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Dear Tracy:

Thank you very much for your comments on "Genetics, Symbiosis, and the Cell Theory"— now (provisionally)retitled "Cell genetics and hereditary symbiosis".

I am sorry too about the condensation, but am not so sure that I had any more ideas to leave out. The stripping was mostly of further experimental detail of the reviewed work. I would have preferred not to add another word (like plasmid) because I am sure that even if it is adopted, it will soon become encrusted in much the same way as all of the other words. However, I did not dare use plasmagene, or virus, as other authors have to cover the whole range of what I call plasmids, for I think these terms should be saved for their connotations of genetic and pathological functions, respectively. Within your own group, I have no doubt you have built up a firm definition of plasmagene, so that you have no difficulty in communication. In talking to different people whose own usages I have had to adopt, however, I have had a lot of trouble on this point.

Your comments were just the sort of thing I needed: it is rather easy to become myopic about something like this. Re the quotation from Beale, I discávered this distortion independently, and have revised it. I did not intend to deprecate him, but the fallacy itself, which is made all too often by the one-to-oneists. I am glad to have your corrections on the Paramecium details.

I tried to warn you that I had no world-shaking comments on gene-reproduction. The whole question of autonomous reproduction (outside of autotrophic organisms taken as a whole) needs more circumspection than it has had for the most part (viz. much of the yeast work). I hope you and other readers will take quite seriously my disclaimer of any originality. There are very few speculations quite new under the sun in a field like this, and the only function of the review is that of emphasis/ and choice (hence "eclectic").

P. 51: "Absolute unit of what?" is just the point! Too many biologists, geneticists included, have seemed to adopt a rather naive monadic philosophy. But I'll try to sharpen this up! You are quite right about mutabilitybeing conceptually independent of complexity. I had in mind a distinction between all-or-none changes, and multiple alleles. OH^- itself would not satisfy the mutability requirement, at first sight, The one point still debatable has to do with the macronucleus as a plasmid. I have tried to visualize what would happen if the macronucleus were not so prominent microscopically, and one had to rely entirely oh genetic observations. I think that its interpretation as a cytoplasmic system would have seemed plausible for the following observations:

Radiation effects exerted only after autogamy (much of this, of course, could result from dominance, and the role of the macronucleus would be paradoxical only for dominant mutations);

Matroclinous determination under conditions of macronuclear regeneration;

Genetic behavior of amicronucleates (nulloploid vs. diploid);

"Cytoplasmic contamination" under conditions of macronuclear-fragment exchange.

If, eventually, several traits were to be studied together, we would come to realize that the persistent cytoplasmic system (usually re-derived from the nucleus) at each reorganization, was highly organized.

Perhaps at this distance I have overemphasized the significance of macronuclear regeneration. But this looks to me like a possible starting point for even a less organized extra-micronuclear system. It might be worth looking for the possibility of macronucleinderived only partly by regeneration.

I had already taken out the implication of duality of micronuclear and cytoplasmic control in different varietied (this was, of course, from the '46 symposium).

Did you find it amusing to see what an interested student can find from your papers? Outdated interpretations have a habit of persisting,longer than they should (like superfluous macronuclear fragments!)

May I confess that my worst trouble writing this thing was thinking there was not much point to it, since you had already stated a similar case, and you yourself would hardly find anything new in it. But there are a few thousand other readers who may be jolted even by a restatement.

I have saved some of my noted on the condensed sections (e.g. lysogenicity). There may be opportunity (if you think it appropriate) for more elaborate discussions in some chapters of the book GOM. This review has taken much more time than it would be worth for its own sake. However, I did learn a number of things myself, and it provided some opportunity to organize my thinking on "cell genetics", so that I will be a little better able to participate with you on GOM. Sometime soom we should perhaps resolve dome of the general questions of organization.

Thanks for your help on this review,

Sincerely,

Joshua Lederberg