3 June 1933.

Professor C.L. Huskins,
McGill University,
Montreal, Can.

Dear Huskins:

Your letter raises so many points of interest that I scarcely know where to begin in answering it. Let me try first to take what I should regard as the simplest possible view of the maize situation, so as to use it as a standard of comparison for the effects of the various complications which may be postulated, some of which may really enter into the situation.

First I am sure that East and Jones have overstressed linkage. If the stock plant which you start selfing is heterozygous for n simple deleterious recessives, then only $(\frac{3}{4})^n$ of the progeny will be free from all of them. If n is about 16, this is as small as 1 in 100. If n = 30 you could try selfing quite a lot of plants without getting any single offspring without some recessive disability, most of them having a good many. This is ignoring linkage altogether and allowing ¼ of the offspring to be homozygote normals for each gene, these normals being assumed to be as good as the heterozygotes. The whole point of bringing linkage in was to make these homozygotes also defective for some other recessive mutant carried in the opposite chromosome and closely linked with the first. But with 10 pairs of chromosomes, and such loose linkage as is found in maize, not more than about 1 per cent. of the chromatin can be so ~~close~~ near to any one locus as to be at all closely linked with it. Consequently close linkage will only be of frequent occurrence when n exceeds 100, and so the introduction of linkage does nothing towards effecting its original purpose of diminishing the number of factors which need to be postulated.

The total number of harmful recessives knocking about a cross-bred population must depend on the frequency of each. If we take this to be 1 in 100 then the average plant will have 30 of them only if there are as many as 1500 in all. In random cross-breeding each will strike one plant in 10,000, or 15 per cent. of the cross-bred population. If this 15 per cent. seems too high you must postulate more factors with a lower individual frequency, but I fancy it might be a good commercial strain that would show 85 per cent. thoroughly sound plants. A sprinkling of weaklings would not matter commercially, and the success of the hybrids from inbred lines shows that there is quite 10 per cent. in yield to be gained over the best commercial strains. So I doubt if the facts do require a larger number of factors than this, though I do not in the lest deny that there may be 10,000.

The simple theory developed so far fails in one respect, which is important for your tetraploid theory. As you say, duplicate factors are common in maize. I think one can get an idea of how common they are from the course of the deterioration curve following selfing. With simple factors half the damage should be done in the first generation. Now I believe this is not so in quite a number of plants. Apart from the strong impression that Darwin acquired, that it was continued selfing that was dangerous, a mistaken view I think, but one that probably has an experimental basis, Rasmusson in the current <u>Hereditas</u> has put forward a rather unconvincing <u>ad hoc</u> hypothesis of the nature of what I call metrical bias, in order to explain why the first generation should not be so damaging as one would expect. Now duplicate factors do this very nicely. With these only ¼ of the ultimate effect occurs in the first generation, and the second generation is actually more damaging than the first. In fact the greater part of the loss is fairly evenly spaced over the first three generations of selfing, after which of course, it falls away as the line settles down to a steady homozygous condition. I have not any metrical data by me, but I should guess that if one took height or yield and grew the seed side by side in the same year one would get a deterioration curve indicating that quite a large proportion of the damage was due not to single but to duplicate factors.

The difficulty may be raised that the foundation plant must be heterozygous for both of the duplicate pair, but this is not really a difficulty, for in a cross bred population the proportion of recessives will rise until the rate of their elimination balances the mutation rate, and with duplicate genes this will give, for the same mutation rate, about double the frequency of double heterozygotes that, with simple genes, you would find of single heterozygotes.

I am not a bit clear about some of your points. If a diploid AA forms an auto tetraploid AAAA I imagine that in the first stage of its evolutionary progress each set of four chromosomes will become differentiated into 2 homozygous pairs AA and A'A'. Exactly how is not very plain to me, but I suppose it must happen during the first 10,000 generations or so. If I understand you right your first point is that once this differentiation is started it had better make haste to finish, else too many of the gametes will be born failures. I think I see this, though a sprinkling of imperfect gametes will not do a plant any harm if it takes care that only good ovules fertilised by good pollen get their full share of the nutriment available, but though differentiation between A and A' may be important, I do not see the bearing of this on selfing, which will normally only increase the similarity of members of the same pair, and this, I should suppose, should, if anything, tend to increase the regularity of their behaviour at the reduction division. I feel pretty sure I must have missed your point here. For what it is worth, now that the production of selfed maize lines has become a minor industry, I should not be surprised to see a homozygous line that would beat your 75 per cent. standard. But the practitioners may be too optimistic and I too credulous.

Yours sincerely,