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Fullerene and the Origin of Life

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ABSTRACT: The role of carbon in the development of life and as the structural backbone of all organisms is universally accepted and an essential part of evolution. However, the molecular basis is largely unknown and the interactions of carbon with nitrogen and oxygen in space are enigmatic. In 1985, the previously unknown form of carbon, coined fullerene, was discovered. We hypothesize that by virtue of the unique properties of fullerene, this hollow, ultra-robust, large, purely carbon molecule was the earliest progenitor of life. It acted as a stable universal biologic template on which small molecules spontaneously assembled and then formed, by further assembly, a surface mantle (here termed rosasome) of larger molecules. We submit that this process, by its inherent flexibility, initiated evolution, allowing the emergence of parallel diverse rosasome lines responding selectively to varying spatial environments. For example, rosasomal lines mantled with nucleotide and peptide layers are conceived as primordial forerunners of the ubiquitous ribosome. Moreover, the parallel independent and interdependent evolution of rosasome lines would be more rapid than sequential development, refute precedence of either DNA or RNA, and explain the evolution of integration of two subunits with different structures and functions in ribosomes and of the triplet nature of the codon. Based on recent astronomical data, this hypothesis supports the concept that life is not a singularity. This concept also suggests a potential vehicle for therapeutics, biotechnology and genetic engineering.

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Clinicians and medical researchers are well aware of unsolved problems in biology that lead to frustration when treating patients. More than most they can appreciate the need for and will welcome any advance in the understanding of the origin of life that may lead to progress in medicine. Throughout their education, physicians hear of theories on the origin of life that focus on informational molecules and chemical machinery critical for self-replication [1,2]. The data reflect experiments which, simulating assumptions about conditions and substrates on primeval Earth, have demonstrated spontaneous self-assembly as well as synthesis of more complex molecules, including many essential amino acids, nucleobases, nucleotides and other molecules not yet identified in space [3]. Yet current evidence on the origin of and precedence between RNA and DNA and on amino acids, their polymers and the initial relationship between them and the nucleotides [3] remains controversial, as does the question of how storage of information required for biological replication developed in relation to cell metabolism.

Although the critical functions of DNA and RNA in maintenance and replication of biological entities and of some of their nucleobases in metabolism, e.g., adenine in ATP, indicate their early essentiality for life on Earth, interest in the possible origin of at least some aspects of life in space is growing. Though theories on whether and how life and its molecules reached Earth have long been proposed [4] and evidence old (membrane-like structures in meteorites) [5] and new (first cometary amino acid identified) [6] claimed, nascence in space (panspermia theory) of non-terrestrial self-replication and its transfer to Earth remains problematic. Similarly uncertain is the identity of the element(s) most closely involved in life's origin; carbon and nitrogen, in particular, as well as oxygen and silicon have aroused interest. However, few would deny the centrality of carbon.

FOLLOW THE CARBON?

In 1985, laser vaporization of carbon revealed a hollow, purely carbon molecular cage, composed of hexagon and pentagon rings. These structures have been coined fullerenes. Interestingly, using the infrared spectrograph of the Spitzer space-based telescope, clean symmetric vibrational bands of non-ionic fullerenes C60 and C70 have now been detected in what appears to be a carbon-rich, hydrogen-poor and dusty inner region of the circumstellar environment of the young planetary nebula Tc 1. This apparently confirms the presence of fullerenes in space and the neutrality suggests possible attachment to dust. No evidence of other major carbon compounds, such as PAH (polycyclic aromatic hydrocarbons), presented in an evidently hydrogen-poor environment [7]. Moreover, fullerenes apparently may also form in a hydrogen-rich region. From the Spitzer telescope, observations have now strongly indicated, for the first time outside of the Milky Way galaxy, the presence of fullerenes C60 and C70 in the nebulae of four stars in the Small Magellanic Cloud. Why this is so is unknown and contrary to a view that it is not possible; it may even be fairly common in some hydrogen-rich conditions [8].

The most recent data from space also support earlier evidence for extraterrestrial fullerenes (C60 to C400) in the Allende and Murchison meteorites from impact events in Cretaceous/Tertiary boundary sediments [9] and from fullerenes extracted from Permian-Triassic boundary (PTB) sediments (mainly C60 and C70) which contained helium (He) and argon isotopes trapped in the cages in ratios similar to those in meteoric carbonaceous chondrites. The PTB data indicate He partial pressure of 2–4 atmospheres during fullerene formation. Only stars or collapsing gas clouds have significant He pressures together with low hydrogen/carbon ratios conducive to fullerene synthesis and imply circumstellar or interstellar formation [9]. The asteroid and cometary data are further supported by experimental and simulation findings of fullerene resistance to exceptional pressures, heat and impact. Reminiscent of graphite, fullerene cages may consist of up to 70 concentric onion-like layers, capable of enclosing small metallic or gaseous atoms. Importantly, for biochemistry, they are strongly hydrophobic and will yield pure carbon crystals on evaporation. In this respect, fullerene C60 is of particular interest.

FULLERENE C60

STRUCTURE

C60 is the most common fullerene and the most spherical molecule known. It has 12 pentagon and 20 hexagon rings. The thirty 6:6 bonds edging adjacent hexagons are shorter and more stable than the sixty 6:5 bonds edging hexagons with pentagons. The pentagon rings relieve planar bond strain, enabling closure of the molecular cage. However, as bonds between adjacent pentagons are less stable, isolation of all pentagons by the hexagons reduces strain in the cage, providing geodesic symmetry with remarkable stability [10]. Isolation of all pentagons is found in all of the most stable fullerenes. C60, the smallest such fullerene, is found under all suitable conditions. Though larger, C70 is the next smallest such fullerene and has some characteristics similar to C60 but is ellipsoid and less robust.

Fullerene C60 displays considerable superconductivity and photostability [11]. Relevant to spatial collision phenomena are fullerene's extreme hardness (more than diamond) after intense heat and pressure, elasticity (immediate, complete recovery from extreme compression on impact), and exceptional heat resistance. Theory and simulation indicate C60 formation at over 2400°C and degradation at 3000–4000°C [12]. Though temperatures within carbon-forming stars are much higher, carbon is ejected to cooler regions, e.g., some circumstellar environments and interstellar gas clouds. If fullerenes could not exist in them, less robust organics would not be found there. Remarkably, fullerene is the largest molecule for which wave interference has been demonstrated [13]. Since electron-rich nucleophiles attach to fullerene carbons [14], covalent, usually mono-adduct, derivatives are common, e.g., Bingel reaction attachment at the ends of a hexagon double bond.

FULLERENE BIOLOGY

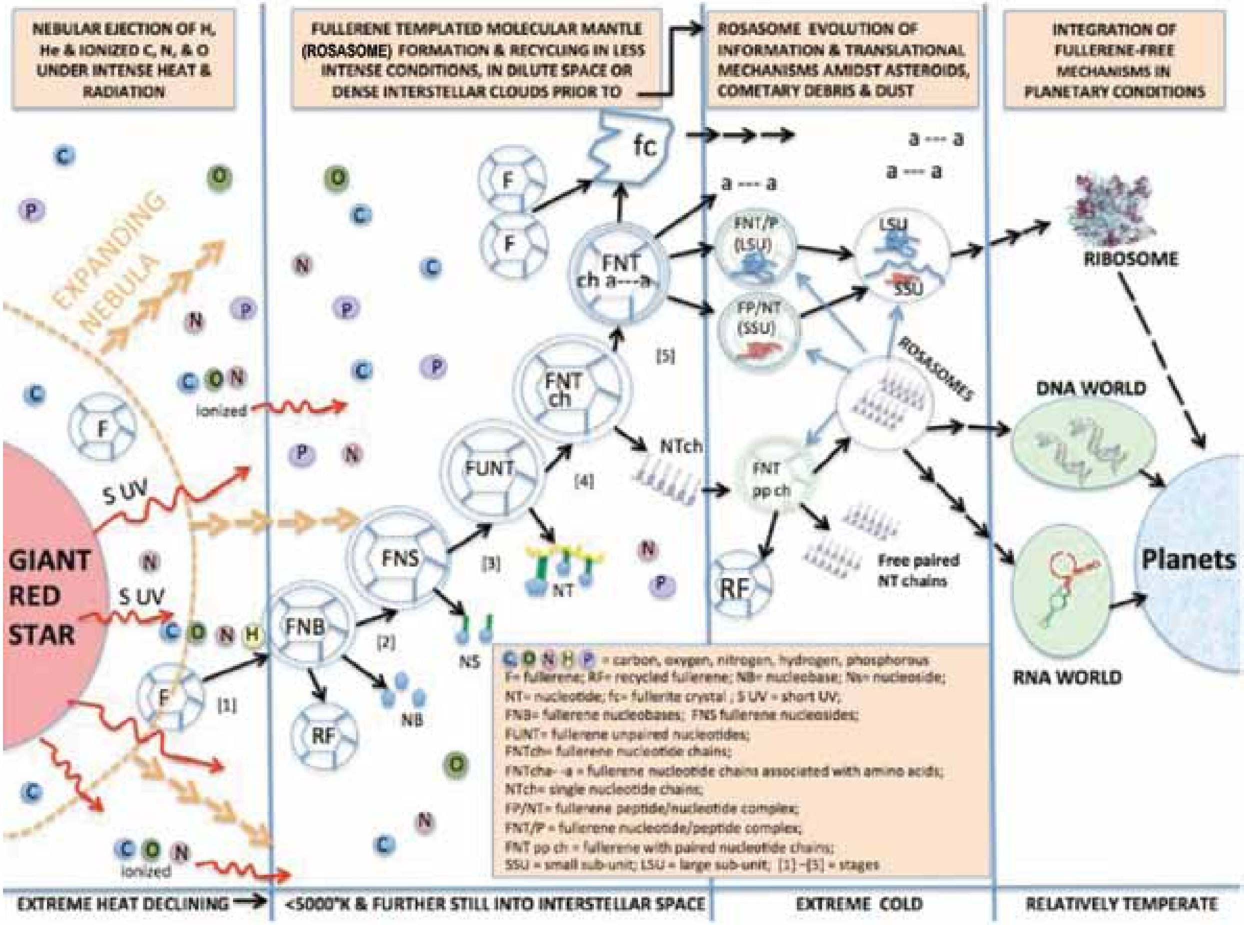
Fullerene hexagon-pentagon double rings may have evolutionary significance; a schema indicating how this may have evolved is reflected in Figure 1. The aromatic, hexagon-pentagon double ring, nitrogenized to a degree – for example in adenine and indole – is ubiquitous in the living world, as are single-ring hexagon pyrimidine bases. Adenine is crucial in genetics, in energy metabolism of all living systems and in much hormonal activity; it is also a neurotransmitter [15]. That the adenine double ring has an ultra-primordial history is supported by the highly conserved adenine at the peptide-transferase center of the large subunit (LSU) of ribosomes from all sources, and by the adenine critical to ribosomal bonding of an additional amino acid to an elongating peptide chain [16]. Similarly ancient in a segment of rRNA in the small subunit (SSU) of ribosomes are two adenines vital for stabilizing the tRNA anticodon mRNA helix [17].

In view of the above, we propose that, driven initially by non-covalent influences, adenine and other nucleobases (long before their conjectured initiation and existence on prebiotic Earth) may have been formed on, or became attached (if previously formed) to the surface of suitable fullerene cages. This contrasts with questioned claims that hydrogen cyanide (HCN) is the source of all pre-RNA nucleotides [3], including early adenine formation from HCN in space and perhaps prebiotically on Earth [3,18]. However, whereas synthesis requires an HCN concentration rarely achievable prebiotically [19], fullerenes may be catalytic in the formation of adenine and other nucleobases and also during related subsequent molecular and macromolecular reactions (below).

FULLERENES AND EVOLUTION

It is proposed that one or more fullerenes were templates in space on which mantles of individual small molecules of different kinds, nitrogenous or not, could form and constitute a basis for the assembly of larger molecules and their polymers. Moreover, from some mantles ('rosasomes') evolved catalytic molecular replication, coded biological information storage and translation. Thus, for example, the ribosome, a ubiqui-

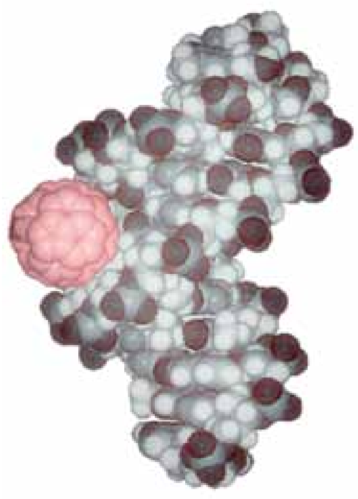
Figure 1. Fullerene ‘rosasomes’: a template process in the initiation of life’s evolution from dying ‘carbon’ stars



tous cellular organelle that consists today of long folded RNA chains intertwined with shorter folded polypeptide chains and translates genetic information into proteins, evolved from rosasomes that were a double-layered integration of nucleotides and peptides on fullerene (possibly C60) surfaces.

The first (nucleotide) layer is initiated, as mentioned, by non-covalent assembly of bases on the fullerene surface. The attached nucleobases become nucleotides by covalent addition of ribose, then phosphates through bonding of templated closely proximate atoms, driven by incident influences (such as shock wave, thermal agitation, high energy radiation and collision) or indirectly by environmentally induced temporary conformational changes in the fullerene cage itself. Independent before or formed during attachment, the ribose attaches to a nucleobase nitrogen via a carbon bond, which angles the ring away from the fullerene surface and enables ribose rotation. Required for most essential biochemical functions, phosphorous is scarce but ubiquitous in the universe, exhibits varied and complex chemistry under different conditions, including a tendency to oxidation, and was possibly first sourced in biogenesis in the interstellar medium [20]. In the context proposed here, perhaps associated with a solid medium such as dust particles, the phosphate group is covalently bonded to a ribose and projects even further away from the fullerene. Depending on the bases attached, up to six nucleotides may form on C60 and when a fullerene hosts two nucleotides or more, short nucleotide polymers may be formed. On C60, double-strand nucleotide formation through non-covalent, dimension-sensitive association of specific purine-pyrimidine bases may be limited to one or two pairs; C70 may host more pairs. Concerning possible steric limitations on sequenced rosasome mantling, it is notable that up to 18 amine molecules may be attached synthetically to a C60 surface [21]. Moreover, short fullerene polymers seem possible [22,23]. Nucleotides may have formed on them, especially if single bonds theoretically enabling rotation [23] are present in the fullerene polymers. Nucleotide chain formation on crystalline fullerene (fullerite) aggregations may also be considered. Driven by environmental forces similar to those associated with fullerene mantle formation of nucleotides, the second, peptidal rosasome layer is formed by de novo dimension-sensitive for-

Figure 2. In a computer simulation, C60 fullerene is docked in a minor groove of double-strand DNA in aqueous solution, remains so and deforms the nucleobase pair angles which it approaches face-on. This apparently supports the proposed non-covalent face-to-face complexion by purine and pyrimidine nucleobases with, respectively, hexagon-pentagon or hexagon elements of the fullerene. Though the binding is hydrophobic, non-covalent binding of fullerene to nucleotides is four times stronger than binding of two hydrophobic C60 molecules in water [38], implying that the attachment of C60 to DNA bases entails non-covalent "pull" as well as hydrophobic "push"



mation of individual amino acids and short peptides strung across the nucleotides of the first layer, probably involving both covalent and non-covalent bonding. (Fullerene aggregates may be candidates for a process similar to the above.)

THE SIGNIFICANCE OF THE FULLERENE ROSASOME

Parallel lines of rosasomal evolution may refute precedence of both RNA and DNA. Moreover, lines of rosasomes carrying three polymerized nucleotides mantled initially on fullerene C60 or C70 may have proved the most viable of the archaic codon lengths currently debated as a basis for today's triplet coding [24]. Fullerene mantles may also support a common view of 10 essential amino acids, as 'early' [25]. They are generally smaller and simpler, as may have been dictated by steric requirements during dimensionally sensitive, non-adaptive assembly on a rosasome nucleotide layer. It has been proposed that a forerunner of ribosomal RNA created peptide bonds between spontaneously assembled amino acids conjugated with single or short oligonucleotides sufficiently robust to survive changing conditions [26]. Rosasome evolution may also explain why the extremely intricate yet reliable ribosome [27] that exhibits replication [28] and catalysis together with decoding peptide-forming functions consists of two integrated subunits, LSU and SSU with different structures and functions [16]. It has been assumed they have independent origins [29]. As proposed here for RNA and DNA evolution, the two subunits could express parallel, different lines of rosasome development that cojoined during the immense period in which the ultra-primordial rosasome evolved into an early ribosome.

FULLERENES IN THE FUTURE

Because of its exceptional nature, fullerene is experiencing intense technological research, e.g., in electronics [30], and in the development and production of new materials [31,32]. Medical research on fullerene [33-36] already includes the possibility of fullerene effects on nucleotides [37]. This is supported by simulated strong, stable non-covalent binding of fullerene to DNA [Figure 2][38]. Such apposition to DNA, or RNA, could prove of clinical value.

Conceived here is an evolutionary process in the archaic past that progressed far beyond the formation of nucleobases on fullerene surfaces. A universal origin of life from dying stars, rapid because it is expressed in parallel rather than sequential lines of development, extends evolution to well before the circa 4.5 billion years available on Earth and invites research with promise for the future.

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Capsule

Antiretroviral dynamics determines HIV evolution and predicts therapy outcome

Despite the high inhibition of viral replication achieved by current anti-HIV drugs, many patients fail treatment, often with emergence of drug-resistant virus. Clinical observations show that the relationship between adherence and likelihood of resistance differs dramatically among drug classes. Rosenbloom et al. developed a mathematical model that explains these observations and predicts treatment outcomes. This model incorporates drug properties, fitness differences between susceptible and resistant strains, mutations and adherence. The authors show that antiviral activity falls quickly for drugs with sharp dose-response curves and short half-lives, such as boosted protease inhibitors, limiting the time during which resistance can be selected for. They find that poor adherence to such drugs causes treatment failure via growth of susceptible virus, explaining puzzling clinical observations. Furthermore, the model predicts that certain single-pill combination therapies can prevent resistance regardless of patient adherence. This approach represents a first step for simulating clinical trials of untested anti-HIV regimens and may help in the selection of new drug regimens for investigation.

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Eitan Israeli

Of all the preposterous assumptions of humanity over humanity, nothing exceeds most of the criticisms made on the habits of the poor by the well-housed, well-warmed, and well-fed

Herman Melville (1819-1891), American writer, essayist and poet. He is best known for his novel *Moby Dick*

The secret of being tiresome is in telling everything

Voltaire (1694-1778), French Enlightenment writer, historian and philosopher famous for his wit and for his advocacy of civil liberties, including freedom of religion, freedom of expression, free trade and separation of church and state