

April 13, 1953

Dr. K. Mather
Department of Genetics
The University, Edgbaston
Birmingham 15, England

Dear Mather:

I am moved to write now partly in recollection of our very pleasant and (to me) fruitful correspondence of six years ago, but primarily from the provocation of Rees & Minks' recent paper in Proc. Roy. Soc. on the mechanism of nuclear adjustment in heterokaryons. It seems to me they have neglected the most likely possibility, namely that hyphae with differing ratios of nuclei are produced by random fluctuations, and that those hyphae with the most adaptive ratios proliferate the fastest. I am writing to you, as their professor, because I am more confident (from past experience) of being able to communicate with you.

Since the linkage analysis, for your help on which I remain indebted, *E. coli* genetics seems to have moved into greater and greater complexity. Despite some current speculations, however, there is fairly explicit evidence that any eliminations of genetic components are post-zygotic. For example, there have been many diploid heterozygotes which, though deficient in the Mal-S segment, have received the Mal allele from one parent, the S from the other (e.g. the Mal+ S^S of table 6A in my 1951 CSH paper). There is still no factual evidence (despite contrary speculation, again) that any agents other than intact cells function in *E. coli* recombination, and we have some hopes (and even some suggestive appearances) from cytological studies in progress. I do not see how selective recovery of prototrophs can play an appreciable role in distorting segregation ratios. Despite minor inconsistencies, which are, by the way less appreciable than the variance for replications of a given cross [which Bailey seems to have overlooked], the ratios from reverse crosses are in too good agreement. Some minor discrepancies may result from competitive suppression, but we have never seen it in reconstruction experiments. The conditions under which most workers have studied reverse mutation in bacteria and *Neurospora*, and their explicit experiments not always mentioned in print, make it unlikely that their results are seriously questionable. However, there was a time when I was emphasizing (perhaps overly) the same point myself, e.g. *Heredity*, 2:162 ff. '48.

With best regards from Mrs. Lederberg,

Sincerely,

Joshua Lederberg
[Associate Professor of Genetics]