

Foreword

Andrew H. Knoll

Harvard University, Boston, MA

aknoll@oeb.harvard.edu

Multicellularity. On the face of it, the concept seems simple and unambiguous: some organisms package everything needed for metabolism, behavior, locomotion and reproduction into a single cell, whereas others contain multiple cells, commonly with varying functions. This is true enough, but it fails to account for the remarkable variety of multicellular organisms, or the nuances of their origins, development, and function. Accordingly, biologists commonly preface “multicellularity” with adjectives that acknowledge various axes of diversity. Multicellular organisms can be aggregative or clonal, emphasizing a fundamental distinction in life cycle. They may be obligate or facultative, changing in response to environmental signals. Or they may be viewed as simple or complex, with complexity variously defined by three-dimensionality, number of cell types, size, or function.

Thinking about this a decade ago, I threw my lot in with function, albeit an aspect of function that correlates with size, three-dimensionality and the differentiation of distinct cell types. As multicellular organisms begin to develop in three dimensions, cells in the interior of the organism become progressively distanced from the ambient environment — their source of food, oxygen and external molecular signals. With increasing size come expanding opportunities for feeding, defense, and environmental occupation, but also a greater need for mechanisms beyond diffusion to support interior cells. For this reason, my attempt to define complex multicellularity focused on the presence of tissues or organs that circumvent the limitations of diffusion. That works pretty well for bilaterian animals, plants, kelps and macroscopic fungi, but, admittedly, presents problems for florideophyte red algae, which pass tests for three-dimensionality, macroscopic size and cell differentiation with flying colors, but fare less well in terms of diffusion and its circumvention.

In fact, all attempts to categorize multicellularity have their strengths and limitations, for the simple reason that multicellular organisms are so various. Although commonly left out of the conversation, bacteria exhibit simple multicellularity in a number of clades; obligately multicellular cyanobacteria have existed for at least 2.5 billion years, and cyanobacteria capable of cell differentiation have been found as fossils in 1.5-billion-year-old rocks. Moreover, myxobacteria aggregate to form macroscopic structures. Among eukaryotes, simple multicellular clades have evolved repeatedly through time, with fossils of simple (presumed) macrophytes found in rocks as old as 1800-1600 million years, and more complex forms entering the record around 600 million years ago, as the age of animals began. In terms of complexity, there does seem to be something different about animals, plants, mushrooms and kelps, but all contain examples that flout the rules. Is *Trichoplax*, for example, complexly multicellular? Were the earliest known animals, preserved in Ediacaran rocks, complex, even though they probably consisted of little more than upper and lower epithelia surrounding a fluid- or gel- filled interior space? The answers may depend on your definition of complexity.

Ways of thinking about multicellularity have expanded along with our inventory of multicellular clades, and many of these exciting new approaches can be found in this volume. Better phylogenies and improved sampling, especially among protists and fungi, now show just how many times multicellular organisms have evolved from unicellular ancestors. And the application of the various 21st century “omics” is illuminating the molecular basis of multicellular development and function, while providing clues to the origins of multicellularity in diverse lineages. Integrating genomics with phylogeny, a number of labs are showing the virtues of molecular comparisons between multicellular clades and a relatively wide range of their unicellular relatives. For example, genomes of the closest sister groups to plants and animals appear to exhibit gene losses as well as gains, evident when a broader range of streptophytes and holozoans is examined.

When does a colony of unicells become a multicellular organism? Such a question emphasizes the importance of individuality in thinking about this subject. At a fundamental level, multicellularity reflects cooperative behavior among cells, but what mechanisms actually underlie the emergence of multicellular structures as evolutionary individuals? And how did nascent multicellular organisms deal with the confounding problem of cheaters, constant threats to the integrity of the system? In these pages, Rick Michod argues that only group selection – long debated by evolutionary biologists – “can make a cell suboptimal were it to leave the group” (Chapter 3).

While increasingly detailed studies of multicellularity emphasize the distinct evolutionary paths traveled by different multicellular clades, some commonalities persist. The evolution of clonal multicellularity – and, therefore, by far the greatest diversity of multicellular species – requires mechanisms of adhesion to ensure that cells remain in place following division. (This, in turn, also puts emphasis on intracellular mechanisms for regulating the geometry of cell division.) Communication among cells is equally key. A number of authors have underscored the evolution of plasmodesmata in photosynthetic clades and gap junctions in animals as key innovations in cell-cell communication. Such structures not only facilitate the passage of signals and other molecular traffic between cells, but provide a mechanism for signaling that is spatially specific. Related to this, the regular morphologies of multicellular organisms require developmental programs in which the fates of individual cells are determined by signals from their neighbors.

Although inherently obvious, it bears repetition that multicellular clades evolved from unicellular ancestors. Therefore, a better understanding of single-celled sister groups can do much to illuminate the bases of multicellularity. Unicells have sophisticated mechanisms for the transduction of signals from the environment and from conspecific neighbors, eliciting a variety of cellular responses. Homologous signaling mechanisms occur in their multicellular descendants, and so knowing signal's function in both ancestors and descendants provides clues to the causes, consequences and mechanisms of multicellular evolution. Life cycles also illuminate aspects of the multicellular program. It has long been known that genes active in the regulation of cell differentiation during the development of *Volvox* also play a role in cell differentiation during the life cycle of its close unicellular sisters. Evidence summarized in this volume also supports the hypothesis that cAMP regulation of multicellular aggregation and differentiation in *Dictyostelium* reflects an earlier evolution of starvation-induced encystment in its unicellular ancestors (Chapters 6-8). Comparable insights are flowing from detailed studies of choanoflagellates and other holozoan relatives of animals (Chapter 13), as well as streptophyte

sister groups of land plants (Chapter 9). Ancestors also impose constraints on multicellularity, for example the rigid cell walls of streptophytes and terrestrial fungi.

Finally, one of the greatest hurdles to the emergence of multicellularity lies in the fitness of early stages in the evolutionary path toward complexity. It is easy enough to appreciate the functional advantages of complex organisms with billions of cells, but what about the early stages of multicellular evolution, populated by organisms with perhaps a few dozen cells? Does predator avoidance furnish both a fitness advantage and scaffolding for the emergence of complexity? To what extent does the coordinated behavior of multiple cells enhance feeding, and does this, as well, provide a sufficient seed for complex multicellularity? Here is where ecology can help. We know little about how many simple multicellular taxa work in nature, and while experiments are providing welcome illumination, more is needed.

Plants, animals, mushrooms and seaweeds shape the ecosystems of our common experience, but they have characterized only the most recent fifteen percent of life's history. How did life expand so remarkably so late in the evolutionary day? And how did innovations in different multicellular clades feed back onto one another? In the pages that follow, readers will find a wealth of new observations, experiments and models that collectively enrich our understanding of multicellularity in all its manifestations. They provide welcome opportunity to learn – and an invitation to think further.