

June 13, 1942

Dear Mather,

I am exceedingly glad you have undertaken this big paper in exposition of what I used to call cumulative factors, especially because we are now at a turning point in the development of Genetics, and your paper may well make many people aware of this who would not be otherwise. Of course it cannot by itself produce a revolution, such as to make all the pottering research throughout the world which is financed for animal and plant improvement, into real quantitative genetics; but it may well be an important step.

As a whole, the paper is expository and stimulating, so that at a good many points I feel, as perhaps you do, that a more critical and analytic approach will also be necessary. I have jotted in the margins a few queries and suggestions.

The finding of abundant recessives in natural populations by inbreeding could have been predicted from the early Drosophila work, but I think it was not. I suppose Dubinin and Timofieff (were they working together?) were the first to do this. I think you should mention Gammerus as an early example carried out by Spooner at Plymouth, though inspired by Ford, who could probably give you a reference to anything Spooner published.

Huxley used the word <sup>clines</sup> ~~clines~~ in a very wide sense. I think he

would include purely environmental differences due to a temperature gradient, as well as various genetic possibilities. In this connection I do not see that polygenic balance in itself explains the stability of polymorphic genes, though modifying factors are obviously important in the different function of controlling the evolution of two or more forms when any important factor is stable, just as both they and environmental factors may control the equilibrium ratio, so as to make it change from district to district.

In respect of the distinction or definition of polygenes as opposed to recognisable factors, should they not be defined as having effects small compared with the total fluctuating variability, rather than with that component of it which is due to environmental variation? A factor making 1 inch difference to human stature would, as things stand, involve a ~~parallel~~ parallelomorphic pair of polygenes, though current environmental fluctuation probably rarely has so large an effect. It is an advantage, too, that the total variance is measurable directly, while the environmental component is not so easy to get at.

I find myself rather sceptical, especially about the last section on breeding systems. I do not see that natural selection will lead to a system controlling the amount of outbreeding in such a way as to make an ideal compromise between current adaptation and adaptability for future use. I think one can say that existing plants have managed to persist in the recent geologic past through long periods of stable conditions and through relatively violent changes. To this extent it is intelligible that the breeding systems they exhibit should, when viewed as a whole, show features

which have helped them in survival. But the contemporary plant does not know whether the last four glacial episodes are going to be followed by four more, or whether Europe is to experience a long period of Pliocene tranquillity. I should say, rather, that many existing plants should be expected to be so ill provided with adaptability that they will probably be exterminated if any extensive changes occur, and that other plants will equally be exterminated, more especially the rarer species, if things remain for long as they are. There is no absurdity in saying that most species, both of animals and plants, are, in fact, heading for extermination, and that only a minority will leave any very remote posterity. I think your last section gives a quite unwarranted impression that the current breeding systems to be observed will somehow see most species through. I don't think this is so, and I don't think natural selection of polygenes would explain it if it were. The *homostyle* *primula* seems to have established a local equilibrium at about 80%. It must, I suppose, have spread, and I should much like to know if it is still spreading. Either way to the benefit of whom?

About the cave animals I must put in a claim. I am sure it was I who suggested to you that the intense selection which must have been needed to develop in a short time the rather elaborate feelers and tactile mechanisms that so many of them have, was a potent cause in upsetting the genic balance needed for any structures, such as the eyes, not protected by selection. This is an effect to be expected from multifactorial linkage, and if the experiment of keeping *Drosophila* in the dark ~~for~~ for 200 generations had been

accompanied by really intense selection for, let us say, scutella bristles, perhaps an experimental demonstration could be obtained of it. This, at least, seems a line worth thinking of.

In places in your paper I got the impression that you were ignoring the independent inheritance of different chromosomes through stressing the importance of linkage in each. This might be worth bearing in mind when you give your paper its final recension.

I do think what you are doing is most important and deserves all the care you can spare to it.

Yours sincerely,

paper returned.