September 21, 1953

Dr. P. Armitage
MRC Statistical Research Unit
London School of Hygiene
Keppel Street, Gower St.
London W.C. 1, England

Dear Dr. Armitage:

I was most pleased to note your article on the statistical theory of bacterial mutation in the last Journal of Hygiene. The discussion at this level should be of considerable value to workers dealing with this problem. But perhaps the most impressive conclusion is how unsatisfactory are the estimates determined from counts of mutants. I think there is little doubt that the technique used by Novick and Szilard (as cited by yourself, and in the Cold Spring Harbor Symposium, 1951) is by far the best approach to the measurement of rates.

In teaching this subject to a class with very poor mathematical preparation, I have found it expedient to focus on the "mean clone size", i.e., $y/m = my\ r/aN = d$, and to explain the effects of phenotypic delay, dominance, and assumptions on the mutational model as they influence d. If I interpret you correctly, we are agreed that the least ambiguous unit for expressing rates is the probability of mutation per bacterial division. Many bacteriologists with a rudimentary training in the calculus have had great difficulty with the unit "per bacterium per division". If we can someday find a system in which phenotypic delay can be discounted, it would be worthwhile to test the mutation models by direct estimation of d, e.g. from a Newcombe's type of experiment.

The enclosed sheet may be of doubtful interest to you.

From other lines of work it is possible to get some assurances on the matter of dominance. Almost all of the mutations that have been exploited for rate measurements are recessive, e.g., resistance to bacteriophages, resistance to drugs, requirement for growth factors. However, the "reversions" to nutritional independence (e.g. histidineless to wild type), and from lactose-negative to lactose-positive, are almost certainly dominant. However, too little is known of phenotypic delay and, correlatively, of the extent to which the existing phenotypes of the cells are tested (rather than that of their descendants) to draw a full picture of any of these systems.

If not too much of an imposition, may I enter a request for a reprint of the present paper for class use. I already indebted to you for a past favor and will reciprocate with any of our papers on subjects of mutual interest.