31st January, 1955.

My dear Kempthorne,

I have been puzzling over your letter and paper for some time, and maybe I have not got it clear yet.

I do not at all agree with the last sentence of the opening paragraph of your introduction, "Later in 1941 (2) Fisher showed that this is true only if the quantity Q^2/PR remains constant..."

What I said on the second page of the paper cited was, "The direct mathematical measure of the average effect of a proposed gene substitution is the partial regression, in the population as actually constituted, of the genotypic measurement on the numbers 0, 1 or 2 of the allelomorphic genes in each genotype." i.e. in that paper I set aside the experimental test of merely introducing more genes of any one kind in an experimental population, and measur~~ing~~ the change in average population value; through recognizing that any ~~general~~ gene substitutions do not merely act by substituting new for old genotypes, but that they ought properly to be regarded as also affecting the environment in which a natural population lives. Interactions with the environment are not, however, specified quantitatively in terms of the genotypic constitution of a population, but would require a full specification of the climatic and ecological situations in which a species finds itself.

For example, dominance deviation favouring, over a large number of loci, heterozygotes, on the average, over homozygotes, would in hermaphrodite plants favour the spread of genes having a variety of effects on flower size, colour, nectar secretion, scent, etc., and also other genes favouring self-sterility, if genes of either of these two kinds existed and ~~are~~ were available for selection. If they are available any improvement in the species, through increase of heterozygotes, may properly be ascribed to these secondary gene substitutions, leaving nothing over to be ascribed to the dominance deviations behind them, for these latter, by themselves, ~~might~~ could produce no effect whatsoever on the evolution of the species; but a change in the attractions offered to insect pollinators, or an improvement in a self-sterility mechanism, would constitute such an evolutionary change.

My point here is that there is no quantitative relationship between the dominance deviation of the numerous effects first mentioned and the rate of evolutionary advance; but there is a quantitative relationship recognizable as speci~~fic~~fied in what I call the 'fundamental theorem', between the genetic variance in fitness to survive due to genes ~~all effects~~ capable of influencing the frequency of cross-pollination.

Equally it should be noticed that external features of the specific environment, such as an increase in the numbers of particular species of insects, or a meteorological change favourable to wind pollination, is capable of raising the specific average through increasing the ~~population~~ proportion of heterozygotes without any evolution being ascribable to the plant species.

Due to all this I am completely puzzled by the statement in your letter that the rate of evolutionary change may be equated to the total variance rather than to the genetic component of variance as I had done. I imagine that by 'total variance' you mean to include the dominance component and the total of epistatic components, but perhaps not the environment components in the actual variance. For my own part I think these are all in the same boat, even the last, for an environmentally induced variance in fitness, i.e. incapacity to leave a remote posterity may, like the others, induce selection in favour of genes capable of enabling the organism to secure for itself an environment of the desirable type, and this, it seems to me, is exactly what happens as a consequence of the other non-genetic but genotypic component of variance.

I have started working lately on a book on inductive inference, partly because I think real progress can now be made in this subject, and partly to dissipate the clouds of opacity arising from Berkeley.

I am returning your paper in case you would care to