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Review article

Symbiosis and Disciplinary Demarcations: The Boundaries of the Organism

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Abstract

Here I explore three interrelated questions: What is symbiosis? How is its study situated in the history of biology? What is the role of symbiosis in the origin of new organisms? I begin with the contemporary conceptual consensus about symbiosis in evolution. I proceed to situate studies of symbiosis within the complex matrix of biological specialization, and offer a broad sketch of the phenomena, movements, debates, concepts and metaphors that have shaped ideas and attitudes about its scope and significance. In reviewing them here, we see that a series of disciplinary aims and doctrines confronted the study of symbiosis in evolution.

The emphasis on conflict and competition in nature, which many critics argue is merely a reflection of dominant views of human social progress, opposed studies of symbiosis. The overwhelming interest in the disease-causing nature of some microbes meant that most biologists were concerned with killing them, or using them as technologies for genetics and biochemistry rather than understanding their behaviour and ecology. The synthetic nature of symbiosis and interdisciplinary nature of studies of cell origins confronted ever-increasing specialization such that few felt competent to properly assess such research. Specialization also posed difficulties for reaching consensus about what counts as an "individual". Finally, until recently, studies of the role of symbiosis in cell origins struggled under the charge of speculation and metascience.

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1. Symbiosis in Contemporary Historiography

Beginning in the 1960s, in the midst of the triumph of molecular biology, a so-called "quiet revolution" in our understanding of ourselves took place. Our evolution, and that of all plants and animals, is not due solely to the gradual accumulation of gene changes within species. We evolved from, and are comprised of, a merger of two or more different kinds of organisms living together. Inside each of our cells are organelles called mitochondria which are responsible for generating metabolic energy using oxygen. Mitochondria have their own DNA, RNA and ribosomes distinct from that of the chromosomes in the cell nucleus. They are now generally held to have originated as symbiotic bacteria some 2000 million years ago (Dyer and Obar, 1994).

The energy generating organelles of all plants, chloroplasts are also derived from independent, self-replicating lodgers: cyanobacteria, formerly known as bluegreen algae. Like mitochondria, chloroplasts have their own DNA, RNA and ribosomes. Similar ideas of bacterial origin have been proposed for the origin of the cell organelles concerned with motility and cell division: cilia and centrioles (Margulis, 1993). Contemporary symbiosis researchers are further urging evolutionists to reconsider other forms of symbiosis as representing a general macro-mechanism for the origin of species (Margulis and Fester, 1991; Saffo, 1991).

Historians have analyzed the ramifications of Darwinism and metaphors of natural selection and "the struggle for existence" in both technical and social contexts. But, in all of their rich and detailed analyses of evolutionary debates, symbiosis as a source of evolutionary novelty is virtually never mentioned. Symbiosis is not included in the historical literature devoted to neo-Lamarckism and the inheritance of acquired characteristics; nor can one find it in historical writings on evolutionists who advocated a role for macromutations in the origin of species. The role of symbiosis in evolutionary change is also absent in historical studies about mutual aid (Todes, 1989) and cooperation in ecology (Mitmann, 1992). This absence reflects the diffidence about symbiosis on the part of biologists themselves.

Yet, the view that symbiosis is a major source of evolutionary novelty paralleled the development of Darwinian theory (Sapp, 1994). The suggestion that symbiosis is a mechanism of evolutionary change was made the moment the term symbiosis was introduced. The possibility that all plant and animal cells had evolved in the remote past from symbiotic associations of two or more different organisms, representing nucleus, cytoplasm, chromatophores, and possibly centrosomes, was discussed by several individuals soon after (Watasé, 1893; Wilson, 1896; Schneider, 1897).

That symbiosis could lead to evolutionary change and the construction of new "individuals" was inferred from associations of algae and fungi in the formation of lichens, of photosynthetic algae in "lower animals", of nitrogen-fixing bacteria in the root nodules of legumes, and fungi in the roots of forest trees and orchid bulbs. From the late 19th to the late 20th century, the scope and significance of such relationships were rather discontinuously debated. At one extreme was the view that such cases were illustrative of evolution in action: how "higher", more complex organisms could have evolved from "lower" simpler ones. Accordingly, there was a range of intimate relations between species, from parasitism to those in which associates mutually furthered and supported one another. A temporal continuum of dependency from transient to permanent interdependence was also recognized.

But many biologists insisted that stable and permanent interspecies integration were exceptions to normal life. These infrequent curiosities only served to detract from proper biological aims and interests. Interpretations of mutual assistance could be dismissed as mere sentimentalism. As Roscoe Pound wrote (1893):

> Ethically, there is nothing in the phenomena of symbiosis to justify the sentimentalism they have excited in certain writers. Practically, in some instances, symbiosis seems to result in mutual advantage. In all cases it results advantageously to one of the parties, and we can never be sure that the other would not have been nearly as well off, if left to itself.

Contemporary symbiosis researchers record anecdotes about how their intellectual predecessors were ignored by an unappreciative scientific community in Germany in the late 19th century, Andreas Schimper (1883) and Richard Altmann (1890) respectively proposed that chloroplasts and mitochondria were symbiotic lodgers inside cells. In Russia during the first decades of the twentieth century, the idea that chloroplasts were symbionts was developed by Andrei Famintsyn (1907, 1912) and by Konstantine Merezhkovskii (1905, 1910, 1920) who coined the neologism, "symbiogenesis" for the synthesis of new organisms from symbiotic unions. Merezhkovskii also developed the idea that the nucleus and cytoplasm represented symbiotic microorganisms. In France, Paul Portier's development of the idea that symbiosis was a universal phenomenon culminated in his book, *Les Symbiotes* (1918), in which he argued that mitochondria had originated as symbiotic bacteria and that symbionts played an essential role in the physiology and development of all organisms more complex than bacteria. His argument was based on the morphological and physiological similarity of bacteria and mitochondria as well as on evidence that such transitions from occasional to permanent symbiont were known to occur.

In the mid 1920s, the French-Canadian bacteriologist, Félix d'Herelle discussed the perpetuation of mixed cultures of bacteriophage and bacteria, or lysogenic bacteria as symbiotic "microlichens". The transformations associated with such phage resistant bacteria as well as other examples of transformations accompanying symbiosis in plants, studied in France encouraged him to believe that symbiosis was largely responsible for evolution. In d'Herelle's words (1926) "symbiosis is in large measure responsible for evolution".

Morphological effects of microbes, inherited and transmitted through the egg of host insects were discussed by the leading German symbiosis researcher Paul Buchner, and popularized in his books (Buchner, 1921, 1965). In the United States, Ivan E. Wallin (1927) proposed in his book, *Symbionticism and the Origin of Species* that the inheritance of acquired bacteria represented the source of new genes and the primary mechanism for the origin of species. Based on intracellular reproduction of mitochondria and their staining properties, so similar to those of bacteria, Wallin argued, like Portier before him, that mitochondria originated as symbiotic bacteria. He emphasized the importance of symbiosis as generator of new tissues and new organs. However, the role of symbiosis in evolution advocated by these individuals was either ignored, ridiculed or rejected. It was not until the 1960s and '70s, with the discovery that cell organelles possessed their own DNA's, that such ideas were taken seriously by mainstream biology.

2. The Untamed Word

Although few biologists would deny that he or she knows what symbiosis means, one finds no consensus in the definition (Saffo, 1992; Sapp, 1994). The term symbiosis was actually coined twice: by Albert Bernard Frank (1877) and again by Anton de Bary (1879) who is generally credited with defining symbiosis as "the living together of dissimilarly named organisms". The term was used by both authors to refer to other relations besides parasitism. It was meant to embrace mutualistic relations (as of benefit to both partners), as well as parasitic ones. Since then, many biologists have limited "symbiosis" to mutual benefit between associated species (Caullery, 1951; Lewin, 1982). Yet, others have argued that this narrow meaning of the term is difficult, if not impossible to apply to real associations (Meyer, 1925; Smith and Douglas, 1987). While some have applied the term to relations between individuals (Dawkins, 1976), others insist that it be restricted to interspecies relations (Lewis, 1985; Saffo, 1992). Still others have limited it further to apply only to relations between species which remain in physical contact throughout most or all of their life (Margulis, 1990, 1991). This imprecision in the semantics is by no means a "fault" confined to symbiosis. One can find the same multiplicity of meaning in many central terms and expressions in science. Species, heredity, gene, "the struggle for existence" all have had multiple meanings.

Despite scientists's intentions to invent technical terms that are untainted by the vagaries of ordinary language and cultural contexts, historians, philosophers and sociologists of science have come to recognize that such ideal language devoid of multiple meanings is, in fact, remote in practice (Keller and Lloyd, 1992). Change in meaning may occur consciously or unconsciously, accompanying the shifts in paradigms that we associate with scientific revolutions. Moreover, in so much as these conceptual modifications are not monolithic, meanings do not simply change but actually accumulate. Different meanings may also reflect different usages – to describe phenomena in different disciplines. Nonetheless, the effort to subdue the power of language, like the effort to attain objectivity, is one of the central aims of scientific activity.

As Evelyn Fox Keller and Elizabeth Lloyd (1992) have argued, because of the large overlap between ways of thinking about the natural world and ways of thinking about human social relations, key terms offer a vantage point for viewing the complex interactions and coupled evolution of science and culture. The permeation of Darwin's theory of evolution by Adam Smith's theory of the market and the division of labour and by Thomas Malthus's law of the relation of population and food supply, has been, and continues to be, the subject of detailed analysis (Young, 1985; Limoges, 1993). The "principle of division of labor" has been used to account for almost every level of biological organization, from interspecies relations in ecology, intercellular relations in developmental biology to intracellular relations in cytology and genetics. To compare the structure of natural forms to the structure of human groups, their inventions and intentions, has remained imaginatively powerful. Nowhere is this more evident than in the history of symbiosis.

Discussions of anthropomorphism and teleology have been central to debates over the semantics of symbiosis for more than a century. A myriad of metaphors of slavery and consortium, the relations between men and women, among nations, and the relations between humans and domesticated plants and animals informed understanding of living arrangements between species. Evolutionary narratives based on these categories were as crucial for theorizing on the origin of symbiotic complexes (Sapp, 1994) as they were in stories about human evolution (Latour and Strum, 1986; Landau, 1991).

The units, their attributes, and the contextual relations chosen are decisive to the kind of evolutionary story told. When groups and species are the focus, cooperation in contrast to conflict and competition has been recognized (Reinheimer, 1915; Gregory, 1951). When descriptions begin with individuals, "cooperation" might rely on individual suffering (Pound, 1893; Spencer, 1899; Dawkins, 1976). If microbes were too virulent, then those which were symbiotic had to have a different phylogenetic lineage: they were called "bacteroids" and "viroids" (Altenburg, 1946). If microbes were cooperative, then it was in ecological contexts, "an over-stepping of boundaries" that made them uncooperative (Thomas, 1974). If they were parasites, then "cooperation" was really a matter of control and domination (Nuttall, 1923; Meyer, 1925).

From the late nineteenth to the late twentieth-century, such discussions went full circle: symbiosis was offered as a model for the study of our human social evolution (Lederberg, 1951; Read, 1958) and as a prescription for our relations with the earth (Reinheimer, 1915; Dubos, 1976). The term symbiosis continues to spill over into various domains. It is used in studies of the origin of "civilization", in which the domestication of plants and animals is considered as a natural evolutionary process based on symbiosis (Rindos, 1984).

A story about the scope of integration in nature and its underlying dynamics as a prescription for our relations with each other, and with other species, the history of symbiosis also offers a citique of the dominant relations which hold between science and nature. It is about constructing concepts of germs, not simply as disease-causing, but as life-giving entities; about understanding microbes as natural historical entities and not simply exploiting them as technologies for biochemistry and genetics; about constructing balanced interdependence as opposed to struggling for control and independence.

For more than a hundred years, symbiosis has remained a meta-disciplinary discourse; no institutionally defined groups monopolized authority over its meaning, or developed a practice based on its definition *per se* – as geneticists did for heredity, for example (Sapp, 1983, 1987). Historically, one can think of symbiosis less as some inherent quality or set of qualities than as a number of ways in which biologists relate themselves to it. Those who converged on the role of symbiosis in evolution came from almost as many backgrounds, and with as many beliefs, interests, and aims as those who criticized them. For some, symbiosis was distinct from and contradicted individual life struggle; for others, it embodied it. For some, it implied a universal mechanism for the synthesis of new individuals. For still others, it represented an exemplar for understanding the totality of the natural world as a superorganism (Spencer, 1899).

The history of symbiosis research is a window from which to scrutinize the effects of ever-increasing specialization in the life sciences. It is well recognized, especially by those who have studied scientific controversy, that specialization and discipline formation, rather than simply a result of a functional division of labor, is a strategy for gaining and maintaining adherents to a particular theory or practice. Specialization serves not only as a locus for funding; it not only affects the way in which concepts are constructed and nature is classified, ordered and parcelled, but also the way in which knowledge claims are assessed. By its very synthetic nature, by questioning the well-defined boundaries of the individual, the study of symbiosis transgressed disciplinary boundaries and confronted the concepts, doctrines, techniques and aims of the major biological disciplines – botany, zoology, bacteriology, physiology, immunology, parasitology, cytology, embryology, ecology, genetics, and virology. Among the aims, doctrines, and social contexts of these disciplines we must search for an understanding of the multiple meanings of symbiosis. Let me focus on two principal meanings: symbiosis as mutualism versus symbiosis as mutualism and parasitism.

3. Parasitism Versus Mutualism

From the very beginning, the notion of symbiosis confronted the widespread view of ecological relations and evolutionary change in terms of ceaseless conflict and competition. Debates centered on whether the living arrangements in particular associations were of mutual benefit to associates, or whether one partner was more or less parasitizing than the other. Early in the twentieth century, experimentalists who examined the underlying dynamics of such relations argued that they were not fixed, but may, at various times in the association, vary from parasitism to mutualism according to environmental conditions. This was as true for the relations between bacteria and plant roots as it was for those between bacteriophage and bacteria, or among the cells composing a multicellular organism (Wells, Huxley and Wells, 1930). Some experimental biologists argued that it was difficult if not impossible to demonstrate mutualism (Meyer, 1925). Still others insisted further that both mutualism and parasitism were anthropomorphic categories that have no real existence: they were both labels for affects not causes (Wallin, 1927; Caullery, 1922, 1951).

Nonetheless, categorisation into "mutualistic" or "parasitic" continued to be the main focus of explanation. To understand why this is so, we have to stand back from the particular phenomenon to be explained, and view it in its socio-intellectual contexts. We can start where explanation of ecological and organismic evolution meets with explanation of human history. The struggle for existence, taken in its narrow sense as a war of all against all, reinforced a narrow meaning of symbiosis as mutualism. Symbiosis as mutualism has been emphasized in opposition to social Darwinism, during the First World War (Reinheimer, 1915), during the Cold War (Nutman and Mosse, 1963), and during the rise of environmentalism of the 1970s (Thomas, 1974; Dubos, 1976). The extent to which symbiosis became equated with mutualism is a measure of the extent to which neo-Darwinism became identified with nature "red in tooth and claw". The every-continuing attempts to disentangle the concept of symbiosis from an essentialist opposition between mutualism and parasitism reflected the difficulty of removing it from the larger context of Social Darwinism.

It would be false to suggest that the dual meaning of symbiosis reflected popular versus technical scientific writing, or that its continued representation in terms of mutualism was due solely to the effects of extraneous political considerations. This view would be was misleading as the suggestion that the diverse and historically contingent political, philosophical and religious representations of symbiosis in terms of mutual aid – as finalist, anarchist, communist, internationalist, environmentalist, or feminist – were solely responsible for deterring scientists from studying symbiosis as a means for synthesizing new organisms (Margulis, 1990).

I do not suggest that the significance of symbiosis in evolution will be fully recognized only when it is divorced from any socio-political connotations. Accounts of the origins of symbiotic complexes have always been inextricably interwoven with assumptions about our human nature and debates about our present and future relations with each other and with other species. The acceptance of the symbiotic origin of eukaryotic cells did not preclude this intermingling any more than had discussions of lichens and lupines before it. The well-known American biochemist, Seymour Cohen (1970) suggested that governments might be interested in the new "revolution" presented by the endosymbiotic theory of cell organelles:

> Just as the Copernican revolution demonstrated that man is not the center of the Universe, so the investigation of this problem may show that a man (and indeed any higher organism) is merely a social entity, combining within his cell the shared genetic equipment and cooperative metabolic systems of several evolutionary paths. We suspect that governments should be interested in such a possibility, although their responses may not be readily predictable.

One could not predict what they would make of it, anymore than biologists themselves. In his text, *An Introduction to Molecular Genetics*, the phage geneticist Gunther Stent (1971) expressed his view of the politics in the cell, not in terms of international cooperation for mutual benefit, but its exact "social Darwinist" antithesis:

> Thus a eukaryotic cell may be thought of as an empire directed by a republic of sovereign chromosomes in the nucleus. The chromosomes preside

over the outlying cytoplasm in which formerly independent but now subject and degenerate prokaryotes carry out a variety of specialized service functions.

Lewis Thomas (1974) assured his readers of *The Lives of a Cell*, that far from being a case of one-sided exploitation,

> There is something intrinsically good natured about all symbiotic relations, necessarily, but this one, which is probably the most ancient and most firmly established of all, seems especially equable. There is nothing resembling predation, and no pretense of an adversary stance on either side. If you were looking for something like natural law to take the place of the "social Darwinism" of a century ago, you would have a hard time drawing lessons from the sense of life alluded to by chloroplasts and mitochondria, but there it is.

It would be a gross error to reduce the antithesis: mutualism vs. parasitism or cooperation versus slavery to whimsical reflections of the political attitudes of individual scientists. They have been embedded in the aims, concepts and doctrines deep within the diverse disciplines of the life sciences every since Darwin. The ever-continuing discussions over the definition of symbiosis — that one could not objectively distinguish mutualism from parasitism, that they were anthropocentric labels, that one had to take into consideration the physiological attributes of partners and their environmental circumstance — were attempts to escape the confines of explanations in terms of contractual relations and conflations of cause and effects, of natural theological finalism on the one hand, and neo-Darwinian reductionism on the other. Again, deflecting the meaning of symbiosis away from fixed conceptions of parasitism and mutualism amounted to removing it from some of the dominant paradigms that have shaped the life sciences in the twentieth century.

Mutualism versus parasitism, and what was to count as symbiosis, was tangled up in the question of what counts as an individual — whether, for example, one should classify lichens as parasitic fungi, enslaving its captive algae, or as a distinct class of organism (Schneider, 1897; Allee et al., 1949). Should one classify the flat worm *Convoluta roscoffensis* as a degenerate worm parasitizing algae or as a "plant-animal" on its way to becoming a plant (Keeble, 1910; Reinheimer, 1915)? The individual was considered as a collection of mutually interdependent elementary organisms (cells or intracellular entities) having a double life, one for themselves, and another – interacting, with a division of labour – for the good of the collective whole (Wilson, 1925). Herbert Spencer (1893) stated this widespread conception:

> An *exchange of services*, – an arrangement under which, while one part devotes itself to one kind of action, and yields benefits to all the rest,

> all the rest, jointly and severally performing their special actions, yields benefits to it in exchange. Otherwise described, it is a system of *mutual* dependence.

C.O. Whitman (1891) was certain that the idea that the living body represents "a commonwealth of cells" was based not on "superficial or fanciful resemblances" but on "analogies that lie at the very foundation of organic and social existence".

> On the same grounds that the sociologist affirms that a society is an organism, the biologist declares that an organism is a society.
>
> A society is an organized whole, the unity of which consists in, and is measured by, the mutual dependence of its members. The living body is an organization of individual cells with the same bond of unity. The principle of organization in both cases is the division of labor or function.

This social construction of the individual lay at the very foundation of cell theory.

The emphasis on "master or slave" or "cost-benefit" analysis in the study of symbiotic associations was reinforced by views of evolution which accentuated the inherent behavioral properties of individuals and their reproductive success. When the outcome of relations among individuals was divorced from understanding ecological contexts, only two choices resulted. Individuals were either inherently selfish or inherently altruistic. In the modern evolutionary construction, any concept which implied that individuals or populations acted for the common good was confusing ends with means, cause and effect, and was teleological. This opposition, altruism vs. selfishness pervaded discussions of the evolution of the evolution of biological organization from Kropotkin to sociobiology (Sapp, 1994).

The germ theory of disease further locked symbiosis discourse. For those who emphasized the inherently hostile nature of microbial infections (Pound, 1893; Lumière, 1919), it was implicit that microbes benefited, but more difficult to accept that plants and animals benefited. They had the opposite problem from many other experimentalists, from the nineteenth century to the present day, who found it difficult to attribute any benefit to the microbial associates (de Bary, 1879; Meyer, 1925; Smith and Douglas, 1987). When Meyer searched the symbiosis literature he found lots of speculation as to the possible advantage to the microbial partner which he himself found difficult to accept. "The function of the microscopic 'symbiotes' and their benefits to the host are explained, but little or nothing is said regarding the possible advantage of the microorganisms" (Meyer, 1925). Symbiosis research was caught in this quandary from which it still has not escaped.

4. A Niche for Symbiosis?

Whether considered as mutualism or not, there were many other aims, doctrines, and social processes antagonistic to studies or symbiosis. Ever-increasing specialization was one of the most salient features of the growth of the life sciences in the twentieth century. Students of symbiosis in evolution were required to seek analyses of symbiosis scattered in various journals with divergent interests. Moreover, synthetic studies of symbiosis confronted established lines of disciplinary competence. Historical evidence is plentiful. A few illustrations make the point. In his plea for studies of the origin of the cell, in 1914, the British protozoologist Edmund Minchin was willing to evaluate the notion that nucleus and cytoplasm were symbionts, but because he was a zoologist, he was reluctant to do the same for chloroplasts [chromatophores]:

> It would be interesting to know exactly what these chromatophores represent...whether, as some authorities have suggested, they originated as symbiotic intruding organisms, primitively independent. I do not feel competent to discuss this problem (Minchin, 1915).

Paul Portier, at the Institut Océanographique de Monaco, in Paris, was judged by his critics in France to be incompetent to discuss cytology or bacteriology. At the Institut Pasteur, Claude Regaud (1919) accounted for Portier's "faulty" cytological evidence for the bacterial nature of mitochondria on the grounds that Portier had "not sufficiently 'lived' the technique for protoplasmic structures". Regaud also labelled Portier's claims with the charge of speculation. He argued that Portier's physiological and morphological comparisons of mitochondria and bacteria did not carry the argument onto purely chemical and physiological grounds. Portier had not shown, and would never be able to show, that bacteria could be transformed into mitochondria. Therefore, Regaud (1919) asserted that to suggest that bacteria had evolved into mitochondria was beyond the scope of experimentation, and beyond the boundaries of proper science.

At the Sorbonne, the botanist Louis Matruchot (1919), offered a more generous interpretation of the tension between Portier's synthetic approach on the one hand, and technical competence on the other:

> M. Portier is above all a physiologist: it is in physiology that he observes and operates, not in bacteriology nor in morphology. And precisely the bacteriologists have the right to ask for greater precision in regard to the techniques employed...
>
> M. Portier works not only in physiology but also in philosophy. He has essentially a synthetic mind; in the relations between things he sees connecting lines, rather than differences which distinguish them.

In the preface of his *Parasitism and Symbiosis* of 1922 (translated into English in 1952), the Zoologist, Maurice Caullery at the Sorbonne also highlighted the tensions between symbiosis and specialization, synthesis and competence:

> This book does not aim at an equivalent treatment of parasitism among animals and among plants which might logically be expected. As a zoologist, I have not been able to avoid giving preponderance to facts drawn from the animal kingdom, if only because I feel myself more competent to deal with them. Also there is a vast domain intimately connected with parasitism which remains almost completely outside the scope of this book, namely bacteriology (Caullery, 1952).

The scientific nation might differ, but the debates remained the same. In the United States, Wallin's critics rejected the validity of his symbiotic theory of mitochondria, in part, on the grounds that his work lay between bacteriology and cytology where no one could properly evaluate it. Edmond Cowdry and Peter Olitsky (1922) asserted:

> Although the evidence presented by Altmann, Portier and Wallin is not convincing, certain inquiries which we have received indicate that the discussion provoked may easily lead investigators from the main problem ... Particularly is this true since the problem lies, as it were, between the sciences of cytology and bacteriology, so that but few investigators can be familiar with both sides of the question.

As intimated in the above quotations, behind these methodological objections were divergent aims of bacteriology and pathology, and conflicting views of the nature of bacteria, and their place in nature. In as much as they emphasized the creative evolutionary effects of interspecies integration, of microbial "infections", that there was something else besides relations in which the parasite destroys its host, studies of symbiosis remained outside the experimental and conceptual foundations of "the modern" consensus.

The disease-causing aspects of such microbes – as "the enemy of Man", emphasized by germ theory and pathology, overshadowed their life-giving properties. Portier's book, *Les Symbiotes* was framed by this opposition. In his dedication to his patron, Prince Albert I of Monaco, he asserted that rather than viewing microbes from "the window of medicine", he looked at "microbiology from the window of comparative physiology". Throughout his book he relentlessly pursued bacteriologists with his rhetoric arguing that to accept his theory would require them to abandon the doctrines which held their practice together (Portier, 1918). He concluded it with the proposed "that we must envisage a new form of bacteriology: physiological and symbiotic bacteriology" (Portier, 1918).

This aspect of the debates was echoed in the United States a few years later by Wallin at the University of Colorado (1927):

> It is a rather startling proposal that bacteria, the organisms which are popularly associated with disease, may represent the fundamental causative factor in the origin of species. Evidence of the constructive activities of bacteria has been at hand for many years, but popular conceptions of bacteria have been colored chiefly by their destructive activities as represented in disease.

The speculative nature of proposals of the symbiotic origin of cell organelles was yet another transnational objection. The American cell biologist, E.B. Wilson wrote in his famous text, *The Cell in Development and Heredity* (1925), "To many, no doubt such speculations may appear too fantastic for present mention in polite biological society; nevertheless it is within the range of possibility that they may some day call for more serious attention". But, as Wilson unwittingly intimates above, speculation was usually a one-sided methodological critique. Those who dismissed such theories never considered their own denial of a symbiotic origin of cell organelles as being equally as speculative. Wilson himself is exemplary. In the first edition of *The Cell*, he categorically rejected the notion that chloroplasts were symbiotic organisms:

> It is but a short step from this conclusion to the view that the centrosome, too, is such an independent organism and that the cell is a symbiotic association of at least three dissimilar beings! Such a conception would, however, I believe, be in the highest degree misleading (Wilson, 1896).

Wilson altered his opinion. In the first edition of *The Cell*, he had insisted that the cytoplasm was the substrate for determinants in the nucleus. But by the mid 1920s, he considered it likely that many of the visible structures in the cytoplasm arose from self-reproducing submicroscopic entities in the cell cytoplasm (Wilson, 1923). His change in attitude was due, in part, to evidence of algal symbionts in protists and "lower Metazoa". In the first edition of *The Cell* he had doubted that such chlorophyll bodies ("animal chlorophyll", as it was frequently called) were symbiotic algae. But by the mid 1920s, the tide of opinion swelled in favour of the symbiotic interpretation.

Nonetheless, the Weismannian doctrine of the isolation of the germ line, and that each organism contained only a single genome was reinforced by Mendelian geneticists' insistence that the nucleus was the sole seat of heredity. Their effect on interest in symbiosis in evolution can be seen by comparing the attention given to Portier's theory in France during the 1920s, and Wallin's in the United States, during the same period. In France, where studies of chloroplasts and mitochondria were prevalent, and where studies of microbes in life processes, nutrition and immunology were emphasized, and where many biologists searched for the effects of the environment on evolutionary change, Portier's *Les Symbiotes* encountered keen interest and intense scrutiny. In the United States, Wallin's *Symbionticism and the Origin of Species* was met with virtual silence.

Wallin's idea about the symbiotic origin of new genes was swamped by a wave of radiation genetics. The same year Wallin's book appeared, H.J. Muller (1927) published his report that the use of heavy doses of x rays could increase the frequency of gene mutations in *Drosophila melanogaster* by 1500 times. The next year, L.J. Stadler (1928) published the results of similar studies on barely. The types of phenotypic changes that occurred were the same as those known to occur spontaneously. Geneticists considered such gene mutations to be the source of new alleles and thus the principal fuel for evolutionary change. As Muller (1929) argued, the ability of genes to vary (mutate) and to reproduce themselves in new form conferred on these cell elements the properties of the building blocks required by evolution. The artificial production of mutations gave geneticists a new burst of life during the late 1920s and the 1930s.

However, there still other movements antagonistic to the study of the role of symbiosis in evolution. Morphological studies of symbiosis conflicted with the main thrust of experimental biology with its emphasis on reducing life functions to physics and chemistry. A physicochemical understanding of life meant studying organisms in isolation. Effects due to the presence of microbes were by definition considered to be contamination and error. This was true in physiology as it was in genetics during the first half of the century when heredity was defined as the sexual transmission of genes from one generation to the next. Anything else, transmitted sexually or not, was by definition foreign, disease, retrogressive.

The metaphor "mutualism", as borrowed from political movements of the 19th century (Boucher, 1983), opposed another metaphor borrowed from jurisprudence: "inheritance". In the sense of hereditary succession to property, rights, etc., the concept of inheritance went through various transformations in the hands of biologists. But as it pertained to infectious microorganisms, the message was always the same: with few exceptions microbes were *thieves*, they were there to steal from the "host" its *rightful inheritance*. Roscoe Pound (1893) phrased this opposition explicitly:

> Mutualism of the kind we meet with in the vegetable kingdom involves sacrifice on the part of the host. The parasite is not there gratuitously. It is there to steal from its host the living it is hereditarily and constitutionally indisposed to make for itself. If the host gains any advantage from the relation, it can only do so by sacrificing by giving the parasite the benefit of its labor that it may subsist.

Forty years later, the American geneticist E.M. East (1934) reiterated this point of view when he assessed the evidence for non-Mendelian, cytoplasmic inheritance:

> Thus there are several types of phenomena where there is direct transfer, from cell to cell, of alien matter capable of producing morphological changes. It is not to be supposed that modern biologists will cite such instances when recognized, as examples of heredity. But since an earlier generation of students used them, before their cause was discovered, to support arguments on the inheritance of acquired characteristics, it is well to be cautious in citing similar, though less obvious, cases as being illustrations of non-Mendelian heredity.

We must also consider, of course, the fact that the views of "the modern biologist" to whom East refers were based on conflict and competition as the driving force of evolutionary change. The British botanist F.G. Gregory (1951) did not fail to make the charge that symbiosis in evolution was ignored as much as cooperation in ecology was ignored, when he proposed that biologists should widen the concept of organism to include symbiotic complexes:

> The "struggle for existence" presupposes antagonism between organisms whether or not they belong to the same or diverse species. On the other hand, the question remains whether associated species tend to provide for each other a favourable environment. The analysis of the relations between organisms has been dominated by the notion of "competition" or "struggle", and the converse notion of "cooperation" has in consequence been disregarded... The data of ecology serve as a challenge to this view of the predominant role of "struggle."

Yet, studies of symbiosis in evolution were not prominent even among those ecologists who emphasized cooperation. "Underground ecology" (bacteria in the roots of legumes and fungi in the roots of forest trees) was largely ignored in ecology texts of the 20th century. Those ecologists who did emphasize cooperation were primarily concerned with cooperation *within* species leading to new individuals, not cooperation *between* them. The cooperation ecologists at Chicago led by W.C. Alee and Alfred E. Emerson denied that many cases of symbiosis including lichens could be considered to be organisms, or cases of mutualism (Allee et al., 1949).

5. The Command of Language: Redefining Heredity

Only after World War II did geneticists discuss the idea of broadening their definition of heredity to include infectious entities and broadening the boundaries of organisms to admit symbiotic complexes. As new genetic evidence for cytoplasmic inheritance came to the fore, geneticists also recognized that there were means other than meiotic sex for transmitting genes from one generation to the next.

Debates over the interpretation and scope of cytoplasmic heredity during the late 40s and early 1950s had often centered on an antagonism between symbiont or virus *virsus* cytoplasmic genetic entity or "plasmagenes" (Sapp, 1987). Leading American geneticists such as H.J. Muller (1951) trivialized the evidence for cytoplasmic gene complexes, dismissing them as mere parasites or symbionts of little genetic interest. After all, Tracy Sonneborn (1950) and his collaborators had shown that one of the exemplars of cytoplasmic heredity, the cytoplasmic factor *kappa* in *Paramecium aurelia* was infectious under certain laboratory conditions. Philippe L'Héritier (1948) had shown the same to be true for the maternally inherited cytoplasmic factor *sigma* in *Drosophila.* Nonetheless, the idea was growing that all cases of cytoplasmic inheritance were due to symbionts, *but* that symbionts had to be considered as part of the genetic constitution of the complex organism.

By the early 1950s it was becoming evident to geneticists that infectious viruses are vehicles of inheritance in bacteria. Their study, when combined with studies of cytoplasmic inheritance in other organisms, reinforced the idea that symbiotic microorganisms could become well-integrated into, and form an essential part of the genetic constitution of the organic whole. C.D. Darlington (1951) and Joshua Lederberg (1951, 1952) attempted to broaden the concept of organism by extending the meaning of the term heredity to embrace "infective heredity". This proposal was supported by studies of lysogeny – that a latent virus or "prophage" could be incorporated and transmitted as bacterial gene(s). It could remain undetected until it developed into an active virus capable of killing its host, and release into the medium.

Darlington and Lederberg argued that recognition of cytoplasmic genetic entities brought heredity, development and infection under a unified view. To resolve the debate over *symbiont* versus cytoplasmic *genetic* entity, Lederberg (1952) offered the term "*plasmid* as a generic term for any extra-chromosomal hereditary determinant. The plasmid may be simple or complex". However, as he well knew the conflict among geneticists themselves arose in part from fixed concepts of the individual organism, Lederberg (1952) argued on operational grounds that an "individual" should be defined by current disciplines rather than as an absolute ontological category:

> The cell or organism is not readily delimited in the presence of plasmids whose coordination may grade from the plasmagene to frank parasites... The geneticist may well choose that entity whose reproduction is unified and hence functions as an individual in evolution by natural selection. The

microbiologist will focus his interest on the smallest units he can separate and cultivate in controlled experiments, in test tubes, eggs, bacteria or experimental animals. Genetics, symbiotology and virology have a common meeting place within the cell. There is much to be gained by any communication between them which leads to the diffusion of their methodologies and the obliteration of semantic barriers.

Bacterial viruses, first used to study the nature of the gene, later became a tool for the development of biotechnology. The importance of virus infections as a source of evolutionary change was virtually ignored. Throughout the 1960s the principle aims of virology and bacteriology remained tied to studies of disease. As the bacteriologist René Dubos (1961) remarked, virologists maintained themselves as "poor cousins in the mansion of pathology". Nonetheless, Dubos prophesied that "there would soon develop a new science of cellular organization, indeed perhaps a new biologic philosophy". The time had come, he (1961) declared, "to supplement the century old philosophy of the germ theory of disease with another chapter concerned with the germ theory of morphogenesis and differentiation".

When symbiosis came to the fore in the 1960s and 1970s, led by the writings of Lynn Margulis (1970, 1981), the focus of debate was much more restricted to a specific problem – the role of symbiosis in the origin of eukaryotic cell organelles. DNA had been detected in chloroplasts and mitochondria. Genetic research programs had begun on chloroplasts in *Chlamydomonas* led by Ruth Sager (1972) and by Nicholas Gilham (1978) and their collaborators in the United States. Those on yeast mitochondria had been initiated by Boris Ephrussi and his collaborator Piotr Slonimski in France (Sapp, 1987). What remained was providing plausible accounts of their symbiotic origin, weighing evidence against alternative theories, and convincing colleagues that this was a legitimate domain of scientific inquiry.

6. Science or Metascience?

During the 1960s and 70s, the symbiosis hypothesis for the origin of eukaryotic organelles developed in conflict with the traditional direct filiation assumption which held that mitochondria and chloroplasts had evolved endogenously by compartmentalization within the cell. The nature of the debates which ensued highlight the difficulties of establishing the validity of any evolutionary account.

Most discussants realized that more than one theory could account for the facts. Since several explanations were consistent with any set of observations, biologists upheld "simplicity" as a criterion for deciding between them. In the debate over the origin of cell organelles, simplicity was most often expressed as an epistemological maxim – that one should choose the "simplest" hypothesis fitting the facts – a principal of frugality attributed to the fourteenth century philosopher William of Ockham: "Neither more, nor more onerous, causes are to be assumed than are necessary to account for the phenomena" (Pearson, 1937).

But reaching consensus about which theory was the simplest was not straightforward and biologists began to recognize the dull edge of Ockham's razor (Sapp, 1994). By the late 1960s, the cytological and biochemical similarities of eukaryotic cell organelles and prokaryotes – their general structural similarity, their similar modes of multiplication by fission, the composition of their DNA – were well recognized. Nonetheless critics insisted that none of this evidence could be taken as direct support for symbiotic theories.

All the striking similarities between organelles and prokaryotes were rather precisely what one would expect if eukaryotes had evolved by gradual transformation of prokaryotes. The similarity of mitochondria and plastids to bacteria could be easily accounted for if plastid and mitochondria genomes had changed more slowly and less radically than nuclear genomes since their common divergence from a single ancestor in a single bacteria-like lineage. Furthermore, geneticists had shown that cytoplasmic organelles were well-integrated into the genetic systems of all organisms. For its advocates, the ships had been placed into their bottles, but for its critics, the bottle-neck was the difficulty of believing that new genes could be incorporated into the nuclear genome through the inheritance of acquired bacteria. The fact that many organelle traits were encoded in the nucleus weakened the case for the symbiont theory. Indeed, many biologists concluded in despair that it was not obvious what kind of research would answer these questions (Kirk and Tilney-Bassett, 1978).

From the outset of the debates of the 1960s and 70s some had argued that theories of cell origins could never be tested and did not belong to the realm of science at all (Woolhouse, 1967). The endosymbiotic theory was a historical theory. It attempted to account for the course of events that occurred more than a billion years ago in terms of present observations. There was simply no sure way of knowing whether what actually happened than and what was occurring now, and therefore one could deny for all such accounts of any degree of scientific validity. The attitude of the microbiologist Roger Stanier (1970) was representative:

> It might have happened thus; but we shall surely never know with certainty. Evolutionary speculation constitutes a kind of metascience, which has the same intellectual fascination for some biologists that metaphysical speculation possessed for some medieval scholastics. It can be considered

a relatively harmless habit, like eating peanuts, unless it assumes the form of an obsession; then it becomes a vice.

It seems unlikely that acceptance of the endosymbiosis hypothesis would ever become truly universal. However, during the late 1970s and 80s new techniques based on nucleotide sequence analysis were developed which, for many, provided the rigor and closed the controversy. The principle work was done by two groups: one headed by Carl Woese at the University of Illinois (Champaign-Urbana) and the other headed by W. Ford Doolittle and Michael Gray at Dalhousie University, Canada. In the 1970s Woese and his colleagues pioneered the use of ribosomal RNA sequencing analysis for phylogenetic studies, and revolutionized the classification of bacteria. He and his co-workers distinguished two fundamental domains, the Archaebacteria and the Eubacteria. Archaebacteria are for the most part restricted to peculiar ecological niches: anaerobic sludges for methanogens, acid hot springs for thermoacidophiles, and salt flates for halophiles. Nonetheless, since a few eubacteria occupy the same niches, molecular characteristics are the only reliable basis for distinguishing between the two groups.

The argument underlying molecular evolutionary studies of organelle origins was straightforward: if the nuclear genome and one of the organellar genomes could be shown to derive from genomic lineages which were phylogenetically distinct before the formation of the eukaryotic cell, then the symbiotic origin of that organelle could be taken as proven. For example, if plastid genomes comprise a branch or branches or the eubacteria, specifically, the cyanobacterial (oxygenic-photosynthetic-prokaryotic) evolutionary tree, and if nuclear genomes arose from within the archaebacteria, then the exogenous origin of plastids could not be questioned. Plastic genomes were traced to the cyanobacteria, and mitochondria genomes were traced to another eubacterial group, the alpha-Proteobacteria.

By 1982 Gray and Doolittle could confidently assert that the basic problem, exogenous vs. endogenous origin, was now to be considered "rigorously and definitively resolved". But that did not exhaust the evolutionary questions generated by the application of nucleotide sequence analysis to cytoplasmic genomes: How many independent symbiotic events gave rise to the diversity of modern day plastids and mitochondria? How plastids insome organisms evolved from eukaryote rather than prokaryote endosymbionts? Could one prove that genetic information brought into the cell from bacterial symbionts was transferred to the nuclear genome? Have organelle genomes evolved at radically different rates in the different major groups of eukaryotes? Startling evidence published by John Hall, Zenta Ramanis and David Luck (1989) at the Rockefeller University indicated the presence of basal body/centrolar DNA, raising the possibility of rigorously testing Margulis's proposed spirochaete origin of these organelles. However, evidence questioning the existence of centriolar DNA was published the next year which, as Gray (1992) saw it, "dimmed considerably" the prospect.

Studies of the role of symbiosis in evolution were not limited to questions of cell-organelle origins. Reconstructed by molecular biology, the symbiotic origin of mitochondria and chloroplasts posed no threat to the major evolutionary consensus as long as symbiotic associations remained exceptions. Throughout the 1970s and 1980s, studies of symbiosis in eukaryotic organelle evolution were largely removed from studies of those 19th and early 20th century exemplars which had originally led to speculation on symbiosis in cell evolution. The symbiotic origin of cell organeles remained virtually an isolated case in evolutionary theory.

During the 1970s and '80s, all those evolutionary and ecological questions that had been posed over the previous hundred years were raised in general discussions of symbiosis. Were there general evolutionary mechanisms operating in nature which encouraged symbiotic complexes? How should one understand the relations making up symbiotic associations? How should one think about the relations between individuals, between species, between organisms and cells, and between cells and genes? If symbiosis played a crucial role in the transition from prokaryote to eukaryote some 2000 million years ago, did it play a major role in other transitions also, or was it a rare exceptional, accidental phenomenon?

Studies of cooperation came to the forefront with the rise of sociobiology, but the focus was on cooperation within species, with an increased emphasis on individualism in evolutionary explanation. Cooperation was reduced to selfish genes; and kinship theory predicted that mutualism between species would be an exceptional occurrence (Axelrod, 1984). Leading neo-Darwinian evolutionists and ecologists continue to assert that the highly interactive interspecies community, the raw material for symbiotic associations, is not a general feature of nature (Law, 1991). Symbiosis is not considered a general characteristic of evolution.

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