

The Concept of Cellular Evolution

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Summary. A central evolutionary question is whether the eucaryotic cytoplasm represents a line of descent that is separate from the typical bacterial line. It is argued on the basis of differences between their respective translation mechanisms that the two lines do represent separate phylogenetic trees in the sense that each line of descent independently evolved to a level of organization that could be called procaryotic. The two lines of descent, nevertheless shared a common ancestor, that was far simpler than the procaryote. This primitive entity is called a progenote, to recognize the possibility that it had not yet completed evolving the link between genotype and phenotype. This concept changes considerably the view one takes toward cellular evolution.

Key words: Evolution — Ribosomes — Genotype-Phenotype — Cytoplasm — Endosymbiosis — Procaryote — Eucaryote — Progenote

Life on this planet began over three billion years ago (Schopf, 1972). While fossil evidence permits a reasonable reconstruction of its history over the past half billion years, it provides only the barest clues to the earlier events that led to the basic cell type (the "common ancestor") and its initial radiation into the major phylogenetic groups. However, the cell itself is an historical record, and, as the biologist is now beginning to learn, this is far more extensive than the fossil record. Through this "molecular paleontological record" it should be possible ultimately to reconstruct a good deal of early evolutionary detail (Zuckerlandl and Pauling, 1965).

While a lack of facts is certainly the major obstacle at present to an understanding of the evolution of the cell, it is clear that our present, crude understanding of this evolution is rooted in outmoded and ill-defined concepts, and so does not even cope adequately with the few facts that are available.

All speculation as to the evolution of cells starts with the assumption that procaryotes evolved first and then gave rise to eucaryotes, which in one sense must be true. The problem is that various writers do not state explicitly what *they* mean by the

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assumption. The crux of the matter seems to be a failure to define "procaryote" and "eucaryote", terms whose meanings have changed considerably with time. Initially "procaryote-eucaryote" meant an organizational distinction. It conveyed the hierarchical nature of biological organization — i.e. metazoa comprise organs, which are formed from eucaryotic cells, which contain procaryote-like entities (e.g. chloroplasts, mitochondria), and so on. This is not basically a phylogenetic distinction. However, the extensive and detailed molecular descriptions of bacteria and of higher cells that are now given are necessarily phylogenetic. No precise formulation of the evolutionary issue is possible if the phylogenetic and organizational aspects of "procaryote" and "eucaryote" are confused.

From an organizational viewpoint it is evident not only that eucaryotic entities evolved from procaryotic ones, but also that the latter ultimately arose from a simpler, unnamed class of entities. However, this purely organizational picture of events need not lead to the conventionally accepted phylogenetic interpretation of the evolutionary sequence — in which an ancestral procaryote gives rise to a procaryotic tree, from whose branches arise certain species that symbiotically conjoin to produce the ancestral eucaryote, and so on (see Fig. 19.1 in Broda, 1975; Margulis, 1970). What this latter view takes for granted — that there existed but one ancestral procaryote and so a single procaryotic tree, but one ancestral eucaryote and so a single eucaryotic tree — is in fact a central and unanswered question.

We would here explore one of the more important facets of this question, the origin of the eucaryotic cytoplasm. The cytoplasm appears to represent the "engulfing" species in the endosymbiosis that is the eucaryotic cell. Its characteristics are sufficiently non-bacterial that some writers have expressed reservation concerning its relationship to bacteria (Stanier, 1970). Nevertheless, the free-living ancestor represented today by the cytoplasm must at some point (before the evolutionary additions of organelles and similar structures) have been a procaryote in the *organizational* sense, — i.e., it was a level simpler than an eucaryotic cell. The question is whether, this ancestor arose from the same phylogenetic tree as did typical, i.e. bacterial procaryotes. For the reasons to be given we feel the eucaryotic cytoplasm came from a line of descent that achieved procaryotic organizational status independently from the typical bacterial line. If this be true then we must revise those attitudes concerning eucaryote evolution that are based on the preconception that the cytoplasmic component arose relatively late in the evolutionary scheme from the bacterial tree, just as the organelles seem to have done.

Discussions of cellular evolution tend to take for granted the nature of the "gene". This is a serious mistake, for at least in its early evolutionary stages the nature of the cell is shaped by the nature of the linkage between genotype and phenotype. Indeed, to a large extent the evolution of the cell is the evolution of the genotype-phenotype relationship. Although we possess no direct knowledge as to its evolution, certain of the properties of the translation mechanism permit us reasonably to infer characteristics of its evolution. The translation apparatus is very large and complex by standards of molecular automata (Haselkorn and Rothman-Denes, 1973). There can be only one reason for this; its size is essential to the accuracy with which the mechanism functions. There exists a direct correlation between the "size" of an automaton — as measured roughly by number of components — and the accuracy of its function (Burks, 1970).

We then infer: (1) that the evolution of the translation apparatus occurred in a series of increasingly complex stages, rather than all at once, and then (2) the stages subsequent to the establishment of the basic mechanism were concerned by and large with increasing the mechanism's accuracy, and possibly speed as well (Woese, 1970).

It is difficult to overestimate the effect on the nature and evolution of the cell that an appreciable translation error rate (a noisy genetic transmission channel) would have. The primary constraint would be on the size and properties of the proteins that could be evolved. This in turn would delimit the specificity of *all* of the cell's interactions. In addition, genome sizes would be considerably smaller than they now are – because they are limited by mutation rate, which is a function of the proteins involved in gene replication. It is fair to say that the cell as we know it today would not exist. Such organisms would necessarily be on a level of complexity far simpler than the procaryotic. Organism of this type, in the throes of evolving the genotype-phenotype relationship, are properly designated *progenotes*.

The question of whether the eucaryotic cytoplasm arises from the same phylogenetic tree as do the typical bacteria, then amounts to asking whether or not their respective lines of descent diverged at the progenote stage. Were two cell lines to diverge at this stage, they would exhibit particular types of differences. All those features which in the progenote were not yet evolved or incompletely so, would be separately fashioned in the two lines of descent. The class of problems having to do with storage and processing of large amounts of genetic information would have been met and solved independently. Thus, genome organization, control hierarchies, (some) repair mechanisms, certain enzymes involved in DNA replication, should appear quite dissimilar in the two cases. Likewise, those aspects of translation having to do with the final "fine tuning" of that mechanism would appear idiosyncratic. The more (functionally) subtle of the ribosomal proteins, patterns of base modification in the RNAs, the detailed aspects of initiation and termination, and so on, would seem dissimilar.

A detailed comparison of eucaryotic and procaryotic translation mechanisms does indeed reveal differences of this sort. Within each group one finds a considerable constancy of structure-function; which tends to disappear when the two groups are inter-compared. Some examples are these: Bacterial ribosomes and ribosomal RNAs are of one size; their eucaryotic counterparts are larger (Wittmann, 1970). Bacterial ribosomal RNAs all exhibit considerable sequence homology among the various species, as do eucaryotic ones; sequence homology between the two groups is far less (Woese et al., 1975; Pace and Campbell, 1971). The bacterial 5S RNA exhibits a constant structural feature, the "procaryotic loop", which has no counterpart in the eucaryotic 5S RNA (Fox and Woese, 1975), and the eucaryotic 5.8S RNA appears to have no counterpart in bacteria (reviewed by Erdmann, 1976). The patterns of base modification in the two types of ribosomal RNAs have little in common (Maden and Salin, 1974; Sogin et al., 1972); it is interesting to note several examples wherein homologous sequence segments in the bacterial 16S and eucaryotic 18S rRNAs are modified, but the modifications are unrelated (Woese et al., unpublished). Each group exhibits characteristic antibiotic sensitivities (for an introduction see Pestka, 1976). It is well known that interchangeability of parts of the translation apparatus among species is the rule within each group, but between the two group many exceptions to the rule exist (for a review see Woese, 1970; also Bellemare et al., 1973; Wrede and Erdmann, 1973; Nomura et al., 1968).

Customarily the differences between the eucaryotic and the bacterial versions of the translation apparatus, if explained at all, are explained in either of 2 ways: (1) The eucaryotic mechanism arose from the procaryotic one and underwent substantial modification due to the requirements of the emerging eucaryotic cell; or (2) The divergence separating the two cell lines is very ancient (compared to divergences within each group), so that time alone (as measured by a mutation rate) explains the differences. Although neither alternative can be disproven at this point for obvious reasons, both are suspect and will ultimately, we feel, be ruled out. The first seems to demand some basic variation in the translation process that confers a selective advantage. It is not clear, however, what this would be. The second rationale is at very least not straightforward: Bacterial ribosomal phenotypes have been basically constant for about 3 billion years (the age of blue-green bacterial fossil evidence — which implies that bacteria had diverged from one *another* by this time) (Schopf, 1972). The divergence of the bacterial from the cytoplasmic line of descent could not have antedated this by more *one* billion years. Thus unless the tempo of evolution were faster at the earlier time, the large number of bacterial-cytoplasmic differences cannot be rationalized. We feel it more reasonable, of course, to assume the mode, not the tempo, of evolution to have changed; the bacterial-cytoplasmic differences reflect the independent evolution of the final, “fine tuning” aspects to translation, after which the functional character of the translation mechanism remained constant, and idiosyncratic, in the two lines of descent.

The possibility that the bacterial and cytoplasmic lines of descent diverged at the progenote stage has subtle but profound conceptual ramifications. Indeed the whole quality of how one perceives cellular evolution is changed thereby. Let us look at a few examples:

1. *The Concept of an “Age of Procaryotes”*

It must be the case, as stated above, that the evolution of the procaryote necessarily preceeded that of eucaryotes. This is true only in an organizational sense, however, in the sense of a simple, procaryotic type of organization arising before the more complex eucaryotic type did. To give the concept a phylogenetic interpretation would (and has) generated the notion that there occurred a primeval “age of procaryotes” a 1–2 billion year period before eucaryotes could begin when bacteria flourished and their major lines of descent were established. From the present viewpoints, however, the line of descent of the eucaryotic cytoplasm would be contemporaneous with the common ancestor of all typical bacteria. Accordingly there would then be no need for the onset of eucaryotic evolution to await the establishment of the major branches of the bacterial phylogenetic tree. There would be no protracted “age of procaryotes”.

2. *The Procaryote-Eucaryote Gap*

Vast differences exist between “procaryotes” and eucaryotes in terms of their genome organization. Although no intermediate types are known, this situation is conventionally seen as representing a gap that was somehow spanned in evolving the former type into the latter. However, this is not a gap spanned by an evolutionary jump; rather it

is a gap created by the fact of genome organization evolving separately in two lines of descent from a *far simpler* common ancestral type of genome organization.

3. *The Nature of Endosymbiosis*

Endosymbiosis is customarily seen as arising when some particular bacterial species lost its wall and then gained a capacity to take in other organisms (Sagan, 1967; Margulis, 1970; Nass, 1969). Such a view makes endosymbiosis a relatively recent and rare occurrence. However, if the cytoplasmic line of descent evolves separately and contemporaneously with the bacterial line, endosymbiosis should probably be considered an aboriginal, not an acquired trait (Stanier, 1970); right from the beginning it would have constituted a major interrelationship between the bacterial and the "cytoplasmic" lines of descent, a relationship whose ubiquity, variety, and full evolutionary impact have yet to be appreciated.

4. *The Uniqueness of the Eucaryotic Cell and of Its Evolution*

It is generally assumed that the eucaryotic cell is evolutionarily unique because of the unlikelihood of the series of events that led to its formation (Margulis, 1970). This uniqueness, this improbability, lies in the paradigm, however, not in the actual situation. If eucaryote evolution is seen in the progenote context, then endosymbiotic events and the like are normal, common occurrences. Consequently, the eucaryotic cell is a condition that could and should have arisen more than once. It also appears that the conventional view of the eucaryote as an aerobic cell containing mitochondria, flagella, and so on, is too restrictive. The "eucaryote" is a general condition, that covers a wide variety of integrated endosymbiotic interactions, not necessarily aerobic, and whose evolution is not necessarily confined to the aerobic phase of the earth's history.

5. *The Predecessor of the Eucaryote*

The context here developed hypothesizes an aboriginal line of descent one of whose manifestations is the cytoplasm, the body, of the eucaryotic cell. A question implicit in this is whether the "pure" form of this organism — i.e. an ameboid anerobic entity free of organelles and the like — exists today. It would probably be recognized as an "anaerobic eucaryote". Entities suspiciously like this do of course exist; in fact, they are common inhabitants of anaerobic environments (Hungate, 1967). The question is whether or not they are fundamentally, aboriginally, anaerobic. The question remains unanswered largely because this particular class of organisms is perhaps the least investigated of all, and this in turn because the concept of an anaerobic eucaryote as distinct from, not derivative of, aerobic eucaryotes is today unrecognized (Stanier, 1970). The best characterized example of an anaerobic "eucaryote" is *Pelomyxa palustris* (Bovee and Jahn, 1973). The organism does not possess mitochondria (but does contain procaryotic endosymbionts), does not perform mitosis or develop spindle fibers, does not manifest the 9 + 2 fibrillar structures and lacks Golgi membranes.

In summary, the conventional concept of cellular evolution — in which the *procaryote* evolves first and eucaryotic cell subsequently arises from (a confluence of) certain branches of the procaryotic phylogenetic tree — appears not only ill-defined,

but wrong in its implications. Eucaryotes did arise from procaryotes, but only in the sense that the procaryote is an organizational, not a phylogenetic distinction. In analogous fashion, procaryotes, arose from still simpler entities. The latter are properly called *progenotes*, because they are still in the process of evolving the relationship between genotype and phenotype. It is at the progenote stage, not the procaryote stage, that the line of descent leading to the eucaryotic cytoplasm diverged from the bacterial lines of descent. This simple realization drastically alters the way in which we conceive the process of cellular evolution.

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