Abstract

Cambrian explosion during which highly advanced lifeforms suddenly emerged is one of the mysteries of biology. Oxygenation of the environment was associated with this event as also a release of methane trapped to a crystal structure of water. Oxygenation made possible the emergence of aerobic respiration and of animals. Stem cells to not however tolerate oxygen. The so called hypoxia-inducible factors (HIFs) make possible to shift metabolism from aerobic to anaerobic in hypoxic environment. In the case of cancer cells so called HIF-2α allows this also in oxic environment. The geobiologist Emma Hammarlund and tumor biologist Sven Phlman conjecture that this true also for the ordinary cells. Moreover, they propose that the event induced a genetic change leading to the emergence of what they call HIF-1 as a predecessor of HIF-2α. This allowed the organism to adapt to environments in which oxygen concentration varied so that stem cells survived in high-oxygen environment. The cause of the sudden oxygenation is not discussed in the article. The so called Great Oxygenation Event (GOE) occurred much earlier than Cambrian explosion, and TGD inspired proposal is that this event drove the primitive life forms under the Earth surface to underground oceans. The pre-Cambrian situation would have been very similar to that in recent Mars. Cambrian explosion was induced by a rapid expansion of Earth size with radius increasing by a factor of 2. This led to the formation of cracks and oxygenation of underground oceans which in turn induced rapid evolution of animals from plant like predecessors.

Keywords: Cambrian explosion, rapid increase, Earth radius, TGD framework.

1 Introduction

There was an interesting popular article in Quanta Magazine titled "Oxygen and Stem Cells May Have Reshaped Early Complex Animals" (see http://tinyurl.com/y86ta45l). The article discusses the work of geobiologist Emma Hammarlund and tumor biologist Sven Phlman: their interdisciplinary hypothesis is published as article in Nature [2] with title "Refined control of cell stemness allowed animal evolution in the oxic realm" (see http://tinyurl.com/y85ufngz).

Here is the abstract of their article.

Animal diversification on Earth has long been presumed to be associated with the increasing extent of oxic niches. Here, we challenge that view. We start with the fact that hypoxia (≤ 1–3 per cent O2) maintains cellular immaturity (stemness), whereas adult stem cells continuously - and paradoxically - regenerate animal tissue in oxygenated settings. Novel insights from tumour biology illuminate how cell stemness nevertheless can be achieved through the action of oxygen-sensing transcription factors in oxygenated, regenerating tissue. We suggest that these hypoxia-inducible transcription factors provided animals with unprecedented control over cell stemness that allowed them to cope with fluctuating oxygen concentrations. Thus, a refinement of the cellular hypoxia-response machinery enabled cell stemness at oxic conditions and, then, animals to evolve into the oxic realm. This view on the onset of animal diversification is consistent with geological evidence and provides a new perspective on the challenges and evolution of multicellular life.

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1.1 The proposal of Hammarlund and Phlman

Cambrian explosion (see [http://tinyurl.com/ntvx38e](http://tinyurl.com/ntvx38e)) during which highly advanced lifeforms suddenly emerged - proliferation and diversification of animal life are the terms used about this - is one of the mysteries of biology. For most of its 4.5-billion-year history, Earth has sustained life but that life was largely limited to microbial organisms: bacteria, plankton, algae. For about 540 million years ago did larger, more complex species are assumed to dominate the oceans, but within just a few tens of millions of years (very short time on the evolutionary timescale), the planet had filled up with all kinds of animals. The fossil record from that period shows the beginnings of almost all modern animal lineages: animals with shells and animals with spines, animals that swam and animals that burrowed, animals that could hunt and animals that could defend themselves from predators. Also many lineages that disappeared were present as one learns from the book of Stephen Jay Gould describing in detail the Burgess Shale finding that revolutionized the picture about evolutionary biology and remains still a puzzle (see [http://tinyurl.com/y9orfy43](http://tinyurl.com/y9orfy43)).

The belief is that the environment became considerable more oxic - that is contained oxygen - and lifeforms had to cope with this change. Before the change the animals in seas (believed to exist!) were anaerobic. The shifting to aerobic respiration was however an enormous metabolic advantage since the effectiveness of metabolic energy gain become roughly 20-fold. Increased metabolic feed in turn made possible the emergence of complexity during Cambrian period.

1. The proposal of the authors is that the evolution of the capacity to maintain stem cells even in an oxic environment allowed the animals to keep stocks of stem cells needed for tissue growth and repair for that this required at gene level new genes coding for so called HIFs.

2. Stem cells require low oxygen levels to preserve their stemness. Heightened oxygen levels cause them to differentiate abruptly. This explains why stem cells are often located in hypoxic regions of the body (say bone marrow) having low oxygen levels. There are however exceptions to this rule: stem cells can also survive in ocix regions such as skin or retina. Cancers also utilize stem cells to achieve growth.

3. Hammarlund and Phlman turned their attention to HIFs (hypoxia-inducible transcription factors), which are proteins, which for hypoxic environment shift the metabolism from aerobic to an-aerobic. For oxic environment they are not needed.

HIF-2α remains however active also in oxic environment and make the cells behave as if the environment were hypoxic. This would allow the stem cells to survive. HIF-2α would however keep the stem cells in immature state also in the case of cancer. The hypothesis of Hammarlund and Phlman was that HIF-2α functions similarly in normal animal tissues. They have seen some preliminary evidence for the hypothesis but further work is needed.

4. HIFs could have helped the animals to survive in oxic environment. Consider an organism as a blob of cells. Before the oxygenation the stem cells would have been forced to the deep interior of the blob, where oxygen concentration was especially low. When oxygenation took place, and oxygen level varied, this trick did not work anymore and HIFs had to be invented.

5. Hammarlund and Phlman postulate what they call HIF-1, which would have helped stem cells to behave as if the environment were hypoxic. Later HIF-2α unique to vertebrates emerged and improved the situation further. Vertebrates are bigger and have longer time spans that invertebrates and they can live in oxygenated environments. Invertebrates such as insects live most of their life as larvae under low-oxygen conditions and they cannot regenerate tissues as vertebrates can.

6. Cancer would be the price paid for this evolutionary advance since cancer cells can proliferate because HIF-2 keeps the stem cells alive. OH present in oxygen rich environment is an oxidant causing cancer.
What caused the oxygenation? So called Great Oxygenation Event (GOE, see [http://tinyurl.com/q7qfd55](http://tinyurl.com/q7qfd55)) is believed to have occurred about about 2.25 billion years ago and thus preceded Cambrian explosion that occured about .5 billion years ago. The time lapse between these events is about 1.75 billion years and much longer than the duration of Cambrian period, which was only tens of millions years. Thus GOE was not the reason for the Cambrian explosion. What caused a further oxygenation or were the effects of GOE somehow postponed (wink-wink!)?

2 TGD view

My own proposal is that life evolved in underground oceans and entered to the surface of Earth in Cambrian explosion (see [http://tinyurl.com/ntvx38e](http://tinyurl.com/ntvx38e)) when oceans were formed at the surface of Earth from cracks formed when Earth expanded rapidly in geological time scale. Before the explosion Earth did not have oceans and continents and was like Mars nowadays: even its radius was that of Mars. This picture follows from TGD based variant of Expanding Earth hypothesis [10, 9] (see [http://tinyurl.com/yc4rgkco](http://tinyurl.com/yc4rgkco) and [http://tinyurl.com/yb68uo3y](http://tinyurl.com/yb68uo3y)).

The habitat changed in the rapid expansion of Earth from hypoxic to oxic and the emergence of the hypothetical HIF-1 transcription factor would have been forced by this evolutionary pressure and made it possible for the lifeforms to adapt oxygen based metabolism. This would have led to a rapid evolution of animals and emergence of vertebrates. One can of course think that oxygenation developed already in the underground oceans as cracks caused in the crust by the expansion of Earth began to develop and provided oxygen. The alternative - not so plausible sounding - option is that the highly developed organisms developed underground slowly and only bursted to the surface of Earth in the explosion.

1. Chemical markers (see [http://tinyurl.com/ntvx38e](http://tinyurl.com/ntvx38e)) indeed indicate dramatic change in the environment at the start of the Cambrian period. The markers are consistent with a massive warming due to the release of methane ice (clathrate hydrate, see [http://tinyurl.com/peq9gmw](http://tinyurl.com/peq9gmw)) trapped within the crystal structure of water. Methane clathrate is found deep under the sediments at the ocean floors. Methane hydrates are believed to form by migration of gas from deep along geological faults (the cracks produced by rapid expansion of Earth [9]!).

2. During the period before Cambrian explosion Earth would have been very much like in recent Mars. Even its radius would have been that of recent Mars! One can ask whether GOE forced the existing primitive lifeforms underground or saved only those already living underground. Situation would have been be very much like in the recent Mars, which also seems to possess underground life.

The development of HIF proteins (hypoxia inducing factor) making possible for stem cells to survive in environments with varying and thus temporarily higher oxygen content would have been a natural reaction to the dramatic changes in habitat.

What can one say about the emergence of animal life in TGD framework?

1. The rapid evolution leading to the emergence of animals - if it was present - would relate to the quantum criticality associated with the increase of the effective Planck constant $h_{eff}/h_0 = n$ by factor 2 increasing the size scale of Earth. The increase of $h_{eff}/h_0 = n$ might have occurred at several levels of dark matter hierarchy, also at biological relevant scales and led to an increase of biological "IQ" (note that evolution corresponds in TGD to gradual increase of number theoretical complexity and $n$ characterizes the dimension of extension of rationals characterizing the complexity [6,7]).

2. Animals use oxygen for breathing and are multicellular eukaryotes having cell membrane enclosing nucleus and other membrane bound organelles. The quantum critical period could have led to the emergence of a kind of symbiosis of various kind of organelles within cell membrane bounded volume. The p-adic length scale $L(k)$ determined by the value of $n$ assignable to the outer membrane of
organelles could correspond to the prime $k = 163$ (or 167). Inside plant cells having no cell membrane these organelles correspond to vacuoles (see http://tinyurl.com/yd879b2d). The outer membrane that emerged in the transition increasing $h_{eff}/h_0$ meant increase of the scale of quantum coherence to a longer p-adic length scale - say $k = 167$ (or $k = 169 = 13^2$ if doubling took place).

3. Mitochondria would have emerged and made possible oxygen based respiration whereas plant like organisms preceding them utilized anaerobic respiration. Methanogenesis (see http://tinyurl.com/yd879b2d) utilizing carbon instead of oxygen and producing carbon-dioxide and methane CH$_4$ (water in O$_2$ based respiration) is the most natural option. The large methane storages underground would be due to methanogenesis. The recent findings (see http://tinyurl.com/y735g9kn) indicate that there is life in Mars: methane emissions occurring periodically with a period of Martian year have been detected. This suggests that solar radiation is somehow able to enter to the interior of Mars or that it heats the underground Oceans. In TGD one can consider also the possibility that some part of solar photons transforms to dark photons and is able to propagate to the underground oceans through the Martian crust [9].

4. What was the primary source of metabolic energy? Direct solar radiation was absent in underground oceans. The immediate source of metabolic energy for the plant like organisms might have been dark nuclei consisting of dark proton sequences and liberating energy in the transitions reducing of $h_{eff}/h_0 = n$. Dark proton triplets give rise to dark variants of DNA, RNA, tRNA, and amino-acids [4, 3, 11]. These dark proton sequences could have formed by Pollack effect at the surface of Earth possibly containing some water and could have propagated along dark flux tubes to the interior: also in "cold fusion" dark nuclei would be formed. Some fraction of them would transform to ordinary nuclei and liberate practically all the nuclear binding energy. Also transitions to dark nuclei with a smaller value of $h_{eff}/h_0$ is possible and liberates energy usable as metabolic energy. Most dark nuclei could leak out along magnetic flux tubes [5]. The hen-egg problem - which came first, metabolism or genetic code - would trivialize in this framework.

For p-adic length scale $L(k = 149) = 5$ nm - thickness of cell membrane - the typical dark nuclear excitation energy was about .5 eV, the nominal value of metabolic energy quantum. For $L(151) = 10$ nm (thickness of neuronal membrane and DNA double strand its value is .25 eV. These estimates are based on the scaling of the typical nuclear excitation energy taken to be 1 MeV and are uncertain by a factor of 2 at least. One of course expects also higher excitation energies - even so high that they correspond to visible ordinary photons. Metabolic energy could have been liberated as dark photons in dark nuclear transitions transforming to ordinary photons and absorbed by the photosynthetic machinery.

The (rough) estimate for the typical value of the dark photon energy is considerably lower than in ordinary photosynthesis. Pollack effect [1] occurring in presence of gel phase bounding water volume suggests that for $k = 149$ the transformation of dark proton sequences to ordinary ones: this mechanism would liberate energy per proton $\sim 1.5$ eV [8], which corresponds to infrared photon. The small value of the metabolic energy quantum need not be a problem: there is recent evidence that IR light with energy 1.76 eV can be used in photosynthesis (see http://tinyurl.com/y735g9kn).
References


