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My dear Ford,

What a splendid little book you have made on Mendelism and Evolution. I am on my back awaiting an operation and have read it through twice, yesterday and to-day. The aim and arrangement strike me as very original, since you are really answering difficulties which, though widespread, have never found coherent expression.

Naturally I am delighted at the use you've made of my work. Of course your acknowledgments are ample. But what is delightful to me is that you have used *it* rather than that you have mentioned it. I have made a lot of notes in the margins mostly on merely verbal points.

P. 46, line 18 - I should prefer 'adapted' to 'evolved'. I suppose its really the same thing but we usually think of men as more highly evolved than echinoderms though I am sure they are often less highly adapted.

On this same page I should somehow like to get into one sentence that there are independent reasons for thinking that beneficial mutations must be small in effect (in highly

adapted species) and that they occur with very low mutation rates (in abundant species) though there may be a great many of them so occurring. But it is rather a lot for one sentence after all.

P. 48, 10 lines from bottom - What about 'paired with' for 'opposed to' and p. 49 line 14 - 'improvement of viability' for 'reduction of recessiveness'?

In the short paragraph on p. 50 I see that you make the mutant acquire dominance before it has supplanted its predecessor. My first thought<sup>†</sup> was that it would not have had time to; but I believe you are right and it would though I cannot prove it.

P. 51, lines 5 - 7 - They will have left too few descendants to have modified much the reaction of the species, even to the heterozygous mutation.

P. 52, opening paragraph - Mice treated with X-rays till their hair falls if heterozygotes regenerate it white. This is a good case of recessiveness disappearing in a changed environment. Cases of its being upset by genetic changes seem more common.

P. 57 - The point about back mutations is excellent.

P. 59 - The numerous genetic substitutions by which our fancy breeds have been built up must fairly often have upset the straight recessiveness of genes which would be quite recessive in the wild.

P. 64. in re Russellism - It is up to the ovist to show that an appreciable amount of the visible variation within a species is naturally inherited. The substantial equality between sire and dam in the biometrical correlations seem to cut away all hope of this, at least in the few species for which we have data. He cannot get away with saying that the ovum controls only inter-specific differences for no conceivable cause of evolutionary change could fail to act unequally and itself cause variability within species.

P. 70 - In the majority of the lines continued selection showed that no measurable heritable variability had been accumulated, though in two lines individual mutations appeared.

P. 72. - Continuous is a troublesome word, to systematists, paleontologists and embryologists, evolution is continuous if the steps are no greater than the ordinary differences between parent and offspring, say 2 ins. a step in human stature. I suppose a genetical selectionist would be surprised if one gene change, worth a  $\frac{1}{2}$  in. or more, swept over the species in a hundred generations. My point is that gene substitutions which for genetic purposes are discontinuous produce evolutionary changes much more continuous than paleontologists have or can have any evidence for.

P. 81 - Hastened by selection. I am tempted to suggest 'brought about by selection or continued mutation'. This is puristry and might force one to take good space to explain.

that the selective intensities must generally be much the greater.

P. 82, line 19 - 'Infertility' for 'lethality', and 'physiological agencies' for 'this latter agency'.

P. 85. The bottom of this is, I think, the only paragraph which, after a critical reading, I should be inclined to re-write.

In these circumstances the genes no longer compete with their allelomorphs independently in pairs but large systems of linked genes or perhaps entire genotypes come into competition as if they were a system of multiple allelomorphs. It is no longer possible for numerous genetic improvements to be taking place simultaneously, they must now take place one at a time, those giving the lesser advantage always making way for those giving a greater. Many advantageous mutations which confer only a small selective advantage may thus be continually crowded out because all the available chromatin is engaged with matters of greater importance. A character involving only small selective advantages such as colour pattern may be, may thus be debarred from the main method of evolutionary adaptation. This opens an opportunity for a duplication, or other chromosome abnormality deleterious when homozygous, to improve the colour pattern and establish polymorphism. The dominance of such factors could not be developed by the selection of modifying factors, for these would enjoy a still

lower selective advantage. In duplications, however, we have provided a tract of chromatin, selection in which is available for modifying the mutant heterozygote and is protected from the competition of the universal recessive gene complex.

Don't take the least notice of all this unless any of it happens to seem useful.

Congratulations again on the book.

Yours sincerely,