

Commentary

Do life's three domains mirror the origins of sex?

Life exists in three fundamental cellular forms, or domains. Along with an almost-universal genetic code, life manifests itself in biota belonging to Monera (bacteria or archea) or to Eukarya. This realization is relatively new, stemming from the seminal discovery of Archea by Woese and colleagues (Woese *et al* 1990). Although data are incomplete, the Monera may have originated soon after life itself started 3.8 billion years ago. The fossil record and molecular phylogenetics suggest that Eukarya are much younger, approximately 2 billion years. Why is this so?

After independent revival in the 1960s of the endosymbiotic theory by Margulis (see Sagan 1967) and Goksøyr (1967), a vast amount of work now supports a symbiotic origin of two eukaryotic organelles (mitochondria and chloroplasts) from bacteria and primitive eukaryotes. But which eukaryotes? And did the nucleus originate by a similar process? What about other structures such as peroxisomes and flagella?

1. Bioenergetics

The origins of Eukarya roughly coincide with the drastic oxygenation of earth's biosphere due to photosynthetic fission of water to energy and di-oxygen. Its accumulation after the pre-cambrian divide threatened with extinction all biota unable to hide or unable to cope with damage caused by reactive oxygen molecules. Today life crops on oxygen by respiration, using mitochondria derived from bacterial species arising 2 billion years ago. However, such symbiosis must have required hundred millions of years judging by the progress of modern symbiotic evolution.

Coping with oxidative damage therefore took place in cells without respiration. Instead bioenergetics (Wrigglesworth 1997) relied on autotrophy (lithotrophy or phototrophy) or heterotrophy. Of these heterotrophy and lithotrophy are thought to be primordial bioenergetics, perhaps active when life originated in the primordial soup. Phototrophy is delayed by the need for complex biomolecules and by the inherent radiative destruction of cells present in the oceanic photic zone with no protective ozone in the atmosphere. Even so, anoxygenic phototrophy is ancient, while oxygenic phototrophy is younger, perhaps 3 billion years old. Which bioenergetics sustained the domains of life when Eukarya evolved?

2. Fusion of Monera to Eukarya

The realization that eukaryotic evolution presented features of genetic fusion of the two moneric domains was a great surprise. In the last decade several penetrating analysis have tried to account for the chimeric nature of Eukarya. Common to these proposals, which space prevents me from elaborating on, is the view that eukaryotes are chimera of permanently fused monera. Only mitosis dissolves temporarily the characteristic karyon. How mitosis arose from microbial fission is not understood, and is implicitly viewed as a distinct problem (Gupta and Golding 1966; Martin and Müller 1998).

The contribution by the moneric domains is asymmetric, since eukaryotic biomembranes reflect only bacterial and not archeal biomembranes. Why such asymmetry? A similar asymmetry is seen in fertilization, but sex has until recently not been implicated in early eukaryotic evolution. When genetic recombination was discovered in prokaryotes, it led to the concept of prokaryotic sex. However, eukaryotic sex is much more than recombination. While eukaryotic sex does not always require gametes, and

gametes may be undifferentiated, isogamous or anisogamous, eukaryotic sex comprises in general three processes: fertilization, syngamy and meiosis. Only the latter involves recombination. This defines eukaryotic sex as a phenomenon distinct from prokaryotic recombination, and distinguishes sexual and mutational adaptations.

3. Sex

Darwin viewed the origin of sex as a mystery. Today sex ranks among the millennial scientific challenges. Sex is an ancient cellular capacity, at least 1.5 billion years old, and thus a *cellular* property present in primitive eukaryotes.

Darwin's two causes of evolutionary selection were challenged by Weismann, who dismissed the heritability of acquired traits. While this challenge was soon shown to be wrong (i.e., Weismann may have misunderstood Darwin), his proposal (1886) on how (eukaryotic) cells acquired sex has survived as a dogma. Inspired by cytology and his theory on germinal substance, Weismann speculated that mitotic cells evolved meiosis from mitosis. Nobody has to this day explained where, when or how this occurred.

Quite the contrary, leading scientists (Williams 1974; Smith 1978) have pointed out that such evolution contradicts Darwinian principles. Species do not survive by dissecting themselves into gametes while competitors continue to multiply asexually. At the cellular level sex is clearly anti-productive. In fact the word sex originated not as a scientific mechanism but from the Latin word "to section", picked by Rudolph Camerarius in 1694 to explain seed formation in certain plants ("De sexu plantarum").

The sex-paradox becomes acute in light of the fact that origins of sex have been explained by the known advantages that sex confers on organisms possessing sexuality: Shedding of mutations in haploid gametes; sustaining mutations in diploid stages; avoiding parasitic susceptibility of progeny by meiotic scrambling of histocompatibility loci. However, explaining evolution of sex by the eventual advantages of sex would be Lamarckism. Evolution is not anticipatory, but occurs in response to present selective pressures (Williams 1974; Smith 1978).

4. The embryogen hypothesis

Over the past years in Norway, we have pursued the theoretical consequences of interpreting gametic morphologies as primordial, viewing undifferentiated gametic morphologies as de-differentiated. We have explored the concept that stereotypic morphologies of gametes relate to functional phenotypes of primordial cells. Thus I developed the idea (1993) that sex originated by the nutritionally advantageous union of two cells with complementary metabolic strategies.

Since two gametic phenotypes (sperm flagellum and oocyte capsule; figure 1) have microbial but few eukaryotic parallels, I proposed that two *bacteria* united their complementary metabolisms in what we now term sexual fertilization. Thus asymmetric gametic contribution to the zygote of genomes and membranes was interpreted (Walther 1998) in the phrase: "Twin phylogenetic roots of life mirror the

Hence, the a-karyotic zygote becomes the *missing link* in the evolution from two pro-karyotes to one eu-karyote, with each gamete sharing common descent with extant microbial species in the two moneric domains: oocyte to eu-bacteria (since eukaryotes have eubacterial membranes), and sperm to archae (Walther 1999).

5. The polar paradise

The reversible union of two such incompatible microbes seems implausible. A solution was sought in photoseasonal polar regions. Two billion years ago these regions probably were both warm enough and cool enough to allow the presence of higher cellular life (< 70°C). Hence the name "polar paradise" for the exo-symbiosis of these two proterozoic microbial species (see figure 1). Each species could survive in this biotope only half a year, but together they could survive all year. The anti-reproductive aspect of sex reflects recurring survival in non-reproductive dormancy.

The “snake” in this paradise would be di-oxygen after the pre-cambrian divide which would force a switch from exo-symbiosis to internalization and syngamy in order to cope with increasing oxic toxicity through reviving archeal oxygen catabolism. That is, syngamy constituted the process by which monera evolved endocytosis, but rendered it a eukaryotic trait, uncharacteristic of monera. Evolving eukaryotes by dynamic sex (with alternating syngamy and gameto-genesis) is quite unlike fusion of symbiotic monera. During hibernative stasis without space or energy for replication, mutations are ineffective for adaptation. Viability in a photozone (figure 1) requires archeal genes to mutate to oxic resistance, and continuously repair radiative damage. Surviving oxic damage during encapsulated hibernation is feasible for a eubacterium if a syn-gametic archean exchanged by recombination the corresponding archeal genes.

A nucleolemma would in this (Embryogen) hypothesis evolve much later when cropping on oxygen for respiration meant incorporating respiratory bacteria, generating a need for genomic protection of the host. The defining eukaryotic feature (karyon) would thus not be fundamental, but rather reflect a secondary adaptation in switching from coping with, to cropping on oxygen. The fundamental step in cell evolution becomes a dynamic syngametic transition to diploidy within one akaryotic cytoplasm. This equilibrium between two moneric species and a resting phase (“zygote”) would generate a new species when meiosis that first served to terminate hibernation (dormancy), was duplicated and simplified to (a-karyotic) mitosis. A biotope prone to drought could select for such evolution since encapsulated

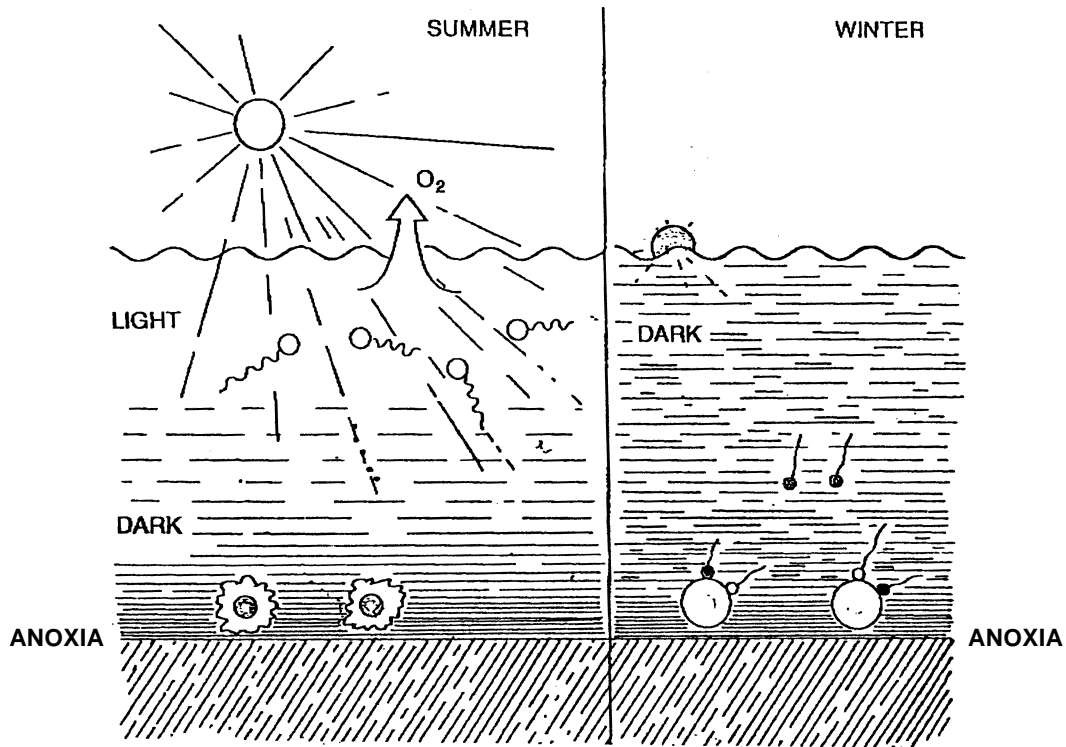


Figure 1. Origins of eukaryotes by sex: The “polar paradise”.

In warm and photoseasonal polar oceans, two proterozoic anaerobic species survived by cooperative metabolisms. An autotrophic (flagellated) Archean with anoxygenic phototrophy flourished in summers, but would perish in winter darkness. Wilting biomass could sustain a heterotrophic (demersal or pycnocline) Bacterium, surviving summer famine by encapsulated dormancy. In spring the photozone was reseeded by phototrophs surviving winter darkness in exo-symbiosis with heterotrophs. Eventually, summer co-encapsulation of revitalized Archean removed toxic di-oxygen from dormant Bacterium, and turned exo-symbiosis into syngamy 2 billion years ago. Di-oxygen in atmosphere derives from oxygenetic photosynthesis in cyanobacteria (not shown), while oceans are practically anoxic.

Wiggled exterior on demersal heterotrophs indicate encapsulation. Prokaryotic cytoplasm in white indicate functional cells, while grey cytoplasm indicate wilting or dormant state.

biota readily resist drought. Given acquisition of organelles the karyon would become as necessary for gametes as for the diploid (mitotic) cell.

6. Conclusions

The sexual theory of cell evolution has clear corollaries. All higher life would be initially sexual, and of two types (A- or Eu-karyotes). Relations would be dynamic with alternative unions and dissolution of the union of the two constituent moneric species, even as their viability as free-living species tended to decline in subsequent evolution. Superior bioenergetics meant eukaryotes were retained in multicellular species. However, some a-karyotes would be phylogenetically older than eu-karyotes, a point which if verified, would render such biota of fundamental significance.

According to the theory, the sexual life cycle may reflect the history of life's adaptation to an oxygenating biosphere. Asexual eukaryotes would by inference have lost their sexuality. Gametes represent moneric biota of the two domains existing before the pre-cambrian divide, with extant microbial relatives. Experimental tests are possible, since relative ages of meiosis and mitosis are predicted oppositely from Weismann's and my model. Other aspects of the sexual theory of eukaryotic evolution are not discussed here, and still unexplored is its integration with evolutionary processes such as horizontal gene transfer (Doolittle 1999).

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