June 30, 1953

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Dear Seymour:

It took me three months, but I finally did get to read your me. It is a beautiful job, and I am sure that I have no reservations that you have not already considered.

The most general assumption is the proportionality of lysis time to enzyme content. Have you been able to construct a plausible function of time and lactase content that will fit the observed lysis/time curves? In heterogeneous populations, I would imagine that the initial physiological heterogeneity of the cells would imply a variable behavior both of lactase and of phage formation, without these being necessarily directly dependent on one another. One could ask how the slopes of figure 8B and of 6C and 7C compare on the basis of equivalent specific activity, or rather how the lysis/time curves compared in your original protocols.

Has the change in optical density been related directly to the lysis of cell populations? Doerrmann once described an independent variation of these, based on some alteration of the optical properties of the infected bacteria.

I am a little surprised that the cells grown without inducer are described as completely devoid of lactase. This was not my experience with K-12. What were your measurements on the specific activity of lactate-grown cells? With NPG it should be possible to measure even 1/4000 of the optimal activity, if a somewhat concentrated cell suspension is used to make the extract.

I have never been entirely happy about the interpretation of "activation" by cell lysis, though the most plausible explanation seemed to be the non-permeationnof sodium into the intact bacteria. Let us hope that it turns out to be so simple, or we may not have known what was being measured in all these experiments. Boris Rotman has just started working here (and at the Enzyme Institute) on a fellowship to study just this, and related problems.

Yours sincerely,

Joshua Lederberg