Dear Watkin Williams,

Thanks for your note of January 22nd. The effective lethality of homozygotes exerts automatic selection against the commoner alleles. When frequencies are unequal, therefore, the situation must have been produced by selection in their favour.

If you regard the 65 varieties tabled as the result of random union among some population of gametes, therefore, the ratios among this hypothetical population must be higher than those observed in the selected resultant, and the differences appears to give the intensities of the selections required in each generation to maintain such a distribution as you have found.

Yes, the proportions I give are the only ones which could yield the observed gene ratios, and are constructed from the marginal values observed. It was the method of doing so that I called 'unfamiliar' and perhaps so far unpublished in the literature.

The second stage of the problem, namely the comparison of observed with expected genotype frequencies, is a more delicate one, and, though I believe the three favoured genotypes I pointed

to are very significantly more frequent, compared with the others, than could be ascribed to chance, I do not know of any experimental examination of the exactitude of the test of significance based on the analogy of  $\chi^2$ ; but it is a big problem.

Sincerely yours,