IOWA STATE COLLEGE
OF AGRICULTURE AND MECHANIC ARTS
AMES, IOWA

STATISTICAL LABORATORY

February 10, 1955

Sir Ronald A. Fisher
Department of Genetics
44 Storey's Way
Cambridge, England

Dear Sir Ronald:

I was very gratified to receive your long letter about my manuscript.

Before taking up this matter, I would like to say that I was very heartened by your remarks on inductive inference. Your new work on inductive inference will be eagerly awaited, not only because it will undoubtedly be of great interest but also because it is badly needed. I am in entire agreement with your remark about Berkeley. I flirted with the Neyman-Pearson ideas of "inductive behaviour" some years ago but have for some years felt their inadequacy and misleading aspects. I have felt for some years that fiducial inference perhaps modified slightly will be shown to be good. The whole trouble it seems to me is that Neyman and the decision function people following him ignore completely the fundamental job of statistics which is the evaluation of data.

Returning now to the manuscript I sent you, I would be very grateful if you can give me some clues on your 1941 paper and on your letter. You do not agree with my statement that you showed that the change in population mean is $2\Delta P\alpha$ only if the quantity Q^2/PR remains constant. It seems to me that my statement is in agreement with yours on page 56. "If λ remains constant the actual change in the mean or total measurement in constant environment will be that due to change of gene ratio only" and just below "If, in fact, the value of λ changes, the change in population mean will differ from that ascribable merely to the change in gene ratio and this whether the change in λ is due to the change in gene ratio or to other causes". Perhaps my statement gives a change in emphasis that you do not favour.

I have gone through the early part of your 1941 paper again and I have no difficulty following until you state on page 54 "--- we are concerned only with those changes of genotypic frequency directly consequent on the proposed change of gene ratio, in the actual conditions of the population ---" I do not see here how one can determine what changes in genotypic frequencies are attributable directly to the change in gene ratio. Also I cannot see how "The direct mathematical measure of the average effect of a gene substitution is the partial regression-". It seems to me that regression coefficients or partial regression coefficients are useful only for making predictions of individuals within the population and not for estimating effects of changes unless the predicting equation is also a functional one giving the effect in terms of determining variables exactly.

On page 55 at the bottom you state, "If the increase of G genes is distributed so as to give an increase of GG homozygotes,

$$dP = \frac{P(Q+R)}{P(Q+R)+R(P+Q)} \; dp$$

the decrease of gg homozygotes will be

$$-dR = \frac{R(P+Q)}{P(Q+R)+R(P+Q)} \; dp$$

----". I do not see how you conclude that "the decrease will be etc".

I have no doubt about your being correct. The greatest tragedy in genetics I feel is that your work has not been understood. I am hoping that I will be able to dispel this to some extent. Otherwise I would not have the temerity to expect you to spend some of your time on my queries.

I can accept the statements in your letter about secondary gene substitutions in that if the dominance deviations favour heterozygotes and hence favour secondary gene substitutions, then the resultant effects should be attributed to the secondary gene substitutions and not to the dominance deviation. However, would your thesis be at <u>all</u> dominance deviations are ascribable to secondary gene substitutions? If so then the Malthusian parameter m would be entirely additive with respect to gene effects and the variance in m would be entirely additive. In that case there would be no conflict between my result which equates the rate of increase in fitness to the total variance in fitness and your fundamental theorem.

I cannot quite understand the main paragraph on page 3 of your letter, in that you seem to state that all variance in fitness, including an environmentally induced variance, would contribute to the rate of increase of fitness. My result was just this, but could not presume from your letter that you accepted my result.

I shall be most grateful for any clarification you can give me.

Sincerely yours,

Oscar Kempthorne

Oscar Kempthorne
Professor

OK:vrs