

Metabolic and Microbial Perspectives on the “Evolution of Evolution”

Short running title: **Metabolic and Microbial Macroevolution**

Authors and affiliations

Russell Powell, Boston University, Department of Philosophy, Boston, USA
powell@bu.edu

Maureen A. O'Malley, University of Sydney, School of History and Philosophy of Science, Sydney, Australia
maureen.omalley@sydney.edu.au

Abstract

Identifying and theorizing major turning points in the history of life generates insights into not only world-changing evolutionary events but also the processes that bring these events about. In his treatment of these issues, Bonner identifies the evolution of sex, multicellularity, and nervous systems as enabling the “evolution of evolution”, which involves fundamental transformations in how evolution occurs. By contextualizing his framework within two decades of theorizing about major transitions in evolution, we identify some basic problems that Bonner’s theory shares with much of the prevailing literature. These problems include implicit progressivism, theoretical disunity, and a limited ability to explain major evolutionary transformations. We go on to identify events and processes that are neglected by existing views. In contrast with the “vertical” focus on replication, hierarchy, and morphology that preoccupies most of the literature on major transitions, we propose a “horizontal” dimension in which metabolism and microbial innovations play a central explanatory role in understanding the broad-scale organization of life.

Keywords: macroevolution, major transitions, metabolism, microbial evolution, sex, competition

Research highlights

- We show that many accounts of major evolutionary transitions, including Bonner’s “evolution of evolution”, are unavoidably progressivist and disunified.
- We argue that the evolution of sex, bodies and brains are insufficient to explain major turning points in evolution; moreover, competitive evolutionary interactions are inherent to life and not unique to complex multicellular organisms.
- We propose shifting the focus onto neglected metabolic and microbial processes and other “horizontal” dimensions of life in order to gain a fuller understanding of macroevolutionary turning points and key evolutionary transformations.

1. Introduction

John T. Bonner (2019) envisions macroevolution as a series of key steps in the evolution of evolvability. His perspective provides a convenient starting point for thinking further about major turning points in the history of life. To contextualize Bonner’s view, we need to take into account

the sizable literature that arose in response to Szathmáry and Maynard Smith's ground-breaking theory of major transitions in evolution (Szathmáry and Maynard Smith, 1995; Maynard Smith and Szathmáry, 1997). In our perspective, we highlight some limitations of the major transitions literature that we believe are shared by Bonner's account. Our aim is to draw attention to the neglected events, processes, and dimensions of life on which an alternative account of macroevolution can be built. Foremost amongst these are microbial activities, particularly metabolic processes, which (we will suggest) inform and complement the standard morphological and replication focus of prevailing major transitions theory.

2. Bonner's account in brief

Like other theorists engaged in the project of identifying and theorizing major evolutionary transitions, Bonner sees macroevolution as punctuated by a series of key evolutionary episodes. These transitions divide the history of life into distinct periods in which the evolutionary process supposedly took on a qualitatively different character and led to novel forms of biological organization. Bonner's account refers to these divisions as "eras," and they correspond roughly to standard geological "eons" (see Table 1). Bonner Era 1 (BE-1), the Archean Eon, is characterized by microorganisms ("bacteria") engaging in asexual reproduction throughout the first 1.5 billion years of prokaryote evolution. BE-2, the Proterozoic Eon, involves the origins and maintenance of sexual reproduction in single-celled eukaryotes, which took up another billion years. BE-3, the Phanerozoic Eon, covers the origins of multicellularity, especially larger bodies, which are widely believed to have generated active competition among animal, plant and fungal lineages. BE-4 is defined by the massive augmentation of information-processing capacities in animals, courtesy of neurons and centralized nervous systems. These innovations eventually give rise to the "miracle of language" that ultimately made human culture and civilization possible.

Table 1: Bonner's schema of evolutionary 'eras'

Bonner's era	Geological eon	Evolutionary driver	Evolutionary achievement/transformation
BE-1	Archaean	Asexual reproduction in unicells	Evolution without competition
BE-2	Proterozoic	Sexual reproduction in unicells (eukaryotes)	More diversity, ongoing non-competitive evolution
BE-3	Phanerozoic	Multicellular sexual reproduction and size increase	Genuine competitive evolution ("the struggle for existence")
BE-4	Pre-Cambrian onwards	Centralized nervous systems: information processing and language	Truly rapid non-genetic evolution

Some of the events that Bonner's schema picks out, such as the origin of sex, complex multicellularity, the radiation of animals, and the development of human language and culture, also feature in other major transition theories. Most of these events are included, for example, in the original and revised versions of Szathmáry and Maynard Smith's theory, which has driven discussion on this topic since 1995. Other authors have followed suit by including some subset of these events in their proffered lists (e.g., Knoll and Bambach, 2000). However, Bonner's framework emphasizes somewhat different theoretical factors from those that supposedly connect the events in Maynard Smith and Szathmáry's original account. As the title of his essay suggests, the "evolution of evolution" is the common thread that is purported to run through the disparate episodes included in Bonner's model. Whereas Maynard Smith and Szathmáry focus on transitional *outcomes* of evolutionary processes (especially shifts in individuality), Bonner's account stresses *drivers* of the evolutionary process (especially innovations that resulted in competitive evolution). However, Maynard Smith and Szathmáry also emphasized the importance of transformations in the evolutionary process itself, which they couched in terms of new modes of information transmission (as reflected, for example, in the genetic code, epigenetic differentiation of cell lines, and cultural inheritance).

There are significant challenges that any theory of major evolutionary transitions must overcome, with respect to both its chosen list of events as well as the thread that is purported to connect them. Examining these common problems allows us to propose an alternative view of major evolutionary turning points in which metabolism and microbes play a more central explanatory role. We begin by identifying two broad problems with major transitions theory (progressivism and theoretical disunity), go on to discuss critically two specific driving forces of evolutionary transformation in Bonner's scheme (sex and multicellularity), and then conclude with a sketch of central events and processes that are missing from predominant views of major transitions (metabolism and microbes).

3. First Broad Problem: Progressivism

A prominent criticism of major transitions theory as it was originally formulated is that, intentionally or not, it paints an "ascent"-like picture of macroevolution that marches from 'monad to man' in ladder-like fashion, with humanity coronated at the pinnacle of this evolutionary trend. This progressive narrative is starkly illustrated by the iconic cover of Maynard Smith and Szathmáry's classic book on major transitions in evolution. Although this problem seems patently obvious to us (see also Ruse, 1996, p. 483), not everyone agrees that these authors display progressivist tendencies. Some macroevolutionists have argued, for example, that Maynard Smith and Szathmáry were simply tracking objective increases in complexity that can be characterized without reference to progress (see in particular Herron, 2016). Another common defence is that Maynard Smith and Szathmáry explicitly deny what they call the "fallacy of progress" in evolution (1995, p. 4), taking pains to point out that not all lineages have undergone the major transitions they identify. One might think this move is sufficient to stop the progressivist objection in its tracks. Rejecting progressivist framings of evolution is a good start. But the absence of a detailed metric and evaluation of alternative trends in the history of life, such as simplification—combined with the failure to distinguish major transitions that are shared by most or all lineages from those that are historically contingent and confined to only a few—results in a picture that is not too dissimilar from one that might flow from a standard progressivist view. Similar narratives could flow from focusing solely on increases in chosen

variables, such as nested hierarchy or body size maxima (McShea 2001; Smith et al. 2016), even though the theorists who describe these trends do not take them to demonstrate progressivist or even selectively biased trajectories. These trends are real and important, but they do not support evolutionary progressivism and they do not in themselves provide a comprehensive picture of the forces and events at work in macroevolution.

We have elaborated on these matters elsewhere and will not revisit them here (for discussion, see <https://freethoughtblogs.com/fierceroller/?p=1677>). Our basic point is that major transitions theory has tended to feature an evolutionary ratchet that cranks up toward increasingly advanced forms of life until it ultimately achieves human civilization. This ratchet makes such accounts vulnerable to charges of progressivism and anthropocentrism. The problem is usefully illustrated by Bonner's scheme, according to which complex multicellular lineages came to "dominate" simpler unicellular ones and humans came to dominate simpler animals. This putative evolutionary dominance appears to provide the main justification for dividing the history of life into four distinct Bonnerian eras. Intuitive notions of dominance and superiority in evolution are notoriously problematic, however. They tend to rely on subjective and value-laden judgments that result in a human, vertebrate, or eukaryote-centric view that glosses over the deeper etiological and ecological structure of life on Earth. Even when properly operationalized, such accounts inevitably abstract away from what Stephen Jay Gould (1997) called the "full house" of life. As Gould and other commentators have observed, evolution is, and forever will be, driven primarily by unicellular ecology and innovation. These processes are marginalized by accounts that have evolution charging in fits and starts toward a human telos. Even the "New Synthesis" supposedly wrought by evo-devo has been restricted to a morphology-based picture of evolution that overlooks unicellular interactions and innovations (as we sketch out in more detail, in our positive account, below).

However, we are not saying that some of the events focused on by Bonner's account and the broader evo-devo program—such as the evolution of animals during the Phanerozoic—are not critically important for the large-scale ecological structure of life on Earth. Even though the 'transition' to animal-grade multicellularity only occurred once in a single clade in the history of life on Earth, attention to metazoan evolution is perfectly justifiable, given that, as Butterfield (2011) puts it, "the biosphere 'as we know it' is a space designed by metazoans." Animals have a strong top-down effect on global biogeochemical cycles and trophic webs through the consumption and transformation of primary producers. Yet it is possible to acknowledge the ecological significance of animals once they evolved without minimizing the equally important role of other complex multicellular lineages like plants, and without marginalizing the role of unicellular innovations in both earlier and subsequent phases of evolution. The latter also include key transformations in the evolutionary process itself, as we will show below. Indeed, it is quite easy to argue that biogeochemically (another way to look at ecology), unicellular organisms have dominated and continue to structure the living world and the evolutionary possibilities of life (see Falkowski et al., 2008). Not giving due recognition to such microorganismal achievements makes any account of major evolutionary turning points appear anthropocentric, progressivist, and value-laden even if there is no such intent or motivation.

4. Second Broad Problem: Theoretical Disunity

There is another familiar problem that Bonner's account shares with the major transitions literature: a lack of theoretical unity among the pivotal events it aims to capture. There are several distinct themes running through Maynard-Smith and Szathmáry's account. These include the emergence of new units of selection (which drove the hierarchical complexification of life), a division of labor (which allowed for the complexification of parts within hierarchical levels), and new modes of information transmission (such as genetic replication, epigenetics, and cultural transmission). Precisely how these themes are related to one another is unclear and remains a matter of debate, even in Szathmáry's recently revised version (Szathmáry, 2015). We and several others have expressed doubts about whether these theoretical threads could ever be combined into a single, unified theory of major transitions (McShea and Simpson, 2011; O'Malley and Powell, 2016). For instance, the transition to complex multicellularity arguably implicates all three theoretical threads, while the molecular division of labor in the early history of life implicates one or perhaps two of the three, whereas the evolution of sex might exhibit none of them.

In order to create a unified theory, several commentators (e.g., Michod, 2005; Bourke, 2011) have attempted to revise Maynard-Smith and Szathmáry's original theory by focusing solely on evolutionary transitions in individuality. These authors purge events in the original model that do not fit this strict individuality criterion, such as sex and language, and focus instead on how independently replicating units merge to become a higher-level unit of selection. A classic example is the endosymbiotic fusion of two prokaryote cells to form the new eukaryote cell (an event we will discuss below). However, evolutionary transitions in individuality are simply one aspect of the complex organization of life on Earth, and thus a purge of all events that do not meet this criterion in the name of theoretical unity comes at the expense of explanatory scope. In particular, individuality falls along what we have called the 'vertical' dimension of life's complexity. Views of macroevolution that are focused solely on the vertical dimension neglect 'horizontal' interactions, such as energetic exchanges, ecological dynamics, symbioses, and communal innovation-sharing. These interactions sustain life on the planet and make vertical transitions possible in the first place (O'Malley and Powell, 2016; Gilbert 2019). We will elaborate later on the importance of this horizontal dimension and why it is better captured by shifting the focus onto microbes and metabolism.

If unity is not an achievable goal given the diversity of events and transformative processes most theorists include, then what is the aim of such theories? As we see it, the goal of major transitions theory is to understand how life came to be organized as it is. Although theoretical unity is a worthwhile scientific pursuit, when it comes to measuring the success of such a broad-scale theory of evolution, unity should not be sought at the expense of explanatory scope and power. We agree with Maynard Smith and Szathmáry and their successors (such as Michod and Herron, 2006) that it is critically important to explain how replication conflicts between levels of selection are solved such that they permit transitions to higher-level individuals. But if we want an overarching account of macroevolution of the sort that major transitions theory seeks, then the single criterion of individuality transitions overlooks far too many other events—including metabolic innovations—that had a profound impact on the large-scale organization of life as we know it today.

Bonner's model attempts a unifying strategy that is rather different from revisions of Maynard Smith and Szathmáry's scheme. He calls his unifying theme "the evolution of evolution," which on one

interpretation refers to the evolution of “evolvability.” Evolvability has numerous definitions (for a review, see Pigliucci, 2008), but broadly conceived, it refers to the ability of a lineage to generate heritable, adaptive variation and thereby respond favorably to natural selection. Evolvability enables a lineage to explore phenotypic space more extensively, which increases the chances that it will stumble upon key evolutionary innovations, some of which may have far-reaching consequences for the organization of life and its future directions. Evodevo research is arguably organized around the concept of evolvability (Hendrikse et al., 2007), though it too has been largely focused on animal evolution and thus has limited evolutionary applicability.

Another way of reading “the evolution of evolution” is to understand this phrase as referring to transformations of the evolutionary process itself. The notion that the very machinery of evolution has evolved has been well explored in the major transitions context (see Calcott and Sterelny, 2011), and was a hallmark of Maynard Smith and Szathmáry’s original model (for discussion, see Sterelny, 1999). Bonner’s take on the evolution of evolution is quite different and more radical. He argues that the unicellular history of life was characterized by non-competitive evolution, and that it took sexual reproduction and body size to break out of this protracted evolutionary Eden. Once these features produced competitive evolution, at least one lineage of brainy multicellular organisms went on to ‘invent’ a wholly new kind of evolution: rapid non-genetic evolution in the form of cumulative culture (see Table 1).

The inclusion of human culture, which is commonplace among major transition theories, exacerbates problems of progressivism and disunity (see O'Malley and Powell, 2016); however, we will leave cultural evolution aside in this essay to focus on the more novel idea of non-competitive unicellular evolution. Bonner suggests unicellular organisms tend to “just exist side-by-side, totally ignoring one another.” We think this claim gives the wrong impression of the ecological and evolutionary processes that characterize the microbial world (see Love, 2019, for a similar interpretation). In the first place, no theorist would suggest that evolution by natural selection was not occurring prior to the Phanerozoic. And if natural selection was occurring in earlier eons of life—as it had to be in order to generate functional complexity and complex adaptive matching—then there must have been competition over resources. The process of adaptation by natural selection simply is a competition between types that vary in relative adaptedness (or fitness propensities) as measured in a common selective environment (Brandon 2014). Moreover, there is a critical Malthusian premise in the Darwinian logic of natural selection: it is resource limitations (along with predation pressures, fecundity, etc.) that result in differential reproduction. Not only are these processes ubiquitous in the microbial world, but – as we elaborate below – they led to transformative evolutionary events well before the origin of animals or even eukaryotes.

The assumption of competition also figures centrally in Darwin’s “principle of divergence”—the competitive separation of lineages—which, along with natural selection and common descent, form the theoretical core of the Darwinian revolution (Richards, 2012). It is also the basic take of competitive exclusion theory, according to which organisms subsisting on the same resource must either evolve to take advantage of alternative resources or else become extinct (Gause, 1934; Hardin, 1960). This generic Darwinian dynamic has been demonstrated in various sophisticated ways, both theoretically and experimentally (see, e.g., Fredrickson and Stephanopoulos, 1981; Levin, 1970), using *asexual microorganisms* as models. Not only are competitive exclusion processes inherent in all unicellular environmental dynamics, but in addition, the ecological and coevolutionary interactions between eukaryotes and bacteria, and between bacteria and viruses, are widely regarded as among

the most significant and pervasive interactions in the history of life on Earth (Matz and Kjelleberg, 2005; Erken et al. 2013; Koskella and Brockhurst, 2014; Rodriguez-Valera et al. 2009). In fact, the predation of unicellular eukaryotes by other unicellular eukaryotes probably explains the origin of some of the multicellularity in which Bonner is interested (Herron et al., 2019). These direct and indirect competitive interactions between unicellular (and acellular) forms of life precede animal arms races by nearly three billion years.

Bonner contrasts his “live and let live” interpretation of microbial ecology with a competitive reading of animal evolution, which we will understand as a claim about direct competition between entire clades. There is evidence that predator-prey arms races may have triggered the Cambrian explosion, as indicated by the widespread and near simultaneous emergence of mineralized skeletons, burrowing behaviors, and masticating abilities in early bilaterian lineages (Vermeij, 1987). These changes have been interpreted as direct responses to the evolution of active predation in arthropods made possible by vision, brains, and active bodies (McMenamin, 1998; Parker, 2004; Trestman, 2013; Powell, 2019). But even if strategic, counteracting innovations transformed the ecological landscape of macroscopic life during the Phanerozoic, the claim that competition for scarce resources, or even the advent of arms races, marks the key ecological difference in the transition from a microscopic to a macroscopic world does not withstand scrutiny.

Indeed, there is probably less evidence for long-term interspecific competition among ‘advanced’ metazoans than there is among microbial species. Ostensibly competing animal clades turn out to be either “ships passing in the night” (Gould and Calloway, 1980), or otherwise are governed by principles of ecological exclusion in which mass extinction events empty saturated ecospace and thereby permit the radiation of clades that were long-suppressed by incumbent advantage (Rosenzweig and McCord, 1991; Benton, 1996; Slater, 2013). There is no reason to think that these sorts of interclade dynamics are not equally applicable to microbial macroevolution. In short, the advent of competitive evolutionary interactions in sexual, complex multicellular organisms is better read as evolutionary business as usual. Competition cannot, therefore, serve as the uniting thread of a view of major transitions that privileges morphological evolution. As we will now show, there are additional difficulties for accounts, such as Bonner’s, that view sex, bodies, and brains as the key drivers of the evolution of evolution.

5. First Driving Force: The Evolution of Sex

According to Bonner’s account, there are two major biological innovations that transformed the evolutionary process: sex and multicellularity. Although sexual reproduction is featured in other major transitions theories (e.g., Maynard Smith and Szathmary, 1997), Bonner makes the strong claim that “any significant evolutionary change requires sexual reproduction.” Although sexual reproduction was included in Maynard-Smith and Szathmary’s original model of major transitions, as we noted earlier it has since been eliminated by revisionary accounts in part because it does not tie neatly into any putative connecting thread. For example, sex does not itself constitute the emergence of a new higher-level individual, even if germline specialization, sequestration, and a single-cell bottleneck are key steps in the transition to complex multicellularity (but see Michod, 2005 for a claim that the emergence of sexual reproduction marks a transition in individuality). Szathmary (2015), in his recent revision of major transitions theory, recognizes sexual reproduction as the “odd man out” and consequently discards it.

However, if the axis of a major transition theory is not hierarchy but rather evolvability, as it is in Bonner's account, then there is a more compelling basis for including sex. There is a long history of discussion about whether sex, which Bonner defines as meiosis and gamete fusion, enhances evolvability. The idea that sex created a genetic combinatorial explosion which dramatically enhanced the "blind variation" component of natural selection, though highly plausible, has been difficult to demonstrate, in part because the impact of segregation and recombination on levels of variation has been hard to gauge (for a discussion, see Otto and Lenormand, 2005). Even if its role in enhancing evolvability explains the maintenance of sex once it originated, other explanations are probably necessary to account for its origins, such its function in DNA repair, the coevolutionary response of host to parasites, and the jettisoning of mutational load that lineages have accumulated through 'Muller's ratchet' (Michod and Levin, 1988; Barton and Charlesworth, 1998).

More importantly, sex is not the only innovation in gene recombination to have achieved these evolvability effects—in fact, it may not even be the most important gene-recombinatory mechanism to have done so. Full-blown sex is not necessary for the increase in raw diversity that enables natural selection to search otherwise inaccessible regions of functional space. Recombination of genetic resources does the same thing by way of similar processes. The most basic forms of this capacity are lateral gene transfer and the prokaryotic version of homologous recombination (Lawrence and Retchless, 2009). Both of these mechanisms evolved in an exclusively prokaryotic world. Lateral gene transfer was of monumental importance to the early phases of life on Earth, as well as to the spread of metabolic innovations (e.g., oxygenic photosynthesis, reduction-oxidation pathways) that continue to sustain life on the planet (Falkowski et al., 2008). In light of this history, we think it is better to interpret sex as a complicated solution to an old problem of how to capitalize on communal innovations (Erwin 2015). The novelty of sex is to solve the perennial problem of innovation-sharing within a new framework of eukaryotic constraints. Such constraints include, first and foremost, the nucleus, which mostly serves to protect the eukaryote genome from parasexual gene exchange, as well as the sequestered germline in animals, which is probably a solution to replication conflicts that arose in transitions to complex multicellularity.

A broader focus on gene sharing throughout the biosphere, rather than a narrow focus on sex in eukaryotes, would enable Bonner's account to avoid progressivist pitfalls and avoid omitting innovations, such as lateral gene transfer and homologous recombination, that by his own criterion of evolvability ought to be included. At the same time, gene exchange mechanisms are not the only innovations that have transformed the space of evolutionary possibility. Modularity—the ability of genes and traits to be modified independently of one another—is also key to evolvability (Wagner and Altenberg, 1996). Adaptations can only be cumulatively shaped by selection if traits can be modified without wreaking collateral havoc on other critical features of the organism (Lewontin, 1978). Sex may contribute to genetic modularity (Misevic, Ofria and Lenski, 2006) and therefore to evolvability, but so too will any number of innovations that play a role in the modular re-structuring of the genotype-phenotype map. It is unclear, therefore, why sex—or even gene recombination writ large—should be the central focus of a theory of major transitions that pivots around the concept of the evolution of evolution. Finally, although the invention of sex probably increased the adaptive potential of eukaryotes, it is unclear how it figures in the emergence of plants and animals, given that the evolution of meiosis predates organ-grade multicellularity by over a billion years (Dacks and

Roger, 1999). This point illustrates once again that any theory that neglects unicellular innovations and their context will fail to capture and explain key evolutionary transformations.

6. Second Driving Force: The Evolution of Bodies and Brains

For the final two stages of his scheme, Bonner homes in on multicellularity and nervous systems (see Table 1). These innovations are widely regarded as having opened up new phenotypic search space (Alberch, 1991; Maynard Smith and Szathmáry, 1997), and thus they fit squarely into the evolvability theme. With the evolution of full-scale bodies, life became truly three-dimensional and hyper-specialized; with the evolution of centralized nervous systems (likely in coevolution with increasingly sophisticated image-forming sensory modalities), life evolved novel capacities for action that allowed for new ecological possibilities. However, there are many other key animal innovations that opened up new adaptive zones to equally significant macroevolutionary effect. Not including these innovations in even a metazoan-centric account of evolutionary transitions makes any chosen list of events look somewhat arbitrary.

For instance, the genetic-developmental 'toolkit' (especially long-range *cis*-regulatory components) that permitted the epigenetic specialization of cell lines and the construction of complex anatomies is unique to metazoans and commonly hypothesized as central to the origin of animals (Sebé-Pedrós et al., 2016; Erwin, 2009; Erwin and Davidson, 2009). Other regulatory genes and mechanisms can be found in the unicellular ancestors of metazoans (Bråte et al., 2018), and the cooption and complexification of these pre-existing machineries made major contributions to the great burst of novelty associated with the evolutionary radiation of animals. Further innovations that were crucial for animal multicellularity include mechanisms for intercellular adhesion and signaling, and these too are found in unicellular predecessors to animals (Grau-Bové et al., 2017). In addition, at least some protein-coding genetic novelty also contributed to the restructuring of the metazoan genotype-phenotype map (Paps and Holland, 2018). Even if sex was a necessary condition for these innovations, a view that focuses on sex is simply not going to capture the key difference-making factors that drove the origin and diversification of the metazoans.

Neither will a focus on nervous systems capture the full range of causal factors underlying metazoan morphological diversification. The gut—an anatomic innovation central to animal metabolic capacities—was arguably as crucial to the advent and diversification of animal multicellularity as the evolution of nervous systems (Hejnol and Martindale, 2009). In fact, nervous systems and guts probably had a dependent evolutionary relationship (Arendt et al., 2015; Holland et al., 2013; Jékely, Keijzer and Godfrey-Smith, 2015). The evolution of the gut also correlates with the evolution of body size (Hejnol and Martín-Durán, 2015), which is a robust trend in evolution that Bonner's account aims to track and explain. Although centralized nervous systems are implicated in the competitive escalations that characterize the Cambrian explosion (see Vermeij, 1987), there are equally crucial metabolic contributions to animal competition, since the latter relies on the evolution of metabolically expensive brains and active bodies. Indeed, there are critical metabolic dimensions to all of the episodes that Bonner and other major transition theorists identify. These dimensions form the basis of our positive account, which we will now describe.

7. Toward a Richer, Horizontal Perspective on the History of Life

The tendency to focus on the role of sexual reproduction and multicellularity in the history of life is symptomatic of a deeper 'paradigmatic' problem with major transitions theory. Namely, such explanations tend to overlook the metabolic innovations that accompanied these key 'vertical' transformations. Theories of major transitions, including Bonner's, have tended to focus on the *vertical dimension* that includes hierarchies (especially of individuality), replication and reproduction down the generations, and three-dimensional multicellular achievements. A focus on *horizontal* events and processes, on the other hand, includes (i) functional complexification within existing hierarchical levels, (ii) ecological interactions between clades and entities at the same hierarchical level, and (iii) innovation exchange across rather than down generations of lineages.

Metabolism dominates and unites all three of these horizontal features of the living world. Metabolism is the biologically structured conversion of energy and carbon, or, more abstractly, how cells and living systems persist in states that are far from thermodynamic equilibrium. All other physiological processes of the cell rely on metabolic functions. As we have already noted, the most consequential metabolic innovations all occurred at the 'level' of the prokaryote cell during the early phases of life. Earth-shaping metabolic innovations proliferated throughout the biosphere via lateral gene transfer, and they continue to drive the Earth's major biogeochemical cycles through symbiotic metabolic linkages that have persisted over eons of geological time and across tremendous turnover in taxa.

We are not suggesting that metabolism is the single true thread that can bind all major evolutionary turning points into a single unified account. Indeed, in light of the grand explanatory goals we attribute to major transitions theory, we are not optimistic that such a monistic theory can be achieved, given the causal diversity and contingent nature of the underlying subject matter. Rather, we are simply arguing that metabolic processes cannot be ignored in any account of macroevolution that tries to understand how life came to be as it is, what the most important turning points in life's history are, and how these key events occurred. Metabolism is indispensable regardless of whether the focus is on evolutionary transitions in individuality or broader notions of evolvability.

There is nothing inherently wrong with black-boxing metabolism in order to explore how certain obstacles to vertical transitions (such as the emergence of higher-level individuals) were overcome. Idealization is an indispensable part of scientific theorizing, model building, and research; whether abstractions are harmful depends entirely on the explanatory goals and context. However, if the goal of major transitions theory is to understand the events and processes that shaped the organization of life in its broadest strokes, including its vertical dimensions, then metabolism cannot be taken as a stipulated background condition. There is no basis by which to privilege replication over metabolism with respect to the defining features of life, its evolution, or key shifts in its organization.

Our previous work sets out how a more interactionist 'horizontal' dimension contributes to major transitions theorizing (O'Malley and Powell, 2016). In brief, we argue that by including networks of energy exchange, various methods of gene exchange (especially of metabolic modules), and key symbiotic dependencies we can gain a fuller view of evolutionary turning points and provide better explanations of classic upgrades in vertical complexity. We would minimally include in such a list the origin of life, the divergence of Bacteria and Archaea, the piecing together of key metabolic pathways able to exploit and transform the Earth (including the emergence of oxygenic

photosynthesis and oxygenation of the planet), the origin of eukaryotic cells, and the acquisitions of plastids. These events had profound evolutionary and ecological consequences and yet they have been largely left out of discussions of major transitions.

How are the events above captured by metabolism, and why are they major? The origin of life is most completely theorized as the encapsulation of metabolic and replication capacities within a cell membrane. Such membranes prevent the diffusion of metabolic processes and products, thus enabling energetic balances to be put toward the making of more cells and self-maintaining biosynthesis (Morowitz et al., 1988). What is most notable in this early phase of life is the great diversification of metabolic functions, with all the major metabolic pathways constructed in the first 1.5 billion years of cell evolution. In this 'aeon of biological innovation' (Falkowski, 2006), two remarkable events stand out. The first is the primeval divergence of cell types into Bacteria and Archaea (Sojo et al., 2014). These are the two basic domains of life, because eukaryotes are probably best understood nowadays as a peculiar clade within Archaea (Williams et al., 2013). What distinguishes these two domains is their membranes, which enable metabolic capacities, and the replication machineries that are sustained by their metabolisms. All the diversity we cherish on the planet today is 'merely' diversification within archaeal or bacterial lineages (or their fusion, aka eukaryotes), whether we examine this diversity genetically or metabolically. Their divergence, therefore, is indisputably major.

The other extraordinary event that brings this first aeon of innovation to a conclusion and opens up a new era of evolution is the bacterial invention of oxygenic photosynthesis (Buick, 2008; Knoll, 2003). Perhaps in itself this metabolic breakthrough is no more functionally remarkable an event than the emergence of any other novel metabolic pathway, but in this case the consequences for the future history of life were profound. We humans are here today because of the Great Oxidation Event that occurred ~2.7 billion years ago and has been maintained by microbial communities and symbioses ever since. Oxygen gains were initially modest under a purely bacterial regime, but with the emergence of eukaryotes a billion years later and the tendencies of some eukaryote lineages to acquire cyanobacterial and then full-blown algal cells endosymbiotically (Archibald, 2009; Keeling, 2010), the oceans and atmosphere attained modern oxygen levels. Any scheme of major evolutionary transitions that does not include the microbial metabolisms that transformed the planet oxygenically is manifestly incomplete.

Microbial metabolic innovations are also implicated in the origin of eukaryotes—a classic major transition that turns up in nearly every account no matter what its theoretical motivations. One influential view has it that eukaryogenesis was initiated and driven by a key 'horizontal' event: the endosymbiotic acquisition of the mitochondrion, which is thought to have provided massive energetic benefits by increasing membrane surface area for ATP-synthesis (Martin et al. 2015). There have been several recent challenges to this view (e.g., Pittis and Gabaldón 2016; Hampl et al. 2019; Lynch and Marinov 2015; Booth and Doolittle 2015), along with vigorous rebuttals (see, e.g., Lane and Martin 2016; 2015; Martin 2017; McBride 2018). Regardless of how this debate is ultimately resolved, adjudicating competing hypotheses of eukaryogenesis requires that we take into account key cellular features involved in making a metabolic living: phagocytosis (cell membrane innovations that allow for the engulfment and ingestion of food sources) or mitochondria. Could the emerging eukaryote cell generate sufficient energy to support complex biosynthesis through phagocytosis alone? Did the evolution of phagocytosis itself require a mitochondrial boost? How did the

protoeukaryote pay metabolically for a larger genome and its associated complexifying cellular machinery? Did the acquisition of the mitochondrion suddenly push this previously unexceptional lineage over a new bioenergetic threshold? Or was metabolism an unperturbed background condition that simply supported classic microevolutionary forces that gradually constructed the eukaryotic cell? Whatever the answers to these questions, a metabolic perspective is critical to an understanding of the origin and evolution of this new cell type, which was of crucial importance for the evolution of complex multicellular life. Merely pointing to the merger of previously independent replicators (e.g., Maynard Smith and Szathmáry, 1997) or sex (e.g., Bonner, 2019) does not provide a sufficient explanation of this event. Metabolism must be an integral part of the story.

Not only does a horizontal metabolic perspective include more events from the first two billion years of the evolution of life that continue to sustain the biosphere today, avoiding progressivist connotations, but it also helps explain other classic evolutionary transitions. For example, the diversification and complexification of animals cannot be understood without analysing feeding modes and their metabolic advantages (Mills and Canfield, 2017). Even the origin of sexual reproduction itself may have a potentially metabolic explanation, in that sex may function as a mechanism to control mitochondria, a key metabolic 'innovation' of eukaryotes (Blackstone, 2013). Other diagnostic features of the eukaryote cell, such as the nucleus, may also be a defensive response to mitochondrial acquisition (Martin and Koonin, 2006). Our point is not that vertical aspects (such as replication conflicts) are irrelevant to these events, but rather that the metabolic side of the equation is equally indispensable for understanding them.

In what ways is metabolism about 'the evolution of evolution'? This occurs in several dimensions. First, and possibly most banally, metabolism is inevitably involved in virtually any event brought to the foreground by any particular theory of major evolutionary transitions. For example, the origin and diversification of animals occurred within an environment structured by the availability of oxygen, which allowed extensive modifications of existing metabolic pathways. Some of these pathways and reactions are unique to and potentially formative of the energy-intensive demands of animal and plant bodies (Raymond and Segrè, 2006). Second, and more interestingly, most transitional events are either initiated by metabolic innovations or strongly canalized by them. The eukaryote cell is a good exemplification of this point, no matter which side of the current debate is favoured. The very nature of eukaryotes is defined and established by metabolic capacities. Third, and probably most importantly, the transformations wrought by metabolism are far-reaching, involving ecological and organismal transitions to new modes of life and interaction. Metabolism in numerous instances has transformed the basic evolutionary forces operating on populations by presenting utterly novel regimes of selection along with brand new organismal capacities for dealing with these pressures. The most groundbreaking of these innovations (the basic metabolic pathways, including oxygenic photosynthesis) all occur early in the course of life and continue even now to shape evolutionary possibilities across the planet, including the most consequential 'vertical' transitions in hierarchy.

Although we have attempted to shift the focus of major transitions theory onto metabolism, we concede that a number of explanatory perspectives are unavoidable if we want to understand major turning points in the history of life. Modes of genetic replication and regulation, morphological innovations, and behavioural novelties are also crucial to understanding the Big Picture of life on Earth. We emphasize metabolism because it is often taken as a stipulated backdrop and its

evolutionary events and explanations are overlooked not only in discussions of major transitions, but also in more clade-restricted contexts such as evodevo. Our aim is to draw attention to the major theoretical benefits of metabolism and its equal centrality to all life, big and small, on Earth or anywhere else it may evolve. Metabolism is undoubtedly a major explanatory force in the first two billion years of life, and it is implicated in all of the classic subsequent events that serve as the focal point of other major transition theories. It also avoids the inherent problems of such theorizing. A horizontal, interactionist picture of life does not result in a progressivist theory that culminates in humans (who can make no claim to metabolic superiority), and metabolism is an explanatorily unifying process that connects events across the entire tree of life—in all lineages, at all timescales. Not all major transitions theorists need to dwell on metabolism at length, but we do suggest they at least justify minimizing its contribution to their accounts.

Finally, some might think that the goal of major transitions theory is to reveal law-like patterns in macroevolution. If this is the goal, then it might justify the exclusion of historically contingent events (such as those we discuss above) no matter how critical they were to the actual history of life. As we understand it, however, the goal of major transition theory is to explain the overarching structure of life on Earth—and explaining this structure will almost certainly require appealing to historically contingent events as well as to law-like processes. Revealing how contingency and necessity have shaped the history of life on Earth should be one of the chief aims of major transitions research.

8. Conclusions

Theorizing and schematizing key events in macroevolution is a valuable exercise. The demands of doing so have been greatly increased since Maynard Smith and Szathmáry set out their thought-provoking manifesto. Even critical responses to their scheme have contributed greater insights into macroevolution, more careful analyses of key concepts such as complexity and individuality, and better explanations for major turning points. Our aim has been to put Bonner's recent efforts into this broader theoretical context and to suggest several general aspects of major transitions that still require attention whatever one's theoretical allegiances. To restate our positive messages: metabolism is a key contributing and innovating process in macroevolution, but it is not the single connecting thread that explains all; microbes and metabolic capacities are deeply implicated in all eras of life and explanations of major turning points, including key events in the evolution of macroscopic life. Although we disagree with several points of Bonner's account, we believe it will stimulate further reflections on how to explain—and celebrate—the history of life in *all* its diversity, complexity, and grandeur.

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