

## Life

LIFE IS A WONDER of its own. It conceivably struck this planet at least some 3.8 billion years ago,<sup>1</sup> arguably the consequence of a phospholipidic layer-bound *quantum leap* in a soup of organic precursors.<sup>2</sup> From that singular moment on, little has been spared in guise of amazement.

The first factual evidence of life on Earth appears inscribed in the fossil record some 3.5 billion years ago. It consists mainly of microfossils and ancient rock structures in Greenland and Australia called stromatolites,<sup>3</sup> the product of the metabolism of photosynthesizing cyanobacteria.

While the fine details of the abiogenic<sup>4</sup> model for the origin of life<sup>5</sup> remain unclear, its primed instances are often depicted as self-replicating units able to regulate their own chemical processes within the confinement of a cellular membrane. Such primeval unicellular organisms were most likely composed of some form of nucleic acid secluded from its external environment by a bilayer of phospholipids.

Nucleic acids, RNA and DNA, are the sole organic molecules fit to direct their own replication and to act as genetic material. RNA was proposed as the original genetic system since it was shown to be able to catalyze a variety of chemical reactions, notably the polymerization of nucleotides.<sup>6</sup> However, as the genetic load stored within cells increased, the lesser stability and reliability of RNA molecules rendered them unsuitable for the furtherance of genetic systems, a stage at which DNA eventually took over as universal hereditary material.

These very simple and self-organized systems emerged in seas densely enriched in organic molecules and therefore didn't require sophisticated toolkits for intake of food or generation of energy. Only when systematic interactions between RNA and specific amino acids became enshrined in the genetic code<sup>7</sup> did evolution start to shape concerted molecular reactions between proteins that animated cells with metabolic activity.

Among the first elaborations of metabolic pathways are likely to have been some simpler form of modern-day glycolysis, the anaerobic breakdown of glucose to lactic acid. Glycolysis is a fixture of all present-day cells and drives the generation of ATP molecules, their universal source of energy. This in turn enabled cellular life to fuel ever more complex metabolic reactions, prime among which was photosynthesis.

Photosynthesis is a metabolic reaction that gathers energy from sunlight to synthesize organic molecules, at the expense of carbon dioxide and water, and generating free oxygen as a by-product. The emergence of oxygen-forming photosynthesis in cellular life, some 2.5 billion years ago, had two major impacts in the course of evolution. Firstly, it liberated cells from the need to directly access preformed organic molecules to sustain their metabolism; and, secondly, it biologically enriched the content of Earth's atmosphere in

<sup>1</sup> Mojzsis et al., 1996

<sup>2</sup> Miller and Urey, 1959

<sup>3</sup> Ohtomo et al., 2014; and Noffke et al., 2013

<sup>4</sup> From the Greek "spontaneous generation", this model posits that autocatalytic polymers able to function as simple molecular replicators are at the origin of life. Alternative models exist, most notably panspermia—the extraterrestrial origin of life.

<sup>5</sup> Much debate has been stirred around the definition of life itself, see for instance Benner, 2010.

<sup>6</sup> Bass and Cech, 1984

<sup>7</sup> The central dogma of molecular biology, postulated by Francis Crick in 1958 and reasserted in 1970 (Crick, 1958, 1970), pertains to the rules that govern the sequential flow of genetic information between DNA, RNA and proteins. It can be summarized as "DNA makes RNA makes protein", which provides the template for the enactment of hereditary information for all living organisms and frames the scope of evolutionary forces on genetic systems.

oxygen,<sup>8</sup> which is thought to have been a pre-condition for the thriving of eukaryotic life.

Up to that stage, all forms of life on Earth could still be modeled from the blueprint of modern Prokaria: a single-celled organism devoid of any membrane-bound organelles, capable of lateral DNA transfer and that mainly reproduces itself through binary fission. The Prokaria taxon comprises both Archae (e.g., *Thermoplasma*-like organisms) and Eubacteria (e.g., *Spirochaeta*-like organisms), which fundamentally differ at the level of the chemical composition of their cell walls; the lipidic composition of their plasma membranes; and the number of subunits in their RNA polymerases.

An hypothetical permanent whole-cell fusion between members of Archaea and Eubacteria has been proposed to be at the origin of the earliest anaerobic Eukarya,<sup>9</sup> of which the first fossil record evidence could date from a 2.1 billion year black shale formation found in Gabon.<sup>10</sup> Eukarya<sup>11</sup> are thus defined by the presence of specialized organelles enclosed within membranes, namely the presence of a discrete nucleus wherein all genetic material is confined.

The evolution of aerobic respiration, now a possibility in an oxygen rich environment, is thought to have occurred about 2.2 billion years ago in prokaryotic cells. The endosymbiotic theory proposes that eukaryotic organelles, such like chloroplasts and mitochondria, evolved from certain types of bacteria that early eukaryotic cells engulfed through endophagocytosis and retained in a mutualistically beneficial relationship.

The appearance of the integrated eukaryotic cell set the stage for a vast collection of evolutionary experiments that propelled a remarkable diversification of life forms. Two critical features were behind this radiation: the advent of sexual reproduction and that of multicellular life.

Sexual reproduction first evolved in a single-celled eukaryotic entity some 1.2 billion years ago.<sup>12</sup> The exchange of genetic information through recombination during meiosis provided cells with a new powerful source of genetic variation, both capable to accelerate adaptation rates to new environmental challenges as well as to supply evolution with novel genetic templates to operate on.

features to be used as templates for the evolution of new traits. resilience of genetic systems

allows for genetic variation meiosis recombination source of variation the benefit of the exchange of information, through recombination, during the sexual process

multicellularity volvox colonies specialization internalization of cellular specialization into the genetic code leading to: embryogenesis Concomitantly, the loss of individualization and increasing social integration of the cellular tapestry into tissular differentiation lead to the evolution of specific cellular pathways

natural selection.

<sup>8</sup> This so called “Great Oxygenation Event”, dated to 2.3 billion years ago, was arguably caused by photosynthesizing organisms whose presence was tracked long before it occurred (Flannery and Walter, 2012). The GOE likely had a catalytic effect in the evolution of life also through the oxidation of exposed rocks, liberating phosphorus and iron that flew into the oceans, there acting as fertilizer (Zimmer, 2013).

<sup>9</sup> Margulis, 1996

<sup>10</sup> Albani et al., 2010

<sup>11</sup> From the Greek, “eu”—true—and “karyon”—kernel.

<sup>12</sup> Bernstein et al., 2012

There is grandeur in this view of life, with its several powers, having been originally breathed into a few forms or into one; and that, whilst this planet has gone cycling on according to the fixed law of gravity, from so simple a beginning endless forms most beautiful and most wonderful have been, and are being, evolved.

How ironic that one of the best models to understand this order of things is actually one of its most harrowing violations: cancer.

## *Cancer*

CANCER IS A DYSFUNCTION OF

## *Microarrays*



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