

Chapter 2

Origin of Prokaryotes and Eukaryotes

*The past the finite greatness of the past/For what is the present
after all but a growth out of the past.*

—Walt Whitman

Speculation on the Origin of Protocells

The fundamental desire to understand the origin of life is demonstrated by the fact that essentially all human cultures contain a story of how life began. From the tribes of ancient times to the mythologies of more modern cultures, there are countless stories of the origin of life. Some are based in pagan beliefs, while others are based on creation resulting from a holy deity. This collection of myths, legends, and tribal knowledge handed down over generations is the collective expression of how man has attempted to explain his world and his place in it. What is common to all these cultures is that their specific story of how life began is accepted without question. The role of the adults is simply to teach the story to the children.

The distinguishing feature of the scientific approach to understanding the origin of life is that it begins by acknowledging the fact that we do not know how life began. Only by admitting that we do not have the answer, is it possible to put forth and test multiple hypotheses.

The origin of life is one of the most challenging problems in biology. The best evidence is that prokaryotic life (microorganisms lacking a membrane-bound nucleus) first appeared on Earth about 3.8 billion years ago (Zimmer 2009). The abiogenesis theory of the origin of life begins with the experimentally supported concept that simple organic compounds, such as amino acids, organic acids, purines, pyrimidines, and simple sugars, could have been produced spontaneously in the earth's primitive reducing atmosphere (Oró and Kamat 1961), containing CH₄, H₂, H₂O, N₂, and NH₃ (Schaefer and Fegley 2010). Further, these molecules could have been concentrated into a "prebiotic organic soup" in evaporation ponds. Whatever the earliest events on the road to the first living cell were, it is clear that at some point the large biological molecules found in modern cells must have emerged. Considerable debate in origin-of-life studies has revolved also around which of the fundamental macromolecules came first—proteins, DNA, or RNA. To gain insight into this question it is useful to consider the functions performed by each of these polymers in existing organisms.

The proteins make up about 50 % of the mass of most cells and are the main structural and functional agents in the cell. Catalytic proteins, or enzymes, carry out the thousands of chemical reactions that take place in any given cell, among them the synthesis of all other biological constituents, including DNA and RNA. However, proteins cannot replicate themselves. They require the information contained within the nucleic acids, DNA, and RNA. In all modern cellular organisms, DNA serves as the storage site of genetic information. The DNA contains the instructions for the manufacture of proteins. In the modern cell, protein, DNA, and RNA are each dependent on the others for their manufacture and function. DNA, for example, is merely a blueprint, and cannot perform a single catalytic function, nor can it replicate on its own. Proteins, on the other hand, perform most of the catalytic functions, but cannot be manufactured without the specifications encoded in DNA and transcribed to RNA. This classic “chicken-and-egg” problem made it immensely difficult to conceive of any plausible pre-biotic chemical pathway to the molecular biological system.

One possible scenario for life’s origins is that two kinds of molecules evolved together, one informational and one catalytic. But scientists studying the origin of life consider this scenario extremely complicated and highly unlikely. Another possibility, currently favored by many theorists, is that one of these molecules, namely RNA, could itself perform the multiple functions of self-replication and catalysis. Catalytic RNAs, also referred to as ribozymes, were discovered in the 1980s (Cech et al. 1981; Guerrier-Takada et al. 1983). Today, RNA molecules are the only molecules known both to store genetic information (as in the RNA viruses and viroids or during transport in the form of mRNA) and to exert biological catalysis, like a protein enzyme. RNA may therefore have supported precellular life and been a major step in the evolution of cellular life. This hypothesis, referred to as the “RNA world” (Gilbert 1986), has gained support in recent years from experiments demonstrating that RNA can perform self-cleavage and autocatalyze its own synthesis (Johnston et al. 2001). The RNA world hypothesis assumes a phase of life, whereby catalytic biopolymers consisted exclusively of ribozymes, hence the name “RNA world.” With the appearance of the prototypical ribosome began the translation of RNA sequences into protein sequences. This gave rise to an RNA–protein world with a step-by-step replacement of ribozymes by enzymes (enzymatic take-over). Much later, according to this theory, RNA as the replicating informational molecule was replaced by the chemically more stable double-stranded DNA (Lazcano et al. 1988). Although criticized by several scientists (Bernhardt 2012), the RNA world hypothesis is considered the most promising we currently have to help understand the backstory to contemporary biology.

Another important issue to consider in the origin of life is boundaries, how molecules might have interacted to assemble into the first cell-like structures, or “protocells.” The origin of cell membranes is a major unresolved issue of evolution (Peretó et al. 2004). Contemporary cells are enclosed by membranes that are essentially made out of phospholipid bilayers (or monolayers in many thermophilic prokaryotes) into which different proteins are embedded. Phospholipids are amphipathic (contain both polar and hydrophobic groups) molecules composed

of a glycerol phosphate moiety and two lateral hydrocarbon chains (usually C14–C20). The membranes of eukaryotes also contain cholesterol. Membranes keep the cell components physically together and form a barrier to the uncontrolled passage of large molecules. Sophisticated proteins embedded in the membrane act as gatekeepers and pump molecules in and out of the cell, while other proteins assist in the construction and repair of the membrane. How on earth could a rudimentary protocell, lacking protein machinery, carry out these tasks? Primitive membranes were probably made of simpler molecules, such as fatty acids (which are one component of the more complex phospholipids). Research has shown that membranes could indeed assemble spontaneously from elementary fatty acids, and molecules as large as nucleotides can in fact easily slip across these membranes as long as both nucleotides and membranes are simpler, more “primitive” versions of their modern counterparts. In fact, it has been shown that fatty acid-based membrane vesicles containing a short piece of a single-stranded nucleic acid could incorporate active versions of nucleotides (Richardo and Szostak 2009). The nucleotides crossed the membrane spontaneously and, once inside the model protocell lined up on the nucleic acid which reacted with one another to generate a complementary strand. Some experimental evidence supports the idea that the first protocells contained RNA (or something similar to it) and little else and replicated their genetic material without enzymes.

We would like to emphasize that attempts to explain the origin of life are rich in speculation and poor on evidence. When a particular concept is tested in a laboratory and yields a result consistent with the hypothesis, then the hypothesis moves from pure speculation to a possible hypothesis. For example, the formation of amino acids from gases in the Earth’s prebiotic atmosphere is a possible step in the origin of life because it has been experimentally demonstrated. The RNA world hypothesis is still primarily speculation since the abiotic formation of activated ribonucleotides has not yet been shown. It should be pointed out that there are other published speculations on the origin of life, such as the “protein interaction world” (Andras and Andras 2005) and the iron–sulfur world (Wächtershäuser 2010) hypotheses.

An alternative to the concept that life originated on Earth by a series of prebiotic chemical reactions is the Panspermia Theory. The word “Panspermia” comes from the Greek language and means “seeds everywhere.” The seeds in this case would not only be the building blocks of life, such as amino acids and monosaccharides, but also small extremophile organisms. The theory states that these “seeds” were dispersed “everywhere” from outer space and most likely came from meteor impacts. Once the earth had cooled sufficiently, these invading microbes from other celestial bodies found the conditions favorable for growth and gave rise to life on this planet.

Recent research has provided some support for the Panspermia Theory. First, we now know that the time from when the earth cooled to permit life and the first evidence of life was relatively short, less than 300 million years; further, the first microfossils were photosynthetic cyanobacteria. Most models of the origin of life have the earliest organisms obtaining energy from reduced chemicals, with the

more complex mechanisms of photosynthesis evolving later. Second, it has been argued that some microbes are resistant to extreme conditions and may be able to survive for very long periods of time, probably even in deep space and, hypothetically, could travel in a dormant state between hospitable environments (Nicholson et al. 2000). Third, researchers have reported the presence of complex organic molecules (Callahan et al. 2011) and possibly extraterrestrial bacteria (D'Argenio et al. 2001) inside meteorites.

The Panspermia Theory has been criticized because it dodges the question. If the earth was infected by microbes, we still have to explain how these microbes came into existence on their native planet. Nevertheless, the Panspermia Theory has been supported by several leading scientists, including Stephen Hawking, Nobel Prize winner Francis Crick, and Leslie Orgel (1973).

Origin of Prokaryotes and Eukaryotes

The oldest direct evidence for life on Earth is well-preserved microfossils of prokaryotes found in 3.9-billion-year-old rocks in Western Australia (Wacey et al. 2011). Prokaryotes (Greek for “before karyon” or “before nucleus”) are simple, single cell organisms that lack a membrane-bound nucleus. Eukaryotes (Greek for “true nucleus”) divide by mitosis and possess a membrane-bound nucleus, an intricate cytoskeleton, mitochondria, and in the case of algae and plants cells, also chloroplasts. Based on the fossil record, single cell eukaryotes first appeared ca. 1.8 billion years ago (Parfrey et al. 2011). According to these data, prokaryotes were the only cellular form of life for 2.1 billion years. During this time, prokaryotes evolved most of the biochemistry present in all forms of life, including DNA replication, the genetic code, protein synthesis via transcription and translation, photosynthesis, and anaerobic and aerobic metabolism. Furthermore, based on differences in their ribosomal RNA gene sequences, molecular microbiologists have concluded that during this time, prokaryotes split into two groups, or domains, titled Bacteria (or eubacteria) and Archaea (or archaeobacteria) (Woese and Fox 1977; Pace et al. 2012).

Since eukaryotes perform the same basic biochemical reactions as prokaryotes, i.e., the unity of biochemistry, it is highly likely eukaryotes descended from prokaryotes. For example, of the approximately 22,000 human genes that code for proteins (Stein 2004), 60 % of them are homologs of prokaryotic genes (Domazet-Lošo and Tautz 2008), primarily those involved in intermediate metabolism. Many scientists assumed that eukaryotes evolved from prokaryotes through the familiar process of mutation and natural selection. However, Lynn Margulis argued that a number of parts of the eukaryote cell were acquired in a radically different way, namely by the fusion of separate bacterial species (Sagan 1967). Many studies have bolstered this once-controversial endosymbiont hypothesis. Let us first consider the mitochondrion, a fundamental organelle of all eukaryotic cells. Mitochondria resemble bacteria in many ways. Both are surrounded by a double layer membrane,

and the structural arrangement of the inner and outer membrane of mitochondria is similar to Gram-negative bacteria. Mitochondria and bacteria can use oxygen to generate chemical energy, in the form of adenosine triphosphate (ATP) molecules. The ribosome coded for by mitochondrial DNA is similar to those from bacteria in size and structure. Mitochondria have their own bacterial-like DNA, which they duplicate when they divide, similarly to bacteria, into new mitochondria. Based on DNA analyses, mitochondria are closely related to the intracellular parasite *Rickettsia prowazekii* (Andersson et al. 1998), the causative agent of epidemic typhus. Using similar arguments, it is now generally accepted that chloroplasts of photosynthetic algae and plants arose through incorporation into cells of symbiotic cyanobacteria (Martin et al. 2002). In fact, the data indicate that chloroplasts were acquired through multiple primary endosymbiotic events (Fagan and Hastings 2002) that occurred long after the acquisition of mitochondria (Perasso 1989). If one accepts the bacterial origin of mitochondria and chloroplasts, then the eukaryote cell, itself, is a holobiont.

One of the fundamental differences between eukaryotes and prokaryotes is the presence of a membrane-bound nucleus in eukaryotes. Because the nucleus lacks an obvious homologue or precursor among prokaryotes, ideas about its evolutionary origin are diverse and highly speculative. One hypothesis is that a prokaryotic cell membrane formed an invagination that enclosed the DNA in a primitive prokaryote (probably an Archaea) and this membrane-bound DNA evolved into the nucleus (Jékely 2003). Another hypothesis is endosymbiosis of an archaebacterium within an eubacterium, with the archaebacterium becoming a nucleus (Martin 2005). The reason for assuming that the archaebacterium became the nucleus is that the molecular machinery involved in information storage and retrieval in eukaryotes is more similar to archaebacterial counterparts than to eubacterial counterparts (Reeve 2003). On the other hand, eukaryotic genes involved in metabolic and biosynthetic pathways reflect a eubacterial ancestry (Simonson et al. 2005).

Recently, it has been discovered that certain bacterial species within the phylum Planctomycetes possess features typical of eukaryotic cells, such as intracellular compartmentalization, a lack of peptidoglycan in their cell walls, and a membrane-bound nucleoid analogous to the eukaryotic nucleus (Fuerst and Sagulenko 2011). However, Planctomycetes are definitely bacteria on the basis of gene sequence trees such as those from ribosomal RNA (Fuerst 2010). Planctomycetes have several other dramatically distinctive features separating them from other prokaryotes (Fuerst 1995). They occur in many marine and freshwater aquatic habitats and in soils, as well as in extreme habitats such as the ultra-dry Mars-like soil of the Atacama Desert (Schlesner 1994) and living stromatolite microbial mats in hypersaline marine shallows (Papineau et al. 2005). They are so different from other bacteria that, when first detected by microscopy of lake water, they were confused with fungi since some have stalks easily mistaken for cellular filaments like those of fungi. The compartmentalization of Planctomycetes challenges our hypotheses regarding the origins of eukaryotic organelles. Furthermore, the recent discovery of both an endocytosis-like ability in addition to proteins homologous to

eukaryotic clathrin in a planctomycete marks this phylum as one to watch for future research on the origin and evolution of the eukaryotic cell (Fuerst and Sagulenko 2011).

A third provocative option for the origin of the nucleus revolves around viruses. It has been proposed that a complex membrane-bound DNA or RNA virus became established in a prokaryote and evolved into the eukaryotic nucleus by acquiring genes from the host (Bell 2001). The eukaryotic nucleus shares several properties with certain viruses, such as mRNA capping, linear chromosomes, and separation of transcription and translation. According to this hypothesis, a large virus would take control of a bacterial or archaeal cell. Instead of replicating and destroying the host cell, it would remain within the cell. With the virus in control of the host cell's molecular machinery it would effectively become a "nucleus" of sorts (Forterre 2006). Through the processes of mitosis and cytokinesis, the virus would thus hijack the entire cell—an extremely favorable way to ensure its survival. The hypothesis that a virus was the origin of the eukaryotic nucleus brings forth the question of the origin of viruses.

The recent discovery of giant DNA viruses has provided some additional support for the viral origin of the nucleus hypothesis (Philippe et al. 2013). These virus particles are large enough to be visible under light microscope and contain DNA genomes larger in size and gene content than some bacteria and simple eukaryotes (Xiao et al. 2009). Amongst the more than 1,200 genes present in the giant viruses are several genes thought to be the hallmark of cellular organisms, including a number of genes coding for eukaryotic-like proteins involved in transcription and translation.

It should be pointed out that the three hypotheses are not mutually exclusive and a combination of them may have been involved in forming the nuclei of eukaryotic cells.

Origin of Viruses

Since their discovery in the late nineteenth century (Bordenave 2003; Iwanowski 1892), viruses have challenged our concept of what "living" means. Initially seen as toxic agents that cause disease (Beijerinck 1898), then as life-forms that multiply only in cells, and then as biological chemicals that could be crystallized (Bernal and Fankuchen 1941), viruses are currently thought of as being in a gray area between living and nonliving (Villarreal 2004). The Nobel laureate André Lwoff wrote (Lwoff 1967), "Whether or not viruses should be regarded as organisms is a matter of taste. A virus is a virus." Regardless of whether or not one considers viruses living organisms, it is now clear that they play a major role in controlling geochemical cycles (Rohwer and Youle 2011), structuring cellular populations and, as we shall see, also in the fitness and evolution of holobionts (discussed in Chap. 7).

Three main hypotheses have been put forth to explain the origin of viruses (Wessner 2010):

- (1) Viruses arose from intracellular genetic elements that gained the ability to move between cells. According to this hypothesis, viruses originated through a progressive process. Mobile genetic elements, pieces of genetic material capable of moving within a genome, gained the ability to exit one cell and enter another.
- (2) Viruses are remnants of cellular organisms. In contrast to the progressive process of hypothesis 1, viruses may have originated via a regressive, or reductive, process. Microbiologists generally agree that certain bacteria that are obligate intracellular parasites, like *Chlamydia* and *Rickettsia* species, evolved from free-living ancestors. It follows, then, that existing viruses may have evolved from more complex, possibly free-living organisms that lost genetic information over time, as they adopted a parasitic approach to replication.
- (3) Viruses predate or coevolved with their current cellular hosts.

It should be pointed out that these hypotheses are not mutually exclusive. To distinguish between these hypotheses it would be useful to date the origin of viruses. Unfortunately, it has not yet been possible to detect ancient viruses in fossils (Emerman and Malik 2010). However, there is strong circumstantial evidence that viruses emerged very early in the evolution of life, before the separation of prokaryotes into two domains: Eubacteria and Archaeobacteria. The evidence is the striking structural similarities between viruses that infect organisms belonging to the different domains of life. For example, archaeal and bacterial tailed phages show remarkable morphological similarity (Zillig et al. 1996), and the *Sulfolobus islandicus* rod-shaped archaeal virus SIRV shows structural and mechanistic similarities to eukaryotic poxviruses (Filée et al. 2003). If the viruses arose after the separation into the three domains of life, one would expect that each domain would have its own characteristic viruses.

Another argument in favor of the early origin of viruses is that some eukaryotic and prokaryotic viruses exhibit a high level of similarity with regard to the organization of their genomes and replication process (Peng et al. 2001). If viruses arose from intracellular genetic elements (hypothesis 1), or are remnants of cellular organisms (hypothesis 2), then one would expect strong homology between virus genes and cellular genes. In fact, most genes in viromes have no homologues in cellular genomes (Wommack et al. 2009). Even more convincing is the fact that so-called hallmark genes that are central to viral replication and structure are shared by many RNA and DNA viruses but are missing from cellular genomes (Koonin et al. 2006). It has been suggested that the first viruses were RNA viruses that originated during the RNA world and played a critical role in major evolutionary transitions, such as the invention of DNA and DNA replication mechanisms (Forterre 2013).

Although the origin of viruses remains an unsolved mystery, it is highly likely that virus-like entities predated the appearance of modern cells. The common dismissal of an early viral origin on the grounds that all extant viruses are intracellular parasites is over simplistic.

Origin of Multicellular Organisms

Multicellularity developed in prokaryotes prior to eukaryote evolution (Bonner 1998). The fossil record indicates the presence of multicellular cyanobacteria about 2.7 billion years ago, whereas multicellular eukaryotes are first seen only 1.2 billion years ago (Fedonkin 2003). Let us consider some theoretical advantages of multicellularity. To begin with, the smaller the cell the higher the ratio of cell surface to volume. This allows for rapid uptake of nutrients and removal of waste products and is one of the traits that enable bacteria to grow rapidly. However, having a high surface-to-volume ratio also makes the cell more exposed and more vulnerable to the environment. To overcome this predicament, a cell can either grow larger or enter into aggregations with other cells, i.e., become multicellular.

Many types of bacteria form biofilms, which are structured cell aggregates. Bacteria inside the biofilm are considerably more resistant to antibiotics and other toxic materials than free-living cells. Still it is crucial that the multicellular structure be constructed such that water, nutrients, and waste products can flow through it. In addition to protection, multicellularity allows for cell density-dependent reactions (Rosenberg et al. 1977). For example, metabolic utilization of nutrients that contain polymers, such as proteins and polysaccharides, requires extracellular enzymes because polymers generally cannot be transported through cellular membranes. An isolated individual cell does not produce a high enough concentration of enzyme in its surroundings to effectively breakdown the polymer to smaller units that can be taken up by the cell. However, an aggregate of cells, each contributing enzymes, can efficiently breakdown the polymer into smaller units which can be taken up by all the cells in the multicellular structure. The same cell density-dependent argument holds for cell signaling. Cell-to-cell adhesion and signaling are two mechanisms that are widespread in the bacterial world. *Myxobacteria xanthus*, for example, when starved of nutrients, produce signals and aggregate by gliding chemotaxis in order to construct species-specific fruiting bodies consisting of thousands of cells (Dworkin 1996). Interestingly, the signals used by *M. xanthus* include molecules, such as kinases and G proteins, in common with eukaryotes. It should be pointed out that most natural biofilms are composed of a cooperating mixture of different species of bacteria; accordingly, they fit the definition of symbiosis.

The origin of the first multicellular eukaryotic organism has been a topic of intense debate in biology, and many hypotheses have been put forth to explain this evolutionary milestone (Grosberg and Strathmann 2007). It is reasonable to

hypothesize that early eukaryotic cells, formed by the fusion of two or more prokaryotes, had the genetic information that would allow for cell-to-cell interactions and the formation of multicellular structures. Support for this hypothesis comes from the discovery that morphogenesis of a choanoflagellate (one of the closest living relatives of animals) is induced by bacteria in the Bacteroidetes phylum (Alegado 2012). Further, it was shown that the inducing factor is a bacterially produced sulfonolipid. This study provides another example of how bacteria may have contributed to the evolution of animals. The relative ease at which unicellular organisms can evolve into multicellularity is supported by the fact that multicellularity has evolved independently dozens of times in the history of Earth, for example at least once for plants, once for animals, once for brown algae, and several times for fungi, slime molds, and red algae (Bonner 1998).

The earliest animal that still exists is the sponge. What can the sponge tell us about the early evolution of animals? Costerton et al. (1995) has compared modern sponges to biofilms because both lack tissues and organs, but are composed of a three-dimensional matrix that allows for the flow of water, nutrients, metabolites, and oxygen. Modern sponges are well known for containing large complex microbial symbiotic communities. More than half of the biomass of some sponges is bacteria (Taylor et al. 2007). The fossil record of sponges demonstrates their ancient association with bacteria, further indicating that prokaryotic symbionts were essential components of animals from their very beginning. Interestingly, some present sponge symbionts produce proteins which have domains that have cell-attachment activity (Siegl et al. 2010). One could speculate that similar bacterial proteins were involved in providing the “glue” for the construction of the first multicellular eukaryotes. Some evidence exists for specific genes involved in early multicellularity (Rokas 2008).

It should be pointed out that not all manifestations of multicellularity are the same. For example, multicellularity in volvocine green algae likely evolved as a consequence of incomplete separation after cell division, whereas in cellular slime molds multicellularity evolved as a consequence of aggregation (Waggoner 2001). Many, but not all, of the molecular components of the genetic toolkit for multicellularity are also present in the DNA records of unicellular relatives, which suggest that these components were likely present in their last common (unicellular) ancestor (Rokas 2008). A large fraction of the additional genes associated with cell–cell signaling and transcriptional regulation observed in these multicellular–unicellular comparisons can be accounted for by gene duplication (Goldman et al. 2006). Genomic analysis of *M. xanthus* identified more than 1,500 duplications that occurred during the transition to multicellularity, and determined that cell–cell signaling and regulatory genes underwent 3–4 times as many duplications as would be expected by chance.

In light of the available information, we propose that animal and plant cells arose from prokaryotic organisms by fusion, aggregated into multicellular complexes, initially using prokaryotic genetic information, and differentiated into animals and plants, always in close association with microorganisms. During evolution, which is discussed in Chap. 8, animals and plants acquired additional

structures and functions either by changing their DNA or by acquiring new symbionts. Good examples of the latter are ruminants (Dehority 2003) and termites (Brune 2011), which evolved the ability to utilize cellulose as a nutrient by incorporating cellulose-decomposing microorganisms, thereby avoiding the very slow process of evolving novel efficient enzyme systems and regulatory elements by themselves.

Key Points

- Life, in the form of prokaryotes, first appeared on earth about 3.8 billion years ago. The abiogenesis theory of the origin of life begins with the experimentally supported concept that simple organic compounds would have been produced spontaneously in the earth's primitive reducing atmosphere. These molecules could have been concentrated into a "prebiotic organic soup," which by chemical evolution gave rise to polymers and eventually protocells. The Panspermia Theory considers that once the earth cooled it was infected with extremophile organisms from other celestial bodies.
- The "RNA world" hypothesis assumes an early phase of life, wherein catalytic biopolymers consisted exclusively of ribozymes. Subsequently, prototypical ribosomes began the translation of RNA sequences into protein sequences. Much later, RNA as a replicating informational molecule was replaced by the chemically more stable DNA.
- Single cell eukaryotes first appeared ca. 1.8 billion years ago, so that prokaryotes were the only cellular form of life for 2.1 billion years. During this time, prokaryotes evolved most of the biochemistry present in all forms of life and split into two groups, or domains, termed Bacteria (or eubacteria) and Archaea (or archaeobacteria).
- The formation of eukaryotes involved endosymbiosis of prokaryotes, mitochondria being derived from a *Rickettsia*-like bacterium and chloroplasts from cyanobacteria. The origin of the membrane-bound nucleus that characterizes eukaryotic cells is highly speculative. Hypotheses include an invagination of the prokaryote cell membrane to enclose the DNA, endosymbiosis of an archaeobacterium within a eubacterium, with the archaeobacterium becoming a nucleus, and a membrane-bound virus becoming established in a prokaryote and evolving into the eukaryotic nucleus by acquiring genes from the host.
- Although the origin of viruses remains an unsolved mystery, it is highly likely that virus-like entities predated the appearance of modern cells.
- The data suggest that eukaryotes arose from prokaryotes by fusion, aggregated into multicellular complexes, initially using prokaryotic genetic information, and differentiated into animals and plants, always in close

association with microorganisms. The earliest multicellular animal that still exists is the sponge which has certain similarities to bacterial biofilms because both lack tissues and organs, but are composed of a three-dimensional matrix that allows for the flow of water, nutrients, metabolites, and oxygen. The fossil record of sponges demonstrates their ancient association with bacteria, further indicating that prokaryotic symbionts were essential components of animals from their very beginning.

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