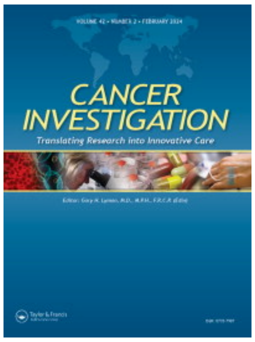

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The Nature, Origin, and Evolution of Life: Part III the Emergence of Complex Life

Gary H. Lyman, Christopher H. Lyman & Nicole M. Kuderer

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EDITORIAL/COMMENTARY

The Nature, Origin, and Evolution of Life: Part III the Emergence of Complex Life

> *I cannot consider the organism without its environment….From a formal point of view the two may be regarded as equivalent phases between which dynamic contact is maintained by the membranes that separate and link them* (1)
>
> *-Peter Mitchell*

Introduction

In the last commentary, we discussed the conditions that likely existed on the early earth which formed about four and one-half billion years ago. The earliest life forms emerged relatively rapidly on the cosmic scale within one billion years of the earth's formation (2). Previously, we discussed the basic logical processes needed for life to develop and evolve (3). These included information storage and replication, metabolic processes facilitated by higher level constraints and some type of semipermeable barrier to both protect the information and metabolic processes enabling the capture of energy sources and the exchange of heat and waste products. We have noted that life, by definition, is associated with organized structures and processes locally reducing entropy and releasing heat and byproducts to the surrounding environment increasing overall entropy in alignment with the second law of thermodynamics.

While the exact processes involved in life's emergence are still not completely known, we have seen that the basic organic building blocks necessary for the eventual formation of living matter were present. These include simple amino acids, nucleotides, carbohydrates and lipids which were present early in the earth's history as well as from likely extraterrestrial sources. The initial energy sources needed for the synthesis of these components likely came from solar, chemical, and other geophysical sources. Therefore, along with the emergence of favorable conditions on the earth's surface, we have evidence for the availability of essential sources of energy and the necessary elements for life. However, exactly how these assembled into the polymers and ordered structures such as proteins and enzymes, RNA and DNA and the complex membranous structures of living cells remains a large gap in our understanding of the emergence of early life. Clearly, a method for energy capture and storage was necessary along with the ability to utilize that energy to form linkages between the building blocks increasing order while releasing excess energy in the form of heat. For life to further develop and evolve into the extraordinarily complex and diverse arrangement of modern cells and living organisms today represents an additional enormous gap in our understanding of life.

Emergence of the increasing complexity of life

The emergence and evolution of living matter is closely associated with the increasing complexity of the various components of life. Such complexity, as evident today, appears to manifest itself through hierarchical controls, each level of which exerts increasing constraints on the various levels of elements at lower levels and increasingly ignoring greater details of the underlying dynamics. This is associated with the appearance of higher-level properties of the overall system not evident based on the dynamic relationships at the lower levels. Such hierarchical control becomes ever more evident and dramatic within multicellular organisms where the basic elements of life, the cells, are controlled in subservience to the whole organism (4).

The increasing complexity of living matter inherently requires energy to move the biological system from one stable state to a higher energy stable state. The resulting increased complexity and local decrease in entropy are generally associated with the formation of new chemical bonds between atoms and molecules. At the same time, the release of energy in the form of heat raises the entropy of the surrounding environment such that the net entropy of the entire system stays the same or increases in accordance with the second law of thermodynamics (1). While the earliest origin of life may have used naturally occurring solar, thermal, and chemical energy sources, further development and the increase in complexity of life required a more predictable and controlled form of energy storage within the living cell itself. While inefficient and less predictable sources of energy storage may have emerged early, a great need existed for a molecular mechanism for accomplishing this task if life was to develop further in complexity.

The prevailing theory of the increasing complexity of life is aligned with our basic understanding of genetic variation and natural selection where altered phenotypic traits offering structural or functional advantages to living cells gain a preferential advantage. An alternative theory proposes that life increased in complexity by a series of symbiotic events where one primitive life form was engulfed or otherwise internalized into another adding additional functionality. This latter approach does not appear to have been a common mechanism for increasing cell complexity, there is compelling evidence that such a process resulted early in life's history with the internalization of a primitive bacterial form with unique energy capture and storing capability and now recognized as the mitochondria present in the cells of all eukaryotic organisms (1). Mitochondria have their own DNA sequences some of which have been integrated into the parent cell's DNA serving as a permanent host (5). The integration of mitochondria into these early cells had a dramatic energizing effect that subsequently enabled the development of greater complexity including the development of multicellular organisms of enormous complexity. In the words of Nick Lane "the acquisition of mitochondria and the origin of complex life was one and the same event" (1).

Phylogenetics and the family tree

The ability to sequence DNA has revolutionized our understanding of the impact of evolution across the lineages of living species. In order to develop a family tree based on the ancestry of genes, studies of genes thought to be critical to life processes have been studied across species. Insight has been gained by a particular focus on intracellular ribosomes constituted from multiple protein subunits and intricately involved in the translation of the genetic code in DNA/RNA into proteins synthesized from individual amino acids. Studies have compared various species of bacteria to very complicated eukaryotes establishing a remarkable new family tree based on genetic relatedness. Three major domains of living organisms have been established including the well-recognized eukaryotes (animals, plants and fungi) with a fairly complex common ancestor population of cells, the more primitive prokaryotes constituted by bacteria along with a new grouping termed archaea. Based on phylogenetics, it can be assumed that any traits persistent in all resulting lineages of eukaryotes were likely present and inherited from their common ancestor including DNA within a complex nucleus surrounded by a double membrane with core proteins embedded in a continuous complex membrane structure within the cytoplasm along with mitochondria and countless intracellular structures hosting the cells metabolic machinery. Likewise, all eukaryotes share the basic cellular processes of DNA replication, protein synthesis including histones surrounding DNA and energy production and storage and thus were almost certainly present in their primitive ancestor reflecting their similar genetic coding and information processing (1). Unfortunately, phylogenetics tells us almost nothing about how all these complex structures and processes actually arose and developed in the period soon after life's emergence. While the Archaea and Bacteria resemble each other morphologically, they are extraordinarily different in their genetic makeup and metabolism from one another as they both are different from eukaryotes. All of this, of course, starkly highlights the enormous gap in our understanding of how such incredible complexity emerged early in the most primitive life forms leading to the eventual emergence of eukaryotes. In our search for even preliminary answers, we turn to the words of Nick Lane: "*The detailed mechanisms of energy harvesting turn out to be conserved as universally across life as the genetic code itself, and these mechanisms exert fundamental structural constraints on cells.*"

Mitochondria and membrane bioenergetics

More recent studies suggest that the origin of the structure that eventually became the mitochondria present in all eukaryotes was precipitated by the acquisition of a primitive bacteria by a host archaea cell and eventual endosymbiosis into eukaryotes (5). Subsequently, genes from both bacteria and archaea were integrated into a mosaic genome prompting the subsequent development of the very complex characteristics of the eukaryote lineage.

All of this complex development appears to be the aftermath and directly related to the unique method of energy generation and storage that takes place in the resulting mitochondria. Ultimately, the energetics of all forms of life, including prokaryotes and eukaryotes, comes from the ability to form proton gradients across the mitochondrial membrane resulting in a flow of protons (6). The core of this unique but universal method of energy production takes place in the inner membrane of mitochondria where a sequence of protein clusters host the respiratory chain where electrons from nutrients are captured. They then move from one protein cluster to another through, what is thought to be, the nearly instantaneous process of quantum tunneling resulting in a sequence of reductive and oxidative steps ultimately donating an electron pair to oxygen (7). For each electron pair acquired from food, ten protons move across the membrane to form a protein gradient due to the tight impermeability of the phospholipid membrane. Thus, some of the energy accompanying the flow of electrons to oxygen, is stored as a proton gradient across a very thin membrane which can subsequently be used to generate ATP through another membrane protein, ATP synthase. This energy, in turn, is used by the cell to generate biopolymers and the complex molecular machinery of the cell including structural proteins, enzymes, nucleic acids and essentially every biochemical process associated with cell growth, differentiation, replication, and metabolism.

As Nick Lane highlights in great detail, the energy produced by mitochondria that energizes the biochemistry of every cell is enormous at the molecular level generating a electrochemical potential difference across the membrane of up to 200 mV (1). Given the short distance across the membrane, this potential difference would be equivalent to approximately 30 million volts per meter (1). A typical cell contains approximately 10,000 copies of each respiratory complex and each cell contains hundreds or even thousands of mitochondria. Among the nearly 40 trillion cells in an adult, more than 10^{21} protons are pumped every second (1).

The key factor distinguishing the evolutionary path to complexity between prokaryotes and eukaryotes, according to Lane, is the availability of energy per gene. While eukaryotes on average are much larger with more DNA than prokaryotes, eukaryotes have a thousand-fold or more energy for supporting a larger genome and gene expression with the formation of peptide bonds between amino acids and thus much greater protein synthesis than prokaryotes (1). It is telling that eukaryotic cells have 1,000–10,000 more ribosomes for protein synthesis compared to prokaryotes (1). Thus, the capacity and perhaps the requirement for the ability of eukaryotic cells to increase rapidly in cellular complexity and eventual multicellularity was forged early. In the end, the key to the enormous energy production to fuel gene expression and cellular complexity in eukaryotes are the mitochondria (8).

Evolution accelerates

With the advent of eukaryotic cells with the unique ability to dramatically generate energy either through photosynthesis enabled by symbiotic chloroplasts in certain cells or mitochondria present in all eukaryotic cells, an energy revolution occurred. This subsequently led to the rapid development of increasingly complex cellular organisms and the eventual development of multicellular organisms. While bacteria and archaea have continued to thrive on the earth, evolution of their complexity has been structurally constrained and they persist as unicellular organisms. On the other hand, the constraints on eukaryotic evolution were released eventually giving rise to the enormous diversity and complexity of life today all of which have been enabled by endosymbiotic events 2–3 billion years ago. At the same time, we must note that all eukaryotic cells and organisms appear to be related having arisen from these early events which set them on a path to rapid increases in complexity and the evolution of modern life. Finally, we must not lose sight of the fact that the evolving complexity of life was largely driven by the intimate interaction of living forms with the environment which has driven the dominance of those complex traits enabling life to compete more successfully and survive.

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ORCID

Gary H. Lyman http://orcid.org/0000-0002-0823-8086

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Gary H. Lyman
Editor-in-Chief, Cancer Investigation Division of Public Health Sciences, Fred Hutchinson Cancer Center, Seattle, Washington, USA
glyman@advancecancerresearch.org

Christopher H. Lyman
Guest Editor, Cancer Investigation
Department of Business Analytics, University of Virginia, Charlottesville, Virginia, USA

Nicole M. Kuderer
Deputy Editor, Cancer Investigation
Advanced Cancer Research Group, Kirkland, Washington, USA