NOVEL CONCEPTUAL DESIGN OF 3D-PRINTED VIBRATORY SCAFFOLD (3DPVS) FOR CELL CULTURE

By

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DOCTOR OF PHILOSOPHY



UniSA STEM

DECLARATION

This work has not been previously submitted for a degree or diploma in any university. To the best of my knowledge, perception and belief, the thesis contains no material previously published or written by other persons except where due reference is made in the thesis itself.



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I also understand that to love someone is to acknowledge the goodness of who they are. Love her now. Realize that the flaws and imperfections are all a part of what makes her.

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ABSTRACT

This thesis proposes a conceptual design of 3DPVS (3D printable vibratory scaffold) for a bioengineered application—cell culture. Compared with conventional scaffold design, which is usually based on laboratory experiments, this study aims to utilise an approach based on TRIZ (Theory of Innovative Problem-solving) to produce an innovation design. This research comprises several key components: a literature review on cell scaffolds, including structural features, fabrication methods and applications of vibration for cell culture; defining the methodology and the techniques for the research; and developing a systematic approach for innovation and evaluation of 3DPVS design.

Firstly, a systematic literature review is performed regarding cell culture, scaffolds, 3D printing and vibration. Although both a 3D scaffold and vibration are beneficial for cell culture, traditional vibration-using cell culture using a mechanical vibratory or shaking platform is hard to match a specific range of frequency and amplitude required at the micro-level. In light of this, an integrated scaffold–vibration system is desirable for design of 3DPVS to achieve vibratory functions that allow the scaffold to vibrate in a non-uniform manner across different parts. It is expected that the 3DPVS can vibrate at required frequencies and generate a shape-changing function at a relatively slow actuation rate.

To enable a novel design of 3DPVS, TRIZ is used for the conceptual innovation, with computer simulation utilised to validate the conceptual design. The conceptual design process includes four main aspects. First, design initiation identifies base and ideal 3DPVS models, and summarises design requirements and objectives. Second, a multi-layer TRIZ approach is used to establish a logical, scientific and structured process, producing basic conceptual solutions for the 3DPVS across a super-system to a system view. Third, by using bone cell culture as an example of application for analysis, a further TRIZ-based process is undertaken to specify initial solutions, which moves the design from the system to the sub-system level. Accordingly, geometrical, mechanical and fabricable properties are also identified. Fourth, computer simulation is used to validate whether the generated 3DPVS can achieve the proposed objectives.

By following this design process, a magnetic-based solution is identified as the most appropriate for actuation compared with others such as the electric-, thermo-, acoustic- and mechanical-based solutions. A conceptual design of the 3DPVS is then generated, with hard-magnetic elastomer 3D-printable materials to shape the scaffold structure and a user-tailored magnetic field to generate and moderate the vibratory stimulation for cell culture.

Simulation results show that the conceptual 3DPVS so generated achieves the proposed objectives. The expected frequency range (50–200 Hz for bone cells) is attainable. The 3DPVS can also generate non-uniform movements when the magnetisation of definite parts

alters. This in turn could benefit a tailored cell culture, where different cellular areas require localised vibratory stimulation.

In summary, this research makes two contributions: it offers a novel approach to scaffold design and puts forward the 3DPVS concept complete with an innovative solution generated and analysed. By drawing together TRIZ and computer simulation, the conceptual design approach developed in this thesis is generic and replicable. In addition to having generated an effective solution for bone cell 3DPVS, this approach may have broad applicability for other cell scaffolds. It could also be applied to other bio-designs following the same procedure, enabling more efficient and effective innovations.

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LIST OF ABBREVIATIONS

2D	Two-dimensional
2PP	Two-photon Polymerisation
3D	Three-dimensional
3DDCC	Three-dimensional Dynamic Cell Culture
3DP	Three-dimensional Printing
3DPVS	3D-Printed Vibratory Scaffold
3DVS	Three-dimensional Vibratory Scaffold
ACM	Altshuller Contradiction Matrix
ACO	Ascending Conflict Octave
AM	Additive Manufacturing
AMSC	Analytical Model of System Conflicts
ARIZ	Algorithm for Inventive Problem Solving
BIR	Basic Ideal Result
CAD	Computer-assisted Design
CCO	Constant Conflict Octave
CI	Conflict Input
CIL	Comparative Importance Level
CO	Conflict Output
CZ	Conflict Zone
DA	Design Attribute
DC	Design Component
DCO	Descending Conflict Octave
DLW	Direct Laser Writing
DR	Design Requirement
ECM	Extracellular Matrix
EDP	Engineering Design Process
FDA	Food and Drug Administration
FDM	Fused Deposition Modelling
FMA	Functional Modelling and Analysis
FMEA	Failure Mode and Effects Analysis
GMB	Geometric, Mechanical and Biological
GMBV	Geometric, Mechanical, Biological and Vibratory
HoQ	House of Quality
IPA	Innovation Principle Analysis
ISS	Innovation Standard Solutions
LCE	Liquid Crystal Elastomer
LENS	Laser Engineered Net Shaping

LSE	Laws of System Evolution
MRF	Magnetorheological Fluid
MSC	Mesenchymal Stem Cell
NSFM	New Substance-Field Model
OT	Operation Time
PA	Polyamide
PCL	Polycaprolactone
PEG	Polyethylene Glycol
PhC	Physical Contradiction
PU	Polyurethane
QFD	Quality Function Deployment
RI	Relative Importance
RP	Rapid Prototyping
SC	System Contradiction
SFA	Substance-Field Analysis
SFM	Substance-Field Model
SFMA	Substance-Field Modelling Analysis
SIR	Senior Ideal Result
SLA	Stereolithography
SLM	Selective Laser Melting
SLS	Selective Laser Sintering
SM	Smart Material
SPA	Separation Principle Analysis
TE	Tissue Engineering
TRIZ	Theory of Inventive Problem Solving
UV	Ultraviolet

LIST OF PUBLICATIONS

Related to this research, several papers have been published or submitted for publication, in peer-reviewed academic journals, as listed below.

Published Papers:

Yuan, H, Xing, K & Hsu, H 2019, 'Generate basic conceptual solutions for 3DPVS via utilizing TRIZ', *Bio-design and Manufacturing*, 2(2), pp. 76–95.

Yuan, H 2019, 'Introducing the language of "relativity" for new scaffold categorization', *Bioengineering*, 6(1):20

Yuan, H & Xing, K 2019, 'A systematic study on design initiation of conceptual 3DPVS', *Biomimetics*, 4(2):31

Yuan, H, Xing, K & Hung-Yao, H 2018, 'Trinity of three-dimensional (3D) scaffold, vibration, and 3D printing on cell culture application: a systematic review and indicating future direction', *Bioengineering*, 5(3):57.

Yuan, H, Xing, K & Hsu, HY 2018, 'Concept justification of future 3DPVS and novel approach towards its conceptual development', *Designs*, 2(3):23

Submitted Papers:

Yuan, H, 'A systematic study on TRIZ for the innovation of 3DPVS', Book chapter, "Artificial Muscles", IntechOpen, Accepted.

Yuan, H, Xing, K etc. 'Simulation and modelling for the conceptual design of 3DPVS', *Journal TBD*, In preparation.

1 RESEARCH BACKGROUND AND SCOPE

1.1 Introduction

The categorisation of cell culture can be defined in two ways—one is through its dimensionality and the other through dynamicity. Knowledge of 'engineering system evolution' (Bukhman 2012; Yuan 2019) is a good indication to understand this. Two-dimensional (2D) towards three-dimensional (3D) cell culture follows the direction of evolution in dimensionality, and 3D scaffolds with 3D printing (3DP) as a popular fabrication tool has played a role in 3D cell culture applications. Dynamic methods for cell culturing, compared with traditional static means, generally follow the evolution line of 'static to motional or dynamic', and vibration is frequently selected as a suitable tool to achieve the dynamicity of cell cultures. This chapter first introduces 2D and 3D cell cultivation, followed by background knowledge on 3D scaffolds, 3DP technologies and vibration stimulation. The novel concept of a '3D vibratory scaffold' is introduced and a new categorisation for scaffolds based on general evolution trends is illustrated. The chapter concludes by discussing the research scope and significance, followed by the thesis structure.

1.2 Cell Culture

Traditionally, cultured cells have been grown on treated-polystyrene 2D surfaces as the standard cell culture plastic-ware. Experiments performed in the classical 2D cell culture system have resulted in a large body of knowledge about basic life science (Greiner, Richter & Bastmeyer 2012; Liu, J et al. 2016). However, the morphology of cells grown in 2D systems is significantly different to cells in real living tissues, given that 2D environments are generally flat and can only control the growth of cells in the x- and y-directions. As such, a thorough cell-to-cell interaction is compromised, which negatively affects protein and gene expression and other cell functions (Greiner, Richter & Bastmeyer 2012; Santos et al. 2012). Figure 1.1 shows the typical negative effect of 2D culture on cell morphology (right) compared with healthy cells in real 3D environments (left).

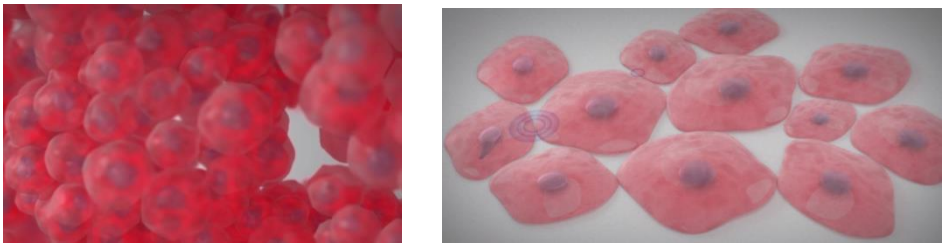


Figure 1.1 Cell morphology differences in 3D culture (left) and 2D culture (right) (from http://www.amsbio.com/alvetex-3D-cell-culture.aspx)

Cells making up real body tissues usually possess a complex 3D architecture, which differs remarkably from the flat monolayer structure of cells resulting from 2D cultures. Considering this, 3D cell culture and its related tools have been developed in recent decades, chiefly for creating suitable 3D surrounding environments used for optimal cell growth, differentiation and function (Greiner, Richter & Bastmeyer 2012; Santos et al. 2012). The vertical axis of the third dimension tends to be in the range of several micrometres to centimetres, which supports cells to form complex 3D interactions with adjacent cells and generate additional layers (Edmondson et al. 2014; Shamir & Ewald 2014). A system of 3D cell culture also enables cells to develop natural, in vivo-like 3D intercellular interactions, providing an ideal environment for real 3D cell growth and issues such as nutrient exchange, which is similar to intra-capillary exchange in living tissues (Khoshroo, K. et al. 2017; Santos et al. 2012; Sawkins et al. 2013). Figure 1.2 illustrates several simplified 3D cultures: (A) 2D monolayer cell culture (B) cell spheroid/aggregates grown on a matrix, (C) cells embedded within a matrix, and (D) scaffold-free cell spheroids in suspension.

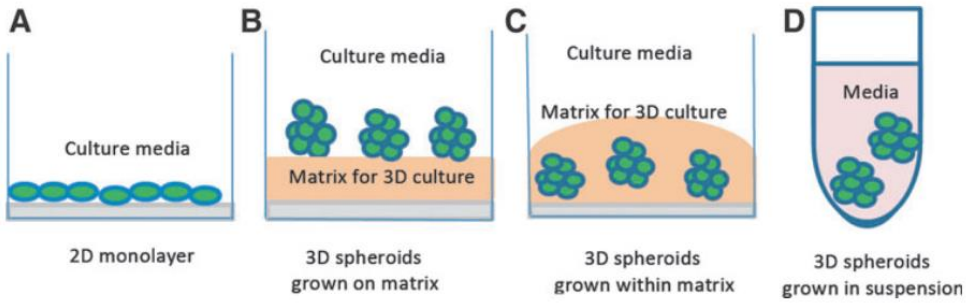


Figure 1.2 (A) Schematic diagram of traditional 2D monolayer cell culture and (B, C, D) three typical 3D cell culture systems (Edmondson et al. 2014)

1.3 Cell Culture Scaffold

1.3.1 *3D Scaffold: Functionality and Use*

As a tendency, 2D cell cultures using 2D plates or 2D scaffolds have been gradually replaced by 3D cell cultures, and 3D scaffolds, as the chief means for 3D cell cultures, have been specifically developed. We first introduce the definition and categorisation of the 3D scaffold. The term ‘3D scaffold’ has been used by previous researchers in most of the literature. In this review, to offer a clearer picture of scaffold engineering, this scaffold will be defined as a 3D static or passive scaffold to make the distinction with the 3D dynamic or vibratory scaffold that will be discussed in a later section.

3D scaffolds have been specifically developed for 3D cell cultivation. The well-defined and micro-porous architecture provides a native 3D environment where cells can invade, proliferate and grow (Benders et al. 2013; Correia et al. 2016; Wu et al. 2017). Two general types of 3D scaffold exist in current tissue and scaffold engineering. The first is the 3D cell culture scaffold, which is mainly applied in regenerative medicine and cell behaviour studies.

The second is the 3D tissue engineering (TE) scaffold, which is used for tissue growth and implantation (Liu, J et al. 2016; Ronca et al. 2016; Shim et al. 2017; Wu et al. 2017). The main difference between them is based on whether the scaffold dissolves or degrades after use. The 3D cell culture scaffold is used in vitro for the purposes of cell cultivation, study or analysis, and will not dissolve or degrade after use (Richter et al. 2013; Sawkins et al. 2013; Shim et al. 2017; Wu et al. 2017). The TE scaffold is a temporary feature used for tissue implantation and tends to disappear after being implanted in the body, which is achieved through dissolution or degradation. Aside from the biodegradability issue as the chief difference, the two types of scaffold can usually be studied together, in terms of their geometric, mechanical and biomedical issues, and the TE scaffold can also be considered part of the cell culture scaffold, given the same nature of culturing cells. Thus, in this review, these two scaffolds will be studied together.

The characterisation and properties of 3D scaffolds vary from one to another. Based on previous literature regarding 3D scaffolds, there are three aspects that generally determine a scaffold's functions, roles and properties in a cell culture: the geometric characters, mechanical controls and biological properties ('GMB'). To help analyse these as one unit, which will assist this study's scaffold design purpose, 3D scaffolds will be defined as having GMB characterisation in this research context, and detailed knowledge regarding such will be discussed in the literature review. Further, material composition plays a vital role regarding the general functions of 3D scaffolds affecting GMB characterisation. A brief introduction will be given below.

In general, materials used for 3D cell culture scaffolds are required to be nontoxic and easily satisfy Food and Drug Administration (FDA) requirements, as well as being biocompatible. The materials used for 3D TE scaffolds typically need to be bio-absorbable (Abdeen & Saha 2017; Chen et al. 2016; Greiner, Richter & Bastmeyer 2012; O'Brien et al. 2015). Previous researchers divided materials into biopolymer and non-biopolymer categories—biopolymer materials include natural and synthetic polymers, while non-biopolymer materials chiefly include glass, ceramics, metals and composites. Varied materials can also be mixed to attain the required biochemical or mechanical properties of the scaffold (Greiner, Richter & Bastmeyer 2012; O'Brien et al. 2015; Perez et al. 2013). Thus, materials play a vital role in controlling the mechanics and biochemical functions of a scaffold, as well as enabling various levels of geometrics in terms of sophistication and complexity.

1.3.2 *Scaffold Fabrication Methods and 3DP*

Following the introduction on 3D cell culture scaffolds and their related characteristics, this section introduces conventional and 3DP novel fabrication methods for 3D scaffold fabrication. As previously studied (An et al. 2015; Cox et al. 2015; Greiner, Richter & Bastmeyer 2012; Kantaros, Chatzidai & Karalekas 2016; Lu, Li & Tian 2015), both traditional fabrication means

and 3DP have been used for fabricating 3D scaffolds. One common approach to distinguish traditional and novel methods is through judging whether the computer-assisted design (CAD) process is used. Conventional technologies do not usually engage the CAD process, and several methods have been generally applied—soft photolithography, solvent casting or particulate leaching, phase separation (TIPS), microsphere sintering, gas foaming and electrospinning.

As a novel method, 3DP plays increasingly important role in advanced and high-quality 3D scaffold fabrication (An et al. 2015). 3DP is a term to describe a set of rapid prototyping technologies that create 3D objects by adding layer upon layer of material, and is sometimes also called 'additive manufacturing' (Inzana et al. 2014; Kantaros, Chatzidai & Karalekas 2016; Murphy & Atala 2014; Rahmani-Monfard, Fathi & Rabiee 2015; Wang et al. 2016). In this research, we will use '3D printed scaffold' to label 3D scaffolds fabricated by 3DP to make a distinction with traditional scaffolds fabricated by other technologies. Three 3DP systems have been used for 3D scaffold fabrication: 3D laser-based, nozzle-based and droplet-based (Inzana et al. 2014; Kantaros, Chatzidai & Karalekas 2016; Serra 2014; Singh, Singh & Han 2016). Detailed aspects of these will be discussed in the literature review. For a typical 3DP scaffold product, Figure 1.3 presents a 3D scaffold sample designed by 3DP laser-based technologies, with (a) displaying the side, (b) displaying the top views of the 3D-printed scaffold product and Figure reprinted from 3Dprint.com and (c) representing bone scaffold to be put into cell culture plate(Tan, J et al. 2010).

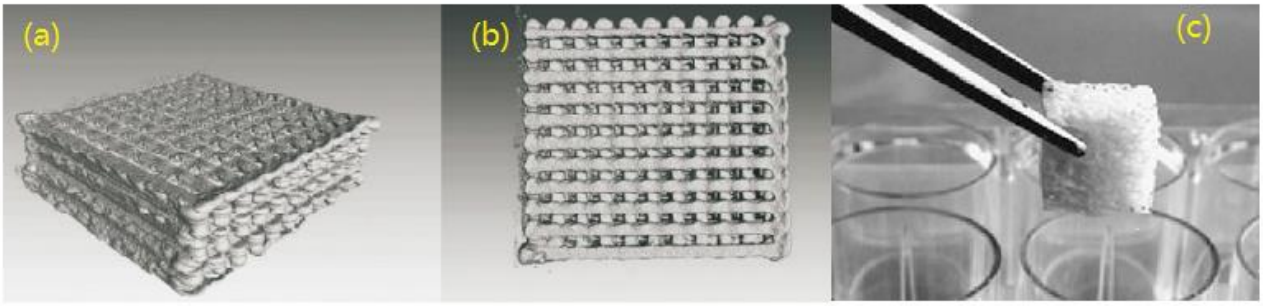


Figure 1.3 one typical scaffold sample fabricated by 3DP

1.4 Vibration for Cell Culture

Previous sections introduced knowledge on changing 2D into 3D cell culture and 3D cell culture scaffolds. This change refers to the dimensional evolution of cell culture and scaffold engineering, while 3DP can be seen as the positive force helping direct this evolution. However, another line of evolution regarding cell culture and scaffolds must also be considered—that is, cell culture and its related platforms tend to evolve from static into dynamic. There are several reasons for this, and vibration mechanisms have been mostly used as tools for achieving this development.

Compared with the roles played by 3D scaffolds, which seek to create in vivo 3D surrounding environments for issues such as optimal cell growth, differentiation and other cell functions, vibration stimulation aims to provide a dynamic or active environment that is similar to in vivo conditions, where cells tend to grow in a better and more natural way, including increased cell adhesion and enhanced differentiation rate (Farran, AJ et al. 2013; Rajapakse et al. 2017). Further, considering the benefits of mechanical stimulation of cell cultures, such as increasing cell growth rate (Matsumoto & Goto 2017; Vining & Mooney 2017), and that cells cultured in the current 2D or 3D artificial environments are usually free of such stimulations, researchers have attempted to develop methods to create dynamically stimulating conditions, where vibration mechanisms have been used as one core part (Farran, AJ et al. 2013; Tong et al. 2014; Zhang, C et al. 2012). The third beneficial effect of using vibration is that cells can be cultured in tailored dynamic conditions, where researchers can study various aspects of cells based on specific biomedical needs (Farran, AJ et al. 2013; Kim, J & Hayward 2012). For example, the intensity of vibration can be controlled in ascending or descending levels to help analyse the difference of cell proliferation in natural in vivo states. Thus, the application of a vibration mechanism has been vitally important in terms of mimicking the real dynamic environment in vivo, creating necessary mechanical stimulus and enabling adjustable intensity in dynamic cell studies. Figure 1.4 provides an illustration of traditional vibratory means using a mechanical vibratory/shaker to stimulate a cell culture scaffold. This is considered an advanced vibrator, which can shake the scaffold in three dimensions.

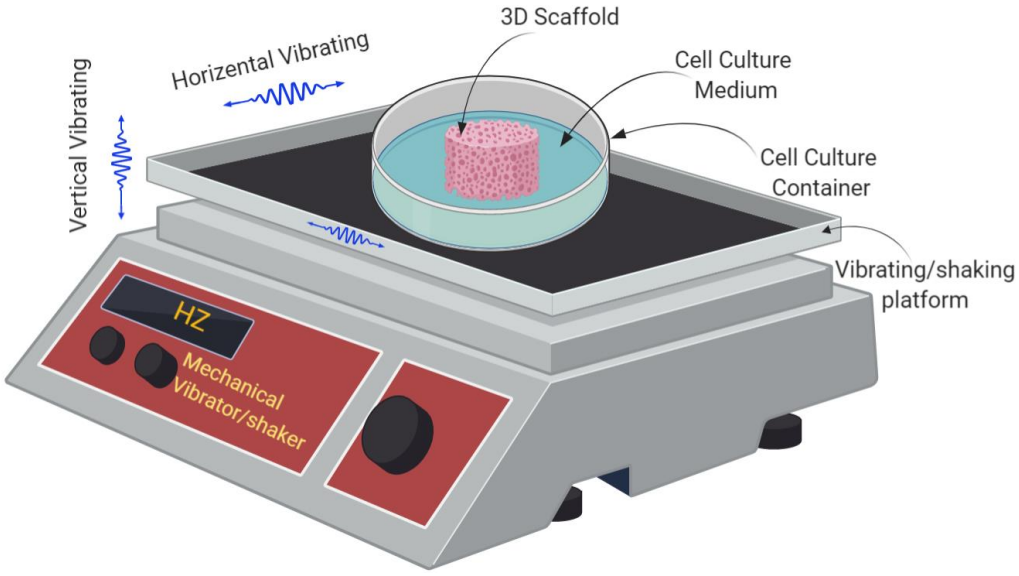


Figure 1.4 Illustration of traditional vibratory method using a mechanical vibrator to shake 3D static scaffold during cell culture

1.5 Trend of Evolution in Scaffold Design

In this section, two aspects are introduced: (i) the evolutional tendency of scaffold engineering in terms of dimensionality and dynamicity, and (ii) the 3D vibratory scaffold (3DVS), which is

proposed as a future novel scaffold category. The 3DVS directly connects with the 3D printed vibratory scaffold (3DPVS), which is the focus of conceptual design in this research.

1.5.1 *Evolution Trends of Dimensionality and Dynamicity*

Parallel with the issues of dimensionality in cell cultures, dynamicity is another vital concept to categorise cell culture systems. Alongside being either 2D or 3D, cell cultures based on dynamicity can be further divided into static and dynamic cultures, and a vibration mechanism has been used as the chief tool to achieve the dynamic purposes. Detailed knowledge has been addressed in the vibration section, while Figure 1.5 briefly summarises the four categorisations of cell culture, as well as the development vision of scaffold engineering. This diagram also indicates general knowledge of the system evolution trends from 2D to 3D culture, and from static to dynamic.

Based on literature studies (Yuan, Xing & Hsu 2018a), the evolution of cell cultures and scaffold engineering can be described as follows: 2D cultures using 2D static or passive plates has largely evolved into 3D cultures using 3D scaffolds, and static cell cultures have partly evolved into dynamic cell cultures with several vibration mechanisms applied. In terms of the research scope of cell culture scaffolds, previous works thoroughly examined the 2D static, 3D static and 2D dynamic stages, while the exploration, attention and studies on 3D dynamic cultures remains at an early stage and much work is yet to begin.

Following the visual illustration in Figure 1.5(a), we know that the current focus of research includes four aspects of cell cultures, where 3D dynamic cell cultures (3DDCCs) have been the chief focus in contemporary research. Scaffold development in (b) started from 2DSS and currently remains at 3DSS. Given the greater usefulness of 3D methods over 2D, 2DVS is less likely to be developed as a product. Indeed, regarding it as one layer of 3DVS is appropriate. To conclude, it is logical to predict that 3DDCCs will continue to be the chief focus for current and future cell cultures, and 3DVS will most likely be developed to first play general roles in cooperating with 3DDCC, and second mitigating the gaps and limitations discussed previously.

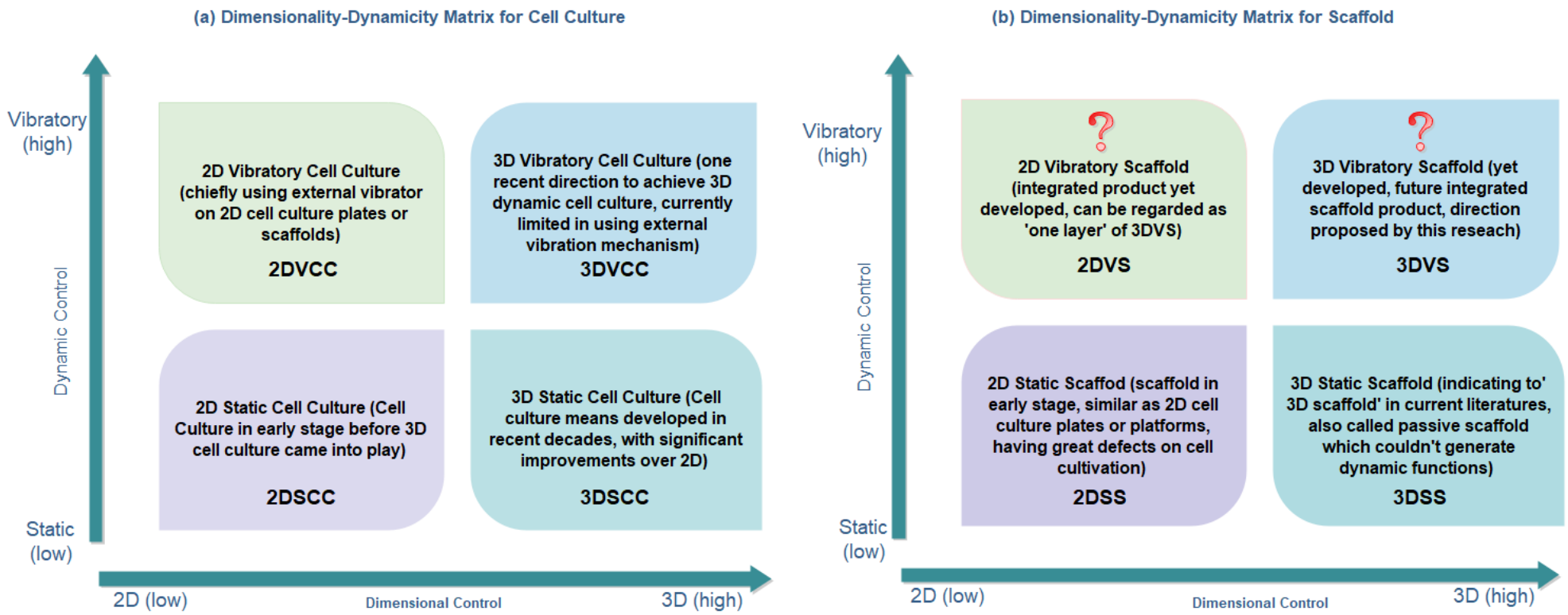


Figure 1.5 Illustration of (a) four main stages of cell culture development and (b) development of scaffold engineering for cell culture applications

1.5.2 *Future 3D Vibratory Scaffold*

The concept of the future vibration-integrated scaffold product, which will play a significant role in 3DDCC, is temporarily named ‘3DVS’, where separate mechanisms of vibration and scaffold provide unified systematic functioning with definite required vibratory functions within the scaffold itself. There are several indications that the 3D static or passive scaffold, as the next stage of scaffold engineering, will most likely evolve into 3DVS. Laws for general system evolution (Bukhman 2012; Cavallucci & Rousselot 2011; Cavallucci, Rousselot & Zanni 2009; Sun, J & Tan 2017) indicate that separate elements of multiple systems generally evolve into a single integrated system with multiple functions. Further, considering the urgent need to address current limitations or gaps, as discussed, developing enhanced vibration mechanisms and 3D scaffolds that could use such scaffold-vibration integration would be of significant value, making the best of both worlds with positive effects from vibration and 3D scaffolds in cell culturing. Scaffolds could potentially generate tailored and localised vibration and frequencies, with higher cell culture accuracy and controllability.

Thus, two chief future trends would follow. First, the combined unit of vibration mechanism and 3D passive or static scaffold on cell cultures has great potential to be developed. In the near future, the 3D passive scaffold has a high possibility of evolving into 3DVS. Second, several evolution laws support and indicate the direction of the scaffold-vibration unification—that is, the passive evolves into the active, the separated into the integrated, and the single-functional into the multi-functional. Following these two trends, along with the increasing call from the scientific world to limit biomedical testing on living animals (Dolgin 2010), the development of potential 3DVS that better mimics real in vivo conditions could be partly used as an alternative for medical testing in animals, which can be considered the third trend. In addition, advanced 3DP methods will likely witness higher applicability as a tendency in future scaffold engineering (Colaco, Igel & Atala 2018; Kim, F et al. 2018; Wallin & Pikul 2018). 3DP will potentially be used as a fabrication method for both advanced/novel 3D static or passive scaffolds, as well as the 3DVS that could emerge in the near future. 3DVS fabricated by 3DP methods is termed 3DPVS, and is the design direction in this research. Concept justification of the 3DPVS will be established in later chapter.

1.5.3 *New Scaffold Categorisation*

As a derivative objective of this research, a seven-layered scaffold classification is developed (Yuan 2019). The philosophical language of ‘relativity’ is introduced to distinguish different scaffolds. Besides the purpose of avoiding ambiguity in perceiving scaffolds, this language also provides high clarity of the ‘evolution stage’, where the focused scaffolds currently stand, where they have been developed, and where in the future they may evolve. Before detailed content is discussed in a future section, Table 1.1 provides a brief summary of these levels of

scaffolds. This provides new understanding of scaffold classification, which expands the vision regarding future issues of scaffold design and development.

To help understand the scaffold evolution line, as well as identifying the position of 3DPVS which is as the object of conceptual design in this research, an illustration is made as Figure 1.6.

Table 1.1 Brief summary of scaffold categorisation by introducing language of ‘relativity’

Time aspects	Previously focused cell culture scaffold			Bridging scaffold	Short-future scaffold	Long-future scaffold	
Categorisation	Scaffold No. 1	Scaffold No. 2	Scaffold No. 3	Scaffold No. 4	Scaffold No. 5	Scaffold No. 6	Scaffold No. 7
Dimensionality	2D	2.5D-3D	3D	3D	3D	3D or beyond	3D or beyond
Dynamicity	Static, passive	Static, passive	Static, passive	Partly dynamic, active	Finely dynamic, vibratory, active	Highly dynamic, vibratory, active	Ideally dynamic, vibratory, active
Chief feature in brief	2D plate or scaffold for 2D cell culture; very limited cell application; mostly replaced by scaffold No. 2 and 3; passive or static; stays at bottom of scaffold’s evolutional ladder	3D scaffold in early stage, simple characterisation and single function, static or passive	Current mainstream 3D scaffold being passive or static, with increasingly tailored characterisations for geometrics and composition	Recent scaffold partly made or designed by smart or dynamic materials; bridging scaffold No. 1, 2, 3 to 5; potentially dynamic or active; inevitable stage to achieve scaffold No. 5	3D scaffold with fully integrated vibratory functions; tailored or self-vibratory properties; 3DPVS as one typical d; currently under conceptual development stage	Bridging scaffold No. 5 to 7; remains a concept; multiple dynamic functions integrated in scaffold might appear; very sophisticated properties	Ideal scaffold in self-perception; fully, ideally controllable vibratility; probably closes the gap between in vitro and vivo
Evolutional ladder	Relatively lowest	Low	Moderate	Slightly high	High	Very high	Relatively highest

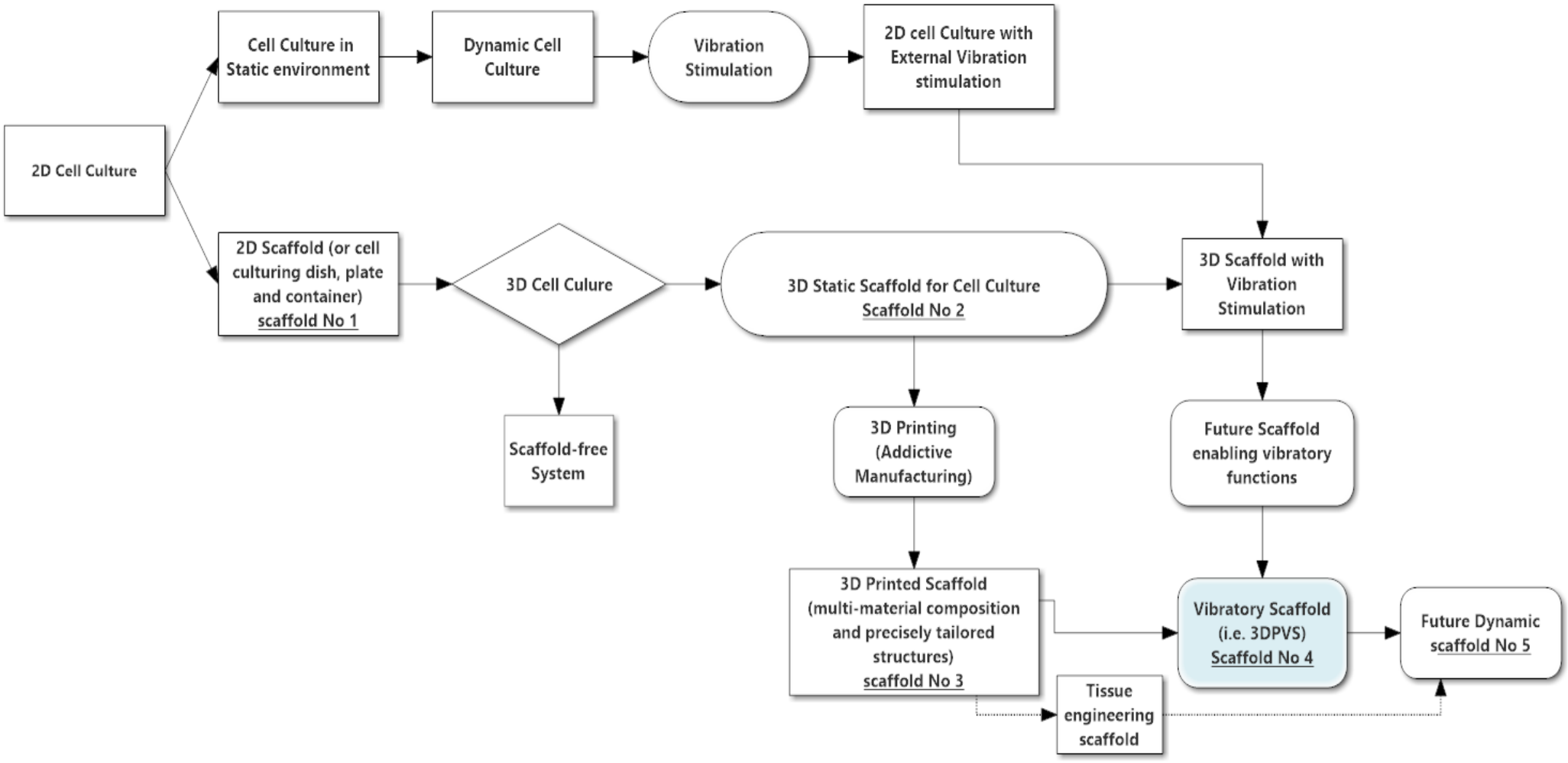


Figure 1.6 illustration of scaffold evolution line and positionality of 3DPVS

1.6 Research Scope and Significance

Regarding the scope, this conceptual design research mainly contains three spheres: cell culture scaffolds, 3DP fabrication, and vibration stimulation mechanisms. Figure 1.7 offers a brief illustration. Another interesting character of this research is using the language of 'relativity' based upon the indication of objects' place in the evolutionary ladder, to study scaffolds. Thus, 'evolution' is the centre of gravity on which to reflect during the full research period.

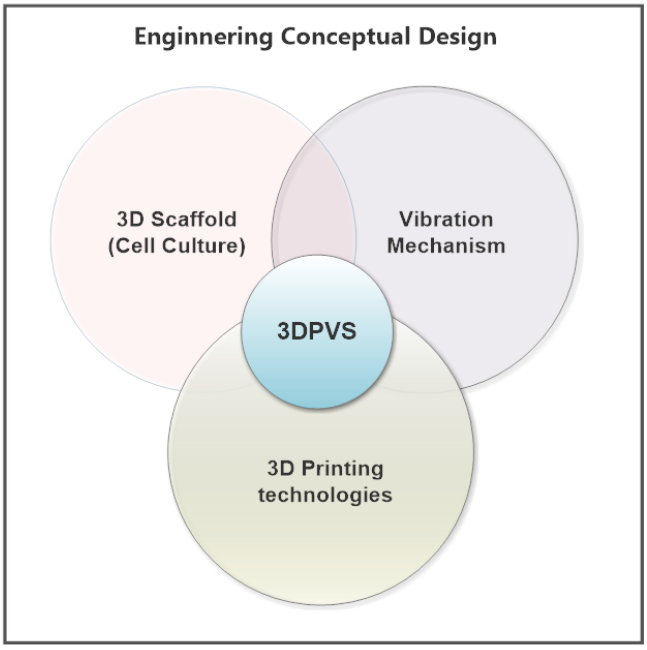


Figure 1.7 Scope of research

There are several reasons for concerning these scopes. First, studying and analysing the responses of different cells to biochemical and physical stimulations in 3D scaffolds has been considered a successful strategy in cell cultures. Researchers have reached some identical understandings of how and which cells can profit from a 3D scaffold culturing environment in terms of three aspects: cell differentiation, cell proliferation and the expression of gene encoding (An et al. 2015; Greiner, Richter & Bastmeyer 2012; O'Brien et al. 2015). Second, along with the development of 3D scaffolds, external vibration mechanisms have been gradually introduced into cell cultures during the last decade. Vibrations can affect cells in these three aspects as well; thus, it is interesting to consider that vibration and 3D scaffolds may have some connections that could amplify the mutual merits and mitigate drawbacks when either works on cell cultures alone. The potential cooperation of 3D scaffolds and vibration urgently calls for further research. Therefore, considering that 3D scaffolds have great benefits for cell cultures, and the vibration mechanism influences cell cultures significantly, it is an interesting direction to find a methodology to design a way to combine

traditional static 3D scaffolds with vibration stimulation in one integrated unit. In other words, approaching future 3DPVS could raise new possibilities for dynamic study of complex physiological, pathophysiological and biomedical processes in vitro. As one might expect, the newly designed 3DVSs would satisfy the functions of a 3D static scaffold. It should also achieve more active and dynamic features and benefits in cell cultures than a static scaffold can achieve. For example, the newly designed scaffold is expected to vibrate with more tailored and precise frequencies, compared with the frequencies generated by static scaffolds stimulated by external shakers. Hence, the designed scaffold should accurately mimic the dynamic characteristics of a real cell culture environment, which is almost impossible to achieve by using outer stimulations, such as bioreactors. Third, this design should ensure that scaffolds can be fabricated by existing 3DP technologies. In the future, the 3D scaffold with dynamic properties could possibly replace the traditional 3D static scaffold, which will take the evolution of scaffold engineering to a higher level.

Along with technical issues, scope regarding the design of this research basically focuses on a non-experimental approach, which applies inventive design methodology (such as TRIZ), innovation steps and a design algorithm for 3DPVS's conceptual design stage. Given that there is no previous formal methodology for scaffold design and that previous designs chiefly focused on experiments, the use of inventive method in the 3DPVS context could be pioneering.

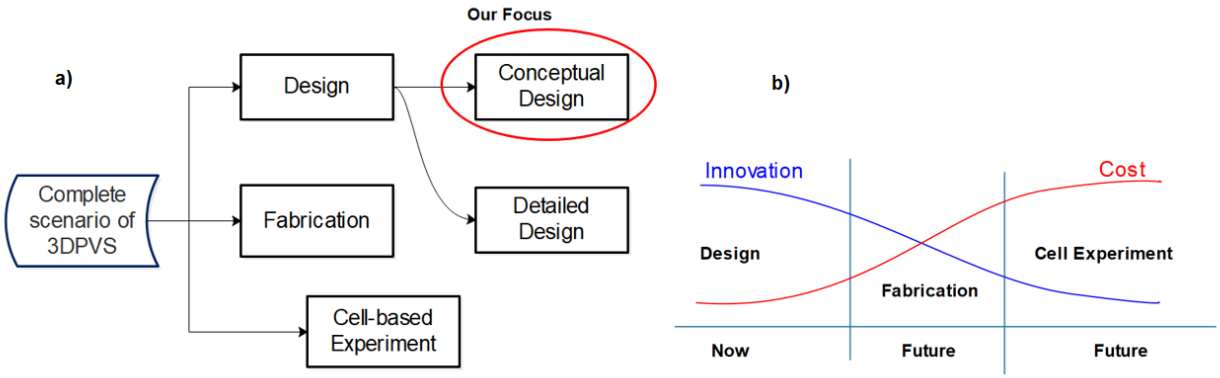


Figure 1.8 (a) Conceptual design as chief focus of research scope; (b) line of innovation of cost in different design stages

Although a complete design process includes different main stages, in this study frame, we chiefly focus on the conceptual design (Figure 1.8) for two reasons. The first reason is the significance of conceptual design in the general engineering design process. Conceptual design has significant effects on the lifecycle cost of the full design. The cost consumed in designing a product is usually about 5%, yet the decisions and solutions developed during the conceptual design process influence nearly 70 to 80% of the cost of product manufacturing and use (Dieter & Schmidt 2009). Thus, the conceptual design determines a much higher

proportion of product costs than other design stages, and this will likely also be the case for 3DPVS design in this research.

Second, conceptual design is an innovative process and designers apply creative thinking to generate conceptual solutions. Although it may be more abstract thinking, conceptual design uncovers flaws in the product design idea, and detailed design work is never completed. Given that the 3D vibratory cell scaffold to be designed is a totally new concept, innovative thinking and concept creating are inevitably the most vital part of this research. Embodiment design and detailed design can only play a role after a satisfactory concept has been established, proved and tested, and after fabrication and vibratory feasibility has been sufficiently evaluated via computer simulation. Further, time and costs are restraints for setting practical goals for researchers. Given the limited funding for our research, focusing on and optimising the conceptual design stage was the most achievable option.

Even though the fundamental conceptual 3DPVS is established, cell culture-based experiments—in terms of selecting materials, testing geometrics, shifting vibration mechanisms and tailoring the cell culture environment—tend to involve 'trial and error'. Further, given the limitations of current methodology in scaffold design, there is no global understanding of whether TRIZ or other design methods can be proficiently used as a formal design method. Thus, a systematic study on design methodology that connects with 3DPVS applications may be promising. To conclude, for a completed design stage of 3DPVS, two systematic stages exist—the philosophical stage and experimental stage—and the former, which contains conceptual design, is of great significance at the current preliminary stage of 3DPVS development. As such, a TRIZ-guided conceptual design could benefit the future model-based detailed design of 3DPVS. Figure 1.9 briefly illustrates this thesis's work focus.

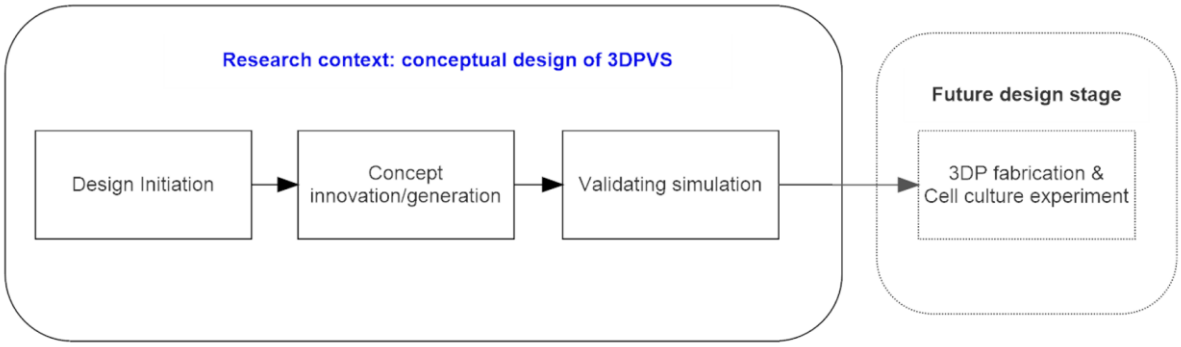


Figure 1.9 Research context of design

Each cell scaffold is different, and there is no 'one-size-fits-all' approach to innovating one. However, there are general innovation principles we can learn to make the design process more straightforward. This thesis is proposed to help achieve this purpose.

In terms of research significance, two main contributions are proposed. First, with the invention of 3PDVS, dynamic cell culture and scaffold engineering could both be benefited. This study

proposes a novel conceptual design of 3DPVS for a bioengineered application. 3DPVS integrating vibration and scaffold into one unit is expected to help the current scaffold engineering evolve into a higher stage. The invented scaffold is expected to provide better and tailored vibratory stimulations to cell culture, especially for bone cells. Second, the design approach for scaffold is reinvigorated. Compared with traditional scaffold design, which is usually based on laboratory experiments, this study aims to utilise an engineering-oriented approach based on TRIZ (Theory of Innovative Problem-solving) to produce innovative design. Benefit of using such design approach includes that it is generic and replicable, leading to broad applicability for other cell scaffolds, and being appliable to other bio-designs following the same procedure, enabling researchers with more innovative and flexible design solutions.

1.7 Thesis Structure

The remainder of this thesis is structured as follows. Chapter 2 presents the literature review, defining the literature's limitations and discussing the research objectives. Besides this, it also justifies the novel concept of 3DPVS regarding the evolution trends of scaffold engineering systems; using 3DP technologies to bridge scaffold and vibration in the present and future is discussed to make the research objectives solid, practical and reasonable. Chapter 3 introduces the conceptual design of 3DPVS and provides the design methodologies and tools that enable the desired innovation. Following traditional engineering design process, the conceptual design process of 3DPVS is also established. Chapter 4 provides the first stage of the conceptual design—design initiation—studying the base model and ideal model of 3DPVS. Basic design requirements are identified in this chapter as well. Chapter 5 connects with the first stage of conceptual generation, which involves generating basic solutions for 3DPVS. The established fundamental solutions are preliminary to complex, and specified design questions come afterwards. Chapter 6, the improvement stage of concept generation, further generate advanced conceptual solution in more specific way based on what is achieved in Chapter 5. Chapter 7, validation stage of conceptual design, uses computer simulation to validate the 3DPVS concept created previously. Finally, Chapter 8, the concluding part of the thesis, summarises the research work, reflects upon the difficulties encountered, discusses the limitations of the study, and indicates directions for future research regarding 3DPVS design. Figure 1.10 below presents a schematic illustration of the thesis structure and research strategy.

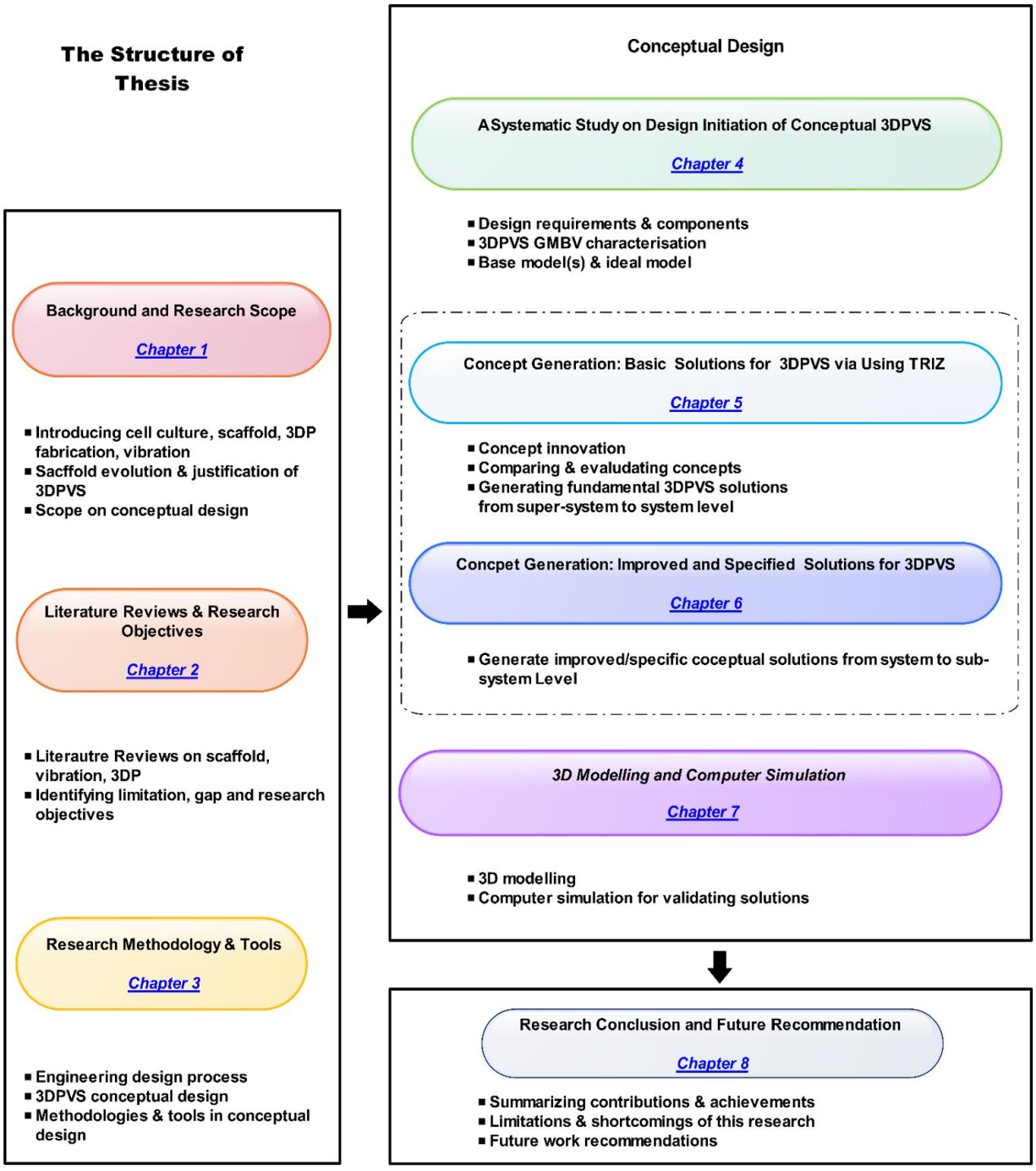


Figure 1.10 Illustration of thesis structure

1.8 Concluding Remarks

Chapter 1 has provided a brief overview of the research background and scope. It introduced 2D and 3D cell cultures, followed by introduction of the 3D scaffold, which is used for 3D cell cultures. Further, it summarised information on fabrication means and 3DP for scaffolds. Vibration, a chief method used for dynamic cell cultures, was then introduced. Further, this chapter discussed evolution trends in scaffold design, as well as future scaffolds. A section on the research scope and significance briefly introduced the value of 3DPVS and conceptual design, while indicating the thesis structure for the work in this research. In brief, this chapter has illustrated the background knowledge and research scope.

2 LITERATURE REVIEW AND RESEARCH OBJECTIVES

2.1 Introduction

This chapter reviews and discusses the literature regarding the research scope. The design characteristics of 3D static scaffolds are first studied in terms of their geometrical control, mechanical properties and biochemical control. Conventional materials used for 3D static scaffold fabrication will be summarised, and smart materials with the potential for 3DVS will be studied. Following this, different kinds of vibration mechanisms for cell cultures will be reviewed regarding their cons and pros, and the possibility of integrating a vibration mechanism with scaffolds will be addressed. In terms of 3DP technologies, the 3DP laser-, nozzle- and droplet-based systems will be studied and their tailored characteristics for scaffold fabrication will be discussed. Following this, current limitations to face and research objectives to establish will be discussed.

In brief, this literature review will thoroughly study 3D cell culture scaffolds regarding several characteristics, vibration stimulation for cell cultivation, and 3DP technologies for fabricating 3D scaffolds. The potential interconnections of these realms will be analysed, and limitations of current 3D scaffolds and vibration mechanisms will be discussed. Further, this chapter will discuss future scaffold engineering regarding 3DVS, as well as indicating 3DP as a positive bridging technology for future scaffolds with integrated local vibratory functions, which contributes to the full concept 3DPVS. Structure of this chapter is as follows:

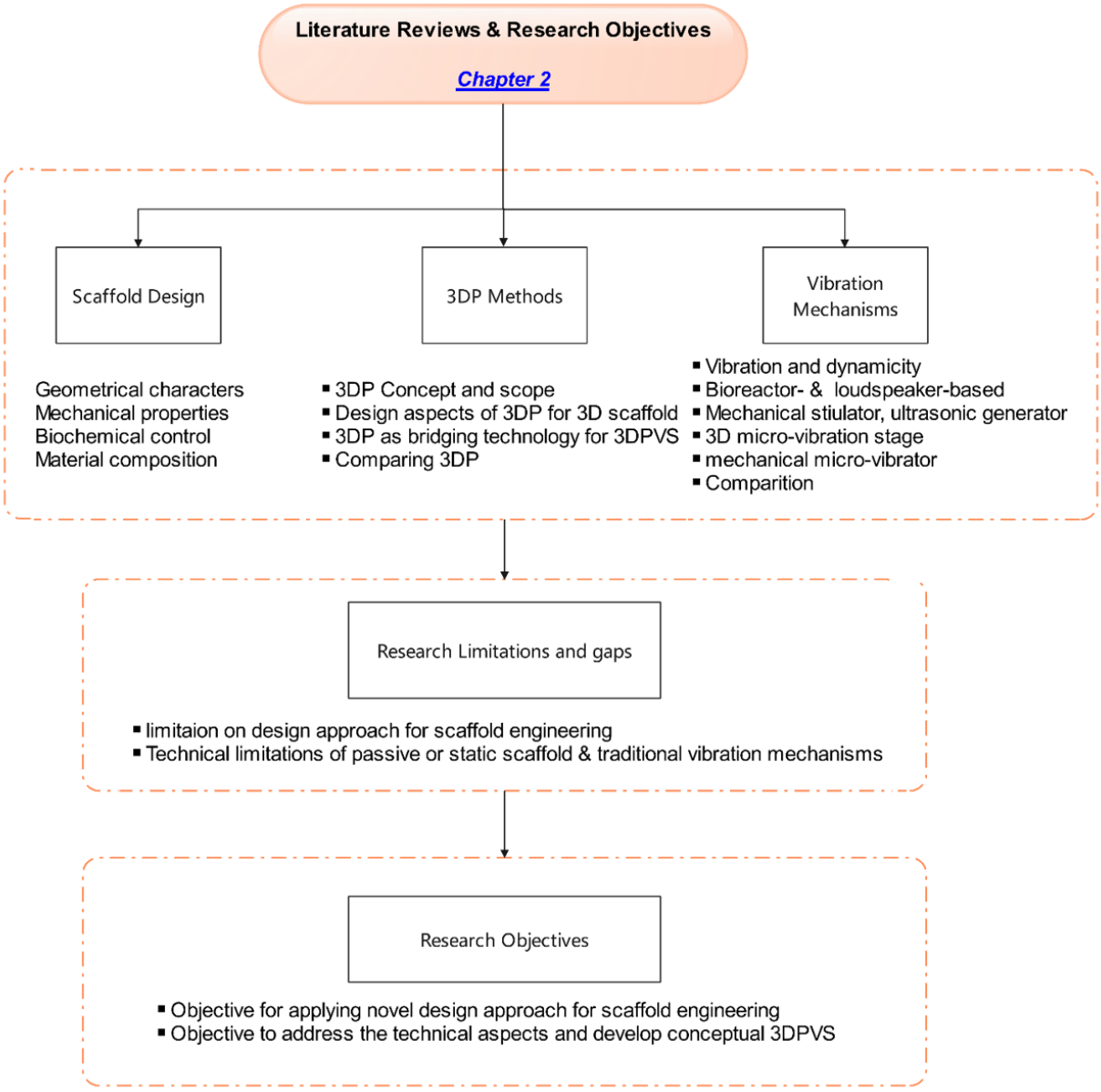


Figure 2.1 Structure of Literature Review and Research Objectives

2.2 Research on 3D Scaffold Design: Characterisation and Parameters

In this section, tailored parameters for the precise characterisation of 3D static scaffolds will be reviewed—that is, the geometrical control, mechanical properties and biochemical control. These three parameters have the most important roles in the design of static scaffolds, and are also predicted in this study to be the key parameters of the 3DPVS design. To realise the vibratory functions, new parameters must be designed on top of the original parameters of the 3D static scaffold, which will be the major direction in new scaffold design. Traditional 3D scaffolds cannot generate dynamic stimulation of cells. Previous studies have chiefly focused on developing or optimising the passive parameters in terms of scaffolds' geometries, mechanical properties and biological control, as introduced in Chapter 1. Therefore, current 3D scaffolds still have great limitations, although they are more sophisticated than a 2D cell culture plate or dish.

2.2.1 *Geometric Characters*

Geometrics have been considered the chief important factor affecting the general functions of 3D scaffolds (Aliramaji, Zamanian & Mozafari 2017; An et al. 2015; Kantaros, Chatzidai & Karalekas 2016). Several concepts related to geometries and pores—pore size, distribution and association—are involved in the definition and classification of mainstream 3D scaffolds (An et al. 2015; Asadi-Eydivand et al. 2016; Kantaros, Chatzidai & Karalekas 2016; Vaezi, Seitz & Yang 2012). First, pore size is generally considered the diameter circumscribing the pores. Porous size of scaffolds tends to vary from nano- to micro-levels. Second, 3D scaffolds can be defined by pore distribution; the numbers of pores per square centimetre vary considerably, generally from around 50 to 600 (Lee et al. 2016; Sun, Y et al. 2016; Tan, Z et al. 2017). The third category of scaffold is defined by association, which generally means the combination of different shaped pores, such as circular and square pores or square and octagonal pores. In terms of the primal effect of geometrics on cells, geometric control leads to tailored surface topography, as well as 3D culturing architectures that help tailored modulation of cell behaviours (An et al. 2015; Chung & King 2011; Kantaros, Chatzidai & Karalekas 2016; Mironov et al. 2017). In addition, two types of architectures—isotropic or anisotropic—have been chiefly applied to 3D scaffolds; both provide specific stimulations of cells, as well as various mechanics for scaffold structures (An et al. 2015; Kantaros, Chatzidai & Karalekas 2016; Shim et al. 2017).

2.2.2 *Mechanics Properties*

In addition to geometrics, the mechanics of scaffolds are important, as they help tissues and cells maintain integrity and proper function. Scaffolds' mechanical properties can be chiefly affected by feature size, structure architecture and fabrication materials. According to previous research (Greiner, Richter & Bastmeyer 2012; Kantaros, Chatzidai & Karalekas 2016; Park, J et al. 2017; Shim et al. 2017), physiological processes can be affected significantly by mechanical properties in cellular environments; these mechanical properties can cause pathological events and affect cells' behaviours regarding differentiation, growing rate and so forth. Mechanical properties of 3D scaffolds in general are tissue dependent, with stiffness of tissue ranging from 0.1 to 3 kPa to intermediate stiffness of 8 to 17 kPa and higher. Thus, tuning the mechanical properties for 3D scaffold design helps ensure tailored physiological stiffness and mechanical supports, which in turn contribute to better cell attachment in ordinary states, as well as a better still–vibration alternating mechanism during dynamic cell cultures (Bose, Vahabzadeh & Bandyopadhyay 2013; Greiner, Richter & Bastmeyer 2012; Lima, Correlo & Reis 2014).

2.2.3 *Biochemical Control*

Compared with the properties of geometrics and mechanics for cell cultures, as discussed, the biochemical properties of 3D scaffolds can be considered the resultant effect of geometrics,

mechanics and the materials composing the scaffold. They mainly influence four aspects of cell culturing: cell adhesion, survival rate, proliferation and differentiation (Bose, Vahabzadeh & Bandyopadhyay 2013; Lee et al. 2016; Ronca et al. 2016). Further, biochemical control specifically deals with the fictionalisation process by biomolecule factors such as fibronectin and laminin, collagen and polylysine, or growth factors of the extracellular matrix (ECM) (Lee et al. 2016; Ronca et al. 2016). In particular, one typical effect of biochemical properties concerns short-peptide sequences that can be derived from ECM molecules. These sequences can benefit cell adhesion, such as the RGD peptide sequence, as well as increase cell membrane proteins, such as E-cadherin (An et al. 2015; Lee et al. 2016).

Among various issues of biological controls, the medium for cell cultures is one of the most important aspects that designers can easily control. Different cell types have highly specific growth requirements; thus, the most suitable media for each cell type should be determined experimentally. There is no solution to systematically design the media previous to experiments. Table 2.1 summarises the cell culture media for six types of commonly used cells.

Table 2.1 Cell culture media used for common primary cells

Cells	Media
Endothelial cells	EndoGRO-LS Complete Media Kit (EMD Millipore), HUVEC Basal Medium CB HUVEC (AllCells), Human Endothelial-SFM (Life Technologies), Endothelial Cell Medium (ScienCell Research Laboratories)
Bone marrow cells	MarrowMAX Bone Marrow Medium (Life Technologies), Bone Marrow Medium Plus (Sigma)
Glial cells	GIBCO® Astrocyte Medium
Epithelial cells	Epithelial cell medium (ScienCell Research Laboratory), EpiGRO primary epithelial cells (EMD Millipore)
T cells	Human StemXVivo Serum-Free T cell Base Media (R&D systems), Stemline T Cell Expansion Medium (Sigma Aldrich)
Hematopoietic stem cells	StemPro-34 SFM (Life Technologies), MethoCult (STEMCELL Technologies, Inc)

2.2.4 *Material Composition*

After illustrating three aspects that determine the functionality of traditional 3D scaffolds, another core issue of scaffold engineering is scaffolds' material composition. The materials used for 3D cell culture scaffolds are generally required to be nontoxic and to easily satisfy FDA requirements, as well as being biocompatible. The materials used for 3D TE scaffolds typically need to be bio-absorbable (Abdeen & Saha 2017; Chen et al. 2016; Greiner, Richter & Bastmeyer 2012; O'Brien et al. 2015). Previous researchers divided materials into biopolymer and non-biopolymer categories—biopolymer materials include natural and synthetic polymers, and non-biopolymer materials chiefly include glass, ceramics, metals and composites. Various materials can also be mixed to achieve the required biochemical or mechanical properties of scaffolds (Greiner, Richter & Bastmeyer 2012; O'Brien et al. 2015; Perez et al. 2013). Thus, materials play a vital role in controlling the mechanics and

biochemical functions of scaffolds, as well as enabling various levels of geometrics in terms of sophistication and complexity. For any type of dynamic properties with which scaffolds may be endowed, material selection is chiefly important.

Synthetic materials have several benefits, including favourable cellular responses, controllable chemical compositions, tuneable physical and mechanical properties, simplicity of processing and synthesis, and compatibility with various 3DP fabrication techniques. One of the most common synthetic materials in 3D scaffold fabrication is organic polymers, such as PDMS-based and polyethylene glycol (PEG)-based chemicals (Greiner, Richter & Bastmeyer 2012; Perez et al. 2013). Although these materials have not been directly used for dynamic purposes, some can become active under different stimulations, such as change in temperature, air pressure and light strength. This may offer some insights into the 3DPVS design. Table 2.2 presents the specific forms of materials and suitable 3DP processes.

Table 2.2 Specific forms of scaffold materials and suitable 3DP

Form	Examples	Suitable 3D-printing processes	References
Solidifiable fluid	Photopolymer resins, temperature sensitive polymers, ion cross-linkable hydrogels, ceramic paste, etc.	Stereolithography, PolyJet, digital light processing, micro-extrusion	(An et al. 2015; Murphy & Atala 2014; Selimis, Mironov & Farsari 2015)
Non-brittle filament	Thermoplastics, e.g., acrylonitrile butadiene styrene, polylactic acid and polycaprolactone	Fused deposition modelling	(An et al. 2015; Mironov et al. 2017; Mohanty et al. 2016)
Laminated thin sheet	Paper, plastic sheet, metal foil	Paper lamination technology, laminated object manufacturing (LOM), ultrasonic consolidation	(An et al. 2015; Cox et al. 2015; Kantaros, Chatzidai & Karalekas 2016)
Fine powder	Plastic fine powder, ceramic powder, metal powder	Selective laser sintering/melting (SLS/SLM), electron beam melting, laser engineered net shaping (LENS), direct metal deposition, Colorjet printing	(Cox et al. 2015; Kantaros, Chatzidai & Karalekas 2016; Ronca et al. 2016)

2.3 3DP: From Design to Fabrication for scaffold

For 3DP, the basic strategy in using computer-based technologies is that the volume of 3D scaffolds can be broken down into multiple layers, which can be then deposited onto each other additively, and this can be achieved by moving the fabricating carriers or devices for material deposition. The 3DP device then reads data from the CAD file and builds a structure, layer-by-layer, from the printing material, which can comprise traditional materials, such as plastic, liquid, powder filaments and metal, or the novel nanomaterials that have appeared in recent decades (An et al. 2015; Kantaros, Chatzidai & Karalekas 2016). Recent advances in 3DP technology, associated with tomographic reconstruction and numerical modelling methods, enable fabrication of complex scaffold architectures with a range of length scales.

2.3.1 *3DP-based Concept and Scope*

In terms of 3DP, different meanings have been attached to the same word and it is difficult to offer a universally identical meaning. Thus, we first require a detailed and clear understanding of three terms—rapid prototyping (RP), additive manufacturing (AM) and 3DP—which are easily mixed in use and sometimes confusing. Some believe that RP and AM are generally the same, sharing the same layer-by-layer or drop-by-drop principles, while 3DP is only one small part of AM or RP. Others believe that RP, AM and 3DP are similar, and 3DP scaffolds refer to the scaffold fabricated by AM methods. A third group think that AM should be a bigger frame than RP, since Inkjet printing is clearly AM, yet would not be seen as a RP process. In the previous literature, 3DP or 3DP has been used as a term that seems to be 'universally known', yet different researchers use it in ways indicating different concepts, and many studies fail to provide a clear idea of what the '3DP' in their context indicates. For example, in studies (Kumaresan; 2015; Vasireddi & Basu 2015), 3DP was used to refer to part of solid freeform or RP technologies—that is, power-based 3DP. However, in research such as (Do et al. 2015; O'Brien et al. 2015; Zhang, Y et al. 2017), 3DP indicated a wider scope containing a range of methods. This can cause ambiguity or confusion for researchers. Thus, it is necessary to define and anchor 3DP clearly to help readers grasp the exact meaning of the term, and understand related or derivative terms, such as '3D printed scaffold'. Similar to many concepts in the scientific world, two terms—general 3DP and specialised 3DP—can be summarised based on the indications mostly used by previous research. General 3DP refers to a range of RP technologies where materials and structures can be additively manufactured in layer-by-layer or drop-by-drop ways; thus, it is usually used similarly to AM. Narrowly defined 3DP generally indicates one small part of the RP or AM technologies that use powder and liquid adhesive. Given this information, studies on 3DP would follow in a logical and straightforward way. In this review, 3DP and derivative products, such as 3DP scaffolds, indicate the first class of 3DP. Table 2.3 presents a brief comparison of the two 3DP uses in the current research. Following this part, novel 3DP meth-ods used for 3D scaffolds will be studied.

Table 2.3 Re-categorisation of term '3DP'

	General 3DP	Narrow or specialised 3DP
Technologies	SLS, SLA, fused deposition modelling, powder-based 3DP, 3D plotting	Only powder-based 3DP
Subcategories	Laser-, nozzle- and droplet-based technologies	Only power-based 3DP
Software	CAD	CAD
Relationship with RP or AM	Parallel, interpenetrating one another	Subordinate part, with RP or AM being fundamental

In this chapter, it is impossible to cover the complete literature on the materials used by 3DP for scaffold fabrication, but several examples are illustrated here with various materials and different architectures employed to study single or multiple cell behaviours in 3D scaffolds.

I. 3DP laser-based systems.

In 3DP laser-based systems, liquid monomers are photo-polymerised or powdered materials are sintered to fabricate 3D scaffolds with complex micro-scale structures (Ambrosi & Pumera 2016; Greiner, Richter & Bastmeyer 2012; Lu, Li & Tian 2015). Stereolithography (SLA) is one typical technology used to fabricate bone-like 3D scaffolds. It consists of photo-polymerisation using an ultraviolet (UV) laser to build layered structures. when exposed to UV light, the liquid photo-curable monomer resins polymerise. The laser scans the top of a bath, polymerises the resin and creates a solid layer. For subsequent layers, the same process is repeated by moving down the platform. A post-process treatment is used to cure the scaffold in the UV oven. SLA allows fabrication with complex and anatomically shaped structures. Besides SLA, two-photon polymerisation (2PP) is another technology, in which Femto-second laser beams are focused on the photosensitive liquid material mixed by a monomeric matrix molecule and a photo initiator. Two photons are simultaneously absorbed, causing high peak energy in the focal volume of the focused laser beam. Once energy exceeds a threshold, the photo initiator molecules are excited, resulting in a highly localised chemical polymerisation event confined to the focal volume of laser (Ambrosi & Pumera 2016; An et al. 2015; Greiner, Richter & Bastmeyer 2012; Kantaros, Chatzidai & Karalekas 2016; Lu, Li & Tian 2015).

II. 3DP nozzle-based systems.

In this category, ink materials can be accurately dispensed through a nozzle following the filament-on-demand principle by fused deposition modelling (FDM) or drop-on-demand principle by 3D plotters. The nozzle treats the materials chemically or thermally. After processing, the ink solidifies via gelation or solvent-induced phase changes. The mobile nozzle determines the X- and Y-resolution and Z- is controlled by a platform (Kantaros, Chatzidai & Karalekas 2016; Lu, Li & Tian 2015; Selimis, Mironov & Farsari 2015). Among the nozzle-based systems, FDM is the most popular. The nozzle pushes out a thermoplastic polymer filament and dispenses the melted polymer onto a platform via a layered process. It has been used to manufacture 3D scaffolds of a honeycomb-like pattern with a fully interconnected porous network, and FDM is also a solvent-free method. However, it is necessary to prepare polymeric filaments before fabricating, which makes the FDM procedure time-consuming and expensive. The narrow range of materials makes FDM harder to achieve for scaffolds with complex filament composition, and the fixed diameter of filament and needle tip limits the printable resolution (Kantaros, Chatzidai & Karalekas 2016; Lu, Li & Tian 2015; Murphy & Atala 2014).

III. 3DP droplet-based systems.

Droplet-based 3DP can produce complex independent 3D patterns with multiple structural constituents and properties. The highly defined control of macroscopic features can affect the growth rate of cells inside the fabricated scaffold, which is a unique advantage of this system. Droplet-based systems are sometimes conceptually similar to SLS, which means that

powdered starting materials are sequentially and selectively solidified to form 3D structures layer-by-layer. The difference is in the use of liquid chemical binders, rather than laser light, to solidify the material (Lu, Li & Tian 2015; Mironov et al. 2017; Selimis, Mironov & Farsari 2015). 3DP droplet-based techniques mainly include Inkjet printing, direct-write printing and micro-pen writing (Kantaros, Chatzidai & Karalekas 2016; Lu, Li & Tian 2015; Murphy & Atala 2014). For precise deposition, this system can use different materials, such as wax, liquid biomaterials or a chemical binder, on a surface to construct 3D scaffolds with specific chemical properties (Khoshroo, K. et al. 2017; Lu, Li & Tian 2015; Mironov et al. 2017).

Table 2.4 briefly illustrates a summary of the benefits and drawbacks of 3DP in current 3D scaffolds.

Table 2.4 Summary of advantages and limitations of using 3DP technologies

3DP family	Advantages	Limitations	Bio-applicability
3DP laser-based system	Hydrogel, high-resolution and accuracy; liquid build material can be easily removed from within complex scaffolding	Limited choice of materials; may require furnace post-processing; high material cost; complex and expensive equipment	Yes, high
3DP nozzle-based system	No trapped materials, minimal material waste, low cost	Materials may thermally degrade during the process; lower range of material choice; medium resolution	Yes, high
3DP droplet-based system	Wide range of material choice, low cost, quick process; multi-material capabilities through multi-print heads	Hard to remove trapped materials; low to medium resolution; powder particles may not bind well; binders are always necessary to bind powders	Yes, high

In conclusion, the laser-based 3DP techniques of droplet- and nozzle-based systems have been applied to process a rich variety of different synthetic materials.

In appendix A1, a comparison of various 3DP technologies and traditional fabrication tools is made, and in appendix A2, an overall illustration in terms of several most typical 3DP tools for scaffold fabrication is generated. In this illustration, all these 3DP methods are supported by CAD technologies during the design and fabrication process. To further understand the details of these methods, and clarify their differences with traditional scaffold fabrication tools, it is necessary to compare each of their characteristics, benefits and limitations.

2.3.2 *Design Aspects of 3DP for 3D Scaffolds*

Future scaffolds will likely need to integrate dynamic or vibratory functions in the scaffold itself, as aforementioned, and the fabrication methods to be developed will be a vital aspect for researchers to reflect on. Among different technologies, 3DP is probably the best solution for fabricating future 3D scaffolds. Advances in 3DP associated with tomographic reconstruction and intellectual modelling allow complex scaffold architectures with a range of length scales, geometric flexibilities and material options. This can assist the design flexibility and

fabricability of 3D scaffolds when cooperating with vibrations. Another benefit of 3DP is that it is feasible with a wider range of 3DP materials, equipped with electrical, optical, dynamic and magnetic properties, all of which could be key factors regarding vibration mechanisms. In addition, as new materials and 'bio-inks' are created or synthesised and novel 3DP methods are discovered, 3DP scaffolds to be used in TE will tend to become more effective, proficient and sophisticated. The 3DP techniques and materials discussed previously are likely to contribute to part of design solutions of generating vibrations from scaffolds. Hybrid 3DP approaches also make the 3D scaffold in the next generation more promising. These hybrid systems, as discussed, have the potential to mitigate the disadvantages of any one 3DP technology and even the limitations of the used materials. In brief, as current techniques are further fine-tuned and more bio-functional materials become available, the design of 3DVS could become achievable in the near future, thus filling the gaps as discussed and keeping pace with system evolution requirements.

To be specific, there are three major parameters for scaffolds when vibration stimulation cooperates with 3D passive scaffolds. Geometrical control is a prioritised factor affecting both the influence of vibrations on objects and the function of 3D scaffolds. 3DP has advantages over traditional tools because it is especially good at producing higher quality architectures. The material composition applied in 3D scaffolds, which is the medium of vibration and cells, must also be designed with great flexibility, as the demand of material composition on different cell cultivations and vibratory stimulations changes. One scaffold sample used for all kinds of vibratory stimulation and cells will be insufficient, and 3D scaffolds may need to be fabricated within short periods to fulfil the timely requirement in vibrations and cells. 3DP is developed from RP, so this fast fabrication from concept to product is its advantage (Hur et al. 2013; Kantaros, Chatzidai & Karalekas 2016; Munaz et al. 2016). The scope of 3DP laser-based systems has potential when highly demanded structures are required for vibratory or dynamic functions. Nozzle-based systems can play a role in complex material fabrication, when multiple materials need to be fabricated on scaffolds at the same time. 3DP droplet-based systems can achieve highly defined control of macroscopic features that greatly affects the growth rate of cells inside the scaffold. This technique has the potential to use complex surface morphology, which may help vibration and biochemical control of cells.

2.3.3 *3DP as Key Enabling Technology*

As discussed, in the next development circle, future scaffolds may integrate vibratory functions into the scaffold itself, and the fabrication methods will thus be one vital aspect to reflect upon when judging whether the designed or proposed scaffold is practically achievable. Among different technologies for traditional scaffold fabrication, 3DP can be predicted as likely the best solution for fabricating future 3DVS, which has been highlighted as a future trend of scaffold engineering in the literature. Several pieces of evidence support this prediction.

Given that 2DVS can be considered one layer of 3DVS, as illustrated, designing 2DVS first and then fabricating it layer-by-layer way to constitute 3DVS would be a highly useful approach. 3DP technologies have the exact layer-based CAD approach, making them likely the optimal tool for achieving 3DVS. Following this, the current and continuously increasing advances in 3DP associated with tomographic reconstruction and intellectual modelling could allow current complex scaffold architectures with a further range of length scales, as well as higher geometric options (Colaco, Igel & Atala 2018; Graham et al. 2017). This could benefit aspects such as design flexibility and structural fabricability in future 3D scaffolds when focusing on the potential design requirements of 3DVS. 3DP is also considered an optimal fabricating tool to stimulate creativity, which indirectly aligns with the innovation-based essence of 3DPVS. In addition, 3DP is feasible with a wide range of 3DP materials equipped with electrical, optical, dynamic or magnetic properties (Crippa et al. 2017; Hendrikson et al. 2017; Kim, F et al. 2018; Vovrosh et al. 2018; Wallin & Pikul 2018); thus, material composition concerns for 3DVS might benefit most from 3DP technologies, compared with other fabrication tools. As new biocompatible materials and 'bio-inks' are created or synthesised (Kim, SH et al. 2018; Moroni et al. 2018; Murphy & Atala 2014), 3DP scaffolds used in tissue and cell engineering tend to become more effective in cell culture applications, which helps cooperate with future scaffolds, which tend to have the same application as cultivating cells. Further, hybrid 3DP approaches, along with novel 3DP methods gradually being discovered (Colaco, Igel & Atala 2018; Ragelle et al. 2018; Seleznev & Prinz 2017; Zhang, Q et al. 2018) make 3D scaffolds promising as the next generation. These hybrid systems have potential to mitigate the disadvantages of any 3DP technology used alone, such as the limited material selection of definite 3DP. Finally, in advanced cell-medical applications, the potential future scaffolds may need the fabrication mode to be of small quantity, yet high quality and rapidly produced (Abdeen & Saha 2017; Wallin & Pikul 2018; Zhang, Q et al. 2018). This is different from fabricating other daily engineering products, where fabrication costs and output quantities would be generally considered a priority.

In brief, as current 3DP techniques are further fine-tuned and more bio-functional materials become available, the design of 3DVS could be partly due to how to make best of the 3DP characteristics enabling user-tailored functions. Studying 3DP techniques and related properties regarding dynamic materials may contribute to design solutions that enable scaffolds to generate tailored vibrations. Therefore, the potential future 3D scaffold product, being both 'vibratory' and '3D printable', as discussed, could be achieved by novel 3DP technologies, which may contribute a new term to the future scaffold engineering world—3DPVS.

2.4 Research on Vibration for Cell Cultures

2.4.1 *Vibration and Dynamicity*

Compared with the roles played by 3D scaffolds, which create in vivo 3D surrounding environments for issues such as optimal cell growth, differentiation and other cell functions, vibration stimulation aims to provide a dynamic or active environment that is similar to in vivo conditions, where cells tend to grow in a better and more natural way, including increased cell adhesion and better differentiation rate (Farran, AJ et al. 2013; Rajapakse et al. 2017). Besides this, considering the benefits from mechanical stimulation of cell cultures, such as increasing cell growth rate (Matsumoto & Goto 2017; Vining & Mooney 2017) and that cells cultured in current 2D or 3D artificial environments are normally free from such stimulations, researchers have attempted to develop methods for creating dynamically stimulating conditions. Vibration mechanisms have been used for this purpose (Farran, AJ et al. 2013; Tong et al. 2014; Zhang, C et al. 2012). The third beneficial effect of using vibration is that cells can be cultured in tailored dynamic conditions where researchers can study various aspects of cells based on specific biomedical needs (Farran, AJ et al. 2013; Kim, J & Hayward 2012). For example, the intensity of vibration can be controlled in ascending or descending levels to help analyse the difference of cell proliferation in natural in vivo states. Thus, the application of a vibration mechanism is vitally important in terms of mimicking the real dynamic environment in vivo, creating the necessary mechanical stimulus, and enabling adjustable intensity and evaluating dynamic cell studies.

Among several factors regarding vibration—such as frequency, amplitude, wave length and flexibility in vibration control—vibration frequency and its related properties, such as frequency range and intensity, may be the most important factor when it comes to vibration in cell cultures. For instance, vibration with different frequencies can easily have different effects on issues including cell lifecycles, proliferation rates and alkaline phosphatase activities. (Pongkitwitoon et al. 2016; Wagner et al. 2016). In terms of the vibration frequency range, cells can be responsive to a broader frequency vibrating strain and sensitised to sinusoidal stimulation under such strain (Nakajama & Hashimoto 2014; Pongkitwitoon et al. 2016; Zhang, C et al. 2012). Continuously changing the frequency under certain ranges can affect the rate of cell differentiation, and vibration with a tailored frequency range can help cells survive relatively longer, compared with a traditional static culture (Hou et al. 2016; Paces et al. 2014; Pongkitwitoon et al. 2016; Tong et al. 2014).

In addition, another important aspect is mechanical stimulation and vibration on bone. Mechanical loading is a potent stimulation factor for bone formation and regeneration. Insufficient mechanical stimulation arising from issues such as bone defects may restrain bone regeneration and cause disuse-induced bone loss. Thus, the efforts of previous researchers have been focused on solving these concerns by using external energy to provide sufficient

mechanical stimulation. Signals of mechanical stress can be transmitted to the nuclear area via the cytoskeleton or intracellular membrane system, and then activate the downstream gene pathway closely related to osteogenesis, thereby regulating bone repair or helping bone regeneration. Some stimulation methods—such as using a mechanical vibrator, a mechanical stimulator, a low-intensity pulsed ultrasound, pulsed electric fields and pulsed electromagnetic fields—have been applied to enhance the cell culturing regarding bone restoration and fracture healing.

In the following section, several mechanisms and methods that have been mostly applied to achieve vibration in cell cultures will be introduced. Several factors must be considered. Based on the literature from previous decades, it seems that the cell culture development from 2D to 3D has occurred more rapidly than the rate of evolution from static to dynamic culture. Advanced 3D scaffolds with increasingly complex geometries and material compositions are becoming gradually popular, whereas vibration mechanisms are rarely seen in recent developments or novel applications in cell culture studies. The reason for this may partly lie with the rapid development of 3DP, which has accelerated the evolution of 3D cell culture, and partly with previous research tending to attribute greater significance to 3D scaffolds for 3D cultures than developing or studying novel vibration mechanisms, which would benefit the dynamicity of cell culture. Taking this into consideration, it is reasonable that many previous studies introducing vibrations to cell cultures tended to use 2D culturing plates or early-stage 3D scaffolds with very simple inner structures and material composition. In the following section, several types of vibration stimulation previously used as mainstream vibration means for dynamic cell culture are introduced and studied.

2.4.2 *Bioreactor-based Vibration*

In many cases, bioreactor-based systems have been used to provide vibration for the cultivation of cells in bone and cartilage applications (Yeatts, Choquette & Fisher 2013). A bioreactor generally provides a continuous or time-controllable inner vibration for cells and culturing platforms or scaffolds that are placed inside the bioreactor. Recent bioreactor systems tend to be used for several purposes, including measuring oxygen content, culturing anatomically shaped grafts, developing a perivascular network, and evaluating the relationships between the scaffold environment and signalling pathways (Al-Qodah et al. 2017; Li, T et al. 2016). Vibrations of nanoscale amplitude provided by a bioreactor system can also differentiate mesenchymal stem cells (MSCs) into mineralised tissue in 3D (Tsimbouri et al. 2017). Besides these, the application of bioreactors creates the possibility for scientists to study the dynamic factors of cells, such as the oxygen content, issues regarding shear and stem cell differentiations (Diban et al. 2017; Kola et al. 2014). Among these factors, the increase of cell differentiation could be a primary benefit of bioreactors.

2.4.3 *Loudspeaker-based Vibration*

Previously, a large number of dynamic systems applying mechanical stimuli on cell cultures were designed to simulate aspects such as stretch, compression and shear stress, yet not vibration (Mohammed et al. 2016). To fill this gap, the loudspeaker-based system was invented to study cell behaviours under cellular vibratory conditions. In one previous study that can be considered typical (Puig, Rico & Almendros 2005), a 12-inch subwoofer loudspeaker driven by a sinusoidal signal at 60 Hz with a power amplifier was used to subject cultured cells to vibratory conditions. The main aim of the study was to test whether vibration could modify cell proliferation, and the experimental result indicated it could, with the proof that the concentration of interleukin-8 (IL-8) had increased.

2.4.4 *Mechanical Stimulator based Vibration*

Several researchers have used mechanical stimulators on dynamic cell cultures, where means such as a piezoelectric actuator or vibratory transducer have been commonly applied to generate vibratory stimulations (Chintavalakorn et al. 2017; Hong, Hua & Guo-zhen 2001; Li, M et al. 2015; Zhang, C et al. 2012). Bone cells, such as osteoblasts, have been frequently studied using such stimulators to compare with cells cultured in static conditions. Specifically, the effects of broad frequencies with low amplitude strains on bone and HESC cells have been studied. The results showed that osteoblasts can respond to a broader range of frequency strains from mechanical stimulators, cells tend to be sensitised to sinusoidal stimulations, and a higher number of cell proliferations resulted after a period of weeks (Kulkarni, Voglewede & Liu 2013; Li, M et al. 2015; Shikata, Shiraishi & Morishita 2008). In brief, mechanical stimulators could affect the differentiation and imply the existence of a frequency-dependent effect from vibrations.

2.4.5 *Vibration by Ultrasonic Generator*

In previous research, after mechanical stimulation with relatively low frequency was applied to cell cultivation, vibration from an ultrasonic system was applied, aiming to break the low-frequency mould and open avenues for vibration stimulation with higher frequencies (Cho et al. 2012). Relevant experiments have studied how cells proliferate, grow and differentiate under continuous or discontinuous ultrasonic vibration. The prominent effect could be due to the created macroscopic flow, generating a stirring or heating effect that in turn changes cell behaviours. Low-frequency vibration causes flow in the liquid, while vibration with high energy could potentially dismantle existing structures of cells. Further, while mild vibration can potentially accelerate cells' proliferation and differentiation, the optimum intensity of such vibration depends on specific kinds of cells (Hino et al. 2016; Nakajama & Hashimoto 2014).

2.4.6 *Vibration by 3D Micro-vibration Stage*

The 3D micro-vibration stage has been developed as a novel system to generate tailored vibrations in each direction, which helps exert vibratory stimulation onto cultured cells in a non-invasive and 3D manner. Its effects have been investigated morphologically, and the experimental results showed that such vibration stimulation can decrease the projected area and increase the slenderness ratio (Konno et al. 2010). Based on the slenderness ratio result, the vibration stimulation made the value of slenderness ratio larger. Given that cellular senescence usually makes the value of slenderness ratio smaller, the results may be evidence that such vibration stimulation could have a beneficial effect on gene expression by affecting the gene expression pattern, and making the cells remain at a genetically younger state (Farran, AJE et al. 2013; Konno et al. 2010).

2.4.7 *Vibration by Mechanical Micro-vibrator*

Biomedical researchers (Gruber & Klein 2011; Hur et al. 2013; Kulkarni, Voglewede & Liu 2013) have demonstrated that, in vivo, there exist multiple mechanical forces, the combination of which can induce cell-to-cell communication, which exerts beneficial effects by refreshing the fluid surrounding cells and eliminating metabolites. Recent studies have sought to achieve higher quality embryos by external stimuli using machines to replicate in vivo mechanical forces. Following this trend, systems of mechanical micro-vibrators have been developed as generating external stimulus. This micro-vibration stimulus has been implemented in cell cultures of mouse embryos, showing a beneficial effect on general cell development, with similar beneficial effects for pregnancy and implantation rates for human embryonic cultures (Hur et al. 2013; Y.X. et al. 2018).

2.4.8 *Comparison of Different Vibration Mechanism*

Table 2.5 provides a comparison of different types of vibration stimulations that have been applied by previous researchers to study cell applications. The table summarises the vibration direction, amplitude and frequency; cultured cells during the vibration; and vibration effects and limitations.

Table 2.5 Previously applied vibration mechanisms for cell cultivation, with functions and properties

Vibration system	Devices applied	Purpose of system	Scaffold applicability	Vibration properties/ frequency	Cell applications	Effects on cell culture	Unique strengths	Limitations	Refs.
Bioreactor Vibration	a device, like a vessel or container, where cell culturing is carried out	study the dynamic factors of cells, including oxygen contents, shear, differentiations	Yes, both 2D and 3D	Most frequency 10-200Hz; Amplitude 0-5 mm etc.	bone and cartilage cells, MSCs cells etc.	increased proliferation; help gene expression etc.; Increased cell viability	Tend to be inexpensive, easily establish-able	frequency cannot be precisely controlled	(Diban et al. 2017; Kola et al. 2014; Li, T et al. 2016; Titze et al. 2005; Wolchok et al. 2009; Yeatts, Choquette & Fisher 2013)
Loudspeaker-based vibratory	A subwoofer loudspeaker, water-proof Mylar speaker etc.	In vitro platform for evaluating cellular responses to vibration	Yes, chiefly for 2D	Frequency 60–1600Hz; Amplitude 0–30mm etc.	MSCs cells, vocal fold cells	Help proliferation, help release some cell product, like IL-8	Relatively accurate and stable	Extra tools needed to calibrate the System; limited in cell application.	(Farran, AJ et al. 2013; Puig, Rico & Almendros 2005; Titze et al. 2005)
Mechanical stimulator	External device, like piezoelectric actuator or vibratory transducer	Investigate the frequency-dependent effect from vibration	Yes, both 2D and 3D	Frequency 10-150 Hz; Amplitude 0–30mm etc.	Majorly in Bone cells, osteoblasts	Benefit gene expression, proliferation and differentiation;	Easily accessible, and widely applied	Limited cell application; inflexibility of frequency control	(Hong, Hua & Guo-zhen 2001; Kulkarni, Voglewede & Liu 2013; Li, M et al. 2015; Shikata, Shiraishi & Morishita 2008)

Ultrasonic vibration	Piezoelectric element, Ultrasonic generator etc.	Study cell behavior under vibration stimulation with higher frequencies	Yes, both 2D and 3D	Frequency 100Hz-1MHz; Amplitude 5-50 μm etc.	Myoblast cells etc.	Increase the proliferation of cells	Capability of generating high frequency	May damage cells and hinder normal proliferation	(Hino et al. 2016; Nakajama & Hashimoto 2014)
3D micro-vibration stage	A micro-vibrator stage basically consists embedded vibrator	Study the cell behaviors in dynamic culture morphologically	Yes, chiefly for 3D	Frequency 10-50 Hz; Amplitude 30-50 μm.	human osteoblast cells etc.	Non-invasively and three-dimensionally vibration;	Affects gene expression pattern and makes the cells remain younger	Limited frequency range; May damage cells;	(Farran, AJ et al. 2013; Konno et al. 2010) (Y.X. et al. 2018)
Mechanical micro-vibrator	A micro-vibrator electric device	Mimic dynamically mechanical forces in vivo, evaluate vibration responses	Yes, both 2D and 3D	Frequency 0-100 Hz; Amplitude 0-5mm;	mouse and human embryo etc.	Precious frequency and time control	Benefits cell's in vitro fertilization and development rates;	Limited frequency range; special device needed;	(Gruber & Klein 2011; Hur et al. 2013) (Feifei, Jigong & Huasong 2014)

2.5 Research Limitations and Gaps

In previous sections, we have studied 3D cell culture scaffolds, 3DP methods and vibration mechanisms applied for cell applications. In this section, the limitations and gaps from two chief perspectives will be discussed to help better understand the current situation and provide potential recommendations for the future.

Limitations and gaps. Based on literature studies, we identified limitations and gaps towards achieving novel 3DPVS from two main aspects, Table 2.6 — first the lack of an innovative design approach to achieve novel 3DPVS, second the technical limitations of 3DPVS itself, compared with current existing technical products, such as 3D scaffolds, traditional vibration mechanisms.

Table 2.6 Limitations identified in this research

Limitations of novel design approach for scaffold engineering
▪ Limitation on experiment-based laboratory approach for scaffold innovation ▪ Lack of method for conceptual development of 3DPVS
▪ Technical limitations of 3D passive scaffold and traditional vibration mechanisms
▪ Limitations of 3D passive or static cell culture scaffolds ▪ Limitation of traditional mechanical vibration mechanisms ▪ Lack of integrity between vibratory functions and scaffold

2.5.1 *Limitations of Design Approach for Scaffold Innovation*

The current literature rarely discusses the scaffold evolution tendency, from ‘static or passive’ to ‘dynamic’, and an innovative approach tailored for scaffold design under this tendency has not yet been developed. The majority of work in scaffold design at previous stages has been laboratory based. The design approach is achieved via conducting experiments, which means trial-and-error attempts are necessary. However, this approach tends to lack the element of innovation. A systematic non-experimental approach that can enable scaffolds with innovative properties remains a gap.

Further, a formal design approach has not yet been developed for innovating 3D scaffolds, although several methods have been attempted, including QFD, TRIZ and axiomatic design. Some of these methodologies aiming for innovation have been successfully applied for a wide range of research fields, including electronic product design and mechanical object innovation. However, these are rarely applied for 3D scaffold innovation, dealing with scaffolds’ microstructural, mechanical and biochemical properties.

To summarise, there exists a gap in the design approach for scaffolds that is non-laboratory based and has innovation as the prioritised focus. Predominant number of researchers focused on experiments to develop new scaffold, which depends on ‘trial and error’ attempts. A new approach therefore is necessary to be applied to scaffold engineering.

2.5.2 *Limitations of Traditional Scaffold and Vibration*

This section discusses the technical gaps in traditional 3D scaffolds with conventional vibration mechanisms. As stated early, the current vibration mechanism for cell cultures is usually generated through placing or attaching a vibrator to the 3D scaffold and shaking it mechanically. In most cases, vibrators are placed at the bottom of the culture dish or scaffold. This mechanism usually lacks localisation functioning, precision control and elaboration. From the view of system evolution, such a mechanism could be improved, and the energy transmitted could be limited.

Scaffold and vibration lack an organic integration. Traditional 3D scaffolds cannot generate dynamic stimulation on cells. Previous studies chiefly focused on developing or optimising passive parameters, such as scaffolds' chemical composition, mechanical property and geometry (Agrawal et al. 2015; An et al. 2015; Farran, AJ et al. 2013; Farran, AJE et al. 2013). Rarely do we see discussion of the evolution trends of scaffolds, and it is difficult to find studies on innovation concepts supporting the principle of laws in engineering system evolution. Thus, the gap between current traditional scaffolds and the novel ones that should be developed to keep pace with evolution demands is an urgent concern.

Resulted from this disintegration, limitation of system energy transmitting also occurs. Researchers find it difficult to accurately control the vibratory stimulation received by cells because there inevitably exists some difference, even slight, in the vibration energy between the generator and the receiver (cells). The main reason for this is that real tissue is an all-in-one dynamic organism; thus, cells can be cultured in exactly the 'required' way by the organism. However, in currently applied vibratory mechanisms, cells are inevitably affected by four 'hierarchies'—that is, vibrations pass through the vibrators, platform, scaffold and inner environment of the scaffold to finally reach the cells (Chintavalakorn et al. 2017; Hou et al. 2016; Laschke & Menger 2017; Wagner et al. 2016). There can be a frictional force between the vibrator and scaffold, the scaffold and culturing media, and the culture media and cells seeded inside the scaffold. Therefore, the frequency generated and received tend to differ, which may compromise the cell culture result, which requires highly and precisely controlled vibration.

Frequency range, accuracy and controllability of vibration must be improved. Current studies illustrate that low-range frequency, such as vibration at around 50 to 200 Hz, tends to have beneficial effects on bone cells. However, a systematic approach of controlling vibrating frequency, as one of the core parts of scaffold design, has not been developed. Thus, scaffolds that can vibrate in a user-tailored way is a design gap. Aside from generating a tailored low-range frequency, current vibration mechanisms working on scaffolds find it difficult to enable vibration with subtler forms. For instance, mechanical vibration can easily achieve a 200 Hz precision, yet current mechanisms cannot achieve 200.01 Hz or subtler frequencies.

This means that specified behaviours in external cell cultures under low-range frequency cannot be effectively studied. Further, recent medical studies confirmed the efficacy of better vibration control. Thus, the question of developing better vibration mechanisms to generate highly-tailored lower-range frequency requires urgent research focus.

Limitation of scaffold in localisation. The current vibration mechanism generates an evenly-distributed vibratory effect among each area inside the scaffold, which could negatively affect cell differentiation and proliferation into 3D tissues. The organs or tissues in the real in vivo environment usually contain many different sub-parts where stems cells will develop, and each sub-part may need different dynamic stimulation to others (Agrawal et al. 2015; Huang et al. 2017; Pongkitwitoon et al. 2016; Tong et al. 2014). For example, cells on the scaffold top, middle or bottom may need different vibrating frequency or intensity. This suggests that a 3D scaffold may need to generate different vibratory stimulations in its different parts to assure a tailored culturing result.

To conclude, considering these aspects and the urgent need for system evolution, as well as the need to mitigate or at least partly address the above gap, a novel vibratory scaffold with tailored localised functions, evolving from a 3D static or passive scaffold, can be logically considered a promising and useful direction.

2.6 Research Objectives

This section proposes this study's research objectives, followed by explanation of each objective in detail.

2.6.1 *Objectives on Applying Novel Design Approach*

First, this research aims to introduce and apply a non-laboratory-based design approach for innovating 3DPVS. Given that the dynamic scaffold is higher up the evolution ladder than traditional 3D static or passive ones, the established methods will be applicable for the design of traditional scaffolds as well. If this attempt is successful, traditional experiment-based design approach for scaffold will likely be reinvigorated. Quality of the new approach should satisfy the following characteristics:

I. Chiefly dealing with innovation aspects of scaffold engineering
II. Enabling traditional engineering design into the bio-design
III. Distinguished from traditional experimental-based design approach
IV. Can be easily replicable and re-usable to developing other scaffolds

2.6.2 *Objectives on Innovating Conceptual 3DPVS*

Second, following this design approach, the conceptual design of 3DVPS will be completed, including concept generation and concept validation. The proposed functions enabled by 3DPVS will include, but not limited to, the following characteristics:

I. 3DPVS will integrate vibration with scaffold into one organic unit.
II. 3DPVS can achieve proactively vibratory functions compared with its traditionally passive vibrating mechanism
III. 3DPVS's geometrics and material composition can enable such vibratory functions and can be designable and modifiable.
IV. 3DPVS is projected to fulfil the following aspects—providing micro-level vibrating amplitude, enabling a vibrating frequency at 50-200 Hz, enabling localised vibration, and generating potential shape-changing functions.
V. It must be fabricable through one or a combination of existing 3DP technologies, and 3DP knowledge will be used for evaluating generated concepts and their fabricability,
VI. It should be modellable by CAD software; Model of 3DPVS should be compatible of simulation tool which will be used to evaluate and validate the proposed functions.

New vibration methods, transcending the ones mostly used with traditional cell cultures, could potentially be introduced to achieve a self-vibratory mechanism of the 3DPVS. This might improve traditional vibration mechanisms, which tend to be rigid and inflexible in vibrational control, and where the scaffold must have a passive role, being vibrated chiefly through mechanical ways. In addition, the designed 3DPVS is projected to work with better vibration control; this will include, cells could be vibrated at a higher precise frequency at micro-level (for example μm), compared with the coarse frequency generated by traditional mechanical vibrations. Considering the uncontrollable evenly-distributed vibrational effect—the acceleration amplitude distribution—the newly designed mechanism aims to ensure tailored and localised vibration. For example, different areas of scaffold can generate different stimulations to cells.

To achieve the design of 3DPVS, several steps in sequence must be completed:

Conduct thorough literature review to support design initiation. Given that 3DPVS is a novel aspect to be developed in the future, its elements must be thoroughly studied, including 3D scaffolds, vibration, 3DP and cell cultivation. This is the focus of Chapter 2. The literature searched will also be needed during later design process.

Establish conceptual design process for 3DPVS and identify research methodology and tools. An engineering design process (EDP) must be applied to 3DPVS development. Based on EDP, the conceptual design of 3DPVS will be established with a multiple-stage plan. Reasonable methodology and tools for each stage will be selected and tailored.

Complete systematic study on design initiation of conceptual 3DPVS. Following the three-stage conceptual design process, focusing and studying on the design initiation will be of significant value at the current conceptual stage of 3DPVS. This study bridges the literature review and contributes to the following stage of concept generation. The base model and ideal model of 3DPVS will also be created at this stage.

Use innovation method to generate conceptual solutions of 3DPVS, from super-system to system and then sub-system. This will be the core part of conceptual design, output of this part will be generic conceptual solutions of 3DPVS. After this part we will have a basic understanding about the useful vibration mechanism, how to integrate within scaffold and what will be its functionality.

Use design method to generate solutions from system- to sub-system level. Output of this part will be a specified scaffold model with possible specifications including geometrics and material composition. This will be used in next-step simulation process which helps to validate and test if the solutions can fulfil the initial objectives as proposed.

Validate generated conceptual solutions by computer simulation. The generated solutions will be evaluated and ranked through theoretic way. Then the specific functions of 3DPVS, such as frequency range, micro amplitude, localization, will be tested through CAD methods to validate the generated concept and to prove the 3DPVS is successful.

2.7 Concluding Remarks

This chapter has reviewed the 3D passive scaffold, 3DP and vibration mechanisms for cell cultivation. In terms of chemical composition, mechanical property and geometry, 3D passive scaffolds have great advantages over 2D cell culturing. Vibration mechanisms and their effects on cell cultivation were also reviewed. Despite the benefits of scaffolds and vibration for cell cultivation, little previous research has focused on how to combine scaffolds and dynamic stimulation into a 'complete organism'. In the final section of this chapter, we discussed the use of 3DP for 3D scaffolds. The combined effects of the vibration mechanism and 3D passive scaffold becoming an embedded unit require further study, although the resultant effect is predicted to be beneficial and useful. In the last two sections of this chapter, we discussed the research limitations and gaps, as well as the research objectives. The following chapter introduces the conceptual stage of 3DPVS and offers a thorough and comprehensive illustration of the research methodology and tools.

3 CONCEPTUAL DESIGN PROCESS AND RESEARCH METHODOLOGY

3.1 Introduction

The previous chapter provided the concept justification of 3DPVS through analysing the limitations of traditional cell culture mechanisms and applied the penetrating laws of system evolution (LSE) to scaffold engineering. Following this, the design process to achieve 3DPVS must be identified, and, in this research context, we propose to establish a tailored design process for 3DPVS based on the EDP, which has been widely applied in traditional designs of engineering products. Given that the EDP has not previously been used for bio-designs and bio-inventions, modification is necessary to make EDP applicable for the 3DPVS context.

In this chapter, we first introduce the basic background knowledge of EDP. The full design of 3DPVS will be divided into two parts: conceptual design and detailed design. Given the significance of conceptual design for 3DPVS at the current stage, in this research context, tasks of conceptual design stage will be prioritised as the focus. That is, the three-stage conceptual design process—design initiation, concept generation and concept evaluation—will be the centre of gravity of this research. In terms of achieving tasks within these three stages, appropriate methodology and tools supporting the selected methodology will be of great value and will be discussed in this chapter.

3.2 Introducing Engineering Design process (EDP)

EDP describes a process to generate the desired result of a product design or complex engineered system design. Before the EDP used in this research is introduced, basic information about traditional EDP is provided in the following section.

3.2.1 *Traditional EDP*

Traditional EDPs generally contain four stages and follow the same four-step principles: analysis of problem as initiation, concept design, embodiment design and product validation. Initiation involves defining the problem, analysing the task restraints and needs, and developing the requirement lists under design specification. Conceptual design is the most vital design phase in EDP. This phase generates the design concepts and validates them. Embodiment design involves developing specifications for function, strength, geometrics, physical compatibility and financial availability. Detailed design involves further identifying and establishing the properties of all components of the product. The simple logic is shown in Figure 3.1.

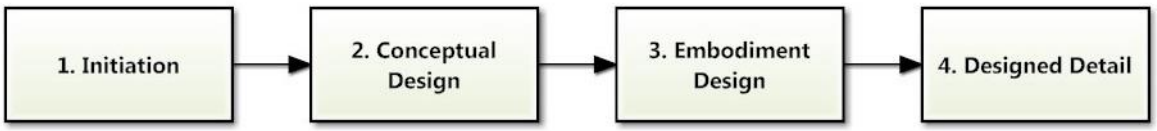


Figure 3.1 Typical EDP process with four stages

In addition to the typical four-stage process, some researchers have suggested that design initiation be integrated within conceptual design, thus reducing the process to three phases. They believe that initiating the conceptual design covers tasks of design initiation regarding defining the problem and gathering information. Thus, conceptual design can be integrated with the design initial stage (Dieter & Schmidt 2009). Figure 3.2 shows a typical three-stage EDP process with eight sub-steps.

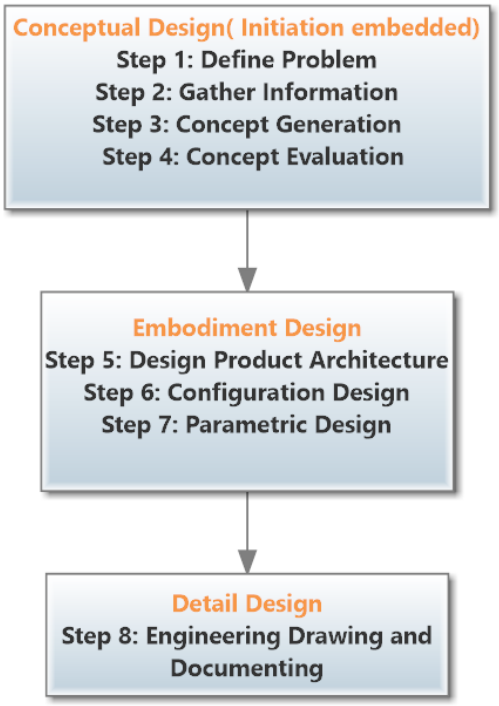


Figure 3.2 Typical three-phase eight-step EDP

Besides the above three-stage EDP process, there is another definition of categorising the design phase, which proposes that embodiment and detail design can be integrated (Matthews 2012). The unified part is named ‘detailed design’ to make a distinction with conceptual design, which includes the full stages. In this way, the design for an engineering product includes only two major stages: conceptual design, which integrates the traditional design initiation and conceptual design, and detailed design, which includes the traditional embodiment design and details design, as shown in Figure 3.3.

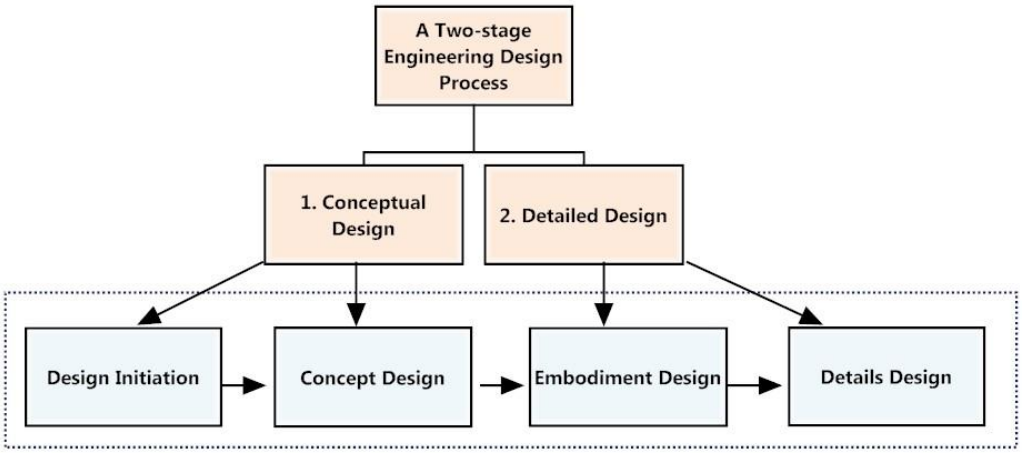


Figure 3.3 Two-stage simplified EDP process

3.2.2 *From EDP into Conceptual Design*

After establishing the 'permanent centre of gravity' in this research—to achieve a full conceptual design of 3DPVS—it is necessary to consider the background information of traditional conceptual design, and then rearrange, modify and tailor it into current context. The traditional conceptual design phase usually includes concept generation and concept evaluation (Taura 2016). Concept generation identifies the system functions and finds possible conceptual solutions, while evaluation compares the possible solutions by criteria, and then determines the principal one. A seven sub-steps illustration is presented in Figure 3.4.

The first five steps belong to the generation stage, while the last two belong to the concept selection stage. The first step concerns identifying the essential problems generated from the requirement list, whose output is a set of functions that should be satisfied by the product. Structure models of these functions are then established and each of these models is decomposed into sub-functions, each of which needs possible principles for its realisation. Searching for these is an innovative process that requires creative thinking. These working principles are combined to generate alternative solutions for the conceptual design, and preliminary combinations are selected, while unsuitable ones are eliminated. Following this, models of evaluation variants of solutions are established and the solution evaluation is available in this stage. Final solutions are evaluated and validated using a set of criteria identified according to the design requirements. The output of this step after the entire conceptual design is the principal and desired conceptual solution for the product.

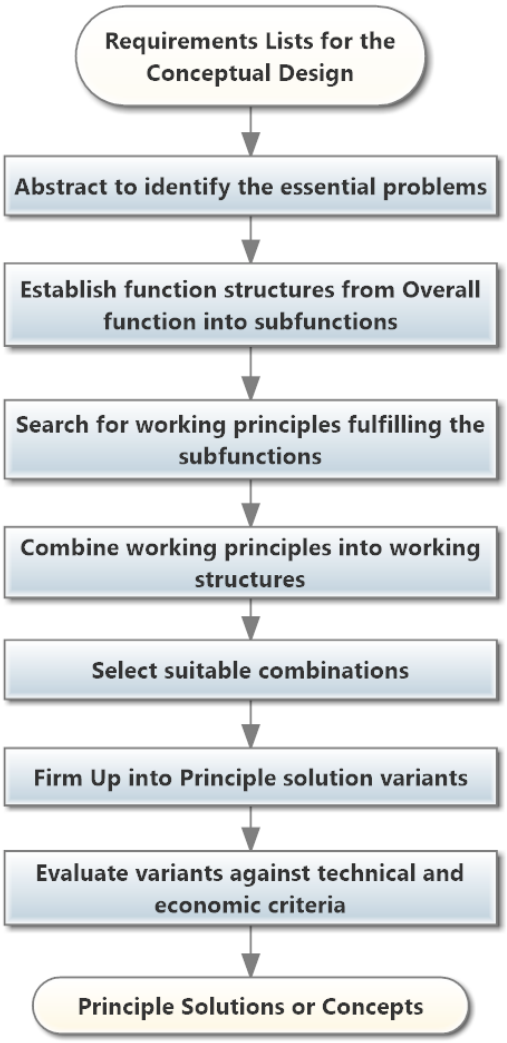


Figure 3.4 Traditional conceptual design process (Dieter & Schmidt 2009; Pahl et al. 2007), adapted

3.2.3 *Conceptual Design of 3DPVS*

Although a complete design process of 3DPVS includes three main stages, as discussed in the previous section, we only focus on the conceptual design in this study frame. There are two main reasons why the conceptual design can and must be the focus of this research. The first reason is the significance of conceptual design in general EDP. Design requirements are transferred to the conceptual level of the solution, and conceptual details should be strictly followed to ensure that the design moves in the projected direction. For many companies, a proposed product design may never make it out of the conceptual stage. Conceptual design also has significant effects on the lifecycle cost of the full design. The cost consumed in designing a product only comprises 5%, yet the decision and solution made during the conceptual design process influences nearly 70 to 80% of the cost of product manufacturing and use (Dieter & Schmidt 2009). Thus, the conceptual design determines a much higher proportion of product costs than other design stages, and this will also be the case for the future 3DPVS design in this research.

Second, conceptual design is an innovative process and designers apply creative thinking to generate conceptual solutions. Although it may be more abstract thinking, conceptual design uncovers flaws in the product design idea, and detailed design work is never completed. Given that the 3D vibratory cell scaffold to be designed is a totally new concept, innovative thinking and concept creating are the most vital part of this research. Embodiment design and detailed design can only play a role after a satisfactory concept has been established, proven and tested, and after fabrication and vibratory feasibility has been sufficiently evaluated via computer simulation. Figure 3.5 shows the four categories when considering the concept and innovation level and product development and fabrication level. In this research context, (A) is the starting point where we initiate the creative design of 3DPVS. The development line from (A) to (B) is the projected aim of this research. After this, (C), the detailed design of 3DPVS, can follow in a scientific and smooth way. Time is another restraint of PhD research to avoid the research goal being set as too impractical or 'imaginary'.

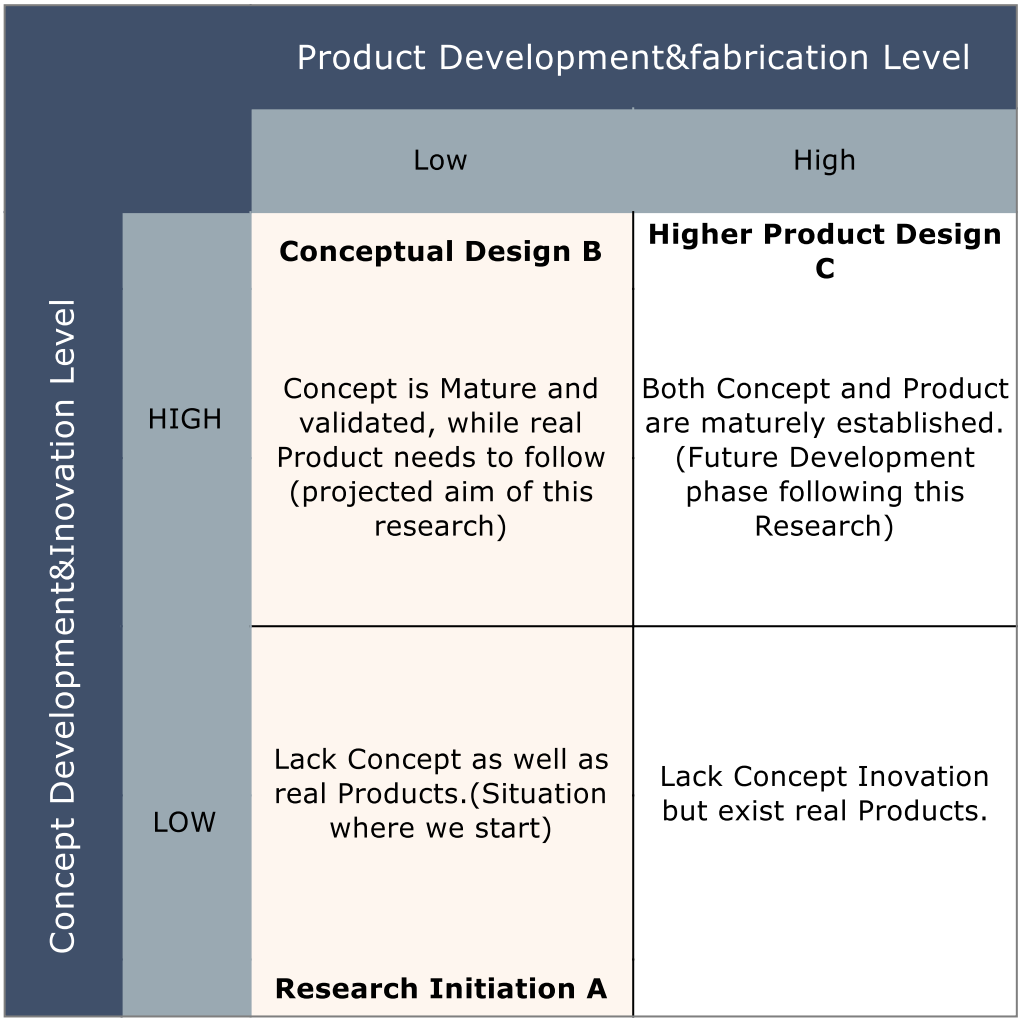


Figure 3.5 Matrix for concept development and product development level

3.3 Conceptual Design Process for 3DPVS

Based on the traditional conceptual design process studied in the previous section, this section proposes a tailored conceptual design process for the 3DPVS development. The input

for the conceptual design is a set of requirements, such as for the cell culture; scaffold; and dynamicity requirements of customers, researchers or companies. This phase is proposed as the design initiation for conceptual design. Fundamental requirements and speculations of the 3DPVS will be acquired here, which will help generate the alternative solutions or concepts for the 3DPVS required. The concept-generating stage is the second stage of the conceptual design process of 3DPVS. The third stage swill be concept evaluation, where optimum conceptual solutions will be selected from the generated alternative solutions, and a process of concept validation will follow. During the evaluation stage, the concepts or solutions that fail to satisfy the initial requirements will need to go through the concept generation phase again to generate alternative solutions or concepts. Although this research focuses on the conceptual stage of the development of 3DPVS, concept evaluation will be extended beyond a philosophical evaluation process, which mainly contains criterion selecting and concept weighting. A phase of computer-aided evaluation and 3DP prototyping testing will be used afterwards to further validate the eligibility of the concepts generated for the required 3DPVS. The logic line of this chapter

3.3.1 *Three-stage Conceptual Design*

Figure 3.6 displays the detailed process created for the conceptual design of 3DPVS. The process comprises seven steps, where the first five steps belong to the concept generation stage and the last two steps constitute concept evaluation. In the figure, the steps of the design process are represented by rectangles, and the outputs of each step by rounded rectangles. However, we propose dividing the conceptual design into three main parts: initiation, concept generation and concept evaluation. The main task of the generation phase is to generate possible solutions to realise all the designed functions of the 3DVS. The evaluation phase judges whether the designed scaffold has fully satisfied these functions, and whether the concept is applicable by 3DP technologies. These three parts are discussed in detail in the following paragraphs.

The core part of the conceptual design is the 3DPVS innovation roadmap, which is essentially a complete set of tools for the conceptual stage of 3DPVS system design. It is an effective way to integrate TRIZ-based technologies; other development and design methods, including DFSS, failure mode and effects analysis, and trimming; and computer simulation and CAD methods.

3.3.2 *Stage 1: Design Initiation*

Design initiation aims to achieve problem selection and requirement identification. This phase is mainly developed to collect requirements and speculations for the 3DPVS design, and the acquired information can be used as the input for the concept design in the next phase. A requirements specification is documented to provide a detailed description of the 3DPVS project, and the requirements identified to make it achievable.

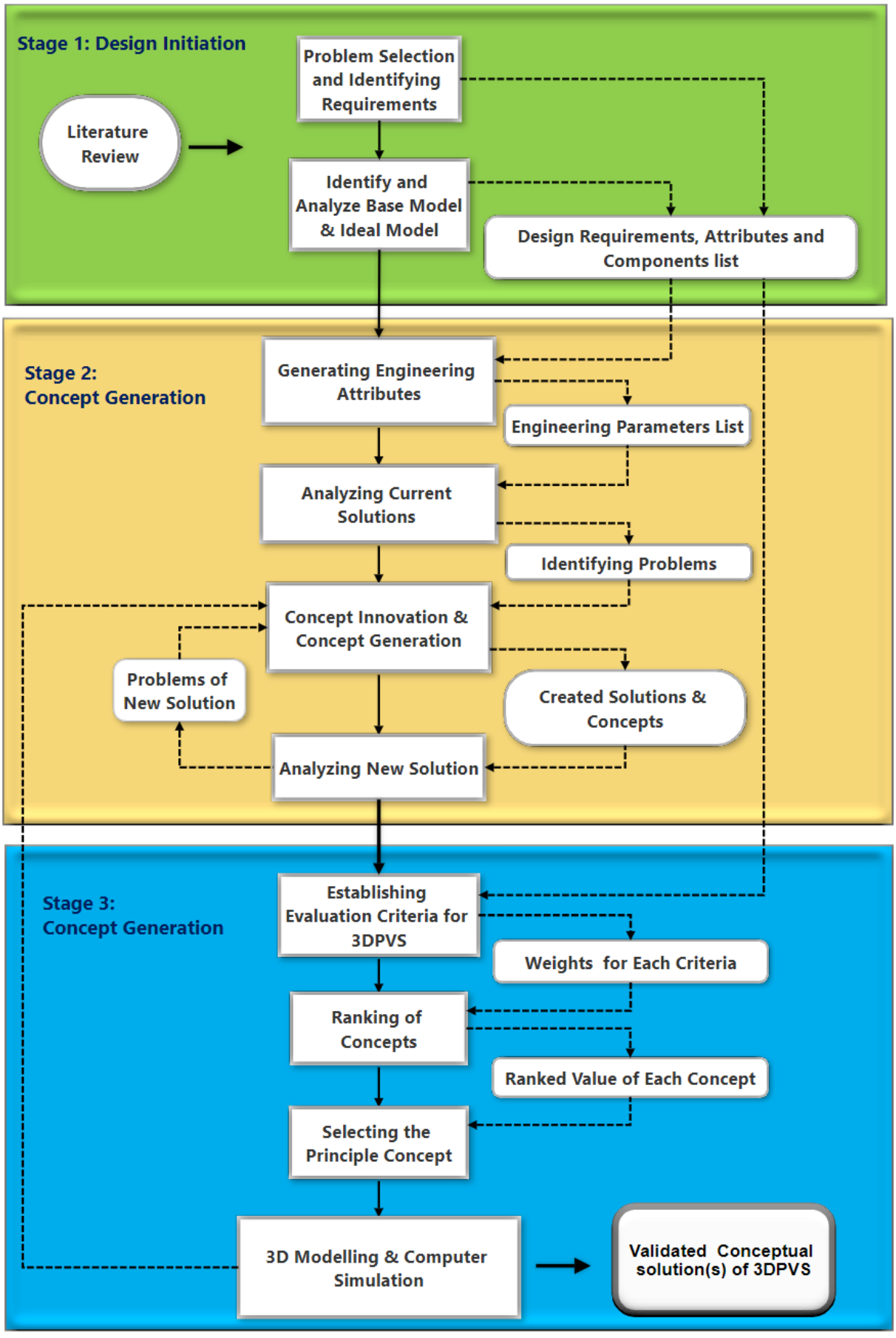


Figure 3.6 Process of Conceptual Design for 3DPVS

The detailed process of this work may occur as follows. Previous work on 3DP fabrication techniques, scaffold architectures, materials, biochemical functions and mechanical properties for 3D scaffold fabrication should be reviewed and compared, and the potential specifications of 3DPVS will include four major aspects: geometrical control, mechanical properties, biochemical control and dynamic functions. For biochemical control, basic 3D static cell culture requirements regarding the viability, proliferation, morphology and differentiation of the cells cultured will be determined first. Then, it is necessary to determine the requirements of the newly introduced vibration mechanism, and the difference between traditional vibration mechanisms and the new vibration-scaffold integration mechanism. This will also contribute to the biochemical and dynamic parts. Base models and ideal models are prepared in the initiation phase. Figure 3.7 illustrates the basic requirement specification list for the 3DPVS conceptual design. Detailed information of each requirement will be discussed in Chapters 6 and 7 and the case study.

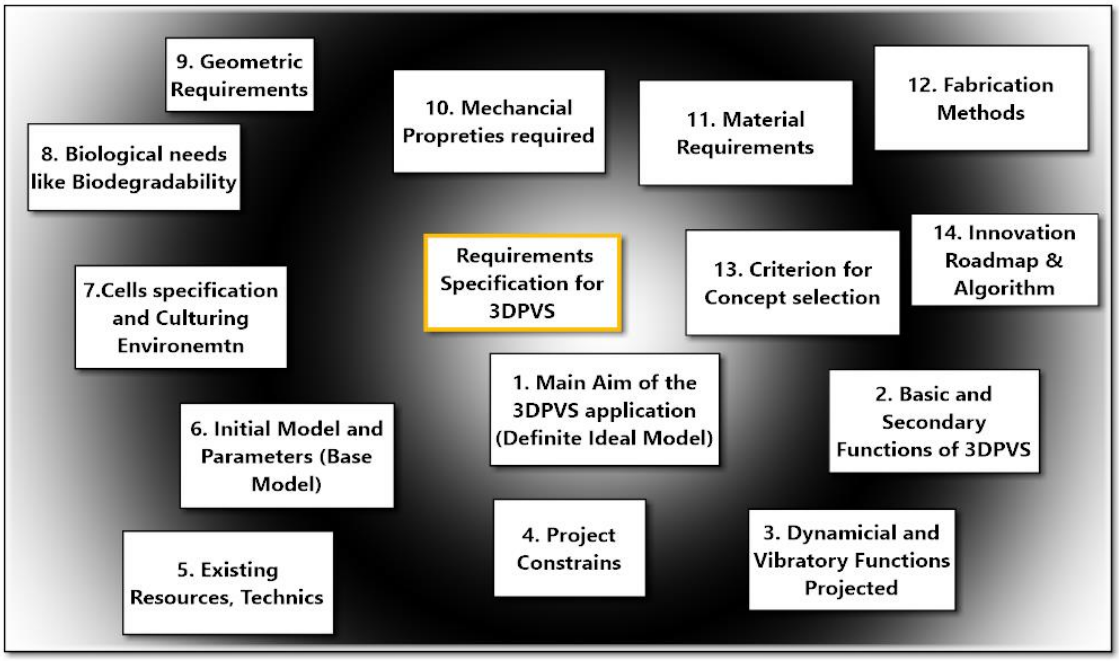


Figure 3.7 14 Key elements for the initiation of 3DPVS design

3.3.3 *Stage 2: Concept Generation and Innovation*

This stage is the second stage in the conceptual design. Its purpose is generating a set of alternative concepts for 3DPVS, and the 3DPVS innovation roadmap and algorithm will be used during this stage. The requirements and specifications output from the initiation stage are the input of this stage. Four steps are involved in concept generation.

I. Step 1: Model of problem creation to identify the attributes and parameters of 3DPVS.
The first step is to establish the 3DPVS ideal model according to the requirements list. This list is the result of obtaining requirements from customer demands, and the current and future needs of dynamic cell culture studies. The attributes are the objectives to be realised by the

3DPVS conceptual solutions. In brief, these attributes chiefly include the perspectives of dynamic and static functioning of 3DPVS:

- scaffold's vibratory functionality
- vibration and frequency cycle performance
- scaffold's geometric and architectural characteristics
- biomedical control factors
- material composition and biocompatibility
- fabrication availability.

The relationships between these attributes as input requirements must be analysed. The weight of each attribute can be determined according to the comparative importance of each requirement. The output of this step is a set of attributes of 3DPVS to be used in both the next stage and the first step of concept evaluation.

II. Step 2: Analysing current or existing solutions.

A novel 3DPVS might be achieved with different types of systems that apply different vibration mechanisms, scaffold designs and fabrication technology. Therefore, one main task of concept generation is to identify an appropriate scaffold base model and vibration and fabrication strategies to create new solutions or improve the current 3D scaffold solutions. The basic conceptual solution is a new scaffold model that has dynamically vibratory functions and generates frequencies in flexibility, which is the gap in traditional 3D cell culture scaffolds with vibrations. In this model, the designed scaffold can vibrate via different non-mechanical vibrations, such as vibrations via acoustic waves or phonic waves. The basic solutions chiefly include:

- a potential vibration mechanism for 3DPVS
- a possible base model to be introduced into the conceptual design
- smart materials that can help the vibratory functions of scaffolds
- tailored characteristics of scaffolds in geometry and surface control
- 3DP fabrication methods available for the geometric and materials requirements.

III. Step 3: Design innovation and concept generation to create new solutions.

Step 3 is the most important step for the innovation roadmap of 3DPVS, the process of which is illustrated in **Appendix G8**. This step contains the full contents of the innovation roadmap, Parts A, B and C. This step will generate ideas to solve the problems identified in Step 2. These problems are normally related to the limitations and gaps to create the 3DPVS in the current solution, and new ideas must be introduced to solve them. In 3DPVS design, this step is the most innovative part, as previously existing ideas cannot realise the proposed functions of 3DPVS. When new ideas are presented, we can improve the basic solution and generate new concepts to realise the 3DPVS's design. These solutions are the alternative conceptual

solutions to be judged in concept evaluation and will be further analysed and improved in the next step. Two tasks of this step are:

- further establish conceptual structures as an intermediary between the base and ideal models
- use innovation methodology and tools to create new ideas.

IV. Step 4: Analysing newly generated solutions.

New solutions and strategies developed in the previous step still need to be improved in the future to ensure their usefulness, practicability and efficiency as a conceptual model. New problems inevitably appear when seeking to solve the old, so we need to return any new problems to the previous step and create updated ideas to mitigate or transform them. Several alternative solutions may thus be generated. Hence, innovation in 3DPVS design is a circular process, following the steps of analysing solutions, identifying and solving old problems, analysing new solutions, and identifying and solving new problems, until the new solution of the design model is sufficient to meet designers' requirements and specifications set before the first design. The final solutions of the innovation process will enter the second phase of concept evaluation.

3.3.4 *Stage 3: Concept Evaluation and Solution Validation*

Comparing concepts with one another requires (unchanging) criteria for evaluation (Salustri 2015). Concept evaluation is the third stage of the conceptual design, and the main objective is to evaluate the alternative conceptual solutions and select the best one as the principal solution. Hence, alternative solutions are the input of this stage, while the principal solution is the output (Liu, Z et al. 2015). For the 3DPVS design, this stage includes five steps. In the evaluation phase, we combine concept evaluation with computer simulation, virtual prototyping and sample product validation, and the final validation is processed through 3DP technologies. The scaffold concept needs to fulfil the requirements of computer simulation and be feasible by 3DP; otherwise, the concept must be regenerated. In brief, the five key elements consist of concept evaluation—the first three are the objectives of this research context, and the latter two are tasks for future work.

Concept evaluation in this PhD research context contains three core aspects:

- concept evaluation through a criterion-based analytic evaluation system
- concept evaluation via collecting experts' opinions
- concept evaluation via adequate experiments undertaken by other research groups.

Future concept evaluation work might include:

- evaluation with computational simulation methods for virtual prototyping
- evaluation of 3DPVS primary samples or parts through 3DP fabrication methods in reality.

Several steps could be undertaken for the 3DPVS concept evaluation work; adjustments may occur by shifting or modifying some elements of each step to tailor to different design needs.

I. Step 1: Establishing evaluation criteria system for 3DPVS alternative solutions

The principles of criteria selection state that the criteria should comprehensively reflect the design requirements and be estimated in the conceptual design phase. These identified criteria should have the capacity to reflect customer requirements of the designed 3DPVS, so they can be selected from the attributes of the conceptual product generated in the first step of the concept generation stage. These attributes should have three characteristics. These criteria should thoroughly reflect the requirements in the initiation phase. Further, they should be condensed and evaluable for alternative solutions in the conceptual design phase; hence, there cannot be too many criteria and the criteria cannot be too detailed. Finally, one or two criteria usually need to be selected from a set of attributes that reflects the same requirement, which can ensure the accuracy of the evaluation. For the 3DPVS concept evaluation, 15 criteria are introduced here:

- design feasibility from base models
- functionality of being self-vibratory, partly or largely
- applicability of new vibration mechanism compared with traditional vibration mechanism
- frequency controllability and flexibility
- time-tailored functionality in dynamic culturing
- affordability and usability for bone cell studies
- safety for cells and researchers
- quality of geometric characterisation, especially for pores
- pore interconnectivity
- mechanical load-bearing capacity
- efficiency of cell penetration
- permeability of culture medium
- maintenance of 3D cell phenotypes (template for 3D morphology)
- adequacy of mechanical properties
- controllable biodegradability or biocompatibility
- availability of smart materials
- fabricability by 3DP method.

After this, a criteria system is established to evaluate the conceptual solutions. Note that difference exists in criteria selection between conceptual and detailed design. For the 3DPVS in this research, because it focuses on the conceptual stage and scaffold innovation, an evaluation system containing criteria that are too specific or detailed is not used. These specific criteria will generally be based on judging sub-system components.

II. Step 2: Ranking concepts by criterion.

This phase traditionally includes two steps: determining the weights of each criterion and calculating scores. For the nature of the 3DPVS design, this part is subjective, as it is generally difficult to define which characteristics of a scaffold are superior to others. In most cases, when a single factor fails to function, the whole functionality of the scaffold is instantly ruined. Thus, after the subjective weighting criterion and obtaining a subjectively calculated score, further objective methods for evaluation are required.

- **Determining weight, significance and priority of each criterion.**

The weights are determined by the relationship between the criteria and related requirements. The importance of each criterion should be determined in accordance with the prioritised requirement for the 3DPVS design. In this research, vibratory functionality is considered the fundamental priority, and this would occupy 50% of the total weight of the concept. Another 50% would be for the normal effect on culturing cells, which could be similar to traditional 3D passive scaffolds working with external mechanism vibrations.

- **Calculating score of each criterion and ranking concepts.**

This step is a preparatory phase to estimate the scores of the alternative solution against each criterion, and neglect inappropriate ones. Detailed information or values for each criterion in each cell culture application is difficult for designers to obtain in the conceptual design phase; thus, each solution in the criteria is essentially judged by the knowledge, information and experience of cell cultivation and 3DP fabrication from companies and academia, and compared subjectively. That is, criterion will be objectively listed as a constant ‘yardstick’ for comparison, but comparison will be a relatively subjective task. The results of this will be used in the next step.

III. Step 3: Selecting the principal (optimal) concept.

When the overall scores or significance of each solution are calculated, the one with the highest potential worth will be selected as the optimal conceptual solution. The overall worth of an alternative solution is calculated according to the weights of the criteria and the score of the solution for each criterion. In this stage, the term ‘best’ is also a term of relativity—that is, the selected concept is best only in that given context from the researchers’ perceptual filters and reasoning. There is every possibility that the selected one is not suitable for practical use. Thus, the following step of validating the concept via computer simulation will help the design become more solid and reliable.

IV. Step 4: 3D modelling and computer simulation

This step involves validating concepts using CAD simulation. While the optimal solution is relatively the best among the alternative solutions, it may still have defects that contradict the design requirements. For example, the optimal solution may have difficulty being transformed into CAD language, limiting 3DP technologies to fulfil real prototyping. Therefore, a solid

evaluation process is needed after Step 3. In this process, the generated conceptual model of 3DPVS, containing a combination of different parameters, will be evaluated through CAD tool first. Computer simulation will be used to chiefly evaluate whether the required characteristics of 3DPVS in a given context can be in tune with the concepts generated previously. Using CAD tool, such as SolidWorks, to construct and simulate the model is to test the function of each parameter in efficient way—especially the vibratory properties.

3.4 Research Methodology and Tools

Through the steps discussed in the previous section, a 3DPVS conceptual design can be undertaken. After illustrating the innovation and design aspects of 3DPVS, the conceptual design of 3DPVS can be separated into three stages, each containing a chief task. Design initiation is for generating system analysis and a problem statement, and the chief task considers how to analyse the problems in existing or previous design solutions, as well as prepare materials for the conceptual design. Stage 2 is about concept generation and problem solving, with the core task being concept innovation, and appropriate concepts for the required 3DPVS will be generated. Stage 3 involves concept evaluation, whose task is to evaluate and validate the generated concepts of 3DPVS in the previous stage, and finalise the concept scenario creation.

Thus, the conceptual design of 3DPVS can be seen as a novel, integrated process of three stages corresponding to three tasks. Several methods and tools will be used to ensure and improve the design efficiency of these tasks in the conceptual stage of 3DPVS, and Table 3.1 briefly summarises these. The literature review in Chapter 2 is used as both a methodology and tool for design initiation, which is the first stage of the full conceptual design process.

Table 3.1 Summary of methodologies and tools for conceptual stage

	Methodology/tools	Tasks	Notes
Design initiation (Stage 1)	Literature review QFD supporting tools	▪ Define base and models ▪ Identify and analyse design requirements, attributes, and components	Conceptual design
Concept generation/ innovation (Stage 2)	TRIZ-based method and tools QFD supporting tools	▪ Identify design criterion ▪ TRIZ-based innovation process ▪ Weight, rank concepts/solutions	TRIZ as the core method for conceptual design will dominate stage 2
Concept evaluation/validation (Stage 3)	Multiphysics COMSOL, CAD tools	CAD simulation for analysing parameters Vibratory solution validation	Validate frequency range, amplitude, vibratory ability
A solution-judging work may be included to gather experts' opinions from cross-domain and miscellaneous fields, which helps evaluate solutions through human experience and expertise.			

For better understanding, an illustration is summarized as follows, Figure 3.8:

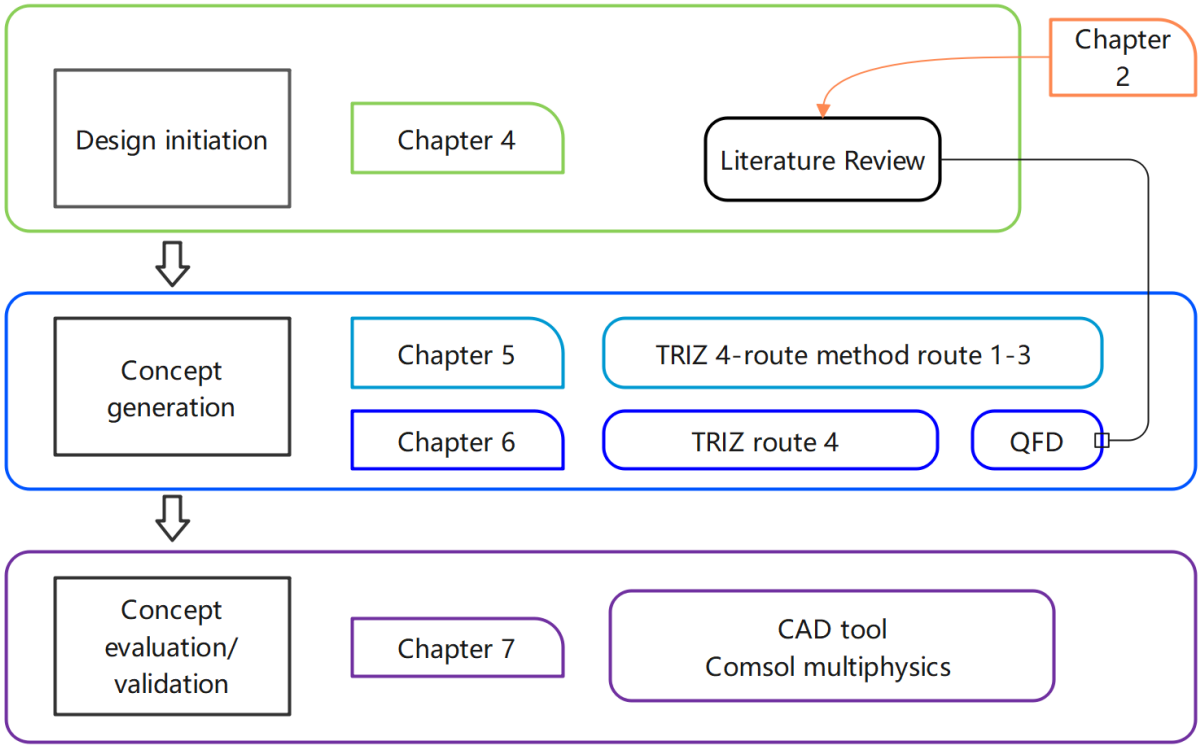


Figure 3.8 illustration of methods and tools corresponding with chapters

3.4.1 *Methods and Tools for Design Initiation*

At the beginning phase of the research, as well as the starting phase of design, two methods can be applied, as follows.

Literature review. Chapter 2, the literature review, continuously plays a significant role in the research. The chief aim of literature reviews is to collect data, identify current limitations and propose practical objectives. Regarding potential data collection in this research, this could include interviews, data extraction, questionnaires and surveys, hypothetical attribute sets, as well as literature reviews—which is the main data collection approach.

The search strategy to conduct a literature review includes an electronic search of databases—mainly including ProQuest, SCOPUS, PubMed, ScienceDirect and Google Scholar. In the 'title, abstract and keywords' search category, several keywords or phrases are used as search parameters: scaffold AND design AND bone, cell culture AND vibration, cell culture AND 3D scaffold, cell culture AND 3D scaffold AND vibration, scaffold AND material (geometry) AND vibration, and so forth. The major search is limited to published works between 2002 and November 2018. The eligibility of publications is based on screening first by title and abstract, and then analysing the level of places where articles are published. In terms of the design methodology for both the scaffold and 3DPVS, articles are analysed via objectives, design process, fabrication technique, metrology materials, geometrics, biological functions, dynamic or vibratory control, and so forth. Manual searches also include examining the reference lists of the selected publications for additional eligible publications.

QFD for design initiation. For generating design requirements from literature reviews, customers, end-users or designers, a methodology to identify, compare and analyse these requirements will also be used in the initiation phase of the research. These income requirements, at super-system level, will be compared and analysed with system-level requirements, called 'design attributes', which will be further compared and analysed with sub-system requirements, called 'design components'. This whole process of comparing and analysing will be conducted through the QFD methodology. QFD will also be used in concept evaluation, which can be considered the chief methodology for Phase 3 of this research. Knowledge and roles regarding QFD, will be introduced in Apx B. The tools incorporating QFD in the initiation phase will be generally the same as those used in the evaluation phase; thus, they will be introduced later.

3.4.2 *Methods and Tools for Concept Generation and Innovation*

As discussed in previous sections, Stage 2 is the most important stage in this research context, and the innovation process is the core part of the concept design. The methodology and tools here chiefly involve generating innovative concepts and ideas to solve design problems, which is also the chief task of Step 3 of Stage 2. Among the three tasks corresponding with the three stages of the 3DPVS conceptual design, the second solves the problems identified in the first stage and generates concepts for the third stage. After design initiation, designers will have a general understanding of the design direction, aim and product requirements of 3DPVS; however, it is impossible to have direct knowledge regarding which innovation concepts will be accessible and how to generate them in a methodological way to fulfil the directed aims. Considering this gap, an effective methodology is necessary to help designers generate novel concepts and solutions in an adequate and effective manner. Thus, in this stage, methodology occupies great weight, and essential work on 3DPVS innovation and creation will occur through this methodology, which helps achieve the 3DPVS conceptual design.

TRIZ innovation method: A TRIZ-based methodology will be used for this purpose. There are several reasons TRIZ will be used as methodology, as the most valuable tool in this design context. Detailed reasoning will be provided in Chapter 5 regarding the methodology for the concept generation of 3DPVS, while a brief illustration is provided here. First, TRIZ has been used worldwide as a relatively mature tool for product innovation and concept design, which is the focus of this research context for 3DPVS. Second, TRIZ can be combined with other proven useful and effective design methods to ensure higher quality of the design, compared with applying only one tool. The eligibility of TRIZ to integrate several other design methods in recent engineering gives it advantages to apply here as a methodology for 3DPVS conceptual innovation. Third, the 3DPVS creation will be an innovative process for cross-domain science and engineering, regarding cell culture, vibrations, scaffold engineering and 3DP technologies; therefore, the innovation process will be different to that of a product from one domain or realm. TRIZ and its related tools have been used for cross-domain designs,

and this is another reason it will be beneficial to use TRIZ-based methodology at this stage. Fourth, the nature of the TRIZ-based process is to solve contradictions. The more sophisticated the contradictions of a design scenario, the more beneficial it is to apply TRIZ-based methods. As illustrated in the next chapter, the conceptual design of 3DPVS will be divided into contradiction solving for geometric, mechanical, biological and dynamic conflicts and contradictions, which leads to the overall contradiction level being complex and challenging. Therefore, TRIZ-based methodology and tools are appropriate to use for the 3DPVS design.

Tool of TRIZ-based components. First, the TRIZ-based tools applied in this research context chiefly contain the traditional parts of TRIZ, including Altshuller's matrix for contradiction solving, innovation principles analysis, standard solution system, and substance-field modelling analysis, as well as the recently developed contents of TRIZ from Oxford Creativity (UK), which offer updated standard solutions for innovation.

These tools or elements of traditional TRIZ or recently developed TRIZ are proposed to fulfil two aims. First, they can be used separately for definite design questions. Each of the tools can be used as one analysing system for definite problems in the design process and generate desirable output for designers. For instance, 40 innovation principles can be directly used to provide solutions to some simple design questions, without the need to change the question into contradiction style and analyse it through the whole TRIZ elements. A detailed illustration of such is provided in Chapter 5 regarding the role and functionality of each TRIZ tool in the 3DPVS design process. Second, the tools of innovation principles, or standard solution system, have been used in the traditional engineering realm, and transforming all the principles or standards to tailor to the 3DPVS design scenario provides a relatively full picture of TRIZ-based analysis for scaffold engineering design, and this could play a beneficial role in the 3DPVS design in this research context and other future scaffolds.

Tool of 3DPVS innovation roadmap. The second tool supporting the methodology is the 3DPVS innovation roadmap, which will be used as the fourth route for established a TRIZ-based four-route methodology (see Section 0). The tool itself is an individual combination of the core parts of TRIZ, other sciences and proven concept development tools, including functional modelling and analysis (FMA), hybrid system and concept design, trimming, and failure mode and effects analysis (FMEA). These together offer a more effective approach for achieving the required concepts of the 3DPVS design and innovative problem solving, compared with the process using TRIZ methods alone. The chief aim of this innovation roadmap is to use elements of TRIZ and other concept development tools to constitute the full and complete conceptual stage of 3DPVS design. Two of the four tools mentioned above will be used in the concept generation stage. The reason for using FMA as the design tool is to analyse the functionality of the 3D scaffold, both static and vibratory, to help designers gain more understanding of the scaffold models and their characteristics, thereby accelerating the

design process. Hybrid system design allows designers to compare different systems performing similar vibratory functions for 3DPVS, and helps combine some useful features of different systems into a hybrid system. This could help accelerate the design process for the concept generation stage.

The innovation roadmap of 3DPVS converts the conceptual design of 3DPVS into an integrated and thorough process. With detailed and accurate requirements input into design initiation, after all steps of the roadmap, the most appropriate conceptual solutions for each case scenario will be created and philosophical evaluation—the first and core part of conceptual evaluation—will be conducted. After the full steps of the innovation roadmap, tools of computer simulation and 3DP can be used to further justify and evaluate the created concepts or solutions. If the generated and previous evaluated concepts cannot be validated at a satisfactory level with computer simulation or 3DP testing, then such solutions must be re-developed to become eligible and appropriate for design needs. The detailed philosophy, analysis and steps of using the innovation roadmap and related tools will be used in the advanced solution-improving in Section 6.3.

3.4.3 *Methods and Tools for Concept Evaluation and Solution Validation*

After illustrating the methodology for concept generation and innovation, which is the core focus of this research context, we now discuss the methodology and tools for concept evaluation and solution selection.

QFD method: The tasks in Stages 1 and 3 to some extent can be considered the same, as both relate to the decision-making or 'identifying-judging-selecting' process. The task in the first stage, design initiation, helps designers decide which problem can be solved and which model is to be established, before any novel concepts are generated. The task in the third stage requires designers to decide the optimal solutions for the concepts generated in Stage 2. Scientifically speaking, these two tasks are not directly part of 3DPVS innovation itself, but are a supporting and necessary part to cooperate with the design. In other words, their respective roles are to generate the inputs and evaluate the outputs of the innovation process. Therefore, the QFD methodology used here will help designers identify the design issues before the innovation process starts, and help select the appropriate concepts after using the methodology for concept generation.

There are three groups of tools that can help the tasks of concept generation and solution selection. The first group of tools evaluates the generated concepts in a theoretical and philosophical way, chiefly using a concept-ranking and solution-weighting tool, as well as several tools in the 3DPVS innovation roadmap. The second group of tools evaluates the solutions in a more practical manner via computer simulation and 3DP testing.

Tools of general design support. In terms of the tools cooperating with the decision-making and concept evaluation methodology, a combination of tools—including traditional criterion-

ranking evaluation methods, hybrid concept design, FMEA and trimming—can be used in definite design scenarios. Concept-ranking and solution-weighting will first be used to judge the generated concepts of 3DPVS in a theoretical way. Establishing a set of parameters and different concepts generated for definite 3DPVS will be weighed with different scores. Higher ranked concepts tend to be more ideal than lower ones. Then hybrid concept design occurs, which is an element of the 3DPVS innovation roadmap, which also helps concept evaluation by creating hybrid concepts based on the best features of multiple generated concepts with the highest values of parameters. It clearly shows the limitations of different generated solutions and thus makes the evaluation process easier to conduct. Trimming uses tools to replace undesirable solutions with others that ensure the same functionality. Generated concepts become simplified after passing the trimming phase, which helps with further evaluation. FMEA will be used as an analysing tool when the 3DPVS solutions are not satisfactorily achieved through 3DP technologies, though they could have been validated through theoretical or computer simulation means. The failure causes will be studied and the generated solutions may be re-processed through the concept generation stage.

Tools for calculating, weighting, and validating. This set of tools can be considered the most important for concept selection and evaluation. House of quality (HoQ) will be used as a means in QFD, which will generate the importance level of different evaluating criteria based on design attributes or components. Quantitative evaluation tools will be introduced, chiefly regarding the calculation of these criteria, design requirements and so forth, so designers can compare the generated concepts in a visually clear way. A set of equations will be introduced in the HoQ, with a Pugh chart being the chief component for concept evaluation and generating the finalised solution scores. Detailed knowledge of these will be discussed in a later chapter. Successfully completing tasks in this phase can be considered the end point of this research and the start point for future 3DPVS detailed design. Moreover, considering the creativity aspect of TRIZ, as well as the nature of this PhD research as a conceptual design, evaluating the generated concept through gaining experts' opinions could be another valuable approach. Different experts from multiple scientific realms could also provide professional and inspiring judgement when it comes to component weighting and concept evaluating.

Tools for concept validation. When designs of 3DPVS pass through the philosophical evaluation tools for the generated concepts, CAD simulation and 3DP prototyping will be used as a further validating means to test generated parameters from the previous stages.

CAD simulation aims to judge the functionality of each parameter of the designed conceptual 3DPVS, and test whether the model is appropriate in terms of vibratory functions. Designed concepts of 3DPVS will be broken into a set of parameters, chiefly regarding geometrical ones, and 3D modelling will be used to validate the properties in relation to the mechanical, biological and vibratory characterisations. Solidworks will play its role in this stage.

3.5 Concluding Remarks

This chapter first introduced the EDP in general and introduced the conceptual design process tailored for 3DPVS, and the methodologies and related tools of the conceptual stage for 3DPVS. Based on analysing the predominant value of conceptual 3DPVS, as well as considering the pros and cons of the research context, the conceptual 3DPVS is the centre of focus of this design, while the real product-based 3DPVS will involve work starting from the future detailed design stage.

The methodology used in this research will focus on conceptual design, which chiefly concerns product innovation and solution generation for the conceptual 3DPVS. As illustrated, the design process is divided into three stages. The first stage involves gathering information about the specifications and requirements of the 3DPVS, as well as generating the tailored base model and ideal model. After this is the second stage of conceptual generation, where the innovative problem solving of 3DPVS and concept generation are conducted. Four aspects in terms of generating concepts are involved: the 3DPVS geometric, mechanical, biological and dynamic (vibratory) configuration and characteristics. The third stage comprises concept evaluation and selection, in which the generated concepts are evaluated and selected both theoretically—such as by using QFD tools or conducting a survey of experts—and practically, by analysing possible environments conducted by related research groups, which could fully or partly support the usefulness of the generated 3DPVS solutions.

In this chapter, future work after the conceptual design was also introduced, which might include works of computer-aided simulation or CAD testing. The design parameters could be validated to ensure the functionality of 3DPVS in terms of different real-world characteristics. Prototyping using 3DP may also be necessary when further validation of 3DPVS is required.

4 DESIGN INITIATION OF CONCEPTUAL 3DPVS

4.1 Introduction

As discussed in the previous chapter, design initiation is the preliminary task on which designers need to focus before participating in any further innovation process. In terms of scope, this includes two main aspects. First, it requires a thorough literature review regarding the cell culture scaffold, 3DP, vibration, system evolutional laws and so on. Second, it requires preparation work gathering the design requirements, analysing characterisation of 3DPVS, generating a base model from which the design process begins, and indicating the ideal model of design, which is considered the ultimate destination that the conceptual product should finally approximate. In Chapter 3, the first task of design initiation was conducted (Yuan, Xing & Hsu 2018b, 2018a); therefore, in this chapter, we aim to focus on the remaining part—the second task of design initiation.

Four basic issues will be sequentially discussed in this chapter. First, we will study several vital elements of design initiation that help prepare the general conceptual stage of 3DPVS. Second, the novel geometric, mechanical, biological and vibratory (GMBV) characterisation of 3DPVS will be analysed, considering GMBV is a unique design prospect of 3DPVS, compared with traditional scaffolds. Third, we will illustrate the base model of 3DPVS and explain the philosophy of the selecting process. Finally, we will discuss the ideality of the scaffold, establish a possible ideal model of 3DPVS and briefly indicate the potential characteristics of such an ideal model. Structure is illustrated as Figure 4.1.

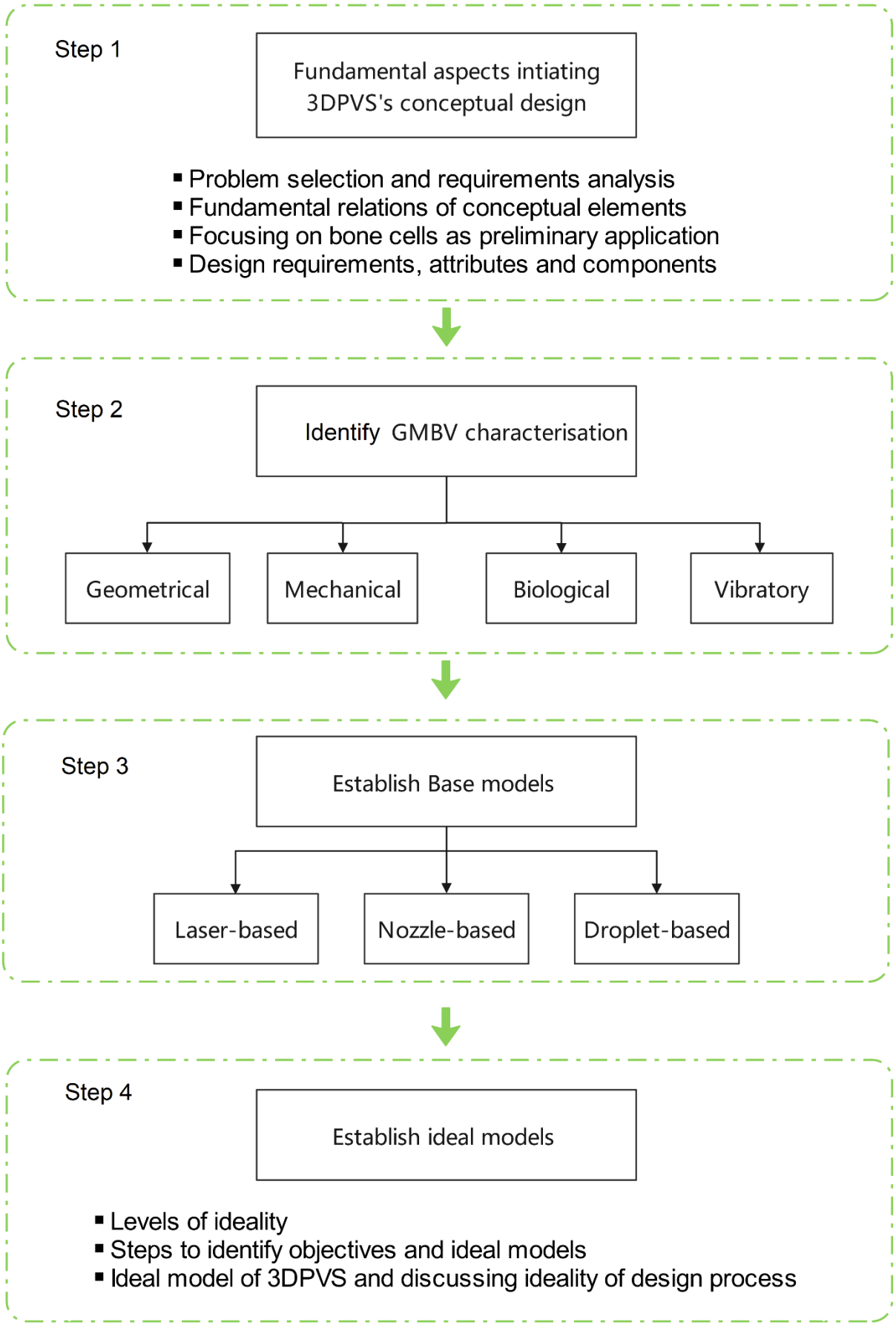


Figure 4.1 Structure illustration for the process of design initiation

4.2 Fundamental Aspects Initiating Conceptual Design of 3DPVS

In terms of the fundamental understanding of 3DPVS, four aspects are examined in this section. First, we discuss design initiation in terms of problem selecting and requirement analysing. Second, we study the fundamental elements that constitute the 3DPVS, as well as the direct or indirect relations between these elements. Third, we discuss why bone cells are preliminarily focused on as a currently proposed application of 3DPVS, along with illustrating several typical requirements of bone cell cultures. Finally, the novel three-layer-based 3DPVS system will be discussed. The corresponding demands during design for the three systems will be named the 3DPVS requirements, attributes and components.

4.2.1 *Problem Selection and Requirements Analysis*

In the literature review of Chapter 2, general information regarding the research problem selected was discussed, after studying the research limitation and gaps, with some possible future objectives presented. However, considering the nature of 3DPVS as the product to fulfil different kinds of requirements for external cell cultures, the way to select problems and determine ideal objectives could vary from one scenario to another; that is, 3DPVS will find it necessary to select different vibratory mechanisms and apply different 3DP tools to achieve functionality. Therefore, if the generic objectives generated in the literature review represent the ‘trunk’ of a tree, then the ‘branches’ would be the 3DPVS to be designed for different and specific scenarios. In this section, such knowledge of the ‘branches’ will be studied, expanding the level of general problem selection and objectives of 3DPVS into one that is detailed. Following this, the corresponding logical aspect is studying the fundamental essence that these ‘branches’ must fulfil. For instance, 3DPVS can be classified by whether it is designed for application with bone cells, other types of cells or both. 3DPVS with bone cells can be further divided into different products tailored for different requirements in bone cell culturing. This sequential categorising may help understand the whole picture of the conceptual design process. That is, the previous literature review chiefly focused on the first, conceptual design and generating solutions focusing on the second, and using the generic solutions of 3DPVS into definite case scenario of bone cells, will be the focus of the third.

Further, the general limitations of previous 3D scaffolds and vibration mechanisms can be segmented into further detailed ones to fulfil the design requirements of different 3DPVS scenarios. It is interesting to consider how to segment general limitations into specific ones for different case scenarios. This might generate new research limitations or design problems that researchers did not anticipate earlier. Design objectives can vary from one case to another, based on what is uniquely required in the cell culture scaffold, as well as the vibratory functionality. Similar to determining newly selected problems from generic problems, the design objectives will result from two elements—the case requirements that need selection of tailored cell culture scenarios, and general 3DPVS objectives, which have been thoroughly

studied via the literature review. In brief, defining such requirements and objectives will be important tasks in design initiation for conceptualising the base and ideal models, respectively.

4.2.2 *Fundamental Relations of Elements Constituting Conceptual 3DPVS*

A justified conceptual 3DPVS is composed of several essential elements. The purpose of this section is to illustrate these elements, including geometric control, material composition, biological properties, and vibratory functionality, as well as the 3DP fabricability towards the future scaffold design. This will be achieved by penetrating deeper into the general knowledge obtained in the literature review (Yuan, Xing & Hsu 2018a) to the detailed requirements gathered in the later stage of design initiation. For the relations of these elements regarding 3DPVS in different cell culture scenarios, possible pitfalls will inevitably exist for designers. Understanding these relations will consequently accelerate the work of design initiation, as well as providing clarity to establish possible base and ideal models of the conceptual 3DPVS.

As discussed earlier, the conceptual objective of the 3DPVS is to evolutionarily transform the traditional passive 3D scaffold and externally attached vibrators or vibration mechanisms into a single organic unit. In design initiation, problems can be attributed to forms tuned with several basic elements, which possess the most fundamental aspects constituting the conceptual 3DPVS. In this connection, solving possible problems resulting from undesired relations can be termed ‘internal’ problem solving. In contrast to this is ‘external’ problem solving. Issues such as undesirable costs of scaffold manufacturing or the low ability to conduct experiments on cell cultures, among others, are important, yet will not be the focus of the current design context, as ‘internal’ issues will be prioritised over ‘external’ ones. In addition, another factor is the current focus on conceptual design. Issues existing in future detailed design should not be prioritised by designers. As a result, the list of elements on which designers should concentrate at the current stage is proposed as the five aspects presented in Table 4.1.

In brief, the basic relations of elements in design initiation, as discussed above, can be considered the fundamental criteria that every possible 3DPVS must fulfil. Further enhancement and detailed specification can occur in future detailed design, which will require designers to address these relations in a more detailed, specific manner. Thus, checking whether the conceptual 3DPVS fulfils these elements in the first place is vital work for designers in the stage of design initiation, which offers insight to identify the novel GMBV characterisation of 3DPVS, as well as benefiting future concept generation and innovation following design initiation.

Table 4.1 Five perspectives focused on by current design initiation

Geometric issues	The scaffold’s geometrics must cooperate with the new vibration mechanism to be designed, and the geometric control of the scaffold should stay at a predetermined state calculable in both conditions when the vibration is switched on and off. Unpredictable issues regarding geometric change during different working states of 3DPVS could negatively alter the scaffold’s proposed

	functionality in a required cell culture scenario. As a result, geometric control of the 3DPVS and cell culture in static conditions could be similar to a traditional 3D scaffold, while this would not be the case when the 3DPVS works in an active state.
Material composition	The material composition of 3DPVS likely varies from that of traditional static or passive scaffolds. Materials of traditional scaffolds will be replaced partly or fully by active materials that help the scaffold generate desired vibrations. Analysis of material composition must be careful, as it not only ensures the scaffold has the required vibratory functions, but also maintains general functionality, such as appropriate mechanical strength and cell biocompatibility. A potential mistake made here, for instance, might be that the scaffold becomes sufficiently vibratory, while it is inapplicable in cell cultures because it is poorly biocompatible.
Biological requirements	In design initiation, biological requirements in terms of cell culture must be fully and accurately understood. Compared with geometric or material properties, which can be separate traits of the scaffold—that is, both can be designed separately without altering the properties of the other—the biological properties of a scaffold tend to be the resultant property of both geometrics and materials. A thorough analysis of the required biological properties of scaffolds in definite cell culture cases will help this issue.
Vibratory dynamicity	The vibratory dynamicity proposed must be applied to a 3D scaffold in an embedded, unseparated manner, the approach to which may differ from traditional means involving connecting an external mechanical vibration to the scaffold. As such, a new way of thinking may be necessary; thus, traditional tools for scaffold design, which chiefly focus on either geometric or material composition aspects, might not be inapplicable, as they cannot tackle the novel vibration issue or trigger the innovation that is the essence of the 3DPVS design.
3DP fabricability	The 3DPVS must be fabricable through 3DP, which fulfils the essence of 3DPVS as a future product manufactured by novel 3DP methods. As such, a single 3DP method or combination of different ones can potentially be used to fabricate the designed scaffold. Products being vibratory, yet not 3DP-fabricable, will not be considered as having an appropriate design.

4.2.3 *Exemplary Application of 3DPVS: Bone Cell Culture*

Given the fundamental elements of 3DPVS, this section selects bone cells as the preliminary application of 3DPVS in this research context, as well as abstract design requirements from general bone cell cultures. This work will help establish the 3DPVS base model and ideal model in design initiation, as well as providing a background for using the 3DPVS design methodology for specific bone cell case scenarios.

I. Focusing on bone cells as current application of 3DPVS.

In this research, the focus of application will be bone cells previously cultured by scaffolds—that is, cells of MG63, MSCs and human MSCs (hMSCs). There are two reasons for this, as discussed in the literature review. First, bone cells have been popular cells, if not the most popular, selected by traditional scaffold engineering in cell cultures. Thus, much existing knowledge and experiment data can be obtained to help designers explore novel 3DPVS in an effective way. The second reason involves the nature of the research context. It seems practical to focus on one definite group of cells in designing the new scaffold and testing the conceptual methodology. A successful approach in this field would lead to the design of 3DPVS for other less-popular cell applications. This will make the research objectives concentrated and relatively convenient to handle.

Given that the application of 3DPVS will focus on bone cells, basic knowledge of bone cells is useful to assist with the design process, and to help designers who lack a specific background in the bone-related biomedical area. There are two types of cells in vivo—osteoblasts and osteoclasts—that work actively in the bone generation process. Both cells stay busy by

creating new bone material at a slow rate. Osteoblasts are cells that build bones, while osteoclasts are cells that dissolve bones. Therefore, determining how to master the functionality of these two cells in vitro is the foundation for research on controlling and regenerating bone cells in vivo (Cox et al. 2015; Ronca et al. 2016; Wang et al. 2016). In brief, for the design of 3DPVS, both in design initiation and the future potential case study, these two types of cells can likely be used as the chief cell culture focus.

For the cell culturing environment, 3DPVS is proposed to use the similar cell culturing media as traditional bone cell cultures with 3D scaffolds. Different cells require different cell growth environments, and determining the most suitable media for each cell culture is challenging and is most likely to be determined via experiments. At the current stage, there is no solution to systematically design the media prior to experiments (Agrawal et al. 2015; Inzana et al. 2014; Taherkhani & Moztarzadeh 2016). This causes difficulty for designers, especially those who focus on scaffold innovation, because it is unclear whether a previously applied culturing medium is adequate, though the effect might be minor. Selecting the medium based on previous researchers' experience can thus be necessary. As such, for base models in the bone culturing environment, the following media will be selected, considering their high applicability in both previous cell cultures and the bone cell focus of this research. The following box provides a typical bone culture media, which will be one part supporting the base model of 3DVPS at the initiation phase:

> A-modified Eagle's medium (aMEM) (Bio-Whittaker, Belgium) containing 10 to 15% (v/v) foetal bovine serum (Gibco™, Thermo Fisher Scientific), 100 to 150 U/mL penicillin and 0.1 to 0.2 mg/mL streptomycin (HyClone, United Kingdom), in a humidified atmosphere at 30 to 40°C and 5 to 7% CO_2 (Bose, Vahabzadeh & Bandyopadhyay 2013; Ronca et al.

II. Abstracting typical cell culture requirements from bone cells.

After illustrating the elementary requirements for 3DPVS, the requirements for general bone cell culture scenarios will be considered here, which will help accelerate the conceptual design process later—namely, concept generation and concept evaluation. The requirements of general bone cases for 3DPVS can be abstracted from the literature (Khoshroo, Kimia et al. 2017; Lai et al. 2018; Mironov et al. 2017; Ronca et al. 2016). In the design initiation stage, some of the most typical requirements of 3DPVS for bone cell applications can be summarised as follows:

- focus on the cell culture aspects, such as osteoblast differentiation and bone formation
- focus on the integrins- and BMP-mediated signalling pathways
- achieve definite activation on the angiogenesis of endothelial cells, which can help in vivo bone formation
- provide tailored and specific biophysical microenvironment for bone cells
- potentially use the scaffold as a tool to regenerate damaged bone tissues

- potentially use external stimulation, such as selective heating, to generate definite stimuli on cells in some areas
- enhance the study's spatial distribution in terms of ligands' physiological aspects, including anisotropic vibration frequencies and isotropic vibration frequencies
- ensure culturing environments are flexible and dimensionally stable
- ensure scaffold materials are biocompatible compounds
- employ high-quality surface of culturing environment, leading to enhanced bone cell attachment
- ensure sufficient and adequate pore size of scaffold for bone cell migration, nutrient transport and vascularisation.

In addition to these typical requirements for bone cell culture, other requirements exist that can be better determined when faced with definite cell culture scenarios. For instance, one critical requirement for tissue scaffolds is regarding the identification and control of mechano-regulation on tissue differentiation by biophysical stimuli, since mechanical integrity is maintained once the scaffold is implanted in vivo. The benefit of bone tissue scaffolds enabling in situ load bearing is thus valuable to the orthopaedic field, as current bone void fillers are non-load bearing. For an external cell culture scaffold, which is the focus of our research, this requirement is less essential, as the scaffold will not be used for tissue implantation. This difference, as well as others discussed in other contexts, can determine the set of design attributes for different scaffold systems.

4.2.4 *Design Requirements, Attributes and 3DPVS Sub-system Components*

From the perspective of system evolution, every product can be defined as a system that belongs to a wider product system, called a super-system, and consists of a components-based product system, termed the sub-system. The 3DPVS system contains a three-level system hierarchy—the 3DPVS super-system, system and sub-system. The three required design elements constituting these three systems can be respectively termed requirements, attributes and components. These concepts will play a significant role in the full design process and are clarified as follows.

I. Categorisation of 3DPVS super-system, system and sub-system.

From TRIZ-based systematic thinking, the requirements during the entire process of design, including the design of 3DPVS, can be divided into three layers. The first is 'requirements'. The design or design initiation requirements in this research relate to the super-system and indicate the application of 3DPVS, such as the requirements for cell culture and dynamic bone cell cultivation. Second, following the super-system requirements are the requirements at system level—namely, the design requirements for 3DPVS, including geometries, material composition and biochemical properties. To avoid ambiguity with the requirements of the super-system, we term this layer of requirements as 'attributes' for 3DPVS design. After this,

the third-level requirements concentrate on the components within 3DPVS—the sub-system requirements of 3DPVS. Parameters such as scaffold height, weight and vibratory frequency are the typical elements constituting this requirement list. Thus, the requirements of this layer are defined as ‘components’ or ‘sub-system components for 3DPVS’ to distinguish them from the requirements in the previous two layers.

II. Structures of 3DPVS requirements, attributes and components.

This section discusses the three-layer structured demands of the design for the 3DPVS system. The fundamental requirements (super-system level) connect with the subordinate (system and sub-system) requirements in a definite way. From the subordinate requirements in the first order come the subordinate requirements of the second order, and so on. The construction of requirements, regarding the whole picture of requirements general or specific from the beginning of design to its very end, can be compared with the construction of a tree. From the straight trunk come boughs on all sides, which in turn divide into branches, becoming smaller and smaller, until they are finally covered with leaves. The same process occurs for the construction of the leaves, the formation of veins and serrations, and so on. Figure 4.2 presents the three-level requirements and their relationships for the three vital elements of the design initiation phase—requirements, attributes and components.

Meanwhile, the fundamental properties of 3DPVS consist of four aspects: the geometric (G-), mechanical (M-), biological (B-) and vibratory (V-) characterisation. From this, we can generate a structured list of input requirements, design attributes and 3DPVS components, which will be analysed using these four aspects in a similar way. This approach will make the entire design process efficient and easily understandable. The establishment of innovation methodology of 3DPVS, which will be studied as a future task, could also benefit from such an approach, since the different level of requirements means more design details, which can increase accuracy—especially in the stage of selecting innovation principles for conceptual generation.

As is often the case, requirements directly obtained from end-users or initiating designers may be general, unstructured or vague. The research objectives regarding the technical aspects of 3DPVS can be considered technical requirements, which the general 3DPVS at system level must fulfil. The attributes and components that respectively act as the role of ‘bough’ and ‘branch’, compared with the ‘trunk’ (which is usually informed by general end-users) are of more significance in the conceptual stage of design. In contrast, further requirements of detailed design—namely, the ‘leaves’ requirements—should be considered after successful finalisation of the conceptual design. In brief, structuring the requirements in language that can be used by designers—such as the language designers use when applying a methodology—as well as identifying the appropriate attributes and components in the design process, are of significant value and will be illustrated in future design work. To conclude, the

construction of 3DPVS requirements, attributes and components has been the focus of this section, following which we introduce the GMBV characterisation of the conceptual 3DPVS.

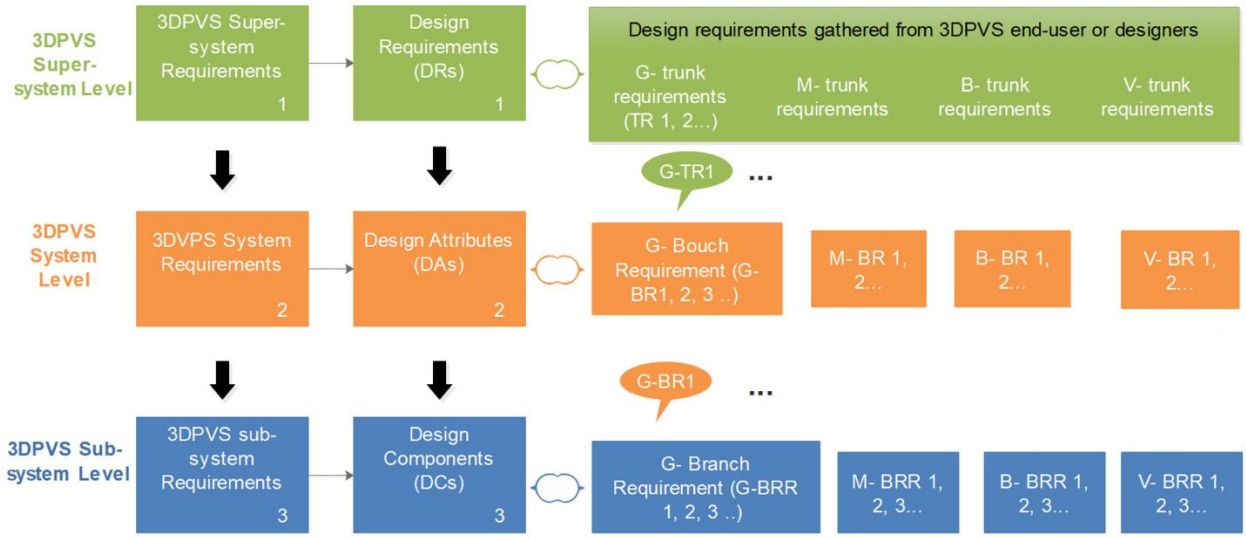


Figure 4.2 Three-level requirements of 3DPVS design: requirements, attributes and components

4.3 GMBV Characterisation of Conceptual 3DPVS

In the previous section, several elementary aspects regarding design initiation were studied, while this section provides a detailed characterisation of 3DPVS, compared with the traditional 3D passive or static scaffold. This knowledge will help understand 3DPVS more clearly and establish suitable base and ideal models for 3DPVS.

As aforementioned, when studying or designing traditional 3D static or passive scaffolds, three characterisations are usually considered: the scaffold's geometric controls, mechanical properties and biological functions. These characterisations could pass into novel future scaffolds and can apply to the study of 3DPVS, chiefly because the essence of scaffolds, static or vibratory, basically remains the same when it comes to the purpose of scaffolds in cell cultures. The only difference for 3DPVS is that vibratory functionality (or vibratory dynamicity) is the prioritised design aspect in the conceptual stage of 3DPVS, as this is the innovative point of the design. Therefore, it is worthwhile introducing a new direction for systematic design of 3DPVS. The characteristics—the elements and parameters of either generic or specific 3DPVS products that suit various requirements of different case scenarios—will be included as a new category, which can be called 'GMBV' characterisation, consisting of the four properties of novel scaffold design: the geometric, mechanical, biological and vibratory properties.

For both base and ideal models of 3DPVS—namely, the base point of scaffold and its related environmental issues to initiate the design, and the ideal end point where 3DPVS is

considered optimal—designers must consider these four characteristics. Design philosophy from base models into desired objectives in terms of these characteristics tend to be invariable from one to another. Parameters and specifications of base models, design objectives and the ideal 3DPVS will be studied and evaluated separately within the newly presented GMBV characterisation. This may make the design process more structured, clear and specific when designers analyse issues in the conceptual stage of 3DPVS.

Following the GMBV analysis, new understandings of base and ideal models can follow naturally. In terms of base modelling, requirements will be established based on the GMBV characterisation—that is, designers will select appropriate 3D static or passive scaffolds with specific G-, M- and B-properties, as well as selecting possible vibration mechanisms as the V-properties to start the design. Within each of the G-, M-, B- and D-characterisations, a relatively large group of parameters or properties can be related, yet many of these will only be considered in future detail design. Considering the priority of the current research of the conceptual development of 3DPVS, the parameters tailored for this stage will be studied and used. Key information regarding this will be discussed in the following sections.

4.3.1 *Geometric Properties (G-characterisation)*

Geometric control is considered vital in both traditional 3D static and passive scaffolds and the potential 3DPVS. CAD of scaffolds chiefly relates to the geometric aspects.

I. Geometrics selected for base model of conceptual 3DPVS.

As studied in the literature review, there have been a wide range of geometrics applied to traditional scaffolds. To tailor geometrical control for the current research aims, four basic geometrics that are most commonly used for bone scaffolds—the cubical, spherical, shifted cubical and shifted spherical porous geometrics—could be used for the 3DPVS conceptual design. These four typical geometrics will be considered the starting point for the geometrics of the base model, given their easily designable nature, which means new features can be easily added. The porosity range generally varies between 30 and 80% for culturing bone cells (Kantaros, Chatzidai & Karalekas 2016; Singh, Singh & Han 2016). Figure 4.3 illustrates the four geometrics that could be used as the base geometrics in the conceptual design of 3DPVS:

- cubical pore model
- spherical pore model
- shifted cubical pore model
- shifted spherical pore model.

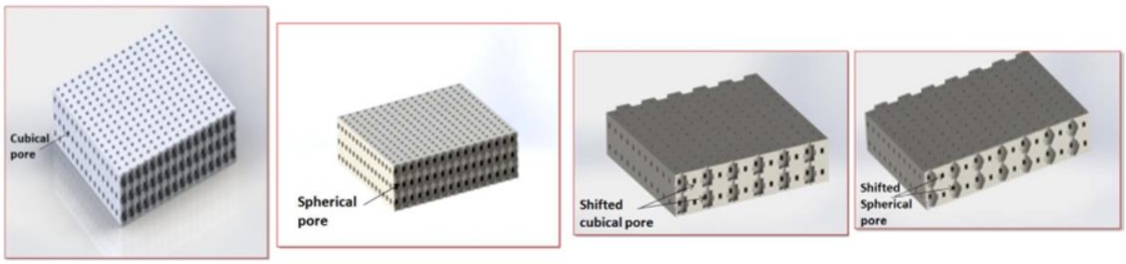


Figure 4.3 Four geometrics of porous scaffolds possibly applied as base models

II. Basic G-characteristics for 3DPVS design.

Following the discussion of the four geometrics, G-characteristics will be defined through the parameters or properties related to geometrics. The following aspects, each containing a pair with the opposite property, will likely be the most vital factors during the geometrics design of 3DPVS:

Volume (high–low), geometric complexity (high–low), porous size (big–small), porous randomness (high–low), surface roughness (high–low), geometrical stimulation (high–low), geometric precision (high–low), scaffold pore size, wall thickness/beam diameters (small–

Aside from establishing basic geometrical perspectives, each parameter or aspect could also be used to judge the idealism level of 3DPVS. Taking the surface roughness for instance, if the desired value of the roughness property must be high to be ideal, based on some design criterion, the value of 'being low' will logically be considered non-ideal, and vice versa. Thus, when studying ideal models, the G-based ideality will be calculated by the proposed properties, or part of them, as listed above. In terms of the geometric characteristics of scaffolds related with 3DP properties (An et al. 2015; Sawkins et al. 2013; Serra 2014), several aspects might be important: flexibility of structural design (high–low), fabricability for free-shaped structures, minimal feature size (large–small), structure minimal precision (high–low), fabrication time (long–short), width of printed line (high–low) and CAD compatibility (high–low).

4.3.2 *Mechanical Properties (M-characterisation)*

Mechanical control of 3DPVS is proposed to be similar to that of traditional 3D static or passive scaffolds, and material composition is the essential factor affecting different mechanical controls.

I. Materials selected for base model of conceptual 3DPVS.

To fabricate scaffolds for bone TE, polymers, ceramic and their composites have been widely used (Serra 2014). Although not every material selected for the base model here will be used in the future 3DPVS design, it is useful as a starting point at design initiation. Several of the most popular polymers could be used as materials for the base model. These materials provide suitable mechanical properties for scaffolds, and are fabricable by different 3DP systems. These materials are naturally static and passive. Comparing these materials with

the novel materials tailored for vibratory functions of 3DPVS could be important during the design process. In brief, the following materials used for traditional 3D scaffolds will be used as the starting point base model materials towards the ideal model materials of 3DPVS:

- polyglycolic acid
- polylactic acid
- PEG
- polyamide (PA)
- polycaprolactone (PCL).

II. Basic M-characteristics selected for 3DPVS design.

Basic characteristics of the mechanical properties for the base model of 3DPVS have been selected, yet are not limited to the following aspects:

Systematic controllability of properties (high–low), anisotropic level (high–low), scaffold syntheticity (high–low), material availability (high–low), mechanical stability of structures (high–low), chemical stimuli (proper–improper), cell study applicability (high–low) and surface biochemical functionality (high–low).

To evaluate the level of ideality regarding mechanical control of 3DPVS, the philosophy is the same as that discussed in the G-characteristics section. In brief, much of the contents will only be used in the future detail design after the conceptual development stage.

4.3.3 *Biological Properties (B-characterisation)*

The biological properties of 3DPVS has a chief difference compared with the G- and M-factors, as discussed previously. Biological properties are usually approached indirectly by designers—that is, biological properties tend to be the resultant by-product of many other factors of scaffolds on cell cultures. Variations of both G- and B- could result in different properties of B-characterisation. However, the quality of biological properties can also be used as criteria by evaluating the idealism or ideal functionality of the scaffold.

I. Biological properties selected for base models.

In terms of the basic B-properties of the proposed 3DPVS, they are currently considered predominantly the same as the biological properties of traditional 3D passive or static scaffolds. The most vital aspects can be summarised as follows:

- can help cell proliferation
- can help cell differentiation
- can help cells remain 3D-shaped
- can help cells make positive contact with other cells
- can help achieve required cell functions (differ from one case scenario to another).

II. Basic B-characteristics selected for 3DPVS design.

Cell culture characterisation regarding biological properties is a sophisticated issue. From a literature study (Moskvin et al. 2018; Munaz et al. 2016; O'Neill et al. 2014), possible characteristics, with pendulum-like opposite values for each property, can include, yet are not limited to, the following:

Cell survival rate (high–low), cell proliferation (high–low), cell viability (high–low), stiffness of environment (high–low), stem cell differentiation (high–low), cell morphology quality (high–low), topography of cellular environment (high–low), spatial patterning of ligands (SPL; high–low), length of ligand (high–low), SPL cell morphology (high–low), efficiency of generating ECM (high-low), presence of biomechanical cues (high–low), experimental model maturity (high–low), integration of different stimuli (physical, biochemical, etc.; high–low), growth factors (low–high), signalling and adhesion molecules (high–low), cell behaviour (high–low), dynamicity of environment (high–low), cell-to-cell interaction (high–low), cell-to-matrix interaction (high–low), cellular force generation (high–low), intracellular structure quality (high–low), cytoskeleton (high–low), cell/matrix adhesion (high–low), natural 3D recapitulation (high–low) and biomolecule immobilisation (high–low).

For the conceptual design of 3DPVS, it is not necessary to focus on every property listed. The most basic properties will be selected for the conceptual stage and other properties will most likely be considered in the future detail design stage. Thus, the way to prioritise different basic properties of scaffolds is important for designers.

4.3.4 *Vibratory Properties (V-characterisation)*

For the base model, the vibration or vibratory dynamicity mechanisms studied in the literature review will be the starting point for the conceptual design. At the design initiation stage, the traditional 3DP scaffolds placed in the dynamic bioreactor, as well as the 3D scaffold attached with external vibrator shakers, can both be selected as the base vibration model.

I. Basic vibratory dynamicity applied to base models.

Based on the study, three vibration modes can be considered the starting point for conceptual design of 3DVPS:

- mechanical vibration through external vibrators
- bioreactor-based vibration
- subtle vibrations, including ultrasonic vibration and vibration using piezoelectric devices.

II. Basic V-characteristics selected for 3DPVS design.

There are several criteria establishing 3DPVS's vibratory dynamicity. The objectives of 3DPVS in this research were discussed in Chapter 2. The integrated self-vibratory functionality of the scaffold—that is, the active capability of the scaffold to generate vibrations—is

considered one of the most vital elements of 3DPVS. As such, several important characteristics need to be summarised, with characteristics further explained for design initiation:

Vibration mechanism applicability (low–high),[1] vibration/frequency range (low–high),[2] frequency accuracy (low–high), vibration localisation level (low–high), vibration feasibility for required cell culture (low–high), vibration stimulation intensity (high–low)[3] and vibration three-dimensionality (high–low).[4]

[1] whether it can be applied on the base model of the 3D static scaffold
[2] range between the affordable frequencies between minimum and maximum values
[3] different dynamic cell cultures require different stimulation intensity

In previous sections, we illustrated the GMBV characterisation for 3DPVS, as well as issues related to establishing base models. In each of the four sets, a list of most frequently used parameters and attributes by designers has been illustrated, which could be used as criteria to judge the ideality level of 3DPVS. For each parameter, a pair of contradictory definitions or labelling values has been identified, with one indicating the parameter as ideal and the opposite as undesirable. For example, porous size is defined as ‘small–big’ and, for a design case where the porous size of the scaffold must be large, a value of ‘big’ will be considered ideal and value of ‘small’ undesirable. Following this philosophy, the level of ideality can be judged by evaluating whether the real value of the attribute is close to the left or right value in this ‘contradictory set’. An appropriate ideality level and ideal model of 3DPVS may be established. In addition, this ‘contradictory set’ approach will tailor the TRIZ-oriented design methodology to help achieve the concept generation after the design initiation phase, making the design process effective and reasonable.

To conclude, GMDV characterisation has been introduced in this section, and aims to provide designers a systematic strategy for analysing, focusing and categorising different design aspects of 3DPVS, which usually have been considered complicated for traditional scaffold designers. Based on this, scaffold innovation will follow in a relatively natural manner.

4.4 Potential Scaffold Base Models

In previous sections, several vital issues of design initiation have been studied, with bone cells as the focused application for the conceptual 3DPVS. GMBV characterisation, which copes with the design issues regarding geometric control, mechanical control, biological properties and vibratory dynamicity, was presented. This section will establish the potential base and ideal model for the conceptual 3DPVS, as a vital task of the design initiation stage.

In terms of the significance of the base model, it is the starting point from which a concept arises. In this study, the practical use of the base model will anchor the design in a practical

realm, which briefly includes two aspects. First, what is generated as the innovation concepts or conceptual solutions in the concept generation stage must be applicable, or at least reasonable, from the stand of view onto the base model analysis; otherwise, the novel concepts are simply ‘imaginary’, in other name it could be just a thought out of practical use. Second, base scaffold models should be applied, studied or investigated by previous researchers at a relatively mature level—that is, the selected initiating scaffolds should not be new, which will ensure that knowledge of their characteristics and effects on cell cultures are already known and accessible.

As such, one key job of using base models in conceptual design is to extract a set of characteristics, or parameters, from the selected scaffold models from where the conceptual innovation can begin. Thus, base scaffold models can be logically defined as a basic version of a 3D static or passive scaffold product, on top of which alterations, additions or enhancements can be designed. It can specifically refer to typical or easily accessible 3D cell culture scaffold models experimented with or used under traditional vibrations—namely, mechanical vibrations, external vibrators and so on.

The next section discusses the base models for 3DPVS conceptual design and establishes three base models corresponding with three 3DP systems. After this, several contents of GMBV characterisation, which can play a bridging role between the base and ideal models, will be studied.

4.4.1 *Selecting Base Models through 3DP Categorisation*

In design initiation, base scaffold models need to be developed. The quality of base models selected and the philosophy behind selecting them is significant, as the whole conceptual design can follow reasonably afterwards. One important question logically arises: what is the basic philosophy to select base models? As aforementioned, 3DP plays a core role for novel 3DPVS, given that 3DP is proposed as a bridging technology between traditional bone cell culture scaffolds and the novel scaffold, and the proposed 3DPVS will be fabricable by 3DP methods. Given this, the base model can be logically classified into three categories corresponding to the three classes that align with the three-group categorisation of 3DP tools. In other words, base scaffold models can be selected as 3D static or passive scaffolds that have been fabricated or approached with laser-, nozzle- or droplet-based 3DP technologies. To enhance design efficiency, in each 3DP category, a relatively popular, easily applicable 3D scaffold will be selected as the starting point to developing it into a possible ideal scaffold model.

Considering 3DP systems and other aspects for conceptual design, base models will be further selected and determined through following criteria. First, the base model must be 3DP fabricable. Scaffolds fabricated by conventional tools tend to be inappropriate. Second, the base model should have been previously applied to cell culture applications and especially

bone cell applications, since the application focus of 3DPVS at the current stage is focusing on bone cells. Novel scaffolds not used for external bone cell cultivation will not be selected. Third, base models must be potentially upgradable and modifiable—that is, their characteristics for geometric, mechanical, biological or dynamic properties should have flexibility to change according to different design requirements. In brief, characterisation of the base model scaffold should be simply and flexibly changeable. In the following sections, the three set of base models corresponding to the trinity of 3DP systems will be illustrated. These models will be used as the starting point towards achieving the ideal model of 3DPVS.

It is also noteworthy that, although base models will be categorised into three classes in accordance with the trinity of 3DP methods, the ideal scaffold model could extend beyond this classification, because that ideal model can either be fabricated by the 3DP that initiated the base model in the same category, achieved with another 3DP method, or even achieved with a hybrid 3DP system that potentially integrates different 3DP fabrication methods.

4.4.2 *Laser-based 3DP Base Model Scaffold*

A laser-based scaffold will be used as the base model. One promising laser-based 3DP is ProJet 1200, which is a recent SLA laser-based 3D printer and is currently available at the University of South Australia. Figure 4.4 shows a typical 3D laser drilling PMMA scaffold used for bone regeneration. It has foaming holes with a diameter range of around 500 μm and depth of about 12 mm, centre distance of about 0.5 to 1.5 mm, achievable porosity at 40 to 75%, and compressive strength at about 20 to 60 MPa (Mironov et al. 2017; Rahmani-Monfard, Fathi & Rabiee 2015; Warnke et al. 2010).

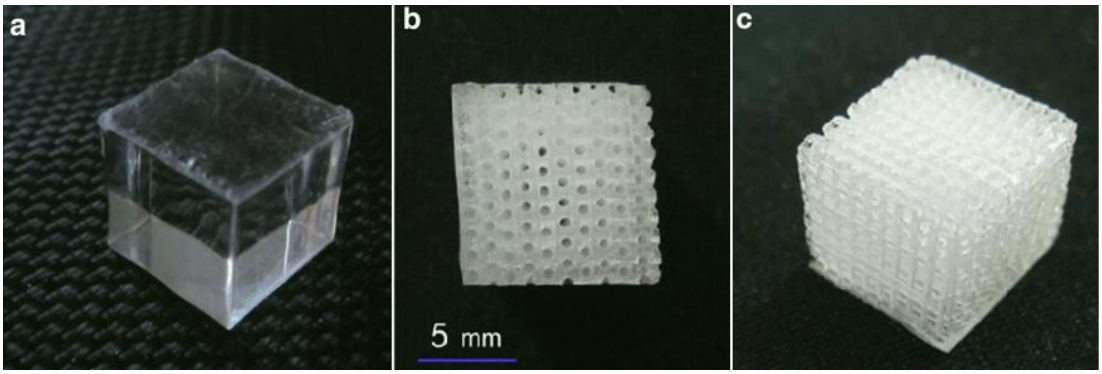


Figure 4.4 (a) Bulk cubic specimen before 3DP laser processing; (b) front view of fabricated PMMA scaffold showing regular pattern of holes; (c) isometric view of scaffold showing inward 3D network

The reason for selecting this scaffold sample as the base model is that different scaffolds with increasing levels of porosity can be fabricated using the same method, and different laser-based techniques easily produce similar products. As such, there is no need to generate fixed parameters for the overall size, porous size and inner mechanical strength of the base scaffold model in this category.

4.4.3 *Nozzle-based 3DP Base Model Scaffold*

The nozzle-based 3DP system plays a significant role for general scaffolds, and will for the novel design of 3DPVS. A typical scaffold model fabricable via nozzle-based 3DP will be selected as the base model of 3DPVS. The following Figure 4.5 shows the 3D printed PTMC scaffold UV cross-linkable graphene/poly (trimethylene carbonate), with the PTMC scaffold of 1 × 1 cm dimensions, and a pore size of 500 to 1,000 μm printed using a KIIM Bioplotter. Single to multi-layered (up to seven layers) PTMC and PTMC-CCG scaffolds can be effectively fabricated with this 3DP method. The accessible mechanical strength of this scaffold model is usually between 3 and 7.5 MPa (An et al. 2015; Sayyar et al. 2016; Serra 2014). The reason this scaffold is selected as the base scaffold model is that the compatibility of this composite scaffold and its equivalent 2D films have been thoroughly tested with human MSCs, and the evaluation effect of this scaffold on MSCs under osteogenic differentiation conditions is considered mature. As such, it may be relatively easy and convenient to develop this base scaffold into the required bone cell culture 3DPVS.

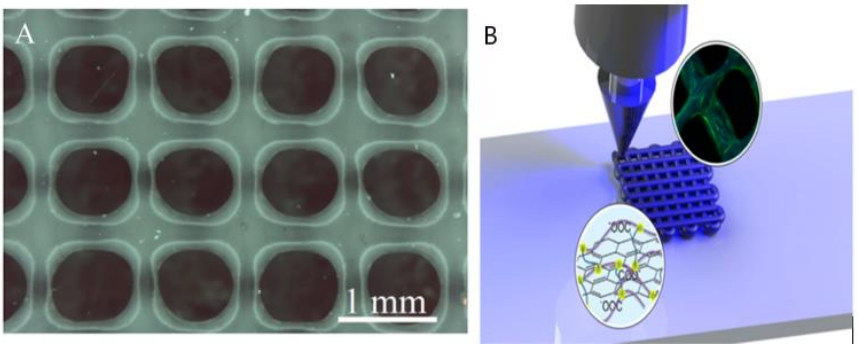


Figure 4.5 (A) PTMC scaffold with 3DP nozzle system and (B) printer nozzle when fabricating (Sayyar et al. 2016).

4.4.4 *Droplet-based 3DP Base-model Scaffold*

In the base scaffold model of this 3DP categorisation, one typical 3DP droplet-based HA scaffold may be selected. This scaffold product typically has matrix structures with an interconnected system of pores ranging in size from 0.5 to 500 mm, with HA content (wt.%) related to PVOH precursor powders between 50 to 60%, pore channels between 1,400 and 1,800 μm, and micropore size between 10 and 60 μm, with numerous topographical irregularities implying a high degree of roughness. The porosity of this scaffold implies an average of 50 to 60% volume use, and the average compressive strength stands at 0.3 to 0.8 MPa, which is relatively lower than the value for scaffolds of laser and nozzle 3DP systems (Cox et al. 2015; Do et al. 2015; Lima, Correlo & Reis 2014). In addition, bioresorbable polymeric scaffolds with specified architectonics for TE can be easily achieved from this base model. Typical materials used are solutions of polylactoglycolide in tetraglycol, with their subsequent solidifying in aqueous medium (Cox et al. 2015; Do et al. 2015). The chief reason for selecting this droplet-based scaffold as the base model is its relatively large size compared

with scaffolds in the laser or nozzle categories. This means that the required 3DPVS developed from this base model can fulfil definite cell cultures when the cultivation or experimentation of a large group of cells is necessary. An illustration of the scaffold and its construction in different stages of the 3DP process is shown in Figure 4.6.

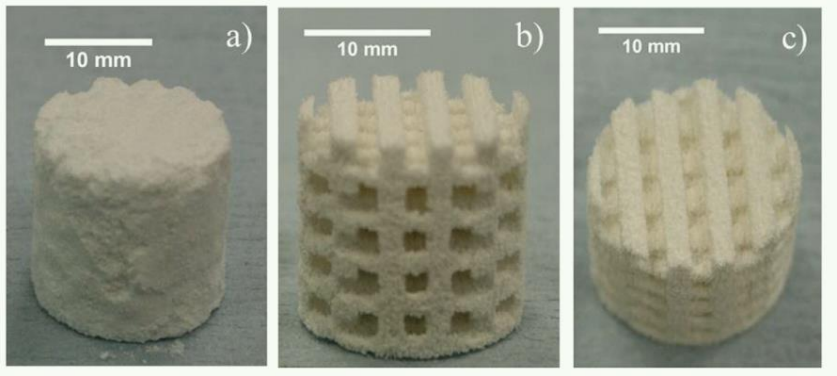


Figure 4.6 (a) Inkjet-printed scaffold as removed from build bed; (b) and (c) de-powdered scaffold

Table 4.2 below summarises the chief features of base models:

Table 4.2 Summarizing the features of the trinity base models

Base model family	Features	Limitations
3DP laser-based	high-resolution and accuracy; liquid material easily removable	Limited choice of materials; post-processing; material cost; complex and expensive equipment
3DP nozzle-based	No trapped materials, minimal material waste, inexpensive printer,	Undesirable degrading issues; lower range of material choice; medium resolution;
3DP droplet-based	Wide range of material selection, fast and economic; enable tailored printing with multi-materials	Hard to remove trapped materials; low to medium resolution; binding issues;

4.5 Ideality of Scaffold and 3DPVS Ideal Models

The ideal destination of 3DPVS, fulfilling its role in the scaffold's evolutionary ladder, is considered the ideal model. The ideal model is also an organisational improvement model that serves as a roadmap for initiating, planning and implementing improvement actions in 3DPVS's design process. For different stages of 3DPVS development—conceptual design, embodiment and detail design—the ideals and ultimately desirable goals will inevitably differ. That is, the ideal model for 3DPVS to achieve at the conceptual design stage will be distinct from the ideal model at the detailed design stage. Thus, two sets of ideal models exist. In this context, the ideal scaffold model discussed here refers to the final ideal 3DPVS product after detailed design. The research objectives discussed in the literature referred to objectives that will be approached during the conceptual design. In brief, a gap will inevitably exist between the conceptual 3DPVS as research objectives at the conceptual level and the ideal 3DPVS as the final real-world product.

4.5.1 *Levels of Ideality in GMBV Characterisation*

For general ideality issues in engineering system, LSE—especially the 'law of increasing degree of ideality'—can help provide a clear vision. The elements of time, cost, space and manufacturing all contribute to some extent to the ideality levels of designs and products. The ideality of the scaffold will be based on this knowledge. This section discusses the ideality aspects specified with 3DPVS.

GMBV characterisation, which was previously presented to understand the basic properties of 3DPVS, can be used to understand the ideality of 3DPVS and the related ideal model(s). That is, designers can establish four levels of ideality corresponding to each of the four properties of GMBV. This will be the fundamental point where ideality can be basically judged. Besides this, another proposal is that the interrelationship of each pair of different properties contributes to the ideality level as well. As such, constructing the six pair of relations—the G-M, M-B, B-V, G-V, M-V and G-B relations—could bring the ideality evaluation to a more sophisticated level. Further, putting three relations together—G-M-B, G-M-V, G-B-V and M-B-V—gives four sets of trinity relations, which can in turn determine some aspects of the ideality level of 3DPVS. As such, a total of 14 ideality relations could exist if designers seek to evaluate the ideality level of 3DPVS in this philosophy. Thus, the ideal models of 3DPVS could be defined as models that fully satisfy the ideal requirements or specifications in each of these related aspects. In other words, the ideal model of 3DPVS would require each of the G-, M-, B- and V-characterisations be ideal, and ensure the different possible relations derived from GMBV characterisation be ideal. In practical reality, this is unachievable, yet it could be sought by designers, which also represents the process of becoming ideal from non-ideal.

Detailed work of establishing and evaluating the ideality levels can only be thoroughly discussed in the future stage of concept generation and evaluation, as well as the stage of detailed design. Thus, gaining a full picture of conceptual specifications and the specifications in detailed design will be of greater necessity. In the design initiation phase, we aim to offer a brief proposal of the idealism evaluating mechanism. The ideality level for the 3DPVS system is to be determined in reverse ratio to the level of contradiction or conflict that inevitably exist in each of these relations. Knowledge regarding contradictions will be studied in the later TRIZ-based methodology chapter. The basic philosophy is that the lower the level of contradiction or conflict in the 3DPVS system—namely, the super-system, system and sub-system GMBV properties and potential relations among the properties—the higher the level of idealism expected. Calculating the sum of ideality value for each separate aspect will give a result of the overall ideality of 3DPVS as an integrated product.

Following concept generation, designers in concept evaluation will create criteria, calculate the contradiction or conflict level directly or indirectly, and analyse the adequacy of the generated solutions or concepts in definite case scenario. To establish ideal models of 3DPVS,

the GMBV characterisation will be analysed, ensuring that the ideal scaffold model is neither so complicated that designers find it difficult to set objectives nor so simplified that following the conceptual stage of the scaffold could lose its innovative value. Figure 4.7 shows the relations in GMBV characterisation that can be used as one approach to set and judge the ideality level of 3DPVS.

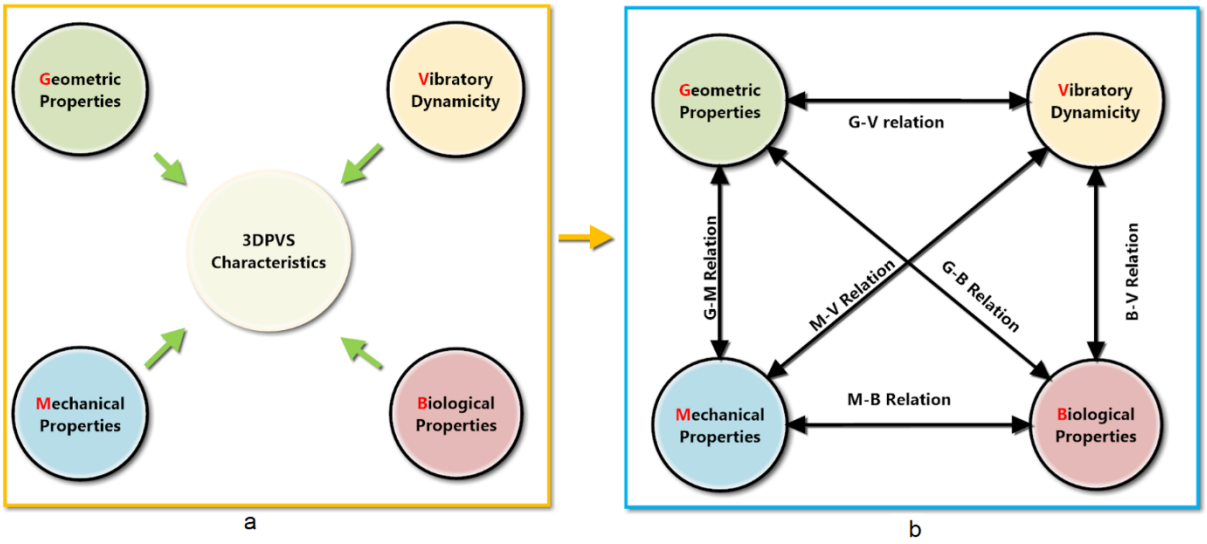


Figure 4.7 (a) Four characteristics of 3DPVS design; (b) pair of relationships for 3DPVS ideality modelling

4.5.2 *Steps to Identify Objectives and Ideal Models*

Several questions can help identify objectives and establish the ideal model of the design. These can be considered decision support, which helps designers analyse the aim to achieve and the possible hindering forces. With hindrance detected, an ideal condition can usually be determined to establish the ideal model. This strategy can help define both the objectives in conceptual design and the objectives of 3DPVS as the ultimate ideal model. A seven-step approach can be summarised, with an example in 3DPVS design for better illustration:

First, designers must identify the ultimate destination of the design. Using one chief goal of 3DPVS as an example, they must to enable the scaffold to generate the required vibrations that can help specific bone cell cultures.

Second, designers must identify the ideal solution. The identification could be that the scaffold becomes self-vibratory under definite stimuli or means. Evolution in this context means a mature change, not the modification of external traits of the traditional scaffold.

Third, designers must identify the obstructions hindering them from attaining an ideal solution; for example, the required stimuli or means that remain yet unknown to designers. Thus, designers lack the inspiration from which innovation could begin, let alone mastering further elements of the design process.

Fourth, designers must identify the elements that constitute the obstructions. For example, one chief cause could be related to material composition, since the materials applied have only been used for static cell culture conditions.

Fifth, designers must identify ways of decreasing or eliminating the effects from the obstructions, directly or indirectly. That is, one possible direction is to change the material composition of the scaffold from using traditional static materials into smart materials, which could possibly be dynamic under definite conditions.

Sixth, designers must identify the resources helpful to make this change. Resources chiefly refer to technical aspects, such as the available science in biological, biochemical and material realms. The expertise of technicians and a sufficient amount of knowledge is always necessary for a successful innovative design.

Seventh, designers must check whether existing tools or methods in other areas could be useful as support. This might include design methodology and related tools. Resources of technology alone are usually insufficient, though they may cover the scope on which the design focuses. To help designers achieve this focus, appropriate methodology is considered important and indispensable.

Following this strategic thinking, the objectives in Step 2 are determined as the summarised ideal model for conceptual design, with a focus on limitations and defects as obstructions, as discussed in Step 3 above. Based on this, ideal models of the 3DPVS, after future detailed design, can be the ultimate extension of the ideal model settled at the conceptual design stage. Understanding this, as well as combining knowledge of GMBV in terms of the multi-relation ideality, we can reasonably establish the ideal model for the 3DPVS product.

4.5.3 *Ideal Model of 3DPVS and Ideality of Design Process*

The ideal model of the 3DPVS means the ideal present-to-future 3DVS model. The ideal 3DPVS model describes the scaffold product as being fully self-vibratory under definite vibration mechanisms and able to generate the required vibration output, such as definite frequencies, via its whole structure or parts thereof. The ideal model should be fully fabricable by one or several existing 3DP systems. In addition, the ideal model should be constructed by materials that fulfil the mechanical and vibratory or dynamic properties expected for a 3D scaffold in different cell culturing cases. In this way, scaffold constructs are enabled with exact mechanical functions as desired, and the cells cultured inside could receive the exact vibrations from the scaffold with the full accuracy required. The geometrics should be flexibly large or small to suit different cell culture environments; therefore, the cell application range should be much larger than the current focus on bone cells.

There is little possibility of fully achieving this ideal model in either the present or future. However, this description gives a partial indication of the ideal future 3DPVS in terms of the

direction of its development. A practical ideal solution or ideal model in design has value as a reference for comparing and understanding where the current design status stands. In brief, the ideal model of 3DPVS could only be infinitely approached during the design process, yet remains unachievable.

I. Chief characteristics of 3DPVS ideal model

This section discusses the ideal model of the 3DPVS in terms of its technical characterisation at the current conceptual development stage. The core idea revolves around the GMBV characterisation at the conceptual level, as well as the basic cell culture requirements in the bone scenario. As aforementioned, for the required conceptual 3DPVS in definite cases, its ideality level can be basically estimated through analysing the contradictory values of each pair of parameters inside the G-, M-, B-, and V-characterisation. For example, ideality in geometric properties will include the ideal pore size, which will manifest at the conceptual level. If pore size is required to be relatively small, then 'small' will be considered ideal and 'large' will be non-ideal. Then, the extent to which it is ideal or non-ideal will be judged specifically for the given case scenario. A scoring method could be necessary when doing this.

In contrast, the ideal model of the 3DPVS in detailed design tends to have more specific, definite and accurate values for each parameter in the GMBV characterisation. In other words, the detailed specification of each parameter during detailed design could present the ideal 3DPVS model with each of the selected parameters being ideal and definite. For example, pore size for a 3DPVS could be set as a precise figure in the micrometre range. This figure could be approximated by designers in detailed design, while it is impossible to make the value of the real product absolutely the same as that of the ideal model. That is, the ideal model of the 3DPVS at its completion would indicate that the parameters or properties of all the elements identified by designers will be ideal and flawless.

At design initiation, only a general introduction of ideality can be summarised. The ideal model of the conceptual 3DPVS is proposed to contain, yet is not limited to, eight aspects. It is worth noting that the following description of the ideal model is only concept based, without detailed specifications, such as the exact pore size the scaffold must have, exact vibratory frequency the scaffold must generate, and so on. This information is only accessible at the stage of detailed design, or in a situation where a definite case scenario is accurately provided by the end-user.

In brief, the chief properties/ features endowed by 3DPVS ideal model 3DPVS are proposed as follows:

- The ideal model should be applicable to different cells that can be cultured by traditional scaffold engineering systems and provide more beneficial effects over the traditional scaffold system.

- Ideal geometrics should refer to ideal interconnected porous networks or structures that allow for tailored cell growth and movement of nutrients, metabolic waste and so forth, and the newly designed geometrics should be in tune with the vibratory functions newly applied by the 3DPVS.
- The ideal model scaffold's fabrication materials should be completely nontoxic, biocompatible and potentially dynamic, as well as having highly appropriate effects regarding mechanical and biological control in different cell culture case scenarios.
- If the ideal model is designed as biodegradable, this would refer to a definite and accurate controllable level of degradation, so that the scaffold can be replaced by bone cell mineralisation in vivo. However, this ideal property is not necessarily required when the scaffold is merely used for external cell culture or cell study purposes.
- Ideal biological control can fully encourage the required cell attachment, proliferation and other biological processes.
- The ideal model of the 3DPVS should have evolved completely from the traditional static or passive scaffold into a novel vibratory scaffold. It can also be used as an ideal 3D static scaffold when the vibratory function is switched off; that is, the ideal 3DPVS model should fully replace the ideal model of the traditional 3D scaffold.
- The ideal model requires its dynamicity to be fully capable of generating tailored vibrations; for instance, vibrations in different areas of the scaffold localised to cells cultured inside, and the range of accuracy for the vibrations, especially the vibrating frequency, should possibly reach microscopic levels (from nanometre to centimetre).
- The ideal model requires the designed 3DPVS to be fully fabricable by one or more existing 3DP systems, endowed with all its properties and characterisations from the CAD process.
- The ideal 3DPVS model has strict requirements for the relations between elements of GMBV characterisation; that is, zero or minimum contradiction should occur between each pair, and the element in each pair should function in an ideal way without hindering the other.
- The ideal 3DPVS could also be used as its own bioreactor. The possibility to switch on/off the dynamic functionality of the scaffold could be used at the same time for delivering biomolecules, as well as stimulating cell adhesion, proliferation and differentiation.

Regarding the most vital target values of properties, several indications should be summarised before conceptual design, which could include: open porosity (50 to 90%); pore body diameter (dozens to hundreds of μm level); pore throat size (usually below 100 μm); surface roughness (dozens to hundreds of nm level); osteoblast proliferation rate (15 to 25 h; doubling time); mass transfer of nutrients (cellular/substrate parameters); compressive strength (0.1 to 100 MPa level); stiffness (Young's modulus; 2 to 10 MPa); and vibration (from micro- to macro-

levels). However, these figures are indication, instead of definite answers, as to what they should be for the future 3DPVS.

In this section, the ideal model of the 3DPVS has been described, with its definition being the future scaffold concept/product fulfilling all criteria mentioned above. However, if the final goal for scientists is achieving the ideal model of 3DPVS, then one condition that must be fulfilled is that the design process for achieving the 3DPVS must also be ideal. That is, if a design process contains defects or problems, the designed product may never be ideal. With an inadequate design methodology or roadmap, the final product will have limitations compared with the ideal goal. Therefore, knowledge regarding the ideality of the design process, such as methodology or design tools that could be used for 3DPVSs, is valuable, though it is sometimes even harder for designers to invent a better-quality process than inventing a novel product.

II. Ideal design process to help achieve ideal scaffold model

After illustrating the ideal model with its possible quality, characterisation and conditioning that the ideal 3DPVS may need to fulfil, this section discusses several key aspects of the ideality of the design process to help designers achieve the ideal model from the base model. The traditional methodology for designing a 3D scaffold chiefly includes CAD. The process contains little about innovation or invention, as it aims to modify and change some existing parameters of 3D scaffolds. However, this is considered non-ideal when it comes to the design of novel scaffolds, such as 3DPVS. Therefore, a new methodology that aims for innovation is necessary, and will be of value if traditional CAD methods used for traditional 3D scaffold design can be embedded within.

After design initiation, concept generation and concept evaluation come into play. We must establish a suitable methodology to help generate and evaluate the concepts of the 3DPVS. Thus, the ideal model of the methodology requires the ideal process of generating and evaluating the novel concepts. In other words, an ideal design process, as well as methodology, would highly accelerate the design innovation and help 3DPVS become more ideal from where it starts. This is very likely a gradual process.

In brief, an ideal design process including methodology can contain, yet is not limited to, the following aspects. First, the ideal methodology will fully cover all stages for the conceptual design of 3DPVS—design initiation, concept generation and concept evaluation. The conceptual solution of the 3DPVS after concept evaluation will be ideal—that is, fully adequate, mature and suitable for the subsequent detailed design. Second, designers can use this methodology to fully fulfil different possible requirements, and solve possible challenges, in terms of the conceptual design process, which means there is no need for designers to resort to strategies in other design processes or systems. Third, the existing conceptual design strategies using CAD must be fully and adequately integrated into the new design process,

which enables the new design process to proceed in two directions: improve the parametric or functional properties of the traditional scaffold (such as the geometric, mechanical and biological controls) and create and trigger innovations and novel functionality following the LSW to help the scaffold reach a higher ideal level in its evolutional ladder.

4.6 Concluding Remarks

This chapter has introduced basic knowledge of the cell culture biomimetic scaffold, explaining its evolution and the position of the 3DPVS. The three-stage conceptual design process was introduced afterwards, and we presented the scope of this chapter's work as focusing and studying on the design initiation, which is of significant value at the current conceptual stage of 3DPVS.

As the essence of this work, four aspects constituting the full stage of design initiation have been studied. First, the authors studied the fundamental aspects initiating the conceptual design of the 3DPVS, which include problem selection and requirement analysis, the fundamental relations of elements building the conceptual 3DPVS, focusing on bone cells as the application context and abstracting related cell culture requirements, as well as indicating the three-level system of the 3DPVS and corresponding three-layer requirements for its design. Second, we introduced the GMBV characterisation of the conceptual 3DPVS, which aims to help analyse aspects of the 3DPVS in terms of its potential requirements, attributes and components at different system levels. Vibratory properties are consequently considered the most unique feature of 3DPVS compared with traditional scaffolds that remain passive or static. Third, we attempted to establish a potential scaffold base model of the conceptual design. Three base models of the 3DPVS were selected, corresponding with the three different 3DP systems—the laser-, nozzle- and droplet-based 3DP. Each base model has its unique benefits, which requires designers to analyse the specific case scenario before applying one or more base models as the starting point of design innovation. Fourth, this chapter discussed the ideality of the scaffold and established potential ideal models of 3DPVS. The ideology of the ideal model corresponds to knowledge of the base model. GMBV characterisation was used to indicate the levels of ideality of the 3DPVS, and the way to identify the objectives or ideal goals in scaffold design was summarised in a seven-step process. Such knowledge provides a clearer picture of the constitution of the ideal model, which could lead to better concept generation and innovation stages following design initiation. As such, this chapter analysed the ideal model of the conceptual 3DPVS regarding what properties it should have and what functionality it should ideally provide. In addition, the ideal design process through which the ideal model could possibly be achieved was discussed in brief.

In terms of future work, several directions could be indicated. Following this design initiation study, future research is expected to have a solid foundation, from which work on the 3DPVS concept generation and concept evaluation could begin. As aforementioned, concept

generation is the most innovative part of the whole conceptual design process, which demands lot of energy, inspiration and expertise from designers. Future researchers from different scientific or engineering realms, including bioengineering, vibration, 3DP manufacturing, mechanical engineering and so on, are welcome to participate in the innovation work of 3DPVS. Further study beyond the current work of design initiation may be necessary in the future if new requirements, constraints or possibilities at this stage of 3DPVS development can be presented.

5 CONCEPT GENERATION: BASIC SOLUTIONS FOR 3DPVS

5.1 Introduction

This chapter seeks to design and solve 3DPVS problems using TRIZ (algorithm of inventive problem solving) in the new bio-dimension. We aim to use TRIZ to conduct a multi-layer problem-solving process to address design concerns of 3DPVS, especially at the super-system to system level. For cell culture scaffold innovation, 3DPVS was indicated as a future novel product, and it currently stands at the conceptual development stage. One essential part of 3DPVS design is innovation, and TRIZ was studied as a promising method for generating novel conceptual solutions. As such, TRIZ is used to address basic constraints and contradictions in the trinity of 3DP, 3D scaffold and bio-based vibratory functionality. In this chapter, five basic conceptual solutions for potential 3DPVS—magnetic-, electric-, mechanical-, light- and thermal-based—are generated. A brief evaluation is also conducted, where magnetic-based 3DPVS shows highest applicability in the potential 3DPVS. Compared with traditional experimental-oriented processes for bio-design, the approach of using TRIZ can be inspiring and reinvigorating, which prepares the ground for future 3DPVS design to address detailed sub-system concerns. This study seeks to fill a gap in scaffold design and TRIZ literature and provide a comprehensive perspective of a timely topic.

5.1.1 *Logic Structure*

In this chapter, a four-layer process for analyzing and problem solving is used. The complexity of this design topic means the document could be difficult to be understandable for all audiences, especially those who are not in background of engineering design and scaffold development; however, a summarized illustration is made as follows, Figure 5.1, to enhance the clarity and expression of the design process and philosophy.

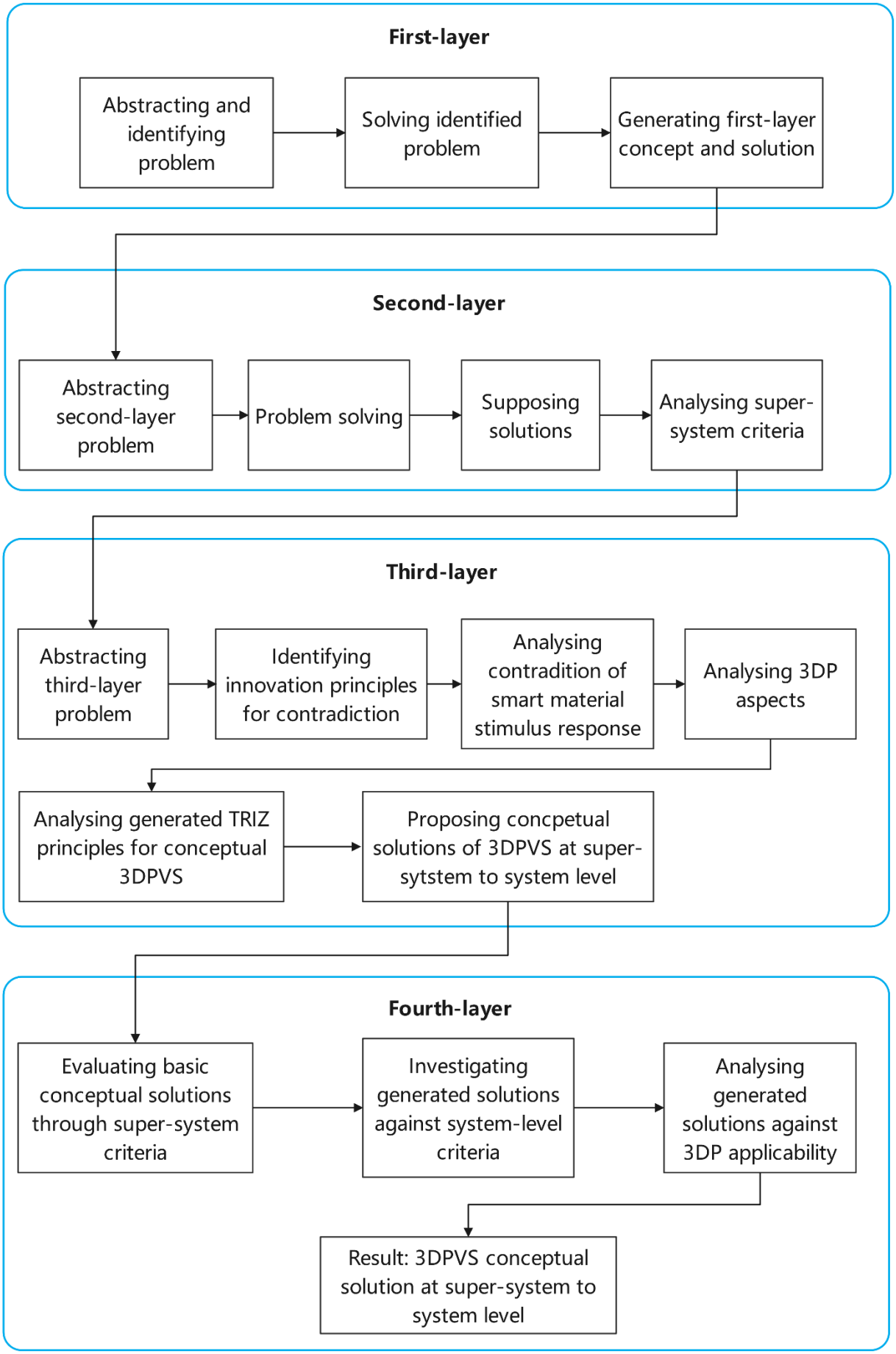


Figure 5.1 Structure of concept generation for basic 3DPVS solutions: four-layer process of analysing and problem-solving

5.1.2 *Background of Using TRIZ*

Prior to detailed design, which is currently unachievable, concept justification of 3DPVS is completed with a basic proposal of conceptual design using three stages: design initiation, concept generation and concept evaluation (Yuan, Xing & Hsu 2018b). Concept generation is identified as the key stage for 3DPVS development, as it focuses on innovation. Given this nature, traditional 'trial-and-error' experimental methods for bio-design seem inadequate, at least at this conceptual design stage. Thus, TRIZ—a Russian acronym for the 'theory of inventive problem solving'—has been identified as a possible innovation method for generating applicable 3DPVS concepts. A three-layer design hierarchy is used by TRIZ philosophy, including a super-system, system and sub-system AltshullerAltshuller, G. S. (2007); (Bukhman 2012). The super-system to system level design aims to identify the basic elements of 3DPVS at its most fundamental and background level, such as what the new vibration mechanism will be, how this mechanism possibly works, and the cons and pros of this mechanism over others being presented during the same design process. Following a successful process of which, system to sub-system level design, dealing with the detailed identification of 3DPVS parameter in terms of its geometrics, mechanical characterisation, biological controls and vibratory properties. Design generally follows a theoretical abstract into detailed concrete flow. In this study, TRIZ will be used to bring out 3DPVS concepts at super-system level, with its typical contradiction-solving philosophy following a multiple-layer problem solving process.

5.1.3 *Multi-route TRIZ design approach*

This study uses a structured problem-solving process containing four layers. The first three layers aim to identify problems and contradictions, and use TRIZ to analyse and address them, as well as generate 3DPVS conceptual solutions at the most fundamental level. The fourth layer is used to evaluate the generated solutions via investigating their relevance, practicality or value in the super-system, system and 3DP fabricating constraints.

Within this four-route methodology, the first three routes are concerned with relatively clear-cut design scenarios, where contradictions can be easily identified, while the fourth route—the newly established tool assisting the conceptual design of 3DPVS—is termed the 3DPVS innovation roadmap and aims for the whole-picture design of 3DPVS in specific cell culture case scenarios. In terms of the further corresponding role of the 3DPVS innovation roadmap in the four-route methodology, several important working places—chiefly including A4, B3, C3 and C4—must receive special attention. Briefly speaking, the input of this four-route methodological process will be the selected problems from the design initiation stage, and these problems can be considered the output of these places. Regarding the final outputs of this four-route process, the alternative solutions for contradiction solving could be the BIR,

MIR or SIR, based on where this process is to be applied. Relevant information could refer to ARIZ-based section.

Chapter 5 will use route 1, 2, 3 and Chapter 6 will use route 4. Detailed knowledge about TRIZ and support information, please see Appendix G. Figure 5.2 illustrates the four-route based approach.

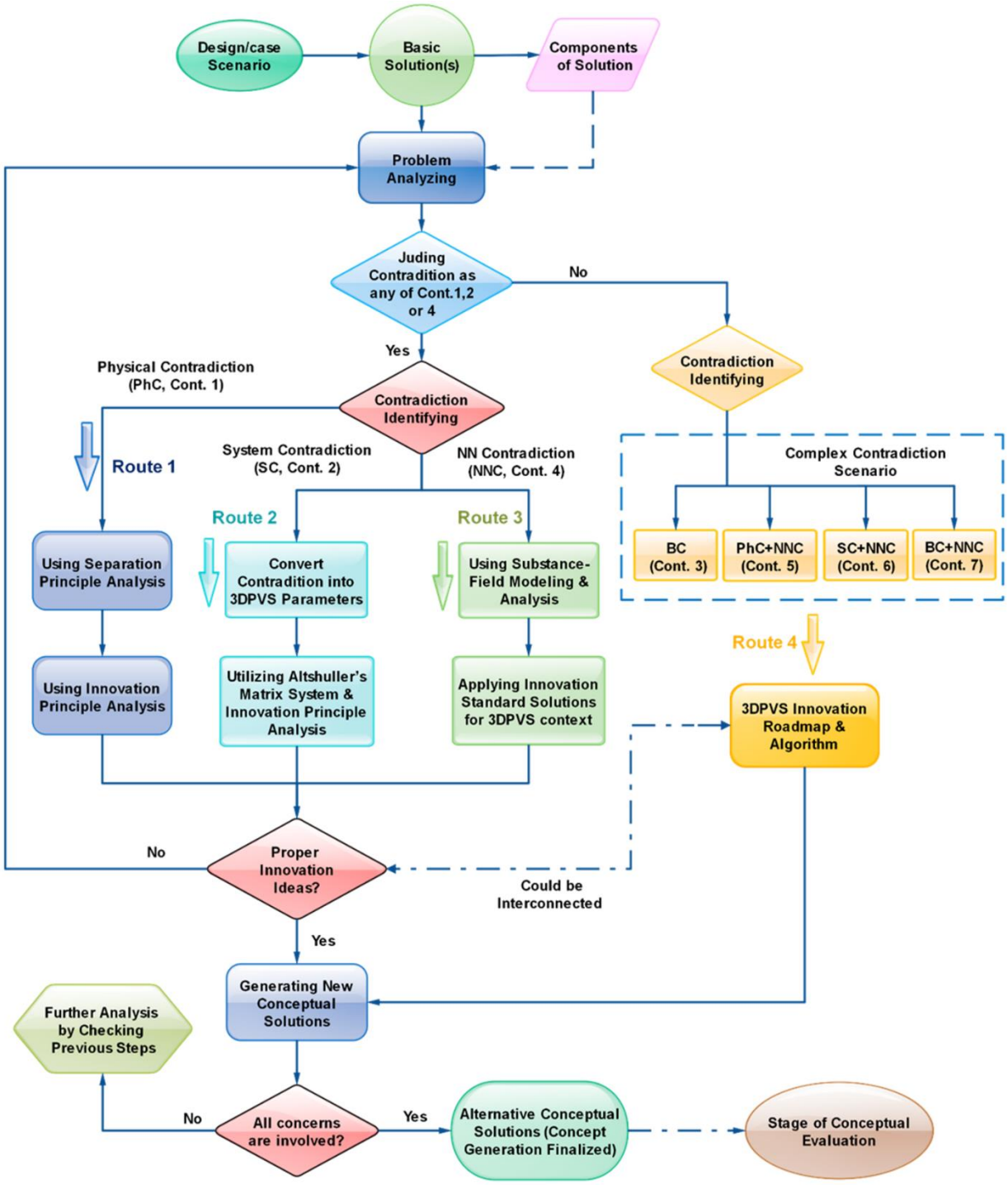


Figure 5.2 Four-route TRIZ-based design approach established for 3DPVS concept generation

5.2 First-layer Analysing and Problem Solving

The first step of concept innovation using TRIZ, as proposed in the TRIZ methodology, is to determine the basic solution (also called current, traditional reference solution) to achieve the potential 'vibrating scaffold' purpose. A scenario of the basic solution was studied in the literature review regarding how vibration was applied and how traditional uses of vibratory cell culture were approached. Studies of design initiation also discussed the components of the basic solution for 3D cell cultures using a vibration mechanism (Yuan, Xing & Hsu 2018a). Summarising which, components of basic solution(s) will be transformed into a tailored format as input for TRIZ process.

5.2.1 *Abstracting and Identifying First-layer Problem*

The aim of the first layer is to identify the most obvious design contradictions and conflicts.

I. Abstracting first-layer problems in basic solution.

After analysing the basic model (a static scaffold connected with a mechanical vibrator), five fundamental problems can be identified, which can be used as input for conceptual design:

1. While designers find that scaffolds being dynamic or vibratory is more valuable for a 3D dynamic culture process, traditional 3D scaffolds remain static or passive, and must be improved.
2. Traditional 3D scaffolds applied together with vibration mechanisms have negative effects on cell culturing, which must be improved.
3. The traditional vibration mechanism cannot generate tailored vibration in different areas of the scaffold, while it is useful to create localised stimulation from different parts of the scaffold on cells.
4. The traditional mechanism of vibration—chiefly 'coarse' mechanical vibrators—cannot generate 'finer' vibrating stimulation, such as sufficient accuracy, which is required for precise dynamic control in cell culturing.
5. 3DP technologies have been previously applied for culturing static scaffolds, while the application of 3DP for dynamic or potential vibratory scaffolds, as what and how, remains unexplored.

II. Identifying first-layer problems using route-based mechanism.

After identifying the problems, the contradictions can be identified through the analysing method, as proposed for 3DPVS design. Table 5.1 presents the analysis result, discussed below:

- The first problem is system contradiction, meaning that the current stage of 3D scaffold being static or passive contradicts some of the requirements of the 3D dynamic culture process, where the scaffold needs to be dynamic or vibratory.

- The second problem belongs to contradiction type 3, whereby the negative or harmful effects of the currently applied scaffold plus vibration mechanism must be addressed.
- The third problem relates to physical contradiction—that is, different parts of a scaffold that are being vibrated or potentially creating vibration must function separately in a tailored way.
- The fourth problem is based on physical contradiction, meaning that the frequency from vibration mechanisms cannot be precise, yet a precise frequency is necessary.
- The fifth problem is a hybrid contradiction, containing both physical and system contradictions.

Table 5.1 Route and contradiction corresponding with the identified problems

	Contradiction type[1]	Contradiction name[1]	Route[2]	Solving approach[3]
Problem 1	Cont. 2	SC	Route 2	ACM, IPA,
Problem 2	Cont. 3	NNC	Route 3	ISS, SFMA
Problem 3	Cont. 1	PhC	Route 1	SPA
Problem 4	Cont. 1	PhC	Route 1	SPA
Problem 5	Cont. 4	BC	Route 1, 2	ACM, IPA, SPA

[1] Cont. = contradiction; SC = system contradiction; PhC = physical contradiction; NNC = contradiction neither physical nor system; BC = contradiction both system and physical.

[2] Multi-route-based TRIZ containing Routes 1, 2 and 3, respectively, deals with PhC, SC and contradiction not easily identified.

[3] ACM = Altshuller contradiction matrix; ISS = innovation standard solutions; SPA = separation principle analysis; IPA = innovation principle analysis; SFMA = substance-field modelling analysis.

5.2.2 *Solving Identified First-layer Problems*

Identified problems could potentially be solved using an appropriate TRIZ route.

I. Solving Problem 1 via Altshuller contradiction matrix (ACM) and innovation principle analysis (IPA) in Route 2.

This contradiction means that the 3D scaffold must be static or passive to maintain its original useful functions on cell cultures, as well as being dynamic or vibratory. Current structures or microstructures of scaffolds cannot operate dynamic functions. Two related parameters are selected as input: ‘structure’ and ‘dynamic function’. This is single parameter–based contradiction; therefore, the traditional 1 × 1 matrix is used. Several solutions can be found, and the one indicating ‘materiality’ will be potentially selected. In this manner, the solution to solve Problem 1 may lie in how and what materials will be applied for the microstructure of 3D scaffold. Changing into dynamic or smart materials can be proposed as a logical solution.

II. Solving Problem 2 via innovation standard solutions (ISS) and substance-field modelling analysis (SFMA) in Route 3.

To address negative or harmful effects from the currently applied scaffold-vibration mechanism, SFMA will be conducted together with ISS. The basic SMA model is to mitigate the negative effects of one part of a system, while maintaining the original positive ones of another part. The original vibration on scaffold is undesirable; S1 is the vibrator, F1 is the

mechanical force to transmit the vibration and S2 is the scaffold to be vibrated. The existing vibration tends to be rough and imprecise, which is undesirable, as we want precise and subtle vibrations. Thus, a subtle vibration mechanism is proposed, which will not negatively affect cells in S2, yet have positivity as F2 compared with F1. Thus, the mechanical vibration—or the scaffold being vibrating in mechanical ways that are usually too rigid or intensive—can be replaced with other vibration mechanisms that tend to be subtler, finer or gentler in terms of vibrating effect. Therefore, the solution indicates using a subtler vibration mechanism, such as light, sound, electronic force or magnetic force, to replace mechanical vibrations.

III. Solving Problems 3 and 4 via separation principle analysis (SPA) in Route 1.

For Problem 3, the essence is a physical contradiction regarding space consumption or occupation. Using the 'separation in space' principle in SPA, a potential solution is generated that can be structured as follows: different parts of the scaffold need different characterisations, so they can respond to the same external vibration in separate ways. Problem 4's essence is frequency accuracy, which needs to be more precise. Based on the principle of 'separation upon conditions', a possible solution is generated: the scaffold can work at different vibration environments, such as changing from a mechanical vibrator to a bioreactor-based mechanism.

IV. Solving Problem 5 via ACM, IPA and SPA in Routes 1 and 2.

In terms of the system contradiction aspects of the question, it is between the requirement of dynamic scaffold and 3DP manufacturing capability. Parameters are related to the adaptability of 3DP on scaffold and usefulness of manufacturing. This is a 1 vs 1 contradiction, where we use the AP as 'ease of manufacture' (parameter 36) and DP as 'adaptability or versatility' (parameter 32). From three principles, 2, 13 and 15—the separation/extraction, action reversed/other way around, and dynamisation/dynamic parts—we choose Principle 2. IPA analysis and corresponding 3DPVS strategies indicate that dynamic scaffolds can be divided into different parts that can be fabricable by 3DP means, single or hybrid.

For the physical part of Problem 5, 3DP has not been used popularly for fabricating bio-based 3D dynamic or vibratory scaffolds via a formal and maturely established approach. However, for dynamic microstructures of objects in other realms, such as tissue or construction, 3DP was used and proven to be applicable for both static and dynamic objects. Thus, using the principle of 'separation from system and sub-system', the original problem is converted into how to use 3DP available materials and structures to fabricate dynamic or vibratory scaffold. Thus, one possible solution logically indicates using 3DP fabricable materials and structures that can operate dynamic functions in the design of 3DVS.

5.2.3 *Generating Potential Concept and Solution*

Based on inspiration and novel ideas created in the last step, a concept can be generated that contains a hybrid of characters corresponding to the problems in layer one. Five characters can be integrated and trimmed into a trinity-component concept:

Character 1: Change materials of 3D scaffold microstructure from traditionally static materials into dynamic, smart ones.

Character 2: Use subtler vibration mechanisms, such as the vibrations created from light, sound, electronic force or magnetic force, to replace mechanical vibrations.

Character 3: Ensure different parts of the scaffold have different characterisations, so they can respond to the same external vibration in separate ways.

Character 4: Ensure the scaffold works at different environments where the vibration is conducted, such as changing from means such as a mechanical vibrator to a bioreactor-based mechanism. The whole scaffold is in contact with the vibration source, not only the bottom.

Character 5: Fabricate 3DVS by 3DP means through designing both materials and geometrics in formats that are achievable by 3DP.

Description of first-layer solution: The potential 3DPVS is a novel scaffold endowed with a trinity of characteristics. First, 3DPVS could have 3D geometrics similar to traditional cell culture scaffolds, while fully supporting subtler vibrations generated from within or without, as well as enabling traditional macro-level vibrations that tend to be coarser. Second, the scaffold's vibratory or dynamic functionality is predominantly achieved through designing material composition. Third, fabrication for 3DPVS could be largely the same as for novel 3D static scaffolds. Specialised vibratory structures or material composition can possibly be segmented from the original scaffold structure and fabricated by 3DP separately, where a single or hybrid 3DP might be applicable.

5.3 Second-layer Analysing and Problem Solving

Based on the trinity-component concept generated for first-layer problems, new problems—termed second-layer problems—distinct from the previous problems naturally arise, which will be addressed via TRIZ.

5.3.1 *Abstracting Second-layer Problem*

The generated concept in first-layer problem solving derives a trinity of concepts that must be further addressed. Using TRIZ language, the first is a '3D traditional scaffold with non-mechanical vibration', the second is 'vibratory biocompatible material', and the third is '3DP fabricable vibratory material', as briefly described below.

3DPVS is the 3D micro-geometrical supporting subtle-form vibration. This characteristic means that the traditionally external mechanism vibrations are transformed into non-mechanism ones, while the structures of the scaffold remain the same because there is no restraint on this.

3DPVS is the 3D vibratory/dynamic through biocompatible and smart materials. This means that the newly applied material on the 3D scaffold must fabricate 3D constructs, being both vibratory in motional control and biocompatible in terms of cell culture use.

3DPVS is the 3DP fabricable, similar to traditional scaffold in geometric and material structuring. This means that the scaffold's constructing material must be fabricable through 3DP technologies, the design requirements of the scaffold must be within the feasibility scope of 3DP, and the 3DP fabricated microstructure can be vibratory or dynamic in some conditions.

Regarding the 3DPVS concept with these characteristics, several contradictions are logically identified, with the chief ones listed as follows:

1. Traditional types of geometrics in scaffold base models were rarely tested in dynamic cell culture studies. However, designers could access knowledge regarding which geometric characterisation plays a more positive role in other engineering contexts. The bridging issue becomes a concern.
2. Some materials that are biocompatible cannot be dynamic, while some dynamic ones cannot be applicable for cell scaffold purposes. If materials are a mixture of both, this may hinder the functionality of either. Thus, how to make best of both worlds remains a vital concern.
3. Regarding the unique benefits of different 3DP systems, the potential of the scaffold may be limited if merely one system is applied as a fabricating tool. Yet traditional cell culture scaffolds chiefly used one fabrication method. Using multiple-3DP for fabricating 3DPVS, how and what, becomes a concern.

5.3.2 *Problem Solving for Second-layer Ideas and Concepts*

Connected with the previous section, three contradictions identified will be analysed, with structured elements shown in Table 5.2.

Table 5.2 Structured analysis for three contradictions identified in second layer

Problem no.	Contradiction type	Contradiction name	Route	Solving approach	Notes
Problem 1	Cont. 5	PhC + BC	Routes 1, 3	ACM, IPA, SFMA	Also solvable in Route 4
Problem 2	Cont. 2	SC	Route 2	ACM, IPA	ISS assisted
Problem 3	Cont. 2	SC	Route 2	ACM, IPA	3DP expertise required

SC = system contradiction; PhC = physical contradiction.

I. Contradiction solving for Problem 1.

We first use the principle of 'separation on space' to give possible direction that different parts of the scaffold can have different geometric structures—that is, a hybrid structural microstructure in the scaffold might be positive to cooperate with some tailored dynamic functionality, while this seems not the design priority at this stage due to higher contradiction revolving materials. Using the established new SFM (NSFM) model, given that 3D geometrics remain a passive force (P) only, the active force of non-mechanical vibration would act as an active force (A). Then the material composition of the scaffold will be chosen as a neutralising force (N) to cooperate the geometrics and vibration. This concept will depend on the vibration mechanism only, and 3D geometrics can be generally those from either of the three 3DP-based models. When it passes to the relationship of vibration and material, it comes to the following stage. Assisted with SEA analysis regarding 'structure' and 'vibration', the following four models, with different unit cell configurations designed for porous structured bone scaffold, can positively be selected with vibrations as follows:

a. cubical pore model with part- or full-structural vibration mechanisms
b. spherical pore model with part- or full-structural vibration mechanisms
c. shifted cubical pore model with part- or full-structural vibration mechanisms
d. shifted spherical pore model with part- or full-structural vibration mechanisms.

Further analysing this scenario, suppose that the geometric structure is not sufficiently stable, then this negatively affects the scaffold's dynamicity. Thus, the material dynamicity and structural stability could contradict each other, which needs further addressing.

II. Contradiction solving for Problem 2.

Addressing this question possibly opens an avenue bridging the traditional static scaffold with novel vibratory ones. According to previous analysis, the 'material' is the basic element transmitting vibrations among geometric structures. Works here will be partly addressed via SEA to first identify suitable materials that are both dynamic and biocompatible, and second determine dynamic yet non-biocompatible materials that could be arranged in some way in biocompatible materials, so cells only interact with biocompatible ones, while general structural vibration is still achievable by the dynamic non-biocompatible ones. Further illustration of this will be in relation to 'material composition'. In brief, solutions for Question 2 must basically fulfil five requirements:

- the requirements of specific smart material(s) to provide the vibratory functions of the scaffold
- the requirement(s) of other dynamic or bioactive material(s) providing similar functions to trigger macro- or micro-vibrations on the scaffold
- the material composition using new materials should fulfil the traditional requirements of the mechanical properties of 3D scaffolds

- the 3DP requirements for dynamically designated geometrics and material composition must be compatible
- the availability of referential studies or scientific resources must be determined—that is, if limited literature supports a definite mechanism, then perhaps exploration from this direction at the current stage would be extremely arduous.

III. Contradiction solving for Problem 3.

The nature of Problem 3 belongs to system contradiction. Using SEA to investigate the general vibration mechanism, as well as studying the relationship between vibration and cells, we propose that, to address this contradiction, the generated vibration from the newly designed mechanism in the first place must fulfil a list of fabricating requirements—namely, the super-system requirements centred on 3DP. Integration of concepts after analysing these will contribute a potential evaluated solution.

5.3.3 *Supposing Solution for Second-layer Problems*

Based on previous contradiction solving, several supposed concepts for the vibration mechanism of 3DPVS could be generated, which may include multiple aspects. Analysing the connected scaffold system, these aspects help formulate contradictions acting as input for problem solving at the next level:

- the scaffold itself as the mechanical shaker system
- a bioreactor system with enhanced control precision plus liquid-active materials
- a scaffold with materials that can react with cells to generate vibratory or dynamic functions
- field-based or non-traditional solutions, such as using a system of electric or magnetic sources plus the electro- or magnetic-active materials, using a piezoelectric vibration system, or using an electromagnetic forces motivation system.

When it comes to this phase, the basic ideas of using vibrations on definite materials have been proposed, yet further analysis is required of their interconnections. The concept here can be called an ‘add-on’ to update the solutions generated in the first-layer problem realm.

5.3.4 *Analysing Super-system Criteria in Second Layer*

When introducing a new vibrating mechanism, new problems will inevitably appear that must be addressed. At the current stage, from design initiation, as well as literature studies (Bettinger, Borenstein & Tao 2012; Díaz Lantada & Díaz Lantada 2016; Herrera-Posada et al. 2016; Tong et al. 2014; Tsimbouri et al. 2017; Tunesi et al. 2016), we generate a list of vital vibration constraints from the super-system level, as shown in Table 5.3.

Table 5.3 List of 3DPVS super-system vibration constraints

No.	Vibration criteria and constrains	Chief contradiction	Design importance[1]	Contradiction level rating[2]
1.	High predictability of vibration mechanism	Predictability–usefulness	1.8	2.0
2.	Better simulation of conditions in living organism	Simulation–living being	1.6	1.7
3.	Positive issues caused by effect of vibration on growth media and expansion of cells	Vibration simulation–cell culture applicability	2.0	2.3
4.	Stimulating effect on hydrogel ECM	Vibration simulation–cell culture applicability	1.9	2.1
5.	Effect on certain tissues that may contain undesirable elements	Vibration simulation–cell harms	3.0	3.2
6.	Integration level of vibration and flow	Vibration–liquid flow	2.9	3.1
7.	More realistic way to grow and treat tumour cells	Vibration–bio-healing effect	3.2	3.3
8.	Throughput effect for multiple scaffolds	Applicability–usefulness	3.7	3.5
9.	Positive connection with other scaffold systems	Applicability–practicality	1.8	2.4
10.	Non-hindering effect on geometric control	Vibration–geometrics	2.5	2.7
11.	Material availability and cost	Usefulness–material cost	3.4	3.6
12.	Further frequency comparison	Frequency–bio-based relevance	4.0	3.9
13.	General benefits on bone cell culture	Vibration–usefulness	1.9	2.7

[1,2] Rated on four-point Likert scale (from ‘none’, ‘slight’, ‘medium’ to ‘strong’) through literature studies and consulting relevant experts in bioengineering, design and manufacturing. [1] Importance indicates weight of element that designers must consider during process. [2] Contradiction level indicates possible conflict intensity that might occur when focusing on identified criteria.

In detailed 3DPVS design, a huge number of minor vibration-based contradictions exist. Thus, analysing fundamental bio-based contradiction—namely possible vibration versus the scaffold’s biological controls—is of prioritised significance. Here, we briefly discuss the listed criterion in relation to vibration mechanisms that will be possibly generated.

High predictability of vibration mechanism. Many vibration mechanisms tend to be unpredictable regarding their effects on cells or biomedical applications—that is, they may have some bio-benefits, yet these benefits remain only partially known, the details are unknown, or they are artificially uncontrollable. Lack of predictability of side effects is also a concern. Thus, a proven beneficial vibration will be used, instead of vibration being investigated. The opposite would increase the cost and failure rate of designing a new vibration mechanism, which is the centre of gravity in this research. The proposed vibration must be relatively predictable to be practically useful for current cell cultivation. For novel vibration approaches, the high potential yet low predictability constitutes a design contradiction.

Better simulation of conditions in living organism. The newly applied mechanism must function through the microfluidics inside the scaffold, which continuously provide nutrients to where cells need them. This means that cells and organs under such a mechanism can grow in a healthy, natural or tailored way, as culturing of conditions in vivo. Some vibration forms might have proven benefits for 'dead' structures, such as engineered constructs or objects, while they become crippled when dealing with 'living' organisms. The applicability of a useful vibration not positively affecting 'living' cells could create a contradiction. It is interesting that the bio-environment tends to use subtler vibration than other engineering realms. Thus, a finer, subtler vibrating form, rather than the traditional 'coarse' mechanical methods, might be a better choice for this question.

Positive issues caused by effect of vibration on growth media and expansion of cells. As cells grow in a 2D or 3D culture, they consume growth media and exude waste. This can result in toxic waste products, dead cells, nutrition depletion and damage of the environment cells cultured. The vibration mechanism must first ensure it will not negatively disturb this process. As a result, other following benefits of the definite cell culture become controllable. Given that 'growth media' is the environment in which cells live, and cell expansion is the basic demand of any kind of cell culturing, limitations on these create vital conflicts in the entire design process. If positive issues are not attainable, vibrating mechanisms must ensure their effects are at least 'neutral'—they do not play any harmful roles in the cellular process.

Stimulating effect on hydrogel ECM. A 3D scaffold provides hydrogel, an ECM in which cells can survive, grow and proliferate. These ECMs usually have tiny pores allowing the passage of nutrients and gasses to give cells an environment for thriving. Well-developed ECMs also provide essential cues to cells, rendering them crucial for the establishment of physiologically relevant 3D tissue cultures. As such, potential conflicts between the vibration mechanism and ECM functionality must be addressed, a better cooperation of which on cell culture inevitably becomes a need when selecting suitable mechanism. For mechanisms that cannot generate a proven or certain effect on ECM, application will be difficult because of instability and other unknown issues. A benefit on ECM yet hindrance on other cell aspects will also create conflict during the design process.

Effect on certain tissues that contain undesirable elements. In rare cases, 3D cultures created from specific tissue types (e.g., basement membrane extracts) can contain unwanted components, such as growth factors or viruses. Definite vibrations may not hinder this process, but instead help or activate the undesirable elements and disturb the aim originally planned for definite culturing. Some mechanisms, such as bioreactor-based, usually help or hinder both useful and harmful elements simultaneously during cell culturing, which contributes to a contradiction if investing further in its application on 3DPVS.

Integration level of vibration and flow. Fluid flow—such as tissue blood flow, interstitial fluid flow and culture medium flow—is crucially important for proper functioning of most tissues. Cells respond to flow through differentiation and metabolic adaptation. Thus, vibration must positively affect the flow, instead of hindering it or causing disturbance to the natural flow, as in traditional static scaffold culturing. Sound- or electricity-based mechanisms sometimes cause such disturbance. Vibration also needs to help oxygen, or other essential nutrients, flow to the right place at the right time. This is especially important for larger-scale cultures, where it can be a challenge to distribute nutrients to definite places in the scaffold. Thus, integration of vibration and flow will be vital in future vibratory scaffolds, since its inner structures may contain several sub-structural areas that require different flow and vibrating stimulations. Considering this, a magnetism-based mechanism may be relatively a good option.

Realistic way to grow and treat damaged cells. 3D cell culture systems are good simulators of diseased tissue, such as cancer tumour cells. They can exhibit healing growth and treatment patterns. Meanwhile, a mechanical field was typically experimented as lacking efficiency in treating damaged cells; hence, mechanical stimulation might have a worse cooperation relationship compared with other vibration forms. As a replacement, a magnetic field could be an option, given the newly emerged bioactive magnetic materials. Other forms of current vibrating forces are chiefly in the research stage, and formal consensus has not yet been reached. As such, practicality becomes a concern.

Throughput effect for multiple scaffolds. Traditional vibration techniques, such as attaching to a vibrator or shaker, are cumbersome and time-consuming, and generally stimulate scaffolds on a one-to-one means—that is, for each 3D scaffold, a vibration device is needed. This limits large cell culturing, such as where many scaffolds are studied simultaneously for drug delivery purposes. Thus, providing the throughput needed for large-scale experimentation will be considered when selecting promising vibration mechanisms. Field-based mechanisms have advantages over traditional mechanical ones. In other words, for expensive cell culturing processes, such as studying cell samples that are precious, a one-to-one-based approach is still of high value; therefore, methods allowing a flexible shift between both vibration modes require contemplation.

Positive connection with other scaffold systems. Two main types of TE exist: scaffold-based and scaffold-free. Scaffold-free systems typically use techniques such as magnetic levitation, bioprinting or whole organ printing. Given that the scaffold is not used to provide simulations, such approaches tend to show a higher appreciation for non-mechanical and invisible stimulating mechanisms. Knowledge of these might offer researchers insights to developing novel simulating methods on 3DPVS. In contrast, scaffold-based systems can be divided because of their chief purpose of culture oriented or tissue implantation. Positive mechanisms could mean the invented vibrating strategies potentially benefit both, though current research mainly focuses on cell culture scaffolds.

Non-hindering effect on geometric control. As a consensus, vibration can shake or even crush construction. The new vibration mechanism should ensure the functionality of the scaffold's geometrics, meaning that applying it will not hinder the structures or promise the functions of geometrics that could be there at 3D static culturing. 'Coarse' vibration mechanisms, such as mechanical shakers, have a higher possibility of damaging microstructures of the scaffold or structured cells during the cultivation process, as well as hindering general geometric controls.

Material availability and cost issue. For this criterion, the selected components of 3DPVS, especially for fabricating materials, are generally required to be inexpensive and easily accessible. This would benefit most researchers who show interest in following 3DPVS development. Compared with traditional materials, novel nanomaterials tend to have advantages because of their bio-based functionality, yet they may be more expensive. Selecting materials with multiple subcategories would provide more availability during design, as another consideration for designers.

Further frequency comparison. As one vital aspect of vibration, frequency-based functionality in 3DPVS must be prioritised after the general selection of the vibration mechanism. Previously mature investigation on effect of frequency on cell culture, especially bone cells, is largely necessary. Some novel vibration forms, such as the newly emerged quantum vibrating method, have promise, yet lack general control in regard to frequencies. Forms with fine vibration yet no capability to generate localised stimulation also create conflicts in application. Among different vibrations, forms that can generate flexible and wide-ranging vibrations that fulfil the needs of frequency accuracy, as well as localised functions, while not contradicting other demands, will be prioritised. It is also important for frequency to be easily controllable. Magnetism-based and other field-based methods could show high promise compared with traditional mechanical means.

General bone cell culture benefit. This will be based on how efficient and effective definite mechanisms work on cells in terms of proliferation, differentiation and tailored cellular growth. Detailed data analysis on cell studies is required to avoid possible contradictions. It is interesting that finer vibration forms generally show a more profitable effect, and are predicted to witness increasing application in bioengineering. During the conceptual process, the designed mechanism could be beneficial, yet cause negativity in practical cell culturing, which is a contradiction that designers must consider at the 3DPVS development stage.

5.4 Third-layer Analysing and Problem Solving

Several problems logically appear at this stage after analysing problems in the second layer. The TRIZ IPA process will be used as the chief tool for generating solutions.

5.4.1 *Abstracting Third-layer Problem*

Attributes of 3DPVS at the system level will be separated into sub-system components as the smallest functional unit of each attribute. Addressing attribute-based contradictions at system level is vital before passing into the components sub-system level. Contradictions between attributes and components—such as 'dynamicity' as one attribute parameter and structural stability within geometric property control, resulting from fabricated materials—is a sub-parameter at the component level. These two 'parameters' at two system levels can conflict with each other. As such, several problems can be identified after second-layer problem solving:

1. The dynamicity of materials can contradict the requirements of scaffolds in terms of mechanical strength. As such, structural stability becomes a vital concern when focusing on material dynamicity.
2. As the problem passes from the second layer, material dynamicity can contradict its biocompatibility or other biomedical properties; for instance, in tissue scaffolds, materials must be biodegradable, while, in cell culture scaffolds, there is no such need.
3. To further address dynamic aspects of materials, with relation to their 3DP fabricability, more dynamicity-based parameters must be identified and selected. 3DP fabricability could conflict with definite dynamicity and this should be detected in the first place.
4. For potential smart materials, suppose they could endow the scaffold with dynamic functions, their biological effect in terms of positive, required cell stimulation may be inadequate. Lack of bio-based research on smart materials may also conflict with the design proposal.
5. After solving issues of the G-, M- and B-parameters conflicting with possible V-properties, inner contradictions—namely, new contradictions in G-, M-, B- and V-, respectively—must be further identified and addressed.

Prior to addressing the above issues, it is important to understand the basic contradiction level between GMBV characterisation of 3DPVS. Table 5.4 summarises the contradiction level when pair of characterisation encounters. From TRIZ, we see that one 3DPVS property may ascend at the cost of descending another, which creates fundamental GMBV conflict. The result is rated on a four-point Likert scale, ranging from 'none', 'slight', 'medium' to 'strong', following the same procedure as previously described.

Table 5.4 Contradiction matrix of 3DPVS GMBV characterisation at encountering

Contradiction ranking matrix of 3DPVS GMBV characterisation				
⬇ ⬆	G-	M-	B-	V-
Geometrics (G-)	1.1	1.4	1.9	2,0
Mechanics (M-)	1.8	2.7	3.1	4.0
Biological properties (B-)	1.9	2.1	3.2	3.8
Vibratory properties (V)	1.7	2.8	3.4	3.2

From this table, we can conclude three main contradictions at super-system level: 'material dynamicity' with 'structural stability', 'material dynamicity' with 'material biocompatibility', and 'material dynamicity' with 'material fabricability'. When mechanical properties meet with vibratory properties, material becomes the centre of gravity. When vibratory properties encounter biological ones, biocompatibility must be carefully addressed. Conflict within vibratory properties itself lies within the constraints of current vibration mechanisms; therefore, enhanced vibration promises to overcome this concern. The following section focuses on these three contradictions.

5.4.2 *Identifying Innovation Principles for Third-layer Contradiction*

This section flexibly applies ACM, with one to three parameters for ascending and descending columns, to the IPA process. For the first problem—the contradiction between material dynamicity and structural stability—detailed steps of the analysing process are illustrated as below.

I. Identifying principles for contradiction between 'material dynamicity' and 'structural stability'.

This part will illustrate how to solve one contradiction, or conflict, between design parameters of dynamicity in material composition and stability in structural design. Five steps, as discussed in the TRIZ methodology, will help achieve appropriate innovation principles:

- Step 1: Designer must determine appropriate material for 3DPVS (EX1),[1] yet lacks the means.
- Step 2: Material dynamicity (PE1)[2] is the most appropriate parameter to evaluate whether the goal is reached.
- Step 3: The most obvious way to make material dynamicity evolve in the desired way is that vibratility (PA)[3] is vibratory (VA).[4]
- Step 4: If vibratility was static or inactive (VAB),[5] structural stability (PE2)[6] would be the most positively affected.

Table 5.5 Simple illustration of combined effect of contradictory element

Contradiction	Vibratility	
	Vibratorily active	Static or inactive
Material dynamicity	Positive	Negative
Structural stability	Negative	Positive

'Vibratility' must be 'vibratorily active' to satisfy the dynamicity of materials, and static or inactive to satisfy structural stability. Table 5.5 displays the four resultant effects when contradictory elements meet. Note that, in this scenario:

[1]: explain with an infinitive verb and a complement; this is the goal of the design process

[2]: explains with which parameter one will estimate when the goal (to determine the appropriate material for 3DPVS) is reached

[3]: explains which parameter is a lever to make material dynamicity evolve in the desired manner

[4]: defines with an adjective the state of vibratility

[5]: defines with an adjective the opposite state of vibratorily active for vibratility

[6]: explains which parameter will be most positively affected if vibratility is static or inactive.

- Step 5: Using TRIZ ACM.

We first select the generic parameters in the matrix that fit the parameters of the proposed contradiction. The inventive principles can be obtained from ACM, which helps solve this contradiction. For this case, 15 principles are obtained. After calculating the rate of these principles, the top several will be prioritised for analysis, and the final number of principles is usually limited to below three. Based on the literature and other evaluation means, one final design principle, separated as one of 40 innovation principles or a hybrid of multiple, will be selected to solve the contradiction. Specifically, in each IPA, more than 10 principles will be available, and designs must select the most suitable ones to ensure efficiency and accuracy of the innovation process. Table 5.6 shows an ACM with calculated rates of applicability of the obtained principles.

Table 5.6 TRIZ IPA focusing on finding principles for the contradiction of structural stability and material dynamicity

IPA analysis	
Structural stability ⇨ Material dynamicity ⇩	8. Volume of stationary object 13. Stability of object's composition 14. Strength
9. Use of energy by moving object 16. Durability of action of stationary object 27. Reliability	35. Change of physical and chemical parameters (18%) [selected] 19. Periodic action (13%) [selected] *5. Combining; 2. Taking away; 39. Inert atmosphere; 11. Beforehand cushioning (each 7%)* *28. Mechanical principle replacement; 24. Intermediary; 13. Other way round; 3. Local quality; 34. Rejecting and regeneration of parts (each 5%)*

From the principles analysed in Table 5.6, a possible solution is to change existing physical and chemical parameters of the 3D static scaffold, such as from static materials to smart dynamic materials. Periodic action, as the second priority, would mean a timely-controlled functionality that does not create too much intensity on the scaffold's structures. Inserting atmosphere could also help protect the stability of structures by creating some supporting forces among geometrics.

II. Identifying principles for contradiction between 'material dynamicity' and 'material biocompatibility'.

After the previous step, the issue arises that, even if the selected materials are dynamically vibratory and ensure the stability of structures built upon these materials, they may be bio-toxic or incompatible with cell culture applications. Thus, the second parameter aside from structural stability arises—that is, biocompatibility of materials. For the biocompatibility parameter, the analysis and calculated rates are shown in Table 5.7.

Table 5.7 TRIZ IPA focusing on finding principles for the contradiction of material dynamicity and biocompatibility

Material biocompatibility ⇨	17. Temperature 26. Quantity of substance 31. Object-generated harmful factors
Material dynamicity ⇩	
9. Use of energy by moving object 15. Durability of action of moving object 35. Adaptability and versatility	35. Change of physical and chemical parameters (17%) [selected] 3. Local quality (16%) [selected] 19. Periodic action (10%) [selected] *2. Taking away (9%)* *39. Inert atmosphere (6%)* *34. Rejecting and regeneration of parts; 27. Cheap short-life instead of costly long-life; 21. Skip; 16. Partial or excessive action* *(Each at 5%):* *24. Intermediary; 23. Feedback (each 4%)* *6. Universality; 15. Dynamicity; 10. Prior action (each 3%)*

The principles obtained here aim to ensure the material composition can guarantee the dynamic functions, and fulfil the end-use cell culture context. Note that, based on the new scenario, three parameters selected for 'material dynamicity' partly differ from the previous 'structural stability' one.

III. Identifying principles for contradiction between 'material dynamicity' and 'material fabricability'.

The third contradiction occurs between material dynamicity and material fabricability. As discussed, the ideal fabrication methods for 3DPVS would be 3DP. However, materials may be both biocompatible and vibratory, yet unable to fulfil 3DP fabrication requirements. At the current conceptual stage of 3DPVS, there could be materials with potential in terms of generating possible vibrations, yet 3DP has not been maturely investigated for their fabrication. Here, three principles for fabricability are selected and the contradiction matrix is shown in Table 5.8.

Table 5.8 TRIZ IPA focusing on finding principles for the contradiction of material dynamicity and 3DP fabricability

3DP fabricability ⇨	29. Manufacturing precision 26. Ease of manufacture 31. Productivity
Material dynamicity ⇩	
9. Use of energy by moving object 15. Durability of action of moving object 35. Adaptability and versatility	35. Change of physical and chemical parameters (15%) [selected] 28. Mechanical system/interaction substitution (15%) [selected] 27. Cheap short-life instead of costly long-life (11%) [selected] *3. Local quality* [selected]*; 12. Equipotentiality (each 6%)* *26. Use of copies (copying); 13. Other way round; 17. Another dimension (5%)*

Local quality could mean using different 3DP methods to fabricate different parts of the scaffold to gain best the advantage of each of the 3DP systems—droplet-, laser- and nozzle-based systems. Changing some mechanical parts with optical or acoustic means may also be applicable.

5.4.3 *Analysing Contradiction Issues of Smart Material Stimulus Response*

Based on the innovation principle, smart material could be enabling with newly designed vibration mechanism. Using TRIZ, the complex contradiction within desired vibration might be transferred into simply a mechanical problem. Part of the solutions to material problems lie in analysing the demands of material to variably 'respond' to different cell culture conditions. Two questions are logically related: (1) What vibration response does this situation require? and (2) What is changing to act as a stimulus to create such a response? We can analyse this problem through TRIZ SFMA. In the vibration mechanism replacement problem, the primary stimulus is the field. Thus, changing the field acts as a stimulus that can trigger a material response; for instance, a mechanical stimulus is used to trigger a mechanical response. The SFM corresponding relationships between smart materials, vibration mechanism and scaffold are illustrated in Figure 5.3. Neutralising force indicates the design elements that either strengthen or hinder definite functions of S1, S2 or F, to help S1 generate normal, desired vibration on S2.

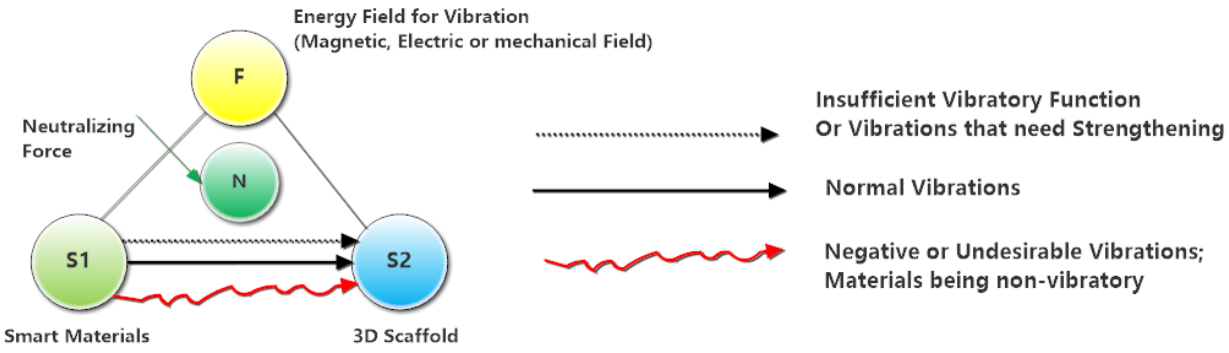


Figure 5.3 SFAN model for smart materials, vibration field and 3D scaffold

Analysing the problem in this stimulus-response manner enables us to classify smart material solutions effectively. Table 5.9 presents the results via arranging already-known smart materials, reworked from previous sources (Khoo et al. 2015; Mann 2009; Miao et al. 2016; Rosso et al. 2005). Several smart material resources are identified that are electrical-, magnetic-, optical-, thermal- and mechanical-based. The different responses listed at the top indicate possible desired results. The stimulus column on the left illustrates what is changing or can be changed at system level to trigger the desired response. Different classes of stimulus provide a range of possible options for the same desired reaction. In the vibration replacement problem, a single stimulus may suffice or multiple stimuli may need to work together, given the definite design requirements. In other words, the table guides a scientific effect to find solutions, and contributes to judging the flexible stimulus-responses of the possible 3DPVS.

Table 5.9 Smart materials stimulus and response potentially useful for 3DPVS

Currently investigated smart material resources					
Response stimulus[1]	Electrical	Magnetic	Optical	Thermal	Mechanical
Electrical		Magneto-electronics, spin-electronics, spintronics	Electro-chromic, electro-luminescent, electro-optic, piezo-chromic, Kerr effect, Pockel effect	Thermo-electric (Peltier)	Piezoelectric, electro-strictive electro-rheological electro-kinetic
Magnetic	Magneto-electronics, spin-electronics, spintronics, Hall effect		Magneto-optic, piezo-chromic	Magneto-thermal	Magneto-strictive, magneto-rheological
Optical	Photo-conductive	Opto-magnetic	Optical bi-stability	Photo-thermic	Opto-mechanical, photo-acoustic
Thermal	Thermo-electric, super-conductivity, radiometer effect, pyro-electric	Curie point	Thermo-chromic, thermo-luminescent		Shape memory
Mechanical	Piezoelectric, electro-strictive	Magneto-strictive	Mechano-chromic, rheo-chromic		Rheopexic, auxetic, shear-thinning, dilatants, non-newtonian, pseudo-plastic

[1] Note: The horizontal represents the desired response, while the vertical indicates the variable stimuli.

However, different field stimuli can also contradict each other. When analysing material contradiction solving with SFM and innovation principles, chemical methods tend to show the least potential. Mechanical-, electrical-, optimal-, thermal- and magnetic-based indicate relatively high practicality for the possible 3DPVS design. Using substance-field analysis (SFA), magnetically vibratory materials (S1) applied with a magnetic field (F) show relatively higher flexible stimulus-response functionality among the possible methods, aiming to fulfil the desired vibratory functions from S1 to the scaffold (S2).

5.4.4 *Analysing Issues of 3DP Systems*

As novel 3DP materials and methods emerge, 3DP for scaffold fabrication tends to be more effective and sophisticated (Maldonado et al. 2019; O'Brien et al. 2015; Serra 2014; Yuan, Xing & Hsu 2018a). Bio-manufacturing is predicted to witness a trend towards multi-3DP fabricated products, compared with previous bio-products, which were generally achieved by single 3DP (Liravi & Toyserkani 2018; Vlasea et al. 2013; Yoon et al. 2017). However, there is no systematic study on how to cooperate one 3DP with another regarding bio-based product manufacturing. Studying 3DP techniques could contribute to design strategies in terms of suitable vibration-based functionality. In real design scenarios, perhaps one solution merely prefers one 3DP as the optimal method if possible, while analysing the hybrid still shows future value.

However, contradiction follows regarding whether to identify suitable 3DP tailored for a definite conceptual solution of 3DPVS in the first place, or to select 3DP first and then conceive a corresponding 3DPVS concept. Output from system-level components, contradictions, will act as parametric input for analysing 3DP materials, geometrics and methods, which helps identify the definite 3DP hybrid system as proposed. Basically, two approaches may exist for the potential 3DP hybrid system. First, multiple direct 3DP technologies could be integrated into one hybrid 3DP system. Second, direct 3DP technologies could combine with indirect 3DP technologies. Before addressing these, which is a vital task for the future design, the basic 3DP criteria corresponding with TRIZ must first be considered.

From another perspective, 3DP creates contradictions within 3DPVS innovation. A fundamental analysis of 3DP-based innovation principles is necessary. From the perspective of TRIZ, we can possibly obtain seven prioritised criteria or requirements concerning 3DP-based contradiction, as shown in Table 5.10. Conflict level is estimated on a four-point Likert scale. Analysing the contradiction, we can seek four basic solutions, which might be universal for all 3DPVS design concerning 3DP: extraction, dynamicity, self-service and copying. Translation of this helps direct the following design process. The contradictions and solutions identified here can be useful for universal application of 3DPVS, regardless of which 3DP will be used. They do not contribute directly to design solutions, yet act as vital support for enhancing the design process.

Table 5.10 TRIZ parameters corresponding with prioritised 3DP-based criteria and possible solutions

	TRIZ CTQs TRIZ classification	TRIZ parameters	Conflict level	Optimisation
1	Dimension between x-y level	Convenience of use	4.0	Ascent
2	Weight between x-y micrograms or grams	Weight of moving object	3.0	Descent
3	Global or localised elasticity	Tension or pressure	2.1	Neutral
4	Fabrication material type and quantity	Complexity of device	2.2	Descent
5	Design and production cost	Manufacturability	3.0	Descent
6	Number of attributes, components	Level of automation	2.1	Descent
7	Mean time between failures (MTBF)	Reliability	1.1	Ascent
	Principles generated from TRIZ innovation principles and translations			
Extraction: This recommendation can be transposed into practice by designing a scaffold containing a single component (extract, remove or separate part or property), yet allowing the scaffold to flex, move or vibrate during cell culturing.				
Dynamicity: This recommendation can be transposed into practice by adding parts of smart, elastic materials so that certain parts of the scaffold are not static and rigid (change position relative to each other).				
Self-service: This recommendation can be translated by reducing the number of moving parts of the scaffold system to eliminate, as much as possible, maintenance of the scaffold.				
Copying: This suggestion can be translated via using a simple and inexpensive scaffold material copy. This could reduce the total number of components of 3DPVS. The resultant scaffold could consist of a single piece with two-part materials—one traditional static and rigid, and the other dynamic and vibratory.				

5.4.5 *Analysing Generated TRIZ Principles for Conceptual 3DPVS*

When analysing the design process, we find that most contradictions concern material dynamicity, biocompatibility and fabricability; thus, we prioritise relationship with the following principles, from which we may address conflicts preliminarily. The sequence of principles follows the relative applicability level during design:

1. change of physical and chemical parameters (92%)
2. inert atmosphere (85%)
3. mechanical principle replacement (84%)
4. local quality (78%)
5. periodic action (72%).

Fundamental solution extracted from these principles: The generated principles contribute to components of a conceptual solution at the third layer of problem solving. 'Change parameters' indicate replacing traditional scaffold materials with novel ones that have different physical and chemical parameters. Thus, the previous assumption of using smart materials can be verified to some extent. Following this, 'inert atmosphere' and 'mechanical principle replacement' may indicate the new vibrating mode as a non-mechanical one, with stimulating atmosphere involved, where the atmosphere could directly control and manifest the vibration functionality. The 'local quality' principle further indicates that a localised parametric scaffold is practical and promising. In scaffold design, this may mean different localisation regarding geometrics, material composition, or both. In this way, vibration stimulation would become localised as well. In addition, material composition within 3DP—which can generate periodic action (that is, periodic vibratory action)—is a possible approach to tackle some cell culture contradictions, as inspired by the TRIZ principle of 'periodic action'. This fulfils one possible technical objective of 3DPVS to generate tailored and localised vibrations on cells cultured inside the scaffold. Concern is raised about what is the periodic control and how to manifest this periodicity. It is also interesting that, for previous contradiction solving between 3DPVS's material dynamicity, biocompatibility and fabricability, the analysed result will not be merely limited for 3DPVS, but may have wider context for other bioengineering designs. That is, the obtained principles could contribute to a universal reference for bio-designs concerning the trinity of dynamic, biochemical and fabricating issues.

Applicability of principles in selecting fields for vibratory functionality: Following the process of principles corresponding, a data-based evaluation is established, as illustrated in Figure 5.4. Multiple fields have possibility to be applied for 3DPVS corresponding with definite smart materials. Among these, magnetic field as the field for vibration (F-element in SFMA) has a relatively higher percentage in terms of its applicability to TRIZ principles, as indicated in Figure 5.4. This means that designing a magnetic-based approach would offer higher convenience and practicality than the other options. However, if system requirements change,

other fields, such as electric or mechanical, may have their own unique strengths over magnetics regarding applicability. Also, the applicability of TRIZ offers a clue, yet not a definite answer, as to which solution is optimal for the real design. Further study and comparison are necessary, as conducted in the next section.

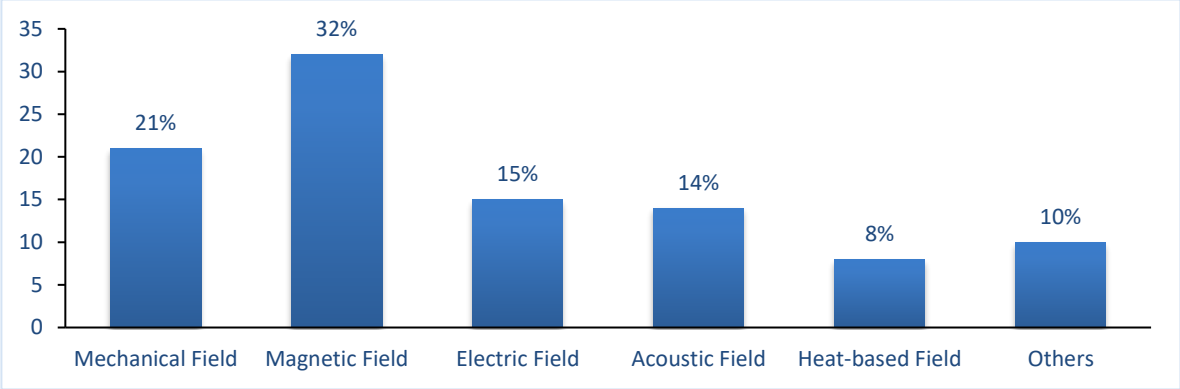


Figure 5.4 Applicability of TRIZ design principles in selecting potential fields

Regarding the vibration mechanisms that correspond with material dynamicity, several mechanisms can be considered suitable, as summarised in the following categories:

- electric field or sources with 3DP electroactive materials
- magnetic field with magnetic-stimulated 3DP materials
- heat-based field with thermosensitive active 3DP materials
- mechanical means with predictable mechanically-reacting materials
- acoustic-based field with acoustically activating 3DP materials
- other fields, such as light-based fields with light-stimulated 3DP materials.

In accordance with these categories, five general solutions are created. Future work will examine detailed sub-system components and generate concepts at the specific level.

5.4.6 *Proposing Conceptual Solutions of 3DPVS Generated at Super-system to System Level*

Five novel solutions indicate potential to achieve 3DPVS using TRIZ. A translation from super-system into system could occur as follows.

Magnetic-based solution: This solution is a 3DP fabricable magnetic nanomaterial, with external magnetic field, using the change in the alternating magnetic field to control the dynamicity of scaffold. The material can mix with traditional materials in the cell scaffold. Magnetic-based shape-memory alloys or shape-memory polymers could come into play. In addition, the magnetic field could positively stimulate cell cultivation and enhance some cell performance. Most cells could receive a tailored reaction under magnetic stimulations. The shift of the field could also be easier in a magnetic-based solution compared with other fields. The challenge lies in selecting magnetic-oriented materials, especially nano-based novel materials that can generate micro-level vibrations. The flexibility of 3DP to fabricate magnetic

smart materials, which has proven methods, is another benefit of employing this solution as the potential 3DPVS concept.

Thermal-based solution: In this solution, the scaffold has a thermal-activated microstructure constituted of timely-controlled shape changing of thermosensitive shape-memory polymers. With an inserted thermal field, shape change of the scaffold can be activated by shifting temperature. The temperature must remain at a level where cells will not be hindered in terms of ordinary growth factors. In most cases, cells must remain at a relatively stable temperature for the usual cultivation process, and this shift, being possibly dramatic and frequent, may negatively affect cells. However, for some specific cell cultivations, such as scientific studies analysing definite cellular reaction based on temperature and vibration, as well studies where cells can tolerate a relatively high or low temperature, such as many types of virus cells, this conceptual scaffold could be an option. For bone cells, the applicability is relatively lower, given the current research needs.

Electric-based solution: In this solution, 3DPVS can be fabricated through a composite of piezoelectric nanoparticles and photo-liable polymer. The scaffold can produce an electrical charge when stress is applied, and vice versa. Electricity stimulates the cells cultured inside. Similarly, a composite of dielectric elastomers and normal biocompatible material may also be applicable, which could produce large strains upon activation by electricity. For definite cell cultures, where electric stimuli can help cell proliferation, this method has unique benefits. The negative issue is the cost of the device. Electricity may be needed for each scaffold to generate the proposed functionality, thereby increasing the economic pressure for large-scale cell cultivation where multiple scaffolds are employed.

Acoustic-based solution: In this solution, biomedical acoustic-active materials can be used in cooperation with definite acoustic fields to generate stimulation in cell cultures. The chief limitation of this approach is that the acoustic wave generally negatively affects cell cultures, harming or hindering cells' normal functions. Researchers have been studying how to mitigate this effect, instead of using it for positive cell cultures. Thus, aside from definite purposes for analysing cells under the acoustic-based solution, this scaffold concept is less likely to be manifested by real designers.

Mechanical-based solution: It is also worth noting that novel mechanical field–based solutions, such as a bioreactor, finer vibrator or subtly-functioning vibration stage, could also be used for generating 3DPVS. In this regard, materials may not be smart materials; traditional ones would be useful if they can pass external vibration to cells cultured inside the scaffold at a satisfactory level. Traditional mechanical vibration contributed the conflict regarding vibration and scaffold, and the question of whether they could successfully evolve in future bio-designs remains a concern, although numerous TRIZ innovation principles assist with this approach.

Among other solutions, a chief example that is considered less practical or applicable is the light-based method. Anti-counterfeiting structures can be applied on the scaffold, using composites such as a quantum dot suspension (mixture of quantum dots and photopolymer resin) to mix with biocompatible rigid material. Quantum dots absorb UV light and emit visible lights that help stimulate cells. The negative side of this method is that it can only provide bioactive stimulation based on light, especially providing with continuous stimuli, yet cannot effectively create tailored vibrations at either micro- or macro-levels. Thus, the way to use methods of this category is a challenge and requires future studies.

This section has generated five chief conceptual solutions for 3DPVS. The problem generation occurred chiefly through TRIZ-based method, Routes 1 to 3. At the current stage, we generated these conceptual solutions without technical evaluation. When the design is anchored by detailed and specific end-user requirements, design attributes and 3DPVS characteristics/parameters, it could it be meaningful to technically evaluate the generated solutions. In brief, the concepts generated in this study are basic structures for the potential 3DPVS. Given that detailed design information and specification tend to vary from one cell culture scenario to another, the selection and optimisation of 3DPVS will differ. A real-world case will be incorporated with the design of 3DPVS to attain optimal solutions.

5.5 Fourth-layer Analysing and Solution Evaluating

This section conducts evaluation work, from super-system to system, to compare the five preliminary conceptual solutions generated previously. It aims to summarise the cons and pros of each conceptual solution, as well as indicate optimal solution at the current preliminary stage.

5.5.1 *Evaluating Basic Conceptual Solutions through Super-system Criteria*

Thirteen super-system criteria for 3DPVS have been discussed previously. A quantitative comparison of five solutions related to these criteria will be conducted, first indicating the normalised weights of the 13 criteria calculated by importance, and second that of each solution as its fulfilling-level against definite criteria. Using the Pugh matrix, the results are presented in Table 5.11. Original estimation is gathered using a four-point Likert scale. Given that different criteria are weighted differently in this case, a normalised calculation is used, instead of using the direct value from the four-scale rating.

Table 5.11 Comparison Pugh chart for generated concepts at super-system level

No. of criteria & constraints	Normalised weight	Solution 1: Magnetic	Solution 2: Electric	Solution 3: Mechanical	Solution 4: Acoustic	Solution 5: Heat
1	0.0641	0.0695	0.0379	0.0433	0.0422	0.0370
2	0.0501	0.0647	0.0729	0.0867	0.0818	0.0438
3	0.0613	0.0624	0.0845	0.1022	0.0897	0.1044
4	0.0529	0.0767	0.0525	0.0619	0.0607	0.0842
5	0.0836	0.0815	0.0904	0.0526	0.0950	0.0707
6	0.0808	0.0839	0.0933	0.1022	0.0923	0.1044
7	0.0891	0.0935	0.0700	0.0867	0.0844	0.0572
8	0.1031	0.0935	0.0758	0.0557	0.0792	0.1044
9	0.0501	0.0743	0.0933	0.1022	0.0897	0.0842
10.	0.0808	0.0695	0.0933	0.0712	0.0739	0.0707
11	0.0947	0.0647	0.0583	0.0712	0.0633	0.0842
12	0.1086	0.0815	0.0758	0.0836	0.0739	0.0572
13	0.0808	0.0839	0.1020	0.0805	0.0739	0.0976
Overall ideality of concept		0.0782	0.0774	0.0760	0.0771	0.0776

From the Pugh chart, we generate overall ideality scores of the four conceptual solutions for 3DPVS in a super-system scenario. The innovative concepts respectively weigh 0.764, 0.965, 1.204 and 0.689, with the datum solution at 0.476. Figure 5.5 below shows a visual comparison of the concepts, indicating that Solution 1—magnetic-based 3DPVS—is considered the most promising concept with highest ideality among all generated concepts. Mechanical- and thermal-based are in parallel positional towards fulfilling the super-system requirements, while electric- and thermal-based solutions tend to be less ideal.

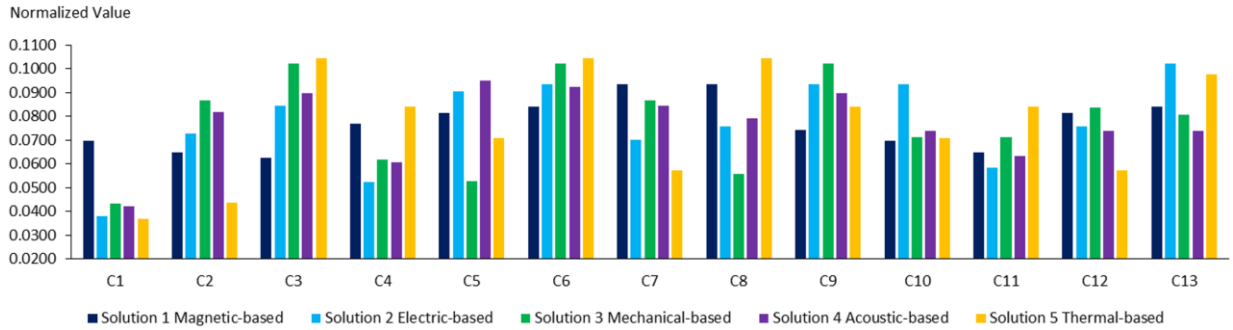


Figure 5.5 Comparing conceptual solutions with super-system cell culture criteria

From another viewpoint, different solutions show a variable rate fulfilling each criterion. Although the average rate for each solution does not present a dramatic difference, the magnetic-based solution indicates the most stable option that essentially fulfils each criterion to a satisfactory level.

5.5.2 *Investigating Generated Solutions against System-level Criteria*

After analysing the super-system perspective, this section investigates the generated basic conceptual solutions of 3DPVS at system level, regarding the 3DPVS product itself in terms of practical use and proposed objectives (Table 5.12). Seven system-level criteria are identified, each of which is considered equally significant. A four-point Likert scale is used via collecting feedback from expert groups, rating 1 (‘none’) to 4 (‘strongly positive’).

Table 5.12 Generated conceptual solutions fulfilling 3DPVS system-level criteria

3DPVS criteria at system level and corresponding rating of various conceptual solutions					
3DPVS criteria at system level	Solution 1: Magnetic	Solution 2: Electric	Solution 3: Mechanical	Solution 4: Acoustic	Solution 5: Thermal
1. Design realisability	2.5	1.7	2.1	1.9	2.0
2. Future potentiality	3.4	1.9	3.1	3.0	3.1
3. Cell culture applicability	3.7	2.1	2.3	2.4	2.3
4. Capability of macro-vibration	2.9	2.1	3.3	2.5	2.7
5. Capability of micro-vibration	3.2	2.9	3.2	3.6	2.6
6. Capability of localised vibration	2.9	2.7	3.1	2.1	3.4
7. Vibration controllability	3.2	2.8	2.1	2.2	2.5
Average rate	3.11	2.31	2.74	2.53	2.66

Analysing from Figure 5.6, all possible solutions show a similar rate in terms of design realisability, which indirectly supports the assumption that the five 3DPVS solutions generated via TRIZ are commonly practical and realisable. In terms of the capability of providing localised vibration, these solutions indicate another similar rating, which can be perceived from the fact that all these solutions use field-based stimulation, which easily manifests different responses inside scaffolds if different parts of the scaffold—namely, characterisation—become non-identical. At the current stage, the acoustic- and thermal-based approaches show a relatively lower application to cell culture, while providing higher future potentiality if bio-scientists can find the right means to use these methods in the right place at the right time. In terms of vibration controllability, the magnetic-based solution shows a higher rate, while the traditional mechanical one shows the lowest. The low controllability of the traditional mechanical solution was the initial motivation of beginning the novel 3DPVS design, which aims to conquer these limitations.

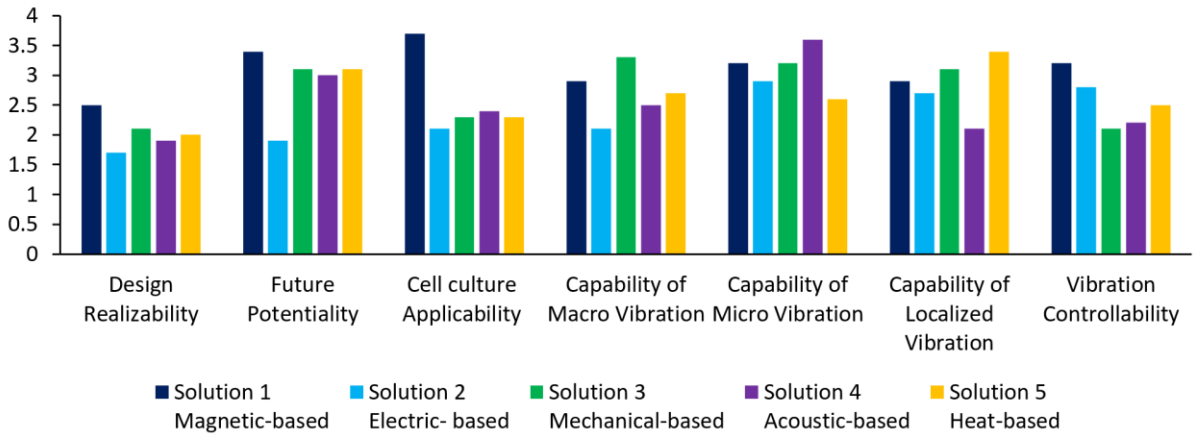


Figure 5.6 Basic conceptual solutions corresponding with system-based criteria of 3DPVS

Despite the aforementioned, magnetic-based solutions tend to show the least deviation rate—that is, it rates at an overall fine level compared with that of the other solutions. It also has the highest applicability in cell cultures, which can be justified via the rapidly emerging magnetic means onto cell engineering. In addition, all solutions show promising future potential, except the mechanical one, possibly because the mechanical approach is the current mainstream strategy to generate vibrations and is stuck at a bottle-neck period where further evolution seems difficult. Regarding vibration capability, the magnetic approach shows a higher rate on average, while the mechanical and acoustic approaches have higher values in macro and micro, respectively. Mechanical approaches are convenient to shake structures, thus creating rough vibration at the macro-level, while acoustics could feasibly create subtle vibrations via sound waves. In terms of localised vibration, which was one proposed aim for 3DPVS compared with the traditional scaffold, the thermal solution tends to be most useful, possibly because controlling thermal issues in different parts of the scaffold may be relatively easier than other solutions, though the others also show fine potential in achieving this aim. For general vibration controllability, such as adjusting frequency or amplitude, the magnetic and mechanical approaches could be relatively more suitable than the other three solutions.

5.5.3 *Analysing Generated Solutions against 3DP Applicability*

Another system-level concern is the future fabricability of generated concepts via 3DP, data in Table 5.13, with graphic analysis in Figure 5.7. As such, a list of applicable 3DP methods are selected. The feature, benefit and property of each can be seen in a previous study (Yuan, Xing & Hsu 2018a).

Table 5.13 Feasibility of generated conceptual solutions vs 3DP fabrication methods

3DPVS conceptual solutions corresponding 3DP methods					
3DP methods	Solution 1: Magnetic	Solution 2: Electric	Solution 3: Mechanical	Solution 4: Acoustic	Solution 5: Heat
1. 2PP	1.4	1.3	1.5	1.6	2
2. LENS	1.6	1.9	2	2.1	2.5
3. SLA	3.3	1.9	2.4	3.4	3.4
4. SLM	1.9	1.6	1.9	2.3	2.4
5. SLS	3.5	3.4	3.5	3.1	3.1
6. LOM	2.9	2.7	2.8	2.8	3
7. Inkjet	3.9	3.8	3.7	3.3	3.1
8. FDM	4	4	4	3.5	3.8
9. 3D plotting	3.8	2.9	3.7	3.3	3.2
10. Indirect 3DP	3.4	3.2	3.7	3.2	2.6

From this study, FDM, the typical nozzle-based 3DP, shows the average highest applicability among all five generated solutions. Inkjet, as liquid-based 3DP, shows generally high applicability, and its application inevitably contains the usage of novel liquid materials. Among layer-based 3DP, both SLS and SLA can be considered promising for achieving the generated solutions, and SLA tends to be a useful method for magnetic-, acoustic- and heat-based approaches, while being less applicable for electric and traditional mechanical solutions. Indirect 3DP could also be applied as a general method for 3DPVS, while 3D plotting shows positivity for some and limitations for others. In addition, these novel field-based solutions tend to be positively applicable for more than half of current mainstream 3DP methods. Some solutions that are not applicable in definite 3DP still have good alternatives regarding possible fabrication. In brief, all generated solutions show a fine level of fabrication applicability via 3DP, which fulfils one core aspect of the 3DPVS requirements—namely, 3DP as the fabricating means for the novel vibratory scaffold.

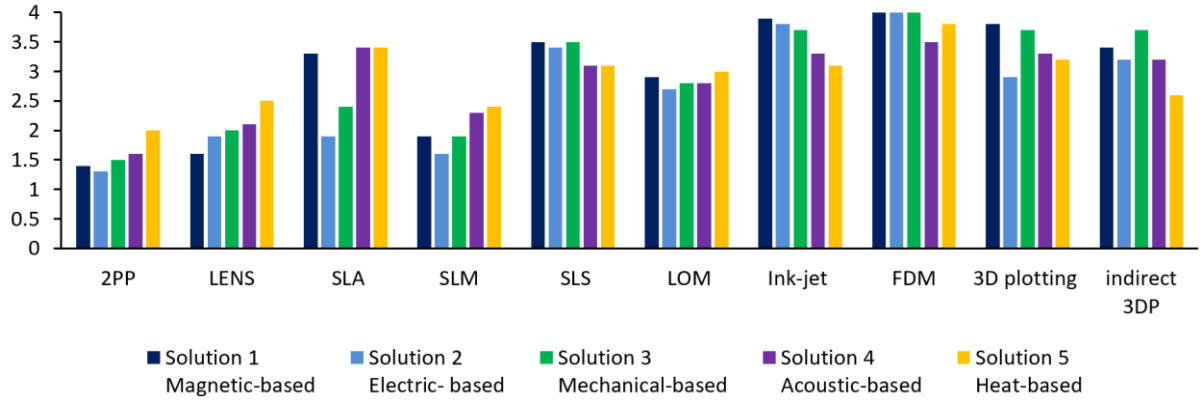


Figure 5.7 Fundamental 3DPVS conceptual solutions corresponding with 3DP applicability

From another perspective, the overall estimation indicates that the magnetic- and mechanical-based approaches rank at a relatively high position, following which are heat-, electric- and sound-based options in sequence. Considering the higher position of the magnetic-based

solution in the other criteria previously analysed, we can recommend this as the optimal solution for conceptual 3DPVS at super-system to system level. The starting point of the novel 3DPVS was proposed to mitigate the limitations of traditional mechanical means, such as attaching the scaffold to an external shaker or vibrating platform. This does not mean that mechanical approaches will fall out of use, as they still have potential among other field-based solutions. Therefore, we may contemplate that mechanical means, such as bioreactor-based or attachment to an external vibrator, will still be practical for a relatively long period, alongside the process of novel mechanical methods being developed. Other novel yet less promising approaches—electric-, sound- and thermal-based—require further effort in terms of developing corresponding smart materials and investigating the appropriate functioning of fields. In brief, although the feasibility of 3DP cannot judge the practical value of conceptual solutions, it indirectly provides evidence to evaluate the flexibility of the solutions. In future study, sub-system requirements, including detailed concerns of GMBV characterisation, will be considered, where a more thorough view of which 3DP tends to play a greater role in a definite solution can be determined.

Further, analysing together with third-layer study concerning 3DP hybrid system, we can reach several conclusions. For a magnetic-based approach, the scaffold product can be fabricated through FDM, PolyJet or a hybrid system of Inkjet and FDM. For a mechanical-based approach, it can be achieved by a hybrid system of FDM with SLS, Inkjet, 3D plotting or indirect 3DP. For a thermal-based approach, 3DPVS can be a fabricated through a nozzle-based 3DP system, such as FDM, SLA or a hybrid system of both. Electric-based 3DPVS could use Inkjet, SLS or a hybrid of both. The acoustic-based solution shows the intimacy towards Inkjet, 3D plotting, FDM, SLA or a relevant hybrid system between multiple of these.

5.6 Discussion

Given that the basic solutions generated remain highly abstract, a fourth-layer study was conducted to evaluate these solutions from various design perspectives. The previously established 13 super-system criteria were initially used to indicate the extent to which the solution would fulfil them. To achieve this, seven system criteria of 3DPVS were used to evaluate the solutions to shift the focus of design from bio-constraints to the 3DPVS innovation itself. Given that 3DP is the fabricating tool for 3DPVS, this chapter completed another study rating each solution against their 3DP applicability. Analysing from the fourth layer, a preliminary conclusion was drawn that the potential conceptual 3DPVS using a magnetic field with materials such as 3DP-fabricable magnetic nanomaterial seems highly promising, with relatively higher practicality, relevance and significance compared with the other novel solutions. The traditional mechanical solutions have numerous limitations, while novel approaches are promising and could be applicable for the future 3DPVS design. Acoustic- and electric-based solutions are novel from a theoretical view, while generally ranked at a

relatively lower position. This may be because there are no mature resources dealing with real-world design scenarios of applying such fields into cell scaffolds. Given the rapid development of material science, perhaps better approaches will arise to make them practical and thus applicable in the future 3DPVS. In brief, this study fundamentally addressed the design contradiction of 3DPVS from the super-system to system level. Different field-based concepts were generated, and the basic comparison and evaluation was conducted from a theoretical level. Study of these concepts is preliminary to future work focusing on how to generate a conceptual solution for 3DPVS at a more detailed, concrete level and solve the sub-system contradictions.

Although concrete future solutions, such as a magnetic-based 3DPVS, cannot be achieved without conducting a further detailed design process, some future perspective on its solution could still be contemplated. A porous magnetic scaffold will serve as a material and structural template for bone cells, such as osteogenesis, while the embedded superparamagnetic material, such as the FeHA microsphere in a polyurethane (PU) matrix, under an external timely-changing magnetic field, will provide useful vibratory stimulation to promote cell cultivation in bone remodelling and regeneration.

However, given the limitations of TRIZ, it is not practical to tackle all challenges in 3DPVS design at one time. Sophisticated, complex problems that remain unaddressed can be assisted by other TRIZ-supportive means. For instance, ARIZ within TRIZ is an algorithm tool for dealing with issues that cannot be easily solvable by traditional TRIZ means. In addition, tools such as QFD could provide more resources in terms of generating a detailed comparison of design criteria, especially the sub-system components that tend to be large in quantity and tedious by traditional comparison. Further, this study is an initial attempt, if not the first attempt, to innovate a bio-scaffold via TRIZ. Therefore, flaws inevitably exist and further investigation is necessary. In other words, 3DPVS design is complex and crosses domains, and finding TRIZ-assisting tools in miscellaneous areas could be useful in 3DPVS innovation. Finally, bear in mind that, for the solution evaluated as conducted in the fourth layer, the rating result should be used as an indication, not a decisive answer.

From another future perspective, the conceptual design of 3DPVS will focus from the system to sub-system level—that is, detailed 3DPVS characterisation will be considered with the fundamental solutions generated in this study. GMBV components of 3DPVS will be studied by considering design problems addressed via TRIZ and other supportive methods. For instance, this includes, yet is not limited to, the following focus: geometric properties, such as porosity, pore size distribution and pore shape; mechanical properties, such as compressive strength stiffness (Young’s modulus); biological properties, such as surface roughness and fluid flow mediated wall shear stress; and vibratory properties regarding how and what vibration will be generated and manifested on the scaffold. In brief, future work will be challenging and further investigation of TRIZ-supportive methods will be valuable.

5.7 Concluding Remarks

This chapter has used basic TRIZ-based design methods to generate conceptual solutions of 3DPVS, especially from the super-system to system level. We sought to identify basic and typical system contradictions, physical contradictions and several non-contradicting-based questions, which stand in the way of the conceptual development stage of 3DPVS. A four-layer systematic approach was used to establish a logical, scientific and structured concept generation process. Each layer presented a definite aim in the whole. From the first-layer analysis, we summarised the design problem from the base model, indicating which TRIZ method and route would be applicable, and generating five characters that the potential 3DPVS solution must fulfil. From the second layer, the generated solution characters were further translated into a trinity of contradictions: 'geometric stability' with 'material dynamicity', 'material dynamicity' with 'biocompatibility', and 'vibrating capability' with '3DP fabricability'. Three design problems were identified correspondingly, with several basic solutions selected. Thirteen super-system criteria, chiefly about bio- and cell cultivation constrains, were identified, which anchors future solution generation. That is, if the super-system criteria are not fulfilled, all other design issues could instantly lose value. We then addressed the third-layer problems, using the TRIZ contradiction matrix to tackle the previously identified problems and select innovation principles to generate potential solutions. Field-based approaches were eventually identified as an essential part of 3DPVS, and smart materials with vibrating or dynamic functionality were perceived as promising scaffold elements. A brief study on the relationship between smart material stimulus and response was conducted, aiming to increase the resourcefulness of further field determination. An analysis of 3DP was also presented, addressing the most fundamental 3DP concerns and design principles. From this layer, five basic conceptual solutions of 3DPVS were proposed: magnetic, mechanical, electric, light and thermal fields, with corresponding 3D printable bio-stimulating materials. Magnetic-based solution has been identified as most promising one at current design stage.

6 CONCPET GENERATION: IMPROVED AND SPECIFIED SOLUTIONS FOR 3DPVS

6.1 Introduction

After generating basic conceptual solutions in Chapter 5, we acquired fundamental ideas about 3DPVS from the super-system to system view. Based on this, this chapter moves the design forward, focusing on the same bone cell culture application, and addressing several important concerns from the system to sub-system levels, as well as tackling some difficult questions that the TRIZ method in Chapter 5 could not satisfactorily solve. In this regard, aside from the first three routes used in Chapter 5, here we demonstrate the implementation of a fourth route—the 3DPVS innovation roadmap—to generate optimal configurations for these detailed, difficult design aspects. Further, the ideal 3DPVS at the current stage is proposed to achieve the trinity of the scaffold's overall functionality of being self-vibratory (vibration-integrated), having a frequency that is finely controllable, and having localised vibration or stimulation enabled. The QFD method will be integrated in the design with TRIZ to better generate conceptual solutions and quantitatively evaluate different requirements, attributes and sub-system components. Further, Chapter 5 chiefly indicated how to achieve self-integrated vibratory properties, yet had limited description of which elements comprise the proposed magnetic-based mechanism. Besides vibratory properties, geometric, mechanical and biological ones must also be addressed, to some extent, to achieve the full GMBV characterisation of the proposed 3DPVS concept. This will be studied in this chapter.

6.1.1 *Logic structure*

The logical process of this chapter, in other words the process of generating improved 3DPVS concepts, is structured as follows, Figure 6.1. For this work, briefly five steps will be conducted, information from literature review in chapter 2 and design initiation in chapter 4 will be partly used as input for Step 1, and the magnetic-based conceptual solution generated in chapter 5 will be used as input for Step 4. Output of Step 5 will be used for evaluation/validation work via computer simulation in next chapter.

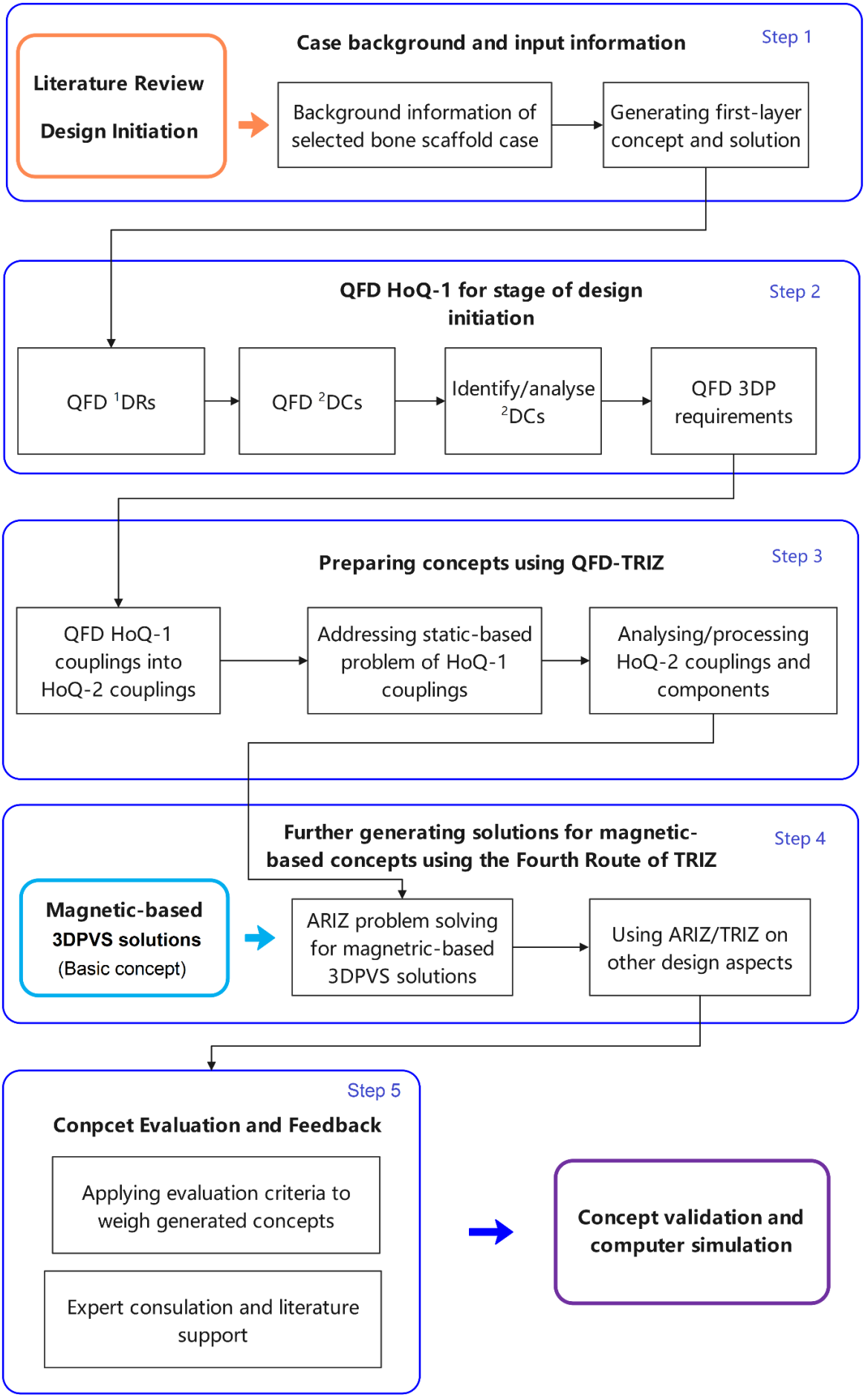


Figure 6.1 Structure for the process of generating 3DPVS improved and specified solutions

6.1.2 *Specification Background and Input Information*

In previous chapter 4, on the fundamental aspects of initiating the conceptual design of 3DPVS, bone cells were selected as the preliminary application of 3DPVS at the current conceptual stage. The design requirements, base model and objective model were identified from a relatively broad view. Fundamental conceptual solutions were generated, with magnetic-based 3DPVS the optimal direction to fulfil these elements. To further concentrate the design focus, a specific cell culture case was used to help understand the solution-generating process by specific real-world end-users. However, the definite requirements of different bone cell culture scenarios could vary one from another, thereby leading to varied conceptual solutions, especially at the system to sub-system level. In terms of design approach, which includes TRIZ-QFD, 3DPVS innovation roadmap and ARIZ, detailed information can be referred to Appendix G.

6.1.3 *Selected Case of Bone Cell Culture Scaffold*

Company A is a Chinese biomedical company focusing on bone cell applications and drug delivery. It focuses on external bone cell culturing and bone cell implantation that achieves regeneration or regrowth of bones that are surgically or accidentally broken. Research Institute B is an institute of biomedical engineering. Research Centre C is a centre for biochemical and nanomaterials located in China. They previously had a project focusing on bone regeneration and bone repair, which applied to leg-lengthening operations for people with disabilities. Part of their objective was to design a novel scaffold product with desired structural and mechanical properties, and good cytocompatibility for bone cell culturing. Mechanical stimulations were necessary to provide dynamic properties for stimulating cell growth. Given that there is no formal methodology for the novel scaffold design, several concerns are presented. The 'trial-and-error' approach in developing a non-traditional scaffold is identified as ineffective and costly. Often, some change in the altered scaffold's characterisation to fulfil one desired aspect can cause other unexpected or undesirable results that disturb the whole cell culture purpose. The leader incentre C stated that:

Change [of scaffolds] under ordinary conditions is difficult because, in wanting to change something, we want to change this one thing only. But everything in the scaffold or cell culturing system is interconnected and every function might be inevitably counterbalanced by some other function or by a whole series of other functions, though we are not aware of this interconnection of the various functions beforehand.

Another researcher at Institute B also remarked that 'a systematic strategy is lacking for tackling with conflicting factors'. From this research's view, this case is interesting. In the following conceptual design, we connect basic conceptual solutions as generated previously, and narrow the end-user 3DPVS product to tailor to this case scenario.

6.1.4 *Overview of Generating Improved and Specified solutions*

Figure 6.3 gives a brief overview of the concept generation process in this chapter. Different color blocks represent different design aspects, namely, magnetic-field, materials, geometrics, 3DP and localization. Detailed knowledge will be thoroughly discussed in following sections.

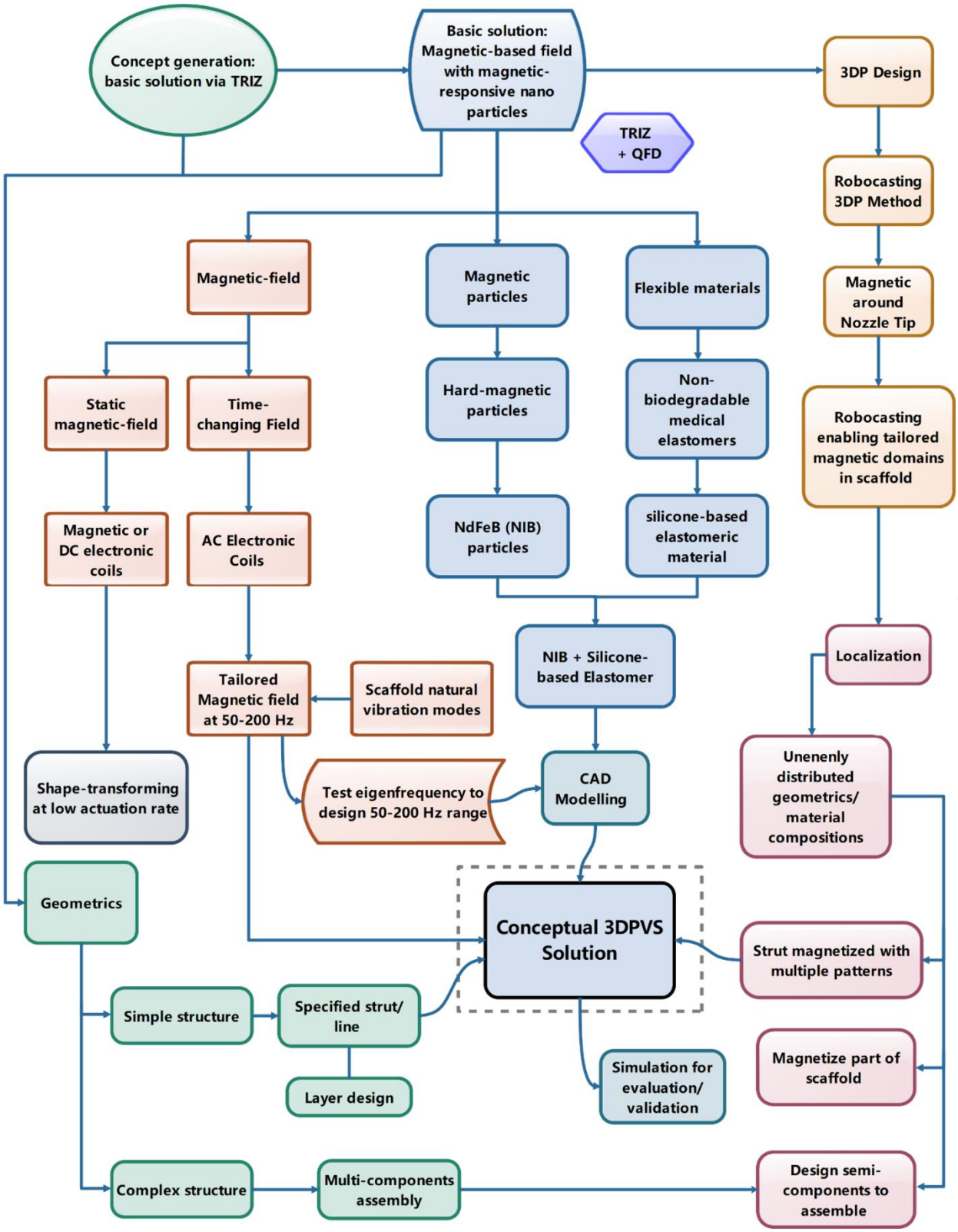


Figure 6.2 Schematic process of generating conceptual solutions

6.2 QFD HoQ-1 for Stage of Design Initiation

After understanding the case background, QFD can be used to undertake the design process.

6.2.1 *QFD for Analysing Design Requirements*

HoQ helps deliver a list of importance scores for connecting design attributes, and indicates possible design problems by analysing the Roof. There are three most vital requirements of design input, as shown in Table 6.1.

Table 6.1 Score of end-user required bone vibratory scaffold, without dynamic properties

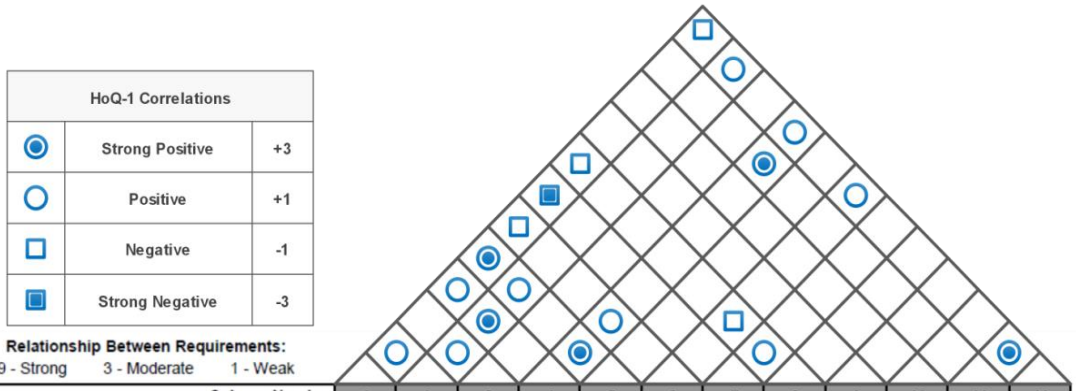
Number	End-user requirements	QFD score (1–9)
1	Ability to maintain blood/liquid medium supply	9
2	Ability to self-vibrate partly or largely	9
3	Ability to remain stable in response to environmental factors	6

In addition to these three most vital requirements, there are other criteria that the proposed 3D bone cell scaffold must fulfil. Integrating with novel dynamic properties, the criteria are identified as shown in Table 6.2.

Table 6.2 List of HoQ system-level importance scores for selected case scenario

Number	Design requirements [1]	(Four-point Likert)	QFD score
1	Acts as template for 3D bone cell growth	4	9
2	Absorbs (or not) during bone cell culturing process	2	7
3	Biocompatible (nontoxic)	4	9
4	Composed of 3DP bioactive and dynamic material	3	7
5	Surface properties promote cell adhesion	4	8
6	Provides sufficient mechanical properties that match host bone cells	3	7
7	Transmits fluid stress across scaffold itself	3	7
8	Transmits compressive stress	3	8
9	Has fabrication process that allows scaffold to fit a differing range of geometries	4	9
10	Is sterilisable and meets FDA standards	4	9
11	Provides dynamic stimulation when bone cells grow	4	9
12	Localised dynamic movements of scaffold	4	9

Given this list of criteria, we can generate the first set of HoQ, HoQ-1, as shown in Figure 6.3.



HoQ-1 Correlations		
◉	Strong Positive	+3
○	Positive	+1
□	Negative	-1
■	Strong Negative	-3

Relationship Between Requirements:
9 - Strong 3 - Moderate 1 - Weak

			Column Number	1	2	3	4	5	6	7	8	9	10	11	12
			Max Relationship Value in Column	9	3	1	9	9	9	3	3	3	3	3	3
			Requirement Weight	750	112.5	62.5	450	337.5	525	300	250	225	112.5	187.5	187.5
			Relative Weight (%)	21.43	3.21	1.79	12.86	9.64	15.00	8.57	7.14	6.43	3.21	5.36	5.36
			Difficulty in 3DPVS Design (0=Easy to Accomplish, 10=Extremely Difficult)	5	5	5	5	5	5	5	5	5	5	8	8
			Minimize (▼), Maximize (▲), or Target (x)	▲	▲	x	x	▲	▲	x	x	x	x	x	x
			Target or Limit Value	9	7	9	7	8	6	7	7	8	9	9	9
Row Number	Max Relationship Value in Row	Relative Weight	Design Requirements (DRs) \ Design Attributes (DAs)	Act as template for 3D bone cell growth	Does (or not) resorb when bone cells are cultured	Is biocompatible (non-toxic)	Composed of 3DP bioactive & dynamic material	Surface properties promote cell adhesion	Provide sufficient mechanical properties that match host bone cells	Transmit fluid stress across scaffold itself	Transmit compressive stress	Have a 3DP fabrication process that allows scaffold to fit a differing range of geometries	Be sterilizable and meet FDA standards	Provide dynamic stimulation when bone cells grow	Localized vibration/dynamic movements of scaffold
1	9	37.50	Ability to maintain a blood/(Liquid medium) supply	9			1	9	3	3	3	3	3		
2	9	37.50	Ability to be self-vibratory/ partly or largely	9	3	1	9		9	3	3	3		3	3
3	3	25.00	Ability to remain stable in response to environmental factors	3		1	3		3	3	1			3	3

Figure 6.3 HoQ-1 regarding end-user three vital requirements into critical design requirements

Calculating design attributes (DAs) into comparative importance levels (CILs), using CIL equations, gives the result: CIL = [0.21, 0.03, 0.02, 0.10, 0.15, 0.09, 0.07, 0.06, 0.03, 0.05, 0.05]. From HoQ-1, DAs [1] with the five highest scores indicate the scaffolds' ability to act as a template for 3D bone cell growth, mechanical properties, 3DP bioactive materials, transmission of fluid stress and transmission of compressive stress. The following relative importance values, 21, 15, 13, 10 and 9, were generated, contributing to nearly two-thirds of the overall design intent. The fourth DA—3DP biomaterial or dynamic material—at the current stage can be regarded a design restriction, which would be prioritised after solving conflicts of the other couplings. Material-based conflicts have been identified when using magnetic-based nano-bio-stimulating materials, as discussed in Chapter 5. Among the whole couplings based on these DAs, several have been previously studied, which from another angle supports the intention to design 3DPVS based on the QFD coupling-identifying process. In brief, Table 6.3 shows a range of couplings identified that can be considered the most vital for the current design focus.

Table 6.3 HoQ-1 identified couplings in current case scenario

Coupling	Coupling comparison		Attribute no.
	DAs-A	DAs-B	X-Y
1	Template for 3D bone growth	Resorbs as bone is repaired	1-2
2	Template for 3D bone growth	Composed of bioactive material	1-4
3	Template for 3D bone growth	Surface properties support cell adhesion	1-5
4	Template for 3D bone growth	Mechanical properties match host bone	1-6
5	Template for 3D bone growth	Transmits fluid shear stress	1-7
6	Template for 3D bone growth	Transmits compressive stress	1-8
7	Resorbs as bone is repaired	Biocompatible (nontoxic)	2-3
8	Resorbs as bone is repaired	Composed of bioactive material	2-4
9	Resorbs as bone is repaired	Surface properties support cell adhesion	2-5
10	Composed of bioactive material	Surface properties promote cell adhesion	4-5
11	Composed of bioactive material	Mechanical properties match host bone	4-6
12	Surface properties promote cell adhesion	Dynamic stimulation	5-11
13	Mechanical properties match host bone	Transmits compressive stress	6-7
14	Transmits fluid shear stress	Transmits compressive stress	7-8
15	Mechanical properties	Bioactive dynamic materials	6-11
16	Composed of bioactive material	Dynamic stimulation	4-11
17	Dynamic stimulation	Transmits compressive stress	11-7

Criteria for 3DPVS: Based on the systematic study of design initiation in Chapter 4, the basic evaluation system can be identified in Figure 6.4, which is summarised in the form of positive, neutralising and negative forces/elements within the 3DPVS design. This corresponds with TRIZ-based SFMA and ISS, which use the same trinity-force structural analysing method.

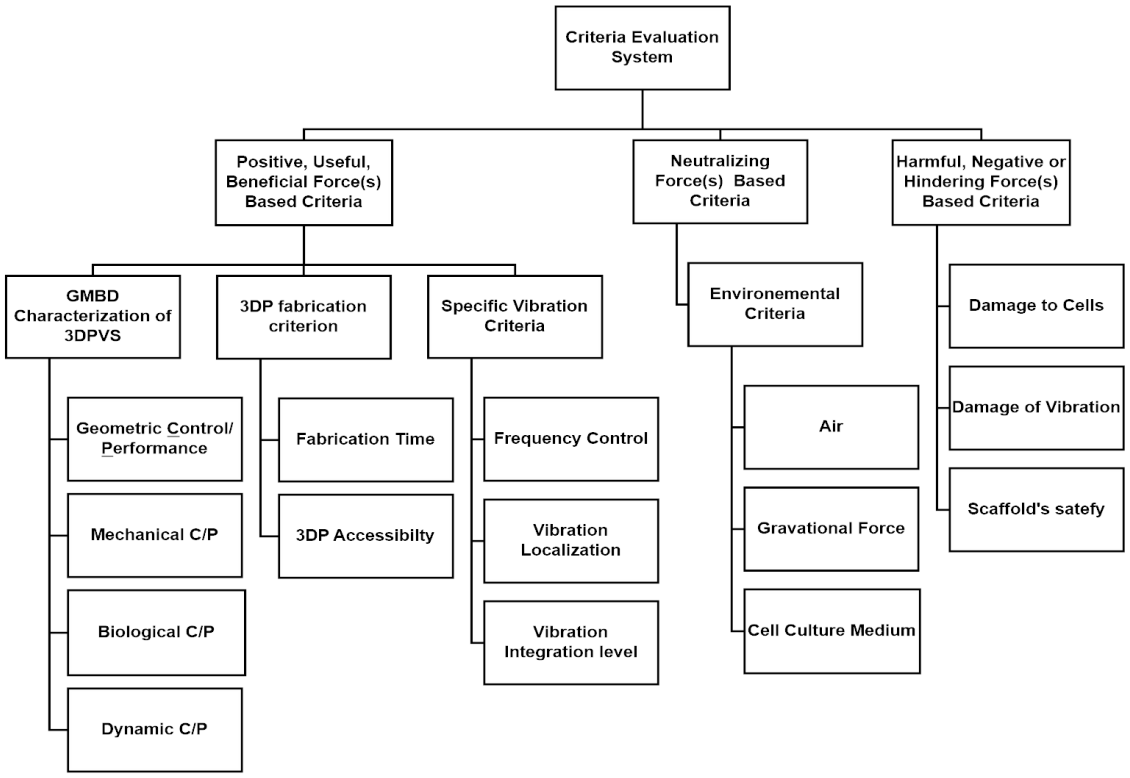


Figure 6.4 Structure of criteria system for 3DPVS conceptual design

Predictability of shape changes: The capability to roughly or accurately predict the final shape under the influence of magnetic interaction is vital to guide the design of the functional structures of 3DPVS based on programmed shape changes.

6.2.2 *QFD to Analyse Design Components*

Based on design initiation, design components (DCs) can be identified, as sub-system 3DPVS elements of GMBV characterisation. The comprehensive illustration is made in *Appendix B*. Following this, we can establish HoQ-2, which focuses on DAs, as shown in Figure 6.5. Within HoQ-2, the weight of each DC will vary in different bone cell culturing applications. In the current case, the weight of each DC is marked with a nine-score hierarchy, where '5' means that the DC plays a neutral role in the 3DPVS design, although it might be valuable in traditional scaffold engineering, and '9' indicates 'significantly valuable' and should be prioritised in the current design process.

When analysing the graphic comparison of different DAs, the basic conclusion can be drawn that 'pore body diameter', 'pore throat diameter', 'strut thickness', 'textural porosity' and 'fluid flow mediated wall shear stress' tend to be of relatively high value, compared with the others. When it comes to establishing engineering targets, as discussed, element (XI) in the proposed HoQ-2 will be discussed in a later section.

Relationship Between DAs and DCs: 9 - Strong 3 - Moderate 1 - Weak	Column Number (DCs)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36
	Requirement Weight	359.2	468.4	374.5	450	349	312.2	254.1	165.3	352	236.7	251	125.5	454.1	142.9	232.7	193.9	175.5	220.4	229.6	229.6	232.7	282.7	282.7	245.9	151	174.5	378.6	256.1	238.8	273.5	140.8	120.4	255.1	266.3	89.8	208.2
	DRs Relative Weight (%)	3.92	5.11	4.08	4.91	3.80	3.40	2.77	1.80	3.84	2.58	2.74	1.37	4.95	1.56	2.54	2.11	1.91	2.40	2.50	2.50	2.54	3.08	3.08	2.68	1.65	1.90	4.13	2.79	2.60	2.98	1.54	1.31	2.78	2.90	0.98	2.27
	Difficulty in 3DPVS Conceptual Design (0=Easy to Accomplish, 10=Extremely Difficult)	7	7	7	7	6	8	8	7	8	7	7	6	8	7	7	7	7	6	5	5	7	8	9	8	8	8	9	9	9	9	9	8	9	9	8	6
	Minimize (▼), Maximize (▲), or Target (x)	x	x	x	x	▲	x	x	x		x	x	x	x								x	x	▲	x	▲		▲	▲	x	x	▲	▼	x	x		x
	Target or Limit Value	9	9	8	8	8	6	6	7	6	9	9	6	6	7	6	6	5	5	5	5	7	7	8	9	8	6	9	7	9	8	8	9	8	9	6	9
Row Number (DAs)	DAs Relative Weight (%)	3DPVS Design Components (DCs) / Design Attributes (DAs)	Open porosity	Pore body diameter	Pore throat size	Strut thickness	Pore geometry (shape)	Pore orientation	Specific surface area	Surface roughness	Textural porosity	Compressive strength	Stiffness (young's modulus)	Fracture toughness	Fluid flow mediated wall shear stress	Flow perfusion rate	Cyclic compression	Cyclic compression induced fluid flow	Rate of ion dissolution	Ion dissolution concentration	Accumulation in major organs	Rate of excretion in urine	Osteo- induction, conduction, integration	Osteoblast infiltration	Cell Proliferation (Osteoblast)	Cell adhesion (Osteoblast)	Nutrients transferring	Angiogenesis	Capable of dynamic stimulation	Vibrational control	Movement of scaffold	Localized dynamicity/ vibration	Vibration frequency	Low Dynamicity/vibration Cell Damage	Personalized scaffold geometry/architecture	Smart Material/ Dynamic materialFabricability	Mass producibility	FDA approved
1	9.18	Act as template for 3D bone cell growth	9	9	9	9	9	9	9	3	3	1	1	1	9	3	3	9					3	9	9	3	3	3	3	1	1	1	1	1		1		
2	7.14	Absorbs (or not) during bone cell culturing process	3	3	1	3			3	3	9				1			1	9	9	9	9	1	3	3	1	1	3		3	1	1						3
3	9.18	Is biocompatible (non-toxic)										1	1	1	1			1	1	1	9	9		1	1	3		1		1	1				1	3		9
4	7.14	Composed of 3DP bioactive & dynamic material	1						3	3	3	1	3	1	9	1			3	9			9	9	9	9	3	3	9	9	3	9	3	3	1	9	1	3
5	8.16	Surface properties promote cell adhesion	3	3	9	3	3	3	3		9				9	1			9	9			9	9	9	9	9	9	1		1			3				
6	7.14	Provide sufficient mechanical properties that match h	3	9	3	9	3	3	3	9	9	9	9	9	9		3	3	1				3	1	1	1			3	1	3			1	9			
7	7.14	Transmit fluid shear stress across scaffold itself	9	9	9	9	9	9	3	3	9				9	9							3	1	1	3	3	3		1				3				
8	8.16	Transmit compressive stress	9	9	3	9	9	9	3			9	9	1	3	1	9	9					1	1	1	1			9		3							
9	9.18	Have a fabrication process that allows scaffold to fit a	3	9	9	9	3	3			3	1	1	1	1	1							1	1					9	3	3	3	3		9	3	9	
10	9.18	Be sterilizable and meet FDA standards										1	1	1						1	9	9							1					1		9		9
11	9.18	Provide dynamic stimulation when bone cells grow	1	3	1	1	3	1	1	1	1	3	3	1	3	1	9								1	1			9	3	9	9	9	3	1	3		
12	9.18	Localized dynamic movements of scaffold	3	3	1	3	3	1	3			3	3		3	1	3												1	9	3	9			9	3		

Figure 6.5 3DPVS conceptual design HoQ-2, DAs with DCs

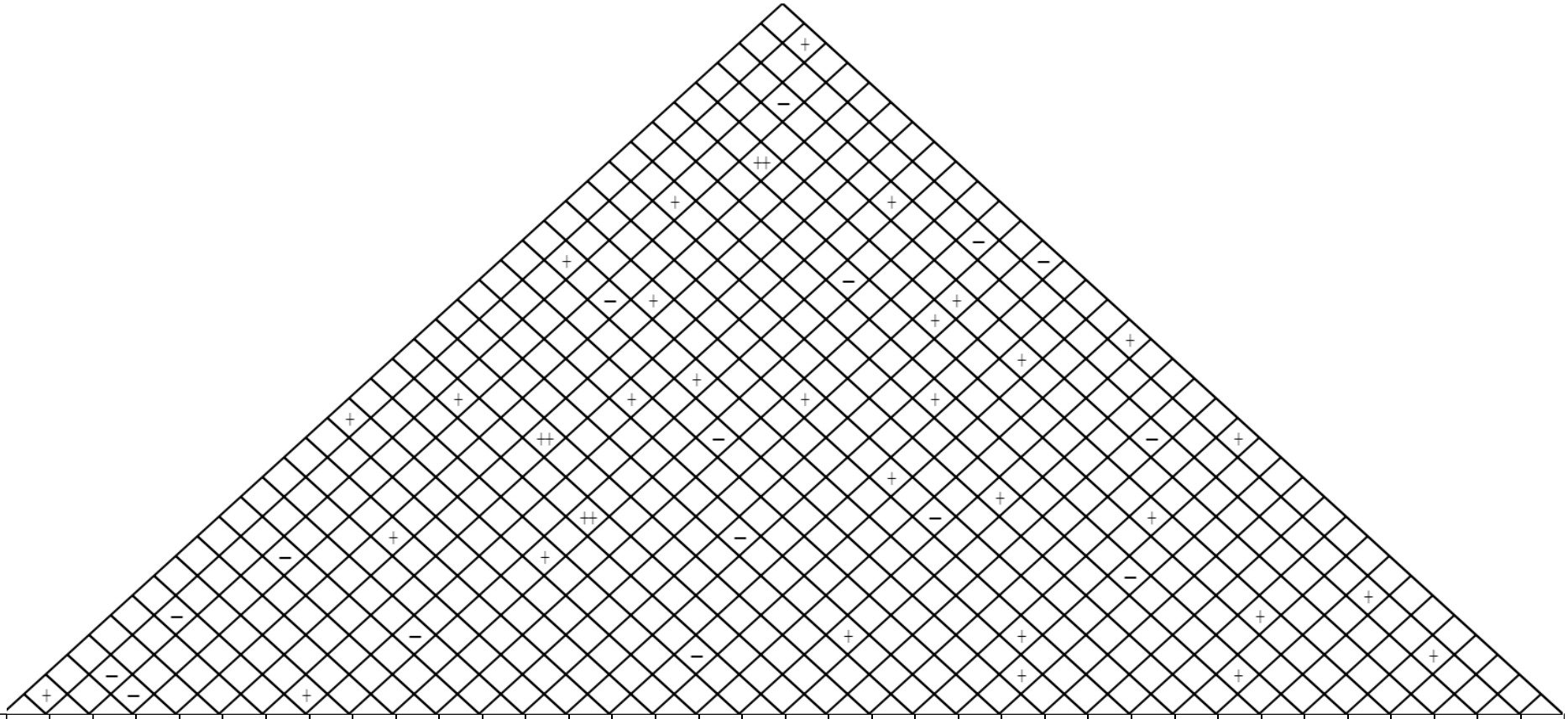
6.2.3 *Identify and Analyse Design Couplings in HoQ-2*

In terms of the relationship between two elements in a coupling, a five-point scale is used to indicate the coupling relationship from ‘very weak’ to ‘very strong’. As discussed, QFD has been newly introduced into scaffold design, and detailed knowledge regarding the relationship between couplings may be unknown or inconclusive. From literature reviews and seeking experts’ opinions, the existence and intensity of coupling is preliminarily judged through whether multiple sources confirm that the coupling exist. We first identify the level as positive (+) or negative (-), and then analyse the existence of strong positive (++) or strong negative (--), see Table 6.4. However, a conclusive answer regarding this requires further research. Next to this, the roof of HoQ-2 can be built, as shown in Figure 6.6

Table 6.4 the relationship between design couplings

Design couplings and their interconnections	Relationship rating	Conceptual design weight
Couplings in pore body diameter		
Strut thickness	++	4
Specific surface area	+	3
Rate of ionic dissolution		
Osteoconduction	+	1
Osseointegration	+	1
Osteoblast/cell proliferation	+	1
Osteoblast/cell adhesion	+	1
Angiogenesis		
Fluid flow mediated wall shear stress	+	1
Vibrational control	++	4
Couplings in pore throat diameter		
Strut thickness	++	4
Osteoconduction		
Osteoblast/cell infiltration	-	1
Couplings in strut thickness		
Rate of ionic dissolution	-	1
Compressive strength		
Stiffness (Young’s modulus)	++	4
Pore throat diameter	+	4
Pore body diameter	+	4
Couplings in pore geometry		
Compressive strength	+	4
Cyclic compression		
Coupling in specific surface area of scaffold		
Textural porosity	+	2
Rate of ionic dissolution		
Stiffness (Young’s modulus)	+	4
Pore body diameter	++	4
Coupling in pore orientation		
Compressive strength	+	4
Cyclic compression		
Couplings in textural porosity		

Specific surface area	+	2
Rate of ionic dissolution		
Coupling in surface roughness		
Osseointegration	+	3
Osteoblast/cell proliferation	+	3
Osteoblast/cell adhesion	+	3
Rate of ionic dissolution couplings		
Ionic dissolution concentration	-	1
Textural porosity	+	3
Specific surface area	++	4
Strut thickness	+	4
Pore body diameter	++	4
Ionic dissolution concentration couplings		
Accumulation in organs	--	1
Osteoinduction	-	1
Osseointegration	-	1
Osteoblast/cell proliferation	-	4
Osteoblast/cell adhesion	-	3
Osteoblast/cell apoptosis	-	1
Rate of ionic dissolution	-	1
Accumulation in major organs couplings		
Rate of excretion on urine	+	1
Ionic dissolution concentration	+	1
Osteoinduction couplings		
Ionic dissolution concentration		
Fluid flow mediated wall shear stress		
Cyclic compression	+	2
Compression induced fluid flow	+	2
Osteoblast/cell proliferation couplings		
Osteoblast/cell adhesion	++	3
Mass transfer of nutrients		
Angiogenesis	-	
Compressive strength	++	3
Fluid flow mediated wall shear stress		
Ionic dissolution concentration		
Surface roughness	+	2
Pore body diameter	+	4
Fluid flow mediated wall shear stress couplings		
Cyclic compression	-	1
Personalised geometry	+	4
Flow perfusion rate		
Osteoblast/cell proliferation	+	1
Osteoblast/cell adhesion	+	1
Osteoinduction	+	1
Pore body diameter	+	3



Column Number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36
3DPVS Design Components (DCs)	Open porosity	Pore body diameter	Pore throat size	Strut thickness	Pore geometry (shape)	Pore orientation	Specific surface area	Surface roughness	Textural porosity	Compressive strength	Stiffness (young's modulus)	Fracture toughness	Fluid flow mediated wall shear stress	Flow perfusion rate	Cyclic compression	Cyclic compression induced fluid flow	Rate of ion dissolution	Ion dissolution concentration	Accumulation in major organs	Rate of excretion in urine	Osteo- induction, conduction, integration	Osteoblast infiltration	Cell Proliferation (Osteoblast)	Cell adhesion (Osteoblast)	Nutrients transferring	Angiogenesis	Capable of dynamic stimulation	Vibrational control	Movement of scaffold	Localized dynamicity/ vibration	Vibration frequency	Low Dynamicity/vibration Cell Damage	Personalized scaffold geometry/architecture	Smart Material/ Dynamic materialFabricability	Mass producibility	FDA approved

Figure 6.6 Roof of HoQ-2 illustrating relationships of couplings and DAs

At this point, we have transferred from HoQ-1 to HoQ-2. At the conceptual design stage, prioritised couplings are selected out, while others are applicable in future detailed design. Simple, easily-solved couplings can be addressed using processes such as TRIZ, ACM and IPA—in other words, the first three routes of the established four-route TRIZ-based method. The fourth route comes into play afterwards, dealing with the unsolved difficult scenarios.

6.2.4 *QFD to Analyse 3DP Requirements*

To estimate the relative importance (RI) among 3DP parameter requirements for 3DPVS, an interrelation matrix can be used, Table 6.5.

Table 6.5 Importance level of 3DP characterisation for 3DPVS

3DP charact.	Scaffold app.	Structural strength	Scaffold custom.	Fabric. speed	Smart material work.	Precision	Thermal resist.	Complex geo. shaping	Reliability /safety
Scaffold applicability	1	1	2	1	1	1	½	1	1
Structural strength	1	1	1	½	1	1	½	1	1
Scaffold customisation	½	1	1	1	1	1	½	1	½
Fabricating speed	1	2	1	1	2	1	½	1	½
Smart material workability	1	1	1	½	1	2	1	2	1
Precision	1	1	1	1	½	1	½	1	1
Thermal resistance	2	2	2	2	1	2	1	2	2
Complex Geometric shaping	1	1	1	1	1	1	½	1	1
Reliability/ safety	1	1	2	2	1	1	½	1	1
RI	0.1086	0.1257	0.1371	0.1143	0.0971	0.1257	0.0629	0.1257	0.1029

This matrix is an instrument evaluating the relationships of dependency or RI among various demands or concepts. It helps define design priorities and establish the optimal sequence of actions that designers could follow. In a dependency matrix, the variable on the columns is considered an unchangeable cause, while the figure in rows is the effect. The dependence can be weak, medium or strong from accountable values. The RI matrix used in the current context evaluates RI among all variables. The following criteria are preliminarily used: (1) the row element has the same importance as Column 1; (0.5) the row element is less important than Column 1; and (2) the column element is more important than Row 1. The decision to use this trinity benchmark is made by analysing the literature regarding importance levels of 3DP elements in scaffolds, as well as seeking suggestions from scaffold engineering experts. Using this instrument, the highest values of ‘sums per row’ indicate the likely most important

variable that tends to have more influence on others. From this, we can identify 3DP elements used in this context with greater understanding. From the previous literature on 3DP, several vital characteristics, which will be used for the current design, are identified as follows. The dependence/independence matrix is built as Table 6.6.

1. cell scaffold applicability
2. structural strength
3. scaffold customisation
4. fabricating speed
5. smart material (SM) workability
6. precision
7. thermal resistance
8. complex geometric shaping
9. reliability/safety.

Table 6.6 Dependence and independence matrix of 3DP characterisation for 3DPVS

3DP characteristic no.	1	2	3	4	5	6	7	8	9	Dependence
1		1	5	5	1	3	1	3	5	0.1206
2	0		1	1	3	3	1	3	3	0.0754
3	3	5			5	3	1	5	1	0.1156
4	5	1	5	5	5	5	3	5	3	0.1859
5	3	1	3	3		1	5	1	1	0.0905
6	5	3	3	3	3		1	3	1	0.1106
7	0	3	1	1	1	1		0	1	0.0402
8	5	5	3	3	3	3	1		3	0.1307
9	5	5	3	3	1	3	3	3		0.1307
RI	0.130	0.120	0.120	0.120	0.110	0.110	0.085	0.115	0.090	

From analysing the matrix, the chief QFD 3DP parameters related to current design can be identified as:

1. scaffold applicability
2. structural strength
3. SM workability
4. complex geometric shaping.

Detailed information of these 3DPVS characters was studied in the literature review (Yuan, Xing & Hsu 2018a). In the following process, structural strength is selected as the possible element in ‘couplings’ when using the TRIZ-based methodology. For 3DP precision, this will be addressed in detailed design. Scaffold applicability is about 3DP magnetic-based stimulating scaffold on external bone cell culture. The SM issue will also focus on considering the 3DP fabricability of the identified magnetic materials.

6.3 Preparing Concepts Using QFD-TRIZ

This section addresses several concerns regarding HoQ-1 and HoQ-2 based on established TRIZ-QFD. This helps generate new concepts and provide enhanced vision for future design questions.

6.3.1 *QFD HoQ-1 Couplings into HoQ-2 Couplings*

We previously identified design requirements (DRs) from end-users, DAs from the current 3DPVS conceptual development context, and DCs of the specified sub-system GMBV characteristics. As such, HoQ-1 can be transferred to HoQ-2, with illustration diagram shown in Figure 6.7.

6.3.2 *Addressing Static-based Problem of HoQ-1 Couplings*

Given the four most important requirement attributes, the nature of the contradiction related to this pairing is system contradiction, termed Contradiction 2. Thus, Route 2 will be used, supported chiefly by ACM and IPA. In the first place, these four DRs must be placed into the appropriate form for TRIZ, as shown in Table 6.7.

Table 6.7 Transforming five prioritised DRs [1] into TRIZ parameters

DAs [1]	TRIZ parameter
Template for 3D bone growth	36. Complexity of device
Mechanical properties match host bone	14. Strength
Transmit fluid stress	11. Stress or pressure
Transmit compressive stress	10. Force
Manufacturing	29. Manufacturing precision

From analysing the 13 couplings previously identified, Couplings 4, 5 and 6 illustrate the highest value to be addressed with priority, given their close relation to these DRs. Possible conflicts in these three couplings belong to system contraction, and the resolving strategy could be Route 1, using a 1 × 1 ACM. The summarised principle searching result for solving problems in couplings is shown in Table 6.8.

Table 6.8 DRs couplings of HoQ-1 with potential solutions referred to TRIZ innovation principles

Coupling no.	Statement of coupling conflicts	Relationships		TRIZ parameter	Possible innovation principles
4	Preferred increase in template porosity for desired bone cell penetration and bone in-growth, but usually causes compromised stiffness of scaffold	↑	Template for 3D bone growth	36. Device complexity	2. Separation 13. Other way around 28. Mechanical interaction substitution
		↓	Mechanical properties match host bone	14. Strength	
5	Desired increase in template porosity by random pore anisotropy, while may lead to negative creation of zones of random fluid shear stresses	↑	Template for 3D bone growth	36. Device complexity	19. Periodic action 1. Segmentation 35. Parameter changes
		↓	Transmit fluid stress	11. Stress	

6	Desired increase in template porosity could result in increased possibility of micro-cracking when scaffold is under compression	↑	Template for 3D bone growth	36. Device complexity	26. Copying 16. Partial or excessive actions
		↓	Transmit compressive stress	10. Force	
16	Dynamic materials vs 3DP manufacturing	This part was studied in Chapter 5, which also included elements such as dynamicity vs biocompatibility and dynamicity vs 3DP fabricability			

For this set of couplings, the problem-solving process is similar to that conducted when generating the basic conceptual solutions of 3DPVS using TRIZ. Input of the solutions will be used, either directly or indirectly, for further-level design process.

6.3.3 *Analysing and Processing HoQ-2 Couplings and Components*

Regarding the couplings and contradictions in HoQ-2, some could have been addressed by Routes 1 to 3; however, because it is a complicated contradiction-solving scenario, which also contains contradictions beyond Contradictions 1, 2 and 3, searching for a solution via the fourth route is preferable.

Relative weight of scaffold DCs. The weight values for corresponding DRs were presented in Figure 6.5. The top seven DRs identified by HoQ-2 include pore body diameter (5.11), fluid flow mediated wall shear stress (4.95), strut thickness (4.91), capability of dynamic stimulation (4.13), pore throat size (4.08), open porosity (3.92) and textural porosity (3.84), where the figures display the relative weight/importance ratings. We find that, for both the traditional 3D static scaffold and novel 3DPVS, QFD can be used in a similar process, and, except for dynamicity-based, the top parameters prioritised in the design remain the same. The value of using QFD shows that DRs/DAs can be identified following a methodology that is repeatable and easily manageable. If there is any disagreement, designers can verify the route through which weights were scored. New DRs or DAs can be added effectively based on established ones.

Analysis based on engineering targets. The scaffold engineering targets—3DPVS characteristic components—are also established through QFD. Difficulty in data interpretation derives from identifying a definite value, as variations exist from designers when undertaking research with variable objectives. Further, when considering the number of different pore body diameters and pore throat sizes, the traditional view of pores and interconnections might be beneficially moved away. Instead of the complexity of a bimodal pore scaffold design with different pore throat diameters acting as interconnections, as is the usual focus of previous designers, combining pore bodies with pore throats in a series of continuous trans-microstructure channels might be an easier, effective alternative. These channels could have controllable tortuosity, which helps create a set wall shear stress under fluid perfusion conditions, which can be considered useful when a dynamic function must be integrated in traditional static components. As such, a scaffold structure consisting of parallel repeated

spiral tubular membranes could be a potential for 3DPVS. Circular spiral columns manufactured by 3DP, such as femtosecond laser microfabrication, may be another useful design candidate.

Previously, to achieve required flow conditions for bone regeneration, scaffolds were most likely seeded with cells and incubated inside a bioreactor or connected with an external mechanical vibrator. This enabled effective perfusion and helped control culture rate, despite the stimulation being continuous or pulsatile. Before 3DPVS was proposed, this seemed the best way to achieve identified perfusion rates or wall shear stresses. It required a hydraulic piston-like incubator to exert a controllable pressure regimen when achieving cyclic compression under bioreactor-based vibration conditions. Currently achieving this seems uncertain. The design of 3DPVS may offer new inspiration in this direction.

Analysing HoQ-2 couplings. From the roof of HoQ-2, the quantity of 'couplings' further indicates the complex task of the scaffold's microstructure design. Several trends are revealed from the groupings of identified couplings. First, osteogenic processes and material characteristics can be coupled with porosity parameters. Second, bioresorption kinetics, which are not used for the current 3DPVS design, yet are still of great significance for TE, could also be coupled with osteogenic processes. As expected, all these couplings have positive interconnections and could be incorporated with each other. Further, of numerous couplings, porosity-based parameters themselves have strong negative couplings, possibly because of conflict between pore struts and the dimensions of internal voids. Larger void spaces easily result in smaller struts, and vice versa, which might cause a design problem for both traditional static scaffolds and dynamic scaffold 3DPVS. The reason may be that larger struts are integral to the overall strength and stiffness of the scaffold itself, yet larger struts also mean smaller dimensions are available to aspects such as fluid flow and cell growth.

HoQ-2 connected with TRIZ-based four-route method. We have previously discussed the benefit of using QFD HoQ-2 for generating thorough scaffold characteristics and providing design inspirations. To proceed further with this design concept, supporting tools are required that organise the identified DRs/DAs into an integrated scenario that is practical and viable. The value and reapplication of this process can be clearly illustrated as Figure 6.7. The identified couplings in HoQ-2 provided greater specificity than their previous counterpart. That is, this process provides higher clarity of interactions based on tangible DRs in scaffold engineering. Further, the analysis results of HoQ-2 can be directly used by the TRIZ-based method proposed in this research, which helps finalise the following conceptual generation. That is, easily-decodable contradictions can be addressed by Routes 1 to 3, while the remaining sophisticated ones can be solved by the fourth route. Following the concepts created from this section, we next use the fourth route—the 3DPVS innovation roadmap—to address the remaining conceptual design issues, which tend to be complex or unsolvable by the first three routes of the TRIZ method.

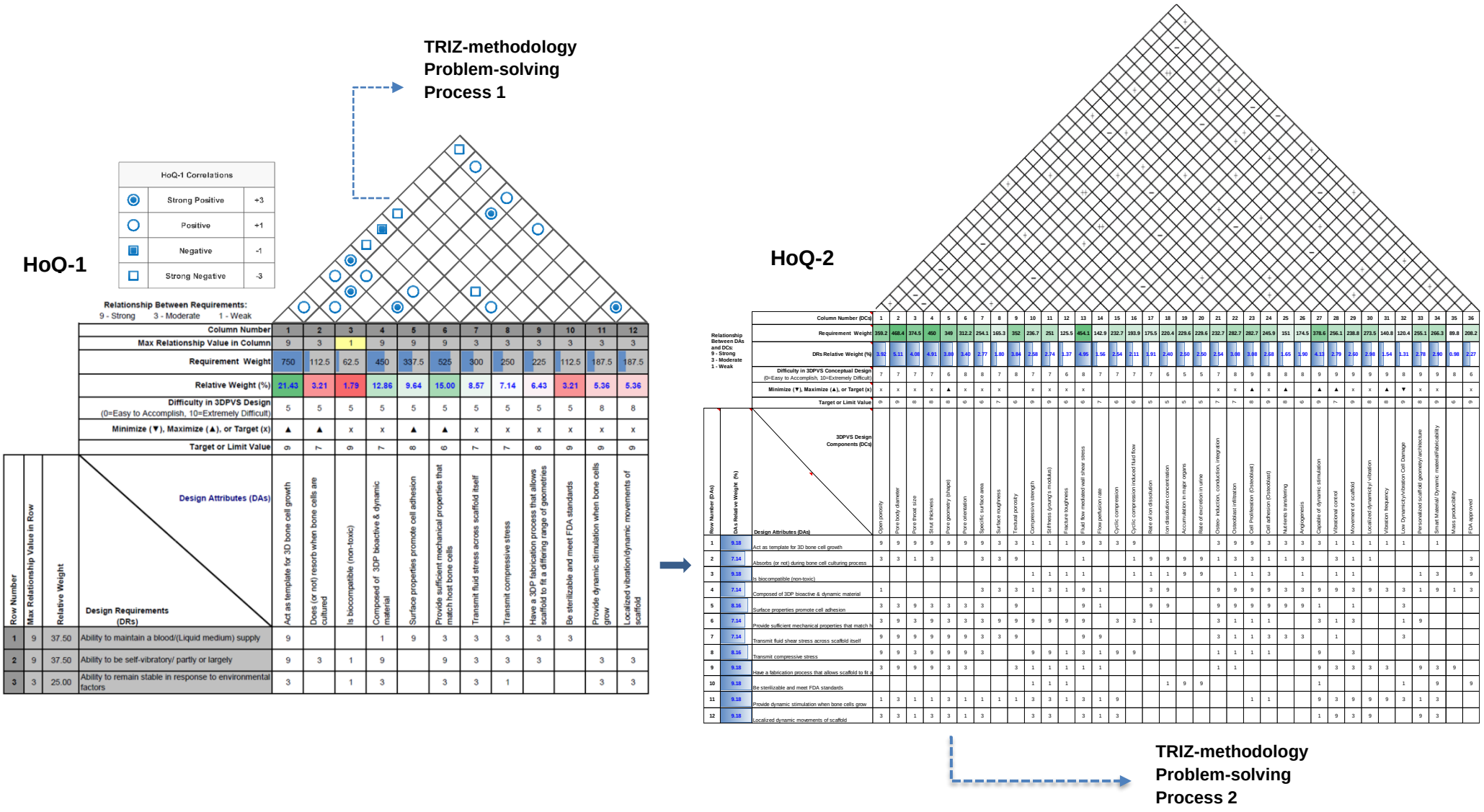


Figure 6.7 Summary diagram of HoQ-1 links to HoQ-2, QFD process in 3DPVS conceptual design

6.4 Further Generating Solutions for Magnetic-based Concepts Using Fourth Route of TRIZ-based Method

The 3DPVS innovation roadmap, as the fourth route of the proposed TRIZ method for the 3DPVS conceptual stage, was previously introduced. Its essential contents have been tailored for the 3DPVS context. The developed algorithm includes three parts/stages, bridging design initiation, concept generation and concept evaluation. Given the complexity of the design algorithm, only the vital elements that help solidify concept generation will be used, in the following sections. Detailed knowledge about TRIZ and ARIZ can be referred to Appendix G-8.

6.4.1 *ARIZ Problem Solving for Magnetic-based Concepts*

I. Part A: Analysing problem and establishing mini-problem model.

Part A helps transform the initial problem, which was considered indefinite, vague or non-structured, into a clearly-constructed model with a simplified description. Particular language that aligns with ARIZ will be used.

A1. Define definite 3DPVS into mini-problems, and formulate the conditioning system.

Table 6.9 Mini-problem definition

	Set 1
a)	The <static cell culture system> for <culturing bone cells in vivo[1]> includes <PU scaffold, bone cells, cell culture liquid, liquid flow>
b)	With limited changes to existing system, <it is necessary to increase scaffold's functionality[3] without a reduction of beneficial effect of PU scaffold on cell culture>
	Set 2
a)	The <dynamic stimulation system> for <generating beneficial effects on bone cells[2]> includes <PU scaffold, bone cells, cell culture liquid, liquid flow, air, external vibrator>
b)	With limited changes to existing system, <it is necessary to create scaffold's new dynamicity[4] without an effect reduction compared with using external vibrator>

Table 6.10 FeHA-based solution transferred into mini-problem

	Set 1
a)	The <static cell culture system> for <culturing bone cells in vivo[1]> includes <PU scaffold, bone cells, cell culture liquid, liquid flow>
b)	With limited changes to existing system, <it is necessary to increase scaffold's functionality[3] without a reduction of beneficial effect of PU scaffold on cell culture>
	Set 2
a)	The <magnetically responsible FeHA-based scaffold> for <generating beneficial stimulating effects on bone cells[2]> includes <FeHA nanoparticles, PU scaffold, bone cells, cell culture liquid, liquid flow, air, external magnetic field>
b)	With limited changes to existing system, <it is necessary to create scaffold's new dynamicity[4] without an effect reduction compared with using FeHA materials>

SC-1: (identity). Formula: If substances or field changes or becomes or be as A, then B happens as positive result; however, C happens as negative result. Table 6.9 illustrates the steps for identifying the mini-problem.

Table 6.10 illustrates the process of transferring a previously generated solution into mini-problem.

A2. Select conflicting pair and define conflicting elements for sub-system.

Identify and formulate the conflicting pair regarding product (S1) and a tool (S2) in the system.

A3. Establish system contradiction and apply ASCM.

Identify four groups of system contradiction (SC). Table 6.11 presents the identified SC groups at A3.

Table 6.11 Identified SC groups at A3

No.	SC description
1 (G-)	***Contradiction in geometrical control***
	G-SC-1: if scaffold's porosity is large+ regarding A, it will increase cell capacity (D-U), but deceases structural stress (I-U);
	G-SC-2: if scaffold's porosity small – regarding A, it will increase structural stress (D-U), but deceases cell capacity (I-U);
2 (M-)	***Contradiction in mechanical composition (material composition)***
	M-SC-1: If scaffold's material composition complex regarding 'A', it will be beneficial for providing multi-functional stimuli on cell culturing (D-U), but hard in providing sufficient stimuli of one particular kind (I-U).
	M-SC-2: If scaffold's material composition is simple regarding 'A', it will be easy for providing definite stimuli selected (D-U), but negative in terms of providing multi-functional stimuli on cells (I-U).
3 (B-)	***Contradiction in biological properties***
	B-SC-1: If the surface of scaffold has higher topology in 'A', then it is helpful for the desired cell attachment 'B' (higher toughness DU), but is negative for the nutrients 'C' passing through pores (IU).
	B-SC-2: If the surface of scaffold has lower topology in terms of 'A', then it is helpful for the nutrients 'C' passing through pores (DU), but is negative for cell attachment 'B' (lower toughness IU).
4 (V-)	***Contradiction in dynamicity and vibration***
	V-SC-1: If scaffold is stimulated continuously for long time, it is beneficial for cell proliferation (D-U) but could not provide the desired favourable synergistic microenvironments (I-U);
	V--SC-2: If scaffold is stimulated with day-night shift breaks, it is positive for creating a favourable synergistic microenvironment (D-U) but cell proliferation could be negatively affected (H);

A4. Select one prioritised SC, detailing analytical model of system conflicts (AMSC).

When analysing contradictions, G-SC-1, M-SC-1, B-SC-1 and V-SC-2, will be selected. First, the main function for geometric control is to increase cell capacity; the main function of the

mechanical property is to provide multi-functional stimuli for cell culturing; the main function of biochemical cues includes that the surface provides with desired cell attachment B for higher toughness; and, for vibration-based functionality, the scaffold mainly enables a favourable synergistic microenvironment, compared with static counterparts. The AMSC formula for these is displayed in Table 6.12.

Table 6.12 Chief SC with corresponding AMSC formula

SC no.	Name	Description	AMSC conflict type
a)	G-SC-1	S1 (D-U) S2-1, S1 (I-U) S2-2	'7'
b)	M-SC-1	S1 (D-U) S2-1, S1 (I-U) S2-2	'7'
c)	B-SC-1	S1 (D-U) S2-1, S1 (I-U) S2-2	'7'
d)	V-SC-2	S1 (D-U) S2-1, S1 (H) S2-2	'4'

The number in quotation marks refers to 11 typical conflicts, as illustrated in an earlier section. Detailed information for core contents regarding 'A1, B1, C1', 'A2, B2, C2', 'A3, B3, C3' and 'A4, B4, C4', as well as function '1' and '2' in each conflict model, will be illustrated later.

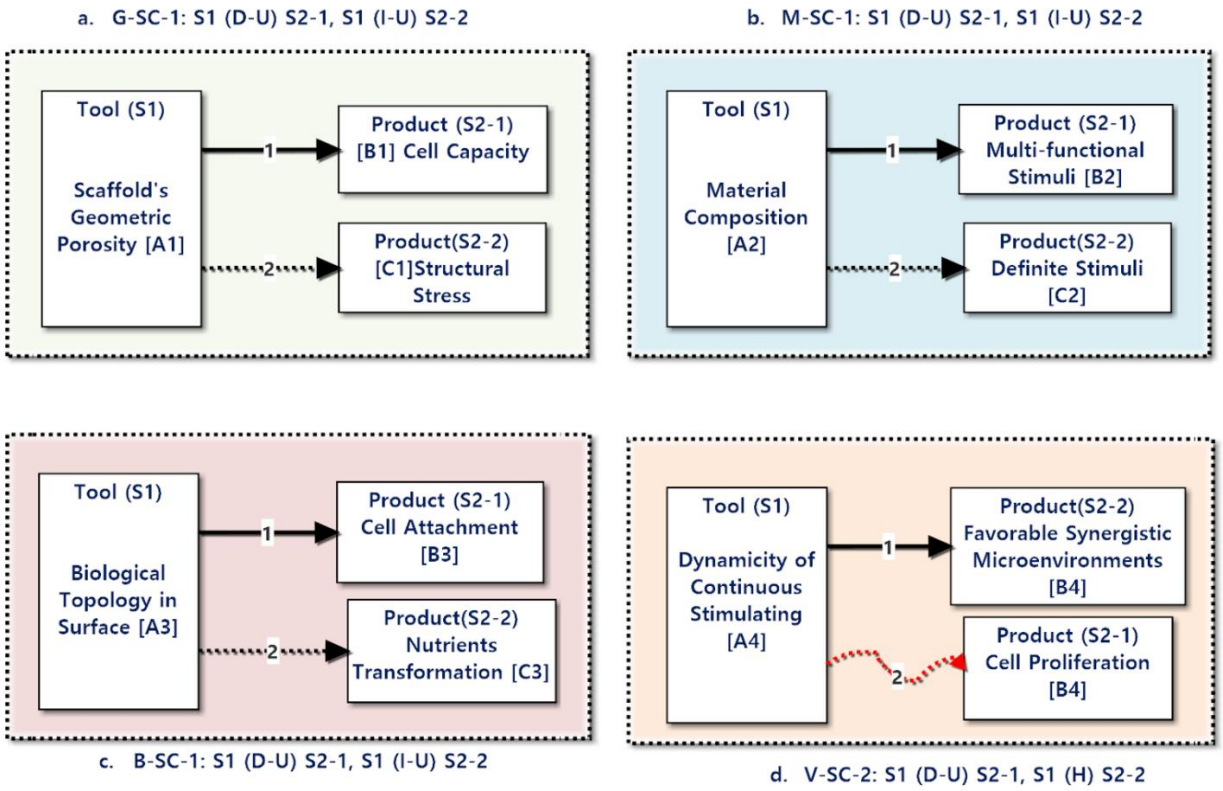


Figure 6.8 Four prioritised contradictions illustrated by conflict diagrams

After four SCs are correctly selected, three parts—IPA, SEA and patent review—come into play. Inventive principles for SC-a, SC-b, SC-c and SC-d, will be selected using IPA of TRIZ. For simplified illustration purpose, the indicated symbol is used. Table 6.13 demonstrates SCs of giving basic solutions.

Table 6.13 SCs with corresponding method and approach to give basic solutions

SC no.	M[1]	SC description
SC-a	IPA	Conflicting parameters: Porosity↑←→Structural Stress↓➔Conflict →(Y8-X11)→(24,35) Inventive Principles: 24, 35→evaluation→(24***, 35*) General solution triggered by IPA, concept G-1: 24^{A} Library units of scaffold that can be finely intersected; General solution triggered by IPA, concept G-2: 25^{B} 3D printing combined with magnetic fields;
	SEA	Scientific Knowledge Data Base will be the chief innovation pool to select proper concepts. General solution triggered by SEA, concept G-3: Fe- magnetic materials. General solution triggered by SEA, concept G-4: Hard-magnetic soft materials.
SC-b	IPA	Conflicting parameters: Material Composition↑←→Chemical Stimuli↓➔Conflict →(Y8-X11)→(24,35) Inventive Principles: 24, 35→evaluation (using Concept Evaluation Methods Ch6) →(24***, 35*) General solution triggered by IPA, concept G-1: 24^{A} : Ferromagnetic materials; General solution triggered by IPA, concept G-2: 25^{B}: Elastic PU materials;
	SEA	General solution triggered by SEA, concept G-3: Ferromagnetic elastic soft material
SC-c	IPA	Conflicting parameters: Porosity↑←→Structural Stress↓➔Conflict →(Y8-X11)→(24,35) Inventive Principles: 24, 35→evaluation (using Concept Evaluation Methods Ch6) →(24***, 35*) General solution triggered by IPA, concept G-1: Composite magnetic materials; General solution triggered by IPA, concept G-2: Support inks for stable 3D structuring;
	SEA	General solution triggered by SEA, concept G-3: external magnetic actuation
SC-d	IPA	Conflicting parameters: localization↑←→Material↓➔Conflict →(Y8-X11)→(24,35) Inventive Principles: 24, 35→evaluation (using Concept Evaluation Methods Ch6) →(24***, 35*) General solution triggered by IPA, concept G-1: variable magnetic domains in different area of scaffold; General solution triggered by IPA, concept G-2: increase structural complexity;
	SEA	General solution triggered by SEA, concept G-3: Printing magnetic domains in different area of scaffold;

[1] Method and approach; '<->' conflicting pair of TRIZ parameters; '->' cause and effect; '↑,↓' ascent or descent of one parameter; '*' priority level.

A5. GMBV conflict set intensification.

Intensifying the conflict of design parameters is a preliminary step towards contradiction solving, as the TRIZ philosophy states. This differs from some traditional designs that intend to smooth or resolve conflicts by creating 'buffers'. As such, reinforced SCs are generated with a specified limit on tools (S1) illustrated on these SCs, respectively, seen in Figure 6.9

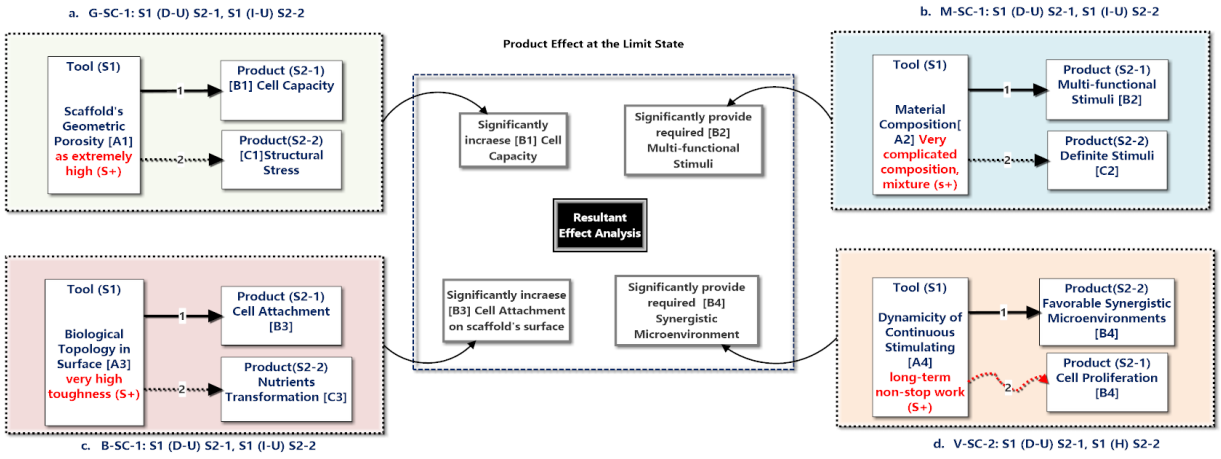


Figure 6.9 GMBV contradiction set with specified limit state

A6. Create specified problem model(s) and hybrid GMBV solution chart.

The problem model of conflicting set, using G-SC-1 as an example, can be formulated into three parts:

1. a tool (S1) of ‘structural porosity’ (high or low porosity size) and two products (S2) of ‘scaffold’s cell capacity’ and ‘scaffold’s structural stress’
2. a scaffold with an extremely high-level porosity increases the maximum capacity for cells cultured inside the scaffold, yet increases the structural stress burdened by the scaffold
3. find an element ‘N’ that preserves the capability of the high porosity scaffold to enable a huge cell capacity, yet does not create a high level of structural stress burdened by the scaffold.

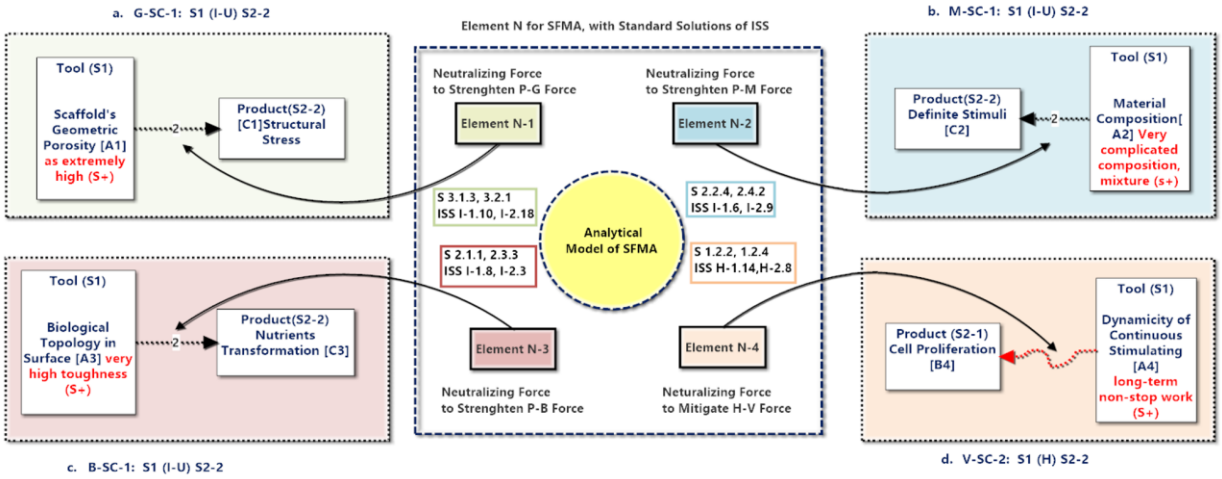


Figure 6.10 Element N for GMBV contradiction set, with TRIZ-based standard solutions and ISS

Other problem models can be formulated similarly, based on analysing the intensified conflict. The model of the problem with element ‘N’ introduced into the GMBV set can be seen in Figure 6.10. In brief, for G-SC, M-SC and B-SC, the solution would be to strengthen the desired yet insufficient functions, while for D-SC it is suggested to use the harm function mitigating solution.

A7. Use ISS to address identified mini-problem model.

In this step, the previously identified AMSC can be transferred into SFMA. Specified fields (F) and a neutralising force (N) would be used in this step. Using both traditional stand solutions and ISS, basic solutions at the current stage can be summarised as follows, Table 6.14.

Table 6.14 Category of SC and solution illustration

SC category	Type[1]	Solution illustration[2]
a. G-SC	TS	3.1.3: Bi- and Poly-systems development of differences inside components; 3.2.1: Transition to the micro-level from the macro
	ISS	I-1.10: Increase the degree of fragmentation by changing original object to a porous or capillary material that will allow gas or liquid to pass through; (5.1.4) I-2.18: Induce the dual- phase state by creating interaction between the parts of the system (5.3.5).
b. M-SC	TS	2.2.4: Transition to Dynamic or Flexible SFM; 2.4.2: Transition to Ferro-substances-field models with Ferro-particles;
	ISS	I-1.6: Change the surface or external layer of the object (object-based, not directly on environment); for example, wearing an armour to protect body. (1.1.3 and 5.1.1.3) I-2.9: Achieve extra action or field by using something already present in system or environment, as the generator of the extra fields or actions acting as media or new focus of old function. (5.2.3)
c. B-SC	TS	2.1.1: Build Chain SFMs, by transforming one of the SFM parts into an independently monitored SFM, then link it as a part of original SFM. 2.3.3: Perform one action in the downtime of the other, if there exist two incompatible actions;
	ISS	ISS I-1.8: Improve a system's effectiveness and controllability by developing one element of system to deliver its own but extra functions, when such extra functions can be identified. (2.1.1) ISS-I-2.3: Improve action's effectiveness by changing Field from uniform or uncontrolled to a field with predetermined patterns being permanent or temporary (2.2.5)
d. V-SC	TS	1.2.2: Remove Harmful interaction or function by modification of the existing substances, usually by introducing a modified third substance already available to the model. 1.2.4: Add a new Field to solve problem by transition to a dual SFM where U action remains beyond F1, and F2 acts as N Force to mitigate H actions or convert it into U.
	ISS	ISS H-1.14: Protect area of the system from harm by adding a protective substance to this area where it is most exposed or easily-affected; (1.1.8.1) ISS-H-2.8: Use element that disappears or becomes identical to components of existing system after fulfilling its work (5.1.3.)

[1] Traditional solution as design reference for ISS; [2] I = insufficient, H = harmful, U = useful.

In this case, V-SC remains highly important among the others; an illustration using SFMA is shown in Figure 6.11. Other SC decoding shares similar models built upon this analysis path.

Standard solution 1.2.4 is selected to solve V-SC-1. A new field F2, magnetic waves, is introduced to the existing system, aiming to help the original function D1, which is to generate nutrition for cells cultured. Using a traditional bioreactor can help this aim, yet remains insufficient because of several limitations. In this situation, magnetic waves/fields could enhance the D1 process, as media stimulated to increase nutrition-generating activity level. Cells, as product S2, can benefit from media and expand gradually. However, when a large number of cells stack, which easily causes stagnation or saturation of definite cell culture by-products, the nutrition-exchanging process by media is hindered and new nutrition is not produced as efficiently as in the beginning. Magnetic waves could help solve this issue and

make the process of producing nutrition more effectively. The process also illustrates the benefit of analysing neutralising force. After establishing F2 as prioritised, it is necessary to consider whether F2 or a new field F2-derived could act as a neutralising force. This could help RPA and SFR analysis following afterwards.

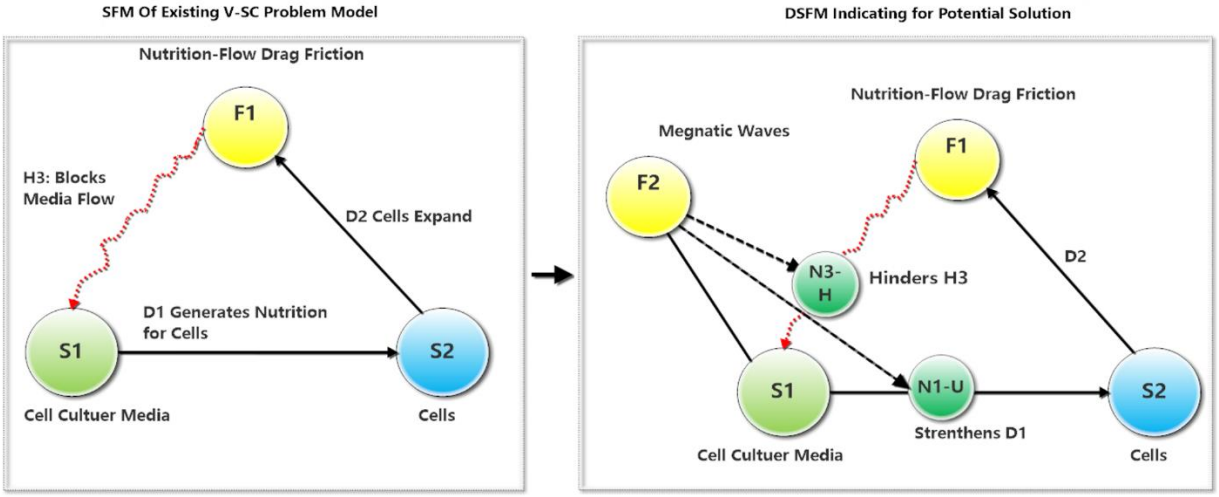


Figure 6.11 SFM illustrating magnetic waves as potential for Field 2

II. Part B: 3DPVS RPA and SFR analysis based on mini-problem models.

Part B aims to create a thorough list of TPSFR and related parameters. Available resources for designing 3DPVS in the current case must also be identified via RPA.

B1. Conflict zone determination for GMBV set.

Based on previous work, a conflict zone (CZ) can be applied to the identified contradiction set as follows. Table 6.15 illustrates CZ about the identified chief SCs.

Table 6.15 CZ with illustration for identified chief SCs

SC	CZ illustration
G-SC - 1	In the porosity characterization [A1] and cell capacity [B1] conflict, the CZ is the place where cells and the porous structures make contact; that is, the inward and external surface of the pore inside scaffold as well as pore's inward space where cells can either pass through or attach with.
SC -2	In the Material composition [A2] and Multi-functionality of Scaffold [B2] conflict, the CZ is the external surface of scaffold, inner surface of pores as well as the solid scaffold body parts where materials compose up.
B-SC -3	In the Biological stimulation [A3] and Cell attachment [B3] conflict, the CA takes place in the scaffold surface.
V-SC -4	In the Dynamicity/vibratability [A4] and cell stimulation or reaction [B4] conflict, the CZ is the whole porous structures in scaffold, cell culture medium, Air, support bottom for the cell couture process, bioreactor.

These CZs will be used in the further Stage C. The same conflict in different places could weigh variably. CZ includes a trinity—the zone for intensifying conflict, zone where the conflict is constant and unchangeable, and zone for decreasing conflict. The same conflicts could result in different intensities in different zones.

B2. Operation time determination for GMBV set.

In the current case, operation time (OT) will be divided into several parts corresponding with the contradiction sets previously identified. To better understand the significance of conflict in 'time', it is necessary to perceive another property of conflicts—namely, 'inner conflicts'. Within conflicts, other sub-conflicts proceed, so that every conflict can be resolved into a great number of inner conflicts. Each section of any conflict can be regarded a conflict on another plane or time. These inner conflicts would proceed simultaneously in different 'media sets', interpenetrating one another, reflected in one another, and giving rise to one another, as well as stopping, impelling and changing one another. As such, chief features of 'inner conflicts' can be applied in describing conflict input (CI), conflict output (CO) and other components for structuring OT, as shown in Figure 6.12.

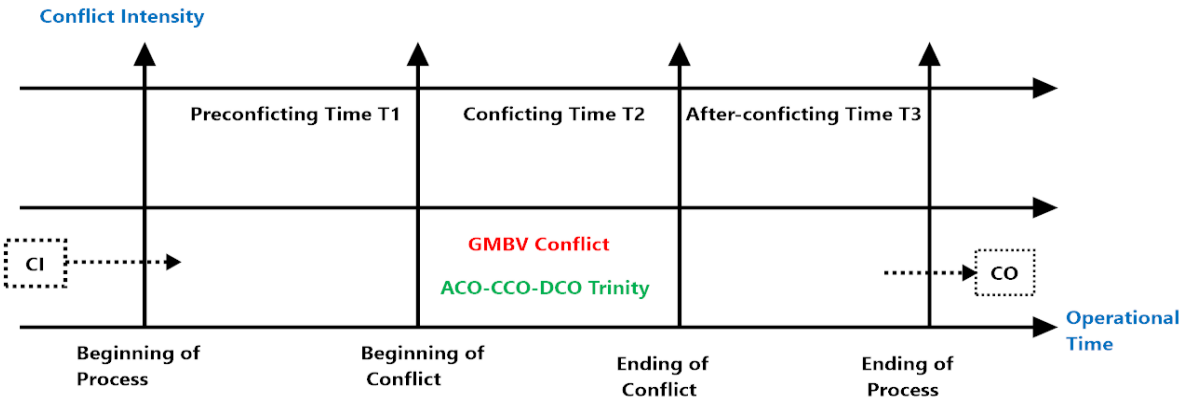


Figure 6.12 Structure of OT dealing with conflicts

The deviation of conflict line, marked 'D', usually occurs at three intervals: between the ascending conflict octave (ACO) and constant conflict octave (CCO), the CCO and descending conflict octave (DCO) and ACO and DCO. Thus, seeking solution at intervals could be a highly useful strategy to solve regarding conflicts. Table 6.16 shows the aspects in different time zones for conflicts.

- ACO: conflict is on an ascending line for a given period
- CCO: conflict remains at a constant level for a given period
- DCO: conflict is on a descending line for a given period.

Table 6.16 Description of aspects in different time zones for selected conflicts

Type[1]	T1 time zone	T2 time zone	T3 time zone	A/D state	Intensity[2]
G-	pre-culture period	full period of cell culture	after-culture period	deviation, ACO-CCO	medium
M-	scaffold 3DP fabrication period	full period of cell culture	after-culture period	deviation, ACO-CCO	strong
B-	scaffold fabrication period	full period of cell culture	after-culture period	deviation, CCO-DCO	medium
V-	before dynamicity or vibration is applied	vibrating or stimulating state	static state after vibration or stimulation	deviation, ACO-CCO-DCO	strong

[1] Selected conflicts corresponding with GMBV characteristic;

[2] Four-scale weights applied: none, weak, medium, strong.

B3 and B4: SFR determination and generate completed SFRP analytical chart.

Here, we generate an SFRP list to indicate aspects of the internal system, external system and general background system. RPA can accelerate solving issues by introducing other SFR if there are insufficient resources available in the current system. In this chart, the existing SFR, with potential SFR as the magnetic field proposed previously, will be established. In part 'C', if more DRs regarding new SFR are detected, the current SFRP chart can also be extended. Table 6.17 summarises the existing and potential SFR.

Table 6.17 Existing and potential SFR of 3DPVS in case study

Internal-System SFR and Parameters for the Case Study			
Substance	***Parameters***	***Field***	***Parameters***
3D Scaffold	length	Fields of forces, energy and momentum	Mechanical force within structures
	Height		
	Area of external		Shape returning force
	Center of gravity in geometry		
	Shape of scaffold 'body'		
	Porous shape		
	Pore size		
	Wall thickness/beam diameters		
	Material constitution		
	Material consumption		
	Mechanical strength		
	Biocompatibility		
	Biodegradability		
	Weight		
	Center of gravity by weight		
	Temperature		
	Scaffold flexibility		
	Speed (moving or shape-changing)		
	Friction force between culturing liquid and scaffold's surface		
	Hydrodynamic resistance		
	Cell/scaffold adhesion		
Cells	Morphology/shape	Fields of forces, energy and momentum	Cellular force
	TCE level		Medium Pressure
	Proliferation rate		
	Survival rate		
	Viability level		
	Cell behavior		
	Cell interaction		
	Gene expression level		
	Cell signaling and adhesion		
External-System SFR and Parameters			
SFR of Immediate Physical Surroundings of the system where conflicts exist			
Substance	***Parameters***	***Field***	***Parameters***
Cell culture media	Temperature	Magnetic Field[1]	Field strength
	Liquid flow speed		Frequency
	Direction		NP size
	Pressure		NP concentration
	Density		Solution viscosity
	Osmolality level		Periodicity
	PH level		Magnetic heating (T)
	Cytotoxicity level		magnetic moment density
	Manufacturing Process		magnetic flux density

	Cell lines		
	Nutrition components	Field of mechanical stimulation/vibration	Strength
Surface of culturing platform	Hardness of surface		Frequency
	Roughness of surface		Periodicity
	Curvature of surface		Stimulation effect
Bioreactor/External Vibrator	Power		
	Dimensions		
	Agitation		
	Control precision		
	Motor speed range		
General SFR for background fields or environments			
Substance	***Parameters***	***Field***	***Parameters***
3D Printer(s)	3DP parameters discussed in Ch2.	Thermal field	Temperature
		Light energy	intensity
Nozzle	Diameter	Gravity	Acceleration of gravity
[1]: Blue color font indicates extended elements generated from future part C.			

III. Part C: Determine basic ideal result (BIR), MIR, senior ideal result (SIR) and solving macro- and micro-levels physical contradiction (PhC).

Part C aims for transition of the established problem model from SC into PhC, and generate the corresponding concepts. Steps C3 and C4 use SPA, SEA and other methods for PhC analysis and concept generation. In this part, the ideal solution of the definite conceptual 3DPVS will be generated. It may not be optimal, but the SIR could point to the most achievable, practical and innovative answers that designers at the current stage could acquire. Following this will be concept evaluation and concept scenario finalisation.

C1. Formulate BIR.

Following the previous conflict solving, we could first arrange the formula of the 'bioreactor' issue, as follows. When the bioreactor is turned on, in T2, there is benefit [U1] towards the desirable cell effect [A + B]; however, a harmful effect [H1 + H2] would be side effects resulting in cell culture aspects [C] that are undesirable. Thus, the core question is how to maintain or strengthen the effect [A + B] while mitigating [H1 + H2]. Rather than analysing B-C, decoding the A-C relationship would be the focus for generating BIR.

V-BIR-1: The bioreactor changes into a time-shifting one, meaning that it can switch on and off automatically or manually. [A + B] would be largely maintained, while [H1 + H2] could be mitigated to some extent. The basic structure is shown in Figure 6.13.

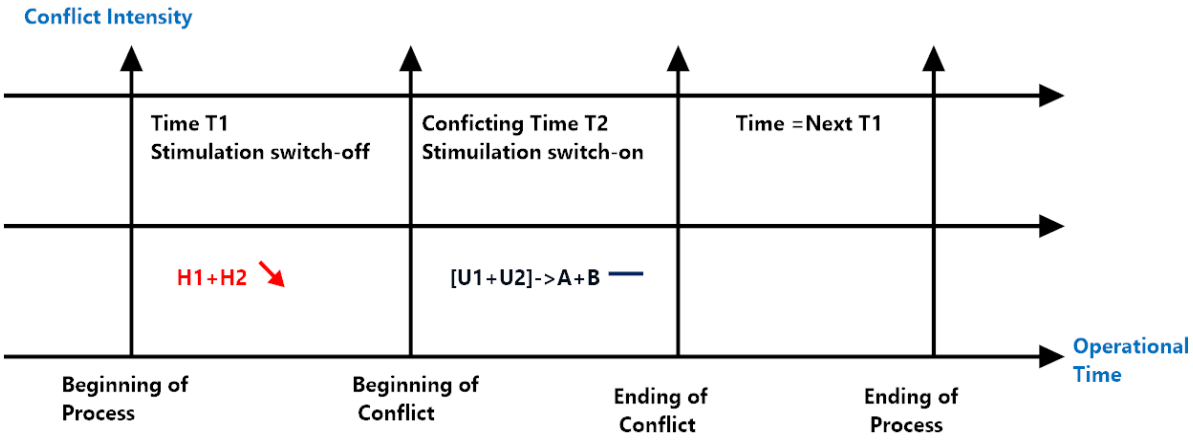


Figure 6.13 V-BIR-1 OT structure of bioreactor's functional time

After identifying specific formulations, these would be used afterwards, where basic SFR replaces element 'X'. The formulation of identified basic ideal results is shown in Table 6.18.

Table 6.18 Formulation corresponding with identified basic ideal result

Type	Formulation with specified language
G-BIR	While neither complicating the existing GMBV contradiction sets nor causing harmful effects in established OT and CZ, G-N acts as the NF[1] to strengthen the mechanical stress [C1] while maintain the beneficial effect from higher porosity characterization on cell culture [A1].
M-BIR	While…, M-N acts as the NF to strengthen the specific stimulation on cells from materials [C2] while maintain the beneficial effect of multiple-mixed material composition [A2].
B-BIR	While…, B-N acts as the NF to strengthen the desired nutrition transmitting [C3] while maintain the capability of higher surface toughness [A3] to help required cell attachment.
V-BIR	While…, D-N (non-bioreactor based) acts as the NF to eliminate or transform the existing harm of current bioreactor' continuous state [D3] while maintain the capability of bioreactor-scaffold [A4] to create cell-benefiting stimulation.

[1]NF: Neutralizing force

C2. Intensify/reinforce BIR with additional requirements.

As discussed, the existing SFR could replace element 'X' existing in AMSF. Analysing CZ and OT, GMBV N-BIR sets could be potentially separated into two groups, G- and B- in T1 state, and M- and V- allocated in T2. As a result, conflict intensity might reach a relatively ideal level based on the following conflict evaluation. Figure 6.14 shows a reinforces BIR formulation.

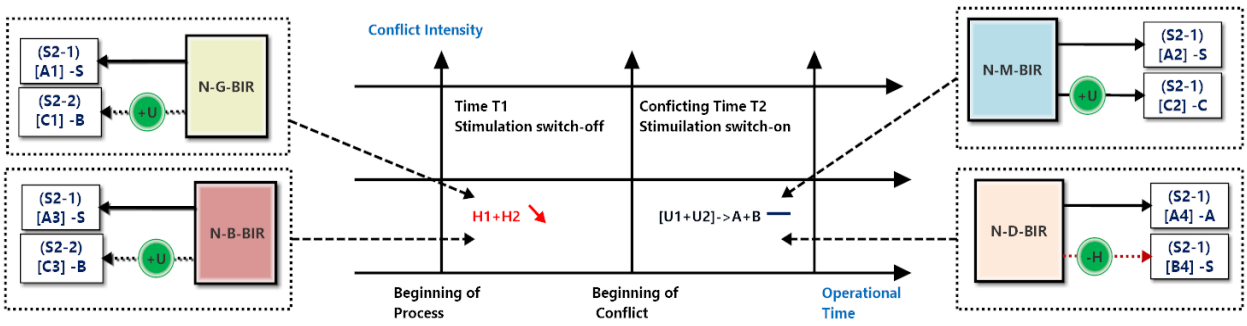


Figure 6.14 Structure of reinforced BIR formulation where selective resources replace element N-GMBV set

Using RPA proposed to analyse and evaluate the parameters of selected SFR, shown in Figure 6.14, gives several possible results—see Table 6.19. In addition, this period also aims to check whether some conflicts in T2 can be separated into T1 and T3 to transform into neutral or even useful functions to definite activities that occur in T1 and T3.

Table 6.19 Using RPA to generate possible results of selected BIRs

Type	Possible indication
G-BIR	A highly interconnected porous with a pore size distribution μm level;
M-BIR	Smart material is applied to generate scaffold's dynamic response, the **HA shell** used for enabling bone conductivity, and original material **PU** will be remained and utilized for foaming porous scaffold with definite tunable structures.
B-BIR	New Influence needs to put on Medium to make it enable the desired functions [D3+D4].
V-BIR	[1] Porous Scaffold with a change of state, from dynamic into static; [2] Rigid scaffold→flexible one;

C3. Formulate PhC at macro-level.

For the generated BIR, conflicting values of selected SFR parameters will be used to create element X's opposite physical macro states in the given CZ-OP process. Table 6.20 illustrates the formulated PhC at macro-level.

Table 6.20 Formulated PhC at macro-level with description in specified form

Type	Possible indication
liquid flow	Liquid flow in the CZ during Operational Time should have high speed for the scaffold moving (vibrating) at fast speed [1] and no speed where the liquid flow contacts the scaffold surface [2];
M-BIR	The pore size distribution μm level needs to be big enough for enabling higher cell capability [B1] and small enough for stabilizing the scaffold structures [C1];
B-BIR	New Influence (magnetic field) on Medium needs to be high enough for enabling the desired stimulation [C2]→[D3+D4], while low to make the side-effects affecting original cell culture process neglectable.
V-BIR	[1] The change of state from cell-stimulating into static needs to be rapid to ensure the cell culture efficiency [B4], and slow to avoid damages and other negative effects on cells [C3].
	Scaffold needs to be flexible enough to fulfill the definite bone growth, [2] Rigid scaffold→flexible, soft one;

To avoid harm from external field, BIR can be formulated as follows. The <liquid column>, during the T2 has to be <magnetic-conductive> to <remove the undesired electromagnetic waves> and needs not to be <conducting> to <prevent absorption of electromagnetic waves>. Thus, the liquid column as medium must be magnetically conductive when there is magnetic stimulation on the T1 cell culture period and should not be conducting for T1 and T3.

C4. Formulate preliminary concept at micro-level.

B-surface particles.

Particles of the 3D scaffold's surface should not to be movable and activated [B-U3] for the scaffold, allowing high speed liquid flow at its surface, as well as function [B3] and [B4]. Particles should be movable and activated [B-U3] for the scaffold, ensuring no speed of liquid flow at its surface:

- Surface travelling waves between the scaffold and liquid culture medium may fulfil both the requirements of the preliminary concept at micro-level.
- A potential way to create such travelling waves is as follows. Using a 'piezoelectric film' preliminary concept (PhC) by IPA, the surface of a scaffold can be covered with a piezoelectric film generating surface travelling waves. The speed of these waves can be changed to the speed of liquid flow, thereby reducing the liquid drag friction to zero or a relatively smaller level.

Scaffold material particles:

Particles of scaffold must be biocompatible for both the T1, T2 and T3 periods, and be capable of generating [B2 + B3] functions at T2, and enable [B4] at T1 and T3. However, particles of the scaffold should not provide [B2 + B3] functions at T1 and T3, or provide [B4] at T2:

- Particles require switch on/off properties, and multiple materials might need to be mixed together.
- A general solution triggered from SM contradiction solving in Chapter 5 could help analysis.

C6. Formulate MIR.

The generated MIR is illustrated in Table 6.21.

Table 6.21 Mid-stage solution formulated corresponding with identified MIR

Type	MIR formulated with illustration
MIR-1	'STW' between scaffold and liquid culture medium activates piezoelectric or magnetic components of scaffold's surface in order to create definite 'STW' in T2, and cease to activating piezoelectric or magnetic components when scaffold works at static state in T1 and T3.
MIR-2	magnetic components of scaffold mix with HA components to provide definite functions [B3+B4]; HA components work through T1, T2 and T3, while magnetic components generate the tailored functions only in T2.
MIR-1+2	Liquid flow in cell culture medium activates one portion of magnetics through applying pressure to help magnetics generate electromagnetic energy. By applying electromagnetic energy other portion of magnetics in scaffold's body will be activated and generate definite TSW waves fulfilling the requirements [B2+B3+B4]. The activating speed of the STW can be adjusted by the external field which controls the activation of magnetics inside scaffold. In this way, the harmful effect [C4] will be mitigated by controlling the T2 activation period to a certain degree based on case requirements.
MIR-3	New Influence needs to put on Medium to make it enable the desired functions [D3+D4].
MIR-4	The specific combination [A4] of magnetic scaffolds with time-dependent magnetic fields could generate synergistic microenvironments favorable for cell activity. This combination will mitigate the cell culture conflicts existing [C4] in T2 as discussed, as well as help other functions in T1 and T3 [B4]. The establishment for this specialized combination needs to go through SEA process as proposed in Chapter 5, which has discussed magnetic field in detail.
MIR-5	A definite combination of frequency, intensity and functioning time (prolonged or shortened exposure time) using a magnetic field (AC or 3D) could affect cell viability both in positive [B3] and negative ways [C4]. Lower frequency (0-100Hz) plus longer time (>6 hours/day) higher frequency (100-300Hz) plus short time (<3 hours/day) would be the possible solution.

C7. Apply ISS to solve identified MIR.

ISS is used to find possible solutions for previously settled MIR. SEA could also be used with ISS. Table 6.22 categorises contradictions into different levels.

Table 6.22 ISS table for MIR

ISS	S	A	B	C
MIR-1	I-1.6, I-1.9 H-1.7	I-2.3 H-2.9	I-2.5	I-2.2
MIR-2	C-1.1 H-2.9	I-1.6, I-1.8 H-1.5	I-2.3	H-2.6
MIR-3	C-1.2, I-2.16 H-2.11	I-2.4 H-1.7	I-2.14 H-2.2	H-1.8
MIR-4	C-1.7 H-2.9	I-1.6, I-1.11 H-2.5	I-2.11	I-2.3 H-1.6, H-2.2
MIR-5	*	I-2.13 H-2.10	I-1.5	H-1.7

SEA concept solution → Alternating magnetic field + magnetic shape memory particles (Effects 1, 2 and 4). This solution aims for the timely control of switch on/off mechanical dynamicity. Further function relating such concept is to generate tailored vibrations under definite magnetic fields.

C8. Use modified SFR for problem solving and solution idealising.

At Step B3, available resources attainable from the existing environment or system elements are identified. This stage aims to further increase the availability of resources to improve the solutions generated at C7. Table 6.23 demonstrates a further process for generating solutions.

Table 6.23 Further solution-generating process with extended resources searching

No.	Further use resources for improving solution generation
1.	Determine the possibility of utilizing a mixture of substance resources. ▪ When introducing new substances, they may result in a more complicated system and harmful side effects. SFRA is used to resolve this contradiction. ▪ In the simplest case, a transition can be from two mono-substances into a non-uniform heterogeneous bi-substance.
2.	Determine the possibility of combining two or more systems into one 3DPVS system. ▪ One method to integrate similar systems is to keep the boarders of the integrated systems in the new system.
3.	Determine if Void resources can be applied on existing SFRA to improve the solution scenario. ▪ An empty space or substances mixture with empty space, sometimes can replace the existing SFR, in order to generate better solutions. Pore, porous structures, foam etc. inside scaffold is the typical example for this application. ▪ The void inside solid can be either the vacuum or be filled with liquid or gas. For SFR at definite level, lower-level structures might act as void.
4.	Determine the possibility of utilizing derived resources or a mixture of derived substances with void. ▪ Changing the phase state of existing SFR can achieve the derived substance resources. For example, derived resources of liquid are ice and vapor. ▪ Derived resources include the products of decomposing the SFR. This application on 3DPVS chiefly lies on shifting the phase of culturing liquid, and 3DP fabricating materials.
5.	Determine if there is possibility to introduce a field (electric field especially) or interaction of two fields instead of a substance. ▪ Electrons exist in most objects, and electrons associated with an easily-controllable field may generate useful functions to the existing system. This is specially the case when conditions of problem situation restrict the use of derived SFR.
6.	Determine if the problem or solution can be improved by applying paired fields and substances; ▪ For instance, magnetic field with ferro-susbtance, thermal field with definite SMA, ultraviolet with luminophor, etc. ▪ Usually this approach will increase the innovation solution to a sophisticated but higher-quality level.

Referring to the fundamental conceptual generation conducted in Chapter 5, several new indications can be created:

1. ‘material dynamicity’ and ‘structural stability’
2. ‘material dynamicity’ and ‘material biocompatibility’
3. ‘material dynamicity’ and ‘material fabricability’.

C9. SIR generation and analysis.

At the C9 step, solutions previously created are proposed to be further improved, leading to a SIR that integrates answers from both C8 and C7 steps. In brief, we will structure SIR solutions as output of the 3DPVS concept generation and problem solving, and use them as input for concept evaluation and concept scenario finalisation. For complex shape changes, patterns can be designed directing the 3DP process, Figure 6.15.

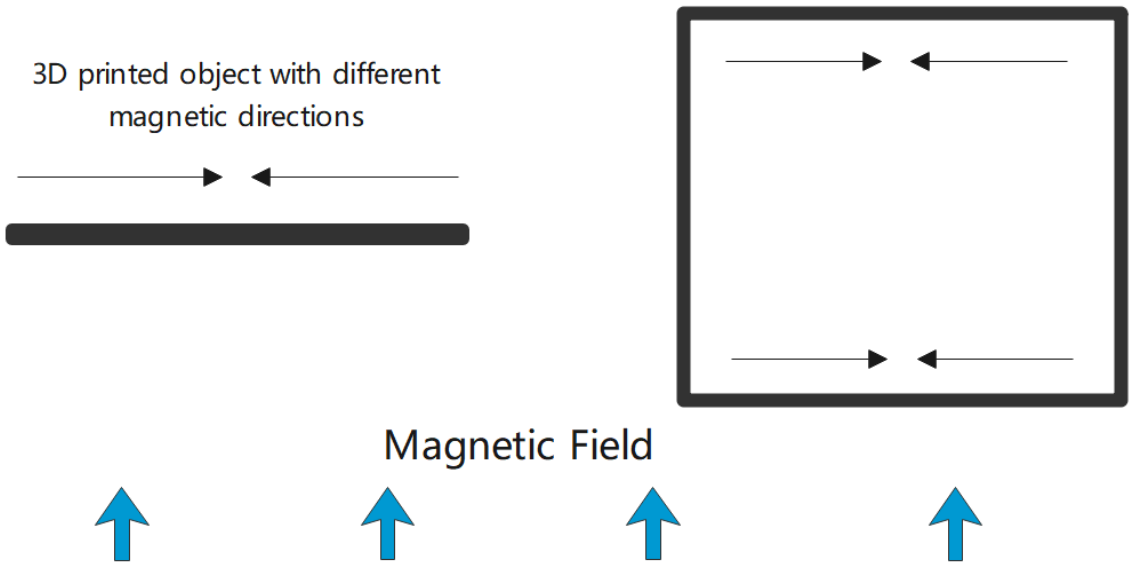


Figure 6.15 Magnetic-printed structures enabling designable changes under applied magnetic fields

6.4.2 *Using ARIZ and TRIZ on Other Design Aspects*

For the selected base scaffold models, different parts of the scaffold can be modified with various properties, such as geometrics or mechanicalness. Designers find it difficult to assemble these parts into a fully workable unit. How to address the ‘connecting’ point, layer or section becomes an issue. For this question, directly identifying a contradiction solution via the usual TRIZ seems arduous. Thus, the ARIZ-based innovation roadmap is further used. Opposite states of patterned magnetic shape changing are listed in Table 6.24.

Table 6.24 Opposite states of patterned magnetic shape changing

	Opposite states	Contradiction	Solution
1	Transformations in a programmable manner	C-1	S-1
	Uncontrollable shape-transforming manner		
2	Slow and simple transformation	C-2	S-2
	Rapid and complex transformation		
3	Intricate patterns of magnetic polarities	C-3	S-3
	Simple patterned magnetic polarities		

Other issues that must be considered include:

- Composite ratio issue: Increasing the mix ratios of the nano-Fe_3O_4/PU composite could significantly decrease the thermal stability of PU. This would hinder the 3DP fabricating process, especially for FDM method.
- Unit library structure vs random, unpredictable structure by a method such as foaming: As a solution, a unit library structure will be used at the conceptual stage.
- Shaping-changing effect must be both small for stability and gentle stimulation, and large to provide sufficient mechanical stimuli.
- Magnetic-based shape change could be rapid, with cycle times of 1 kHz or above. A real-world shape-transforming function could not achieve this.
- Non-biocompatible magnets should be properly coated with a bio-safe material.

From round 2, the magnetic-based contradiction and solution is shown in Table 6.25.

Table 6.25 Magnetic-based contradiction and solution in Round 2

Con.	Materials	Example	Coercivity	Features	Result
C-4	Soft-magnetic materials	iron and iron oxides (Fe_3O_4)	Low, usually one field applied;	Inadequately retain strong magnetism once external field is removed;	simple elongation or compression; generally unsuited for complex transformations;
	Hard-magnetic materials	neodymium-iron-boron (NdFeB)	High, multiple fields applicable;	Retain high magnetism in absence of field once saturated;	programmable and complex shape changes;
Solution	magnetically-hard particles could be incorporated in mechanically-soft materials; 3D-printable hard-magnetic elastic (soft) materials;				
Con.	Controllability	Predictability		Patterns	Effect
C-5	Uncontrollable shape-transforming manner	Low		Simple	Simple shape-changing;
	transformations in a programmable manner	High		Intricate	Complex shape-transforming
Solution: Each line of filament is printed with definite programmed domains. Simulation is required for predicting and developing rapid and complex transformations in a programmable manner. Helps address slow and simple transformation.					

Soft vs hard magnetic materials: Using soft magnetic materials, the programmed domains could be easily reverted by the applied actuation fields, making it difficult to achieve desired

shapes in a controllable manner. Given this limitation, hard-magnetic materials may be preferred to fill the gap.

Orders of magnitude: The actuation rates and power densities achieved by existing 3DP shape-transforming elastic materials tend to be insufficient, and should be improved to ensure enhanced, rapid structural transformation. As such, ways to increase their orders of magnitude could be an interesting question for designers. From TRIZ, several indications can be acquired.

Magnetic intensity: Static moderate-intensity fields (1mT-T level) are capable of affecting a number of biological phenomena, such as cell proliferation migration, with no lethal effect on cell growth (D'Amora et al. 2017; Fassina et al. 2006). Thus, magnetic stimulation should remain at micro-tesla range.

Magnetic concept 1: The magnetic composite microsphere of Fe_3O_4–HA is proposed to be prepared via a homogeneous precipitation method. Fe_3O_4 NPs will be dispersed and used as a substrate in a Ca-P solution to deposit HA on the Fe_3O_4 spheres by gradually increasing the pH with decomposed urea, and urease can be employed as the catalytic. Following that, the Fe_3O_4–HA/PU composite scaffolds with a reasonable weight percentage of Fe_3O_4–HA could possibly be fabricated via (in situ) 3DP layer polymerisation and a simultaneous fabrication, such as gas foaming. Based on the current proposal, the feasibility of 3DP of uniform foam structures through a process called direct-ink-write could be a better alternative to traditional foaming, which would be applied for future fabricating 3DPVS.

With regard to durability and long-term mechanical performance, 3D-printed foam also works better than standard cellular materials. Compared with their traditional counterparts, 3D-printed materials age slowly, better retain mechanical and structural characteristics, and enable 3DPVS work to occur for longer in external cell culture applications. This helps tackle the typical contradiction between foaming method and scaffold mechanicalness. Further, 3DP of foams provides tremendous flexibility in creating programmable architectures and customisable shapes, which simultaneously helps address G-based concerns in 3DPVS design.

Magnetic concept 2: This concept is to activate large shape changes in oriented liquid crystal elastomer (LCE) networks via magnetic heating. A contactless electromagnetic trigger can be used, generating reversible, well-defined change. Change in the relative sample length along the tensor could be predicable around 20 to 30%. LCE nanocomposites could be used, which contain superparamagnetic particles performing local heat dissipation upon irradiation with electromagnetic fields. The heat issue during cell cultures should be considered when using this concept.

Magnetic concept 3: Detailed information on this concept will be presented in the summarisation section for the sake of brevity, as this concept is evaluated as the most ideal one. In brief, hard-magnetic elastomer will be used together with tailored magnetic field.

Printing 3D structures with DIW (Direct-ink-Writing): Difficulties typically arise because of structural instability as deposited filaments are stacked up. Therefore, using DIW as a fabricating tool is useful, yet the instability creates conflicts.

I. Material-based solution searching steps

Based on the previous process, several conceptual solutions have been generated regarding the magnetic scaffold—that is, the magnetic scaffold will be the 'truck' for the required 3DPVS in this case scenario, and the conceptual solution for this case study can be summarised as follows, Table 6.26.

Table 6.26 Steps of generating concepts corresponding materials

No.	Concepts generated with description
1	Porous magnetic scaffold will be served as material and structural template for osteogenesis, while the 'embedded superparamagnetic material under an external magnetic field' will provide useful mechanical stimulation to promote cell cultivation in bone remodeling and regeneration.
2	Superparamagnetic properties [SEA] on biomedical applications from magnetic composites will provide effective mechanical stimulation [B2+B3] under an external magnetic field to promote desired biomedical functions including bone cell growth and bone regeneration.
3-a	Concept generated for material composition**:** PLGA scaffold→PU scaffold→HA/PU composite scaffolds→ NPs-HA/PU Scaffold);
3-b	Superparamagnetic FeHA**:** Fe_3O_4–HA microsphere into the PU matrix to develop a novel magnetic composite 3DPVS that integrates superparamagnetism, cytocompatibility, and osteostimulation. ・PU, a versatile elastomeric block copolymer, enable 3D scaffold with biocompatibility and tunable properties. ・HA can endow magnetic materials with bone cellular conductivity and bone-bonding bioactivity. ・Fe_3O_4 core is applied to generate desired superparamagnetic response for this 3DPVS case, with the HA shell used for enabling bone conductivity and PU utilized for foaming porous scaffold with definite tunable structures.
4-a	The PU/FeHA weight ratio (w/w) 70%+ is studied as most suitable ratio for [A3+A4] functions. Polyurethane magnetic nanoparticles need to be analyzed in separate case.
4-b	Nanocomposite scaffolds are proposed by embedding FeHA nanoparticles into PCL matrix.
4-c	FeHA magnetically-responsible material is to be mixed with material [X]
5-a	Elastic polymer polyurethane could be alternative of traditional PU that used in scaffold.
5-b	hard-magnetic materials identified;
6-a	Mechanically-responsive shape-transforming soft materials identified;
6-b	Fabricating method corresponding such hard-magnetic soft materials;
7-a	Localization of vibratory scaffold is proposed as achievable by altering material weight ratio.
7-b	Localization via printing same materials with specially designed magnetic patterns;

For simplicity purposes, the multiple-layer material identifying work can be condensed as follows, Table 6.27.

Table 6.27 Composite material 1 with illustration of part functions

No.	Name	Material 1	Function
1	L-1 material solution	Fe_3O_4 Core	Providing superparamagnetic response;
		HA Shell	Enabling bone conductivity;
		PU-1	Structuring porous scaffold;
3	L-2 solution	POMaC	Candidate base material as soft elastomer;
		LCE	Liquid crystal elastomer supporting shape-changing;
2	L-3 solution	magnetized NdFeB particles	elastomeric composite ink containing magnetized NdFeB particles;
		silicone rubber matrix	Elastomeric particles as scaffold support;

For the elastomer particles used as a potential scaffold matrix, a calculating table is illustrated in Table 6.28. As discussed, values were basically ranked and transferred via literature study and consulting experts. Analysing the table, silicone-based elastomers might be the optimal candidate for structuring our proposed scaffold. Styrene-based rubbers might be also useful, while biostable PUs tend to show the least application potential in the current design context. From literatures, silicone also has proven applicability for scaffold (Xu et al. 2020).

Table 6.28 User-defined matrix calculation for ranking elastomers potentially used in 3DPVS

	Criteria no.	C1	C2	C3	C4	C5	
No.	Candidate biomedical elastomers[1]	3DP	Cell culture scaffold	Dynamic functionality	Magnetic cooperation	Design efficacy	Overall score[2]
		0.2062	0.2062	0.1959	0.1959	0.1959	
1	Silicone-based	0.2000	0.1762	0.1798	0.2160	0.1916	***0.1919***
2	biostable polyurethanes	0.0895	0.0994	0.0988	0.0969	0.0828	0.0937
3	polyvinyl chloride	0.1085	0.1009	0.0822	0.1073	0.0794	0.0959
4	cis-polyisoprene	0.1369	0.1123	0.0970	0.0773	0.1176	0.1092
5	polyolefin and polydiene	0.0793	0.1225	0.1322	0.1395	0.1333	0.1209
6	styrene-based rubbers	0.1388	0.1306	0.1524	0.1243	0.1436	0.1380

[1] Given the current research focus on external cell culture application, instead of tissue implantation, materials are selected from biocompatible yet non-degradable elastomers. [2] Normalisation values for ratings of criteria and material overall score.

II. Characterisation of scaffold design

In this scenario, conceptual solutions of desired 3DPVS are generated via multiple layers. First, as in Chapter 5, we indicate a magnetic-based scaffold—a scaffold with magnetically responsible nanoparticles plus an external magnetic field—as a relatively optimal solution, compared with other generated candidate solutions. This is considered the super-system solution scenario, which prepares the ground for further design process. Second, to penetrate deeper based on first-layer problem solving, as well as considering the definite bone cell case scenario, we generate a novel magnetic porous 3DPVS concept that can integrate superparamagnetic properties, cytocompatibility and osteostimulation by using FeHA

composite with PU, with the product's aim of promoting the required bone repair and regeneration aspects. This design would choose, for instance, a Fe_3O_4–HA/PU composite integrating both magnetic properties and biocompatibility, which could be possibly used as an ideal candidate material for dynamic properties required by the current case and other cell culture applications. Thus, magnetic stimulation and magnetically responsive scaffolds may be the solution to promote desired bone repair and regeneration. Third, concept generation has progressed further. We chiefly seek to address, at least to some extent, the constraints of vibration requirements proposed by this research. This part has focused on the trinity of vibrating properties—being non-mechanically vibratory, enabling localised vibration, and allowing for vibrating in desired frequencies—and several solutions, or, more precisely, conceptual indications, have been generated. Given the nature of conceptual design, loops or gaps inevitably exist, and require further solving in later detailed design. In the new concept generation, material has become the main stumbling stone for designers.

Unlike previous shape-memory materials, the proposed material could consist of a polymer and embedded droplets of definite magnetorheological fluid. Magnetorheological fluid (MRF), a recent SM, illustrates well-functioning vibration and impact control fields. A definite MRF must be mixed with magnetically responsible materials. Following this, the second magnetic-based solution, especially material aspect, has been generated with LCE and NIP, respectively. Conceptual design of the composite consists of two components: magnetically responsible nanoparticles and small droplets of liquid mixture. Latter particles provide material with magnetic properties and its shape-memory character. The composite material is first forced into a certain shape and then exposed to a definite magnetic field, where it retains its shape. When the magnetic field is removed, the material returns to its original shape. A repeated process of this could generate slow vibrations, as expected. Thus, speed shape-changing properties play a vital role in manifesting desired scaffold changes, simply via the 'flip' of a magnetic switch. Using the mixed material as composite ink for 3DP, we could possibly use nozzle-based direct ink writing of a biocompatible elastomer composite containing ferromagnetic microparticles. As a result, the 3DPVS tends to be elastomeric, biocompatible and speedily shape changing, as well as appropriate for bone cell culture applications.

In terms of other innovative aspects, for the cell culture process, there may be two intervals where specialised stimulation is necessary to make cells grow as the desired line. (These two intervals generally occur at the 40% and 90% state.) It is suggested to increase the vibration frequency at these states to solve the contradiction in OT. For further design, we could incorporate hard-magnetic nanoparticles within super-elastic microparticles, which is proposed to be remotely controllable by a definite magnet field in such a way that they can be actuated and manipulated in a highly controlled manner. This method has the potential to

generate extreme shape changing, while maintaining good mechanical toughness. Thus, the vibrating stimulation based on this method could play more roles that we did not identify.

III. Localised workability

A single unit is combined with other units to compose a complex matrix structure for the scaffold. It is designated to be symmetrical in all directions of x-, y- and z-axes. To combine different parts of the scaffold—in other words, multiple sub-scaffolds with variable properties—the priority issue considered by the current design context is identified as creating sufficient contact surface between these design parts. That is, if the designed contact surface design is not compatible with that of other designs, using 3DPVS consisting of two scaffold parts, for instance, it could possibly cause high stress levels at junctions between the separate parts. This would in turn lead to undesired aspects or failure of the overall scaffold. Localisation needs to take three criteria into consideration.

- Criteria 1: Compatibility of 3DP methods.
- Criteria 2: Combinability of different design parts.
- Criteria 3: No pores enclosed during assembly.

3DPVS must be porous, as discussed, where a definite pore size is required to ensure cell proliferation, nutrition distribution and waste removal. During undesired assembly, pores could be enclosed, blocked or negatively deformed because of geometric defects. This would cause negative scaffold deformation, where space within cannot be used. High porosity scaffolds generally have low mechanicalness, and vice versa. However, porosity cannot be sacrificed to ensure high strength, as a basic function of the scaffold is to benefit the transportation of fluids, nutrients and wastes, as well as enhanced proliferation of cells. A highly porous scaffold may not tolerate the loading conditions and fail rapidly. In connection with this, two suggestions therefore can be made, firstly using line-based structure with each line or group of lines fabricated/postprocessed with invariable properties, which can result in different localised functionality, and secondly, use special semi-scaffold parts with different geometric/mechanical properties to assembly the full scaffold, which can result in another type of localised functionality.

6.5 Conceptual Evaluation and Feedback

In this section, the concepts previously generated will be evaluated, and the optimal concept scenario will be established. Regarding magnetic-based concepts, three finalised concepts in terms of material composition in current scenario are as follows:

- Conceptual Solution 1: FeHA + PU
- Conceptual Solution 2: Tailored LCE
- Conceptual Solution 3: hard-magnetic soft materials NIB.

6.5.1 *Applying Evaluation Criteria to Weigh Generated Concepts*

Thirteen criteria for the selected super-system, system and sub-system conceptual generation will be reapplied to analyse the generated magnetic-based scaffold concepts, with data and scores shown in Table 6.29.

Based on the quantitative analysis, Solution 3 may be the most ideal, compared with the other two solution alternatives and traditional datum solution. Other evaluation based on 3DP methods and the geometrics or mechanical properties of unit library was conducted during the design process, as discussed.

Table 6.29 Generate concept weight using evaluation criteria

Category[1]	No.	RI[2]	Description	Weight 1[3]	Weight 2	Weight 3
Useful/ positive forces	1	0.039	Open porosity	0.039	0.039	0.042
	2	0.039	Pore diameter and pore geometry	0.041	0.041	0.045
	3	0.043	Pore throat and size strut thickness	0.047	0.047	0.045
	4	0.151	Compressive strength	0.151	0.151	0.172
	5	0.172	Scaffold stiffness	0.182	0.185	0.180
	6	0.025	Quality of fluid flow mediated wall shear stress	0.035	0.046	0.065
	7	0.025	Cell proliferation	0.035	0.025	0.027
	8	0.083	Cell adhesion	0.083	0.083	0.083
	9	0.043	Dynamic/vibrational functionality	0.141	0.145	0.183
Neutralising forces	10	0.043	Localised dynamicity/vibratability	0.113	0.103	0.192
	11	0.065	3DP dynamic materials fabricability	0.095	0.092	0.105
Harmful/ negative forces	12	0.065	Costs/ technical conflicts	0.075	0.069	0.045
	13	0.153	Possible risks from scaffold and vibration	0.153	0.153	0.153
			Overall score of concepts	*1.105*	*1.032*	***1.235***

[1] Category based on trinity forces for evaluation purpose; [2] Normalised RI for each criterion; [3] Weight 1, 2 and 3 represent the three newly generated concepts.

6.5.2 *Expert Consultation and Literature: Experiment Support*

To analyse and partly validate the conceptual design, we consulted experts from multiple academic institutions, with information illustrated in Table 6.30. Unfortunately, only limited replies were received, which did not provide any definite answer.

Table 6.30 Consulting experts to partly validate the scientific soundness of conceptual solutions

Group	Institution of experts	Consulted direction
1	Research Centre for Nano Biomaterials in ChengDu, China	FeHA/PU scaffold with experiment
2	Institute of Biomaterials and Biomedical Engineering, University of Toronto, Canada	Elastomeric scaffolds; shape-memory functions
3	Massachusetts Institute of Technology, United States	Elastomer composite containing ferromagnetic; microparticles

To help validate part of the conceptual solutions, the generated solution is separated into three aspects: core materials, such as FeHA or NIB; the elastomeric scaffold; and the shape-changing composite containing magnetic particles. It can be preliminarily considered acceptable if all three aspects have solid literature or experiment support. This is followed by the next stage of detailed design, ensuring the product is promising, realistic and scientifically-sound. Given that our generated concept is novel, it can be decoded into these three parts, each of which can be studied by existing resources. This is also supported by using the TRIZ RPA process. Although these cannot provide a definite answer to the full 3DPVS concept, several experiments could still partly provide support for the design, which possibly benefits the further validation process.

We searched for an FeHA/PU scaffold in cell culture studies, and the experimental effect could help justify whether the generated solution is eligible to fulfil definite requirements. One selected experiment using a Fe_3O_4–HA/PU composite scaffold was conducted at the Research Centre for Nano Biomaterials in ChengDu, China. The experiment (Yan et al. 2017) showed positive magnetic properties and fine biocompatibility for bone repair. Such scaffold could allow for a highly interconnected porous structure, with 'μm' pore size distribution and a fine compressive strength. This suits the design object using TRIZ. For the NIB-based solution, there has not yet been such experiments on scaffold studies. However, an analogous study conducted by MIT showed the positive functionality of NdFeB particles and demonstrated its advanced shape-changing property (Kim, Y 2018; Kim, Y et al. 2018). This to some extent supports our design guided by TRIZ as promising and inspirational.

Currently available literature with experiments that correspond with some aspects of 3DPVS could partly support the eligibility and practicality of the basic concepts generated. However, further computational stimulation may still be needed to analyse 3DPVS and evaluate the conceptual solutions at further detailed characterisations. In brief, the current 3DPVS concept was conceived in a multidisciplinary way following a concurrent engineering approach. Four different specialties were involved: design, mechanical engineering, advanced manufacturing and bioengineering. At least three professional experts from each specialty were consulted by our research group to participate in part of the decision-making and criteria-making process.

6.6 Concluding Remarks

To conclude, this chapter further generates the conceptual 3DPVS solution based on the fundamental magnetic-based solution from previous chapter. Hard-magnetic elastomer materials NIB under user-tailored magnetic field has been identified as the most promising solution, considering current research needs on bone cell culture application. Using novel 3D printing techniques that enables creating ferromagnetic domains can result in user-tailored magnetization, which in turn endow 3DPVS with possible localization functionality and higher dynamicity. Line-structured scaffold has been identified to be useful sample to structure

3DPVS. Through controlling the geometric properties, chiefly the number of layer and strand size, the eigenfrequencies of 3DPVS are expected to be centre at around 50-200Hz, compared with traditional scaffold that usually has much higher eigenfrequencies. After simulation test, an 18-layered strand-made 3DPVS has been identified as optimal, considering all design requirements for vibration as well as the general needs for bone cell culturing. Other solution can contain a combination of multiple structures that could lead to higher localization properties, though this one can be more difficult to achieve in reality world at current stage.

7 3D MODELLING AND COMPUTER SIMULATION

7.1 Introduction

7.1.1 *Background of simulation*

Multiple analysis software can be used to perform finite-element analysis and simulations for mechanical designs. We can create a user-defined virtual environment where a replica of actual conditions can be created for testing or validating purposes. Simulating the designs and calculations can be done to estimate the flaws in structures. This cost-effective and resource-saving approach means designs can be validated, at least to some extent, before passing into the embodiment design stage. Purpose for simulation during design can be summarised as Figure 7.1.

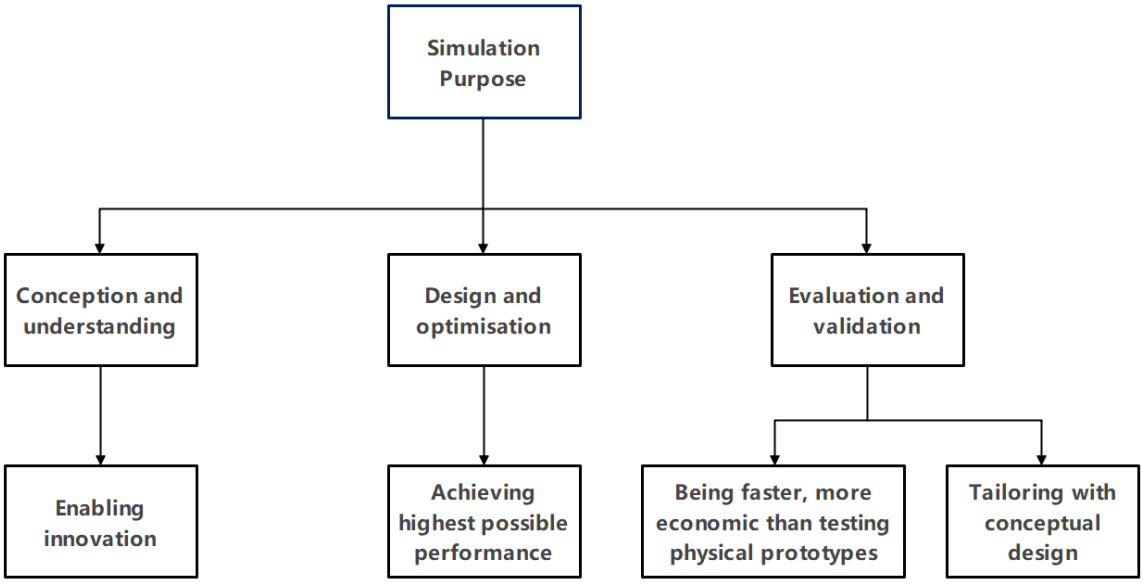


Figure 7.1 Purpose for simulations during design

In this study, concepts generated previously will be evaluated using theoretical means, such as QFD, via mathematic calculation. Concepts will be compared with optimal solution(s) as output. Following this, further validation is proposed using SolidWorks and FEA (Finite Element Analysis) software, COMSOL. 3D modelling of the scaffold will be built and tested under SolidWorks, with models transferred to ABAQUS to further validate two functions: the predictable shape-transforming of structures, and the localised functionality of the scaffold. A brief illustration of simulation is shown in Figure 7.2.

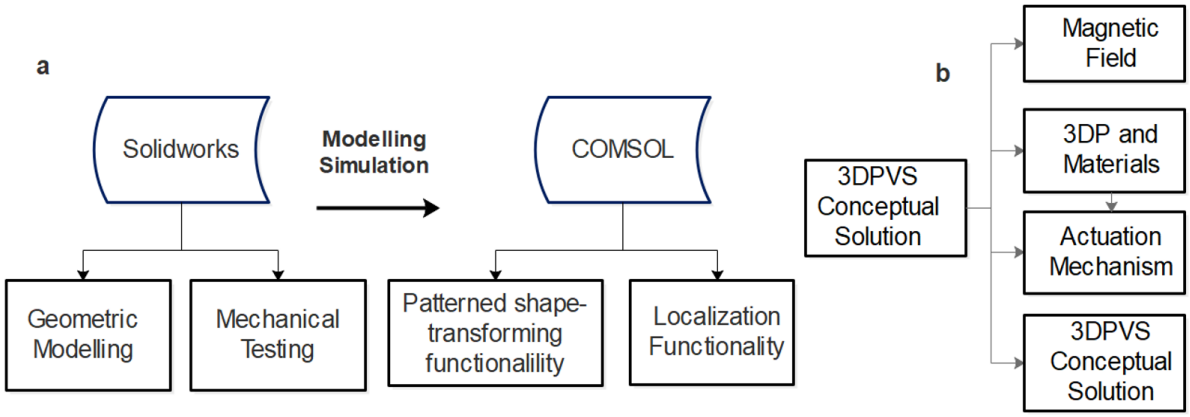


Figure 7.2 (a) Scope of computer simulation for conceptual design; (b) presenting generated solution from four angles

A magneto-mechanical model is presented for the magnetically designed scaffold in surrounding external magnetic field. Multiple physic-vibrational response mechanisms are characterised, including the scaffold's magnetisation, shape-changing and vibrational deformation. Four case studies are conducted: (i) 3DPVS subject to static and alternating uniform magnetic fields, and (ii) 3DPVS in a non-uniform magnetic field. In an alternating magnetic field, the scaffold stretches along the magnetic field direction, with the displacement exhibiting a pulsatile change. As a result, the present multi-physics model may provide guidance to optimally design the 3DPVS with the magneto-mechanical coupled field, which could benefit a future more complex coupled field, such as a magneto-chemical-mechanical one, when the cells, culture medium and heat transfer enter the design scenario.

7.1.2 *Logic Structure*

For readers' convenience, logics of the chapter is summarized as Figure 7.3. with the previously generated solution as input, there are three steps of work to conduct the simulation. This includes firstly preparing the 3D modelling and simulation input, secondly identifying the conditions and parametric setting, and thirdly proceeding the simulation process.

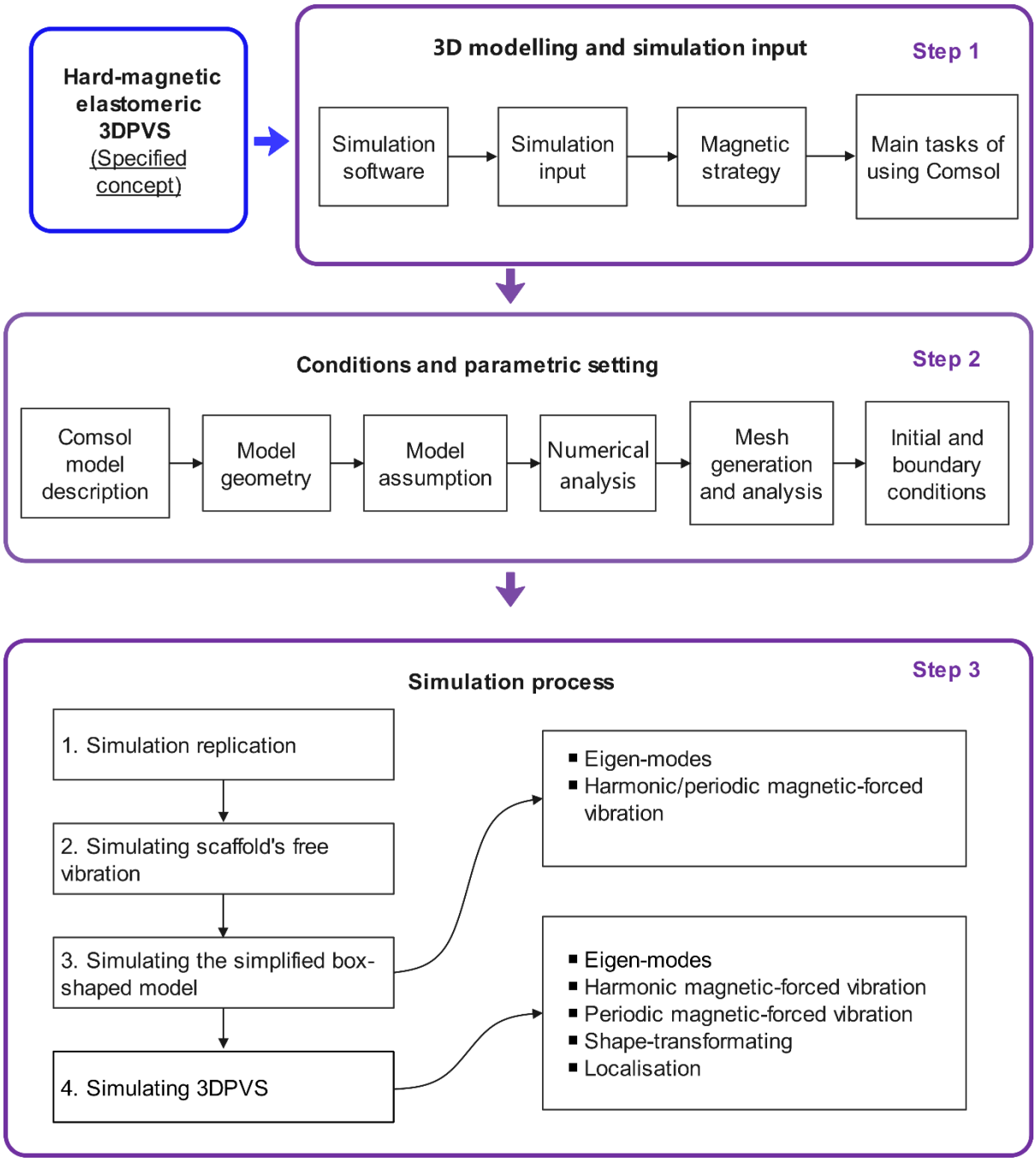


Figure 7.3 Logical illustration for the structure of simulation work

7.2 3D Modelling and Simulation Input

7.2.1 *Simulation Software*

COMSOL is selected to conduct the simulation over other software for several reasons. One main benefit of COMSOL for this study may be solving inverse problems—that is, once the user is comfortable with the software, it can be applied to a wide range of physical problems. Additionally, COMSOL's 'Multiphysics' capabilities allow several physical equations to be intrinsically coupled; thus, the multi-physical domains that appear in the future design and experiments may be easier to address via COMSOL. The drawbacks of using COMSOL

include that its solution time can be slower than that of other highly specialised forward models.

7.2.2 *Simulation Input*

From the previous design process, the parameter range for the ideal scaffold, between NIB magnetic particles and silicone elastomers, was proposed as between 15 and 25%, based on TRIZ contradiction solving weight/density/magnetic property, as well as previous experimental proofs.

I. Material input

An average-level ratio parameter of 20% is selected for the following simulation input. First, we searched databases for 'NiFeB' and 'silicone elastomer', and then completed a literature review on previous research who completed exact studies using 20% NIB with silicone elastomers, with partial experimental data information acquired from the MIT research centre (Kim, Y 2018; Kim, Y et al. 2018). Other information about NiFeB and elastomeric polymers were attained from university libraries.

II. Magnetic property input

For the printer's nozzle size, the average is between 300 and 600 μm for Robocasting or FDM 3DP. Given that nozzle size can affect magnetisation strength, previous experimental data using a nozzle with diameter 410 μm under a magnetic field of 50 mT at the nozzle tip is studied for simulating purposes. The measured magnetic moment density varies almost linearly from 15 kAm-1 to 83 kAm-1 as the volume fraction of NdFeB particles increases from 5 to 20%. As such, the structural magnetisation for our simulation study is identified as 82 kAm-1.

Simulation input: The following input parameters were used for simulation, Table 7.1. These parameters will be directly used for establishing the models of scaffold and magnetic field.

Table 7.1 the input information for COMSOL simulation

Input	Symbol	Value
Density	rho	2.434 g cm-3
Shear modulus	G[1]	330 kPa
Poison's ratio	nu	0.499
Magnetisation	M[2]	82 kAm^{-1}
Young's modulus	E	989.3 kPa
Bulk modulus	K	275,000 kPa
Magnetic intensity	B	At mT level

[1] G is 245 kPa when printed without external fields; M remains below 2 kAm^{-1}; G is 380 kPa when uniformly magnetised at 2.7 T after normal fabricating, where M will reach 124 KAm^{-1}; [2] M is 70 kAm-1 when using a smaller printer nozzle at 200 um.

7.2.3 *Scaffold with Magnetic Vibration*

There are several different magnetizations in relation to scaffold's fabrication, which can be summarized as Table 7.2.

Table 7.2 Illustration of magnetization methods in regards of 3DP fabricating

No.	Method	Prior to fabricating	During 3DP	Main vibratory principle
1	Non-magnetised	Scaffold material paste/ink remains neutral	None	Eigen- [2]
2	Magnetised	Scaffold is magnetised after 3DP fabrication	None	Eigen- + field stimulation
3	Locally magnetised	Material is partly magnetised previously	None	Eigen- + field stimulation
4	3D printed in tailored magnetic domains	Material paste is fully magnetised previously	Magnetic installed around nozzle	Eigen- + field stimulation
5	Geometric unit library design	Cooperated [1]	Cooperated	Eigen-

[1] Geometric designs could potentially cooperate with four magnetic-based solutions to generate more complicated vibrating or dynamic functions. [2] Eigen- means tuning magnetic field frequency with eigenfrequency of structure.

For conceptual 3DPVS, structural material, such as paste or ink, could be treated differently to induce multiple effects that can be actuated afterwards via an external magnetic field. Thus, multiple categories can be proposed.

7.2.4 *Main Task of COMSOL Simulation*

Two main tasks will be concluded for the simulation, one is scaffold is fully magnetised at z-axis, along the same z-direction of magnetic field, Table 7.3. Another is scaffold magnetised in tailored ways. Modelling the magnetic field with different directions and patterns can be an interesting future work.

Table 7.3 Chief simulation tasks using COMSOL

No.	Magnetisation	Task	Aim	Main principle
1	Scaffold magnetised at z-axis, with magnetic field along z-axis	a. Basic shape-changing functions (field turn on/off) at lower actuation rate	To demonstrate the designed 3DPVS could generate shape-changing/vibrating functions as expected	Eigen- [2]
		b. Eigenfrequency stimulation (50 to 200 Hz as designed) at higher vibrating rate		
2	Scaffold magnetised with different parts + magnetic field along z-axis	a. One layer of scaffold is magnetised in x-axis, with another layer in y-axis, alternately	To demonstrate the special functionality of our design, which means localisation	Eigen- + field stimulation
		b. One layer of scaffold is magnetised, with another layer non-magnetised		

Note: In (1), scaffold is magnetised after fabricating, under a magnetisation machine, to achieve uniform magnetisation along z-axis. In (2), scaffold is magnetised through the specially designed 3DP technique, with magnetising direction along with the printing direction.

7.3 Conditions and Parametric Setting

7.3.1 *COMSOL Model Description*

A 3D computational model of a single magnetic field is set up in COMSOL Multiphysics® 5.4 to investigate the vibration of the designed scaffold. The physics package of 'magnetic fields', with 'no currents' and 'stationary' state, is selected. The interface of physics mainly solves Gauss's law for the magnetic field, and takes scalar magnetic potential as a dependent variable. Extra finer mesh size is selected to improve simulation accuracy.

7.3.2 *Model Geometry*

I. Scaffold geometry

A designed scaffold with a regular geometrical structure measuring 14.75 × 14.50 × 13.77 mm (length × width × height; total volume, 2.95 cm^3) is designed. The geometry is designed within COMSOL graphical user interface after being imported from SolidWorks. From concept generation, geometric is the key factor for eigenfrequencies in case that material composition is determined. Different parameters in terms of the strut's length, width, and height were tested, which generates a good solution enabling maximum number of natural vibrations at 50-200 Hz. 18-layer 3DPVS with this specification is considered as optimal, Figure 7.4.

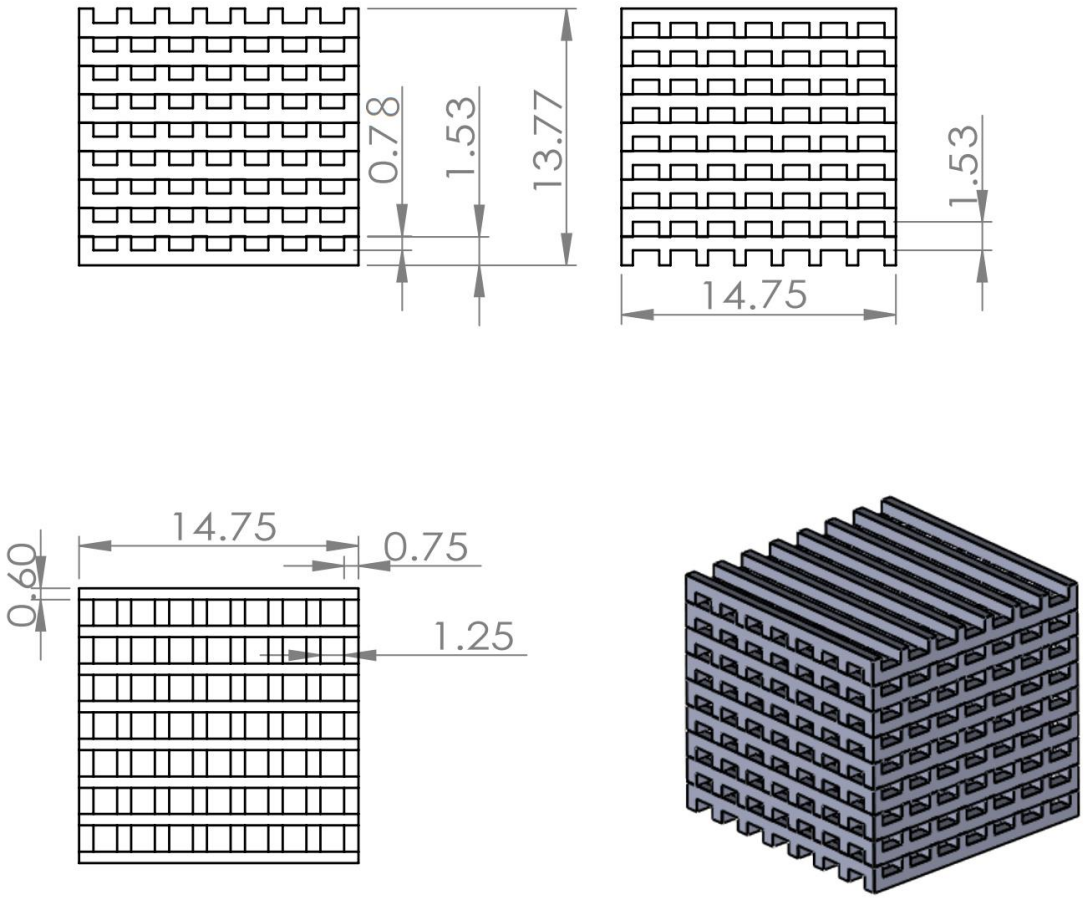


Figure 7.4 Geometric specifications of strut-based 3DPVS model by Solidworks

II. Magnetic field

COMSOL Multiphysics 5.4 is used to simulate user-tailored magnetic fields. Models of the external permanent magnet field is established via the current-free module under magnetic field to calculate the magnetic force of particles. It is set twice the size of overall scaffold, Figure 7.5. Different magnetic fields can be set from Background Magnetic Field. In this study, Z-axis field is most frequently used for simulation. Moving mesh focusing on particles' transient movement is not used, which will be useful in future work when cell culture medium and cells are considered.

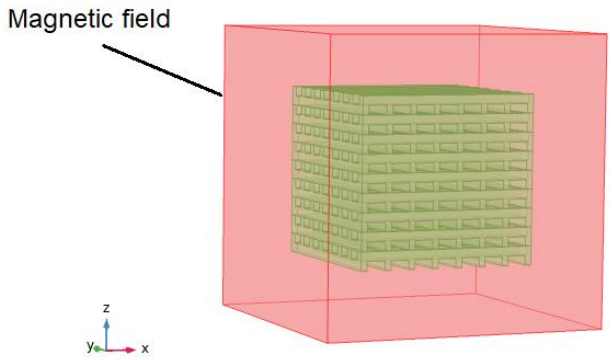


Figure 7.5 Model of magnetic field in position with 3DPVS

7.3.3 *Model Assumption*

To simplify mathematical modelling, several assumptions are made regarding boundary conditions and initial conditions, when modelling the scaffold in the magnetic field. First, the effect of heat dissipation from shape changing of the scaffold is neglected. Second, air is considered the medium between the scaffold and magnetic field. Third, the partial bottom of the scaffold is fixed.

7.3.4 *Numerical Analysis*

COMSOL 5.4 is used to perform numerical simulations, studying the magnetic field around the scaffold and the deforming behaviour of the scaffold because of the magnetic presence. The magnetic field strength can be generated in two ways—magnets or AC circuits—and a magnetic flux density of 1mT/1T is simulated. Methods to alter field strength are also investigated. Given that the magnetic field is being simulated without electric currents, the model is solvable with a scalar magnetic potential defined, as follows: $H = -\nabla V_m$, where V_m is the scalar magnetic potential and H is the magnetic field strength. The magnetic flux density can be written as $B = \mu_0 (H + M)$, where M is the magnetisation and μ_0 is the permeability of free space. Then the gradient of magnetic flux density can be expressed using Gauss's law as $\nabla . B = 0$. After using this expression equation, the gradient can be written as $-\nabla . (\mu_0 \nabla V_m - \mu_0 M) = 0$.

Structural mechanics in COMSOL implementation are based on the principle of virtual work, the sum of which from internal strains is equal to that via external loads. The implementation for hyperelastic materials is similar to that of linear ones. The strain tensor is replaced with the Green-Lagrange strain tensor, while the stress tensor is replaced with the second Piola-Kirchhoff stress tensor, which describes a material's nonlinearity. Thus, the principle of virtual work solved via COMSOL can be expressed as $W = A_1\left(e^{C_1(J_1\text{-}3)}\text{-}1\right) + A_2(J\text{-}1)^2$. Connecting with this, the principle of virtual work solved in COMSOL Multiphysics is expressed as:

$$\delta W = \int_V (-\varepsilon : s + uF_v)\ dv + \int_S (uF_s)\ ds + \int_L (uF_L)\ dl + \int_p (u^t F_p) \qquad \text{Eq. 7-1}$$

where u is the displacement variable tensor, F_v is the volume force, F_s is the area force, F_L is the line force and F_p is the point forces acting in the domain. W denotes elastic energy in the case of hyperelastic materials.

An understanding of PDE (partial differential equation) is a requisite for analysing the simulation process of COMSOL. Implemented in the finite-element software, several weak forms construct the magnetic–mechanical coupled system, given the strong capability of COMSOL in handling a coupled partial differential equation (PDE). Three interfaces implement the fully coupled PDEs with corresponding constitutive equations: (i) PDE interface adopted for the magnetic actuation, (ii) AC/DC interface used for the distributive magnetic and electric fields, and (iii) solid mechanics module used for the shape deformation of 3DPVS. From previous studies on hard-magnetic elastic materials, the first Piola-Kirchhoff stress can be calculated as:

$$P = GJ^{-\frac{2}{3}}\left(F - \frac{I_1}{3}\boldsymbol{F^{-T}}\right) + KJ(J-1)\boldsymbol{F^{-T}} - \frac{1}{\mu_0}\, B^{applied} \otimes B^r \qquad \text{Eq. 7-2}$$

where G is the shear modulus, K is the bulk modulus and $I_1 = \mathrm{tr}(F^TF)$, B^r indicates the residual magnetic flux density, and $B^{applied}$ is equal to $\mu_0 H$. The elastic contribution can be expressed as $\sigma^{elastic} = GJ^{-\frac{5}{3}}\left(FF^T - \frac{I_1}{3}\boldsymbol{I}\right) + K(J-1)\boldsymbol{I}$, which can be tuned with COMSOL hyperelastic neo-Hookean models as incompressible. Meanwhile, magnetic contributions, expressed as $\sigma^{magnetic} = -\frac{1}{\mu_0}\left(B^{applied} \otimes B^r\right)$, must be transformed from the first Piola-Kirchhoff stress into the second, with the transforming equation $P = (FS) = (I + \nabla u)S$, because magnetic problems are solved by COMSOL via the second Piola-Kirchhoff stress tensor.

7.3.5 *Mesh Generation and Analysis*

After constructing geometry, adding physics, studies, materials, ICs and BCs, the mesh of model is generated, where the details of this mesh are described in the caption.

Table 7.4 Mesh independent analysis

Mesh type	Max. element size (mm)	Min. element size (mm)	Max. element growth rate	Curvature factor	No. of elements	Solution time (s)	Global error (%)
Extremely fine	0.295	0.00295	1.3	0.2	662,023	24	NA
Super fine	0.516	0.0221	1.35	0.3	116,726	4.28	0.5
Extra fine	0.811	0.059	1.4	0.4	37,595	3.31	0.7
Finer	1.18	0.148	1.45	0.5	25,858	2.89	7.7
Normal	1.48	0.266	1.5	0.6	17,774	3.29	9.1
Coarse	2.21	0.413	1.6	0.7	17,535	3.17	9.3

To select the appropriate mesh size, we undertake a mesh independent study, where the mesh size increases gradually, and compare the magnetic intensities along the coordinate X = $L_{x/2}$. Table 7.4 shows the mesh independent study under different scales. Global error is computed between specified mesh scale and reference scale (i.e., extremely fine). The table shows that by decreasing the mesh size, the number of elements increases and the global error drops. When the mesh scales are coarse and normal, the global errors indicate 9.3 and 9.1%. When the mesh scale changes from finer to extra fine, the error lowers from 7.7 to 0.7%. However, when the mesh changes further from extra to extremely fine, the number of computational elements increases significantly by about 279%. Therefore, extra fine could be adopted as the optimal mesh scale for our simulation. As shown in Figure 7.6, the sweep/mapping method is used in meshing the scaffold, and the free tetrahedral mesh is employed in the rest of the numerical model.

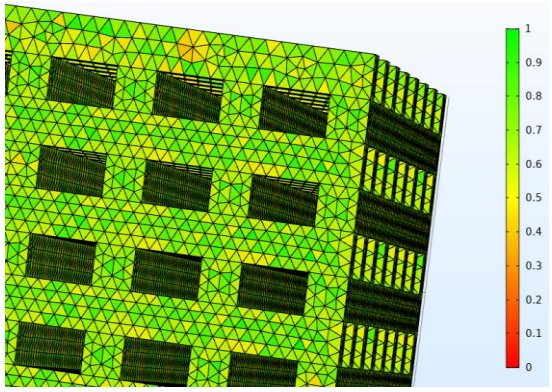


Figure 7.6 Illustration of scaffold meshing via extra fine mode

To ensure the stability, convergence and accuracy of the numerical results, a finer mesh of approximately 5,000 elements and a fine time-step (3,000 time increments, unit time-step size) is used.

7.3.6 *Initial and Boundary Conditions*

Real-world cell scaffolds usually need to be at a fixed position during cell culturing; therefore, a mechanical boundary condition is set in the bottom plane of the scaffold. Multiple fixing manners can be adapted to deal with different user demand cases. In our study, one possible

optimisation requires the scaffold to be both ‘attaching’ to its bottom support, while playing the most flexible role regarding resonant (vibratory) functions. The magnetic ground is applied on the boundaries, as well as inside the scaffold domain. For boundary conditions, no prescribed displacement is applied at the scaffold, while the bottom side can be either partially or fully fixed.

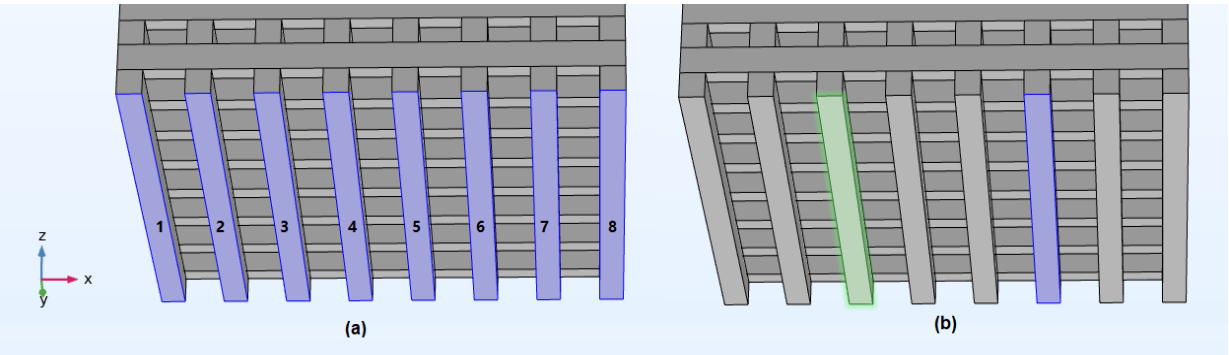


Figure 7.7 Scaffold boundary condition fixing manner: (a) eight lines fully fixed; (b) third and sixth lines fixed

A detailed study is conducted to investigate the relationship between bottom-fixing manners versus the scaffold’s vibration, example shown in Figure 7.7. Considering the asymmetric characteristics of the scaffold, optimal fixing manners may be chosen asymmetrically as well—that is, to fix two, four, six or eight lines, depending on the tailored cell culture requirements. In this study, four lines are selected, as a relatively balanced, neutral mode during simulation studies. Different fixing modes can affect the vibrating functions.

Using number to indicate previous numbered lines, six modes are analysed, which includes 1-2-3-4-7-8, 2-4-6-7,2-4-5-7, 1-3-6-8, 3-6 and 4-5. From this study, fixing two lines is selected as one optimal option. Characteristic frequency number indicates the number of eigen-modes at the range of 50-200 Hz, which is desirable characteristics by 3DPVS, Figure 7.8.

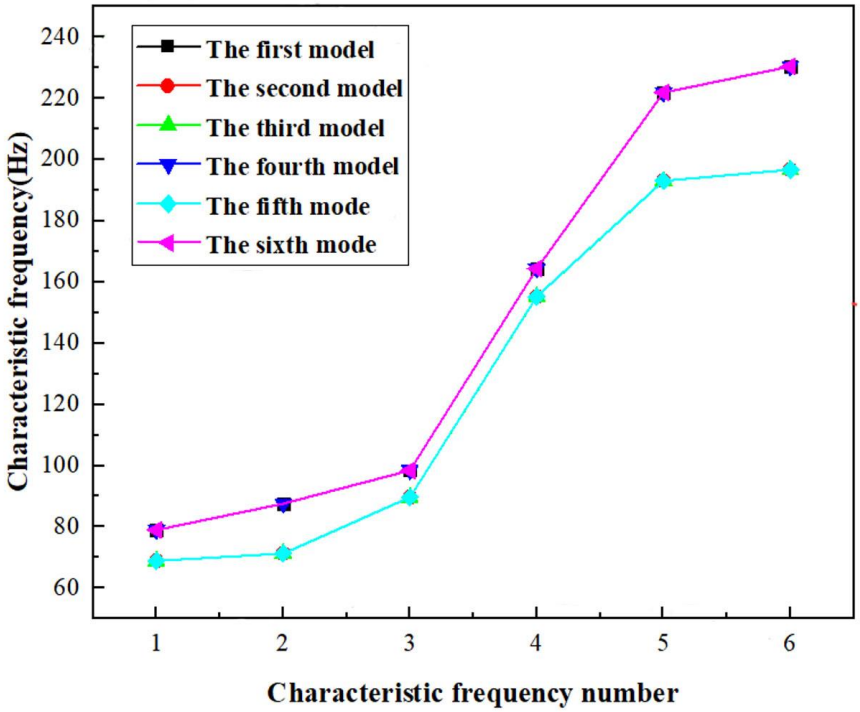


Figure 7.8 Comparing characteristic frequency number in different fixing modes

From this analysis, different modes show relatively small difference regarding numbers, while the frequency varies between different modes. Selecting two or four lines is optimal as it provides highest flexibility.

7.4 Simulation Process

7.4.1 *Simulation Replication*

Regarding hard-magnetic soft materials, there was previous research studying their domain-tailored shape-transforming functions. Figure 7.9 shows an example of previous simulation work (Kim, Y 2018; Kim, Y et al. 2018), with magnetic-domain printed on a line-structure that generates m-shaped change. Here, we use COMSOL to replicate this work. Comparing with previous simulation results, we demonstrate that the COMSOL software settings and parametric settings are reasonable by generating the same results. The constitutive relation used for calculating magnetic-stress induced deformation was implemented as a user-defined element subroutine in the FEA software ABAQUS for model-based simulation.

In brief, simulation work here will help facilitate the rational design of magnetically-activated functional structures and scaffolds based on quantitative prediction of complex shape changes, making the further study of vibratory properties easy and effective. In the following part, a line structure with programmed ferromagnetic domains will be simulated first to analyse predictable shape changes under applied magnetic fields. This is undertaken because, before reaching the level of mastering full scaffold deformation, basic analysis of one filament, one library unit of scaffold or a single layer should be implemented in the conceptual design stage.

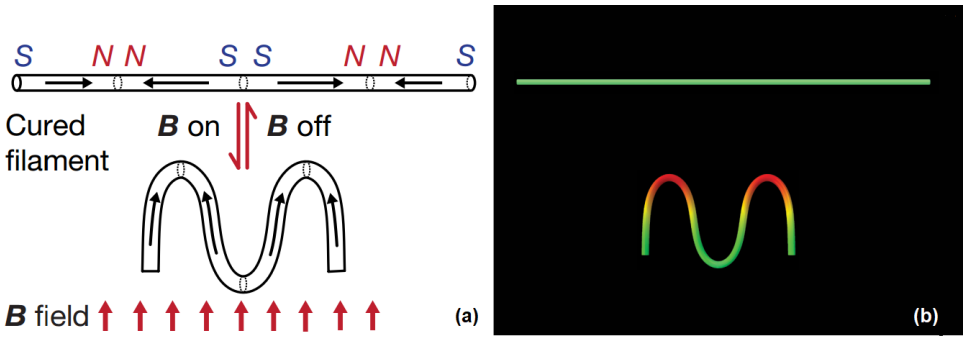


Figure 7.9 (a) Schematic sample of single 3D-printed filament and (b) finite-element model ABAQUS simulation under magnetic field stimuli

COMSOL work is conducted as follows. First, a 2D modelling (fixed bottom, 100 mT) is used to predict the m-shape of transformation. Second, a 3D model is built, generating both U-shaped and M-shaped simulation results, with a fixed bottom at a 100 mT magnetic field. Figure 7.10 shows the one-line magnetic domain simulation; two-pattern magnetisation with U-shape, a, and four-pattern with M-shape. There is a visual difference between M-shaped line between this work and previously ABACUS work done by Kim, Y et al. 2018., because the two ending points and middle point of COMSOL simulated one is fixed with boundary condition.

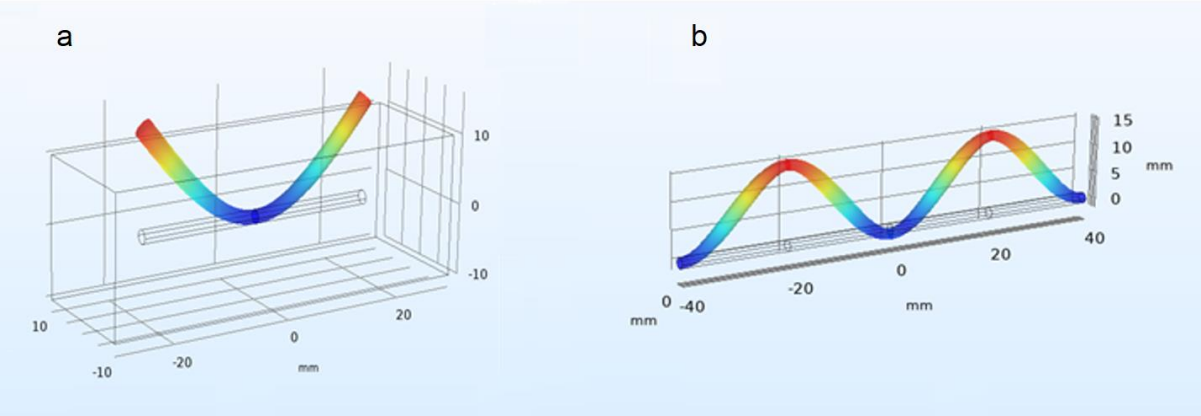


Figure 7.10 COMSOL for simulating/replicating one-line transformation, (a) U-shaped, (b) M-shaped.

Another simulation work is on the complex 3D model, as shown in Figure 7.11. Work of COMSOL in B shows similar shape-changing in shrinking compared with the ABAQUS result in A. Difference is due to the amplification ratio of visual setting.

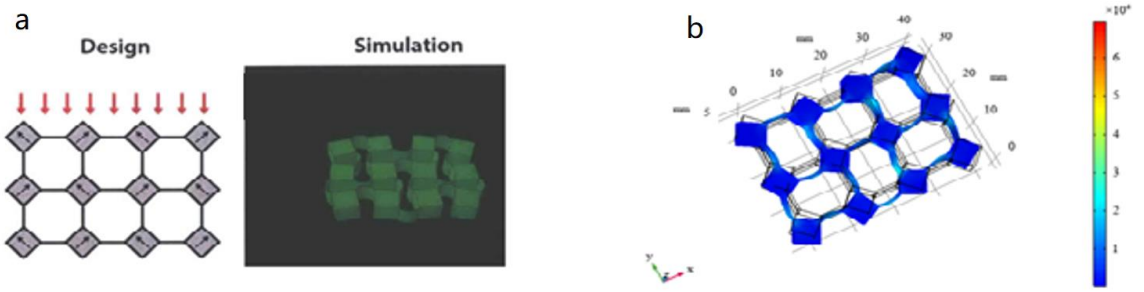


Figure 7.11 (a) Replicating box-shaped simulation work: design and ABAQUS simulation, (b) COMSOL replicating work

In brief, a single 3D-printable elastomeric fibre encoded with alternative localised ferromagnetic domains is proposed to generate the ‘m’ shape in a short time (within seconds) when applying a magnetic field at mT level, and this can be successfully replicated. Another benefit for this single line work is that simulation—including the filament’s magnetic and mechanical properties and the applied field—will guide designing complex line-based structures in scaffolds with definite programmed ferromagnetic domains.

Though there exists some visual difference, the general magnetised shape-changing principles simulated by both software types remain the same. Work conducted previously with ABAQUS is successfully replicated with COMSOL. This proves the early idea that COMSOL is fully capable of modelling hard-magnetic elastomer structures.

7.4.2 *Simulating Scaffold’s Free Vibration*

CAD model is built by either COMSOL or Solidworks. In first place, an eigenfrequency study is conducted, setting the scaffold as hyper elastic material, with density, Young’s modulus and Poisson's ratio. Mode shapes of scaffold is analysed at multiple resonance frequencies.

The first goal of this part is to validate the design scaffold, which has low-level eigenfrequency. Therefore, a traditional scaffold is used as a comparison reference. The traditional static scaffold (one base model) using PCL has the following parameters, which are used for simulation: density at 1.146 kg/m^3, Poisson’s ratio at 0.42 and Young’s modulus at 20 MPa.

Eigenfrequency of PCL static scaffold tends to be at high values. This means that resonance cannot be triggered by hundred-level frequencies required by definite bone cell studies. Scaffold building is modelled by SolidWorks. The geometrics of the both traditional scaffold and 3DPVS are set as same for comparison. Using COMSOL, the desired eigenfrequency number is set at 15, with first real values selected.

Note that the eigenfrequency analysis can only provide the shape of the mode, not the amplitude of vibration triggered by external force. To calculate the amplitude of 3DPVS inside the magnetic field, magnetic strength and frequency need to be determined.

7.4.3 *Simulate the Simplified Box-shaped Model*

Due to excess work of calculating magnetic field with full scaffold, here we use a box-shaped model to for simplification. Basic principles using magnetic vibration as per design can be validated at more effective and easier way. This include two tasks, firstly to identify the eigenfrequencies of the model and analyze its shape-mode; secondly simulate the model using domain-frequency magnetic field at the range around previously generated eigenfrequencies. The magnetic-actuated modes will be compared with the natural vibrating modes. It is expected that a structure deforms into a corresponding shape under magnetic vibration at around its eigenfrequency. However, whether this shape has relation to its eigenmode remains unknown. An edge point is selected to help analyze the displacement, Figure 7.12, left, the box inside magnetic field, right, one edging point of box selected.

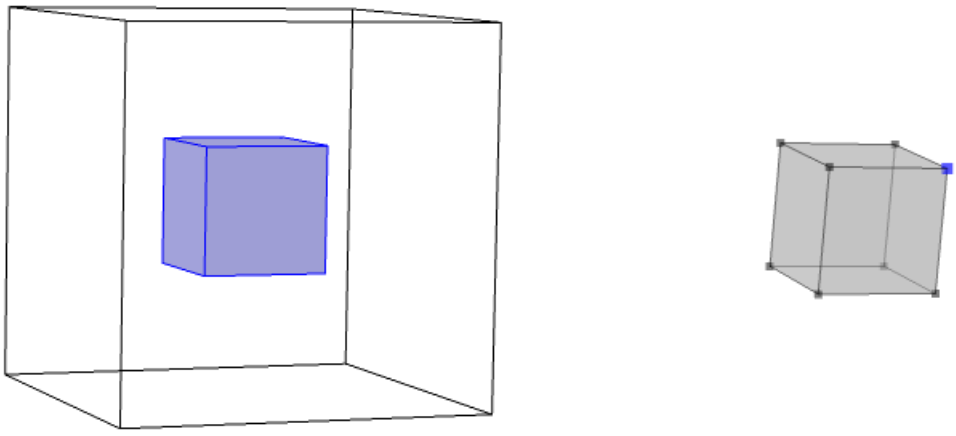


Figure 7.12 Box-shaped model inside magnetic field with one point selected

Purpose of simulating box-shaped model. There are several advantages of using this simplified model. First, several design principles/solutions generated in the previous conceptual process can be validated with this model, which is easier and more effective than with the complex 3DPVS model. Second, this box-model can be used as reference to compare with 3DPVS which will be simulated under same procedure. This provides feedback and helps future designs. Third, to fully simulate 3DPVS model, a high-performance workstation is needed, which we currently don't have. Using the currently available hardware, the calculation time for one model could take up to weeks, which is unpractical. This results in a limitation that several simulations of 3DPVS model cannot be satisfactorily conducted. Simplified box model therefore is used for analysis.

7.4.4 *Simulating 3DPVS*

I. Simulating the Magnetic-actuated Vibration of 3DPVS

Two modes will be analyzed, first the harmonic vibration and second the periodic forced vibration. Under harmonic vibration modes, it will validate if 3DPVS can generate required micro-level amplitudes among the selected 50-200 Hz range, and study how scaffold vibrates in definite frequencies for example those close to the eigenfrequencies. For periodic forced vibration. Magnetic input will be set as the function sin(2πft) to test vibratory properties under selected frequencies and strength of magnetic field.

II. Shape-changing Functions of 3DPVS

For this part, scaffold is magnetized at z-axis with the 200mT magnetic field at the same direction. First, stationary study is used to analyse the shape-transforming properties of 3DPVS. With the triangle magnetic field input, scaffold is predicted to generate regular shape-changes. Displacement magnitude will be studied. Second, time-based modes of 3DPVS in slow-shifting magnetic field will be simulated, assuming there is an alternating magnetic alone z-axis.

III. Localisation

A three-layer scaffold is simulated to analyse the possible localised functionality. Different magnetic patterns are designed Figure 7.13, with a curved shape changing as expected result.

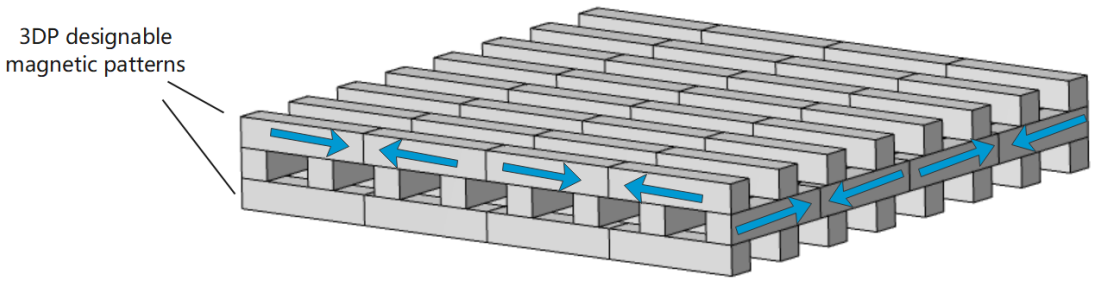


Figure 7.13 3DP designable magnetic patterns for localization

The eigenfrequency of three-layered model will also be analysed. From the conceptual design, it generates the solution that small layer scaffold in such structure will enable 50-200 Hz natural vibrations, which will be validated.

7.5 Results and Discussion

7.5.1 *Free Vibration of 3DPVS*

From the simulation, we see that the designed 3DPVS can reach the lower-range vibrating frequency (50 to 200 Hz), as proposed. Using the magnetic-based elastomer material, 3DPVS could generate tailored vibrations when changing the layer of scaffold. An 18-layer scaffold can enable the largest number of appropriate frequencies.

The simulated results need to be compared with the analytical results for the free vibration case. Due to 3DPVS remaining at conceptual stage, there is no experimental data yet. But for the agreement, authors predict that the accuracy will increase with increasing complexity of fine mesh, as it's limited for using relatively coarse mesh to describe such complex shape.

I. Comparing Traditional Scaffold vs. 3DPVS

Eigenfrequency of traditional static scaffold. As a reference, the geometrics of PCF scaffold are modelled the same as 3DPVS. Results show that such traditional static scaffold tends to have a natural frequency above thousands of Hz or higher.

Low-level eigenfrequency enabled by designed 3DPVS. For 3DPVS, its natural frequency must be settled at hundred level, even reaching 50 Hz and below. In this case, the magnetic-based scaffold could achieve multiple eigenfrequencies at levels at the range 50-200 Hz, which is the proposed vibrating frequency by this research.

II. 3DPVS Eigenfrequency Models

The FEM helps evaluate various parameters, such as the internal stress and strain distribution, which is difficult to measure using experimental methods. Given that cavities are uniformly distributed on the scaffold, only one part is modelled. The simulation is performed in the following steps: geometric solids are created, including the scaffold, magnetic field (without current) and air region. Current excitations and Ampere forces are ignored. Suitable boundary conditions are loaded correctly, and a definite selection part is chosen for meshing. Then, the magnetic field distribution and strain can be calculated, with derived data being analysed and visualised in post-processing. Figure 7.14 shows the 3D eigen models of 3DPVS at the desirable range about 50-200 Hz. Note that meshing strategy can affect the calculation result. From the simulation result, we can see that the eigenmodes between 50-200 Hz vary significantly and each frequency can generate a specific shape-modes.

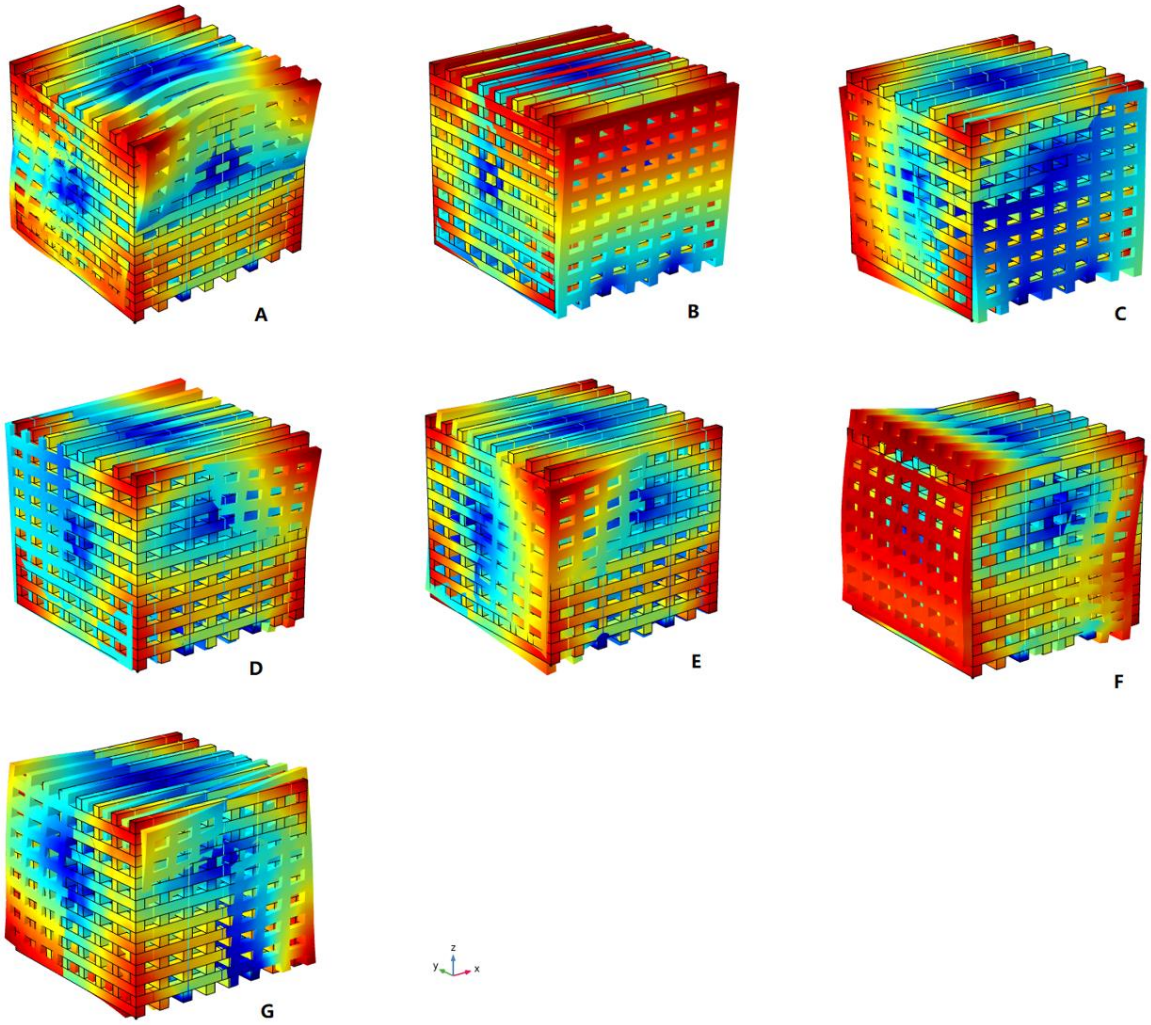


Figure 7.14 Comparing vibration modes of 3DPVS with different eigenfrequencies: (A) 60.866 Hz, (B) 74.798 Hz, (C) 153.26 Hz, (D) 153.64 Hz, (E) 154.04 Hz, (F) 183.21 Hz and (G) 203.58 Hz

III. Magnetic Flux Density

The magnetic fields with definite magnetic field strength and direction can be modelled under Ampere's law. In this case, field-resulted magnetic flux density is shown as Figure 7.15. Result shows that the connecting points between struts tend to have higher density.

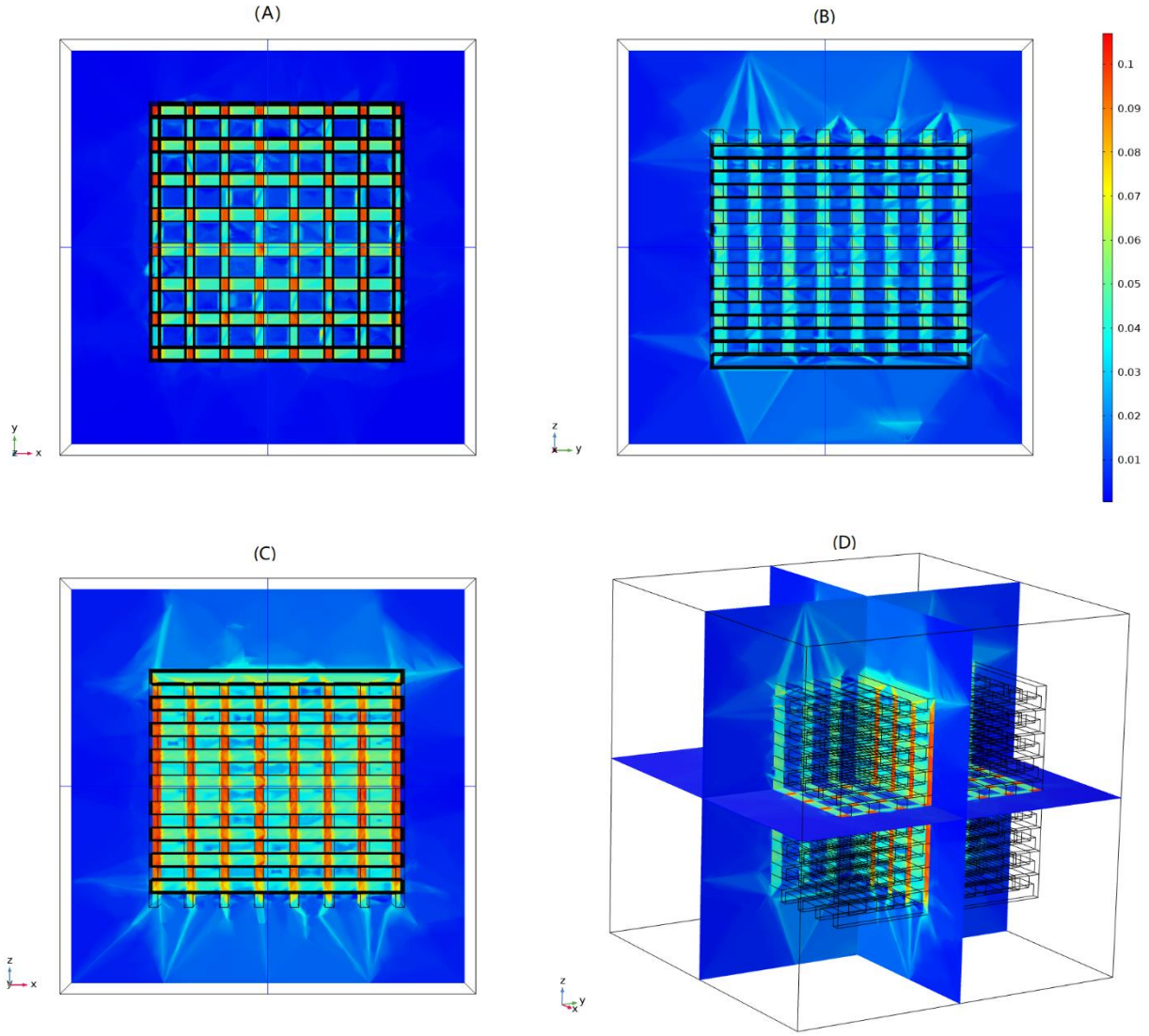


Figure 7.15 Magnetic flux density illustration within the scaffold, (a) top view, (b) x-axis view, (c) y-axis view, (d) 3D view.

IV. Displacement with Multiple Planes Inserted

Inserting multiple planes inside scaffold could help analyse scaffold's inner status. Different points are also selected in comparison. The COMSOL simulation shows the result as Figure 7.16. Vibrating modes analysis comes from (a) and (b) ½ intersection plane, (c) and (d) ¼ intersection plane, (e) and (f) 1/8 intersection plane. Numbers inside bracket indicate the position of x- and y-axis.

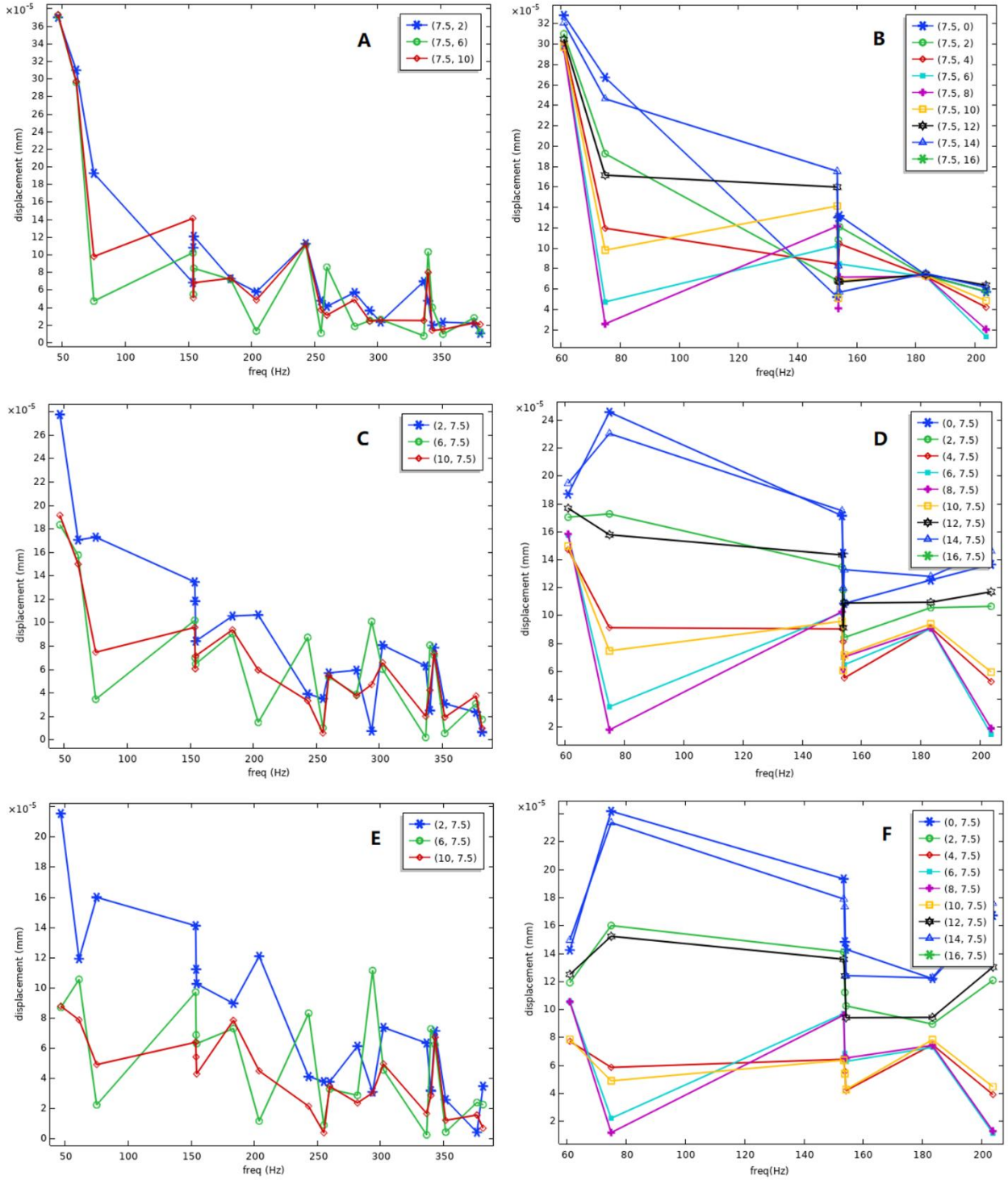


Figure 7.16 Comparing 1/2, 1/4 and 1/8 intersection planes in scaffold during vibrating modes

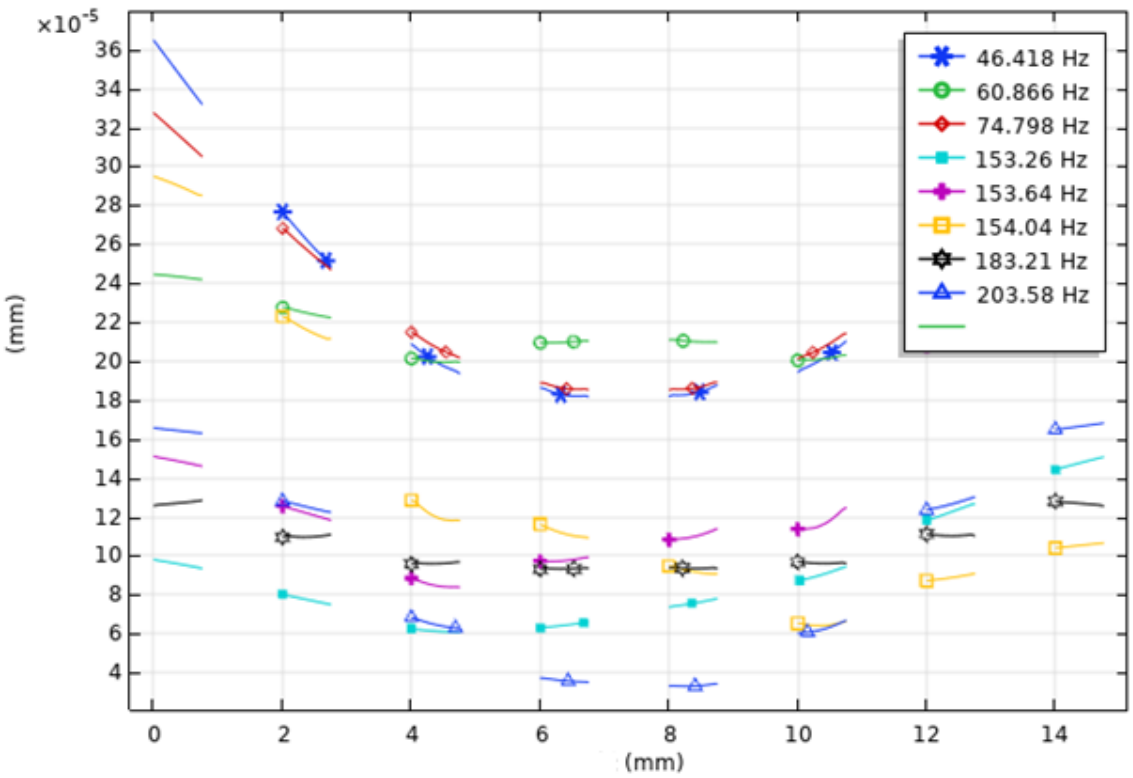


Figure 7.17 Displacement of different vibrating frequencies

With the change of vibrating frequencies, as shown in Figure 7.17, result shows that, as frequency increases, the amplitude displacements demonstrate a U-shaped curve. Middle point of scaffold tends to have lower displacement than edging point.

7.5.2 *Simplified Box-shaped Model*

With this simulation, we arrive at two understandings. First, magnetic-vibration modes of the box have close relations with the natural frequencies. Around the definite eigenfrequencies, the displacement curve will either reach a peak, or bottom, or show a deviation. Second, magnetic-based vibration can generate different shape-changing modes than natural eigenfrequency modes. This is possibly due to the magnetic reaction inside scaffold, as well as the user-tailored magnetic direction. Figure 7.18 shows the comparison of several typical eigenmodes with magnetic-vibrating modes of same frequencies. Basic conclusion is that under definite eigen-values, scaffold can generate shape-changing, while this changed shape has no obvious relationship with the shape of eigen-modes. Reason and why can be an interesting question for future research.

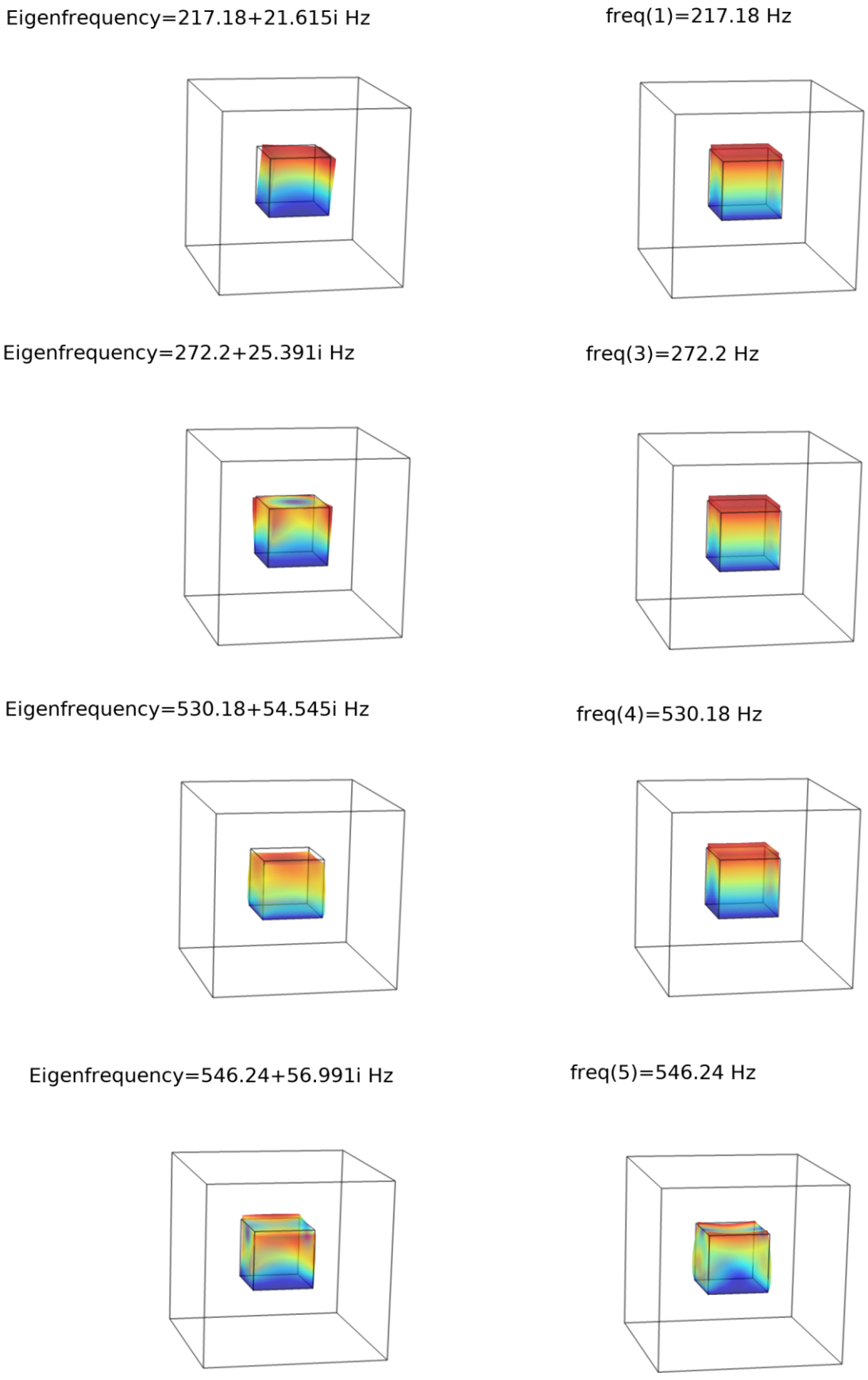


Figure 7.18 Natural vibrating modes vs Magnetic-actuated vibrating modes at same frequencies

I. Harmonic Magnetic-forced Vibration

After comparing the natural vibrating modes with magnetic-stimulated vibrating modes of the same frequencies, several conclusions can be made. First, natural vibration modes are quite unpredictable in each of the eigenfrequencies, while magnetic-based vibration can be precited based on the direction of externally-applied magnetic field. Result shows with z-axis magnetic field, the box-shaped model has the tendency to change its shape alone z-axis. Second, at around 500Hz, magnetic-triggered vibration shows the similar shape-mode compared with that of the eigenmode. Third, the maximum displacement of the magnetic-actuated models generally is in tune with that of eigenmodes. On other side, from the displacement analysis, we test that from 20-700Hz (the range where the natural vibration of box most occurs), the displacement curve increases gradually until around 375 Hz, then fluctuates and decreases until reaching another small peak at around 600 Hz then falls to 700 Hz followed by another peak at around 800 Hz; see Figure 7.19.

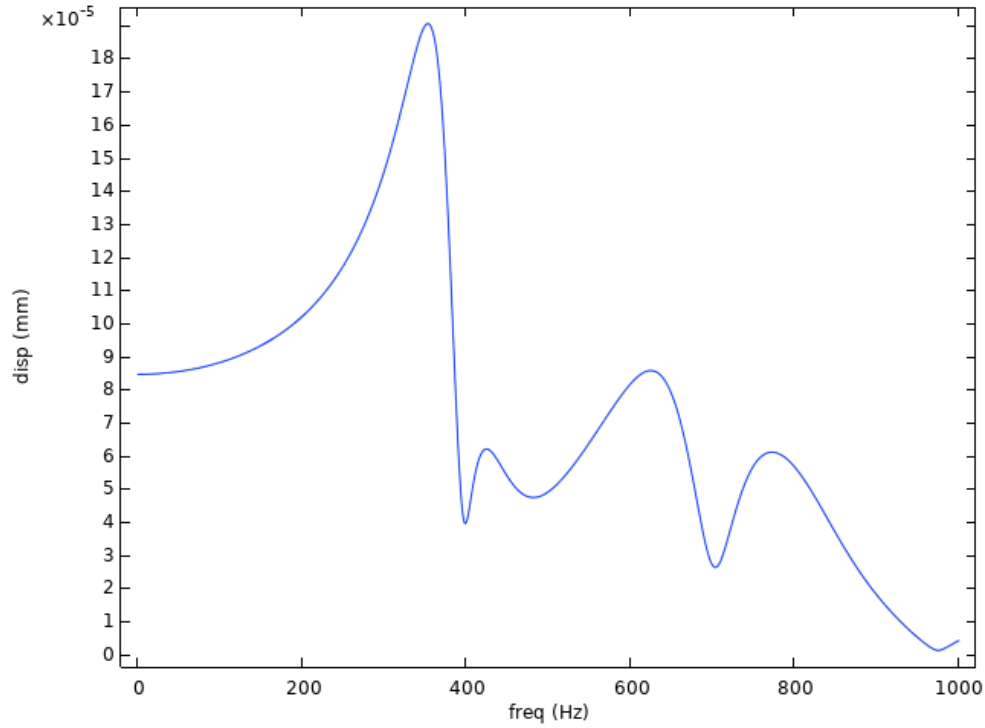


Figure 7.19 Displacement alone with the increased magnetic field frequency from 1 to 1000Hz

II. Periodic Magnetic-forced Vibration

A corresponding magnetic field is applied to induce vibrations. Different points of the scaffold can have invariable displacement. As time passes, the external magnetic field changes its strength, resulting in a corresponding displacement in scaffold that is predictable. Different geometrical points are compared, showing the outside point could enable relatively larger displacement compared with the inside point.

With a sinuous magnetic field input, box model shows predictable shape properties. In terms of the shape-changes, the box shows regular changes when simulated under z-axis magnetic

input; Figure 7.20 shows three states, namely, a, normal state, b, maximum state, c, minimum state.

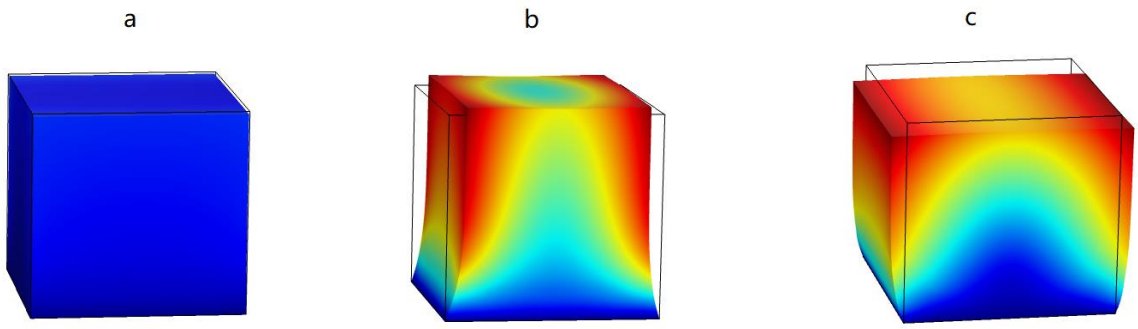


Figure 7.20 shape modes of box model under time dependent stimulation along z-axis

Analysing from Figure 7.21 to Figure 7.24, it shows that the displacement of model is strictly corresponding to the input functions of magnetic field. This is in tune with the concept solution generated previously; that is, the shape-changing of such hard-magnetic elastomer model can be predictable and determined by designing the input of magnetic field. Magnetic strength seems to be dominant factor affecting the displacement, compared with magnetic frequency. Under 1T field, displacement of 500Hz and 350Hz show quite similar result, although in resonance analysis displacement of 350 Hz is much higher than that of 500 Hz.

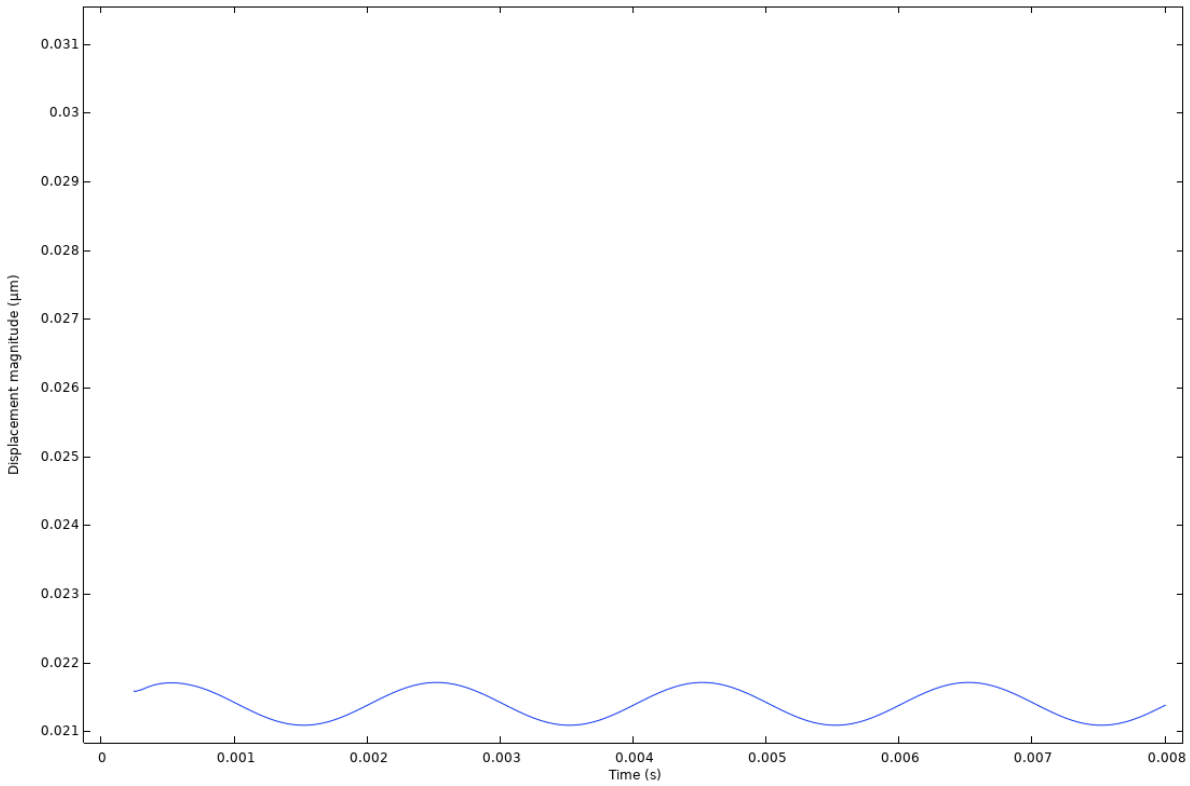


Figure 7.21 Time-domain displacement by shifting magnetic field, 500Hz, 1mT.

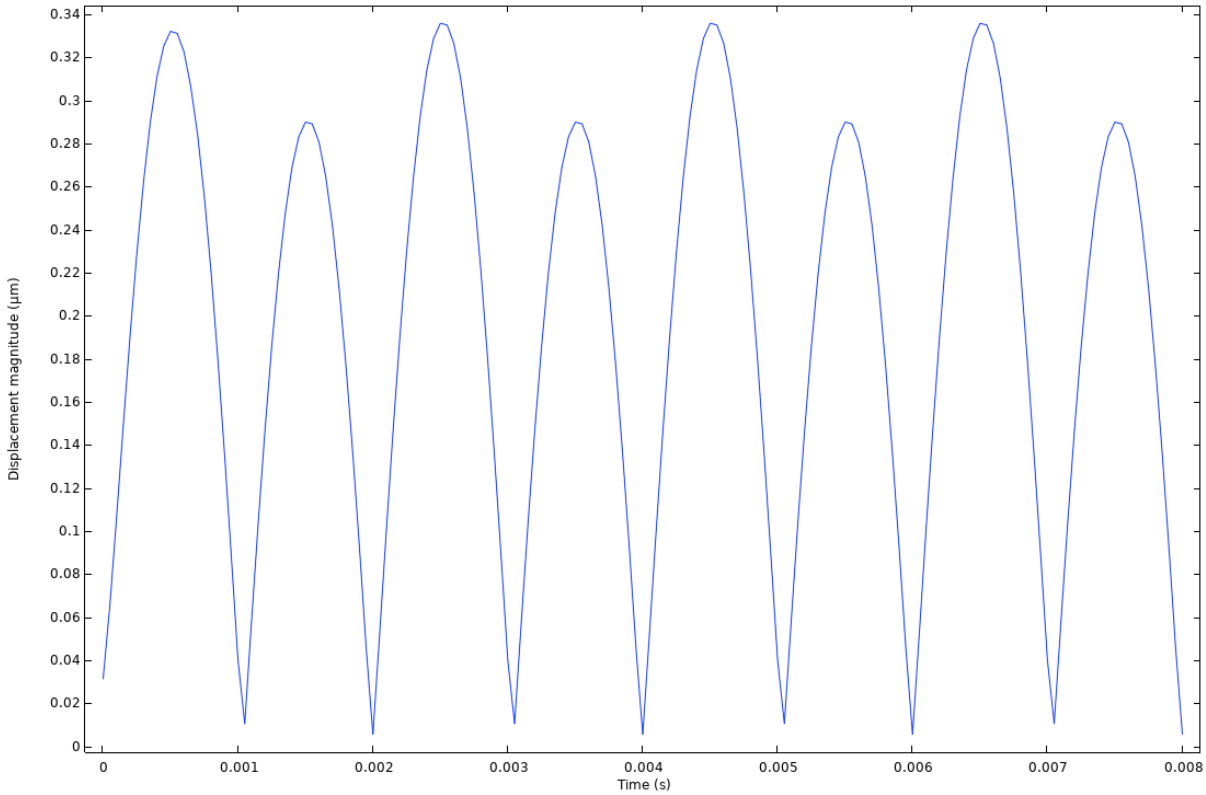


Figure 7.22 1T, 500Hz magnetic-actuated vibration

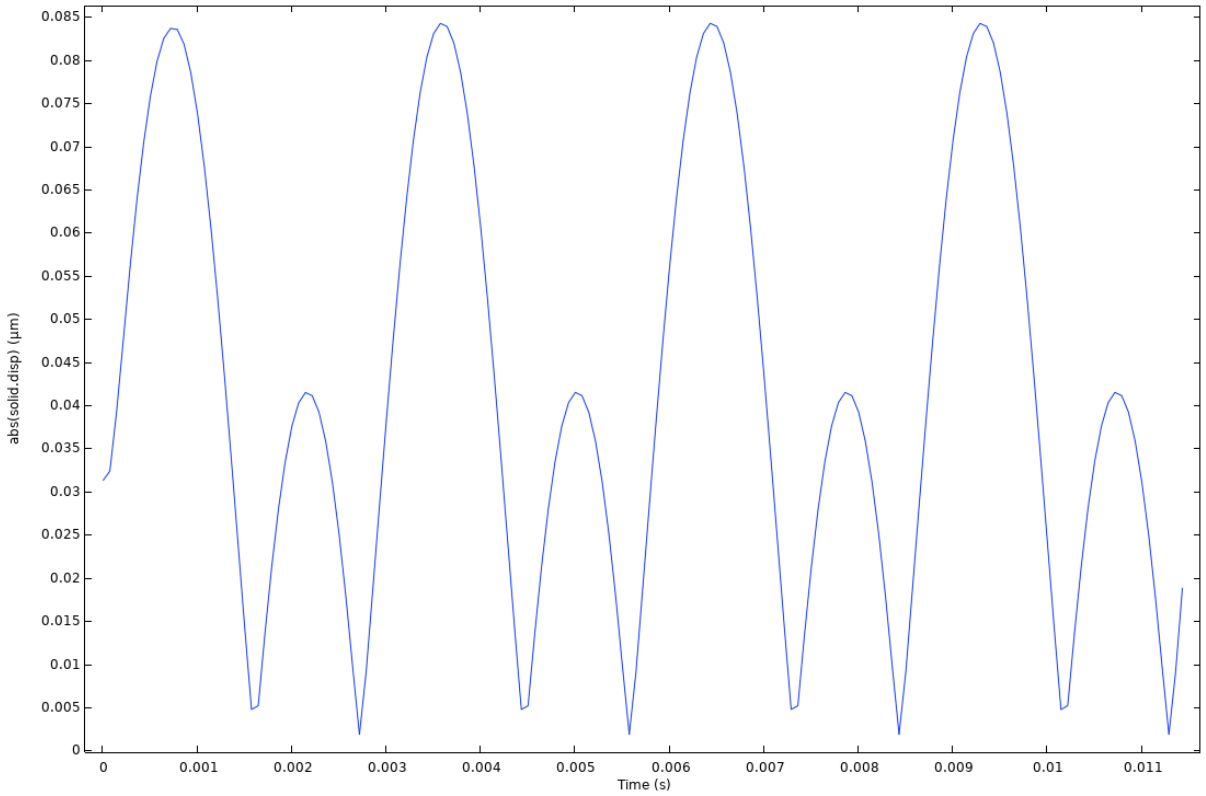


Figure 7.23 350Hz, 0.2T magnetic-actuated vibration

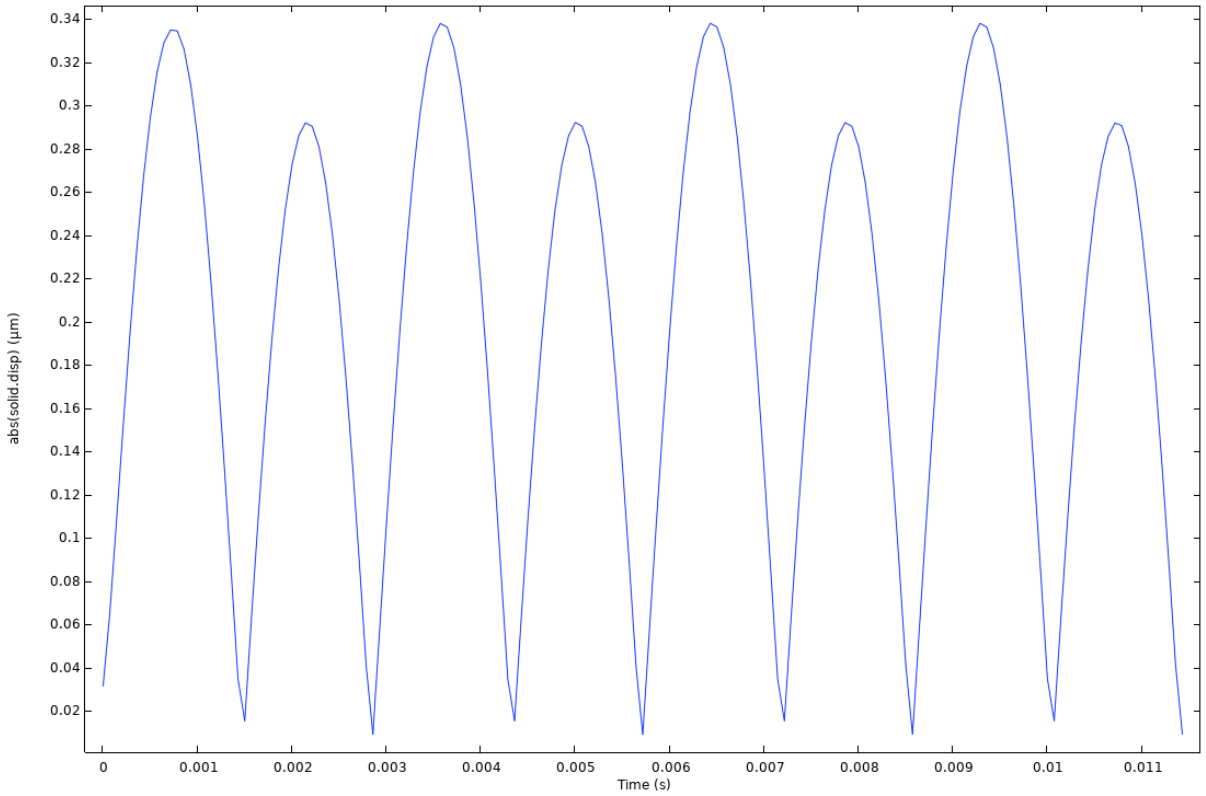


Figure 7.24 1T, 350Hz magnetic-actuated vibration

7.5.3 *3DPVS: Magnetic-actuated Vibration*

As early illustrated, the 3DPVS as designed can enable proper eigenmodes at around 50-200Hz range. For this simulation, Figure 7.25, a 200mT magnetic field is applied at frequencies from 40Hz to 210Hz. We could see that there are two peak magnitudes around 65Hz and 150Hz. As previously simulated, two eigenmodes exist around these two frequencies. However, in other eigenfrequencies, displacement tends to be at relatively low level. Displacements of different points were compared. Point on the edge tends to have larger displacement with the increasement of frequencies compared with that inside mid part of surface.

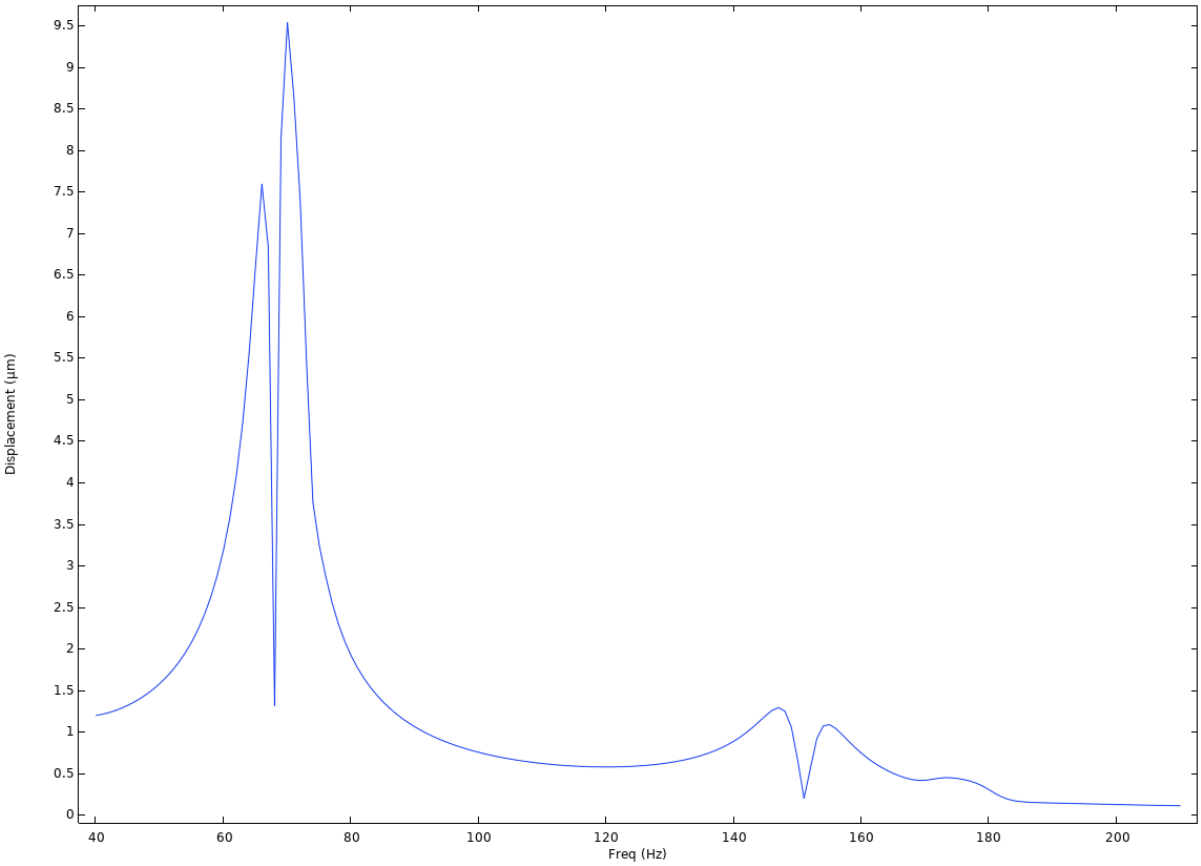


Figure 7.25 Displacement magnitude against frequencies

The 3D models from magnetic resonance are also generated. We see that in each model scaffold shows quite different shape changes, which is unpredictable. To generate thorough shape-transforming in as much part of scaffold as it can, a useful vibration way might be to use gradually increasing or decreasing magnetic field. This helps achieve thorough simulation on scaffold, compared with the simulation under only one or two definite frequencies.

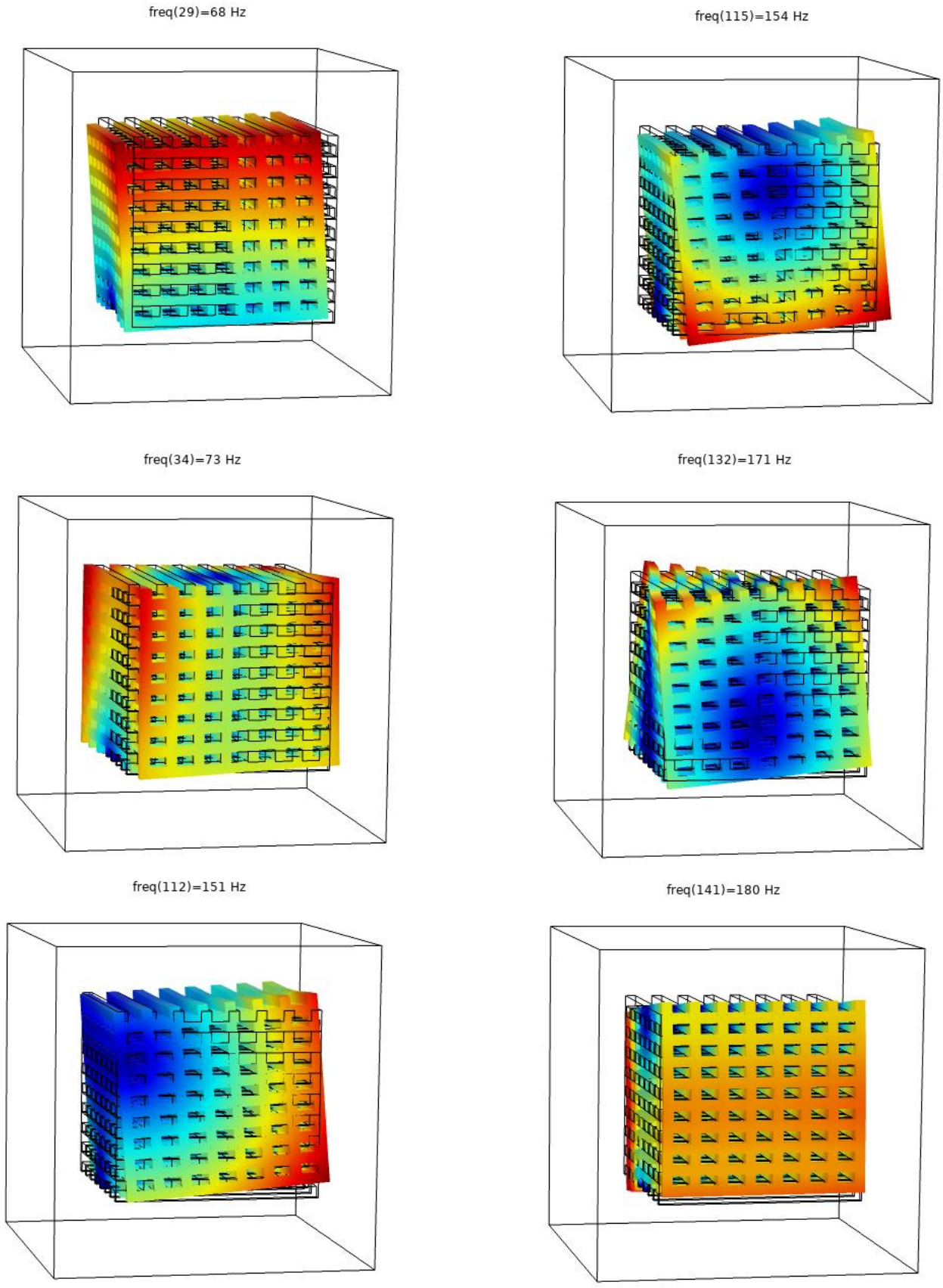


Figure 7.26 shape-changing modes of 3DPVS with invariable magnetic field shifting from 40Hz to 210Hz, with six eigenmodes inside the design range to be identified.

I. Harmonic Forced Vibration

Harmonic response indicates to 3PDVS's reaction of magnetic vibration under 50-200 Hz range. Peak displacement (μm), peak stress (Pa) and frequencies (HZ) were computed; In terms of the harmonic forced vibration case, the results are in good agreement with the expected outcomes proposed via the design process. Table 7.5 illustrates the computed harmonic responses.

Table 7.5 The computed harmonic responses of 3DPVS model

Mode number	Eigenfrequency COMSOL result (Hz)	Peak displacement (μm)	Peak stress (MPa)	Type
1	60.866	35.5	14.2	Flexural
2	74.798	102.3	34.3	Torsional
3	153.26	65.4	24.3	Flexural
4	153.64	63.5	23.5	Extensional
5	154.04	61.3	21.2	Torsional
6	183.21	40.2	15.7	Flexural
7	203.58	20.3	7.8	Extensional

Figure 7.27 illustrates the displacement of 3DPVS versus frequency, at harmonic response under 2mT magnetic field; Figure 7.28 shows the vibration stress at corresponding frequencies.

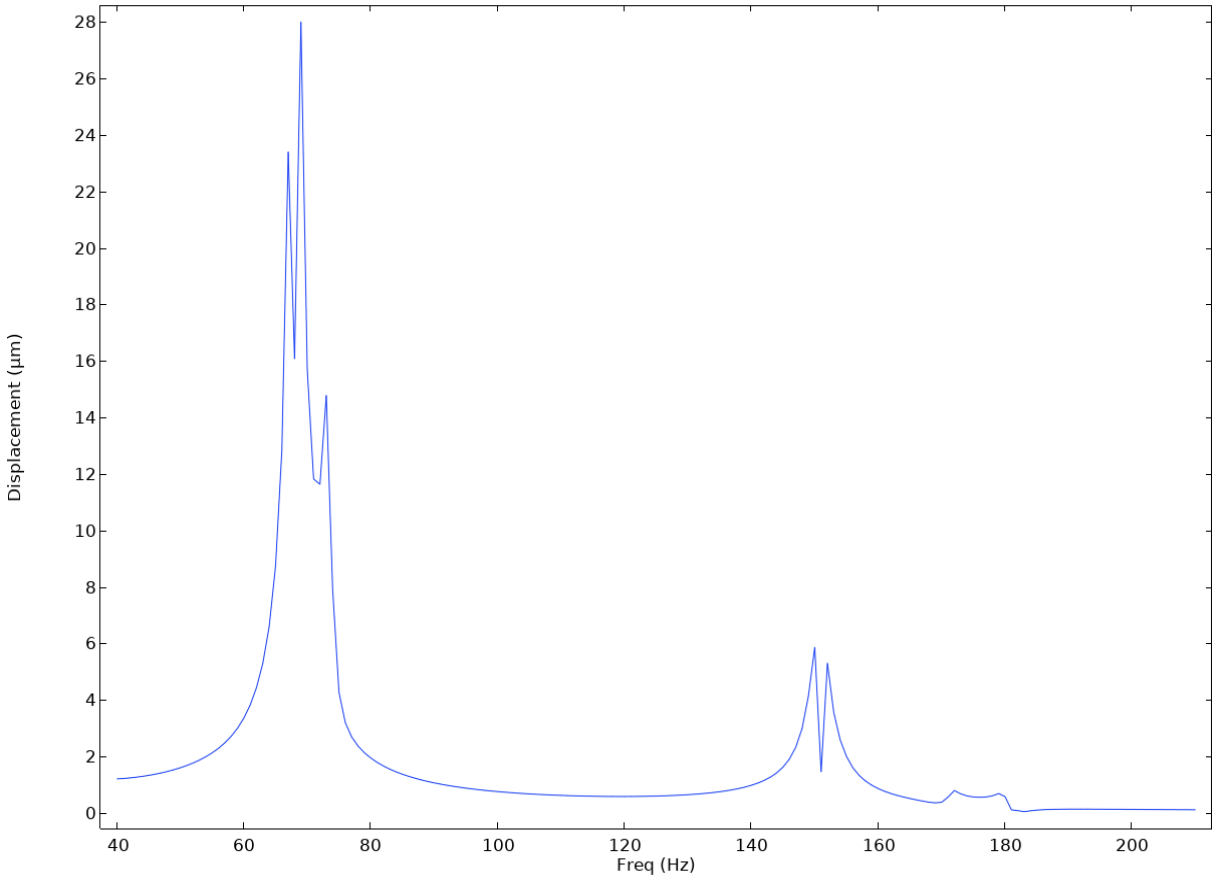


Figure 7.27 Displacement versus frequency, harmonic response under magnetic field

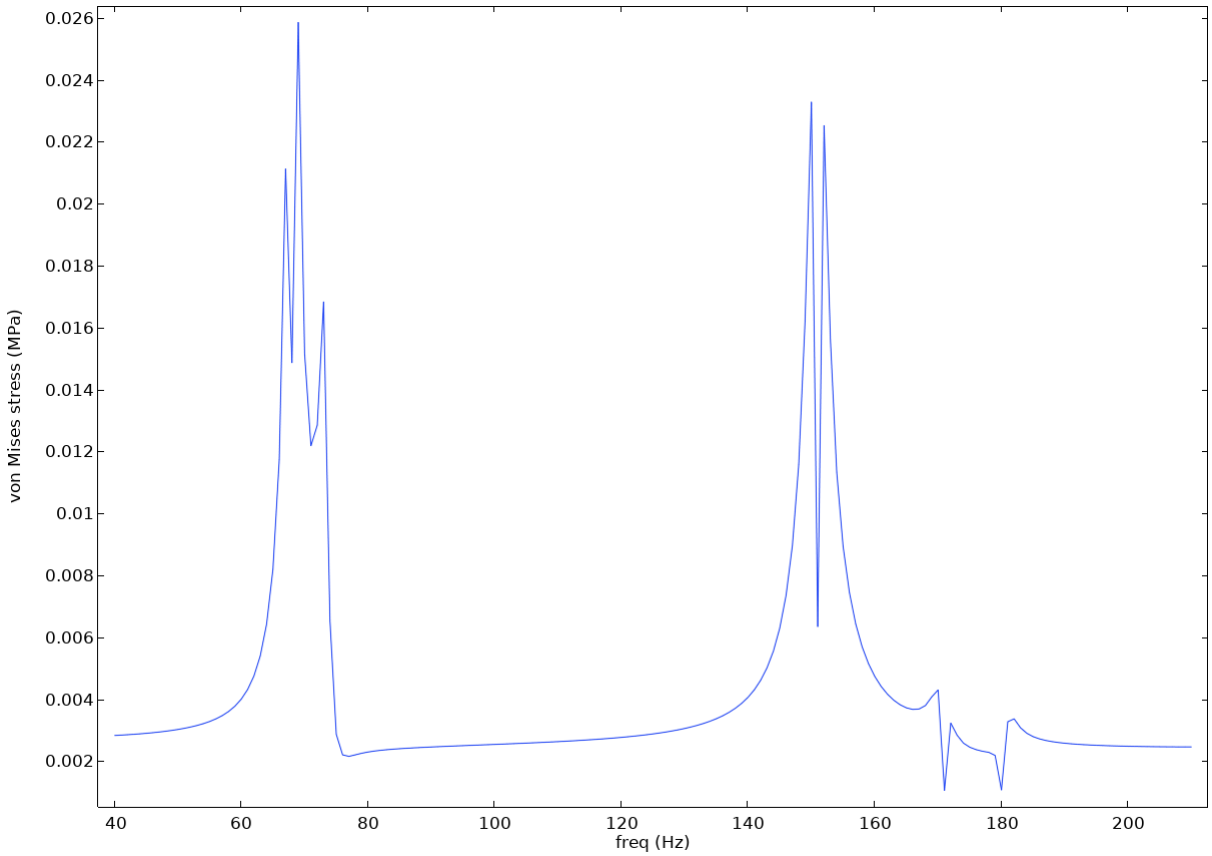


Figure 7.28 Vibrating stress versus frequency, harmonic response of magnetic field

After identifying the eigenfrequency of the scaffold, we use the magnetic field with the same frequency to stimulate the scaffold. Figure 7.27 shows, at around 70 Hz, there is a peak displacement at around 30 μm, followed by another peak 25 μm at around 150 Hz. It is interesting that around both there are sharp fluctuations, first between 10-30 μm, and second 5-25 μm. The stronger the magnetic field strength, the larger will be the displacement. Thus, a magnetic field varying between 50 and 200 Hz is used to simulate the scaffold to validate the design proposal. The von Mises stress, shown in Figure 7.28, shows the similar tendency corresponding to the displacement, with peak stress around 0.025 MPa, 0.024 MPa at around 70 Hz and 150 Hz respectively.

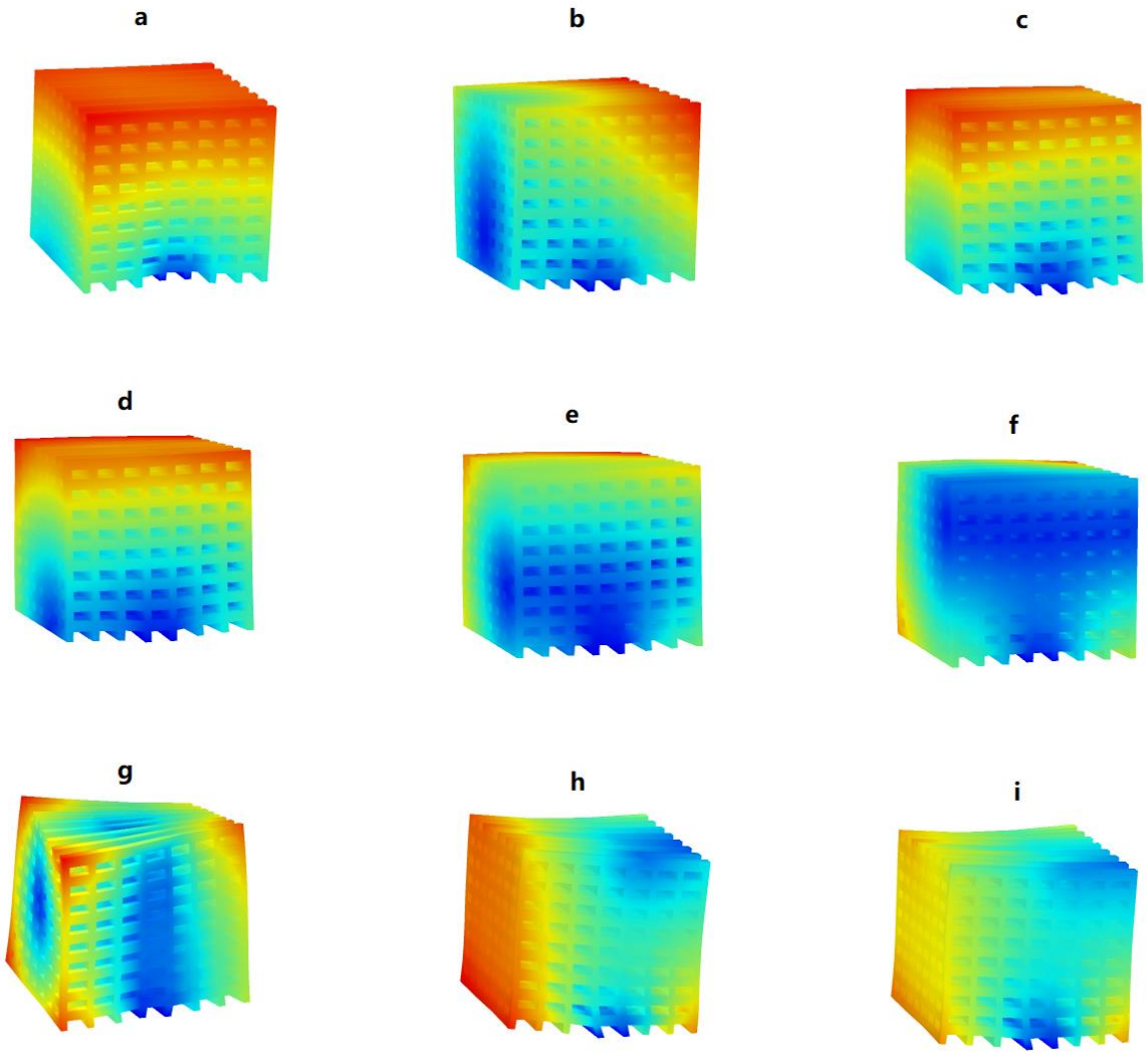


Figure 7.29 Magnetic vibrating modes from 50 Hz field towards 210 Hz

From Figure 7.29, we can see that the magnetic vibrating state remains in tune with the previous natural vibrating stage of the scaffold. With magnetic field strength at mT level, the vibration amplitude remains around macro-meter level. Each mode represents a definite frequency: (a) 50 Hz, (b) 70 Hz, (c) 90 Hz, (d) 110 Hz, (e) 130 Hz, (f) 150 Hz, (g) 170 Hz, (h) 190 Hz, (i) 210 Hz.

II. Periodic Forced Vibration

Compared with the simulation conducted on simplified-box model, displacement result of periodic 3DPVS shows a similar tendency. With a sin(2πft) input, model shows a regular and predictable shape-changes, a large peak followed by a smaller one. The amplitude is about micrometres range, which validates the early design proposal about generating micro-level vibrations.Figure 7.30 demonstrates the displacement of three typical points, a, b the two points at top edges and c the midpoint of side edge. Top four edging points show the relatively largest displacement.

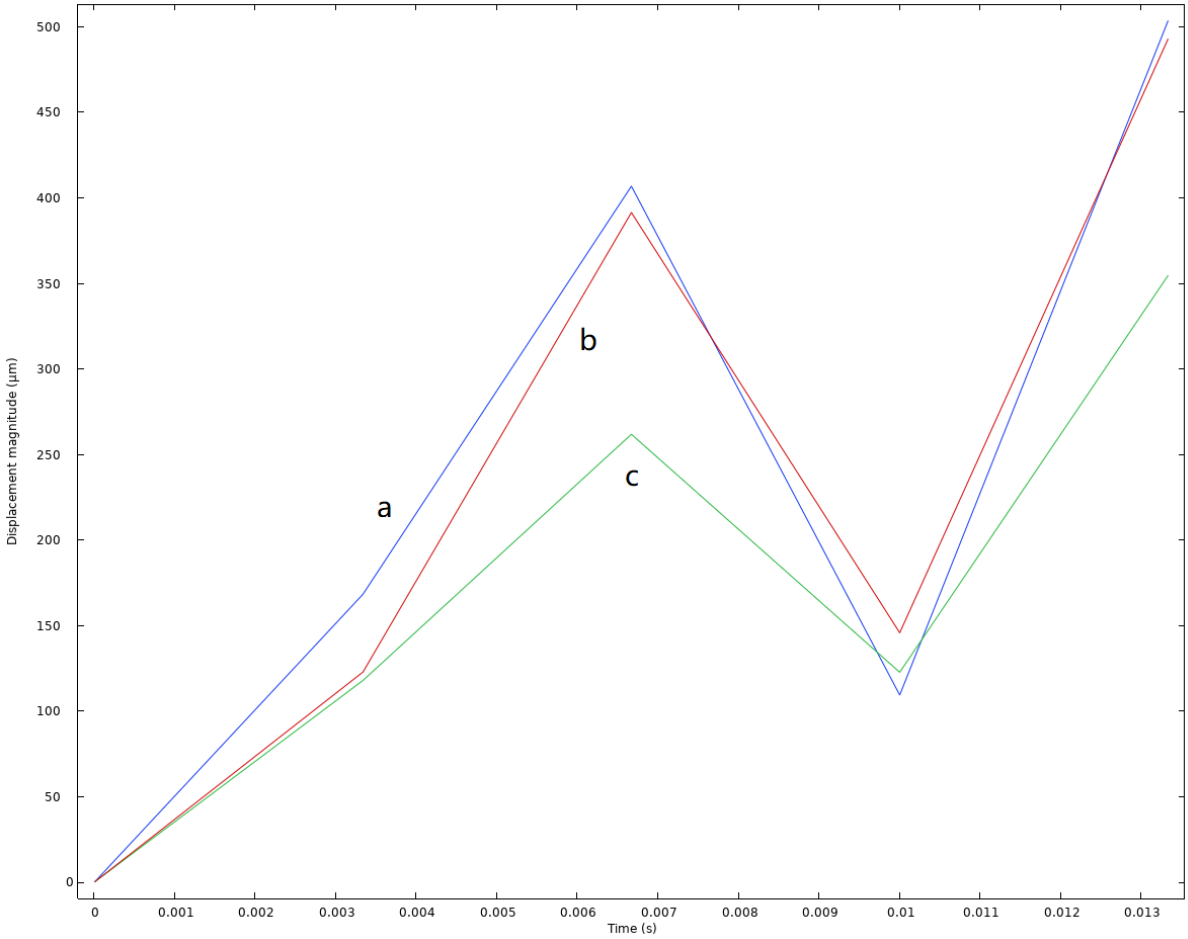


Figure 7.30 3DPVS displacement of periodic forced vibration

7.5.4 *Magnetic Shape-transforming*

Different models have been tested, including a two-layered scaffold, 13-layered scaffold (a) and the optimal design option of 18-layered scaffold (b), see Figure 7.31. The simulated result shows that 3DPVS can generate z-axis shape-changing movement, when the magnetic field runs at sine function. The shape-changing amplitude is about micro- to millimetres, which satisfies the initial proposal.

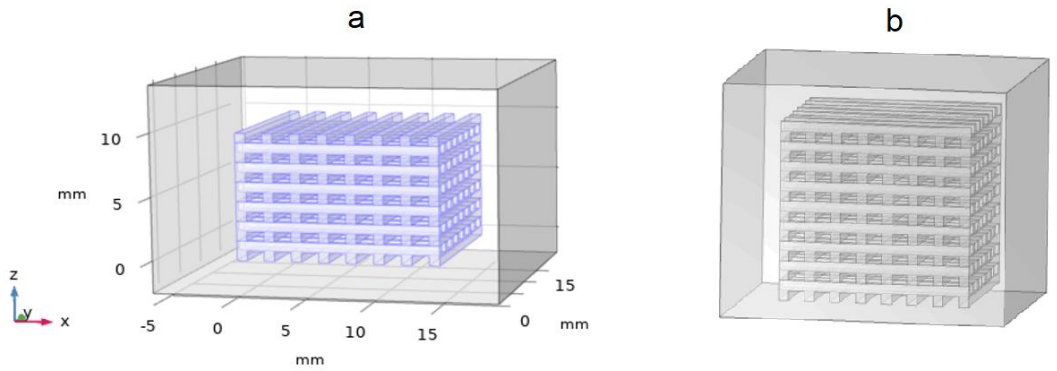


Figure 7.31 Testing two modes of scaffolds for analysing layer issues



Figure 7.32 Comparing z-axis displacement between 13-layered and 18-layered scaffold

From Figure 7.32, we can see that the higher the layered scaffold becomes, the more displacement it can generate in general, and the top side illustrates more shape changing compared with the lower parts.

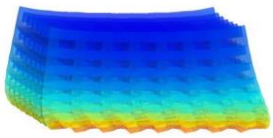


Figure 7.33 High magnetic strength resulting in undesirable flat shape

From another simulation, Figure 7.33, a huge magnetic field results in a flat shape, which is undesirable in scaffold design.

After multiple testing, shape-changing degree in this case is determined by magnetic strength. Model is tested under seven fields, Table 7.6.

Table 7.6 shape-changing functions against various magnetic field

Mode number	External magnetic field (mT)	Peak displacement alone Z-axis (mm)	Peak stress (MPa)	Peak actuation rate(s^{-1})
1	1	0.02	9.24	22
2	10	0.65	19.3	14
3	20	1.02	24.3	14

4	50	2.34	28.5	12
5	100	4.65	31.2	12
6	200	6.52	35.7	10
7	300	8.54	42.5	10

7.5.5 *Localisation of Scaffold*

Different layers of scaffold can be magnetised with tailored polarity, which may result in various shape-changing functions. From this simulation, Figure 7.34, we know that the shape-shifting remains basically the same as the single line structure. Regular magnetisation in tailored parts of scaffold can generate predictable changes in shapes.

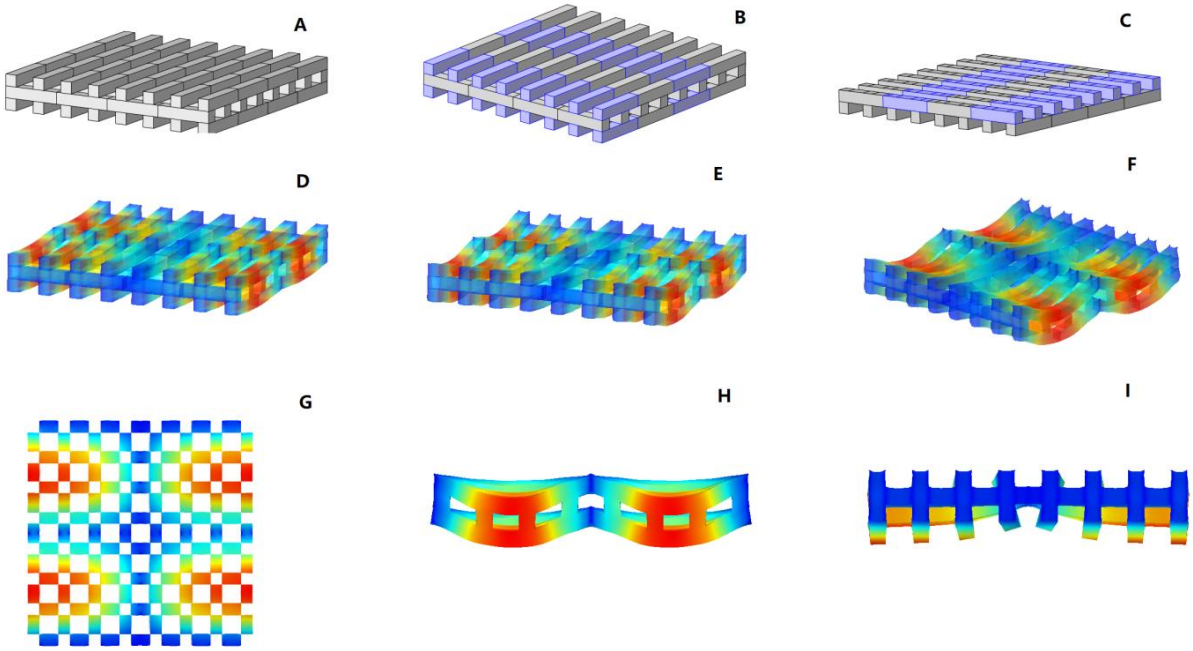


Figure 7.34 Three-layer scaffold sample to test the proposal of localised design

7.5.6 *Traditional Vibrator Shaker vs. Magnetic-actuation Mechanism*

Using the same scaffold geometrical design, this part simulates compares traditional mechanical vibration with the novel magnetic-based actuation. First sample is for 100 HZ mechanical vibration at Z axis with 0.5 g acceleration, Figure 7.35, and second sample is for 100 Hz magnetic-based actuation, Figure 7.36.

Traditional Vibrator method.

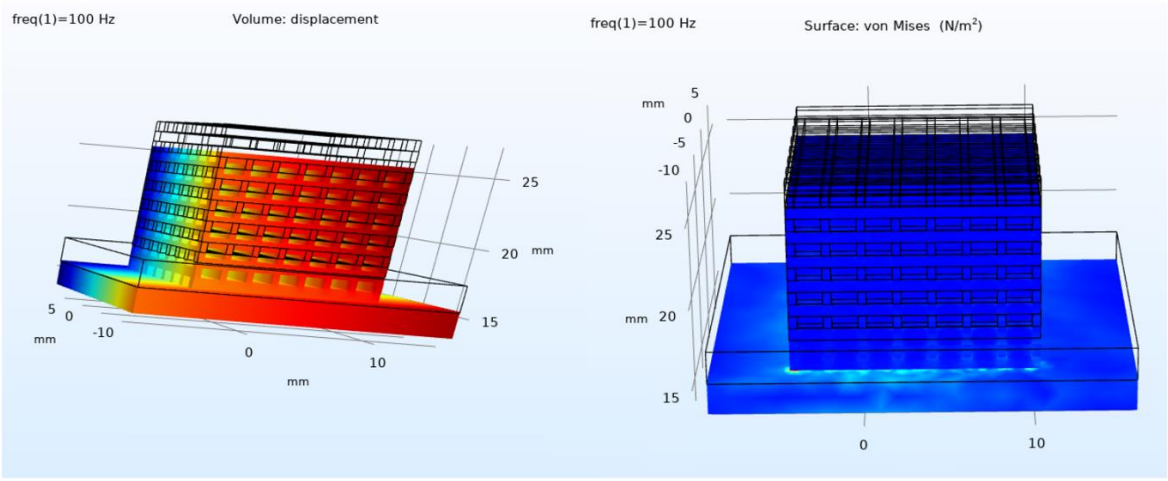


Figure 7.35 Simulating the traditional mechanical vibration

Magnetic-based vibration.

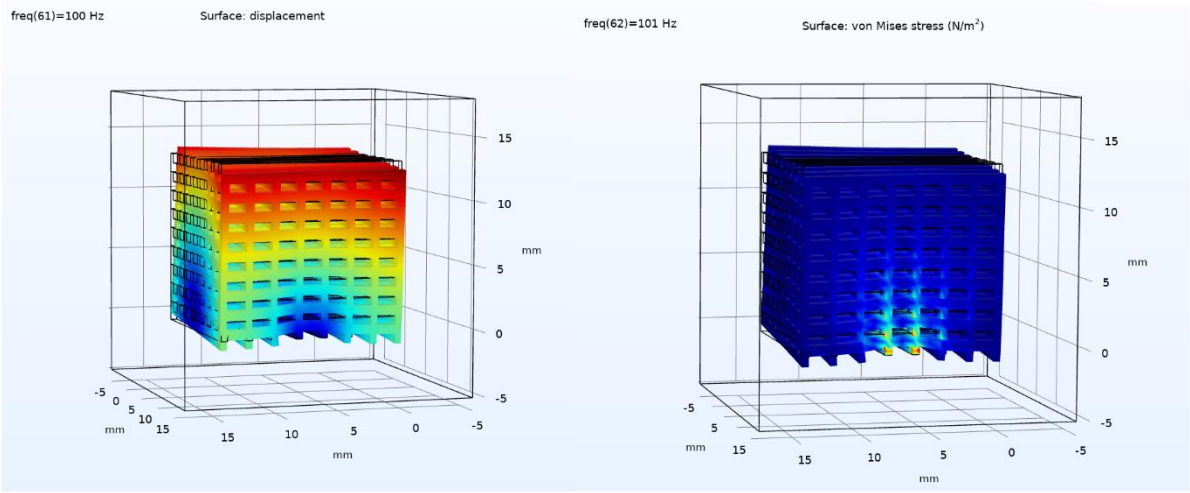


Figure 7.36 Simulation the novel magnetic-actuated vibration

From this we know that, the designed vibrating principle could vibrate scaffold in multiple ways, based on the natural eigenfrequency shape-changing modes, while the traditional mechanical one could only follow the platform's movement which seems to be less flexible. For the surface stress, we can see magnetic-based vibration tends to show more stress within than without. Traditional vibrator tends to show highest von-mises stress at the interacting surface between scaffold and the vibrating platform. This can be very likely result in higher stress in bottom cells seeded inside scaffold. To ensure an average-stress distributed cell culturing atmosphere, magnetic-based mechanism could be the better option, based on current simulation study.

7.5.7 *Discussion*

In this study, firstly several concepts were evaluated via the box model. Firstly, it is validated that model magnetized can vibrate under magnetic field. The vibration amplitude around definite eigenfrequencies tend to be higher than around others. Secondly, displacement of

model is predictable through designing magnetic field and model's magnetization. Under sinuous input, displacement and stress correspond in same sinuous way.

For simplicity purpose, a box geometric model is used at the beginning for testing natural vibration mode, magnetic resonance modes and period vibration models. This simulation has proven that, if the frequency of magnetic field has approximating model's eigenfrequency, model could be actuated resulting in definite shape-changes.

For 3DPVS simulation, free vibration study shows that scaffold has quite predictable shape modes in different eigenfrequencies. Using corresponding magnetic field does create resonance of scaffold, but most of the shapes under resonance have significant difference compared with eigen-modes.

In terms of frequency range, the designed 3DPVS successfully enable the range of around 50-200 Hz with more than five candidate natural frequencies. Under 50-200 Hz magnetic field, scaffold shows special shape changes under these candidate frequencies. The peak amplitude occurs at about 75 Hz and 150 Hz. Average displacement stays at micro to nano level, which fulfils the early design proposal.

For the periodic simulation, we did not fully simulate this model due to high requirement on CPU that we currently don't have. Meshing strategy remains extremely coarse and time calculation for step setting is set as T/4 compared with the relatively precise T/40 for box model setting. Full model of designed 3PDVS can be tested with high-performance workstation. This saves CAD modeling time and decreases the difficulty of simulation.

Result show similar shape-changing tendency of the box model. That is, with sinuous input, scaffold generates sinuous output in terms of its amplitude. With magnetic strength increasing from 1mT to 0.2T, the maximum amplitude increases significantly, from about 18nm to 1μm. Another interesting finding is that the input magnetic field affect more the displacement than the frequency of magnetic field. Thus, it is easier to design magnetic strength to achieve definite amplitude.

In terms of magnetic shape-transforming at low-actuation rate, scaffold can generate obvious Z-axis displacement around millimeter range, which fulfils the design expectation. For localization, the tailored magnetization manner can result in user-controlled shape changing. In this simulation, only one magnetic domain is applied, but it is predictable that different domains can result in different shape changing, based on designers' requirements.

To sum, the evaluated characteristics of 3DPVS and the completion degree is made as Table 7.7:

Table 7.7 Evaluated characteristics of conceptual 3DPVS

	Proposed characteristics	Simulated characteristics	Completion degree of simulation
Integration of scaffold and vibration	3DPVS should integrate external vibration mechanism with scaffold	Proposed integration is workable	Completed
Frequency	50-200Hz	Enable of generating 50-200Hz vibrations	Completed
Amplitude	Micrometer μm level	Enable of generating μm	Completed
Localisation	Different parts of scaffold can enable tailored vibratory fucntions	Magnetic domain works	Partly completed with one domain designed
Harmonic vibration	Eigen-modes determine vibration	Magnetic vibration occurs at eigen-frequencies	Completed
Time-based periodic forced Vibration	In tune with input stimulation	Similar wave with input signal	Partly completed using simplified-box model
Shape-transforming	Generate low-actuation rate shape-transformations	Z-axis transforming	Partly completed, but needs further simulation to validate and improve

7.6 Concluding Remarks and Future Work

In this chapter, simulation is used to validate the conceptual ideas—that is, the magnetic-based vibrating strategy is workable. First, background of simulation was introduced. Second, 3D modelling was introduced and input specifications of 3DPVS were identified. Third, conditions and parametric settings of building models were discussed, followed by which was the illustration of simulation process. This process contains a replicating work, simulating natural vibration of scaffold, simulating the simplified cube model and simulating 3DPVS. Results of each were illustrated in next section with a through discussion of what this study found out.

To be specific, magnetic-based vibration was simulated, with the eigenfrequency of scaffold being identified. Multiple elements, such as fixing manners in scaffold's constraints and layers, were simulated. Magnetic-based shape changing—namely, shape-transforming along the z-axis—was studied, which is the case when the magnetic field shifts in a regularly controlled manner, such as sinusoidal. Localisation was tested and demonstrated that the transformation is predictable and easy to control. Finally, the newly designed vibrating strategy was compared with the traditional mechanical vibrator/stage, which shows the novel mechanism is more flexible. In terms of future validation, 3DP prototyping is necessary to further validate the selected concepts. 3DP prototyping and cell culture experiments will evaluate the full properties of conceptual 3DPVS.

8 RESEARCH SUMMARY AND FUTURE WORK

8.1 Introduction and Overview

The previous chapters presented literature studies of all vital aspects of 3DPVS, provided concept justification of 3DPVS, identified TRIZ-based method, used TRIZ and tools such as QFD to generate 3DPVS solutions, and validated the solutions via computer simulation. We focus on bone cell as 3DPVS application and demonstrate a positive vision on the implementation of the design philosophy, as well as the exploration of its effectiveness in designing a scaffold product with practical attributes derived from a real-world context. This chapter provides a concluding summary and description of this research's contributions and limitations, and the lessons learnt during the study process. This chapter also suggests several key aspects on which further research could focus.

8.2 Summary of Research

Through this research, it is reasonable to conclude that a TRIZ-based design approach, which was not previously used for scaffold design, can contribute to design solutions, offering innovation and enhancement to the novel field of 3DPVS design. 3DPVS, evolving from the traditional 3D passive scaffold, could contain multiple conceptual solutions, among which magnetic-based 3DPVS may be the most promising for current bone cell applications. As a continuation of this research, future designs could move forward with good foundation from conceptual solution into real products.

Eight chapters make up the main body of thesis. Chapter 1 provided the research background and scope. Chapter 2 presented the literature review, identifying current limitations and proposing research objectives. Chapter 3 introduced the conceptual design of 3DPVS and provided the design methodologies and tools which enable the 3DPVS innovation. Chapter 4 demonstrated the design initiation—the first stage of the conceptual design—with basic design requirements identified. Chapter 5 and chapter 6 focused on concept generation—the second stage of the conceptual design, which respectively generates the basic solutions of 3DPVS and the improved/specified solutions. Chapter 7 worked on evaluation/validation—the third stage of conceptual design, using computer simulation to validate the 3DPVS concept created previously. Chapter 8, as the concluding part, summarises the research work, reflects upon the difficulties encountered, discusses the limitations of the study, and indicates future directions.

Output of this research can be presented as follows. The magnetic-based solution is evaluated as optimal compared with others such as the electric-, thermo-, acoustic- and mechanical-based solutions. A detailed concept of the 3DPVS is generated, with hard-magnetic elastomer 3D-printable materials making up the scaffold and a user-tailored magnetic field providing the stimulating force for the vibration. Simulation results show that the conceptual 3DPVS so

generated achieves the proposed objectives. The expected frequency range (50–200 Hz for bone cells) and amplitude range (around micrometer) are achievable. 3DPVS can also generate non-uniform movements when the magnetisation of definite parts is changed. This in turn could benefit a tailored cell culture, where different cellular areas require localised vibratory stimulation.

8.3 Contributions of Research

This research makes two contributions: first it provides a novel approach to scaffold design and second puts forward the 3DPVS concept complete with a generated innovative solution. The novel design approach developed in this thesis is replicable and re-usable. In addition to having generated an effective solution for bone cell 3DPVS, this approach can have broad applicability for other cell scaffolds and can be applied to other bio-designs following the same procedure. Aside from the potential future use of 3DPVS, this work also provides a thorough review of the connection between TRIZ and scaffold design—an area that has received scant research attention.

From the theoretic, methodological, and practical points of view, contributions can be summarized as follows, with the schematic illustration in Figure 8.1.

Methodological contributions. This research has used a novel approach for developing/innovating the conceptual 3DPVS. Traditional engineering design process was used for the bio-design scenario, which helps establish the tailored conceptual design process. For innovation purpose, TRIZ was adapted from traditional engineering/industry field into scaffold design, which can be considered as novel and unique. Previous bio-design methods were chiefly based on laboratory works, which could be sometimes trial-and-error. A novel method from TRIZ, and TRIZ associated with tools like QFD, therefore can be considered as reinvigorating. This research also deeply studies TRIZ and its key elements, considering that a formal TRIZ-based methodology for scaffold design can be established following this study at near future.

Theoretical contributions. This research contributes to theories on conceptual design of 3DPVS. Through a systematic review, this study succeeds to connect 3D scaffold, 3DP, vibration into an organic unit. The concept of 3DPVS an contribute to the theory and knowledge base for scaffold engineering. With this concept, magnetic-based solution has been generated through two stages, basic concept generation and concept improving/specifying. In addition, this study expands the current scaffold categorization with the language of relativity. layers of scaffold were theoretically defined from the view of ‘evolution’. This can help future designers better understand scaffold and follow a crystallised path.

Practical Contributions. This study focuses on the application of cell culture, with bone cells selected as the primary design focus. Detailed and specific design requirements, components and attributes were attained, which makes this research down-to-earth and practical. Computer modelling and simulation considers the reality problems encountered by researchers in terms of vibration and scaffold. 3DPVS can be fabricated following such simulation work and can pass into cell experiment for better testing/evaluating the properties of 3DPVS. Also, this study provides practical implications to the future development of 3DPVS, regarding frequency control, localisation, application of magnetic field. This can potentially enable and accelerate 3DPVS to become real-world product.

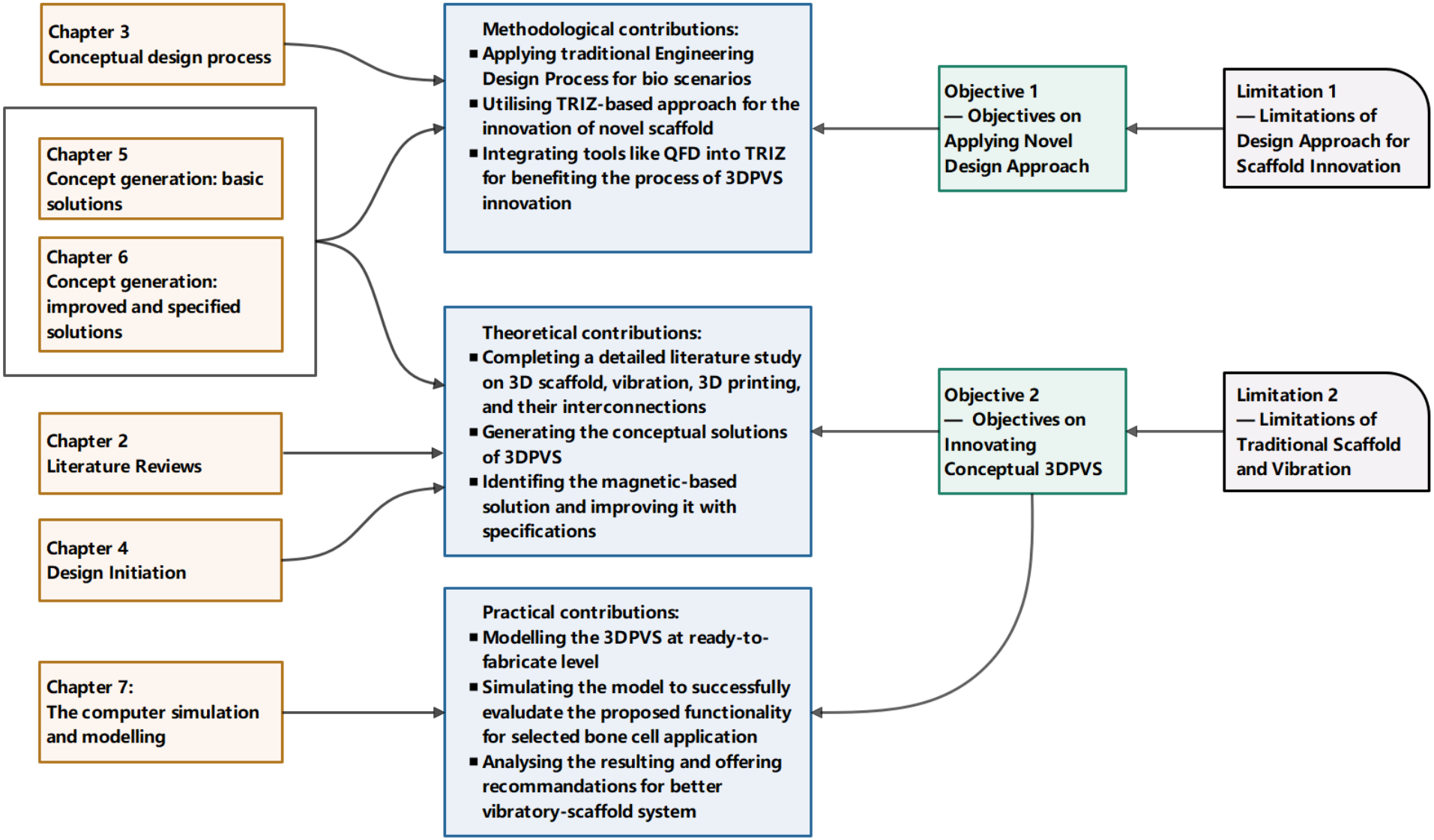


Figure 8.1 Contributions of the research in view of theory, method, and practice

8.4 Research Limitations and Lessons Learnt

There major limitations were identified during the study process.

There lacks formal and mature methodology for design and innovation of 3D scaffolds. Despite the increasing application of TRIZ, QFD, 3DRTC, axiomatic design and so forth to engineering design, we can barely find any thorough or exact approaches to using one or multiple of these design methods to achieve novel scaffold products. The established method of this research itself can be considered an attempt from which nobody could predict the result before suitable solutions are successfully generated. Although we successfully used TRIZ-based method to generate solutions of 3DPVS, whether this approach can be globally adapted as a formal methodology for scaffold design still remains a concern, requiring further exploration and examination by future research.

More biological and economic factors should be included in design process. The modelling of 3DPVS characteristics predominantly focuses on representing the roles of vibration mechanisms and 3D scaffolds. Biological factors, especially those purely related with cells and tissues, were not considered as of high importance to form design requirements. As such, future researchers in the cell or biomedical realm who continue this study may find it necessary to design the biological functioning in a more exact and through manner. Also, current design scenario generates non-biodegradable cell culture scaffold for external use, but wider applicability for 3DPVS shall also cover bio-degradable scaffolds. Improving concept regards this needs further research works. In addition to the biological factor, another factor we will consider is the economics or costs of 3DPVS. Economic factor is often a major determinant for judging the applicability of new product. Thus, cost-based concerns of 3DPVS must be included in the detailed design stage.

Technical and hardware limitations. After generating conceptual solutions, computer simulation is used to evaluate the 3DPVS model and validate the key design concepts. Due to a lack of high-performance workstation, the simulation work cannot be fully conducted especially for two scenarios. Time-oriented study such as periodic forced vibration is fully simulated on simplified-box model; however, it becomes extremely difficult when it comes to the full 3DPVS model. Regarding localisation, a three-layer scaffold is simulated instead of using the full scaffold. This hardware limitation occurs to other situations as well, for example when meshing becomes finer and when magnetization is complexly localised.

8.5 Future Work and Recommendations

Given the limitations abovementioned, several recommendations are provided:

- Further investigation should be undertaken on TRIZ-based methodologies and tools that can be applied to the design and innovation of scaffold.

- More detailed effects of biological and economic factors should be embedded inside the 3DPVS design process.
- The design parameters of 3DPVS require continued computer optimisation, chiefly in terms of localization and tailored vibration control. A high-performance workstation therefore is of urgency.

From design perspective, several tasks could follow immediately after this research. This also helps bridge current conceptual design into next design stage:

- Solutions should be further evaluated using CAD, computer simulation and 3DP working prototypes in 3DPVS detailed design. Generated concepts should be further evaluated, when fabricable and experimental feedbacks are received.
- The relationship between elements inside GMBV characteristics should be further explored.
- Beginning with 3DPVS for external cell culture applications, further investigation in 3D TE scaffolds should be undertaken, where implantation becomes a concern.
- Despite the potential offered by 3DPVS, it remains far from being implemented in clinical practice. Designers can gain a clearer picture of the detailed bicellular roles of vibration and microstructure that affect cells.

In terms of the generated 3DPVS solution, future improvement suggestions could contain:

- Further study on magnetically responsible soft materials, which includes exploring the suitability for a wider range of cell culture applications, analysing on materials' mechanical properties, and studying of different ratio of material mixture about NIB with soft elastomer. More interesting materials, especially those biodegradable ones, could also come into play in next design stage.
- Design new geometrics to evolve 3DPVS from current struct-based structures, which includes designing the assembly of multiple scaffold parts into one unit, using non-uniform sized struts for same layer of scaffold, and testing different geometric architecture than the struct-based.
- Use 3DP to fabricate real 3DPVS samples, which includes testing the vibratory properties such as frequency and amplitude with real experiment and using fabricated samples to culture bone cells. Together with this, it would be interesting to propose a study based on the design of experiments.
- Simulate scaffold considering the in vitro cell culture environment, which includes using higher-performance workstation to simulate full 3DPVS model, and adding the cell culture medium and cells into current simulations.
- When cell culture medium and cells are considered at simulation, future works might need to explore whether the 'current' will be generated by the altering magnetic field, and what the effect it will be, especially for the culturing medium and cells inside.

Among these future tasks, author of the research is currently undertaking the assembly design, where a sophisticated 3DPVS model can contain an assembly of multiple library design units. The geometric models of two typical designs are as follows, Figure 8.2.

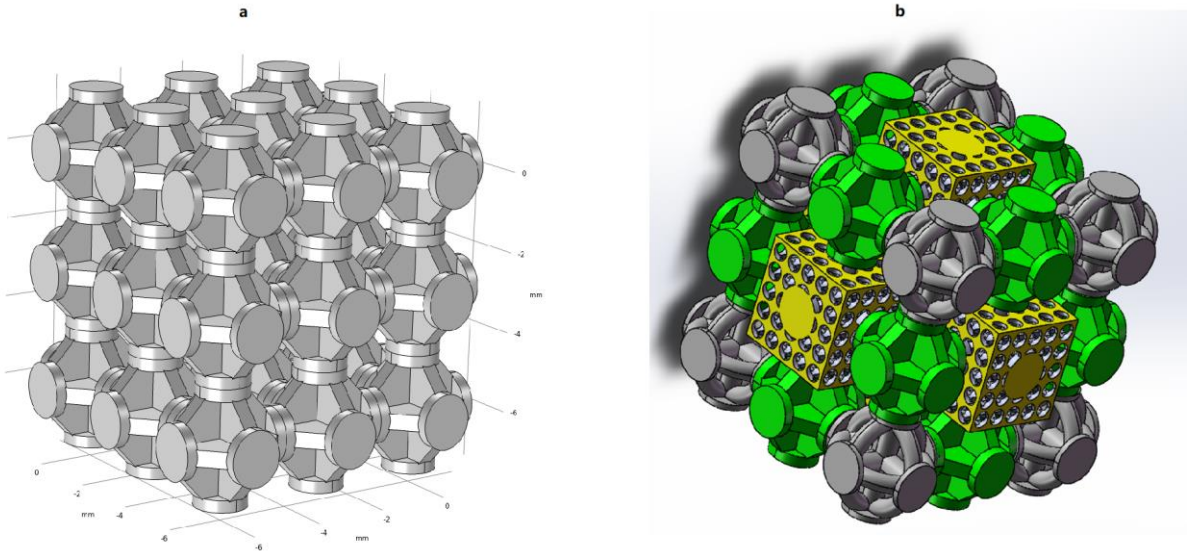


Figure 8.2 demonstration of assembly design of 3DPVS, a, single-unit assembly, b, multiple-unit assembly

Using this assembly design, scaffold is proposed to achieve new vibratory functions compared with the struct-based 3DPVS. It also provides high localisation when scaffold is designed with multiple library units. The detailed effect about such scaffold, and the optimisation about design process, will be an interesting question for us in next stage.

To conclude, there inevitably exist limitations and unknown loops than those identified, which could be detected by fabricating real prototypes and performing cell experiments. Current success of the conceptual design is only the first step in the full innovation process. Thus, significant improvements are likely, and future design stages are warranted.

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APPENDICES

Apx A. 3DP Technologies Used for Scaffold Fabrication

A1: Illustration of multiple 3DP technologies

Figure A-1 demonstrates six types of 3DP technologies used for cell culture scaffold fabrication: (a) SLA; (b) liquid 3DP or droplet 3DP; (c) FDM, which is the typical 3DP method in nozzle-based systems; (d) (e) 3D plotter or Bioplotter, which belongs to the 3DP nozzle-based system, but uses liquid or biological materials, such as real cells, as materials for fabrication; (f) SLS, the typical laser-based 3DP; and (g) indirect 3DP, of which the most typical method is wax printing, which can be regarded a hybrid 3DP approach.

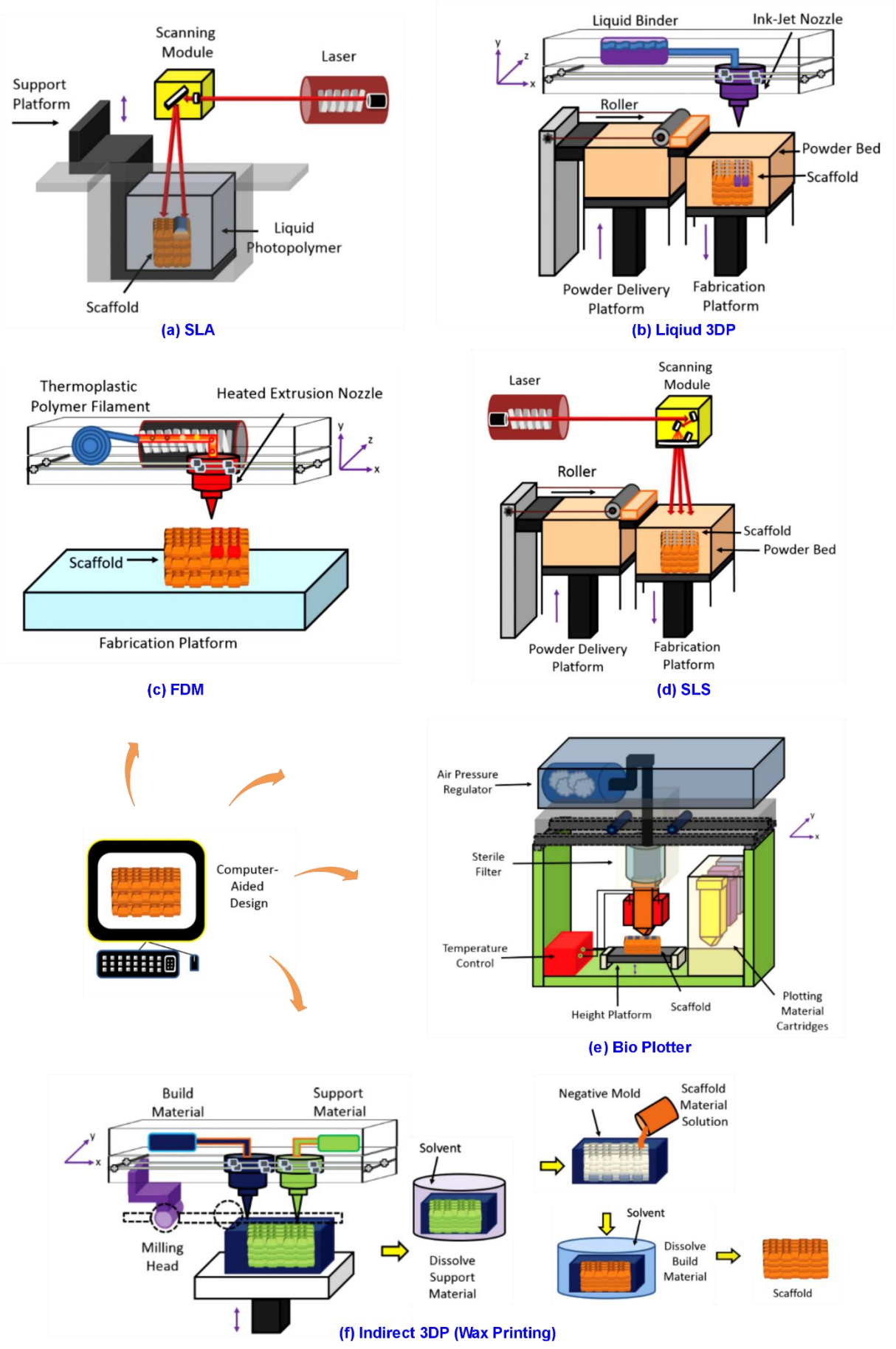


Figure A-1 Illustration of six typical 3DP technologies, modified from (Do et al. 2015)

A2: Comparing table for various 3DP technologies and conventional fabrication tools

Table A-1 Comparison of various 3DP technologies and traditional fabrication tools

3DP methods	Chief feature and mechanism	Materials	Cells studied	Architecture	Dynamic applicability	Advant.	Disadvant.	Refs.
2PP	laser beam is focused onto a liquid material; CAD	Solidifable fluid: photosensitive materials	Bone cells, human stem cells;	Mesh-like, Wheel-, pyramid-, cube-like; pattern in hydrogel;	High	Homogeneous and two-composite polymer	Excess of initially powdered material hard to remove;	(Greiner, Richter & Bastmeyer 2012; Murphy & Atala 2014; Zhang, LG & Kaplan 2016)
LENS	Metal powders used to build or repair scaffold parts;	Fine powder: plastic, metal etc.	General tissue cells;	Mesh-like network;	High	Able to repair old parts and fabricate new; secondary firing process not needed; excellent material properties;	Low geometrical control in dimension;	(Kumaresan; 2015; Vasireddi & Basu 2015)
SLA	Laser onto liquid photopolymer to generate scaffold; CAD;	Solidifable fluid: photopolymer resins, temperature sensitive polymers, ion cross-linkable hydrogels, ceramic paste, etc.	Rat bone, rabbit trachea, pig tendon cells	Mesh-like, Honeycom-Wheel-, pyramid-, cube-like; porous cylinder;	High	High surface quality; high resolution; high complexity; fast speed.	Limited to specific polymers (photopolymers); need support system; moderate strength; expensive	(Do et al. 2015; Gu et al. 2016; Park, HK et al. 2018; Serra 2014; Vasireddi & Basu 2015; Zhang, LG & Kaplan 2016)
SLM	Using small diameter wire-frame elements;	Fine powder; Plastic, metal , ceramic or composite powders,	Mouse bone cells;	Mesh-like, Honeycomb-Wheel-, pyramid-, cube-like network;	High	Controlled pore interconnectivity and porosity; greater durability of mould; free from temperature-related defects	Low surface quality;	(Deng & Kuiper 2018; Murphy & Atala 2014; Vasireddi & Basu 2015)
SLS	Laser-based CAD technique; include laser and power bed;	Fine powder: Plastic, metal ,ceramic or composite powders,	Mouse bone, rat heart, rat bone, mouse skin, mouse heart cells.	mesh-like network; porous cylinder;	High	Good mechanical strength; complex structures; high resolution; large part size; no support structure needed;	High materials requirements (heat, shrinkage resistant); require high processing temperature; powdery surface; costly; time consuming	(Do et al. 2015; Greiner, Richter & Bastmeyer 2012; Serra 2014; Vasireddi & Basu 2015)
LOM	layers of adhesive-coated laminates being successively glued together and cut to shape with laser;	Laminated thin sheet: Ceramics—alumina, silicon nitride, and zirconia and metals	General tissue cells;	mesh-like network	High	Large part size; layer builds quickly; fine accuracy and resolution low cost;	Materials limited;	(Kumaresan; 2015; Vaezi, Seitz & Yang 2012; Vasireddi & Basu 2015)

Inkjet printing (3DP in traditional terminology)	Liquid binder jetting; drop-on-powder; CAD	Hydroxyapatite; magnesium phosphate; cement; polyurethane;	Rat bone, rabbit bone and mouse bone cells.	mesh-like network; porous cylinder;	High	Materials versatile; powder can be trapped inside body; don't need support structure; high speed; cost-efficient;	May be toxic; low mechanical strength compared with Laser printing; time consuming in post-processing;	(Bose, Vahabzadeh & Bandyopadhyay 2013; Do et al. 2015; Greiner, Richter & Bastmeyer 2012; Serra 2014; Vaezi, Seitz & Yang 2012)
FDM	Thermoplastic polymer through heated extrusion Nozzle to create scaffold onto platform; CAD	Non-brittle flament: Thermoplastics like ABS, PLA, and PCL etc.	Rat and Swine Bone cells	mesh-like network; porous cylinder;	High	Relatively inexpensive; low cytotoxicity; good strength; no support structure needed; no power trapped; good mechanical anisotropy; speed control by strand diameter;	Limitation on materials (thermoplastics); materials non-biodegradable; support structure required for complex geometrics; post possessing needed; low resolution; low speed;	(Bose, Vahabzadeh & Bandyopadhyay 2013; Do et al. 2015; Greiner, Richter & Bastmeyer 2012; Serra 2014; Vaezi, Seitz & Yang 2012)
3D plotting (Bioplotter printing)	Air pressured system to extrude material from bioink cartridges;	Solidifable fluid: ion cross-linkable hydrogels etc.	Rabbit cartilage, rabbit trachea, rat cartilage, mouse cartilage, mouse skin cells etc.	mesh-like network; dot-like structure;	High	Viable cells printable; soft tissue applications; wide variety of natural and synthetic materials; processing at room temperature;	Nozzle may be cytotoxic; support structure required when printing complex structure; low dimensional accuracy;	(Bose, Vahabzadeh & Bandyopadhyay 2013; Tan, Z et al. 2017; Vasireddi & Basu 2015)
Wax printing (indirect 3DP)	Wax being printed as a negative mold where scaffold solution is cast;	Wax	Rat bone cells, mouse stem cells;	mesh-like	High	Benefit on preproduction; versatility on material casting following obtained mold;	Materials may fail to be biocompatible; Low resolution; always need a mold; low speed in fabrication	(Deng & Kuiper 2018; Do et al. 2015)
Conventional materials	Chief feature and mechanism	Materials	Cells studied	Architecture	Dynamic applicability	Advant.	Disadvant.	Refs.

Electrospinning	Polymer solution forced into a capillary to form a jet of solution a tip; high voltage applied between tip and collector	biodegradable polymers like PCL;	Rat bone, mouse bone, rabbit vascular tissue cells.	mesh-like structure; microchannel	Low	Fast speed; cell printing available; soft tissue application; similar to ECM; better mechanical control (shear stress); high aspect ratio and surface area	Fibers printed in random orientation; pore sizes not uniform; high voltage demand; organic solvent needed;	(Do et al. 2015; Greiner, Richter & Bastmeyer 2012; Serra 2014)
Solvent casting/ particulate leaching	dissolute polymer in an organic solvent and casting into a mould;	Composite like PLA/Calcium phosphate	Bone cells	mesh-like	Low	High geometric control; easy processing; fast speed;	Organic solvents have to be used;	(Serra 2014; Taherkhani & Moztarzadeh 2016)
Phase separation	Polymer and solvent mixed pass through a freeze-dryer;	ceramics, i.e. glass	Bone osteoblast cells	homogeneous and highly porous structures	Low	High porosity; easy to cooperate with other techniques	Possible shrinkage issues; organic solvents used; anisotropic pores;	(Deng & Kuiper 2018; Durgalakshmi & Balakumar 2015; Serra 2014)
Gas forming	using a process with high-pressure carbon dioxide at room temperature;	polyesters polymers; biodegradable polymers;	Bone cells;	mesh-like; microchannel	Low	Organic solvents not needed; room temperature processing; macro-porous scaffold	Poor geometrical and porous control;	(Deng & Kuiper 2018; Serra 2014; Sun, Y et al. 2016)
Microsphere sintering	sintering polymer microspheres thermally or chemically;	Polymers;	Bone cells;	mesh-like; microchannel;	Low	Pore size being gradient; complex shape fabricable;	Lack of control in interconnectivity;	(Deng & Kuiper 2018; Khoshroo, K. et al. 2017; Serra 2014)

Apx B. QFD-based Conceptual Design Support

Although ideas can be generated through the multi-route problem-solving process, as established with TRIZ, these ideas may not necessarily be optimal solutions. Thus, a further approach regarding how to evaluate these concepts is necessary, which may assist the general efficacy of conceptual selection and help better identify DRs.

B1: Introducing QFD into 3SPVS Conceptual Design and Concept Evaluation

QFD is an end-user-driven quality design methodology used for designing complex products. The chief purpose of QFD is to strengthen the value of requirements in design or deployment from end-users, where end-users intimately influence the design process. This has tremendous significance for novel product design, where a clear list of requirements sometimes outweighs the design process itself. QFD can be applied with TRIZ-based methodology (Blogg 2013), where QFD performs requirement identifying and conceptual selection. To achieve the implementation of QFD, HoQ has been used frequently as an effective approach to identify requirements and make thorough comparisons.

The general philosophy of QFD is that the effect—either positive, negative or neutral—can be tracked visually along the design process. Designers thus easily detect conflicts among requirements, attributes or components. One defect of QFD is that it cannot generate innovation; therefore, it is considered a method for requirement-based strategic thinking, instead of an innovation-oriented design method. In terms of the role of QFD in scaffold design, especially bone cell scaffolds, it helps analyse multiple requirements in scaffolds, vibrations, cell cultures and 3DP, as well as determining the optimality of generated solutions via TRIZ. In the following, we illustrate this TRIZ-supporting QFD method established for our research.

Core Terms and Definitions of QFD

Several terms should be clearly illustrated to help better understand the methodology and process, as displayed in Table B-1.

Table B-1 QFD terms used with illustration

Term	Illustration
House of Quality (HoQ)	A tool which has been widely used in the initial stage of QFD for developing novel or new product.
Design Requirements (DRs)	DRs can be defined as the description of desirable performance of the scaffold product and its functions, either from ‘customers’, ‘end-users’ or ‘designers’. DRs tend to be at super-system level.
Requirement Importance (RIs)	The level of importance attributed from end-users to each DR. In the case of 3DPVS conceptual design, a five scale was applied, namely 1, extremely significant, almost useless, into 5, extremely useful and important.

Design Attributes (DAs)	There is the design 'how' and 'what' statements at scaffold or 3DPVS system-level. DRs can be segmented into various DAs, which depends on how designers perceive the initial requirements.
Relationship Matrix (RM)	A visual illustration regarding the relationship between DAs and DRs. The relationship could be defined by correlation intensity from four scales, namely none, weak, moderate and strong.
Engineering Targets (ET)	A set of targets whose values could allow designers to technically benchmark the scaffold or 3DPVS design concept. ETV will indicate the Engineering Targets Values.
Couplings	A pairwise comparison of the DAs establishes the roof of HoQ. Three aims generally exist here, first is to indicate whether there is a relationship between DAs and second, whether some DAs are in conflict or friendliness with others; last, to judge the intensity level of the interaction.

HoQ and Steps for 3DPVS Conceptual Design

This section introduces seven elements of a basic HoQ that will be used for the design of 3DPVS. The steps of establishing useful HoQ, as well as using HoQ with the TRIZ-based four-route methodology, will also be discussed.

Seven elements of HoQ: Figure B-1 illustrates the core elements of HoQ in the QFD method. It is termed HoQ-1, distinguishing it from HoQ used in later phase.

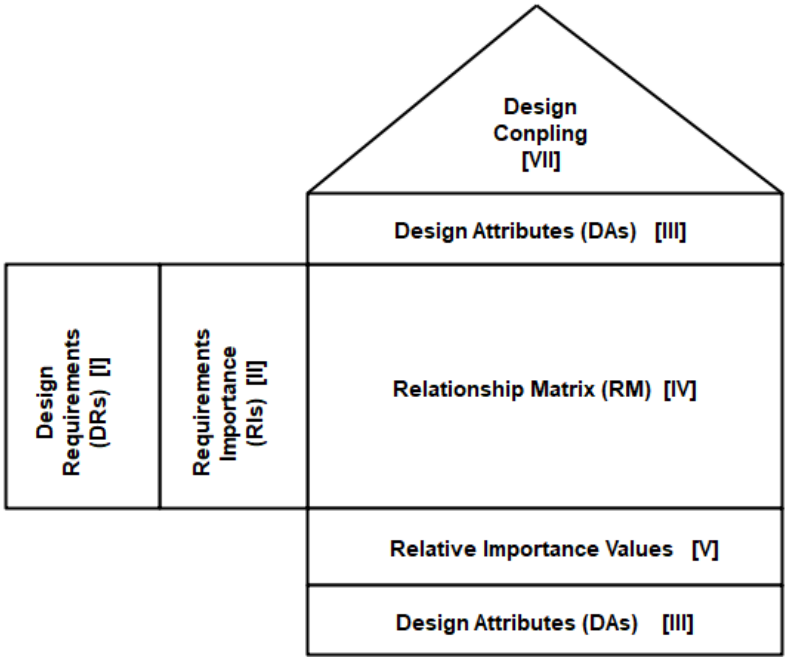


Figure B-1 Seven components up HoQ-1 in this research

To implement this HoQ, the main steps would be as follows.

Step 1: Identifying and validating DRs.

DRs could be collected from direct customer engagement (interviews or expert surveys), market research (questionnaires, media and trade journals) and literature reviews. Requirement importance ratings will be generated here. [I] and [II] will be conducted here. Table B-2 briefly illustrates the DRs of traditional bone cell culture scaffold (static and passive). This helps understand the base models of 3DPVS. Importance level serves only as an indication, not a definite answer, of the relative significance of each requirement.

Table B-2 DR statements and five-scale importance ratings for traditional bone cell culture scaffold

DRs no.	DR statement	Importance level
1	Act as template for 3D bone growth	5
2	Resorbs at the same rate as bone is repaired	3
3	Is biocompatible (non-toxic)	5
4	Being biodegradable	3
5	Composed of a bioactive material (class A/B)	4
6	Surface properties promote cell adhesion	5
7	Exhibit mechanical properties that match host bone	2
8	Transmit fluid stress across itself	3
9	Transmit compressive stress	4
10	Have a fabrication process that allows scaffold to fit a differing range of geometries	4
11	Be sterilizable and meet regulatory standards	4

In this research, customers exist as potential bone cell culture researchers, where DRs and DAs have been created generally from literature reviews on 3D scaffolds, bone tissue scaffolds, vibrations, dynamic cultures, 3DP and so forth, as well as from seeking opinions from multiple-domain experts. DRs and DAs have also been discussed, first via survey with identifiable professional researchers in related fields of scaffold engineering, and second via communication with our research group.

Step 2: Identifying and validating DAs

This step involves deriving the DAs responding to generated DRs, and determining RI ratings of these DAs. See the detailed relation between DRs and DAs in Chapter 4, focusing on the study of design initiation.

Step 3: Establishing HoQ-1 to assess concept of cell culture scaffold

HoQ-1 consists of the input of DRs, importance level values and DAs. Here, the relationship matrix of interactions between DRs to DAs will be compared for analysis. The result is largely derived from whether and how a definite DA could cause, affect or disturb a DR. For instance, the scaffold acting as ‘a template for 3D bone cell growth’ is likely to endow the scaffold with the capability to ‘assist or support dynamic culture’. This interaction will thus be marked as strong (intimate).

Step 4: Identify the design couplings (potential pairs that conflict each other)

This step establishes the attribute-requirement correlation via the HoQ roof.

Step 5: Resolve above couplings-1 via TRIZ-based method

In couplings-1, the contradiction tends to be detectable when designers use the TRIZ method, such as ACM and IPA, to help solve it.

Step 6: Identify GMBV characterisation components of 3DPVS

GMBVs here would include system to sub-system components of 3DPVS. This process helps analyse detailed requirements above levels where stand DRs and DAs. DCs refer to the parameters or attributes of the scaffold, such as vibration frequency, length or weight of scaffold, and pore size. Sometimes DCs can be used as DAs during the simple design scenario.

Step 7: Conduct second HoQ, comparing and connecting DAs and DCs

This step determines the functional components of 3DPVS corresponding with input DAs. This step can be skipped when DRs and DAs remain generally the same. In addition, when it comes to analysing the required vibratory functions of 3DPVS, designers could possibly include GMB components in HoQ-1, while setting V-components separately in HoQ-2. In brief, the structure of HoQ-2 will basically remain the same as HoQ-1, both with seven components, as illustrated.

Step 8: Input second group of couplings into TRIZ-based four-route methodology

Four couplings-2, which tends to be sophisticated and complex compared with couplings-1, the four-route TRIZ-based methodology is used to resolve potential contradictions from these couplings. Detailed knowledge of using the TRIZ method for solving conflicts has been discussed previously. Figure B-2 presents the role of QFD in connecting with the established TRIZ-based methodology.

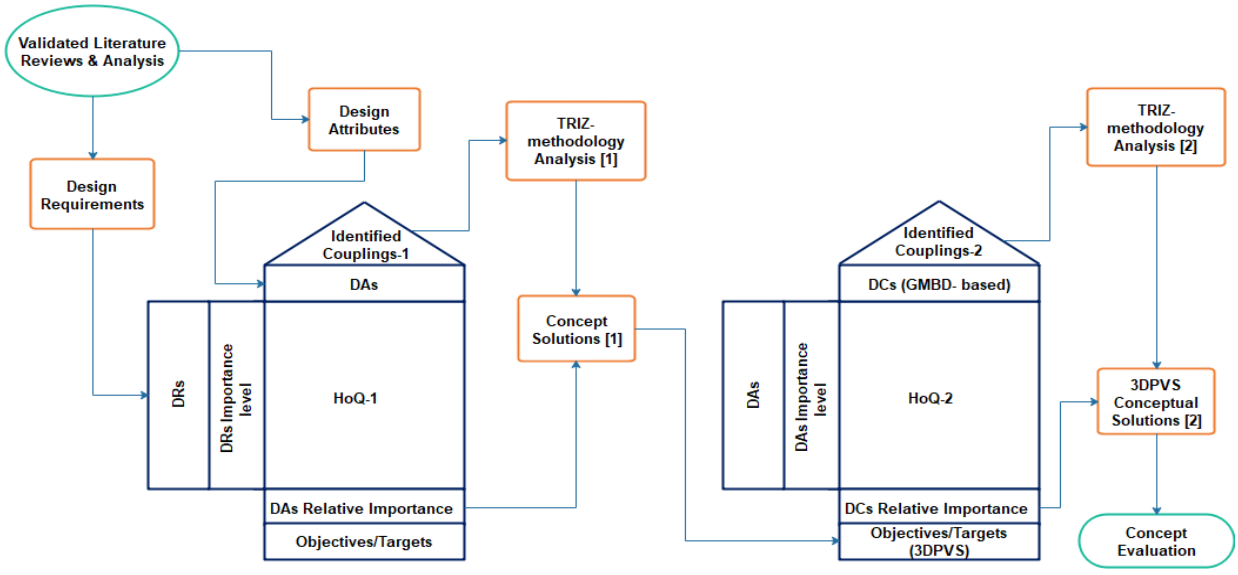


Figure B-2 QFD methodology incorporated with TRIZ methodology established for 3DPVS conceptual design

For the 3DPVS scenario, a scale of 1 to 5 for importance level or intimacy relationship will be used, instead of the traditional 1 to 9 scale, for two chief reasons. The first is to simplify the number of graduations and help the design criteria be more concise. Given that our research seeks to use the TRIZ methodology for scaffold design, the HoQ parts must be trimmed and simplified as much as possible while maintaining all useful functions. Second, for the

conceptual design stage, a 1 to 5 scale is sufficient. A 1 to 9 scale may be better applied in the scenario where elements illustrate a huge difference in their values. For 3DPVS, we only select the most relevant and practical elements, especially at the conceptual stage. In addition, tailored HoQ in 3DPVS design differs in some ways from traditional HoQ; for instance, competitive benchmarks and limits are not used, as there is no physical market competitor at the current conceptual design stage, and this helps prevent possible interference from designers prior to applying TRIZ.

B2: Quantitative evaluation tools assisting QFD-based design approach

In this research, where TRIZ-based methodology and related tools have been integrated into the conceptual development of 3DPVS, there must be a sufficient tool for evaluating the conceptual solutions. After using the TRIZ-based method and before the whole design passes into detailed design, basic theoretical evaluation of the generated solution is vital, after which laboratory experiments or computer simulation can be applied with a more realistic foundation. As such, quantitative evaluation tools can be proposed that support TRIZ-based innovation process in terms of generating reasonable solutions, as well as judging values of different concepts at variable stages of design. In brief, several core aspects will be included, as follows.

Analysing multiple weights in 3DPVS conceptual design. As studied early, DRs, DAs, sub-system components and conceptual evaluation criteria are four aspects with a specific weight or value to incorporate in the judging process, including selecting solutions. When 'requirements' is used, it indicates that the demand derives from the super-system level—from either end-users who need specific 3DPVS products or designers who intend to improve current 3DPVS solutions. 'Attributes' indicates the system level, concerning several aspects of geometric, mechanical, biological and vibratory properties. For 'components', parameters of DA are the focus.

Calculating weights follows the same philosophy—comparing the relative significance of one 'character' with others in the same elementary category. Weights are interconnected, having relations with one another. Judging weight directly between different categories—for instance, DR with DA—could be confusing without HoQ. A TRIZ matrix can also be used to analyse relationships of elements in cross-categories—for example, DR 'to vibrate at a higher frequency' with DA 'scaffold's geometry'.

CILs between DRs. 3DPVS DRs have been systematically studied in design initiation. The analytic hierarchy process, traditionally used to subjectively determine requirements, can be partly applied for conceptual design. Four levels of significance, ranging from 1 to 4, where 1 indicates similar importance between pairs of requirements, while 4 means one requirement is much more significant than the another. All requirements selected for 3DPVS can be analysed with the four-level hierarchy.

DR CIL can be represented by a vector that identifies the weight of each requirement, where an equation established by (Yang 2013) can be introduced. First, a number called G_j, as the geometric of the i^{th} requirement, will be calculated, where g_{ji} is the dominance importance of requirement i over the j^{th}. value of $g_{ji,}$ and thus ranges between ¼ and 4. After generating G_j, a normalisation value can be used to acquire the importance level of the i^{th} requirement. I_j (N) means the normalised CIL level for DRs. After this analytic process, designers must further check the calculated level as applicable and reasonable:

$$G_j = \left[\prod_{i=1}^{n} g_{ji}\right]^{1/n} \quad \text{Eq. B-1}$$

$$I_j(N) = \frac{G_j}{\sum_{j=1}^{n} G_j} \quad \text{Eq. B-2}$$

In regard to analysing the CIL between a pair of DAs or DCs, the same philosophy can be employed with the four-point Likert scale. Thus, a hierarchy of different significances among 3DPVS attributes and components can be established.

Analysing relationship between requirement and attribute. To achieve this, a four-point Likert scale can also be used, which helps quantitatively analyse definite attributes before passing into TRIZ contradiction solving. Along with generating the weight of attributes via designers' experience, a quantitative strategy could help better. In the below equation, $W_i(A)$ indicates the weight of the i^{th} DA, I_j is the importance degree of the j^{th} DR, R_{ji} is the degree of relationship between the j^{th} requirement and i^{th} attribute, and n is the number of total DRs where R_{ji} varies between 1, 3 and 5:

$$W_i(A) = \sum_{j=1}^{n} R_{ji} I_j \quad \text{Eq. B-3}$$

Analysing relationship between attributes and components. The priority of components can be determined by human experience. A component with high weight leads to establish a contradiction pair with a higher value, where the TRIZ method comes into play. To support efficiency when analysing a range of components, a quantitative method is considered positive. In the following equations, V_j represents the value of one component of GMBV characterisation, such as the scaffold's porous size or weight; l represents the total number of components; R_{ij} indicates the relationship of the j^{th} component to the i^{th} attribute (for example, porous size and geometric complexity); and W_i denotes the weight of the i^{th} attribute. In addition, the normalisation of the value for each component is sometimes useful, via generating the comparative weight (W_j). For DRs and DAs, normalisation can also be used to achieve enhanced clarity in data analysis:

$$V_j(DC) = \sum_{i=1}^{l} R_{ij} \times W_i(A) \quad \text{Eq. B-4}$$

$$W_j(N, DC) = \frac{V_j}{\sum_{j=1}^{l} V_j} \quad \text{Eq. B-5}$$

This process helps researchers identify the most valuable parameter or component pair in TRIZ-based contradiction analysis. It is especially important for cross-domain designs, such as 3DPVS, where a large number of components for cell cultures, scaffold engineering, vibration mechanisms and 3DP might be considered simultaneously, and designers must focus on the main contradictions.

Determining weights of evaluation criteria. After introducing several analytical tools for DRs, DAs and 3DPVS sub-system components, this part introduces the weight of evaluation criteria, which will be used in both phases of concept generation and evaluation. Criteria are first selected from the attributes of scaffold engineering. Some attributes will not incorporate criteria selecting; thus, normalised calculation of criteria is sometimes used. That is, W_i is the weight for the i^{th} criteria, with n the total number of criteria identified. After normalisation, the weight of criteria can be used for evaluating generated solutions with enhanced clarity. The normalised weight also shows the relative difference, which helps comparison between criteria:

$$W_i(N) = \frac{w_i}{\sum_{j=1}^{n} w_j} \quad \text{Eq. B-6}$$

B3: Introducing Pugh matrix to incorporate with QFD

The basic philosophy of the Pugh matrix is that an optimal concept can be selected from a set of alternative solutions through comparison with the reference concept (called the 'datum concept' in the Pugh matrix). Criteria are analysed with results from comparison, generally leading to three levels: better, equal or worse. The datum concept for 3DPVS can be regarded the base concept or solution initiating the innovative problem, while new concepts refer to solutions generated using the TRIZ-based method. The basic solution, conceptual solution and relative level of ascent or descent are the three essential elements when using the Pugh matrix.

In addition, the ideal concept indicates an ultimate solution form that can be perceived as a 'perfect state', while being 'unachievable' in reality. The ideal concept can be perceived as the ultimate 'reference state', between which ideal and current states exist, and inventive solutions gradually mitigate the gap. Thus, the datum concept can play two roles—first acting as an ideal solution that evaluates newly generated solutions, as well as basic ones, and second functioning as a basic solution that only evaluates new solutions. The relative difference between solutions will be the output of concept generation and solutions can also be judged from the perspective of ideality. Table B-3 shows the basic structure of the Pugh matrix used for 3DPVS conceptual evaluation. It was used while generating basic conceptual solutions in Chapter 6.

Table B-3 Basic structure of Pugh matrix to be used in 3DPVS conceptual stage

Evaluation criteria	Weight	Datum solution	Solution 1	Solution 2	……	Solution m

Useful and positive forces (elements, performance) related	Criterion 1	W_1	E	D_{11}	D_{21}	…	D_{m1}
	Criterion 2	W_2	E	D_{12}	D_{22}	…	D_{m2}
	…	…	…	…	…	…	
Harmful and negative forces (elements, performance) related	Criterion x	W_x	E	D_{1x}	D_{2X}	…	D_{nx}
	…	…	…	…	…	…	
	Criterion n	Wn	E	D_{1n}	D_{2n}	…	D_{mn}
Score of ideality			IS_d	IS_1	IS_2		IS_m

The Pugh matrix traditionally had two categories defining criterion—benefit-based and harm-based (Pugh 1991), such as 'performance' and 'consumption or risk' (Yang, Xing & Ness 2016). Introducing three forces, with neutralising force integrated, provides a tailored Pugh matrix for 3DPVS. In the Pugh matrix, the value of each entry represents the dominance degree of the generated solution to the datum solution, judged by corresponding evaluation criterion. For example, D_{32} indicates the value of dominance degree between 'solution 3 to datum solution' based on 'criterion 2'. Dominance degree of the datum solution to itself always remains equal, with 'E' marked. Multiple levels or scales for evaluating dominance degrees can be established (Yang, Xing & Ness 2016), and, in the 3DPVS evaluation context, an 11-level criterion can be primarily identified from [0.01–0.99]. Specifically, (0.01) indicates the concept being almost useless, (0.1) extremely negative, (0.2) very negative (0.3), negative (0.4), slightly negative, (0.5) equal (E), (0.6) weakly positive, (0.7) positive or useful, (0.8) very positive, (0.9) extremely positive and (0.99) almost equal to the ideal concept. Such classification would also incorporate with TRIZ ISS.

Overall score of generated solution. By calculating each alternative conceptual solution, comparison helps judge the relative betterment or negativity of concept quantitatively. It will be based on literature studies and researchers' experience. For a definite alternative solution, its overall score is calculated based on dominance degree considering the weight of criteria. That is, n points to the total criteria number, S_i is the overall score of the i^{th} solution, w_j is the weight of the j^{th} criteria, and D_{ji} is the dominance degree of the i^{th} solution to datum 1, built upon j^{th} criteria:

$$S_i = \sum_{j=1}^{n} w_j \ D_{ji} \qquad \text{Eq. B-7}$$

Calculating ideality of each solution. The score for each conceptual solution generated will be calculated by the equation of ideality:

$$IS_j = \frac{\sum_{i=1}^{a} w_{ij} D_{ij}}{\sum_{k=1}^{b} w_{kj}(1-D_{kj})} \qquad \text{Eq. B-8}$$

Here, IS_j is the total ideality score for solution j (j = 1, 2, …, n), a and b respectively indicate the number of criteria representing positive/useful effects and harmful/negative effects, where n is the total number of criteria that equals the sum of a and b. The value of w is the

weight of the corresponding evaluation criteria. IS indicates the ratio between positive and negative aspects of a solution. The higher the IS, the higher the positivity the definite solution endows. In addition, the concept or solution with the highest IS could be further used as the datum concept or basic solution for the next-stage design, thus gradually idealising the conceptual solutions.

Apx C. Design Components on GMBV Characterization and 3DP Fabricability

Table C-1 DCs for GMBV characterization and 3DP fabricability

Category			No.	DCs	General value for scaffold (literature)	Target value for 3DPVS in this case
G-characterisation	G- characterisation	Geometric properties (porosity)	1	Open porosity	80-90 %	≈ 85-90%
			2	Pore body diameter	< 10 µm, 10 – 100 µm, 100-300 µm, 300-500 µm, >500 µm	≈ 150-300 µm
			3	Pore throat size	10 -50 µm, 50 -100 µm,	≈ 10-50 µm
			4	Strut thickness	300-600 µm, 0.6 – 1.0 mm, >1.0 mm;	400; 700 µm
			5	Pore geometry (shape)	Cube / hexagonal prism; Tubular; Spherical; Cylindrical	Cube; Spherical;
			6	Pore orientation	Cubic/hexagonal stacking; Cubic stacking; Gyroid/Salt-leached;	Cube; hexagonal;
			7	Specific surface area	100 – 120 m^2/g; 120 – 180 m^2/g;	108.3-125.2 m^2/g
M- characterisation		Characteristics of porous materials	8	Surface roughness	10 – 100 nm	15-80 nm
			9	Textural porosity	2 – 10 nm; 10-50 nm;	5-40 nm
			10	Compressive strength	0.05 – 0.5 MPa; 1-15 MPa; >80 MPa	At 4-5 MPa
			11	Stiffness (young's modulus)	1-5 MPa; >5 MPa;	D.
			12	Fracture toughness		
		Mechano-transduction	13	Fluid flow mediated wall shear stress	0.1 – 2.0 MPa; 2-5 MPa; 1.5 – 12 dyn/cm^2; >100 dyn/cm^3	
			14	Flow perfusion rate	0.1-1.5 ml/min;	D.
			15	Cyclic compression	Around 0.1 MPa; 500 – 5000 macrostrains;	D.
B-characterisation		Bioresorption theory	16	Cyclic compression induced fluid flow	1.5%, 1Hz, 1 hour daily / static	Bioresorption is for TE scaffold. 3D CC scaffold in this research need not to be biodegradable.
			17	Rate of ion dissolution	Positive gene-expression profile on osteoblasts	
			18	Ion dissolution concentration	Positive gene-expression profile on osteoblasts; ion release lowers pH	
			19	Accumulation in major organs	Negligible	
			20	Rate of excretion in urine	1.8 mg/day (tested on rabbits) for >20 weeks	None

D-characterisation	Ossification/ osteogenesis	21	Osteo- induction, conduction, integration	yes		
		22	Osteoblast infiltration	10 µm/min		
		23	Proliferation (Osteoblast)	Proliferation rate: 20 hours (doubling time)		
		24	Cell adhesion (Osteoblast)	Surface roughness 10-120 nm		
		25	Nutrients transferring	At cellular/substrate parameters		
		26	Angiogenesis	20-50 µm/h (rate of vessel growth); total growth >300 µm		
	General dynamicity/vibration	27	Capable of dynamic stimulation	Mechanical stimulation	Tailored mechanical or non-mechanical stimulation	
		28	Vibrational control	No	Yes	
		29	Movement of scaffold	No	Yes	
		30	Localized dynamicity/ vibration	No	Yes	
		31	Vibration frequency	0.1-10 HZ, 10-100 Hz, >1MHz		
		32	Frequency controllability	Low	Moderate	
3DP characterisation	3DP fabricability	33	Personalized scaffold geometry/architecture	Computer Aided Design (CAD)	CAD	
		34	Smart Material/ Dynamic material fabricability	Partly	Yes	
		35	Mass producibility	General RP/SFF fabrication technologies	No	
	Bio-safety	36	FDA approved	Yes	Yes	
		37	Cell Safety	Yes	Yes	

Apx D. TRIZ Innovation Principles Translated into 3DPVS Contexts

Table D-1: Illustration of TRIZ Innovation Principles and Translated Contents on 3DPVS

1. Segmentation

a. Object divided into independent parts:
- A large truck replaced by a truck and trailer

b. Making object easily disassemble:
- Quick disconnect joints

c. Increasing the degree of fragmentation/segmentation:
- Use powdered welding metal instead of foil

Applicability on 3DPVS:

- 3DPVS can be disassembled into 3D static scaffold and separated vibration mechanism;
- Large 3D scaffold segmented into several small 3D scaffold;
- Scaffold divided into several parts with different material composition or inner structure;
- Tissue divided into different group of cells;
- Some afterwards processing in 3DP: divide the fabricated scaffold from mold or support materials.

2. Separation/Extraction

a. Separate a disturbing part or component from object:
- Locate the air-conditioner outside room to avoid noise during cell culture;

b. Select out the useful part or property of the object:
- Bio- automation removes humans' definite functions;

Applicability on 3DPVS:

- Separate harmful vibrations from useful ones;
- Extract damaged cells from healthy ones;
- Extract useful parameters, like geometrics, from 3D static scaffold into dynamic ones;
- Separate useful functions of various 3DP technologies and create hybrid system;

3. Local Quality

a. Change property from uniform to non-uniform;
- Material surface treatment such as coating;

b. Make each part of object work in conditions suitable most for its operation
- Freezer compartment in refrigerator

c. Make each part fulfil a tailored and useful function;
- Multi-functional knife;

Applicability on 3DPVS:

- Frequency improves from uniform into non-uniform patterns;
- Localized vibrating frequency from area to area inside scaffold;
- Localized material composition inside scaffold;
- Localized geometrics and pore structures;
- Smart material for vibration while traditional material for mechanical strength of scaffold;
- Localized cell culture in different scaffold areas;

4. Asymmetry/Symmetry Change

a. Shape of an object is change from symmetrical to asymmetrical;
- Asymmetrical chip mounting reduces the ground lead inductance;

b. Increase the degree of asymmetry for asymmetrical object;
- Special connectors with complex configurations in shape or pin;

Applicability on 3DPVS:

- Traditional asymmetry geometrics of 3D scaffold change into asymmetrical ones;
- Asymmetrical material composition;
- Symmetrical cell growth into asymmetric one;
- Asymmetric vibration stimulation to achieve definite cell growth requirement;
- Asymmetric 3DP process;

5. Merging/Consolidation

a. Merge identical or similar objects, assemble them to perform parallel operations;
- Cartridge of multi-colour ink

b. Make operations contiguous or parallel in time.
- hillside combine harvester

Applicability on 3DPVS:

- Merge the cell culture benefit of 3D scaffold and vibration stimulation;

- Merge multiple materials generating vibratory functions;
- Dynamic cell culture via 3D scaffold (dynamicity merges with dimensionality);
- 3DP 'design and build' process;

6. Multi-functionality/Universality

a. A part performs multiple functions, so to reduce the need of other parts;
   - Cordless drill functions as screwdriver, sander, polisher;
   - USB used as a storage medium for multiple data types;

Applicability on 3DPVS:

- One scaffold provides both ECM-mimicking functions and Dynamicity Creating functions;
- 3DPVS replaces the 3D static scaffold even in static cell culturing;
- Diminish the needs for external mechanical vibrators;
- New vibration mechanical both provides vibration frequency as well as other dynamic stimulation;
- One 3DPVS design methodology that fulfills all requirements in future scaffold engineering;

7. Nested Doll

a. One object is placed inside another;
   - Voids in 3D structures

b. Dynamically makes one part passing through a cavity in another;
   - Vacuum cleaner has retractable power-lead;

Applicability on 3DPVS:

- Cells reside inside culturing liquid which is inside 3D scaffold;
- One or more micro vibrators can be placed inside 3D scaffold;
- Transition from mono- to poly-layer design of 3DP scaffold;
- Inside large pore there can exist small porous structures;
- Make one vibration field inside another field to generate special multiple-field vibration;

8. Weight Compensation/Anti-Weight

a. Merge the object with others that provide lifting function;
   - Aerostatic plane with lighter-than-air pockets;

b. Make the object interact with environment, using aerodynamic, hydrodynamic, buoyancy or other forces;

c. Maglev trains apply magnetic repulsion to reduce friction;

Applicability on 3DPVS:

- Cells in 2D culture tend stays at bottom of the plate by gravity force, while 3D culture substances help cells remain 3D morphologies.
- Anti-weight 3D scaffold for cell culturing;
- Anti-weight function provided by definite vibration mechanical, to slightly lift upcells cultured;
- In each layer of 3DP structure, make the vacuum filled with up-lifting air or gas;

9. Preliminary counteraction/anti-action

a. Deal with harmful actions or effects first before undertaking useful ones;
   - To prevent harm from extremes of pH by buffering the solution;

b. Oppose undesirable functions during action by creating other countering functions in prior;
   - Decompression chamber prevents divers from getting the bends;
   - Pre-stress the rebar before pouring concrete;

Applicability on 3DPVS:

- Put definite solutes beforehand inside culture environment for absorbing the toxic substances created during cell culture;
- Deal with useless vibration first than apply useful ones;
- 3DP process using preliminary counteraction to avoid fabricated product changing shapes when temperature drops;

10. Preliminary action/ Action in advance

a. Act before needed
   - Pre-impregnate the carbon fibre to saves lay-up time and increase its wetting degree;

b. Pre-arrange objects to ensure their coming into action efficiently;
   - flow-lines in modern Manufacture;

Applicability on 3DPVS:

- Make Vibration mechanism ready before dynamic culture starts.
- Store cell previously with nutritious fluid before putting into scaffold;
- Pre-arrange the hybrid 3DP system before fabrication is needed;
- Remove all negative influences from cell culturing before cells being damaged;
- Predict the tendency of cell growth first then select tailored vibration stimulation;

11. Beforehand compensation/Beforehand cushion

a. Means for emergency need to be prepared beforehand to compensate for the low reliability of the object;
   • Multi-channel control system;
   • Computer programs with automatic save operations;

Applicability on 3DPVS:

- Multi-channel vibration control system to change vibration in time;
- Emergency preparation for 3DP process with sophisticated material composition that might have chemical reactions during fabrication process;
- Vibration induction methods to help cells isolate from harmful vibrations or electromagnetic field waves;
- Removing strategies for dead or damaged cells during culturing from healthy cells;

12. Equipotentiality

a. Limit the changes of object's position in a potential field, to avoid the necessity of moving, lifting or lowering object during processing (usually by redesign the field or environment);
   • The Industrial Canal Lock in New Orleans;
   • Put a spherical lens between the LED an photodetector to eliminate the reflection light from photodetector that will affect that LED's performance, while still ensuring the function of photodetector to measure the light of LED;

Applicability on 3DPVS:

- Adjust vibration amplitude in different areas of scaffold to avoid moving scaffold up and down;
- Cells in bottom and top side of scaffolds move to receive definite gravitational force ;
- Put spherical lens or glass between focal based scaffold and the light source;
- 3DP process using fixed platform but moving nozzle head;

13. Action reversed/Other Way Round

a. Invert the action for problem-solving;
   • Varying pressure outside instead of inside to test pressure vessel;
b. Shift the parts states between static and movable;
   • Rotate the part rather than the tool;
c. Make the object or process 'bottom-upside';
   • Cleaning bottles by inverting and injecting water from below;

Applicability on 3DPVS:

- Increase the frequency when cells require lower ones or vice versa;
- For definite cell culture results, shift the 3DPVS from static and vibratory;
- Turn an assembly scaffold 'upside down' Turn an assembly upside down to insert fasteners;
- 3DP fabricates the scaffold in reversed layer-patterning way comparing with previous fabrication;
- Reversed geometrics to test scaffold's cell culture functions with normal ones;

14. Spheroidicity / curvature

a. Use curvilinear, spherical and ball-shaped structures to replace rectilinear, flat or cubical parts;
   • Arches and domes for strength in architecture
b. Apply balls, rollers, spirals;
   • Archimedes screw
c. Changes Motion from linear to rotary and uses centrifugal forces;
   • Rotary actuators in hydraulic system

Applicability on 3DPVS:

- Design Inner geometric structures as curvilinear, spherical or ball-shaped;
- Surface of scaffold becomes rounder and less cubical;
- Morphology of cells in 3D culture versus 2D;
- Linear vibration into rotary vibration;
- Bio-reactor using centrifugal force
- Rotary vibrating system

15. Dynamization/ Dynamic Parts

a. Change the object or environment for optimal performance, or find the optimal operating condition:
   • Shape memory alloys/polymers
b. Object to be divided into parts being capable of movements relative to other;
   • Articulated lorry
c. Make the rigid or inflexible process into movable or adaptable;
   • Bendy drinking straw

Applicability on 3DPVS:

- Use Smart materials to generate dynamic functions;
- Use subtle energy field to generate vibration for optimal vibrating condition;
- Scaffold divided into two centers, moving center and stationary center;

- Rigid scaffold into relatively flexible, soft or adaptable ones;
- Cells grow into soft tissues;

16. Partial/Excessive Actions

a. Complete partial work then 'add';
   - 'Roughing' in structure and slow 'Finish' in coating

b. Complete excessive work then 'substract';
   - Over spray when painting, then remove excess

Applicability on 3DPVS:

- Over printing when using some 3DP techniques, then remove excess;
- 3DP for part of the product then build other parts upon it;
- Increase or decrease vibration frequencies from required level;
- Ascend or descend the vibratory function intensity of 3D scaffold;
- Add or remove some quantity of cells cultured inside;
- Partial or excess material composition;
- Partial or excess structural building;

17. Dimensionality/Dimensional Change/Another Dimension

a. Add an additional dimension;
   - Spiral staircase using less floor area;

b. Decrease the dimension level;
   - 3D paper box pressed into flat form to save space;

c. Single-layered to or multi-layered arrangement;
   - Traditional fabrication to additive manufacturing;

d. Re-orient the object or use its different side;
   - Electronic components mounted on both sides of circuit board;

Applicability on 3DPVS:

- 2D cell culture into 3D; 2D scaffold into 3D;
- Spiral or curved inner structure to replace line-based one;
- 3DP fabrication process;
- Set the vibrator from scaffold's top into bottom;
- Dimensional scaffold system evolution process;
- Combine multiple 2D scaffold into 3D layered one;

18. Mechanical Vibration

a. Make an object vibrate or oscillate;
   - Vibration exciter removing voids from poured concrete;

b. Ascend the vibration frequency
   - Non-destructive crack detection using ultrasound

c. Use an object's resonant frequency;
   - Increase a catalyst's action by vibrating it at its resonant frequency;

d. Use piezoelectric vibrators than mechanical ones;
   - Piezoelectric vibrator improves fluid atomisation from spray nozzle;

e. Use combined ultrasonic and electromagnetic field oscillations;
   - Sono-chemistry;
   - Ultrasonic drying of films;

Applicability on 3DPVS:

- Cause 3D static scaffold to vibrate;
- Increase the frequencies of traditional vibration mechanism on cell culture;
- Increase the frequency to ultrasonic level for definite cell culture aims;
- Design the scaffold's resonant frequency by different material composition;
- Scaffold's resonant frequency by different geometric structures;
- Tailored vibration to disintegrate or remove dead cells while help the culture of healthy ones;
- Use piezoelectric vibrator instead of traditional mechanical vibrators;
- Use piezoelectric vibrator may help save energy consumption;
- Use inner vibration generated from scaffold instead of externally applied vibrations;
- Field-based vibrations for scaffold's higher performance;
- Mixed field vibration instead of single field vibration;

19. Periodicity/Periodic Action

a. Use periodic or pulsating action than continuous ones;
   - Pulsed water jet cutting;

b. Change periodic action in terms of its frequency or magnitude;
   - Transmit information by AM, FM, PWM means;

c. Perform a different action by using pauses between impulses or actions;
• Inkjet printer cleans heads between passes;

Applicability on 3DPVS:

- Periodic vibration to replace continuous one which may have negative effect on cells cultured;
- Pulsating vibration to generate better cell culture results in definite aspect;
- Design tailored period vibration regarding the frequency and amplitude;
- Periodic dynamic culture with static cell culture;
- Information transmitted between cells;
- Periodic functioning of Smart Materials;

20. Action Continuity/ Continuing beneficial action

a. All parts of object work at full load during the period without break;
• Continuous process of melting and discharging steel from furnace;
b. Remove or decrease idle or intermittent actions or performances;
• Print during the return of a printer carriage in inkjet printers;

Applicability on 3DPVS:

- Continuous vibration applied during cell culture;
- Continuous growth of cells into definite ECM;
- Use specified vibration to make cells continuously produce definite products;
- Majority of 3DP printing process needs to be continuous to ensure fabrication quality;

21. Skipping / Rushing through/hurrying

a. Conduct a process or stages of it at high speed to avoid destructive, harmful or undesired effects;
• Cut plastic faster than heat propagating to avoid deforming the shape;
b. Acceleration of present to achieve positive effects in future;
• Increase efficiency in doing small tasks so more time will be allocated for bigger ones;

Applicability on 3DPVS:

- Rushing the dead cell cleaning process to guarantee healthy culturing environment;
- Accelerate the frequency shifting between tow values to avoid negative effects on cells caused by the shifting process;
- Hurrying the cell culture process to avoid cell stagnation or attachment in scaffold;
- Skip the trivial details in scaffold 3DP fabricating to ensure a better quality in whole;
- Complete the after-fabrication process of 3DP in fast speed;

22. Transmutation/ Converting harm into benefit/ Blessing in Disguise

a. Use harmful factors, especially harmful effects of environment or surrounding, to achieve positive effect;
• Use waste heat to generate electricity;
• Recycle scrap material as raw materials for other application;
b. Eliminate the primary harmful action by adding another harmful action to it;
• Eliminate both nitrogen narcosis and oxygen poisoning from air and other nitrox mixes by using a helium-oxygen mix for diving;
c. Amplify a harmful factor to such a degree that it ceases to be harmful;
• Laser-knife cauterises blood vessels as it cuts;

Applicability on 3DPVS:

- Useful harmful vibrations to eliminate negative by-products cells from cell culture;
- Two non-beneficial vibrations work together to achieve positive effects;
- Hybrid 3DP system to make use of one system's limitation into another's advantage;
- Apply useless geometric structured scaffold for definite cell culture purpose;
- Harmful factors of multiple materials mitigated by 'intellectual' material composition;

23. Feedback

a. Improve a process, function or action by introduce feedback, referring back or crosschecking;
• Thermostat controls temperature accurately
b. Change feedback's magnitude or influence if it is used;
• Change sensitivity of an autopilot when close to an airport;

Applicability on 3DPVS:

- Vibration management system based on cell culture processes;
- Change sensitivity of vibration when descending vs ascending, since it uses energy less efficiently when vibration descends;
- Feedback on material composition based on vibration generated;
- Change sensitivity of scaffold's materials toward definite external vibration field;
- Feedback on structural controls based on vibration requirements;
- Automatic frequency control in potential future's 3DPVS;

24. Intermediary/Mediator

a. Use an intermediary object, carrier article or process;
- Dwell period during a manufacture process operation;

b. Temporarily merge one easily-removable object with another;
- Abrasive particles enhance water jet cutting;

Applicability on 3DPVS:

- Use scaffold as the intermediary object between cells and vibration stimulation;
- Intermediary vibration embedded inside main vibration;
- Traditional materials mixed with Smart Materials to help mechanical strength;
- Vibrator connected with 3D scaffold;
- Intermediary structure to support scaffold for further 3DP fabrication;

25. Self-service/ Serve Itself

a. Make an object serve itself by performing auxiliary useful functions;
- Self-cleaning oven / glass / material;

b. Use waste resources, energy, or substances;
- Pressure difference used to reinforce seal action;

Applicability on 3DPVS:

- Passive vibrating mechanical of 3D scaffold into self-vibratory mechanism;
- Use waste products during cell culture as vibrating stimulator or receiver;
- Use heat generated from mechanical vibration on scaffold to maintain cell culture temperature;
- Self-service by cells cultured inside scaffold;
- Self-disassembling scaffold during culturing process;

26. Copying/ Virtuality Replacing

a. Use similar or inexpensive copies to replace unavailable, expensive or fragile object;
- Imitation jewellery or Astroturf

b. Use optical copies to replace an object or process;
- Virtual mock-ups / electronic pre-assembly modelling;
- Video learning replaces learning of face-to-face;

c. Use infrared or ultraviolet copies if visible optical copies are used.
- A stethoscope with a microprocessor;

Applicability on 3DPVS:

- 3D scaffold to mimic real tissue environment for cell culture
- CAD modelling to help study scaffold's functionality;
- Computer simulation and analysis to replace real cell culture experiment;
- Virtual vibration stimulation;
- Virtual 3DP process;

27. Commercial Short-living objects

a. Replace an expensive object with several inexpensive objects, compromising its service life
- Disposable paper-cups, plates or cameras etc.

Applicability on 3DPVS:

- Use multiple not-expensive scaffolds to replace large, expensive ones;
- Disposal scaffold for one-time cell culture purposes;
- Use not-expensive vibrator to replace complicated vibration devices;
- Use cheap dynamic materials to replace expensive ones;

28. Mechanical System/interaction substitution

a. Change a mechanical system with sensory means, like the optical, acoustic, taste or smell;
- Finger-print/retina scan instead of a key

b. Use energy fields (electric, magnetic and electromagnetic) to interact with the object;
- Field activated switches

c. Fields change from stationary into moving, unstructured into structured;
- Magnetic Resonance Imaging (MRI) scanner

d. Utilize fields in conjunction with field-activated (e.g. ferromagnetic, magnetic, or electronic) particles;
- Ferro-fluid stays attached to the surface that requires lubrication;

Applicability on 3DPVS:

- Change mechanical vibration into subtle and non-mechanical one;
- Mechanical interaction of vibrator and scaffold changes into field-based;
- For material composition, electrostatically charge one positive and the other negative to mix two material powders;
- Mechanical cell culture process into field-based culturing;
- Scaffold into subtler form to have better interaction with cells;
- Static field vibration into moving field one, to generate tailored non-uniform vibrations;

- Heat scaffold containing ferromagnetic material by using varying magnetic field, to create suitable temperature for cell culture;
- uses ferromagnetic particles and variable magnetic field to alter the viscosity of the fluid where cells are cultured, to help cell growth;
- use field-based means to associate with 3DP process;

29. Aerometry(pneumatics) and Hydraulics

a. Use gas parts of an object instead of solid parts (inflatable or air cushion)
   - Acoustic panels with Helmholtz resonators; Hovercraft;

b. Use liquid parts of an object to replace solid ones(filled with liquids hydrostatic, hydro-reactive)
   - Transition from mechanical to hydraulic drive

Applicability on 3DPVS:

- Gas-filled 3D Scaffold
- Liquid 3D Scaffold
- Scaffold vibrated through liquid or gas;
- Use gas or liquid means to help cell growth;
- Change liquid nutrition for cell culture into gap ones;
- Use pneumatics or hydraulics 3DP process
- Solid materials for 3DP into liquid ones;

30. Flexible Membranes/Shells/Thin Films

a. Replace 3D structures with flexible shells and thin films;
   - Accumulators in hydraulic system, storing energy in stretchable bags;

b. Use flexible membranes to isolate object from external environment;
   - Shrink wrapping

Applicability on 3DPVS:

- Surface of 3DPVS made with flexible membranes;
- To cover scaffold by flexible shells to associate with vibration stimulation;
- Use thin films to isolate cells from external environment;
- Coating scaffold's structure with definite materials in thin layer;
- 3DP fabrication with original materials and thin-layer other materials to fulfil definite requirements;

31. Porous Materials/Density Change

a. Change solid object into porous or add porous elements, like inserts, coatings;
   - Sponge-like structures as media to absorb fluid;

b. Change the porous complexity or level if an object is already porous;
   - Porous structure density determining object's weight;

c. Use the pores of porous object to introduce a useful substance or function;
   - Cavity wall insulation;

Applicability on 3DPVS:

- Solid part of scaffold into porous;
- Make the porosity of scaffold non-uniform, that is, some parts are more porous than the other.
- Solid part by non-dynamic material as supporting structure and porous part by Smart Material as dynamic cell culture media;
- Porous characterisation to increase or decrease vibration magnitude or frequency;
- Porous control for cell culture purposes;

32. Colour characterisation/ Optical parameter change

a. Change the colour of the object or its external environment;
   - Electrochromic glass;

b. Modify the transparency of object, or its external environment;
   - Photolithography changing transparent material into solid mask for semiconductor processing;

c. Use the optical parameter of object or its environment to introduce a useful function or substance;
   - Change the emissivity object subject to radiant heating;
   - Use coloured additives or luminescent elements to increase object's observability;

Applicability on 3DPVS:

- Change scaffold's colour coordinating with definite vibration stimulation;
- Electrochromic or light-sensitive 3D scaffold;
- Use colour parameters to assist cell cultivation purposes;
- 3DP fabrication enabling complex colour characterisation;
- 3DP process undertaken in different colour lights;
- Add or decrease coloured additives or luminescent elements of scaffold to change the its transparency which could be connected with scaffold's vibratory functions or its properties for cell culture;
- Increase or decrease the light-level during cell culturing for optimized result;

- Introduce electromagnetic waves to affect cells in definite aspects;
- Use optically transmissive material to create an transparent shield (A glass device body covered with a thin layer of definite material) protecting cells from undesired electromagnetic waves that help generate vibration, so scaffold is vibrated while cells are not negative affected by the electromagnetic field;

33. Homogeneity/ Compatibility

a. Use materials with similar or identical properties for interacting object;
   - Container made of same material as its contents, to reduce chemical reactions;

b. Change the level of homogeneity or compatibility;
   - Add special additives to increase homogeneity between two metals during fusing;

Applicability on 3DPVS:

- Biocompatible materials for the homogeneity of 3D scaffold with cells;
- Homogeneity of different cells during culture process;
- Interaction between different semi-scaffolds;
- Use material homogeneity in 3DP application;
- Use the homogeneity of vibrations;
- Merging smart materials (dynamic materials) and traditional materials with special interacting substances;

34. Discarding and Recovering/Rejecting and regenerating

a. After objects completing or fulfilling their functions, discard them by dissolving, evaporating, or modify then during the process into new objects;
   - Bio-degradable containers;

b. Restore or recover the parts of an object after consumed or used;
   - Automatic rifle;
   - Self-charging energy accumulator;

Applicability on 3DPVS:

- Discarding the consumed cell culture media;
- Scaffold regenerating itself after being consumed by cells;
- Biodegradable scaffold;
- Discarding the support-structures for scaffold after 3DP process;
- Create scaffold's tunnel with complicated configuration with temporary substance, like dried ice, which can be vaporized.
- Automatic scaffold which can change shape to some level then come back;
- Vibration part of scaffold can be regenerated and discarded based on requirement;
- Regenerating required structures during cell culture;

35. Parameter Change;

a. Change object's physical state between gas, liquid and solid;
   - Water changes into gas to provide energy for engine;

b. Change object's concentration, density or consistency; crystallization;
   - Transport oxygen gas as liquid;

c. Change the flexibility degree;
   - Compliant brush seals instead of fixed geometry seals;

d. Change the temperature, volume or pressure;

e. Other parameters (39 parameter list);
   - Shape-changing parameter;
   - Field-based parameter, like magnetic property;
   - Conductivity;

Applicability on 3DPVS:

- Change scaffold from rigid-solid form into flexible solid form;
- Develop liquid-based scaffold and gas-based parts in scaffold for definite functions;
- Shape-changing materials generate vibratory functions;
- Change the density and consistency of vibration;
- Change the multiple parameters during cell culture simultaneously;
- Tailor the temperature and other aspects for better dynamic cell culture result;
- 49 parameter list for 3DPVS;

36. Phase transition

a. Utilize the generated or by-product phenomena occurring during the phase transitions, like volume change, heat loss or absorption, conductivity change and process;
   - Latent heat effects in melting;
   - Volume expansion by liquid-to-gas transition;
   - Superconductivity;

Applicability on 3DPVS:

- 3DP printing head can be designed with a cavity filled with frozen lubricant-coolant before printing to increase the cooling-efficiency;
- Use phase transition to absorb or generate heat generated during cell culturing;
- Cooperate with vibration frequencies with phase-transition phenomena;
- Volume-changing phenomena of scaffold results in dynamic stimulation on cells;

37. Thermal expansion

a. Use materials' thermal expansion or contraction;
   - Shrink-wrapping;

b. Use multiple materials with different coefficients of thermal expansion;
   - Bi-metallic strips in thermostats;

Applicability on 3DPVS:

- Thermal shape memory alloys/polymers for scaffold fabrication;
- Two-way shape memory alloys to create dynamic function;
- Combine scaffold's materials with positive and negative thermal expansion coefficients to achieve tailored expansion properties for dynamic functions;
- Utilized the thermal expansion effect on cell culture;
- Thermal insulation during cell culture;
- Use thermal expansion properties to cooperate with vibration frequencies;

38. Increased Oxidation

a. Use oxygen-enriched air instead of common air;
   - asthmatic patients placed in oxygen tent;

b. Use pure oxygen to replace the enriched air;
   - Treat wounds in a high-pressure oxygen to aid healing;

c. Use ozonized or ionised oxygen;
   - Ionising the oxygen to help chemical reaction process;

d. Use ozone to replace ozonized or ionized oxygen;
   - Use ozone to destroy harmful micro-organisms in plant like corn;

Applicability on 3DPVS:

- Accelerated oxidation together with 3DP process to achieve definite fabrication results;
- Using ozone to help or hinder cell culture;
- Oxidation cooperates with definite vibration mechanisms;
- Oxygen-enriched air to help general cell culture process;
- Oxidant work with fields, like electromagnetic;

39. Inert Atmosphere / environment

a. Inert environment to replace normal one;
   - Conduct electron beam welding in a vacuum;

b. Add Inert additives or neutral parts to object or process;
   - Add fire retardant elements to titanium;

Applicability on 3DPVS:

- Inert atmosphere during 3DP process to avoid undesired chemical reactions of definite materials;
- Inert atmosphere associates with vibration mechanism;
- After-fabrication processing of 3D scaffold;
- Culture cells inert environment with definite density;
- Inert atmosphere helps fabricating definite geometric structures that cannot be fabricable in normal air;
- Material composition inside inert atmosphere;

40. Composite Materials

a. Use composite, multiple or mixed materials instead of uniform one;
   - Glass- or fibre-reinforced plastic and ceramics;
   - Composite photo-catalyst materials;

Applicability on 3DPVS:

- Material composition for 3D scaffold with both traditional materials and smart materials;
- Composition design for vibratory functions of 3D scaffold;
- Use composite materials to generate multiple stimuli on cells;
- Fabricate tailored geometrics with composite materials instead of uniform one;
- Adapt composite materials to single or hybrid 3DP system;

Apx E. TRIZ-based ISS Proposed for 3DPVS Design

Table E-1 ISS assisting the TRIZ IPA process for 3DPVS Design

ISS	No.	Aim	No.	Description and Example on 3DPVS Innovation
Incomplete or Inadequate SFM	8 Solutions	Creation of SFM from incomplete model;	5	1.1. Creation of SFM from incomplete model 1.2. Add a tool, substance (S1) if system is required to provide the extra functions 1.3. Add an object (S2), when S1 and F cannot provide sufficient functions for system 1.4. Use a copy or model of the object where additives can be used, when additives are not available to be applied in the original 1.5. Transition from simple S1-S2-F models to complex SFM, to constitute whole picture of system functioning
		Delete, simplify excessive elements of SFM,	2	2.1. From complex SFM generate multiple SFM which only contains three elements, S1, S2 and F. 2.2. Delete the irrelevant elements that affect nothing on present analysis from original SFMA and build the simplified-most model;
		Transform SFM into NSFM containing analysis of Three Forces;	1	3.1. Establish the positive force, negative force and neutralizing force for each interaction given on the desired functions by such interaction. Complete the 3-interaction-9-forces (3I-9F) model; Analysis the model in terms of the effect of neutralizing force on positive and negative ones;
Consciousness Identification Standards	4 Solutions	Contradiction Re-structuring	3	1.1 Solving contradiction by shifting focus onto more significant contradictions which are parallel with original ones but have higher weights. Higher design contradiction emerging, previous ones considered as significant tend to lose their weights. 1.2 When there exists only one set of conflict or contradiction, hypothesized ones with higher weights needs to be established to serve the purpose of non-identified comparison. 1.3 Separate definite function or action in both positive and harmful based on design criterion, then analyse the Useful (U), Harmful (H) Force and Neutralizing force (N).
		Identification Patterning & Dismantling	2	2.1 Mental inertia frequently is caused by identified with one problem while ignoring others, that is, trees nearest represent the whole wood. Solution is that to disidentify with ‘wood’ and see the ‘forest’; 2.2 Reverse design process to some extent, changing elements with ABC sequence into CBA; Identified ‘cause’ and ‘effect’ might be on the contrary to truth.
Harm-based Elements	27 Solutions	Eliminate the Harm or Decrease its Degree	18	1.1. Remove the components whose functions are not needed; 1.2. If the S2 (object) can perform the useful action, then trim S1 (subject) and transfer responsibility for the useful action to the S1. 1.3. If another component can perform the useful action, then trim S1 (subject) and transfer responsibility for the useful action to the component. 1.4. If a resource can perform the useful action, then trim S1 (subject) and transfer its responsibility to the resource. 1.5. Trim the subject further after it has performed its useful action; 1.6. Partially trim the harm-generating or harm-receiving parts, if this does not affect useful functions; 1.7. Counteract the harmful action with an opposing field which neutralizes the harm 1.8. Change the object’s sensitivity so it becomes immune to harmful actions; 1.9. Change the zone and/or duration of the harmful action to decrease its effects; 1.10. Avoid harmful action by introducing a substance from elements of existing system; 1.11. Avoid harmful action by introducing a new substance from external; 1.12. Use a sacrificial substance to absorb the harm 1.13. Apply the required field indirectly or link it with other substance or put it elsewhere, if it harms the system; 1.14. Protect area of the system from harm by adding a protective substance to this area where it is most exposed or easily-affected; 1.15. Use a weaker field or action and enhance it locally in required area; 1.16. Use sub-system elements to stop or mitigate the harm; 1.17. Use super-system elements, like environment, to stop the harm;

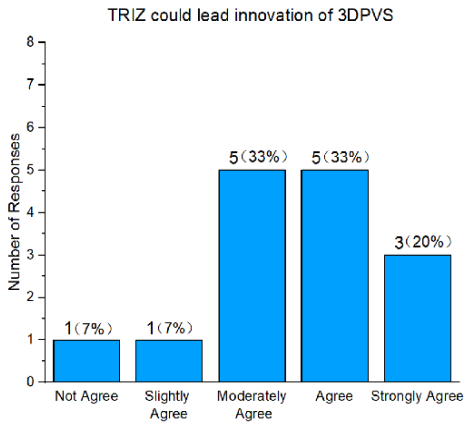
				1.18. Remove the harms by switching them off partially or fully;
		Transform Harm into Positive or Neutral	9	2.1. Use definite harm to deal with original harm, by finding the right context; 2.2. Use definite harmful function or activity to eliminate or dismantle another harm; 2.3. Use the harm to generate some positive elements, by finding right context; 2.4. Add another harm so that the combination of the two harms is no longer harmful; 2.5. Amplify the harm until it delivers benefit; 2.6. Eliminate its harmful consequences in time after a harmful action takes place; 2.7. When there is an inevitable harmful effect of an action, add an anti-action which controls/counteracts the harmful effect; 2.7.1. Create prior or simultaneous anti - harm to counteract the harm 2.8. Use element that disappears or becomes identical to components of existing system after fulfilling its work 2.9. Useful action noy found in given process where only two harmful actions are available, choose the less harmful one which has higher possibility to be modified into neutral or useful
Insufficiency based elements	37 Solutions	Change, evolve the system' components or add something to them	19	1.1. Add elements directly to or inside the S1 or S2 (subject and object); 1.2. Add something between the S1 and S2 which enhances the required function; 1.3. Use the existing external environment or substances to enhance the actions; 1.4. Add new elements into the environment, when external environment does not contain ready solutions. 1.5. Replace the external environment with another one by decomposing it; 1.6. Change the surface or external layer of the object (object-based, not directly on environment); for example, wearing an armour to protect body. 1.7. Degenerate or decompose other elements in substances or environment so required function can be enhanced, when nothing new can be added; 1.8. Tailor the external environment for localized substances, to enhance general function required; For instance, move heat-activating scaffold parts to higher temperature zone and heat-repulsive parts to cold zone, where both zones are available in the system; 1.9. Segment the object by dividing the elements into smaller units, when an improvement is needed but components cannot be added with anything new; 1.10. Increase the degree of fragmentation by changing original object to a porous or capillary material that will allow gas or liquid to pass through; 1.11. Change the subject or object by introducing voids, fields, air, bubbles, foam, when we need 'large amounts' but we can use 'nothing'; 1.12. Increase the efficiency of the system by making it more flexible/adaptable/dynamic (less rigid/fixed); 1.13. Improve system by multiplying some system elements (similar or dissimilar) or combining it with another system (similar or dissimilar), when such elements or external system is available; 1.14. Develop the linking function between the elements of system, by making links more flexible or more rigid, when links have obvious features to modify 1.15. Achieve system transition, by increasing the 'differences' between elements partly or up to opposites; 3DPVS for instance: Higher-vibration scaffold for one group of cells' culturing, Lower-vibration scaffold for another. Vibratory-functioning mode for dynamic cell culture, and Static-functioning mode for ordinary 3D static culture; 1.16. Improve definite function of system by delivering opposite incompatible functions at different system levels, when distinctive functions of three systems exist. 1.17. Improve definite function by changing transition function delivery to micro-Level;

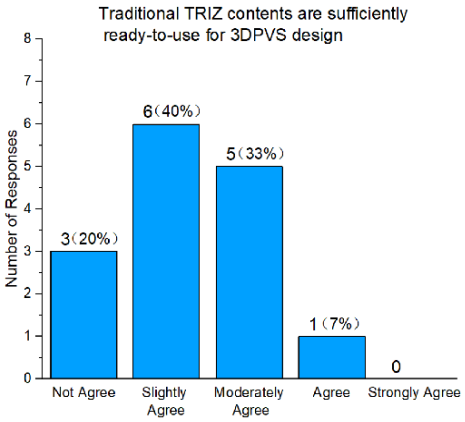
			1.18. Improve a system's effectiveness and controllability by developing one element of system to deliver its own but extra functions, when such extra functions can be identified. 1.19. Improve a system by changing the components/substances to deliver exactly what is needed in time and/or space, that is, certain functions will not be needed except certain areas or at particular times. For instance: changing in space includes from a uniform substance or uncontrolled substance, or to a non-uniform substance with a predetermined spatial or other structure; changes in time could be permanent or temporary;
	Enhance, strength, improve the Action focusing on Insufficient or Missing Field (F)	18	2.1. Get an action by adding an appropriate Field, or extra Field, when the existing system elements cannot be easily changed 2.2. Replace an inefficient or poorly-controlled field with a better one; take 3DPVS for instance: Replace a gravitational field with a mechanical field, a mechanical field with an electric field etc., such as using mechanical field to replace mechanical one for dynamic cell culture; Use a field to replace a substance; (5.1.1.2) Using vibrating field to replace vibrator; 2.3. Improve action's effectiveness by changing Field from uniform or uncontrolled to a field with predetermined patterns being permanent or temporary 2.4. Improve action's effectiveness by matching or mismatching the natural frequency of generated by F with the natural frequency of S1 (tool or subject) or S2 (object or product) 2.5. Improve action's effectiveness by matching or mismatching the frequencies of the different fields being used 2.6. To achieve two incompatible actions by performing one action in the downtime of the other, when field can be closely related with such actions 2.7. Use field-based actions or fields in system to create another field 2.8. Use actions or fields that are present in the environment, when factors like gravity, ambient temperature, pressure, sunlight can be used. 2.9. Achieve extra action or field by using something already present in system or environment, as the generator of the extra fields or actions acting as media or new focus of old function. 2.10. Use excessive action or extra intensity of field, then decrease; ▪ Use an excess of what is required and remove the surplus, such as post 3DP fabrication process; ▪ Surplus substance is removed by a field and surplus field is removed by a substance; 2.11. Use a small amount of highly active additive; ▪ Use a large amount of very inactive additive to generate reverse effect; 2.12. Concentrate the additive at a specific location 2.13. Introduce the additive temporarily or at a given time 2.14. Improve an action/field by changing the phase of the existing field/substance 2.15. Achieve an action by using the phenomena which accompany phase change 2.16. Achieve an action with dual properties by using substances capable of converting from one phase state to another 2.17. Replace a single- phase state with dual-phase (or multiple-phase) state 2.18. Induce the dual- phase state by creating interaction between the parts of the system

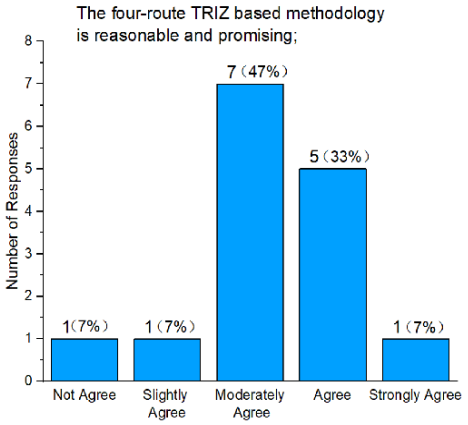
Apx F. Result & analysis of Expert Survey

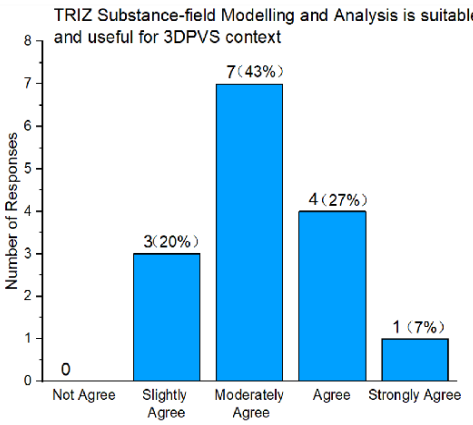
F1: Feedback of the TRIZ-based approach

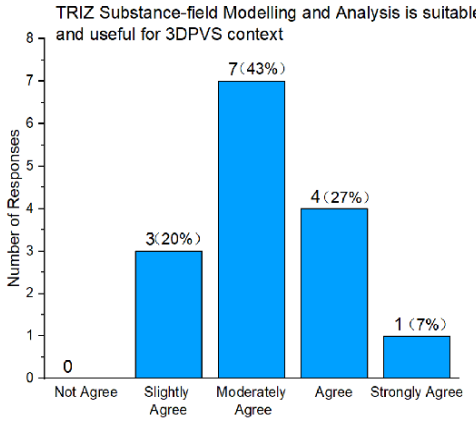
Figure F-1 Result & analysis of Expert Survey

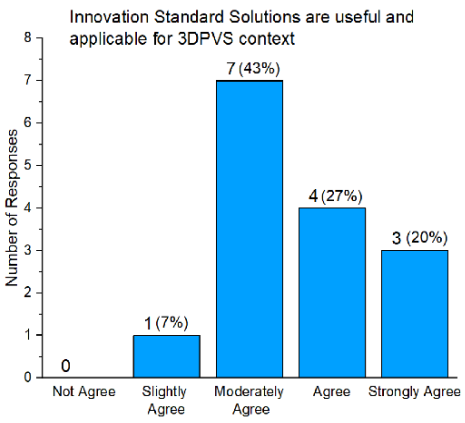

TRIZ could lead innovation of 3DPVS
Number of Responses
1(7%)
1(7%)
5(33%)
5(33%)
3(20%)
Not Agree
Slightly Agree
Moderately Agree
Agree
Strongly Agree

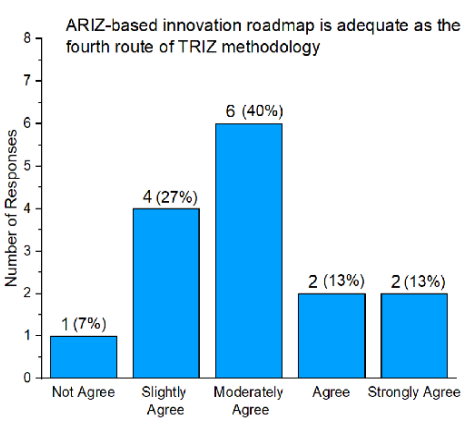

Traditional TRIZ contents are sufficiently ready-to-use for 3DPVS design
Number of Responses
3(20%)
6(40%)
5(33%)
1(7%)
0
Not Agree
Slightly Agree
Moderately Agree
Agree
Strongly Agree

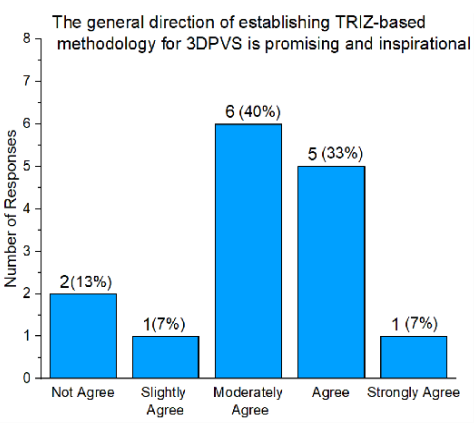

The four-route TRIZ based methodology is reasonable and promising;
Number of Responses
1(7%)
1(7%)
7(47%)
5(33%)
1(7%)
Not Agree
Slightly Agree
Moderately Agree
Agree
Strongly Agree

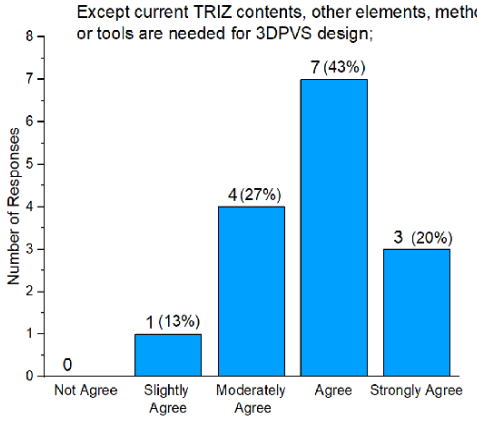

TRIZ Substance-field Modelling and Analysis is suitable and useful for 3DPVS context
Number of Responses
0
3(20%)
7(43%)
4(27%)
1(7%)
Not Agree
Slightly Agree
Moderately Agree
Agree
Strongly Agree

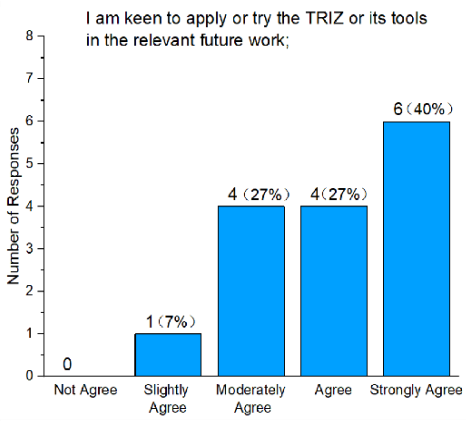

TRIZ Substance-field Modelling and Analysis is suitable and useful for 3DPVS context
Number of Responses
0
3(20%)
7(43%)
4(27%)
1(7%)
Not Agree
Slightly Agree
Moderately Agree
Agree
Strongly Agree

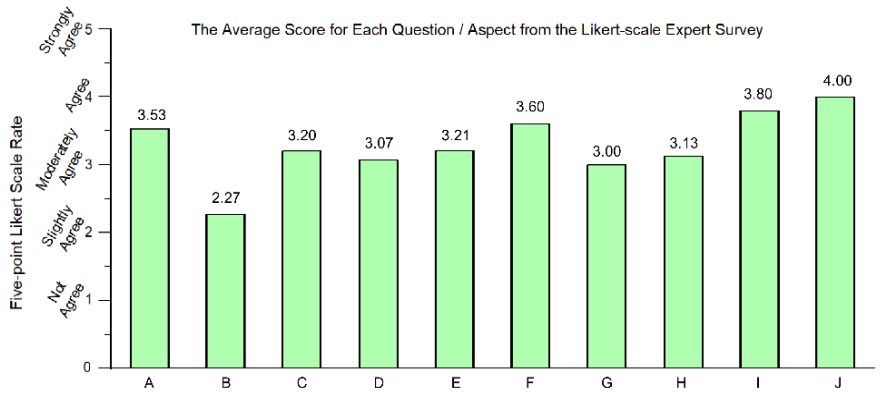

Innovation Standard Solutions are useful and applicable for 3DPVS context
Number of Responses
0
1(7%)
7(43%)
4(27%)
3(20%)
Not Agree
Slightly Agree
Moderately Agree
Agree
Strongly Agree


ARIZ-based innovation roadmap is adequate as the fourth route of TRIZ methodology
Number of Responses
1(7%)
4(27%)
6(40%)
2(13%)
2(13%)
Not Agree
Slightly Agree
Moderately Agree
Agree
Strongly Agree


The general direction of establishing TRIZ-based methodology for 3DPVS is promising and inspirational
Number of Responses
2(13%)
1(7%)
6(40%)
5(33%)
1(7%)
Not Agree
Slightly Agree
Moderately Agree
Agree
Strongly Agree


Except current TRIZ contents, other elements, methods or tools are needed for 3DPVS design;
Number of Responses
0
1(13%)
4(27%)
7(43%)
3(20%)
Not Agree
Slightly Agree
Moderately Agree
Agree
Strongly Agree


I am keen to apply or try the TRIZ or its tools in the relevant future work;
Number of Responses
0
1(7%)
4(27%)
4(27%)
6(40%)
Not Agree
Slightly Agree
Moderately Agree
Agree
Strongly Agree


The Average Score for Each Question / Aspect from the Likert-scale Expert Survey
Five-point Likert Scale Rate
Not Agree
Slightly Agree
Moderately Agree
Agree
Strongly Agree
3.53
2.27
3.20
3.07
3.21
3.60
3.00
3.13
3.80
4.00
A
B
C
D
E
F
G
H
I
J

F2: Survey contents

This material presents the survey used in the validation process of the chapter work.

Introduction Context

I am contacting you and requesting for you to participate in a survey, since you are involved in the relevant research of 3DPVS. I think that your participation could make some contribution to knowledge in the field of scaffold design and innovation. Answering the survey statements below might take only a few minutes of yours.

Reasons of Conducting the Survey

During the research of developing 3DPVS, I have studied TRIZ and relevant tools and found that TRIZ could have high potentiality to applied as design methodology to the design of novel 3DPVS, as well as possibly other novel scaffolds. The motivation of this survey is to subject the potential ideas and methodology plans, which resulted from my work, to the scrutiny of regarded experts. Since the TRIZ methodology, and its tools have not been utilized as formal methodology for scaffold innovation, the study level of my work tends to be abstract and remains at theoretical level at this stage. Although it is challenging to do so and difficult to arrive at definitive answer, I would like to hear experts' ideas and consider whether the proposed work can be validated to certain extent.

Instructions

The views of the participants will be held anonymously. For each element of the proposed methodology work, five-score statements are posed in the form of a questionnaire. The survey is designated, and answers can be selected by a tick box method, where each statement requiring one response. If you have additional comments or concerns, please feel free to write them down. Any and all contributions would be sincerely appreciated.

Survey Questions sent to Experts

After analyzing this design element, please tick the relevant box which best describes your answer to the following statements:

Answer Type: [Five-point scale for each, Strongly Agree, Agree, Moderately Agree, Slightly Agree, Not agree];

Table F-1 Survey questions sent to experts and five-point scale answer box

No.	Survey questions	Five-point Scale
1	TRIZ could lead to innovation of 3DPVS;	☐ ☐ ☐ ☐ ☐
2	Traditional TRIZ contents are sufficiently ready-to-use for 3DPVS design;	☐ ☐ ☐ ☐ ☐
3	The 4-route based TRIZ methodology proposed is reasonable and promising;	☐ ☐ ☐ ☐ ☐
4	TRIZ Innovation Principles & Parameters presented are applicable and adequately adjusted to tailor 3DPVS context;	☐ ☐ ☐ ☐ ☐
5	TRIZ Substance-field Modelling and Analysis proposed is suitable and useful for 3DPVS context;	☐ ☐ ☐ ☐ ☐
6	Innovation Standard Solutions proposed are useful and applicable for 3DPVS context;	☐ ☐ ☐ ☐ ☐
7	ARIZ-based innovation roadmap presented is adequate as the fourth route of TRIZ methodology;	☐ ☐ ☐ ☐ ☐
8	The general direction of establishing TRIZ-based methodology for 3DPVS is promising and inspirational;	☐ ☐ ☐ ☐ ☐
9	Except current TRIZ contents, other elements, methods or tools are needed for 3DPVS design;	☐ ☐ ☐ ☐ ☐
10	I am keen to apply or try the TRIZ or its tools in the relevant future work;	☐ ☐ ☐ ☐ ☐

Free Text Comments:

Apx G. Explore and Tailor TRIZ Method for 3DPVS Conceptual Design_ Supplementary Chapter

Work of this has been converted into full manuscript for publishing.

G1: Introduction

Regarding cell culture scaffold innovation, 3DPVS has been proposed as a present-to-future novel product, which currently stands at the stage of conceptual development. Design studies on 3DPVS concept generation show high value, and one essential part of this could establish a suitable design methodology that has innovation merits. TRIZ and its tools have proven valuable for creation and design innovativeness, but have not yet been used for scaffold design at a mature level. In this chapter, we seek to study and explore the design aspects of TRIZ and its most relevant tools for the context of 3DPVS, as well as preliminarily establishing a TRIZ-based methodology that could tailor the design aspects of 3DPVS. Based on this, a four-route TRIZ-based methodology for 3DPVS has been preliminarily established, with several essential components structured, adapted for 3DPVS context. Validation has also been conducted to investigate design aspects of this study. In brief, this chapter explores using TRIZ in a new realm potentially preparing the ground for future 3DPVS innovation, which indicates that a TRIZ-based method can be applicable to bio-design and scaffold science. It also, to some extent, fills a gap in the scaffold engineering and TRIZ literature and provides a comprehensive overview of a timely topic.

G2: Selecting TRIZ for 3DPVS Innovation

Five levels of innovation are identified by TRIZ. Level 1 indicates a simple improvement of a technical system with parametric changes, and Level 2 involves resolution of a technical contradiction. Level 3 invention contains a resolution of a PhC that requires knowledge from other industries. Level 4 is the second-highest innovation, where new technology is developed from a breakthrough solution that requires knowledge from various fields of science. Level 5, the top innovation, means the discovery of new phenomena. For example, Nobel Prize winners could be in such an innovation position. Based on this, nearly 80% of patents only belong to Levels 1 and 2. Predominant scaffold designs (90%+) studied from the literatures are at Levels 1 and 2. However, this study is predicted to help designers, with practical use of TRIZ, elevate the innovative solution to Levels 3 and 4. Therefore, systematic study of TRIZ, tailored practically to 3DPVS, is promising and could possibly broaden the vision for future scaffold innovation.

Innovation as Essence of 3DPVS Design

Following the laws and principles of scaffold evolution, it is reasonable to reach the conclusion that traditional 3D scaffold systems, vibration systems, as well as cell culture systems, will develop simultaneously and meet at a cross-roads in the near future, which indicates the

appearance of novel 3DPVS. There have been no previous studies on 3DPVS, either in terms of its conceptual philosophy or product realisation. As such, an appropriate methodology, or methodological system, must be selected, adapted or even invented in the first place to help achieve the 3DPVS at the conceptual design level.

Compared with traditional scaffolds, the development of a novel product 3DPVS is an innovation process, which is different from that of other bio-products that can be better approached by an experimental 'trial-and-error' strategy from the beginning. An experimental focus at this stage of 3DPVS is considered less vital than a conceptual design at philosophical level. In other words, the former can be useful and efficient only after a successful approach of the latter. In addition, the core task of 3DPVS conceptual design revolves around the idea of 'innovation', which means creating new concepts where the newly proposed vibratory functionality could innovatively integrate with the 3DP fabricability and 3D scaffold. This integrating process is novel, and it is more promising to achieve when the selected method tackles this 'novelty'. Thus, TRIZ has potential because it was especially developed with a blueprint for 'creativity' and 'innovation'.

Compared with TRIZ, another innovation method is Extenics, which focuses on solving incompatible problems by formularized methods in management and engineering. Extenics has solved many engineering incompatible problems and has been practised as suitable for special fields. However, there is no systematic theory on knowledge-based innovation (Li, X, li & Chen 2014). Extension innovation methods needs further improvement to be used as general operable methods for innovative activities. Regarding bio-innovation, TRIZ shows more applicability. Therefore, TRIZ is considered as better approach for 3DPVS scenario.

In contrast, as studied early (Yuan 2019), tackling contradictions in GMBV characterisation of 3DPVS, increasing the ideality level of 3DPVS to gradually approach its ideal model, and viewing the whole design process from the idea of system evolution are several essential focuses that the selected methodology must fulfil. In this way, TRIZ methodology has been identified as highly suitable, since the TRIZ 'contradiction matrix', 'innovation principles' and 'evolution patterns for ideality' exactly tailor to the requirements of those three cores, which is also consideration criteria when selecting a design method. Considering this, TRIZ is used for the innovation process of 3DPVS development. The contents of TRIZ and its innovation mechanisms are discussed in the following section.

Innovation Mechanisms of TRIZ

TRIZ is a set of tools used by engineers, inventors and scientists to systematically create new innovative ideas and solutions. It has been used to analyse and study artificial engineering systems (Bogatyrev & Bogatyreva 2015; Kamps et al. 2015). Instead of waiting for random inspiration or using trial and error to innovate, TRIZ enables designers to attain breakthrough ideas, methods and solutions on demand. Created in Russia, TRIZ tools have been developed

from the study of millions of patents. Rather than playing psychological games, brainstorming or guessing-and-trying, as in ordinary designs (Sarkar & Chakrabarti 2011), TRIZ solutions are systematically derived based on the information abstracted from studying how others solved problems and created innovation.

TRIZ methods, as discussed, have been created, tested and analysed based on millions of patents and innovations, aiming to transform the subjective innovation process, to some extent, into a relatively objective, scientific and easy-handled process. The basic philosophy of TRIZ indicates that, when an innovation problem is broken into required elements in TRIZ as input, following a series of 'alchemical work', the being of the original problem, filled with contradictions, splits and conflicts, can change into a new being which is of integration (Hua et al. 2006). In brief, TRIZ analyses the hidden determinants of creative works by previous innovators and packages their essence into TRIZ. Technical contradictions and PhCs are the cornerstones of TRIZ. Traditional TRIZ generally contains three mechanisms, as follows (Altshuller, G. S. 1984; Bukhman 2012; Chechurin 2016).

Table G-1 Mechanisms of TRIZ for problem solving related to different contradiction cases

Problem-solving mechanism related to SC
Thirty-nine parameters and 40 inventive principles may be applied. For a software contradiction, use 24 parameters and 40 inventive principles.
Problem-solving mechanism related with PhC.
Five separation principles can be used for solving a PhC.
Problem-solving mechanism related with non-contradiction issues.
The system of standard solutions is used to address problems where no contradiction can be abstracted or where the contradiction is too challenging to be categorised as either SC or PhC.

Specifically, the categorisation of mechanisms depends on the essence of the contradiction. The process of using the contradiction matrix to solve a problem occupies the most significant role in TRIZ methods (Altshuller, G. S. 1984, 2004; Fiorineschi et al. 2018). SC is the conflict between two or more parameters in a system, while PhC is the conflict between two or more values of one parameter. An SC could mean that, when improving one design parameter of the product, another design parameter will deteriorate, so improving one parameter could conflict with the properties of others. For instance, in the design of 3DPVS, when the pore size increases to the desired level to cooperate with vibration, the geometric stability may decrease and negatively affect the cell culture process. Thus, elimination of this conflict could indicate that designers must find a solution that fulfils both requirement of scaffold pore size for possible vibration, and avoids the deterioration property of its geometric stability. In contrast, a PhC could mean that when pore size changes to a desired level—say, highly precise at nano-micro-level—the fabricability of this pore decreases or becomes impossible. Thus, identifying a suitable pore size that is both as precise as required and fabricable, will be key in this scenario.

In terms of system evolution, it is guided by defining and resolving SCs and PhCs in terms of performance demands. Software contradictions are modified from SCs tailored to software and informational technology related problems (Cascini & Russo 2007). If there is contradiction, then, based on its nature—that is, whether it is a PhC or technical contradiction—the problem can be approached using either the five separation principles (physical) or contradiction matrix and 40 principles (technical). If no contradictions can be recognised or the contradiction is at beyond level, certain tools can potentially be applied to solve the problem, such as evolution principles and laws and 76 standard solutions.

For another instance, when enhancing the print resolution of 3DP, we usually require more printing materials; thus, the resource consumption of 3DP will increase. The conflict between printing resolution (increase) and material consumption (decrease or preserve) requires that both 'more and less' printing materials be used, which is a technical contradiction. In terms of customer aspects, a 3D printer tends to be complex and sophisticated equipment and more operations are required to maintain the functions of the printer. However, customers may be unwilling to spend excessive time operating this and prefer to use simple, easy approaches, even if these cannot fabricate fine-resolution samples. Thus, low maintenance and fine resolution become a SC. In terms of PhC, enhanced resolution does not always lead to a high-quality printed sample. Cells may not pass through the fabricated scaffold if the resolution is too fine. A resolution that is neither too fine nor too coarse leads to a PhC.

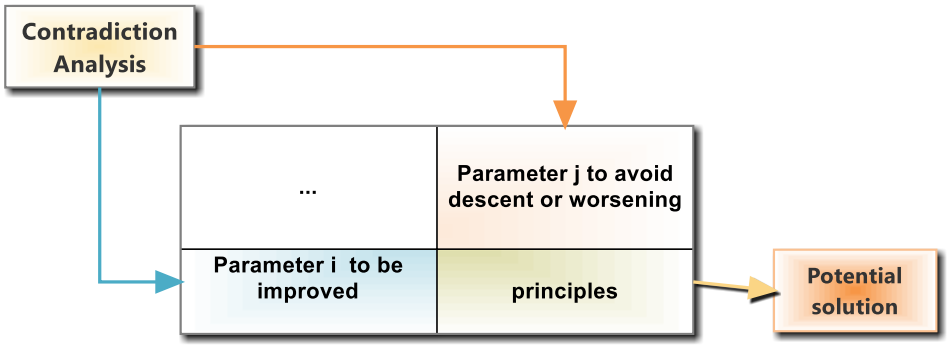


Figure G-1 Process of using TRIZ contradiction matrix

Possible Cons and Pros of Applying TRIZ on 3DPVS Design

Despite the potential benefits of TRIZ for product innovation and novel design, it inevitably entails some limitations. Identifying these limitations early can help provide designers gain better clarity of TRIZ in terms of pros and cons. This section studies two aspects: (i) the limitation of TRIZ in general engineering, and (ii) the possible challenges when using TRIZ for specific scaffold design.

I. Possible limitations of TRIZ in general.

Based on the literature reviews on TRIZ and TRIZ design case studies, TRIZ limitations are chiefly recognised by its difficulty of use in several aspects. This includes: (i) translating problems or innovation issues from specific to generic, (ii) identifying TRIZ-based solutions for

these generic problems, and (iii) translating the generated solutions back to the specific problems or issues. In terms of using TRIZ innovation principles or standard solutions, careful work and thorough preparation of 'translating' them into a context where product innovation can directly take advantage is always necessary (Blogg 2013; Ilevbare, Probert & Phaal 2013; Jia-Yen & Shih-Tian 2016). This usually takes much time and effort. Although TRIZ innovation principles and philosophy remain the same for every designer, expertise or understanding of them varies. Lack of efficiency and precision in this translating work can be an obstacle to those who attempt to use TRIZ for innovation designs. In addition, it tends to be challenging when applying TRIZ for innovation in bioengineering scenarios, since TRIZ has not been explored and used for this specific context.

From another perspective, it is rare to find previous studies on the use of TRIZ methods for novel scaffold innovation. Although TRIZ methods have been used and approved by researchers in general, knowledge of TRIZ for scaffold innovation is lacking. In particular, there is no formal research on analysing contradictions and selecting principles for scaffold innovation. Considering this, a TRIZ-based system for scaffold design is needed, aiming to translate TRIZ principles into scaffold-tailored scenarios specifically for 3DPVS. TRIZ methodology has been used in cooperation with other proven supportive design methods, such as QFD, root cause analysis, system function analysis, hybrid system design, FMED and trimming (Blogg 2013; Cameron 2010). There is no systematic study regarding how to link these proven supportive methods in scaffold innovation cases. Therefore, a thorough process combining TRIZ and these supportive methods for scaffold innovation remains a gap and requires urgent development.

II. Potential advantages of TRIZ for scaffold innovation.

Comparing TRIZ methodology with traditional methods of EDP—a series of steps that engineers follow to generate solutions to a definite design problem—offers several advantages. Traditional methods of generating product design concepts or solutions can be based on processes such as brainstorming and 'trial-and-error' methods (Fouchal, Hassan & Loveday 2014; Sekar & Jayakrishna 2014). Although such approaches are easy to implement, they tend to lack the innovation essence resulted from core of creativity (Dorst & Cross 2001). In addition, following the traditional problem-solving path, which can be considered 'linear' (Chakrabarti & Bligh 2001), we may find something negative and start making efforts to alter it, or we may succeed in obtaining a certain result, yet another unexpected or undesirable result might occur. Using cell scaffolds as an example, an additive added to scaffolds could directly help cell adhesion, yet this may cause unknown proliferation effects that designers could not predict. Correcting this usually means re-conducting the cell culture experiment, which makes the whole process repetitive, costly and time-consuming. Given this, a more efficient approach for generating innovative, useful and effective concepts for scaffold designs

has attracted much attention. As such, TRIZ has been proposed as an appropriate method and the four-route process is established.

For a scaffold engineering system, everything within may be interconnected and every function may be inevitably counterbalanced by some other function or a series of other functions, though they are not easily detectable in linear patterns. As such, the new path to be developed should not be linear, but dimensional, which means that the possible supplementary changes, or side effects, as far as possible contradictions inside GMBV is concerned, must be considered beforehand. Given that TRIZ allows a non-linear contradiction-solving path, it could logically help designers become better aware of the interconnection of the various properties within the cell culturing scaffold system. Further, given the complex, sophisticated design issues for 3DPVS as a bio-design and cross-domain, ARIZ within TRIZ may be a suitable tool, since it was specifically developed for complex design questions. Thus, introducing ARIZ to complex bio-product innovation could break new ground.

Transferring TRIZ Elements into 3DPVS Context

The innovation work at the current stage of 3DPVS needs to focus on its conceptual design. To ensure a high-quality innovation process, systematic methodology is of significance (De Carvalho & Back 2000). As such, TRIZ has been identified as a potential methodology for 3DPVS innovation and, in the following sections, we aim to tailor the traditional TRIZ method and its related tools to a systematic methodology that can be specified for the conceptual innovation and design of 3DPVS. Using this methodology system, designers could possibly generate required solutions and concepts for 3DPVS. To establish such methodology, this section is structured as follows. First, TRIZ and its basic mechanisms are introduced, with justification of why TRIZ is an optimal means to help accomplish the conceptual innovation of 3DPVS. Following this, the core part of the research chapter is to tailor and adapt original TRIZ-based methods into a structured methodology that tackles innovative tasks in the conceptual design of 3DPVS. Given that the nature of 3DPVS currently remains a future novel concept and the real-world product has not yet been approached using TRIZ, the major proportion of elements within TRIZ need to be transferred, at least to some extent, into a set of specific languages, codes or forms that can be directly applicable to novel scaffold design. Besides the novelty of 3DPVS, the very process of this transferring may also be considered a novel aspect.

G3: Studying Basic TRIZ Contradiction-solving Process for 3DPVS Concept Innovation

For TRIZ, systems evolve towards gaining ideality by overcoming contradictions. Conceptual solutions of 3DPVS will be the output of the TRIZ innovation process, and a vital part of this innovation process is achieved by identifying ‘contradictions’, and then solving them (Fey &

Rivin 2005). Contradiction solving is the unique mechanism of TRIZ, which may be considered an evolutionary aspect advantaging TRIZ over other design methods.

In this research, a large part of work in conceptual development of 3DPVS revolves around the centre of gravity of contradiction solving, which is achieved through generating identified contradiction and conflict pairs and solving them in a scientific manner. The philosophy behind this could be that the innovation and problem-solving process is the process of eliminating contradictions, which is achieved through intensification of conflicts, not by smoothing them or using buffers to 'avoid seeing' them. As such, the contradiction-solving process will potentially penetrate every stage of the conceptual concept generation and evaluation tasks for 3DPVS.

Introducing TRIZ Contradiction Solving to Scaffold Innovation

The TRIZ-derived methodology developed in this research context is for solving contradictions or conflicts in the design scenario of 3DPVS. It requires a systematic approach on how to apply this process in design. Traditional TRIZ contradiction solving has often been used as a three-route process, while, in this study, we expanded this process into four routes to better tailor it to a sophisticated design scenario. Given the nature of 3DPVS being miscellaneous, the innovation process requires cross-domain knowledge and expertise, which makes the 3DPVS innovation relatively complex and sophisticated, compared with single-domain innovation of a product. Given this, traditional contradiction-solving methods will be fully applied, and we also attempt to explore whether some novel aspects can be developed, which will help existing methods more effective for scaffold innovation. In brief, the innovation of 3DPVS first requires integration of three core set contradictions—the contradictions between 3D scaffold and 3DP, 3D scaffold and vibration mechanism, and vibration and 3DP—and second requires addressing of the set of pair-based contradictions in GMBV characterisation of 3DPVS—the contradiction between relations of G-B, G-V, B-V, B-M, G-M and M-V.

Figure G-2 shows the scope of this contradiction-resolving approach of six set contradictions between four design aspects—the, geometric, mechanical, biological and vibratory properties. It is worth noting that, besides these six contradiction relations, each G-, M-, B-, V-characteristic of the 3DPVS design could produce conflicts to contradict with themselves, which would create four sets of the most typical PhCs—that is, G-G, B-B, M-M and V-V contradictions.

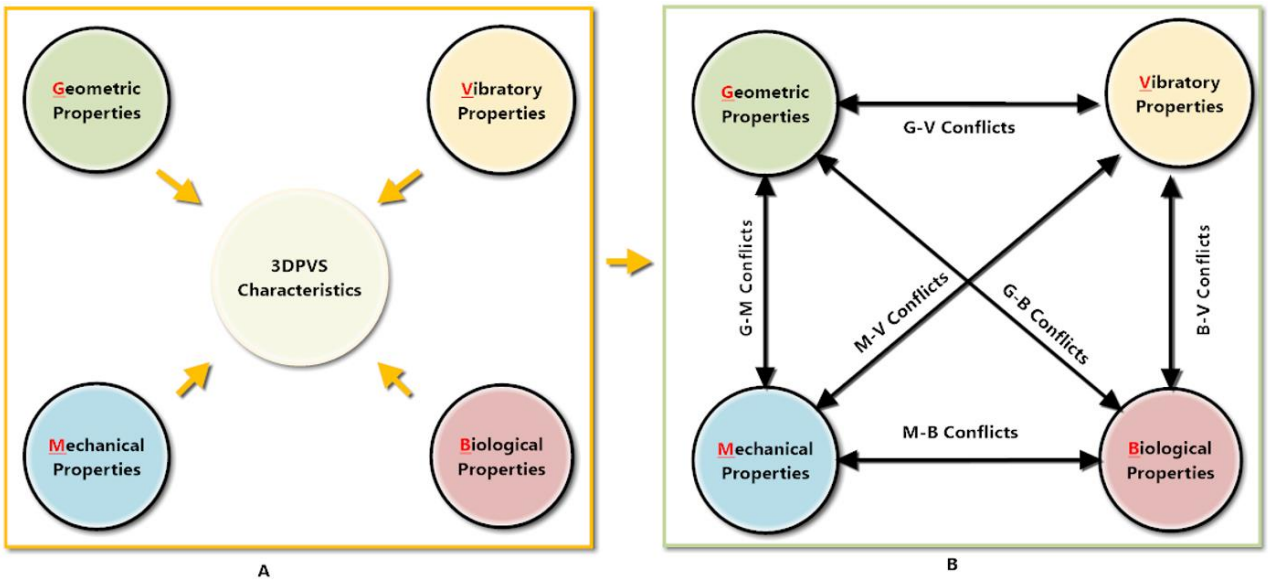


Figure G-2 Six relation sets of contradictions existing for 3DPVS design

Establishing Four-route Contradiction-solving Process for 3DPVS

The four-route process proposed, as shown in Figure G-3, can be regarded the expanded version of the traditional TRIZ-based contradiction-solving process that aims to solve SCs and PhCs in both simple and sophisticated design scenarios. Learning from the previous literature, one successful approach to establish TRIZ in a route-oriented methodology was conducted by (Yang 2013) for conceptual innovation of a service product. Although the design context differs to the bio-design 3DPVS, the basic contradiction-solving philosophy is considered the same, while the 3DPVS design tends to be more cross-domain and sophisticated. As such, we attempt to further explore the potential of traditional TRIZ-based contradiction solving and restructure it into a new four-route process model tailored for a highly complex design scenario that includes the conceptual design of 3DPVS. In brief. this four-route process, which contains the 3DPVS innovation roadmap as the fourth route, is illustrated in Figure G-3.

Within this four-route methodology, the first three routes are concerned with relatively clear-cut design scenarios, where contradictions can be easily identified, while the fourth route—the newly established tool assisting the conceptual design of 3DPVS—is termed the 3DPVS innovation roadmap and aims for the whole-picture design of 3DPVS in specific cell culture case scenarios. In terms of the further corresponding role of the 3DPVS innovation roadmap in the four-route methodology, several important working places—chiefly including A4, B3, C3 and C4—must receive special attention. Briefly speaking, the input of this four-route methodological process will be the selected problems from the design initiation stage, and these problems can be considered the output of these places. Regarding the final outputs of this four-route process, the alternative solutions for contradiction solving could be the BIR, MIR or SIR, based on where this process is to be applied. Relevant information could refer to ARIZ-based section.

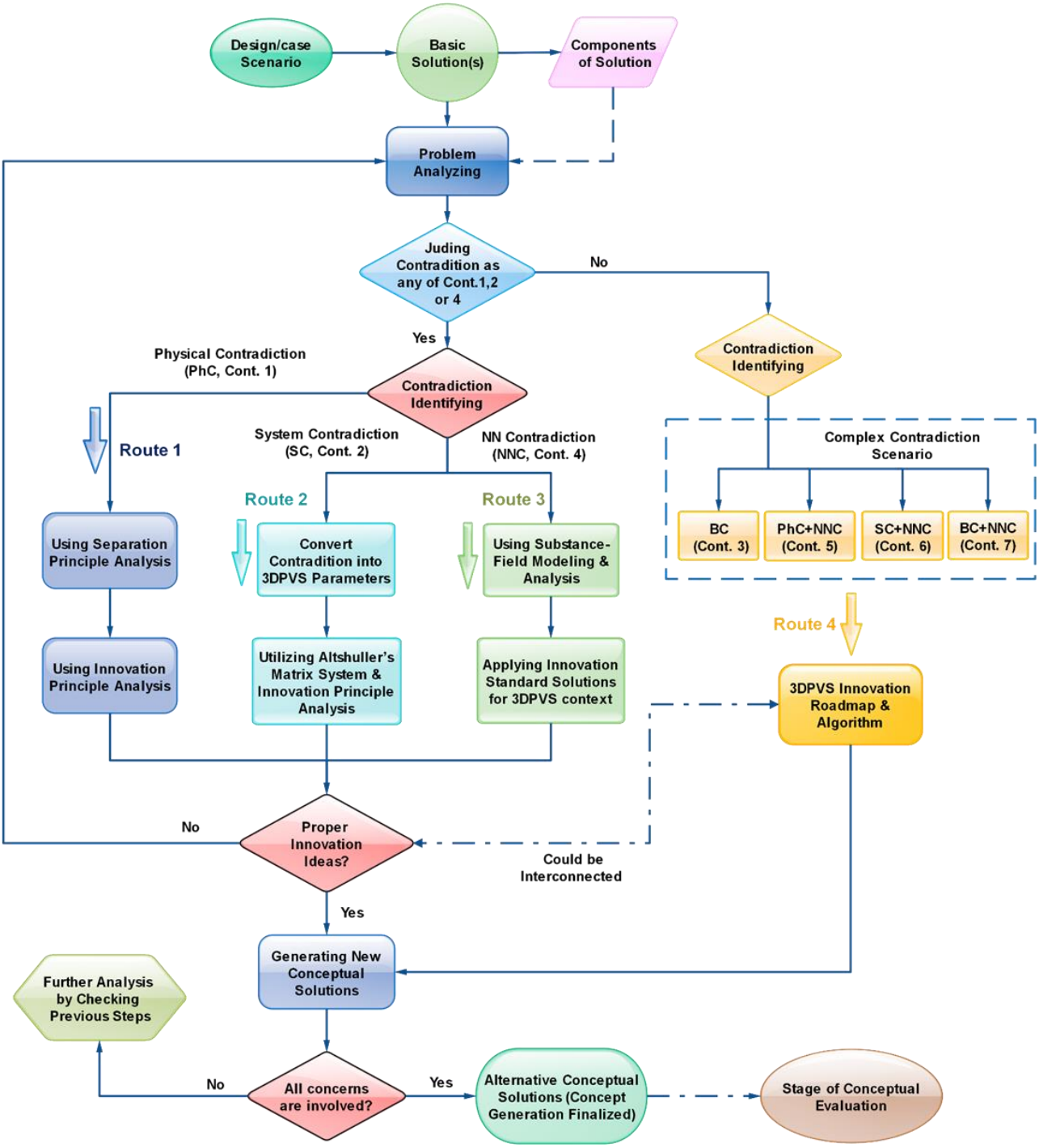


Figure G-3 Four-route TRIZ-based methodology established for 3DPVS concept generation

Steps of Using Established Four-route Methodology

Three chief steps can be taken when using this four-route methodology for scaffold innovation, as follows.

Step 1: Analysing contradiction from selected problems.

As the first task, designers must analyse the contradiction level of the problems selected. For a simple scenario, problems can be directly categorised into two groups: technical contradictions and PhCs. Using 3DPVS's GMBV for example, a technical contradiction occurs when improving one parameter of G-characterisation deteriorates the parameter of either M-,

B- or V-characterisations. A PhC is when altering the value of this G-parameter for a positive effect towards an expected attribute shows a negative effect on another G-based parameter simultaneously.

Step 2: Searching routes for contradictions.

Searching for solutions is the core step of the entire process for developing innovative ideas, and these ideas can be identified through four routes, as follows.

Route 1: TRIZ traditionally identified 40 principles that can be used for eliminating technical contradictions and 39 parameters of technical systems that can be used to develop and describe the technical contradiction. Route 1 resolves the contradiction via application of the 40 inventive principles, as well as gaining specific recommendations to overcome the contradiction. If the conflict belongs to a technical contradiction (contradiction type 2), we transfer the two conflicted attributes into a pair of engineering TRIZ parameters. The invention principles that may solve the contradiction can be identified using the contradiction matrix.

Route 2: A PhC is a conflict between two mutually exclusive physical requirements to the same parameter of an element of the system. Route 2 overcomes a PhC (contradiction type 1) using four 'physical' principles and a database of physical phenomenon and effects. In most cases, designers need to transform the technical contradiction into a PhC and solve this issue at a physical level. Thus, the transformation process is a task on which Route 2 needs to focus.

Route 3: If no clear contradictions can be extracted from the problem analysis, designers can consider using other tools, such as SFA, to generate new ideas. In some cases, contradiction is difficult to identify at the beginning, yet becomes clear after using these tools.

Route 4: Regarding a complex contradiction scenario that may arise with Contradictions 3, 5, 6 or 7, the first three routes of the methodology could be insufficient for designers to obtain a satisfactory innovation answer, as these three routes classify problems as technical or physical, given traditionally single-dimensional dualistic thinking, yet, in reality, problems can be complex and multidimensional, meaning they can consist of different aspects of contradictions simultaneously. It seems challenging if designers force themselves to clarify the contradiction scenario in the first place. As such, for a multiple-dimensional contradiction scenario, a fourth route—the 3DPVS innovation roadmap—will be introduced with its design algorithm.

Step 3: Generating alternative concepts as output of contradiction-solving process.

Following one of the four routes and its working inner process, new ideas or solutions may be generated. This is usually obtained through using ACM, IPA, SFMA and so forth. Despite the unique advantage of these tools in innovation design, there is no guarantee that all solutions are appropriate for real-world 3DPVS. A suitable evaluation process will be necessary,

provided that no innovation ideas can be generated. In terms of the contradictions identified in Step 1, at this stage, those contradictions might need to be re-established to find better alternative solutions.

Introducing Seven-layer Contradictions for Entire Scenario Design

The TRIZ philosophy believes that design problems can be decoded using the language of 'contradiction'. Thus, clarifying contradictions before design begins is of tremendous value. Two types of contradiction are recommended by TRIZ for problem solving—PhC and SC (technical)—where TRIZ provides great resourcefulness in solving them. However, it tends to be difficult to abstract and identify contradictions from real design scenarios. That is, sophisticated design cases make the contradiction-abstracting process challenging. In other words, TRIZ allows designers to conduct innovation after identifying contradictions, while the art of abstracting contradictions, especially in sophisticated scenarios, is challenging. Chief concerns subconsciously indicated by TRIZ is a dualistic contradiction categorisation, which means the contradiction has two layers—either physical or system. As a matter of fact, this is not accurate. During the practice and design research, we found that a systematic contradiction-categorising process could be useful to help understand the exact contradiction levels of a definite case. As such, a seven-fold logic to define the level of contradiction is introduced and integrated with the TRIZ process. This seven-fold logic was first developed by an ancient Indian philosopher and has been studied in contemporary set mathematics (Jech 2003; Tourlakis et al. 2003), and inspiration was also acquired from (Karen & Jean Paul Van 2007). A brief illustration of its basic structure is shown in Table G-2.

Table G-2 Seven-category contradiction for entire design scenario

Name	Cont.1	Cont.2	Cont.3	Cont.4	Cont.5	Cont.6	Cont.7
Ctr. type	PhC only;	SC only;	both PhC and SC	neither PhC nor SC	PhC, and neither PhC. nor SC	SC, and neither PhC nor SC	both PhC and SC, and neither PhC nor SC
Design priority	High	High	Low	Moderate	Low	Low	Low
Methodology route	2	1	4	3	2 and 3	1 and 3	4

Note: Ctr. = contradiction; PhC = physical contradiction; SC = system contradiction (or TC for 'technical contradiction'); route represents the route number in the four-route methodology. Priority is determined based on the corresponding role of definite contradiction in the specified design scenario. Details of this will be discussed in a later section.

In terms of the philosophy, four areas can be delineated for the entire problem scenario, which is represented by the white canal background. In Figure G-4, area (a) indicates that the problem is only concerned with PhC, and area (c) is concerned with SC. The crossing area, represented by (b), indicates a problem that is entangled simultaneously with both contradictions, and area (d), as the remaining area in the picture of the design problem,

indicates that the selected problem does not belong to either PhC or SC. Here symbol '+' is used to represent the 'both' relation in set theory, as shown on the right side of Figure G-4.

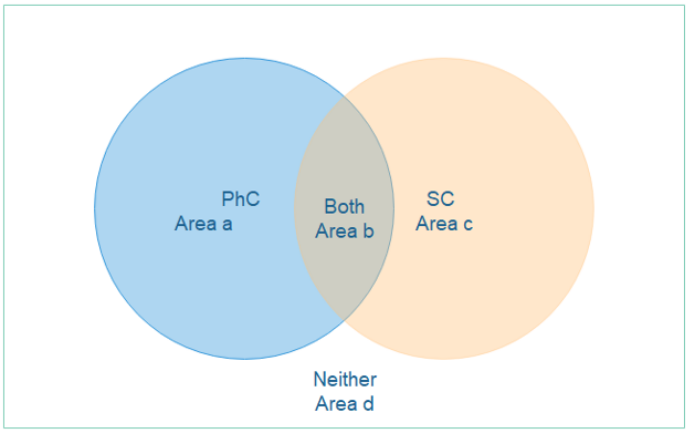


Figure G-4 Diagram demonstrating interconnection of seven contradiction types

The seven-fold logic helps display the interrelationship of various relations that designers may face during 3DPVS design. Contradictions in the 3DPVS scenario may arise from three system levels—the three levels of 'requirements' during the design—that is, the requirements of the end-user, attributes of the design, and components of the sub-system of 3DPVS. A complicated scenario such as this benefits from the newly proposed contradiction-categorising method. Here, we use 3DPVS as an example to briefly illustrate the seven-layer logics—see Table G-3.

Table G-3 Seven-layer logics tailored for four-route TRIZ-based methodology

Ctr. no.	Illustration
Ctr. 1	A problem that is only structured with PhC, such as a geometric contradiction regarding scaffold height and weight. Elements belong to sub-system level, or components, parameters of 3DPVS.
Ctr. 2	A problem when material changes or the scaffold's geometry conflicts with mechanics. Geometry and mechanics are SC. They belong to the attributes level.
Ctr. 3	A problem that has not been divided into a mini-problem yet, so two types of contradictions exist simultaneously. The first stage of analysing a problem usually encounters such a case.
Ctr. 4	For example, when analysing geometry of a scaffold's height and conflicts arise or something needs improving. The attribute of 'geometry' and component of 'height' cause the problem. In brief, when contradictions are not in the same hierarchy or category, they cease to construct either PhC or SC.
Ctr. 5	PhC is entangled with contradiction type 4. For instance, the attribute of 'geometry' and component of 'height' cause problems, while 'height' simultaneously conflicts with the scaffold's length.
Ctr. 6	SC is entangled with contradiction type 4. For instance, the attribute of 'dynamicity' and component of 'frequency' cause problems, while the attribute of 'dynamicity' simultaneously conflicts with another attribute of 'geometry'.
Ctr. 7	Contradiction 7 could indicate the ultimate form of contradiction—that is, all contradictions exist. This is usually the initial state of any sophisticated design problem. It usually needs to be transformed into Ctr. 5 or Ctr. 6 first, then into 1 and 2 ultimately.

To conclude, a systematic analysis based on seven-fold contradiction could increase the design efficiency, especially at the preparing stage when contradictions need to be identified and the methodology route is selected. It could also help broaden the general perception of designers anticipating complicated design scenario where multiple elements—such as both

attributes and components—need to be identified simultaneously. Innovation of 3DPVS is a typical design example, since multiple contradictions at the same system level could affect each other, while contradictions at other system levels may simultaneously influence them as well.

G4: Studying ACM and Applying to 3DPVS Conceptual Design

As an essential part of TRIZ, ACM helps solve SC, where improving one parameter of a system conflicts with the requirements of other parameters. To define a SC for a system and find relevant parameters of the SC, four steps are required. To select effective inventive principles for this contradiction, another four steps are needed, comprising an eight-step process for the whole contradiction defining and solving. We can embed the 3DPVS design into this eight-step process as follows.

Table G-4 Eight-step process for 3DPVS contradiction defining and solving

Step no.	Tasks
1.	Generate the parameter list for the 3DPVS system, the detailed process of which could be generated in design initiation stage.
2.	Select a parameter at 3DPVS system level and change its value;
3.	Analyze the interconnection between the selected parameter and other remaining parameters; select out conflicting pairs, each of which will represent a System contradiction.
4.	Choose the most appropriate parameters in the 39 parameters list which correspond to the 3DPVS system parameters as selected above.
5.	Utilizing ACM, from the vertical list identify 3DPVS parameter whose value is to be improved.
6.	Identify the worsening or descending parameter inside the horizontal list.
7.	Identify the inventive principles from the matrix intersection.
8.	Study these principles in detail and analyze the applicability of each on 3DPVS design.

For Step 3, the question arises as to which pair of the contradicting parameters should be analysed as a priority. The possible ranking order will depend on the requirements and conditions of the given cell culture case scenario, and the different aims at different stages of 3DPVS design.

Corresponding Characteristics of 3DPVS with List of TRIZ Parameters

To gain a better understanding of 3DPVS parameters, it is important to know which parameters TRIZ summarises as most vital. The traditional TRIZ 39 parameters are for engineering and technology systems, and for the 3DPVS design context, we find that the majority could be appropriate parameters for the design of 3DPVS.

At the stage of design initiation, relevant parameters for 3DPVS are collected and analysed regarding the possible contradicting interconnection between each of the parameters. The selected 3DPVS parameters that compose a SC must to transformed from commonly used attributes of 3DPVS into the general parameters recognised by TRIZ. Further, there might be gaps between the commonly used parameters for scaffold engineering and the TRIZ

parameters generated in the universally possible realm of engineering and science. Parameters of the latter tend to be more generic and conclusive and could be directly used together with the 40 TRIZ principles, which exist as generalised innovative abstracts or concepts for triggering innovation. In brief, GMBV characterisation of 3DPVS must first be transferred into the TRIZ language. Table G-5 converts the GMBV types into potentially corresponding TRIZ parameters.

Table G-5 Translating 3DPVS GMBV attributes into general parameters of TRIZ

3DPVS GMBV Type		Explanation	Corresponding parameters of TRIZ
G-	1.	Geometric Parameters (Pore characterization, porous connection)	1, 2, 3, 4, 5, 6, 7, 8, 12, 18, 25
M-	2.	Material Composition (Chemical Parameters)	2,5, 7, 9, 36
M-	3.	Mechanical parameters	3, 9, 14, 17, 19
B-	4.	Biological parameters	5, 9, 17, 20, 28, 30,
V-	5.	Dynamic/vibratory functionality parameters	2, 4, 6, 12, 26
V-	6.	Vibration mechanism parameters	17, 19, 25
Others	7.	3DP Fabrication parameters	27, 32, 34, 35
Others	8.	CAD Design and computer simulation	28, 38

Using TRIZ Parameters in 3DPVS Context

In this section, the most applicable use of the 39 TRIZ parameters in 3DPVS context has been discussed; however, extension of these parameters for novel future bio-design could also occur, as an interesting direction for future TRIZ innovators.

Optimising Innovation Principle Selection from ACM for 3DPVS

In terms of ACM for the 3DPVS context, we propose a new multi-level principle selecting mode, in comparison with the traditional ACM, which uses a single-level one-to-one principle selecting mode. That is, traditional ACM selects one improving parameter and one decreasing other that causes conflict, then manually searches the 40 innovation principles and receives recommended solutions, which tend to be a combination of three to five principles. For such a one-to-one selecting method, several points must be considered by designers. First, there is no ranking or evaluating tool to judge the weight of the selected three to five principles; designers must compare them with subjective experience, which can make the process time-consuming and inaccurate. Second, for the pair of parameters creating conflicts, each of which may be a combined parameter resulting from several other parameters, simply choosing one parameter for the x-axis in ACM and another for the y-axis would be inadequate. If the parameter ‘X’ contains three elements (X1, X2 and X3 parameters as a unit) and the decreasing Y parameter includes another three elements (Y1, Y2 and Y3), then traditional ACM could find it challenging to solve this. Starting from this new Metrix-searching process

comes into the IPA, which would contain a similar process of selecting generic parameters in the matrix through fitting with the parameters composing SC. Designers obtain the inventive principles and associated percentage ranking, which is a special trait of the new ACM, to help solve contradictions effectively. Each pair of parameters that create conflict can be divided into one, two or three sub-parameters, based on the parameter evaluation criteria—that is, the parameter weight calculated by specific DRs as four levels, represented by ‘S’, ‘A’, ‘B’ and ‘C’. For the IPA in the 3DPVS context, we would use ‘S’, ‘A’ and ‘B’, where S is the chief feature parameter in the given scenario, A is the secondary and B is the minor. ‘C’ is considered a trivial determinant that does not affect the decision making in the innovation process. If the conflicting parameter is the exact one inside the 39 parameters list, the IPA matrix can be used similarly to the traditional matrix, with one difference—the weight of principle by percentage among other principles is calculated as well. For this instance, as well as transforming traditional ACM into the new ACM IPA, an example is shown in Figure G-5, which illustrates the basic development from a traditional single-dimensional matrix into a novel multidimensional one.

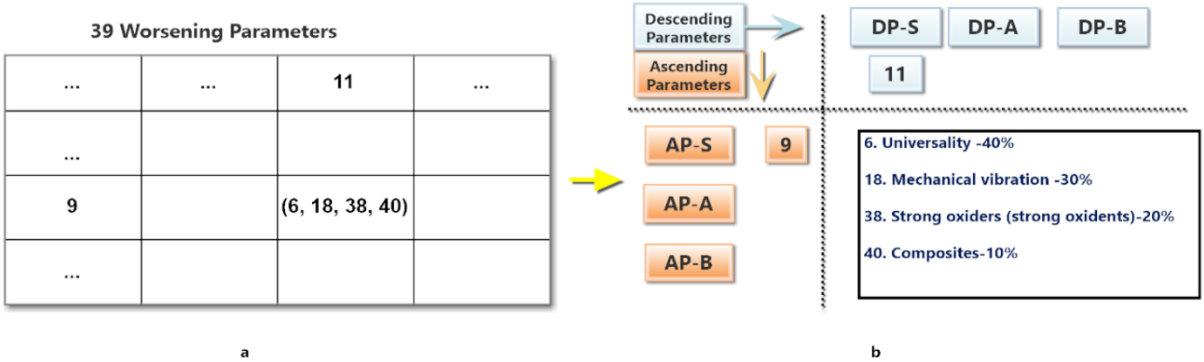


Figure G-5 Change from (a) traditional 1–1 matrix solution into (b) developed 3–3 matrix IPA, and IPA results for traditional 1–1 conflict

Within IPA, two or three sub-parameters constituting the states or functions of the original parameters are used to fill the X or Y ACM column before the principle searching begins. The total searching time will be a number between nine and one, and a proportion ratio based on the appearance frequency of selected principles in this one-to-nine scenario will be calculated. The company time to innovate used such a calculation philosophy in their TRIZ application and demonstrated higher design efficiency. The resulting top principles will be considered prioritised solutions for the given scenario. To better understand this 3 × 3 matrix, an example is given here of a specific 3DPVS scenario. In this scenario, cells move rapidly in a culturing environment as the chief feature parameter (S). The definite duration (A) must be ensured, as well as maintaining the cell temperature (B). In one rapidly moving state, cells create negative pressure on the scaffold, making stress or pressure the chief feature parameter (S) of the descending parameters (DP). Also, more energy could be used by such higher movement of cells, so other cell processes may be affected, making the energy lost the secondary feature (A). The shapes of cells may also be negatively affected, resulting in an undesired

morphological effect. The shape issue is not vital for this scenario, yet is also a negatively affected factor, so it is the support feature parameter (B). Designers must maintain the ascending parameters (AP)—speed of cells, speedy period and cell temperature—while not affecting the DP pressure, energy used/lost and shape. In this instance, the IPA result from ACM is shown in Figure G-6.

From this IPA, we can see that Principles 19 and 35 represent the highest weight, and Principles 15, 14 and 6 follow. These principles are considered the most promising direction when solving the problem, while the principles weighing less can be used as a reference to help innovative thinking. In this case, a possible innovative suggestion is to use dynamic materials so the scaffold's physical and chemical parameters change at a periodic level. Based on this, we could explore further detail.

To conclude, IPA is proposed to play a vital role in the four-route TRIZ-based methodology. In the next section, we present detailed knowledge on TRIZ innovation principles, as core contents for IPA and TRIZ, as well as discussing the most likely direction when applying each principle for the future 3DPVS design.

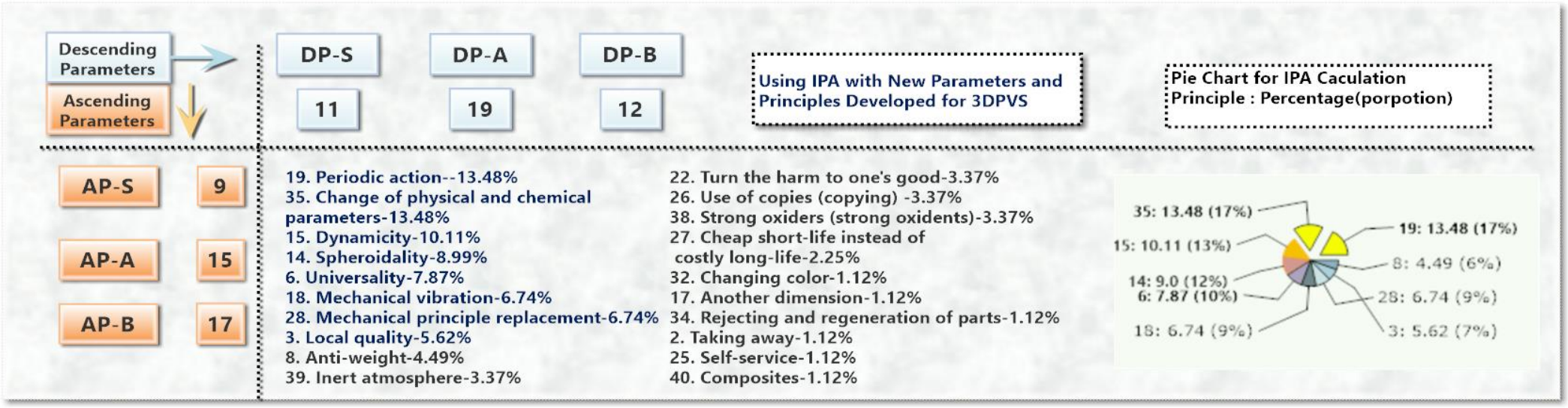


Figure G-6 IPA matrix illustration for solving complicated 3 × 3 parametric cell culture issue

G5: Studying TRIZ Innovation Principles in 3DPVS Context

After introducing IPA and its philosophy, in this section, we study the details of IPA and the most likely manifestation of each principle in the 3DPVS design context. We first discuss the significance of translating the TRIZ innovation principles, and then discuss the 40 innovative principles and principle-related expansions, as well as 3DPVS design strategies using corresponding principles.

Need to Translate Innovative Principles into 3DPVS Context

One core element of TRIZ is to recommend innovative principles that potentially stimulate the designer's creative thinking in solving design conflicts or contradictions. However, TRIZ-based inventive principles have not been developed for bioengineering products or used for scaffold innovation. This means that existing principles may not be applicable to scaffold design, including conceptual development of 3DPVS. Therefore, the key of identifying a TRIZ-based innovative solution for 3DPVS lies in translating a set of scaffold-based conflicts into the generic conflicts established in TRIZ. Simultaneously, the potential solutions, inspired from innovative principles, need to be translated into solutions tailored to the 3DPVS scenario. As such, a wide degree of analysis, interpretation and new understanding on TRIZ innovative principles is necessary when using TRIZ in 3DPVS design. Thus, the process of translating solutions from generic TRIZ-based traditional ones into specific, tailored solutions applicable to scaffold design, specifically 3DPVS, is of great significance, and is discussed in the following section.

IPA and 3DPVS Potential Strategy

TRIZ-based techniques traditionally use 40 inventive principles to eliminate SC. The way to use these innovative principles for 3DPVS tends to weigh significantly regards its proportion inside entire design process. However, for the novel cross-domain aspects in 3DPVS, old explanations may be limited, and new interpretations tailored to novel bio-design require urgent exploration. In this research chapter, aside from understanding the 40 principles of traditional engineering perspectives (Altshuller, G. S. 2005), perception of 3DPVS based on bio-design, especially for 3DPVS, has been explored—see **Appendix D**. As such, examples from general engineering world will be illustrated to help clarify the definite principle. These examples have been selected as 'inspirable' and indicated to have close interconnection to the context of 3DPVS.

While SC for 3DPVS is a conflict between two parameters at system level—different parameters at the 3DPVS super-system, system or sub-system levels—PhC is the conflict between two desired values of one parameter at the same 3DPVS system level. These PhCs could be eliminated by four separation principles, as shown in Table G-6. In terms of the

relationship between separation principles and the 40 TRIZ innovation principles, we could categorise the latter into four classes. This categorisation fully suits the 3DPVS product.

Table G-6 Relationship between separation principles and 40 innovation principles

Separation principles	Indication	Corresponding innovation principles
Separation in Space	Object has parameter value A and B at Time '1' and '2' respectively.	1,2, 3, 4, ,7, 13, 17, 24, 26, 30
Separation in Time	Object has parameter value A and B at Space '1' and '2' respectively.	9,10, 11, 15, 16, 18, 19, 20, 21, 29, 34, 37,
Separation upon conditions	Object has parameter value A and B on condition '1' and '2' respectively.	12, 28, 31, 32, 35, 36, 38, 39, 40
Separation between the Parts and the whole (system and sub- or super-system）	Object has parameter value A at system level, while value B at super-system level (or A at system while B sub-system level)	1, 5, 6, 7, 8, 13, 14, 22, 23, 25, 27, 33, 35

As is usually the case for design, the first three classes of principles tend to be applied simultaneously to solve PhC, so combining them can help achieve rapid analysis. Figure G-7 maps the resolution strategies of PhC in space, time and condition corresponding to the 40 inventive principles. For the 3DPVS context, 11 principles will be considered less applicable than the remaining 29 principles classed into either condition, time or space. Analysing the crossing area, we might predict that Principles 2, 3, 4, 5, 12, 22, 24 and 34 tend to be highly applicable to solve 3DPVS PhCs.

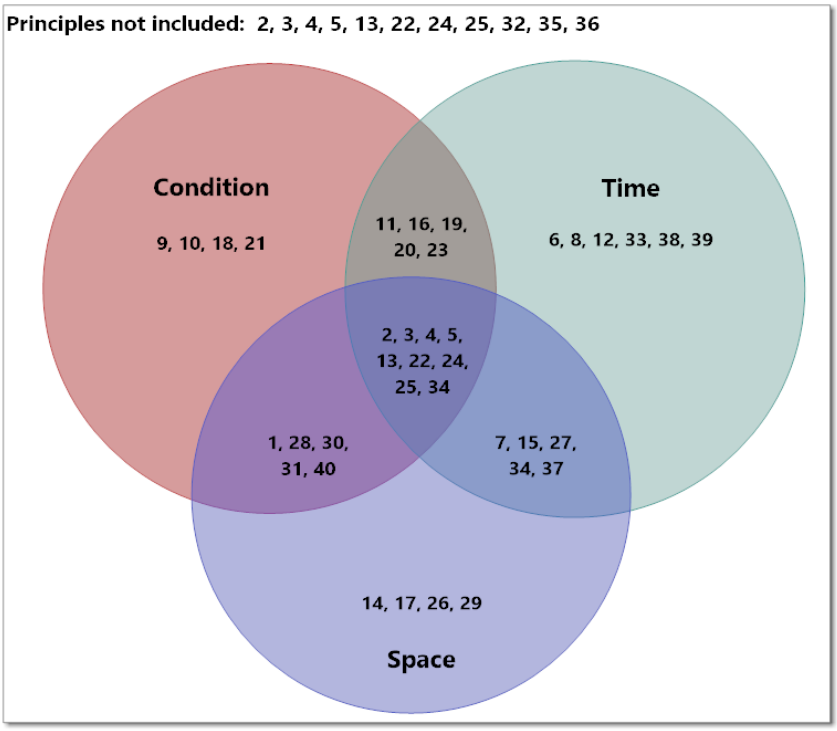


Figure G-7 Analysing PhC solutions to 40 innovation principles of 3DPVS

Alongside direct analysis of PhCs, the transition from SC into PhC can help understand SC, as well as transforming it to an easier-level problem for solving. For the sake of efficiency in 3DPVS design, SC to PhC can be coded as follows:

{A higher scaffold contains more cells, WHEREAS has poor stability during dynamic cell culture.

Two conflicting parameters: 'height' of scaffold <-> 'stability' of scaffold

PhC: One parameter, 'height' of scaffold, should have different values of low and high.}

Software contradictions, such as CAD aspects, might also exist. Software principles are abstract rules that could help solve contradictions in CAD aspects. As proposed by the three-stage conceptual design, concept evaluation could use CAD software to build or simulate 3DPVS models. Using software inevitably encounters conflicts as software contradictions. Predicting this beforehand and providing possible solutions could improve design effectiveness. Thus, several issues will be discussed here to address this. In brief, the computational design of 3DPVS indicates that its CAD process is similar to for traditional 3D product designing. Among the 24 TRIZ parameters in software contradictions, Principles 1, 4, 9 and 10 are selected, since they have a relatively intimate connection to the context of 3DPVS. Four principles and their corresponding contradiction solving are shown in Table G-7.

Table G-7 Software principles and corresponding contradiction solving in 3DPVS scenario

Software principles	Corresponding conflict solving
Adaptability	Conflicts in transforming traditional CAD design to 3DPVS context
Date access	Conflicts in accessing design data from existing CAD resources
Flexibility	Conflicts in adapting CAD parameters of traditional scaffold into 3DPVS parameters;
User capacity	Conflicts of CAD file or codes in terms of its simplicity and understandability to end cell culture users

Note that software contradiction will potentially play a role when the conceptual design stage is completed and computer modelling using CAD software begins. For other stages, it will remain as a study reference.

G6: Studying SFMA in 3DPVS Scenario

SFMA is one vital part of TRIZ engineering. SFMA is potentially of high value to the four-route methodology established previously. In this section, several aspects of SFMA and its application to 3DPVS will be studied.

Studying SFMA and its Philosophy

Invention and separation principles of the TRIZ methodology, as discussed, could be applied to 3DPVS design. Cooperating with this, another tool of TRIZ for innovation and problem solving is SFMA, which aims to provide standard solutions not related to specific areas of

technology, but that enable the solution to transfer from one scientific branch to another. This system—the system of standard solutions—is especially beneficial for solving complicated problems using a combination of several standard solutions. Its philosophy is built on the foundation that, in different domains of science and industry, there exist a definite a number of graphic models that describe the oceanic amount of problems; thus, a definite number of transformed graphic models can illustrate possible solutions. Each standard solution proposes one pair of such graphic models for solving similar, standard problems when SCs or PhCs in Routes 1 and 2 cannot be effectively anchored. In brief, SFA is the unique language of this system. For tailoring the novel 3DPVS design, SFR could be potentially used in the design algorithm with several steps, which will trigger innovation and help generate fine ideas.

Substance-field Model and Three-class Analysis

I. Studying substance-field model (SFM).

SFA contains three main elements—S1, S2 and F—as represented in Table G-8, with possible application examples for 3DPVS design.

Table G-8 SFA elements, description and 3DPVS application examples

SFA elements	Description	3DPVS application example
Substance S1	a 'tool' or 'instrument' utilized for producing a product, manipulate a function, control, measure or change values of product's parameters;	materials and solid items like water, cell, cell culture medium, scaffold, vibrator, 3D printer etc.
Substance S2	the 'product' or 'object' which is to be produced, manipulated, measured or changed;	materials and solid items like water, cell, cell culture medium, scaffold, vibrator, 3D printer etc.; S1 in one design scenario could be S2 in another;
Field F	the energy or energy field or medium utilized for the interaction between S1 and S2;	energy like magnetic, mechanical, electrical, chemical, thermal, acoustic field etc.

The analysis of two SFMs—one of the existing problem and another of its possible solution—is called SFA. Study of the evolution of substance-field structures is also part of SFA. This model illustrates the situations, problems, challenges, limitations and possible solutions in a graphic, abstract form with three basic components, as shown in Figure G-8.

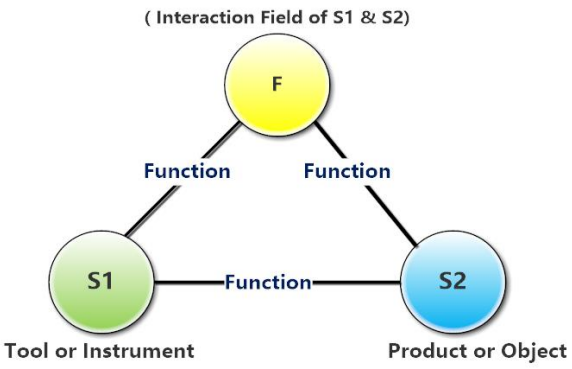


Figure G-8 Illustration of SFM containing three elements and three functions

II. Three-class analysis for function between S1 and S2.

To understand the basic components of SFA, it is important to have a clear picture of the interconnected relationship between these three components—namely, the relationship between S1 and S2, S1 and F, and S2 and F. Three classes can be summarised corresponding to the relations, with three definite symbols representing different types of functions, shown in Figure G-9.

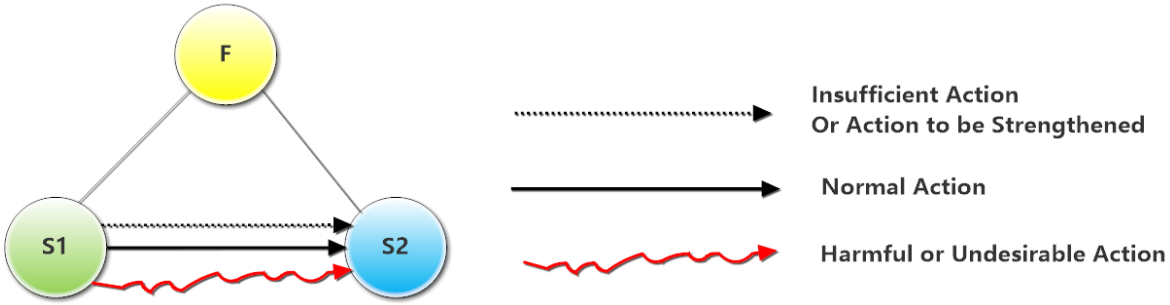


Figure G-9 SFM and representing symbols for function between substances

Table G-9 Three levels of SFA with possible application to 3DPVS

Class no.	System indication	Description	3DPVS application example and solution
Class 1	system with Incomplete or Inadequate SFM	Merely S1 exist and the system lacks F and S2, therefore S1 could not generate the Desired Functions. To solve this issue, F and S2 can be introduced to create a complete model;	Take S1 as Scaffold for instance. S1 is to have vibratory Functions, so Field or Vibratory Filed F provided by S2 needs to be introduced to provide the Vibratory Functions to S1. F can be a magnetic field and S2 the magnetically vibratory materials.
Class 2	System to Eliminate Harmful or Hindering Actions	The sub-field model is complete but exists harmful, negative actions. Designers need to integrate new substance or field to eliminate, counterbalance that negativity. That is, S1 here has normal and negative actions to S2 through original field F1. Solution might involves introducing new elements into system, i.e. S3 and F2 having positive or counterbalancing effect on S2 is introduced so original harms will cease to some extent.	For undesirable vibration frequency: S1 is vibrator, F1 the mechanical force to transmit the vibration and S2, the scaffold to be vibrated. Existing vibration is rough and imprecise; the function is not desirable since we want precise and subtle vibrations. Then a subtle vibration mechanism, a vibrator with higher controllability in frequency can be introduced as S3, and F2 will be a more subtle and controllable frequency effecting S2 scaffold.
Class 3	System to strengthen or enforce insufficient Action	Model is complete with S1, S2 and F, but effect from S1 onto S2 through F is deficient or inadequate. Solution for this comes as introducing new Substance S3 and Field F2, so the combined effect from S3 and F2 act as the Neutralizing Force which strengthens the original Deficient Action.	Scaffolds made of Smart Materials may lack strength on mechanical properties, i.e. the structures remain unstable and easy to break: Smart materials as S1, mechanical influence as F and Scaffold's structural stability as S2. Realizing other materials S3 helps strengthen structural solidity not hindering original dynamic functions of S1 onto Scaffold; mixing traditional Materials S3 with S1, effect of F2 can strength F1 then help achieve the desired structural stability.

The three classes within SFA—that is, the class concerning a system with incomplete or inadequate element or function, class concerning a system to eliminate harmful or hindering

actions, and class where the system is to strengthen insufficient action—are summarised asTable G-9, which also illustrates suitable application to 3DPVS.

SFMA into AMSC

From the three-class SFA, several models of typical conflicts for SC could be used in design methodology. These models are called AMSC. Due to study, 11 AMSC could have practical use for the 3DPVS context. In this section, we illustrate these AMSCs with description, analysis and connection to the 3DPVS scenario, Table G-10.

Table G-10 Description of AMSC and examples for 3DPVS scenario

No.	AMSC	Description and analysis	Direction on 3DPVS
1	Counterwork	Positive Action or function from S1 to S2 is accompanied by the reverse negative or harmful action or function.	Scaffold holds cells and cells gradually damage scaffold.
2	Mated function A	Positive Function from S1 to S2 is combined with a negative function from S1 to S2, that is, same function can be both positive and harmful at different stages or aspects.	Vibration can accelerate cell growth while damage cells.
3	Mated function B	S1 generate positive function to part 1 of S2, while damage part 2 of S2.	For vibratory cell culture, a definite vibration can help cell proliferation but hinder gene expression.
4	Mated function C	For a S1, S2-A, S2-B system, function from S1 helps S2-A, while hinders S2-B.	Heat from 3DP can melt one material of the material mixture, but damage another.
5	Self-compensating function	While S1 generate useful function to S2, it generates negative aspects on itself.	Some magnetic materials act to magnetic field vibration while their magnetic power is running out. It needs to be charged during the period or after use.
6	Incomplete or Absent function	There are three types. First, S1 generates several useful functions but one or more is absent; second, S1 generates one useful function and strength of which is weak, and third means only product S2 exist while Tool S1 is missing.	Vibration could help proliferation but does little on differentiation; Vibration does not generate sufficient frequency; traditional 3D static scaffold which lacks vibratory stimulation;
7	Insufficient Function	Like the fifth model, useful function from tool S1 to product S2 is not enough.	Cells require a 500HZ frequency of vibration, but mechanical stimulator can generate 300 at maximum.
8	Excessive or Overloaded Function	There are excessive actions generated from S1 to S2 than required.	Mechanical vibration tends to be rough compared with subtle vibration means;
9	Uncontrollable or low-controllability Function	S1 generates useful action to S2, but it is not controllable.	Vibration generated is continuous, while cells need periodic vibration.
10	Incompatible Function	Two tools (S1-A and S1-B) generate useful functions for product (S2), while these two functions contradict or hinder each other.	Definite scaffold's material composition helps cell growth and definite pore structure of scaffold helps cell growth, while the material cannot be fabricated into that pore structure.
11	Mutual-damaging Function	S1 generates harmful action to S2, and S2 have negative effects on S1.	Scaffold hinders the movement of fluid medium for cell culture, while the fluid can corrupt some material of scaffold.

Using these AMSCs, identifying types of problems and possible solutions tends to be easier and more effective. By analysing AMSC with potential ISS, as discussed later, designers can practically find innovation concepts for most design issues.

Analysing Three Forces with SFMA for 3DPVS Design

For the novel design of a bio-product, such as 3PDVS, three forces—positive, negative and neutralising—are used together with traditional SFMA to accelerate design efficiency and raise the accuracy of SFMA analysis, thereby supporting the general product innovation process.

I. Philosophy behind three forces.

The principle of three forces is simple yet useful when applied to a design scenario (Cescato 2005; Kroes et al. 2008). The first force is active or positive; the second is passive or negative; the third is neutralising. In practice, all three forces are equally active and appear as active, passive and neutralising in relation to one another at their meeting points and at a given moment. The first two forces are easily comprehensible, while the third may sometimes be discovered either in the ‘medium’ or the ‘result’. Several reasons may exist to explain why the third force is sometimes not easily accessible. First, it could be due to the functional limitations of ordinary psychological activity. Second, it may be due to the fundamental categories of our perception of the phenomenal world—that is, the sensation of space and time resulting from these limitations. It might be similar of perceiving, observing the third force directly than spatially perceiving the 'fourth dimension’. Although it may seem complicated, the application of three forces to design is understandable. For a scaffold application, such as a cell culture, any useful design elements can be termed positive, and any hindering termed negative. Neutralising refers to elements that either support the active, or hinder the negative, to help the design better achieve the aim. This simple logic aligns with the TRIZ SFMA approach, where objects and elements are defined as ‘useful’ or ‘harmful’, and the key point of dealing with them is to strengthen some and decrease others. The element of ‘neutralising’ in this context would be the inspirational aspect during design, since finding such would mean finding a powerful solution to existing design ‘inertia’, as is usually the concern of TRIZ users.

II. Corresponding three forces with three functions of SFM.

SCs are called interactions in the system in the following conditions: (i) a profitable (P) action causes a simultaneous harmful (H) action, and (ii) introducing or intensifying a P action, or eliminating or reducing a H action, results in a deterioration of one of the system parts or the whole system. Understanding these interactions helps establish SFM and acts as the foundation introducing three forces to SFM. The core element is to combine the ‘neutralising force’ with existing positive and negative forces, and this is vital not only for 3DPVS design, but for general TRIZ innovation contexts.

Our approach is presented in Figure G-10, which illustrates the symbols and process of unitising three forces in SFA. The red circle represents S1, which generates a positive force to a desired phenomenon or projected design aim; S2 is blue, as the generator of negative force; and the green N is the neutralising force to either strengthen S1 by N1, affect the medium process by N2, or minimise S2 by N3. Detailed use of this for 3DPVS design could occur in the concept generation stage. Regarding the function between S2 and S2, we can see there are two opposite forces, positive and negative, and the neutralising force can affect three points—S1, S2 and the function process.

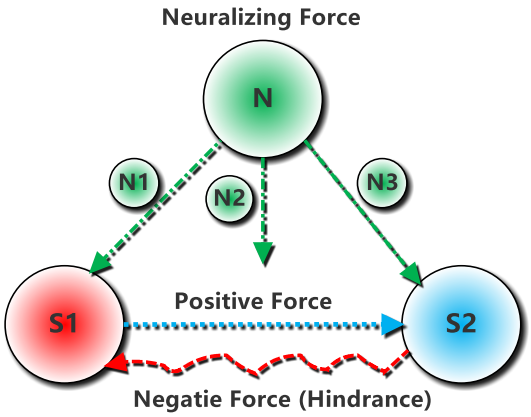


Figure G-10 Applying three forces to function of S1 to S2 in SFA model

After establishing the aim or objective of the function between S1 and S2, we use P to name the positive or profitable force to help, support or strengthen this aim, and use H to define harmful or hindering forces to cripple, disturb or negatively affect the aim. The neutralising force is N, which must be found to help the P and hinder, repress or transform H. An illustration of the three forces within SFM is shown in Figure G-11.

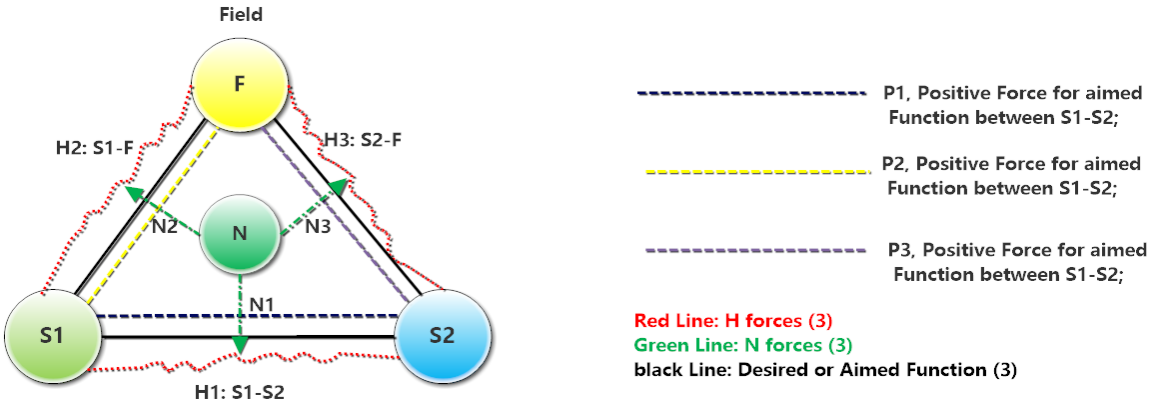


Figure G-11 Three basic functions and nine forces illustration for new SFM

From this model, we can see there will be three functions: function 1 between S1 and S2, function 2 between F and S1, and function 3 between F and S2. There are three forces, P, N and H, for each of these three functions, to make nine forces in sum. After introducing three forces to SFM, it shows more efficiency in terms of analysing the three functions between the

three elements, S1, S2 and F. In practical use, the new model can be temporarily termed NSFM to distinguish with the one without using three forces.

III. Steps of using NSFM in design.

We propose that four steps of NSFM can be used in the 3DPVS design as follows.

Table G-11 Four-step process using NSFM in design

Step 1: Establish SFM Function Trinity Establish the function 1, 2, 3 between S1-S2, S1-F and S2-F; if the system only need analyse one function, then other two can be absent.
Step 2: Establish the P Force Lists ▪ For each Function, analyze the Positive force in the question form, such as what can help this function and what helps achieve this aim. Anything that helps the desired function will be called force 'P'. Make a list of each 'P', that is, there will be three 'P' representing three functions established in step 1. If there are multiple P forces existing for one function, then use the evaluation method to build a hierarchy.
Step 3: Establish the H force lists ▪ Similar as the process of analyzing positive forces, harmful or hindering forces, factors, will be established in this step. Except from the H forces hindering the established function, any factors, elements or forces hindering, harming P force established in previous step, will be considered as H force as well.
Step 4: Establish the N force Lists ▪ Establishing Neutralizing force lists will be the core of this methodology. The centre aim of N can include three realms. ▪ N will support P while remain neutral or positive toward N, so P will conquer N toward achieving the aim. ▪ N will minimize the force of H, while remain neutral or positive toward P, so H will be conquered by P as well. ▪ N will transform H or part of H into P, which helps P to grow while H weakens. This is the prioritized solution for any system. ▪ N will help P and H simultaneously, but P ascends in more significant ratio compared with the rate of H, then as a result P dominates H and helps the function to reach the projected aim. N will both weakens P and H, but the level or proportion toward H is heavier than P, then P will conquer H in same way, and help achieve the aim.

To conclude, the established NSFM is proposed as a useful tool for the 3DPVS design. It can be used to solve problems in Route 3, as well as cooperating with ISS, which will be discussed in the following section. This method boosts the efficiency of traditional design philosophy and gives designs more freedom to see the whole picture of the problem.

G7: ISS Assisting 3DPVS Design Methodology

TRIZ ISS have been demonstrated to be a powerful tool for product innovation and novel design (Goddard & Gadd 2011; Savransky 2000). As illustrated in the four-route methodology, ISS can help solve contradictions, especially in Route 3, where contradictions cannot be easily identified as a technical contradiction or PhC. Further, ISS can be used separately as a philosophy of general innovation thinking, which can help designers be more practically creative.

Knowledge and Concerns of Dual ISS

In recent years, Oxford Creativity, by Karen Gadd and her teams, updated TRIZ ISS into new formats to make it easier to implement (Goddard & Gadd 2011). Both types of solutions can benefit the design purpose, and, in this study, we first learn from the philosophy and then adjust the solutions to be tailored for the 3DPVS design context. We initially study traditional TRIZ-based standard solutions. Altshuller and his associates generated the '76 standard solutions' in TRIZ between 1975 and 1985. These solutions are grouped into five categories, as shown in Table G-12(a). Despite its popularity, there are several concerns when using it in the 3DPVS innovation context. SFA connected with this solution system offers innovative solutions, yet some tend to be difficult to apply when solving problems. For a given problem, researchers sometimes need to read through every principle to find the suitable one—that is, the traditional five-class categorisation might not be effective in rapidly indicating the correct direction for problem solving. Meanwhile, some solutions may be too general, and others too specific and focused only on one application. For example, ferromagnetic was a novel product 30 years ago, so TRIZ used it as an innovation solution. However, taking this to current innovation world is narrowed, that is, 'ferromagnetic solution' needs to be put together with antiferromagnetic, diamagnetic, ferromagnetic and paramagnetic, to make this solution more generalised and practical. In this regard, for tailored ISS used for novel design, especially 3DPVS, while the core philosophy remains, some of the solutions may need to be adjusted or rearranged to enhance effectiveness and efficiency.

Studying the standard solutions adjusted by Oxford Creativity is also important for restructuring work in the 3DPVS context. Oxford Creativity restructured a new standard solution system from the traditional one, aiming to pattern the 76 principles into easily understandable formats so more people can use them rapidly. Its classification is shown in Table G-12(b).The new standard solutions are easily understandable, especially for those unfamiliar with TRIZ and who want instant solutions. However, there are several concerns in this categorisation. Before adjusting their solutions to ISS for 3DPVS, understanding these concerns is necessary. TRIZ solutions focus on system development, which contains sub-system, system and super-system components. Oxford Creativity does not prioritise in system. As such, some definitions of solutions may be vague. For example, the formula of solutions of '1.1 Add something to/inside the subject or object' and '1.3 Use the environment' seem too general and not practically helpful. In addition, some definitions of the class seem debatable. For example, to 'Eliminate, trim out the harm' occupies six solutions, and to 'stop, block the harm' occupies another 11. However, these two classifications describe the same harm-elimination process, just at different levels. Eliminating harm means fully stopping and partially stopping means eliminating. A further concern is regarding field and action. In TRIZ, action is a by-product resulting from the reaction of F, S1 and S2—the consequence of elements or process generated by elements. Field and action are not the 'phenomenon' in

one level. Field can contain an action, but is not action itself. Additionally, congruity is a concern. For example, the first two solution classes of Oxford Creativity—harm and insufficiency—are based on functions between field (F) and Substances S1 and S2, while the third one—measurement—is based on requirements by researchers at the product level or function level of the product. As another example, measurement also includes two functions: harmful means of measurement and insufficient means measurement. Thus, solutions in the measurement category seem as repetitive as solutions in the first two categories. In practical use, this might cause repetitiveness in solution searching (Goddard & Gadd 2011). Some standard solutions are partly repetitive with 40 principles. Therefore, rapid solution searching while maintaining general congruity is needed. These concerns may need to be addressed, to a certain extent, in the ISS established for 3DPVS design.

Table G-12 (a) ISS by traditional TRIZ vs (b) adjusted innovation principles by Oxford Creativity

(a) Innovation principles by traditional TRIZ			
Class no.	Description	Notes	3DPVS applicability
1	Improving the system with no or little change	13 Standard Solutions	Yes, high
2	Improving the system by changing the system	23 Standard Solutions	Yes, high
3	System transitions	6 Standard Solutions	Yes, high
4	Detection and measurement	17 Standard Solutions	Yes, low
5	Strategies for simplification and improvement	17 Standard Solutions	Yes, low
vs			
(b) Innovation principles by Oxford Creativity adjusted TRIZ			
Class no.	Description	Notes	3DPVS applicability
1	Harm	24 Solutions with 4 Sub-class	Yes, high
2	Insufficiency	35 Solutions with 3 Sub-class	Yes, high
3	Measurement	17 Solutions with 3 Sub-class	Yes, low

Restructuring and Re-contextualising ISS for 3DPVS Design Context

To assist with the four-route methodology established by this research for the novel development of 3DPVS, we attempt to adapt and restructure the ISS based on Altshuller's 76 standard solutions and the simplified version of Oxford Creativity. As aforementioned, the essence of 3DPVS development is a cross-domain scientific design covering realms of scaffold engineering, vibration science, mechanical science, 3DP and so forth. Therefore, standard solutions or principles must be tailored to or at least compatible with these realms to ensure design proficiency and convenience. The proposed ISS contains most of the original standard solutions in both traditional TRIZ and Oxford Creativity, with new extensions and modifications; that is, part of the TRIZ and Oxford solutions has been simplified to make them more scientifically specific and accurate, part has been modified to be general and applicable

for a wider context, and several derived new solutions have been added to cover novel cross-domain innovation aspects. In brief, ISS for innovation of 3DPVS, as well other similar bio-product designs, is proposed to make the best of both worlds of traditional TRIZ and Oxford Creativity, while addressing some limitations they potentially have in the 3DPVS context. Traits of ISS include, yet are not limited to, the following aspects: (i) it can be directly anchored with the 40 innovation principles to solve 3DPVS SC; (ii) it potentially provides greater effectiveness, clarity and integrity when cooperating ISS with SFMA methods; and (iii) new formula for most solutions are uniform—'what action'+ 'how to act'+ 'where/when is the context'—to make each solution understandable, specific and accurate. As such, four classifications are established, with philosophy and focus as follows.

Consciousness- and contradiction-solving based. In this category, five solutions revolve around solving concerns related to consciousness and contradiction solving. Consciousness from one engineering realm towards others, especially cross-domain ones, always seems challenging, and understanding and addressing this is thus necessary for every designer. Given that contradiction is the core of problem solving in TRIZ, better understanding and analysis of contradiction, and making it applicable, is another vital issue. It is also worth noting that, before analysing the solutions for usefulness or harm (as discussed later), the system model itself must be established in a suitable way; otherwise, the following analysis to tackle the 'harm' or strengthen the 'usefulness' will be ineffective or even faulty. The process of establishing a suitable SFMA is predominant, and can be considered 'neutral' in terms of the desired or undesired functioning of a real system, represented by 'usefulness' and 'harm', respectively.

Usefulness-based standard solutions. In this category, eight solutions are concerned with a useful action, function or activity that is needed by the system, while seems lacking, incomplete or inadequate. First, four solutions focus on 'creation of SFM from incomplete model'; second, two solutions focus on 'delete excessive elements of SFM, and make it simplified'; third, one solution focuses on 'transform traditional SFM into NSFM, which contains the analysis of three forces'.

Harm-based standard solutions. As the opposite of 'usefulness', 'harm' must be mitigated or decreased during the design process. This category contains 26 elementary solutions with two basic strategies for problem solving. Eighteen solutions deal with 'eliminate the harm or decrease its degree', while eight solutions focus on 'transform harmful functions, activities or objects into positive'. Similar to usefulness-based solutions, harm-based solutions could potentially be applied not only to technical engineering aspects for 3DPVS, but also useful to solve other harmful actions or functions, as they represent the H force in the law of three. These solutions could potentially be universal standard solutions for the engineering, scientific and philosophic world, which deals with 'harm' and 'usefulness'.

***Insufficiency-based elements*.** Two basic strategies composing 37 solutions are included in this category, which aims to help improve, change or enhance definite functions by changing the substances (S1 or S2) or the action/ field (F) that acts between them. Nineteen solutions deal with the 'change, evolve the system' components or 'add new elements to them'. Eighteen solutions focus on 'enhance, strengthen or improve the action focusing on insufficient or missing field'. In this category, to find the right F when there is an object (S2) that needs to provide some extra function or change, a subject or tool (S1) with a field (F) to deliver/complete such a function is key. This group of standard solutions also helps find a solution, particularly when cooperating with scientific effects analysis.

ISS as Assisting Tool for TRIZ IPA Process on 3DPVS Design

In previous SFMA, we illustrated the four classes of standard solutions and introduced their basic philosophy. The contents of the ISS could be considered a core part assisting with the TRIZ-based methodology, as proposed previously. Thorough details of ISS standard solutions are presented, with description of each solution and potential applicability to the 3DPVS design.

To conclude, ISS established within TRIZ-based methodology could increase the speed of generating innovative ideas and creating novel and practical concepts, which is especially necessary in the 3DPVS conceptual developing scenario. ISS could not only be used for Routes 3 and 4, where no easy identification on SCs or PhCs of definite design question can be obtained, but also as general innovation standards for much wider multi-cross-domain designs and innovations.

G8: ARIZ-based Innovation Roadmap for 3DPVS Concept Generation

In this section, we focus on three aspects. First, we introduce the fourth route of the established TRIZ methodology—the ARIZ-based innovation roadmap. Second, we illustrate the roadmap with its specific work in each step. Third, alongside functioning as an independent design route, the ARIZ map could also cooperate with the first three routes to boost their design efficiency and innovation resourcefulness.

ARIZ-based Innovation Roadmap as Fourth Route of Design Methodology

As previously discussed, the conceptual stage for 3DPVS chiefly contains three stages (Yuan, Xing & Hsu 2018b), and the TRIZ-based methodology for the 3DPVS conceptual design includes four routes. In terms of the simple format contradiction or problem solving, the first two routes could be playing with better potentiality. For problems that tend to be relatively complex, where identifying the contradiction initially seems challenging, the third route comes to play its role, using SFMA and ISS elements. However, the real 3DPVS design tends to be more complicated—especially when DRs and specifications are directly from end-users—and approaches could be less effective when directly using the first three routes. As such, a fourth

route has been proposed as a separate route tailored to such complicated or entire-scope scenarios.

Before using ARIZ, which helps solve dimensional and difficult questions (Chou 2014; Kim, S-K 2017), several limiting aspects of traditional scaffold design may be first perceived. Philosophy of which tends to be a 'linear' and 'single-dimensional' design process, and generally follows six sequential steps: obtain requirements; search previous scaffold information by other researchers; compare the difference of application; modify (minor or major) materials, geometrics or other aspects through brainstorming, thinking and trial-and-error experimental work; and finally generate a 'suitable' model. Such steps are adequate for simple questions or design concerns, but for complicated products, such as 3DPVS, compared with traditional 3D passive or static scaffolds that have been used as mainstream tools for cell cultivation, they seem less effective. Thus, a systematic design algorithm or process is needed, so scaffold designers can follow a series of steps and achieve optimal conceptual solutions. In other words, for quantitative scaffold improving—namely, updating products with changes on external traits—it is convenient to use the traditional linear path. When novelty or innovation needs to be integrated to endow a scaffold with a new essence, a better approach might be necessary, which is partly due to the limited resources supporting such design purpose and partly by the 'mental inertia' possibly caused by 'trial-and-error' design practice. This traditional scaffold design process could break the mould to achieve innovation of 3DPVS. 'Trial-and-error' designs cost both time and resources. Thus, a novel guide that helps researchers tailor the design path and find the best way to achieve 3DPVS is of significance. The innovation roadmap proposed in this research aims to provide end-users with a relevant, efficient and practical approach when innovation is the chief focus for designing scaffolds. Given that ARIZ was basically unexplored in previous scaffold design, much work may be needed to further improve it after establishment. Further, other TRIZ-derive methods, such as OTSM-TRIZ, were developed for complicated designs (Cavallucci & Khomenko 2007; Fiorineschi, Frillici & Rissone 2015). However, considering its lack of applicability to integrate in existing routes, and the unfamiliarity of engineers not with TRIZ expertise, ARIZ is considered more convenient and suitable.

Cooperating with the basic philosophy of 3DPVS development—that is, increasing the scaffold ideality level to achieve a higher position in its evolutionary ladder—ideality focus is one merit of using the ARIZ-based design roadmap. It helps create concepts and solutions with ascending ideality. Ideal concepts generated from the innovation roadmap with a design algorithm can be divided into three levels: basic ideal concept, mediate ideal concept and senior ideal concept. The term used is classified by the language of 'relativity': one senior ideal concept generated in definite phase can be the final ideal concept in this phase, while it might become only the input as basic ideal concept for another further design scenario. These three concepts aim to provide ascending ideality at a sequential level following the design process.

Illustration of ARIZ-based 3DPVS Innovation Roadmap

Studies of ARIZ are based on (Altshuller, G. S. 2007; Bukhman 2012). The innovation roadmap with basic algorithm contains three chief parts, A, B and C, containing seven, four and eight steps, respectively. An illustration is shown as Figure G-12, indicating its basic structure and indication. The meaning of each symbol in the roadmap is briefly illustrated in Table G-13.

Table G-13 Representation of symbols in 3DPVS innovation roadmap

Symbol	Representation for design
Solid square (yellow)	Definite design process for stage A, B and C stand 7, 4 and 8 steps, respectively
Solid circle (blue)	Methods applied during conceptual stage
Dashed square	Input or output from definite process
Dashed circle	Supplement methods assisting chief methodology
Green solid circle (green light)	Process passing into next one, without returning or re-processing; evaluation will be introduced here
Red solid circle (red light)	Stagnated or hindered stage or step, whereby it is necessary to return to the definite previous step and re-conduct the process; evaluation will be introduced here as well

Regarding the aim, motivation and task of each step, the content is proposed in Table G-14, illustrating Parts A, B and C in a systematic way. From this, the philosophy and design aspects of the ARIZ-based innovation roadmap for 3DPVS can be explained for perception.

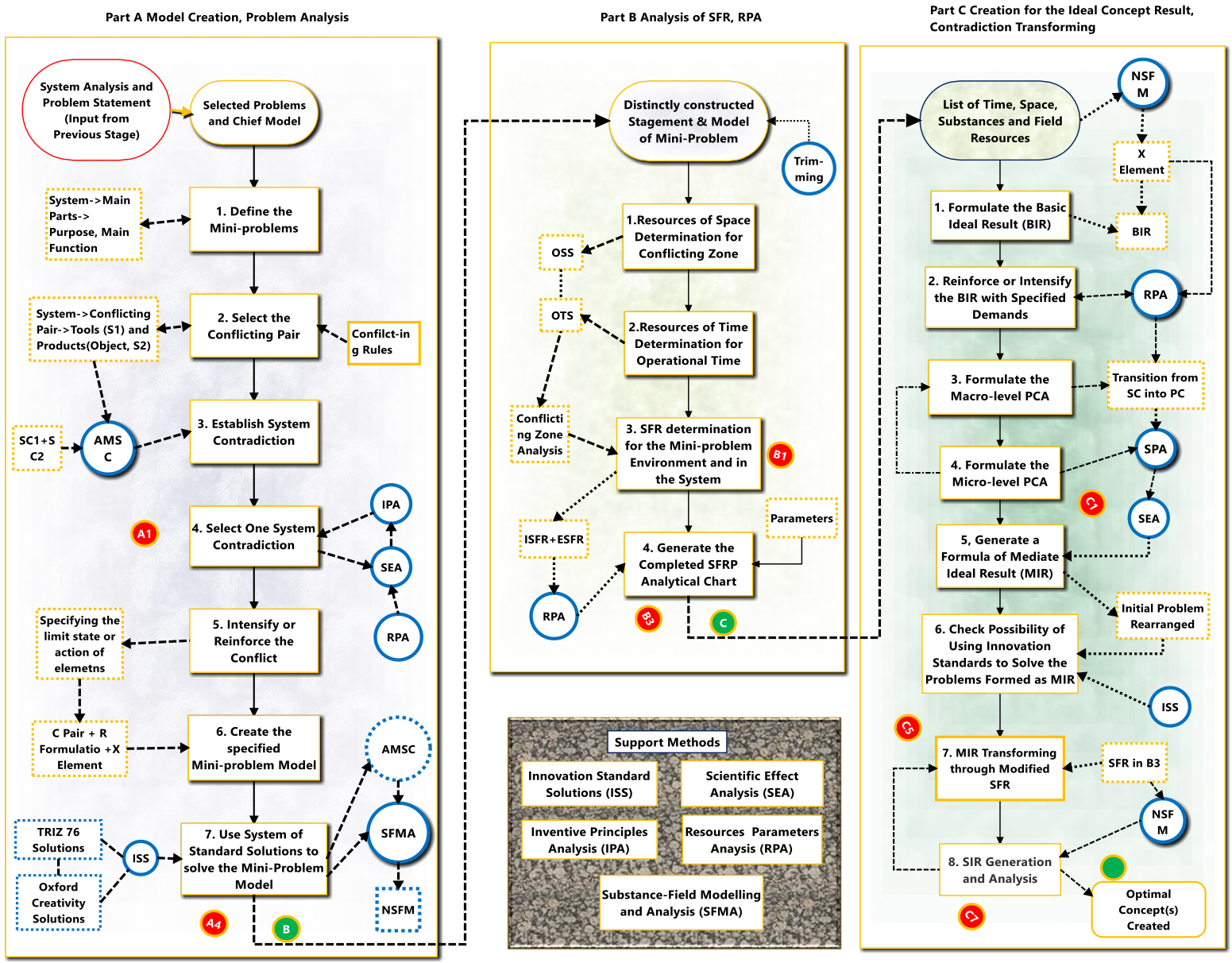


Figure G-12 3DPVS innovation roadmap as Route 4 of TRIZ-based methodology

Table G-14 ARIZ-based innovation roadmap for conceptual development of 3DPVS

Part A: Analysing the Case Problem, establishing Mini-Problem Model	
The chief aim of Part A is to transform an indefinite, vague or non-structured initial problem of a required 3DPVS scenario into a clearly constructed, simplified description Model. The language needs to be tuned with the design methodology/Roadmap in this research context.	
A1	Define Case 3DPVS into Mini-Problems, and formulate the Conditioning
A2	Select the Conflicting Pair/define Conflicting elements for Sub-system of 3DPVS
A3	Establish System Contradiction, applying Analytical System Conflict Models (ASCM)
A4	Select the Prioritized System Contradiction, detailing AMSC
A5	Intensify and Reinforce the GMBV Contradiction Sets (Intensification Simulation)
A6	Create the specified Mini-problem Model(s) with Element N, Generating Hybrid GMBV Solution Chart
A7	Use System of Standard Solutions and ISS to solve the GMBV Mini-Problem Models
Part B: 3DPVS RPA and SFR Analysis based on Mini-problem Models	
Part B of the Innovation Roadmap aims to create a through list of TPSFR (time, space, substance and field resources) and their related parameters. Available resources for a definite 3DPVS context need to be identified, and an RPA will be conducted afterwards.	
B1	Resources of Space Determination for Conflicting Zone
B2	Resources of Time Determination for Operational Time
B3	SFR determination for the Mini-problem Environment and in the System
B4	Generate the Completed SFRP Analytical Chart
Part C: Determination BIR, MIR, SIR, and Solving Physical Contradictions on macro- and micro-levels of 3DPVS System	
Purpose of Part C of Innovation Roadmap for 3DPVS is to make problem-model transition from System Contradiction into Physical Contradiction. For steps of C3 and C4, they can be effectively associating with analyzing, utilizing separation principles, scientific effects and previous scaffold innovation studies. The application of part C directs designers toward the Ideal Solution of the required 3DPVS product. It will not be the perfect Ideal Solution, but the SIR (Senior Ideal Result) point to the most achievable, practical and innovative answers.	
C1	Formulate the BIR based on NSFM
C2	Intensify/reinforce BIR with additional requirements
C3	Formulate PhC GMBV sets at macro-level
C4	Formulate the PhC GMBV sets at micro-level
C5	Formulate the MIR
C6	Apply the inventive standards to solve the MIR
C7	Use modified SFR for problem solving and solution idealizing
C8	SIR Generation and Analysis
At this step, the proposed ARIZ Algorithm for 3DPVS as fourth Route of TRIZ methodology has been basically finalized. This multi-step process is considered to make up the essential design of 3DPVS as far as scenario draws to Route four, and the practical application of which could be on conceptual Case studies regarding generating innovative concepts.	

In this section, we introduced the fourth route of the established TRIZ-based methodology for conceptual 3DPVS—the ARIZ-based innovation roadmap. As mentioned, Route 4 is chiefly concerned with a relatively complicated design scenario, and can also cooperate with the previous three routes and help increase design efficiency. How and where the connection lies between the fourth route and previous three is discussed next.

Possible Interconnection of 3DPVS Innovation Roadmap with Other Routes of TRIZ-based Methodology

Corresponding interconnection with Routes 1, 2 and 3. In Chapter 5, we established a four-route methodology for the conceptual design of 3DPVS, and the 3DPVS innovation roadmap was proposed to play a role in complicated contradiction scenarios—that is, scenarios mingled with Contradictions 3, 5, 6 or 7. Design questions or aspects involving Contradictions 1 and 2, which are relatively linear and easy to solve, will be solved by Routes 1 and 2. Route 3 concerns relatively complex yet still simply structured design questions. For other questions that tend to be the most challenging and sophisticated, Route 4 is proposed as the possible problem-solving path. However, each route can function both dependently and interdependently. Figure G-13 presents a brief illustration of the connection between the fourth route and others. In this illustration, the dashed line indicates the potential interconnection between the solution generation of the first three routes and the fourth one. After problems have been segmented into set mini-problems—that is, the problem which basically contains either SC or PhC, Route 1 could cooperate with A4, while Route 2 with B3, C3 and C4. Four steps in Part A of the 3DPVS innovation roadmap could be integrated into the Route 1 typical approach, while five steps initiated by B3 in Part B and two steps initiated by C3 in Part C help deal with PhCs. Parameters and resources in Part B could become part of input for a definite step in Routes 1 and 2. The created micro- or macro-PhCs in Part C can also be transferred into Part 2 for Route 2. IPA and SPA would help generate both typical solutions corresponding to both types of conflicts, with the output evaluated by tools regarding its appropriateness in a definite design scenario. If unsatisfactory, the generated output could be analysed using ISS, which is an element in Route 3. In this way, the design of the mini-problem can be resolved at a relatively comprehensive level.

To conclude, after discussing the innovation roadmap for conceptual generation of 3DPVS regarding ‘what’ during the design process, we attempted studies regarding ‘how’. The algorithm established in this research context is based on the traditional ARIZ, with its essential contents modified, reconstructed or tailored to accurately fulfil the 3DPVS design context. Elements of EDP have been integrated into the algorithm as well, together with other specified means developed in this research, such as NSFM, ISS, RPA and SEA, which mostly play an essential role in TRIZ. This algorithm generally includes around 60 steps (at the current stage of proposal) corresponding to the innovation roadmap, and one detailed application on how to create concepts of 3DPVS with specified requirements by a real end-user was illustrated in the case study chapter. The algorithm developed chiefly includes three aspects. It is worth noting that these stages continue from the design initiation of 3DPVS and bridge to the concept evaluation and concept scenario finalisation. Considering the complexity of the design algorithm, knowledge and expertise from TRIZ resources and 3DPVS context

may be required. Therefore, more work is recommended to study TRIZ thoroughly and attain a better understanding of the innovation roadmap.

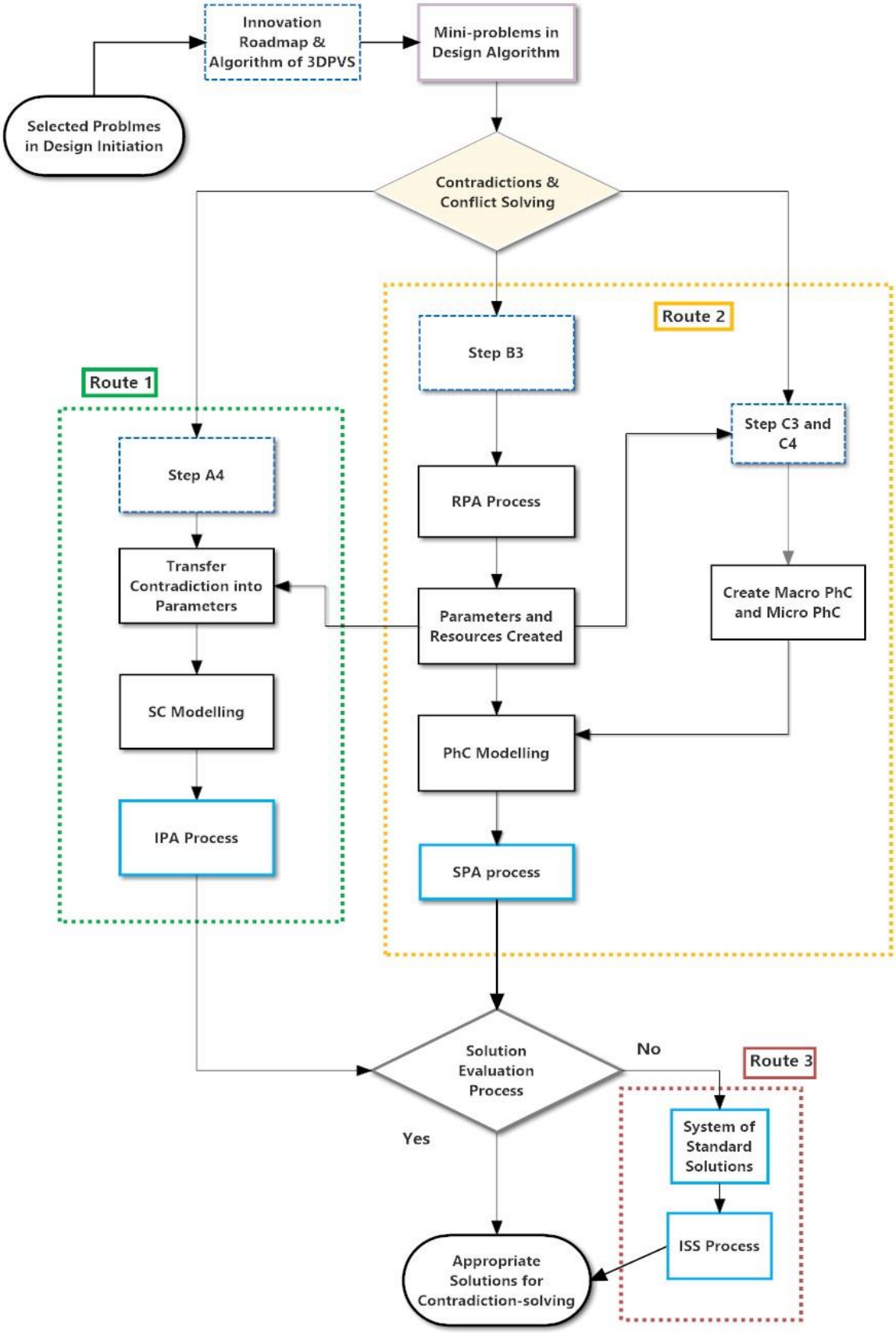


Figure G-13 Interconnection of 3DPVS innovation roadmap with other routes in TRIZ-based methodology

G9: Expert Survey as Support for TRIZ Method Evaluation

A survey of experts can be useful in conceptual stage of product innovation (Blogg 2013). This section contains the survey details of the proposed method and design tools through collecting opinions of experts via email, Skype, telephone or face-to-face. Experts were chiefly surveyed from four realms: the bio-realm concerning cell culture scaffolds; structural engineering realm regarding vibration and dynamicity; mechanical and manufacturing realm regarding 3DP, properties of scaffolds and material composition; and design realm regarding theory and methodology. Experts were identified via academic literature, conference participation lists and members of international design organisations. Each expert was identified as having an influence on the discussion of design aspects of engineering or bioengineering. The professional experience of the participants ranged from three to 17 years, with an average of 10.2 years. Apx F. provided the survey questions and result.

Of the 35 surveys sent, 15 experts had responded at the time of writing (43% survey response). If a survey response was not received, non-responders were contacted periodically, once per week, until a response was received or three contacts were made. An additional four experts declined to participate. Despite several follow-up contacts, no further participants showed intention. Therefore, while the results generated in this section help validate to some extent the TRIZ methodology and tools proposed for 3DPVS, they indicate a future research direction, instead of providing a definitive answer.

The survey questions are available as supplementary material, reflecting the expert opinion of TRIZ-based factors and elements that may influence the methodology established for 3DPVS design, as rated on a five-point Likert scale, ranging from ‘strongly agree’ to ‘not agree’. Participants could also provide free comments on each question. Introduction and instructions for the survey were provided, and 10 survey questions considered most vital for this study context were sent to experts. A three-level result was generated: (i) summarising the institutional information of experts, number of experts invited to participate, participants’ expertise, and number of respondents categorised by expertise or institution; (ii) summarising feedback information for each question in the survey; and (iii) qualitative analysis of experts’ feedback for both validation purposes and to help contemplate the pros and cons of this research.

Based on the feedback of experts, we attained indications from several aspects. First, the proposal of TRIZ for 3DPVS innovation is basically considered promising, with an average score rating at 3.53, and more than 80% experts ranked it from ‘moderately’ to ‘strongly agree’. When inquiring whether the current TRIZ contents on 3DPVS design are sufficiently ready-to-use, as the second listed question in the survey, experts generally showed moderate to negative opinions, with an average rating of 2.27—the lowest average ranking among the 10 inquired aspects. This answer may show that traditional TRIZ contents are not at a ready-to-

use level when focusing them directly on 3DPVS design. It is interesting to link this question to survey Question 14, where experts were asked whether other tools or methods are needed aside from TRIZ for design scenario of 3DPVS. Surprisingly, the majority of experts responded with a positive answer, with an average rating at 3.8—the second-highest score of all 10 factors surveyed. This could mean TRIZ alone is insufficient to tackle all possible design issues that would appear during 3DPVS development, although TRIZ could possibly lead to innovation. Considering this with one of the author(s) previous discussion indicating TRIZ as a potential tool for the concept generation part of 3DPVS design, we can conclude that other tools are necessary for concept evaluation, which is the following stage in the 3DPVS development. Therefore, exploring and establishing a methodology for the future concept evaluation work might be an interesting direction, following the innovation achieved by the TRIZ methodology proposed in this study.

Focusing on methodology, several indications can be summarised. First, besides the relatively positive attitude towards TRIZ for 3DPVS innovation, when surveying whether it is inspirational and promising to establish a TRIZ-based methodology for conceptual 3DPVS, the experts similarly provided relatively positive feedback, ranked 3.13 on average, and around 80% of experts agreed with this at a moderate to strong level. This could to some extent support the motivation of this study. Passing from the generation methodology proposal to the four-route TRIZ methodology established for 3DPVS in this study, about half of the experts showed moderately agreement, while another third responded with ‘agree’. This may mean that most experts considered the four-route proposal reasonable, at least from a theoretical level, though detailed works using this four-route approach for 3DPVS design have not yet started. Further design studies regarding the proficiency and effectiveness of using this methodology are considered necessary.

In addition to the generic methodology aspect, the surveyed results on aspects of selected tools and elements in this study could also provide useful information. As such, the TRIZ innovation principles, SFMA, ISS and ARIZ innovation roadmap, were asked for knowing experts’ views on the basic feasibility and scientific soundness of using them for the 3DPVS conceptual design. In the corresponding responses, the feedback showed an average rating by experts of moderate agreement. This could partly support the proposal of using these tools, which functioned as vital elements in TRIZ methodology for 3DPVS innovation, as being realistic and applicable. Among these, ISS attained the highest average scale (3.60) and nearly 90% of experts regarded this at or above ‘moderately acceptable’ level. This is possibly because of ISS’s high coverage in tackling universal innovation solutions, and that the generated ISS solution is relatively easily understandable by designers. In contrast to ISS, ARIZ seems less attractive and barely passed the line of moderate acceptance. While about 30% stated ‘agree’ and ‘strongly agree’, a similar number of experts rated ARIZ as ‘slightly agreeable’ or below. After further inquiring about this, it may be partly perceived that ARIZ

requires much more expertise compared with other TRIZ elements, which means it is not ready-to-use for everyone and the need for specific training could occupy much time. Some experts held a neutral attitude and wished to provide further comments after seeing the detailed implemented work of this ARIZ algorithm to the 3DPVS design.

It was also interesting to note the surveyed result of Questions 2 (B) and 9 (I) as the opposite polarity—that is, while the statement of 'current contents of TRIZ are sufficiently applicable for 3DPVS design' attained the lowest approval among all questions (nearly 20% disagreed and another 40% slightly agreed), the declaration of 'keen to attempt TRIZ in relevant future work' gained the highest rank among all other aspects, with about 40% of experts indicating 'strongly agree'. This could mean most experts were interested by this research and would like to further understand TRIZ and its tools' possibilities, yet mostly did not feel very positive that the current content of TRIZ is directly applicable to designing 3DPVS. Regarding the second indication, it is indeed reasonable, which also to some extent validates the direction of re-contextualising TRIZ and adjusting its tools to the 3DPVS context. This was part of the work in this chapter and perhaps further work is needed in that direction. Further, some experts held the view that new TRIZ parameters or innovation principles could be added to the existing pool, since these parameters or principles were presented decades ago and many innovations have since occurred that could offer other parameters or principles. Whether these could fully satisfy the innovation requirements for 3DPVS is a concern and needs further validating.

Based on the free comments coded in post-processing (nine received of 15 participants), several issues were indicated. First, it was generally considered positive to attempt to integrate the TRIZ toolset in the conceptual design of 3DPVS. The four-route methodology of TRIZ was perceived as useful, even though it has not been used for formal conceptual design of 3DPVS. Several experts suggested presenting follow-up surveys of each part of the tool in the presented work to achieve higher understanding for validation purposes. Several questioned whether TRIZ is sufficiently scientific to contribute to complicated bio-designs, such as 3DPVS. Some stated that validation at the current stage can only be preliminary for future work, since real validation should always pass experiments and detailed designs.

From another perspective, in this survey, experts from realms related to design generally had greater confidence in applying TRIZ to new realms such as bioengineering, while experts with relatively less expertise in design studies tended to show more negative attitudes towards applying TRIZ for 3DPVS. This could possibly be perceived from the fact that, in traditional or predominant bio-innovation, laboratory experiments have always been considered the priority, and theoretical knowledge or philosophy such as TRIZ does not attract much attention. This also gives an indication for future TRIZ workers that, until more solid practicality is demonstrated, TRIZ may not be easily accepted by bioengineering designers which basically remained as design theory.

To conclude, the survey results showed that most TRIZ aspects raised by this study were considered by experts at an average 'moderately agreeable' level, and the ratio to reach the second-highest scale ('agree') was approximately 26%. The ratio at the highest scale ('strongly agree') was around 15%. At a preliminary design study stage, these data offer a positive and promising indication for the general work frame. In addition, when validating the appropriateness of TRIZ and its tools for the 3DPVS scenario, more than 80% of feedback indicated 'moderately agree' to 'agree' and beyond. For the four-route TRIZ-based methodology, proposed for tailored design for the 3DPVS scenario, while some experts had concerns regarding the proficiency and effectiveness of using this methodology for future practical 3DPVS design, most experts showed a promising attitude. Finally, from the expert survey, we can conclude that the basic relevance, practicality and reliability of the TRIZ-based methodology for the 3DPVS conceptual design was supported, at least to some extent. Although several concerns existed, the general work of introducing TRIZ and four set of tools in the 3DPVS design received relatively positive feedback and appeared promising.

G10: Concluding Remarks

In this study, exploring and selecting TRIZ methods for the concept generation stage has been illustrated and discussed systematically. The methodology derived from TRIZ methods and other useful philosophical design aspects. Considering the possible limitations of traditional design approaches for scaffold engineering and that of existing TRIZ, we chiefly tailored and transferred traditional TRIZ-based methods into the new context, which can be directly applicable to future concept generation of 3DPVS.

The four-route methodology using seven-layer contradiction logics preliminarily focused on providing a useful, effective and accurate cross-domain aspect of innovation and design for a novel scaffold. Thirty-nine parameters of the TRIZ matrix and 40 innovative principle for SC were studied and, with their core elements, transferred into scaffold contents, especially tailoring to the 3DPVS conceptual design. The original explanation of TRIZ principles and parameters, their possible and extended indication, as well as the application to 3DPVS were illustrated comprehensively. SFMA was studied and proposed with some new functioning, with the three forces embedded, which aims to function as the third route of methodology to achieve greater proficiency and effectiveness. Following this, the traditional TRIZ-based ISS and Oxford Creativity standard solution were studied, and a format with the same yet restructured format was generated, which aims to deal with the comprehensive design aspects potentially appearing in the innovation work of 3DPVS. The ISS for 3DPVS relates to innovation principles, making SC using innovation principles easily achievable, and making the process using standard solutions in SFM more solid, accessible and convenient. Through design studies on ARIZ, as an essential part of TRIZ, this study sought to apply the 3DPVS innovation roadmap, which focuses on works in the fourth route of TRIZ-based methodology, while potentially dealing with sophisticated design works directly from end-users of 3DPVS. It

also aims to provide TRIZ methodology with greater resourcefulness and flexibility. The ARIZ-based algorithm basically contains the full steps, starting from the end point of design initiation and ending by finalising the basic conceptual innovation works of 3DPVS. It is also important to embed useful TRIZ-based methods and other proven design in this ARIZ-process. In brief, this study to some extent established a ready-to-use content bridging TRIZ innovators and those who focus on novel conceptual 3DPVS designs. Other novel designs in similar positions to 3DPVS may benefit from this 'text-book' content as well. Through using the TRIZ-based methodology, the conceptual design—especially concept generation—is expected to occur with increased convenience and efficiency. The works in this study may also to some extent fill a gap in the scaffold design and TRIZ literature and are preliminary to preparing future works of establishing a formal TRIZ-based methodology for novel scaffold innovation.

Validation of the work partly depended on the expert survey conducted with experienced experts in relevant academic realms, and partly depended on the design efficiency of 3DPVS itself, meaning the following design works connected with the established TRIZ methodology and the newly adapted TRIZ tools. From analysing experts' feedback, we can draw the preliminary conclusion that the basic relevance, usefulness and practicality of the TRIZ-based methodology appears to be scientific, logical and promising, at least to a certain extent, in terms of the attempt to use TRIZ and its tools for the 3DPVS conceptual design. The experts generally rated the work at the level of 'moderately agree' and beyond. However, this will not be the end of the study. Given the limited sample quantity of the experts, as well as their expertise, detailed information regarding each element of this study might require further exploration and analysis to draw a more accurate conclusion and a thorough future improving plan. This work can be combined with the following concept generation work of 3DPVS. Through practice, perhaps some defects and limitations of current methods can be detected, and we can enhance the TRIZ-based methodology to a finer level.