

21 December 1931.

Major L. Darwin, Sc.D.,
Cripps's Corner,
Forest Row,
Sussex.

Dear Major Darwin:

Many thanks for your letter and for sending me Mrs. Barlow's paper which I had not before seen. If I may, I will keep it by me until I can compare it with a later paper by East who has worked out a more complicated system, which he seems to be quite confident of, though it does not everywhere seem to tally very well with Mrs. Barlow's data. His scheme involves, like hers, a single factor, A, which distinguishes short from long- and mid-styled plants, but the difference between mid and long he ascribes not to a single factor but to two factors, both lethal, one or the other or both of which will turn a plant from long to mid. Moreover, these two lethals are in his scheme somewhat closely linked, with the result that there are in all ten possible genotypes, one of which is long, four mid-styled, distinguished according to whether the plant has one, or the other, or both in the same chromosome (coupling), or both in opposite chromo-

somes (repulsion), and five short genotypes corresponding to both the long and the mids with the addition of A.

The close linkage of the two lethals, giving apparently only about 10 per cent. recombination aroused my curiosity, and I thought it must have an evolutionary significance. You see I am suspecting that Natural Selection will have left its traces on linkage as well as on dominance. So I thought it worth while to work out the proportion of the numbers of the different genotypes arising from the 29 legitimate types of mating, assuming, what is quite possibly inaccurate, equal viability and fertility for all genotypes and thence finding at what frequencies a population mating according to the rules would come to an equilibrium. It seems to me proper to ignore differential viability and fertility at this stage, partly because it would be almost impossible to obtain data on these points appropriate to the wild conditions except indirectly by comparison with the consequences of the simpler theory, and partly because this theory might itself suggest ways in which the system might be led to depart from the simple condition of equal viability and fertility.

The existence of a condition of equilibrium is ensured, if we can ignore illegitimate unions, by the fact that if any one style type is exceptionally rare each plant of it will have to do more than its normal share in pollinating

the other style types, and so will be at a selective advantage and increase in numbers, until equilibrium is reached, and this works fairly rapidly; I mean that you could start a colony in almost any proportion, provided all the necessary genes were present, and in fifty generations there would be only very trifling departures from the equilibrium proportions.

The lethal genes are always tending to die out, for whenever two of the same kind meet the zygote is inviable. Consequently the number of mid-styled plants must be depressed in order to give the lethal genes which they contain a compensating selective advantage. It will be sufficient to do this if, out of a thousand plants, the population contains 377 long-, 283 mid-, and 340 short-styled. Of the two lethal genes the more numerous will be at a greater selective disadvantage through the elimination of homozygotes, but they will share the same selective advantage, due to the comparative rarity of the mid-styled type, and consequently will come ultimately to be equally frequent. I find, leaving out decimals, that the 283 mid-styled will be made up of 135 each for the two single lethals, 6 for the double lethal coupling, and 7 for the double lethal repulsion; while the ³⁴⁰ short types will be 221 non-lethal, corresponding to the long-styled, 54.9 each for the single lethals, only 2.6 for double lethal coupling, and 6.6₁ double lethal repulsion. These are the proportions which would exist at any one time in the wild population, when a state of equilibrium had

been reached, under the assumed rules of legitimate mating. The counts quoted by your father do not suggest that the mid-styled are in fact rarer than the long-styled, at least not in so high a ratio as 3:4, and it may well be that the higher fertility which he found for the mid-styled as seed-parents, though compensated by an apparently lower fertility as pollen parents, may be a further compensating mechanism, which brings the numbers closer to equality, than they would be on my simplified assumptions. However, that may be, one may first follow out the consequences of these assumptions somewhat further. For though the numbers I have given represent the frequencies of plants in a population in equilibrium, yet, owing to their unequal frequency of parentage they will not represent the proportions they contribute to a remote future generation. One can see this even in the first generation for the 377 longs will become the parents of 720 plants of the next generation, which counts only 360 to their long parents; and the final reduction will be somewhat greater than this, because these 360, though comprising all style types, will yet contain more than the normal proportion of longs. My next stage was therefore to work out the reproductive value of each of the ten genotypes, in the sense of its probable contribution to the ancestry of a remote future generation. Thus a thousand longs I find to be worth about 950. Of the middles, 1000 of either single

lethal kind is worth about 1673. A thousand of the double lethals in coupling is worth 1080, and 1000 of the double lethals in repulsion is worth 1121. Similar figures with smaller differences are found for the five short types.

The point that I think matters is that, whereas the introduction of a single lethal increases the value by 123 per thousand, and a second lethal in repulsion increases it further by 48, yet the extra lethal if introduced in the same chromosome, (coupling), is only worth 7. Consequently it is advantageous to get what lethals you have into different chromosomes, and ^{to} keep them there; which can be done by tightening up the linkage. The amount of linkage only affects the progeny of the four rare double heterozygotes coupling and repulsion in mid and short, which together constitute only 22 per 1000 of the population. Moreover for the coupling plants looser linkage will be desirable as enabling the two lethals to get separate, while, in the slightly more numerous repulsion plants, tighter linkage will be desirable in order to keep them from getting together. The net selective advantage may be found by working out the increased value of the progeny of each of these double heterozygotes in each of its possible matings, and striking a balance. Thus a 1 per cent. change in linkage intensity, say from 10 to 9 per cent. recombination, gives a net advantage of 5.9 per million from the repulsion plants against a net disadvantage of 4.1 per million for the coupling plants, or

a balance of 1.7 per million, measuring the selective advantage which such a change would enjoy.

For aught we know this tiny selective intensity may be unbalanced by other causes, and be slowly tightening the linkage between the two lethals, until ultimately, in the kind of sense in which one speaks in the theory of the moon, they become completely linked, and incapable of being brought together into the same chromosome; in which case they will appear as though they were two lethal allelomorphs of the same gene, whose heterozygote is viable; and on this view we must suppose that selective intensities not much greater have brought them to their present condition of close linkage. Alternatively, this minute selective intensity may be balanced by other causes, and the system ^{may have} now reached the point of balance with those other causes, having been brought to its present condition by the still more minute intensities of its previous unbalance. The only third alternative to these two views is to say that the linkage is a sheer coincidence, and that it has just happened that two mutations having the same effect have happened to occur very close to each other on the same chromosome, and this alternative, as you will guess, I dislike intensely, though one must admit it as a possibility.

One could wish there 10 trimorphic species of Lithrum showing different stages of this lunar process. I wonder if

Mrs. Barlow knows what others sufficiently nearly allied there may be. Anyway, when I can possibly get down to any ^{serious} writing I mean to set the whole thing out at length, and set the Royal Society the problem of deciding whether it is a botanical or mathematical paper!

It was tremendously good of Mrs. Darwin to think of the sweets. They will enjoy them immensely, and I believe Harry has perpetrated a letter on the subject. My wife joins me in good wishes to yourself and Mrs. Darwin for Christmas.

Yours sincerely,

P.S. I am enclosing two recent reprints of mine. The last paper of mine on dominance pulls the thing together much better than I had previously done. I am returning at the same time the two letters you were good enough to let me see from Ford and the one to Freeman.

R.A.F.