MATHEMATICAL MODELLING OF HEARTS

by

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Thesis submitted August 1968 - recommended November 1968
Technion, Israel Institute of Technology, Haifa.

Thesis submitted for the degree of
Doctor of Philosophy
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August 1977
\textit{Approved: F. Mac. 1978.}
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SUMMARY

The objectives of the research described in this thesis are: (1) the derivation of the differential equations of motion of muscle, and (2) the development of methods for physical and mathematical modelling of animal hearts in general and of mammals in particular. The thesis succeeds in laying the foundation toward accomplishment of these rather complicated tasks, and it provides some meaningful results and conclusions regarding the behaviour of cardiac muscle and the performance of hearts under various normal and abnormal conditions.

At first an outline of the structure and function of animal hearts is given, describing a variety of hearts ranging from that of the simplest animals in the chain of evolution to that of the most complex, i.e., man. Additionally, some fundamental properties of striated muscle are described. This provides the essential physiological background necessary for mathematical modelling of muscle and of the complex movements of the walls of the heart.

To model the cardiac musculature, which is the most important structure of the heart because its contraction is responsible for forcing the blood out of the cardiac cavities, two approaches are used: a "black box" approach, and a more fundamental approach based on molecular biology. In the simpler "black box" approach, the general theory of linear viscoelastic muscle mechanics is developed using arrangements of three basic elements: a spring, a dash-pot and a contractile element.

In the molecular biological approach, attention is focussed on the electrochemical, biochemical, mechanochemical energy transduction and mechanical muscle subsystems controlling the contractile behaviour of muscle. The following models are developed. (1) Excitation-contraction coupling, describing calcium movements in muscle fibres and the action of the regulatory proteins troponin and tropomyosin. (2) The biochemistry of myosin (HMM S-1) cross-bridge interaction with actin, enzyme kinetics and the contractile cycle of a single cross-bridge, based on the Lynn-Taylor kinetic reaction scheme.
(3) The energetics of contraction, i.e., mechano-chemical energy conversion. A synthesis of these models along with consideration of the mechanical properties of the biopolymer heavy meromyosin (HMM) leads to the differential equations of motion of a single cross-bridge. Then the molecular cross-bridge equations of motion are used to extend the theory to obtain the one-dimensional and three-dimensional equations of motion of muscle.

Two important conclusions follow from the above muscle model. First, the above-mentioned excitation-contraction coupling model provides a sub-model which could shed light on the complex mechanism of cardiac flutter and fibrillation. Second, from the above differential equation of motion of muscle, we find that under steady-state conditions, the contractile behaviour of muscles is governed by a general force-velocity relation, which includes the well-known hyperbolic A. V. Hill's equation as the simplest special case. This general force-velocity relation is capable of modelling many features of the normal and abnormal behaviour of cardiac muscle which cannot be modelled by the simple Hill relation. Furthermore it can be used to determine muscle constants and molecular parameters (E-C coupling, biochemical, energy conversion, and mechanical) from physiological experiments on a whole anatomical muscle. It should be noted that this is mainly due to the unconventional approach adopted here in developing the cross-bridge biochemistry model.

Finally, combining the simplified three-dimensional differential equations of motion of muscle with the equations of motion of fluids, a physical and mathematical model of forced blood flow from contractile vessels, tubular and chambered hearts is developed, and a general solution is obtained by Laplace transform. In addition, an electrical analogue of these hearts is developed which can be used for analog computer simulation of normal and abnormal expulsion flows from muscle cavities.