18 May 1934.

Dear Mr. Mather,

TThank you for your long and interesting letter, which has quite confirmed the recommendation of your ability which I had from Winge. I have now no hesitation in offering you the appointment, if you can give me a firm answer at once, so that I can get the business through with the College authorities.

About Sewall Wright, he has changed his ground so frequently since I first published on Dominance in 1928 that I am not quite sure what his alternative theory is supposed to be. After all I suppose that a theory must always be an attempt to deduce some admitted phenomenon, which is regarded as requiring explanation, from causes, the working of which is supposed to be understood. Wright makes a good many general assertions, many of them quite acceptable, but I cannot disentangle any coherent theory from them. This may be because I am still occasionally trying to work in points of view which he has now abandoned.

It is quite obvious that in a chemical reaction one ingredient may be present in excess, in the sense that small variations in its amount have very little effect on the speed of t the reaction, while a large diminution of it would slow the reactio down. That this is probably the case with the products of s ome

genes is shownby Stern's "bobbed" allelomorphs. It is a relatively obvious way of producing dominance against mutations which partially inactivate the mutant genes. It might, as far as my theory is concerned, be the only mechanism by which dominance is produced, though I do not imagine that this is so. But if this were so, the occurre nce of dominance would be just as much inneed of explanation as if dominance were produced by some other mechanism. For the fact that one component of a reaction is present in excess implies that its speed is regulated by other components, and that mutations affecting these, if they occurred, would not show dominance, whether the mutation reduced the activity or enhanced it. On the theory of components in excess we should have to say that the organism had been so modified that the speeds of all biochemical processes were regulated only by the products of genes incapable of mutation.

Actually I think Rasmussen's case and much of Wright's argument turns on the very well authenticated fact that the wild type is much less variable than are the mutant types. This seems a good fact of observation which can be understood if modifiers have been worked into a system of checks and counter-checks to stabilise the normal course of development, but which naturally fail when development is in any important degree abnormal. I am not at all unwilling to regard dominance as a particular case of this more general phenomenon, but I am quite unwilling to say that we understand this general fact except as due to an evolutionary

process by the selection of modifiers, or that it is available on its own merits as an explanation of the particular case offered by dominance.

Some time I should like to hear in more detail how your system works for explaining the recessive suppressors. If I have your theory right it involves, in one link of a chain, a recessive mutation which decreases the speed of reaction and in another link a recessive which increases the speed. Tell me how this last can be so if inactivation is the simple explanation of recessiveness.

On the partially dominant mutations in Drosophila you have listed all the explanations except the one I give, which is that they reduce the viability of the heterozygote so greatly that the process of modification is exceptionally slow and even its first stage is not completed. They are as, indeed, you mention in your letter, an exceptionally inviable lot, and relative viability is, in fact, extremely influential on the rate of modification. But there are other large unknown factors which prevent one from laying down absolute rules, of which one of the most important is the frequency of the heterozygote in the wild population. In respect of recessive mutation these frequencies seem to be turning out to be surprisingly high, and I have no doubt that Harland is right in suggesting that this is often due to the heterozygote being actually at a slight selective advantage, though he does not seem to see that the more frequent

they are themore rapidly will the modifers be selected. It was not Harland, by the way, who saw the importance of the behaviour of crinkled dwarf to the Dominance Theory; but Hutchinson's who was at that time, his assistant. Hutchinson's verbal account of the material have always differed somewhat from Harland's, who who has never been very willing to admit, as I think in time he will have to, that Huhchinson was right about it from the start. His published papers are always more intelligently read as though they were arguments with Hutchinson than as though they were discussions of the views I have put forward. I doubt if he knows what I have and have not said on the subject.

Yours sincerely,