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1

Biocosmology: Part I

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ABSTRACT

Twenty years ago (King 1978) I proposed the biocosmological thesis that the form of life's origin and evolution is a cosmological interactive process defined in the cosmic symmetry-breaking at the origin of the universe. With the passage of time, the pendulum has shifted from the improbability of life as a random molecular accident to an awareness that central biomolecules may be cosmologically abundant products of the clouds forming young stars leading to an RNA-era in which both catalysis and replication emerged from one cosmologically dervied molecule RNA. This paper unveils the non-linear quantum foundations of biocosmology as the founding science of life. Part I of this paper covers the following topics: 1. Paradise on the Cosmic Equator; 2. Generating a Complex Twisted Universe; 3. The Abudantly Fecund Universe; 4. Quantum Chemistry as Non-Linear Complexity; 5. The Non-recurrent Table and the Elementary Bifurcation Tree; 6. Structural Dynamics of Core Polymerization Pathways; 7. RNA and Cosmology; 8. Diverse Horizons of the RNA Epoch; 9. Universal Stability Structures in Molecular Biology; 10. The Last Universal Common Ancestor; and 11. The Precocious Origins of Life on Earth.

Key Words: cosmology symmetry-breaking, molecular evolution, chaos, complex system, neurodynamics, quantum non-locality, transaction, consciousness.

1. Paradise on the Cosmic Equator

Could biological structures such as tissues, and organisms be cosmological interactive structures as fundamental as stars and galaxies to the cosmic design? The conventional objections are obvious. Life is a fragile insignificance among the immense energies of black holes, galaxy formation and the big-bang. Its tiny entropy-reducing photosynthetic energy budget and fragile chemical bonds are insignificant on the cosmic scale. Biological structures are genetically coded in a vast variety of ways by specific nucleic acid sequences. Biological evolution is a stochastic process combining random mutation and selective advantage, many of whose manifestations are opportunistic. Nevertheless many features of life as we know it on Earth may be the product of cosmic factors determining the laws of nature which make life possible.

Although traditional chemistry, despite its quantum foundations, treats molecules as arbitrary building blocks which can be arranged in almost any combination using suitable reagents and conditions, there is clear evidence for optimality of many prebiotic and biological molecules, giving life as we know it a cosmological basis as a culminating interactive structure.

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Fig 1: Paradise on the Cosmic Equator: Darwin, the serpent and the hoopoe in Eden: Biological systems form a central cosmological manifestation of interactive complexity in the universe. When space-time is considered as a 4-manifold, biology's 'equatorial' position is as fundamental in cosmological terms, even though biological energetics are too weak to withstand either the polar big-bang at the origin nor the possible final fates, whether they are heat death by attrition in an ever-expanding universe, a big crunch, or fractal inflation, as shown at the left.

This paper explains how and why the origins of chemical life, major aspects of biological evolution and the elaborate emergent structures of tissues, from biomolecules up to cellular organelles and even to the doors of perception of the conscious brain, are a fractal interactive consequence of the non-linear laws of nature established at the cosmic origin. This reverses the Copernican revolution, putting life and with it ourselves back to centre stage in the cosmic arena.

Biology is a product of the twisted laws of nature dervied from cosmic symmetry-breaking. The rich diversity of structure in molecular systems is made possible by the profound asymmetries developing at the cosmic origin, between the nuclear forces, gravity and electromagnetism. The diversity of the elements and their asymmetric charge structure, with clusters of negatively charged electrons orbiting a massive nucleus containing all the positive charges in a concentrated nuclear 'droplet', is made possible only through the divergence of symmetry of the four fundamental forces. Without these asymmetries there would be only one or two simple atoms and none of the richness of the almost unlimited variety of molecular structures which can be generated by the over one hundred complex atoms occurring in nature as we know it. Chemical bonding is a consequence of the non-linear inverse square law of electromagnetic charge interaction in space-time. This non-linearity also gives rise to a succession of weak bonding interactions, generating the complex non-periodic secondary and tertiary structures of proteins and nucleic acids.



Fig 2: Galaxies and galaxy clusters illustrate the fractal self-similar nature of large scale fluctuations in the universe. According to some versions of inflation theory these may be inflated quantum fluctuations. Left: Galaxy MC 100. Right: a distant gravitationally-lensed red galaxy beyond a closer cluster, including blue galaxy lover right. Top right inset large scale structure of the universe including the 'great wall'.

2. Generating a Complex Twisted Universe

The four fundamental forces of nature - the strong and weak forces mediating nuclear binding and neutron decay respectively, along with electromagnetism and gravity are believed to have emerged from a single superforce, perhaps a form of higher-dimensional string, or membrane theory, in twelve, or so dimensions, immediately after the big bang, fig 3(a). The higher-dimensional space, containing a single generalized superforce compactified most of its dimensions to sub-particulate scales, leaving the four dimensions of space-time and broke symmetry to form the different forces we see today, in much the way a ferromagnet is polarized at minimum energy, breaking symmetry in space, so that at the lowest energy, all domains point in one direction. The forces nevertheless do appear to converge at extremely high energies - the unification temperature.

The strong force is a secondary effect of the colour force between the three red, green and blue quarks comprising a proton or neurtron in much the same way that molecular bonding is a secondary consequence of the formation of atoms. The colour force has three colours and three anti-colours instead of two charges. It also comes in two ground flavours so that the proton and neutron are a composite of up and down flavours uud and udd as well as three different colours. The quarks' charges of u = +2/3 and d = -1/3 thus generate precisely the integral charges of the proton and neutron. The weak force has become very short range because it is mediated by massive particles, which are believed to gain the required extra degree of freedom by assimilating another concealed particle, the mysterious Higg's boson (Georgi 1981, t'Hooft 1980, Veltman 1986).

bubble universes such as ours.

Complementing this picture at the quantum field theory level is a description on the cosmic scale in which a central theme is inflation. Although recently questioned by difficulties finding enough dark matter to halt the universe's slide towards hyperbolic expansion (Krauss 1999, Bucher and Spergel 1999), inflation concepts remain central to understanding how symmetry-breaking of the forces may have generated the expanding universe we know. In summary, a seed universe in the symmetrical state, below the unification temperature is in an unstable high-energy false vacuum, like a super-cooled liquid which could freeze to form a polarized magnet. The false vacuum in the Higg's field causes a gravitational repulsion representing the negative energy difference between temperature and that required to maintain the Higgs field. Under this 'antigravity', the empty universe, expands exponentially, smoothing quantum irregularities to structures on the scale of galaxies (Guth & Steinhardt 1984). The breakdown of the false vacuum (in 10⁻³⁹ sec) halts this inflationary phase, releasing a shower of high-



energy particles as latent heat, forming the hot expanding universe under attractive gravitation we are familiar with. The gravitational potential energy gained almost exactly equals the kinetic energy of the particles, making the generation of the universe possible from a quantum fluctuation. Indications are that the universe will continue to expand suggesting a hyperbolic inflation or fractal cosmic inflation (Linde 1992), in which the active tips of the universe are permanently inflating, to leave behind non-inflating

Fig 3 (a) Divergence of the four forces from a single superforce. (b) The three non-gravity forces converge in strength at the unification temperature.

What interests us here are the interactive consequences of this symmetry-breaking differentiation, because it leads to all the complex structures we see around us today. Cosmology is traditionally preoccupied with alpha and omega - initial and final causes - the origin and fate of the universe. But there is another perspective in which life and its complexity is as central to cosmology, fomring the central nonlinear interactive processes that make the universe the complex one we know and exist within, during the vast epochs of its mature evolution.

Although life may be created and annihilated during the evolution of the universe from alpha to omega, just as the creation and anihilation of virtual particles are essential to quantum field theory, the biological forms and processes can have a cosmic origin as generic structures and a cosmic significance as culminating interactive complexity (fig 1). Although fragile, on the cosmic scale of energies, the complexity of life is the supreme culmination in complexity of the interactive quantum process initiated in the quantum symmetry-breaking.



Fig 4: The standard model of particle physics involves half-integer spin fermions which obey the Pauli exclusion principle and form matter and integer spin bosons which mediate force and radiation. Right: the composite structure of symmetry-broken fermionic matter is molecular.

The interaction between the wave-particles emerging from the cosmic origin results in distinct effects on microscopic and cosmic scales. On the cosmic scale we find fractal structures - galaxy clusters, star and planetary formation, mediated by gravity, through contraction, heating and the ignition of the strong nuclear force, producing the energy of stars and the secondary photosynthetic energy of visible light. On the quantum scale we find integration of quarks to protons and neutrons then atomic nuclei in stars, then supernovas in the formation of chemical elements, and finally molecules, in the lower energetics of second generation sun-like stars. Quantum interaction of fermions reaches its full interactive complexity only in the molecular assemblies of biochemistry and finally, in tissues, organs and organisms, the brain being the most complex global expression of chemical non-linearities so far known, forming "the three-pound universe" (Hooper ad Teresi).

The hierarchical process leading to molecular complexity involves all the forces in sequence. Quarks are bound by colour force gluons into composite particles, such as the proton p+ and neutron n. These then interact by the strong force, via the nucleosynthesis pathway, to form the elementary nuclei. The nucleosynthesis pathway generates over a hundred atomic nuclei from the already composite proton and neutron. Parity between protons and neutrons is mediated by weak decay and is slightly broken at lowest energies to balance filling nuclear quantum levels with increasing electromagnetic repulsion of the positive protons, fig 6(b). Nucleosynthesis is a complex process catalytically moderated by several of the isotopes of lighter elements such as carbon and oxygen. Subsequently the weaker electromagnetic force interacts, firstly by formation of atoms through aggregation of electrons around nuclei and then by secondary interaction of complete atoms to form molecules. Molecular bonding is a non-linear quantum interaction, which is never fully resolved and thus perpetuates in a sequence of stages through successive strong and weak bonding interactions, making possible the complex tertiary structures of biomolecules.



Fig 5: The extreme variety of conditions on our own planets and between the moons of Jupiter and Saturn are only a foretaste of the bizarre variety of planets detected around other neighbouring stars. This extreme variety is consistent with the non-linear nature of gravity under inverse square law attraction in four-dimensional space-time and the resulting capacity of the universe to explore its own space of possibilities through chaotic dynamical interaction.

- <u>Super-Earth discovered in a habitable zone</u> 2011
- Impacts 'more likely' to have spread life from Earth 2011
- Comets may be creating oceans on alien planet 2011
- Fifty new exoplanets discovered 2011
- Exoplanet near Gliese 581 star 'could host life' May 2011
- Exoplanet hunt turns up 54 potentially habitable worlds Feb 11
- <u>'Trillions' of Earths orbit red stars in older galaxies</u> Dec 10
- <u>New exoplanet like 'one of ours'</u> Mar 10 <u>First life-friendly exoplanet may not exist</u> Oct 10
- Not too hot, not too cold: New Earth-like planet could sustain life Sept 10
- Billions of Earths in our Galaxy and 32 Discovered in 2009
- <u>Cool find in hunt for exoplanets</u> Dec09
- <u>'Super-Earths' orbit nearby stars</u> Dec09
- Keeping the young Earth cozy 09

Generation of the chemical nuclei requires a cosmic cycle through the supernova explosion of a shortlived hot star, generation of heavier elements like gold possibly involving the collapse of twin neutron stars after supernova formation (Rosswog). In the second phase, these elements are drawn into a lower energy long-lived sun-like star, the lighter elements associated with terrestrial biology occur in relatively high abundance as a result of nucelosynthesis dynamics, fig6(a), and can become concentrated on midrange planets. The final re-entry of the forces occurs through irradiation of molecular systems from photons emitted by stellar thermal radiation, representing the final re-interaction of the residual lower energy electromagnetic bosons with their fermionic counterparts in the electromagnetic orbitals of molecules. The typical coupling of the 5000°C surface temperature of sun-like stars provides photonic energy suitable for energizing weak-bonded molecular structures, without destroying them. A pivotal environment in which this final negentropic low-energy re-entry occurs in abundance are the surfaces of rocky planets in the temperature belt where water is liquid. The variety of planetary systems so-far discovered demonstrates the capacity of the universe to explore through chatoic non-linearities in gravitational orbits, a diverse array of planetary surfaces, ensuring the phase space of potential molecular environments is well explored on a cosmic scale (fig 5).



Fig 6: (a) Cosmic abundances of the bioelements. (b) The neutron excess of the stable nuclei reflects the interaction between the strong and electromagnetic forces via the weak force

The Anthropic cosmological principle introduces the existence of observers as a boundary condition, effectively imposing the existence of life as a cosmological constraint. It asserts that fundamental properties of the universe may have been selected by the fact that only with such constraints on the laws of nature would there be a (complex biological) observer to witness the universe and examine its laws (Barrow and Tipler). Forms of many-universes or many-histories cosmology likewise allow for a spectrum of possible universes, only some of which would have laws of nature which would permit the complex interactive states we associate with living systems. Some cosmologies suggest selection principles may regenerate the universe as a whole, and predispose it to the complexity we find evident (Smolin).

A key approach which seeks to define the laws of nature uniquely derives from super-symmetric string theories. In supersymmetry, each half-integer spin matter-forming fermion (e.g. electron, proton, neutrino, fig 4) is matched by a force/radiation-generating integer spin boson (e.g. Higgs, photon, Zo, gluon, graviton, fig 4). In string theories point particles become resonant loops, strings or membranes in higher dimensional space as distance shrinks, avoiding the infinite singularity of point particles. Consistent super-'brane' theories (Green 1985, 1986, Mukerjee 1996, Duff 1998) require a large number of dimensions, between 10 and 26 in which all but four dimensions (space-time) curl up on microscopic scales. Despite millions of possible compactifications, none has so far been defined which matches our particles and forces. Regardless of the fine details of the ultimate theory resolving the origins of the universe in unification, the formof the forces as we know them is consistently described as a conseuqence of symmetry-breaking.



Fig 7: The Orion nebula contains newly forming stellar systems possibly including the propylid (tiny black dot centre) with a dark 'planetary' disc (top and centre right) (Buhl). Some of these newly forming stars are also surrounded by clouds of HCN and HCHO (inset bottom-left) (Hubble telescope image).

• <u>Stars concoct complex molecules</u> 2011

3. The Abudantly Fecund Universe

As time passes, more and more evidence is accumulating that, the universe and its galactic gas clouds are abundant in organic chemicals, from the simplest molecules to sugars, amino acids and nucleic acid bases. Since Fred Hoyle coined the term "wooden universe" based on infra-red spectral data indicative of carbohydrate emission, there has been an awareness of the potential of galactic gas clouds to be cosmically abundant sources of prebiotic molecules.

Radio-telescope data as early as 1974 (Buhl) demonstrated clouds of multiple-bonded HCN and $H_2C=O$ spanning the region in the Orion nebula where several new stars are forming, fig 7. These are key precursors of complex polymerization pathways discussed below. Glycine has also been found in interstellar gas and adenine is an abundant product in simulations of collapsing interstellar gas clouds containing a dozen elements including hydrogen, carbon, oxygen and nitrogen (Chakrabadi 2000). Along with amino-acids, all of A, U, G, and C have been detected in carbonaceous chondrites (Hua et. al. 1986), such as the Murchison meteorite. These also contain amphophilic membrane forming products (Deamer and Pashley 1989). Cometary impacts are believed to have coated the Earth in a rich endowment of organics from the earliest stages of solar system evolution when impact rates were high.



Fig 8: Left: The cloud from which glycoaldehyde has been detected Right Droplets made by harsh radiation under interstellar conditions (Dworkin et. al.)

Glycolaldehyde has recently been detected by Jan Hollis (2000) in a cloud of gas and dust 2 light years across of a type from which new stars are formed. He notes "Interstellar clouds are spread throughout the galaxy and you often find the same molecule in many different clouds. Since these organic molecules are so widespread, it may mean that pre-biotic chemical evolution is an ongoing process." Glycoaldehyde can combine with other carbohydrate molecules to produce ribose.

A team led by David Deamer, Jason Dworkin, Scott Sandford and Louis Allamandola has also formed complex organic molecules under the harsh condition sof outer space. The main ingredients of interstellar ices are simple chemicals frozen together. Mostly water, some ammonia, carbon monoxide, carbon dioxide and methanol. The team froze a mixture of these chemicals into a thin solid ice at temperatures close to absolute zero $(-441 \hat{A}^{\circ} F/ -263 \hat{A}^{\circ} C)$ under extreme vacuum and exposed this to harsh ultraviolet radiation that mimics the radiation in space produced by neighboring stars. Instead of finding a handful of molecules only slightly more complicated than the starting compounds, hundreds of new compounds were produced in every mixed ice studied. The types of compounds produced are strikingly similar to many infalling meteorites and interplanetary dust particles. Thus much of the organic material found on the Earth in its earliest years probably had an interstellar heritage." (Dworkin et. al. 2001).

The capacity of complex organic molecules generated in space to enter Earth's atmosphere intact has also been confirmed. Jeffrey Bada has found evidence that "mother lodes' of buckyballs, football-shaped molecules made up of carbon atoms, have fallen intact to Earth from outside the Solar System from Sudbtlry, Ontario, where a meteoroid the size of Mount Everest crashed 2 billion years ago. They were loaded with helium, an element rare on Earth, but abundant in inter-stellar space. The single impact site contained about 1 million tons of extra-terrestrial buckyballs. If complex buckyballs could fall on earth without burning up so could complex organic molecules (Cohen 1996).

4. Quantum Chemistry as Non-Linear Complexity

The complex expressions of chemistry particularly in biology are manifest as a final non-linear interactive consequence of cosmological quantum symmetry-breaking. The stability of the nucleus with increasing nuclear mass number and charge permits an unparalleled richness and complexity of quantum bonding structures around the diverse chemical elements. Electron-electron repulsions, spin-obit coupling, delocalized orbitals and other effects perturb the periodicity of orbital properties and lead to the development of higher-order molecular structures. Although quanta obey linear wave amplitude superposition, chemistry inherits an inverse quadtaic non-linearity in the form of the attractive and repulsive charge interactions caused by re-distributing electrons between orbital systems. Such non-linear interaction, combined with Pauli exclusion, is responsible for the diversity of chemical interaction, from the covalent bond to the secondary and tertiary effects manifest in the complex structures of proteins and nucleic acids. The quadratic nature of charge interaction, leads to a situation in polymeric chemistry akin to the Mandelbrot set, (fig 22a) and which is central in making complex molecules (fig 10) and the scale-dependent structures of tissues possible (fig 22b).



Fig 9: Although all wave functions obey quantum superposition, the non-linear nature of electronic charge distribution and its resulting occupancy energetics, the Pauli exclusion principle and additional electromagnetic effects results in the non-linear energetics of chemical bonding. This non-linear interaction is never fully resolved by any single bonding step and gives rise through subsidiary weak-bonding interactions to the global interactivity of complex biomolecules and cellular organelles.

The source of this non-linear interaction is the foundation of all chemical bonding, the electric inverse square law of charge interaction. Although the state vector of a quantum-mechanical system is a linear combination of base states, exemplified by the formation of linear combinations of *s* and *p* wave functions to form the four sp³ hybrid orbitals, the electrostatic charge of the electron causes orbital interaction to have fundamentally non-linear energetics. The total energy is represented by the resonance integral of the Hamiltonian composed with the wave function, divided by the normalizing overlap integral S.

$$E = \frac{\int \varphi^* \mathcal{H} \varphi \ d\tau}{\int \varphi^* \varphi \ d\tau}.$$

DNA Decipher Journal

Published by QuantumDream, Inc.

In the case of the one-electron Hydrogen molecule ion, with Saa= Sbb normalized to 1, we have 2 solutions, as indicated:



The capacity of orbitals, including unoccupied orbitals, to cause successive perturbations of bonding energetics results in an interaction bonding sequence, from strong covalent and ionic bond types, through to their residual effects in the variety of weaker H-bonding, polar, hydrophobic, and van der Waals interactions, merging into the average kinetic energies at biological temperatures (Watson et. al. 1988). These are responsible for secondary structures such as the a-helix of proteins and base-pairing and stacking of nucleic acids, and result in the tertiary and quaternary sturctures determining the global form of large biomolecules and the globally-induced active-site effects central to enzyme action.

By contrast with the periodic crystalline or random amorphous structures of most minerals, the nonperiodic scale-dependent primary, scondary and tertiary structures in proteins and RNA that are critical to establishing the richness of their forms and their bio-activity, fig 10. The almost unlimited variety of monomeric primary sequences induce higher-order secondary and tertiary structures through subsequent folding of the polymer. These are possible only because the non-linearity of charge interaction which causes chemical bonding also gives rise to further residual interactions at lower energies which are resolved by cooperative weak bonding. Proteins are powerful catalysts because the global coherence of action arising from cooperative weak bonding makes for very powerful and responsive active sites. Despite being genetically coded, such molecules form fractal structures both in their geometry and their dynamics, fig 31(e, f) (Ansari et. al. 1985, Liebovitch et. al. 1987, 1991).



Fig 10: Global t-RNA and protein [enzyme] tertiary structures are the result of hierarchy of strong and weaker chemical bonding interactions operating on a non-periodic secondary structure. Both derive their structures in association with water.

Non-equilibrium thermodynamics (Glansdorff and Prigogine 1971) and the associated oscillating chemical systems such as the Beloushov-Zhabotinskii reaction (Epstein et. al. 1983) demonstrate the capacity of auto-catalytic chemical systems, and membrane electrochemistry (Chay & Rinzel 1985), to enter into non-linear dynamics and chaos (Epstein et. al. 1983, Agladze et. al. 1984). Quantum chaos and its suppression is also an emergent issue (Gutzwiller 1992).

The prebiotic polymerizations leading to the chemical origins of life share an informational paradox in which a small number of simple reactant lead to a large array of complex interacting products with many potential catalytic interactions. The initial conditions are thus insufficient to causally determine the products, except for a few predominant products such as adenine, leading to a huge variety of possible end states with increasing complexity. This allows for a high degree of polymeric variability which can be influenced both by auto-catalytic feedback and stochastic effects.

5. The Non-recurrent Table and the Elementary Bifurcation Tree

Although the discrete quantum aspects of orbital occupancy are periodic, (fig 11 b, c) the properties of successive atoms in the same periods in the table are not exactly, or even approximately, periodic. Successive members of the same group differ significantly in nuclear charge, atomic radius and electron repulsion, resulting in trends which permit interactive bifurcations between their properties. For example the properties of sulphur are significantly different from oxygen, although they are a period apart. The same goes for sodium and potassium through to fluorine and chlorine. When this non-linear non-periodicity complicating the underlying periodicity of the *s*, *p*, *d* and *f*orbitals is further extended to molecular systems, the parameter space of possible interactions resembles a quantum Mandelbrot set (fig 22) forming an atlas of configurations in which the atomic interactions fig 11(a) and resulting molecular species supporting biogenesis (fig 14, 15) play a pivotal generic role.

Such trends are illustrated in polar and H-bonding properties of hydrides for which H_2O is optimal (fig 11(b)), atomic and ionic radii in which the properties of elements like Na and K differ sufficiently to induce distinct H_2O bonding structures, and electronegativity, fig 11(c) in which O is even more electronegative than Cl. Such partial, or quasi-periodicity is also illustrated by the intrusion of the transition element d-orbital series between the subsequent s and p series (Moeller et. al.).



Fig 11: (a) Symmetry-breaking model of selection of bioelements, as an interference interaction between H and CNO, followed by secondary ionic, covalent and catalytic interactions. (b) Boiling points of hydrides illustrate the optimality of H2O as a polar H-bonding medium. (c) Electronegativities illustrate optimality of O and water as a hydride and emphasize the unique role of first row covalent elements C, N, O demonstrated in primitive polymerizations. Atomic and ionic radii also result in a two-way bifurcation of the properties of K, Na, Ca and Mg. Transition elements introduce unique catalytic activities partly through bringing the d-orbital into play.

The stable aspects of quantum orbital interaction in biochemical evolution can be classified into a tree of fundamental bifurcations which distinguish the elements structurally and cause divisions between their properties in interaction. This forms a generative sequence in which the bioelements have key roles (fig 11(a)). Each bifurcation gives rise to a reaction phase with added degrees of freedom and consequently greater interactive complexity. Describing the evolution of interactive chemical quantum structures in terms of fundamental force bifurcations sheds constructive light on the broad categories into which molecular free interaction differentiates and determines both the degrees of freedom and the constraints for development of interactive complexity in bio-molecules. Successive bifurcations are as follows:

Principal Bifurcation : The Covalent Interaction of H with C, N, O.

The central covalent quantum interaction in the table of the elements is between the two-electron 1s orbital and the eight-electron 2sp³ hybrid. This is the fundamental covalent 1-2 shell quantum interaction and the bifurcation through which biocosmology comes into existence. All the members of the CNO group have tetrahedral sp3 bonding geometry and form a graded sequence in electronegativity, from carbon in rough parity with hydrogen to electronegative oxygen, with one and two lone pair orbitals appearing successively in N and O. The resulting 3-D covalent bonds give C, N and O optimal capacity to form complex, diverse polymeric structures. Symmetry is split, because the 1s has only one binding electron state, while the 2sp³ has a series from 4 to 7 with differing energies and varied occupancy, as the nuclear charge increases. The 1s orbital is unique in the generation of the hydrogen bond through the capacity of the bare proton to interact with a lone pair orbital.

Some of the strongest covalent bonds known to chemistry are the multiple-bonds such as -CC-, -CN, and >C=O. These can be generated by applying any one of several high-energy sources such as u.v. light, high temperatures (900°C), or spark discharge to the respective atoms. Because of the higher energy of the resulting p-orbitals, these bonds possess a specific type of structural instability, in which one or two p-bonds can open to form lower energy partially s-bonded heterocyclic and other oligomeric structures. Most of the prebiotic molecular complexity generated by such energy sources can be derived from mutual polymerizations of HCCH, HCN, and $H_2C=O$, and realated hybrids in association with 'sister' molecules such as urea H_2N -CO-NH₂. These include purines such as nucleic acid bases adenine and guanine, their pyrimidine complements uracil and cytosine, key sugar types such as glucose and ribose, amino acids, polypeptides, porphyrins etc. They form a core pathway from high energy stability to structurally unstable polymerization, and to complexity, which we will elucidate.

The formation of conjugated double and single bonds in these reactions results is delocalized *p*-orbitals (Pullman and Pullman 1962). Such orbitals in heterocyclic (N-C) rings with conjugated resonance configurations also enable lone pair $n > \text{\&pi}^*$ and $\text{\&pi} > \text{\&pi}^*$ transitions (Rich and Rajbandry 1976),

resulting in photon absorption and electron transfer. These two effects in combination play a key role in many biological processes including photosynthesis, electron transport and bioluminescence.

Secondary Splitting between C, N, and O: Electronegativity Bifurcation

In addition to varying covalent valencies, lone pairs etc., the 8-electron 2sp3 hybrid generates a sequence of elements with increasing electronegativity, fig 11(c), arising from the increasing nuclear charge. This results in a variety of secondary effects in addition to the oxidation parameter, from the polarity bifurcation discussed below, to more subtle effects such as the complementation of $-CO_2H$ and $-NH_2$ as generalized organic acidic and basic moieties.

Differential electronegativity results in several coincident bifurcations associated with water structure. A symmetry-breaking occurs between the relatively non-polar C-H bond and the increasingly polar N-H and O-H. This results in phase bifurcation dividing the medium into polar (aqueous) and non-polar phases in association with low-entropy water bonding structures induced around non-polar molecules. This is directly responsible for the development a variety of structures from the membrane in the context of lipid molecules fig 20, to the globular enzyme form and base-stacking of nucleic acids fig 10.

Critical in this process are the optimal properties of water H_2O among all molecules, making possible in turn polarity interactions, aqueous acid-base bifurcation, ionic solubility and hydrogen bonding. The optimal nature of water as a hydride is illustrated in boiling points Fig 11(b). Water provides several other secondary bifurcations besides polarity. The dissociation H_2O &harr H^+ + OH lays the foundation for the acid-base bifurcation, while ionic solubility generates anion-cation. Many key properties of proteins and nucleic acids, are derived from water bonding structures in which a counterpoint of H-bonding and phase bifurcation effects occu, determining the form of the alpha helix and nucleotide base pairing. Hydrophilic-non-polar bifurcation is central to the tertiary structures of globular proteins as 'micelles' and hairpins of RNAs, fig 10. The solubility or otherwise of a variety of molecules and ions is derived from the energies and entropies of their induced water-bonding structures. The large diversity of quantum modes in water is demonstrated by its very high specific heat, contrasting with that of proteins (Cochran 1971). Polymerization of nucleotides, amino-acids and sugars all involve dehydration elimination of H₂O, giving water a central role in polymer formation. It has also been suggested water is a two phase medium containing quantum-coherent domains, in association with boundaries such as macromoleculaes and membranes (Mae-wan Ho ISIS Report).



Fig 12: The diversity of snow crystals illustrates the complexity of water bonding structures and their diversity under very slight perturbation of initial conditions (Bentley and Humphries).

Ionic Bifurcation

The cations bifurcate in two phases : monovalent-divalent, and series (Na-K, Mg-Ca). Although ions such as K^+ and Na⁺ are chemically very similar, their radii of hydration differ significantly enough to result in a bifurcation between their properties in relation to water structures and the membrane. Smaller Na⁺ and H₃O⁺ require water structures to resolve their more intense electric fields. Larger K⁺ is soluble with less hydration, making it smaller in solution and more permeable to the membrane (King 1978) . Ca²⁺ and Mg²⁺ have a similar divergence, Ca²⁺ having stronger chelating properties. This causes a crossed bifurcation between the two series in which K⁺ and Mg²⁺ are intracellular, Mg²⁺ having a pivotal role in RNA transesterifications. Cl⁻ remains the central anion along with organic groups. These bifurcations are the basis of membrane excitability and the maintenance of concentration gradients in the intracellular medium which distinguish the living medium from the environment at large.

P and S as Low-energy Covalent Modifiers

The second-row covalent elements are sub-optimal in their mutual covalent interactions and their interaction with H. Their size is more compatible with interaction with O, forming e.g. SiO_3^{2-} , PO_4^{3-} and SO_4^{2-} ions including crystalline minerals. The silicones are notable for their O content by comparison with hydrocarbons. However in the context of the primary H-CNO interaction, two new generic properties are introduced.

PO43- is unique in its capacity to form a series of moderate energy dehydration polymers, both in the form of pyro- and poly-phosphates, and in interaction with other molecules such as sugars. The energy of phosphorylation falls neatly into the weak bond range (30-60 kj/mole) making it suitable for conformational changes. The universality of dehydration as a polymerization mechanism in polynucleotides, polypeptides, polysaccharides and lipids, the involvement of phosphate in adenosine

triphosphate (ATP) energetics, ribonucleic acid (RNA) and membrane structure, and the fact that the dehydration mechanism easily recycles, unlike the organic condensing agents, give phosphate optimality as a dehydrating salt.

The function of S in biosystems highlights a second optimality. The lowered energy of oxidation transitions in S particularly S-S > S-H, by comparison with first row elements, gives S a unique role as a mediating mild covalent linkage both in terms of tertiary bonding and low energy respiration and photosynthesis pathways.

Transition Element Catalysis

Transition elements add key d-orbital effects, forming a catalytic group. Almost all of the transition elements e.g. Mn, Fe, Co, Cu, Zn are essential biological trace elements (Frieden 1972), promote prebiotic syntheses (Kobayashi and Ponnamperuma 1985) and are optimal in their catalytic ligand-forming capacity and valency transitions. Zn2+ for example, by coupling to the PO43- backbone, catalyses RNA polymerization in prebiotic syntheses and occurs both in polymerases and DNA binding proteins. Both the Fe²⁺-Fe³⁺ transition, and spin-orbit coupling conversion of electrons into the triplet-state in Fe-S complexes occur in electron and oxygen transport (McGlynn et. al. 1964). Other metal atoms such as Mo, Mn have similar optimal functions, e.g. in N₂ fixation.

These five processes between them constitute the major quantum bifurcations in the free interaction of the elements. They are also the central processes operating in biogenesis. Put together this says the following: The central biogenesis pathways are themselves results of the central interactive quantum bifurcations of symmetry-breaking and its resulting non-linear interactions. While life may be possible from other combinations of elements and other temperatures and pressures, life as we know it has taken the sang raal or blood-royal route of quantum cosmology.



Fig 13: (a) The perturbing effect of the neutral weak force results in violation of chiral symmetry in electron orbits. Without perturbation (i) the orbits are non-chiral, but the action of Zo results in a perturbing chiral rotation. (b) Autocatalytic symmetry-breaking causes random chiral bifurcation (i).Weak perturbation breaks stability to one chiral form (iii)

Kenso Soai (1998) and his team have demonstrated the autocatalytic bifurcation framework as well They took a mixture of compounds containing a small excess of one enantiomer of the amino acid leucine. In the presence of this imbalance, the components of the solution reacted to form a compound called a pyrimidyl alkanol, also with a small excess of one enantiomer. But this molecule then acted as a catalyst in its own formation, and soon almost all the pyrimidyl alkanol in the solution was of this sort. (see also New Sci 12 Dec 98 16)

Did exploding stars shatter life's mirror? May 10

Tertiary Interaction of Mineral Interface

Both silicates such as kaolinite clays (Strigunkova et. al. 1986) and volcanic magmas (Lavrentiev et. al. 1984) have been the subject of intensive interest as catalytic or information organizing adjuncts to prebiotic evolution. Clays have been proposed as a primitive genetic system and both include adsorbent and catalytic sites (Cairns-Smith 1982, Weiss 1981). Clays also appear to play a key role in stabilizing ribonucleotide polymerization (Ferris 1996). The mineral interface involves crucial processes of selective adsorption, chromatographic migration, and fractional concentration, which may be essential to explain how rich concentrations of nucleotide monomers could have occurred over geologic time scales.

6. Structural Dynamics of Core Polymerization Pathways

The initial polymerizations of energetic multiple-bonded monomers in the reaction in figs 14 and 15 form a particularly interesting problem from a quantum-mechanical point of view, because they provide some of the richest examples of growth in quantum-mechanical complexity, in which a relatively small number of simpler entities give rise to increasingly complex structures whose properties cannot be fully predicted from the initial conditions.

H2C=O in aqueous solution gives rise to 4 to 7 carbon sugars, including ribose, as well as branched polysaccharides. HCN gives rise to heterocyclic purine and pyrimidine nucleic acid bases, and in addition several amino acids, polypeptides, porphyrins, and many other types of biomolecule (Lowe et. al. 1963, Calvin 1969, Mizutani et. al. 1975). A similar array of products arises from hybrids such as cyanogen NC-CN (Schwartz et. al. 1975) and cyanoacetaldehyde NC-CH₂-H₂C=O. Although several of these products, such as the ring polymers adenine (HCN)₅ and ribose (H2CO)₅ are stable product structures, many of the more complex products, such as particular oligopeptides are metastable or stochastic products of the reaction. These conditions differ markedly from the current biochemical regime in which structurally-stable metabolic pathways are maintained through genetically-coded enzyme catalysis except where recombinational stochasticity is specifically initated as in generation of antibody immuno-diversity.



Fig 14: Known product structures and pathways in HCN polymerization.

Since the initial conditions do not contain sufficient information to determine the final products, the system contains many potential outcomes. The lower energy configuration of key products, such as adenine's resonance stabilization, leads to some stable conformations based on free energy. Stochastic indeterminacies in the interaction of simpler molecules lead to multiple branching pathways. Products of increasing complexity such as polypeptides possess increasingly active catalytic potential, which may alter the structural-stability of polymerization to favour certain types of product. The dynamics may trigger a sequence of autocatalytic bifurcations, some of which may result in the formation of attracting molecular products. These reaction pathways are capable of producing a vast variety of complex molecules with generic relationships to key biomolecules, including amino acids, polypeptides, HCN polymers, purines, pyrimidines and porphyrins.

Both HCN and HCHO polymerizations have prominent cyclic products which act as spontaneous end points of polymerization, because cyclization mutually neutralizes reactive moieties. The purines, pyrimidines, ribose and porphyrins all display structure consistent with being cyclic terminators. The capacity of polymers for non-periodic primary sequencing gives rise to complex tertiary structures, which are fractal as a result of structure on several overlapping scales from the atom, through local groups, to structures such as a-helices through to global conformation changes. This fractal nature is reflected both in the geometry and the quantum energetics of molecular transformations (Ansari et.al. 1985, Liebovitch & Toth 1991). Substrate form is dependent firstly on local active sites, and in turn on the global tertiary structure of catalytic molecules.



Fig 15: (a) One of several synthesis pathways for pyrimidines. (b) Sample HCHO polymerization routes. Phosphorylation of the oligo-aldehydes causes the reaction to favour ribose. (Eschenmoser 1992).

Although the first syntheses produced the purines adenine and guanine readily, cytosine and uracil, the complementary pyrimidine bases making up the other half of the pair A-U and G-C, however Stanley Miller, forty three years after his original pioneering experiment in spark synthesis, with Michael Robertson, discovered a way for the primordial pond to make them in high yield. Although urea is produced in Miller's original experimental setup, it never reaches a high enough concentration. When he added more urea, it reacted with cyanoacetaldehyde, another by-product of the spark synthesis, churning out vast amounts of the two bases. Urea would have been able to reach high enough concentrations as shallow pools of water on the Earth's surface evaporated. (Cohen 1996, Horgan 1996).

Eschenmoser (1992) has found that glyceraldehyde phosphate in the presence of HCHO will produce 5carbon sugars with up to 33% ribose. In the absence of HCHO the reaction tends to produce 6-carbon sugars. The phosphate-induced reaction is key here because RNA, ATP and glycolysis all involve phosphate dehydration energy. This indicates a specific link to phosphate energy primordial to the formation of oligonucleotides and even ribose.



Fig 16: (a) MgATP-complex illustrates linkage between primal stability structures. Cyclic pentamers of HCN (adenine) and HCHO (ribose) are linked by phosphate dehydration, stabilized by cation and water structures. (b) Heterocyclic form of heme. Porphyrins have also been detected in primal syntheses. (c) Nucleophilic attack of adenine N9 on ribose.

7. RNA and Cosmology

In 1981 Francis Crick commented that 'the origin of life appears to be almost a miracle, so many are the conditions which would have to be satisfied to get it going." (Horgan 1996) Now, several findings bolster the dominant theory of genesis - that life began in an era in which RNA was both the genetic and catalytic basis - the RNA era (Gilbert 1986, Benner et.al.) in which simple replication and 'enzymatic' process based purely on RNA catalysis established evolutionary biochemistry.

The general outlines are clear. Ribose, unlike the deoxyribose in DNA, has plausible prebiotic syntheses. RNA's capacity to both form double-helices, like DNA and to also three-dimensional tertiary structures similar to proteins through base-backbone bonding to ribose fig 10(a), causes RNA to have both genetic and catalytic capacity. Simple biological RNAs have been demonstrated to have autocatalytic self-assembling capacity. The catalytic activity of polynucleotides, hinges on various forms of proton transfer fig 17(a,b,c) (Pace and Marsh 1985), in particular transesterification.

The essential core of the protein-assembling ribosome remains RNA as does the signal recognition particle which shepherds nascent proteins through the membrane. The ancient fossil nucleotide coenzymes including ATP, NAD, coenzyme-A and Vitamin B12 are all ribonucleotides. Eucaryote organisms continue to have a massive commitment to RNA processing within the nucleus, including the use of many small small nuclear ribonucleotides or snuRps involved in RNA splicing. This suggests eucaryotes have never fully transferred from an RNA-based metabolism. Reverse transcriptases also remain ubiquitous and essential for such basic functions as telomere extension, and have a common evolutionary tree, giving retrotransposons and retroviruses a potentially ancient origin in the commonality of the RNA era.

There is still debate about whether RNA was actually the primordial genetic molecule and other hybrid molecules such as peptide-nucleic acids which use peptide rather than sugar linkages also have genetic potential and plausible prebiotic status (Nelson et. al.), however it is clear RNA itself has generic status as a cosmological molecular structure on several grounds. Adenine is a principal thermodynamic product of HCN polymerization in industrial yields. All of A, G, U and C now have prebiotice status as favoured products of such reactions. Ribose is an optimal sugar conformationally in terms of permitting complementary double helix formation, and has a synthesis route from glyceraldehyde phosphate. The complementations of A-U and G-C posses a type of structural optimality among the bases. The heterocyclic polymers are restricted in their variety by the positions of N atoms required by the polymerization process. The tautomeric states of A, U, G and C indicate AU and GC may be optimal for base-pairing among close prebiotic variants.

The nucleotide unit, as exemplified in ATP consists of a direct concatenation of key products of HCN and HCHO polymerizations. Adenine and ribose are the cyclic pentamers of HCN and HCHO linked via dehydration to a dehydrating oligo-phosphate giving it the statues of a generic structure, fig 16(a) stabilized by water and Mg^{2+} , Positive ions also play an important role in stabilizing mono- and oligo-nucleotides. It was originally synthesized under primitive conditions by Ponnamperuma et. al. (1963). Mg^{2+} ions are also bound to transfer RNA and play a critical role in transesterification, balancing the negative phosphate suggests that phosphate was the active moiety linking of the base-sugar-phosphate complex, fig 16(c) and thus drove the entire formation of nucliec acids.

RNA proved difficult for a time to induce into complementary replication in enzyme-free systems, but its relative difficulty of synthesis may be essential to its function. It is necessary that RNA be thermodynamically unstable, or life could not exist dynamically but would 'crystalize' all the way to non-genetic polymers. A variety of partial model systems of complementary replication have been realized by Orgel and his coworkers, however instabilities in polymerization have hindered experimental enzyme-free complementary polymerization of RNAs (Orgel 1992). It is clear that a regime of polynucleotide chemistry would have to have occurred stably over evolutionary time scales for an RNA-based form of life to evolve to the point where it had established translation and captured metabolic synthetic pathways.

Ferris reported (1996) that he had found a means by which the first large chains could have been forged. When his team added montmorillonite, a positively charged clay believed to be plentiful on the young Earth, to a solution of negatively charged adenine nucleotides, it spawned RNA 10-15 nucleotides long. If these chains, which cling to the surface of the clay, were then repeatedly 'fed" more nucleotides by washing them with the solution, they grew up to 55 nucleotides long. Ferris notes the clay gets RNA off the hook of having to take on the tasks of information storage and catalysis in one fell swoop. It would catalyse RNA synthesis, stocking pools with a large range of RNA strands that, as Szostak and others have shown, would evolve a catalytic capacity of their own. (Horgan 1996). Thus complementary replication can come into existence after a phase of single-stranded polymerization has given rise to a fractal RNA environment with a diverse array of oligomeric and polymeric structures, which in turn feedback autocatalytically on replication and monomer synthesis.



Figure 1 | Pyrimidine ribonucleotide assembly options. Previously assumed synthesis of β -ribocytidine-2',3'-cyclic phosphate 1 (blue; note the failure of the step in which cytosine 3 and ribose 4 are proposed to condense together) and the successful new synthesis described here (green). p, pyranose; f, furanose.

In 2009 <u>Sutherland</u> discovered that pyrimidine nucleotides can be readily synthesized from simple prebiotic molecules bypassing the more difficult routes depending on synthesizing ribose, bases independently and trying to then attach them to phosphate. In fact phosphate was pivotal in producing new intermediates which would then in good yield polymerize to nucleotides.

Chemist Shows How RNA Can Be the Starting Point for Life May 14, 2009

Since then he and his colleagues have proposed one-pot pathways to both purine and pyrimidine nucleotides (Powner, Sutherland and Szostack 2010 *Chemoselective Multicomponent One-Pot Assembly of Purine Precursors in Water J. Am. Chem. Soc. 2010, 132, 16677â€*"16688).



" Solid arrows, reported chemistry; dashed arrows, proposed chemistry.

Hypothetical pathways to both purine and pyrimidine nucleotides fro the above paper

Powner and Sutherland have also investigated interconversion of sugar bases between ribo and arabino nucleotide intermediates (Powner MW, Sutherland JD. 2010*Phosphate-mediated interconversion of ribo- and arabino-configured prebiotic nucleotide intermediates*. Angew Chem Int Ed Engl. 49(27):4641-3).

A central scenario out of many, including volcanic hot pools, and hydrothermal vents, is the three-phase boundary of a phosphate-rich, clay shore line under tidal or weather-related variations in a pool in which the margin is reversibly dehydrated e.g. by sun-drying. Both clays and volcanic basalts have been cited as possible mineral interfaces. Precipitated phosphate at 37° , leads to pyrophosphate formation and hence phosphate bond energy (Hermes-Lima 1990). Since the energy for nucleotide polymerization is driven by H₂O removal, reversible dehydration of a medium containing phosphate, bases and sugars provides one of the most direct and simple routes to polynucleotide formation.

8. Diverse Horizons of the RNA Epoch

A whole new field of RNA research has developed from the discovery of spontaneous splicing of RNAs in living systems by Tom Cech and the demonstrated capacity of such RNAs to function as catalysts in transesterifications and the work of Jack Szostack's teams in selective RNA catalysis (Cech 1986a). This immediately made the idea of the RNA world before proteins a natural hypothesis. This work has grown with artificial selective evolutionary studies, culminating with the development of a ribozyme which is capable of high fidelity complementary replication of short RNA oligomers of arbitrary sequence (Johnston et.al. 2001). This has become a turning point in the credibility and maturity of the RNA world as a precursor to DNA-based life which can develop as an autonomous molecular system.

The model has been extended to others for RNA-based error-correction, synthetases and the ribosome (Bass and Cech 1984, Cech 1986b, Zany and Cech 1986, Garriga et. al. 1986, Weiner and Maizels 1987). Modified ribozymes are capable of acting as polymerases which can replicate complements to subsections of themselves (Green et. al. 1990, Doudna et. al. 1991).

The discovery that RNA appears to be the agent of peptide-bond synthesis in the modern ribosome (Guthrie 1992, Pace 1992, Noller et. al. 1992) and the capacity of modified ribozymes to act as aminoacyl esterases (Picarilli et.al. 1992), the first step of ribosomal action in protein synthesis, establish RNA has the potential to act as synthetase as well as transfer, messenger and ribosomal functions. This gives RNA the capacity to act on its own to catalyse both its own replication and the ordered polymerization of proteins. Simpler model systems have also been advanced of the stereospecific capacity of Dnucleotides to act as a catalyst of L-amino acid polymerization (Lacey et. al. 1990). These results enable RNA to be the key prebiotic molecule generating ordered polynucleotide and polypeptide structures.



Fig 17: The ribozyme world: (a) Phospho-imidazole. Proton transfers in (a) imidazole, (b) in base tautomerization, (c) in Tetrahymena intron. (d) The first effective ribozyme RNA polymerase (iii) - a 172 unit molecule bred by molecular selection from a ligase ribozyme (i) through selective evolution of a pool of other intermediates (ii). This ribo-RNApolymerase will faithfully perform complementary replication of oligo-ribonucleotides of arbitrary sequence up to 14 units long with accuracies of up to 98% per base pair. (e) The RNA polymerase ribozyme tC19Z, that was able to synthesize a spectrum of RNA sequences, including the accurate synthesis of an enzymatically active RNA

Szostak and Wilson (1996, Wilson and Szostak 1995) have evolved ribozymes capable of a broad class of catalytic reactions. The catalysis of previous ribozymes tended to involve only the molecules' sugarphosphate "backbone," but these could also promote the formation of peptide bonds (which link amino acids together to form proteins) and between carbon and nitrogen. (Horgan). David Bartel a former member of Szostak's team, has evolved RNAs that are as efficient as some modern protein enzymes. The problem with most ribozymes is that they are as likely to snip an RNA molecule apart as stitch one together which makes copying a molecule fifty nucleotides long (the minimum size necessary to catalyse a chemical reaction) difficult or impossible. Bartel's new ribozymes, on the other hand, can stitch small pieces of RNA together without breaking larger molecules apart. These ribozymes use high-energy tri-phosphate bonds similar to ATP as their fuel, speeding the reaction up several million-fold. "We've got ribozymes doing the right kind of chemistry to copy long molecules" says Szostak "We haven't achieved self-replication from single nucleotides yet, but it is definitely within sight". (Cohen)

Zhang and Cech have reported a step towards the goal of linking amino-acids. They isolated RNAs that could efficiently link specific amino acids together (Zhang and Cech 1997). These pseudo-ribosomes were selected from a random pool of 1015 synthetic RNAs. They then elicited a trans-acting by coupling one of the amino acids to a short RNA with complementary sequence to the ribozyme achieving a ribozyme which whould join a ribosynthetase-amino acid to form a peptide bond with another thus relicating even more closely ribosomal function. They also found that a small region of many of the RNAs they selected was 70 per cent identical to some regions of the ribosomal RNA. "We not only copied ribosome function, we seemed to have recapitulated its evolution," says Cech. The two researchers then removed or mutated these sequences in the synthetic RNAs (Zhang and Cech 1998) any change to this region cut the activity of the RNA by a factor of between 20 and 600. This suggests this region in both the modern ribosome and the synthetic RNA may have the same role in the fusion reaction, such as holding the amino acids in the correct position and that they may have converged on the same molecular solution.

In 2011 a breakthrough has been made by recombining traits evolved separately in different ribozyme lineages in combination with in-vitro evolution and engineering producing an RNA polymerase ribozyme (tC19Z in fig 17), capable of synthesizing RNAs of up to 95 nucleotides in length, that was able to synthesize a spectrum of RNA sequences, including the accurate synthesis of an enzymatically active RNA, a hammerhead endonuclease ribozyme (Wochner A, Attwater J, Coulson A, Holliger P 2011*Ribozyme-Catalyzed Transcription of an Active Ribozyme* Science 332 209-212).

The alternative hypothesis is that life may have begun as a molecular hybrid, PNA or peptide nucleic acid. PNA has a similar structure to RNA except for having a peptide backbone based on prebiotically abundant glycine and can co-instruct complementary RNA sequences and vice versa (Bohler, Nielsen and Orgel). The bases of PNA are joined together with peptide links like those in proteins which may not present the instabilities which sugars may have faced on the early earth. Matthew Levy and his colleagues (Nelson, Levy and Miller) persuaded up to 78 per cent of plausible prebiotic chemicals to transform into PNA backbone subunits amino-ethyl glycine or AEG. The acetic acid derivatives of the bases A, G U and C can likewise be generated from prebitotic reagents including NH₄CN with glycine and cyanoglyceraldehyde. AEG units link up readily at 100 deg C, which may have been common temperature four billion years ago when our planet was rich in volcanic activity. PNA is clearly an alternative route to establishing the RNA era which also has a good cosmological foundation. However researchers concede that there is no evidence such alternative molecules have existed in Earth's history

"You don't see a smoking gun," says Gerald Joyce, of the Scripps Research Institute. (Marshall M 2011 *First life: The search for the first replicator* New Scientist 15 Aug).

CCY Pro	CGY N-base	CUY VL D	H O	CAY
GC Y Ala ←	GGY Gly abu	ndant GUY	P	GAY Acid
UCY Ser ACY Thr	UGY Cys	ALTA ALTA	P 0 1	UAY J Stop
	SH AGY Ser	AUY VII P	a	AAY N-base

Fig 18: The genetic code contains evidence for several primal bifurcations (King 1982). Centre position AU selects polar **[10]** /non-polar **[10]** as broad groups. VLIP are Val-Leu-Ileu-Phe. First position G initially determines primally abundant **[10]** amino acids. Expansion: first codon C, A become fixed in relation to synthesis routes from Glu **[10]** and Asp **[10]** Subsequent bifurcations include H-bonding block **[10]** and acid-base.

9. Universal Stability Structures in Molecular Biology

The previous discussion of the RNA era can unravel a double-bind that is central to biogenesis - how did the core biochemical pathways become generated? The traditional viewpoint is that they were successively created starting from a simple chemical-feeding heterotroph, through mutational evolution, building one-by-one the protein components necessary to make a working whole. This however does not explain how integrated systems such as electron transport and the citric acid cycle could have functioned at all with only a vestigial complement of enzymes.

This suggests that many of the major features of molecular biology are generic structures which can come into existence under suitable conditions, through bifurcation, independently of the emergence of genetic RNA, and that these were subsequently captured by genetic takeover as genetic complexity permitted. Such generic structures include the polymeric structure of proteins and nucleic acids, nucleotide coenzymes, bilayer membrane structure and the topological closure of the cell, ion transport and membrane excitability, membrane-bound electron transport, glycolysis and the citric acid cycle.

Such a perspective has far-reaching consequences for molecular biology in cosmological terms, for while the details of mutational evolution will be unique to each environment, the major features underlying biology could be universal.

(a) Nucleotides and the Nucleotide Coenzymes.

The nucleotide co-enzymes are widely regarded as ancient molecular fossils retained from the RNA-era. In addition to the key role of ADP and ATP as energy currency in the bio-metabolism, GTP is used in protein synthesis, and the nucleotides UDP and CDP are carriers of glucose and choline and other membrane components. Model prebiotic reactions have successfully coupled UDP and CDP to glucose

and choline (Mar et. al. 1986). Both NAD, and FAD function as carriers of redox energy. Coenzyme A consists of adenosine coupled to pantothenic acid and functions as a carrier of acyl and other groups via the terminal SH bond (Reanney 1977). Vitamin B_{12} also illustrates how a di-nucleotide can bind a metallic porphyrin ring. Eschenmoser (1988) has also discovered a plausible prebiotic pathway generating the more complex B_{12} molecule which involves two nucleotides and a Coporphyrin.Prebiotically such a molecule could have also utilized a lowered Fe²⁺- Fe³⁺ activation energy as a carrier of electrons.

(b) Translation.

According to the genetic takeover hypothesis, evolution of RNA captured existing stability structures in the prebiotic medium. The most central of these is clearly the use of proteins as coded enzyme catalysts. Such a process could only have occurred in an environment in which RNAs coexisted with amino-acids and in which a very small additional genetic advantage could capitalize on simple coding of existing structures to good effect.

A variety of amino acids and oligopeptides are common products of prebiotic syntheses. The polymerization of amino acids and the development of peptide backbones with cyanide side chains from the linear HCN oligomer fig 14, provide alternative routes to oligopeptide structure. A natural propensity for $-NH_2$ and -CO2H moieties as basic and acidic groups arises directly from the electronegativity bifurcation.

The discovery that ribosomal, synthetase, messenger and transfer functions of protein synthesis can all in principle be carried out by RNAs alone leads to a natural interpretation of the development of the genetic code from a protein-free translation system. The major partitions of the genetic code have structural features consistent with an origin in underlying chemical bifurcations. The fundamental bifurcation sequence, fig 18 is as follows:

(1) **Polarity bifurcation:** There is a major bifurcation in polarity between amino acids with anticodons having centre bases U & A. Uracil is correspondingly more hydrophilic than adenine, as reflected in their dominant split in hydrophobicity A(3.86)>G(2.3)>C(1.5)>U(1.45) and water solubilities A=1/1086, U=1/280. This leads to the idea that the polarity bifurcation was a principal symmetry-breaking factor in the origin of the nucleic acid code (King 1982).

(2) Abundance and GC: The initial base G also codes the most abundant amino acids, consistent with a GXY code starting with GAY=polar (anticodon U), GUY=non-polar (anticodon A) providing binding strength of GC and frame shift suppression (Y=pyrimidine).

(3) Four-fold code: Extending to include GGY, GCY, provides a fourfold specificity for polar (Asp/Glu), non-polar (Val and larger), along with Gly, and Ala as most abundant.

(4) **Eight- and Twelve- fold codes:** This could have then doubled to and 8-word code by including CAY, CUY, CGY, and CCY coding for non-polar and basic groups, and then a similar series based on AAY, AUY, AGY, and ACY Wong (1975) originally noted a correspondence between the first codon base and biosynthetic pathways in primitive organisms such as sulphur bacteria with Pro, Arg, Gln Leu, His derived from Glu and having first codon base C and Ser, Thr, Ile, Asn, Met, Lys being derived from

Asp having first codon base A (Knight, Freeland and Landweber 1999). OH- and SH-containing amino acids also form a single additional block (UA)(GC)Y, suggesting a third bifurcation for H-bonding, with UAY reading stop. Notably these is significant stereospecific affinity between certain amino acids such as Ile and Arg and their codons (ibid).

(5) Evolutionary takeover: From this point evolutionary selection begins to optimize the bifurcations caused by stereospecificity and the growth of these interactions into synthesis pathways, based on error minimization and the incorporation of the last of the amino acids. Later assignments such as Trp are consistent with evolutionary adaptions.

Freeland and Hurst (1998), have shown that strong selective pressures must have acted on the code during its evolution. Hurst found that single-letter changes to a codon, inserting the wrong amino acid into a protein, tended to specify amino acids that were very similar chemically to the correct ones, minimising the impact on the protein. Freeland then reasoned that the code should minimise chemical differences most between the correct and incorrect amino acid at the third base in the codon since translation misreads this base 10 times as often as the second. In an analysis that gave extra mathematical weight to the vulnerable sites most likely to be mistranslated, Freeland showed that no more than one in a million random codes was better at reducing the impact of errors than the natural code. The possibility of evolutionarty change in the code is affirmed by both mitochondrial and nuclear variants (Knight, Freeland and Landweber 1999).

Following on from this Freeland et. al. (2000) have analysed other work showing that more optimal global solutions do exist to propose that stereochemical and synthesis path constraints fixated the code ealy on into one which was later evolutionarily optimized on error minimization constraints, the modern code being optimal under these constraining conditions. This analysis gives strong weight to the idea that the form of the code is derived from chemical, historical and selective factors rather than being a frozen accident which happened to the predecessors of the last common ancestor of living cell lines.



Fig 19: Left and centre: Microcellular formations generated by the author from HCN and HCHO. Right: Spores of a psilocybe species at the same magnification for size comparison (King 1991b).

(c) The Membrane, Excitability and Ion Transport

All life as we know it is dependent on maintaining a distinct internal micro-environment as an open farfrom-equilibrium thermodynamic system (Glansdorff and Prigogine), through the topological closure of the cell. Viruses for example all depend on cellular life. The structure of the bilayer membrane is a direct consequence of the polarity bifurcation. The formation of amphophilic lipid-like molecules, joining a linear non-polar hydrocarbon section to an ionic or H-bonding polar terminal, leaves 2 degrees of freedom for layer formation. Backing of the non-polar moeties to one another, fig 20(b), completes the bilayer. Cell structure can then arise directly from budding of the bilayer, as illustrated in budding in several types of prebiotic reaction medium. Microcellular structures are abundant in many origin of life syntheses, fig 19. The use of CDP associated with choline, inisotol & lipids in membrane construction is consistent with membrane formation in the RNA era. The structure of typical biological lipids such as phosphatidyl choline display a modular structure similar to ATP, consisting of fatty acid, glycerol, and substituted amine again linked by dehydration and involving phosphate, fig 20(e).

The existence of the membrane as a non-polar structure leads to segregation into ionic and non-polar reaction phases. Ion transport is essential in maintaining the concentration gradients that distinguish the cytoplasm from the external environment and thus must develop in the earliest cellular systems (MacElroy et. al. 1989). Ion transport is a source of significant electronic effects, because the membrane under polarization is piezo-electric and is capable of excitation in the presence of suitable ions. Model systems using the simple 19 unit oligopeptide Na-ionopore alamethicin and artificial membranes display action potentials (Mueller and Rudin 1968). Similar results have been reported for microcells produced by prebiotic techniques containing light irradiated chromophores (Przybylski and Fox 1986), demonstrating that such effects are fundamental to the quantum architecture of lipid membranes (King 1990). Four groups of non-polypeptide neurotransmitters: acetyl-choline, catecholamines, serotonin and histamine are amines, the latter three being derived from amino acids tyrosine, tryptophan and histidine by decarboxylation. Two others are amino acids and thus also contain amine groups. Notably alamethicin also has glutamine amides located in the core of the pore (Fox & Richards 1982). The catecholamines are linked to indoles such as serotonin by a prebiotic pathway, fig 20(c).



Fig 20: (a) NAD structure permits linkage of other energies to a redox bifurcation. (b) H+ and etransport linked by H2 in membrane due to insolubility of e- and solubility of H+. (c) Prebiotic link between catecholamines and indole via quinone-type photoreduction. (d) Hypothetical form of primitive electron transport as a non-equilibrium limit cycle. (e) Acetyl-choline and phosphatidyl choline compared. Phosphatidyl choline lipid stacks tail to tail as shown in the clothes pegs (b).

(d) Electron Transport

The fact that the proton is soluble in water to form the hydrogen ion, but the electron is not, unless attached to another group such as a protein, causes a physical linkage to exist between the polarity bifurcation and the charge bifurcations associated with electron and proton transfer, fig 20(b) mediated by H transport through quinone reduction, (c). Despite the complexity of modern electron transport in photosynthesis and respiration, there is considerable evidence that membrane electrochemistry could have arisen before translation could produce coded enzymes. Firstly there is a consistent basis for the existence of many of the components of electron transport during the RNA era, since the nucleotide coenzymes NAD, FAD, a nucleotide-bound Mg & Fe-porphyrin ring similar to B₁₂, a cysteine-bound FeS group (Hall et. al. 1974), possibly based on glutathione (g-glutamyl-cysteinyl-glycine) and quinones provide all the key components of electron transport in an RNA dependent but protein-free form, fig 20(d) (King 1990). Both porphyrins and quinones have obvious prebiotic syntheses and the primal role of nucleotide coenzymes has already been discussed. Secondly, membrane structure and the solubility differences between the electron and proton guarantee a link between electron and hydrogen ion transport fundamental to quantum symmetry-breaking. Electron transfer does not require the complex coded active sites required to catalyse specific molecular transformations. Model systems using Feporphyrins and imidazole can couple oxidative electron transport to phosphorylation (Brinigar et. al. 1966) and photo activated Mg-porphyrin to phosphate link (Goncharova and Goldfelt 1990, Lozovaya et. al. 1990).



Fig 21: (a) Di-phosphorylation of sugars leads to glycolysis through interaction of charged phosphates. (b) Generic examples of group transfer in the tricarboxylic acid cycle.

(e) Glycolysis

Glycolysis forms a bridge between six and three carbon sugars, reversing the structural pathway from H2CO, glycoaldehyde and glycderaldehyde to cyclic sugars, fig 15(b). Glycolysis is made energetically possible by phosphorylation, and releases high energy phosphate capable of driving other phosphorylations (Hermes-Lima and Vieyra 1989), fig 21(a). It is notable that glycolytic diphosphorylation of fructose is homologous with the route for nucleotide formation of fig 16(c). The high phosphate environment leading to RNAs would then naturally lead to similar phosphorylation of other sugars, and release of the high-energy phosphate bond through cleavage of the sugar. Mineral catalysis associated with phosphate gives the glycolytic pathway a natural basis for lysis of sugars as a dissipative

structure. Biological UDP-glucose coupling is consistent with nucleotide-dependent glycolysis in the RNA era.

(f) The Tricarboxylic Acid Cycle

forms a pool of multiply carboxylated molecules which carry CO_2 in various states of energy, and result in reducing energy via nucleotide coenzymes NAD and FAD, which coupled with the use coenzyme A provide a basis for the tricarboxylic acid cycle in the RNA era. This could have existed as a limit cycle of di- and tri-carboxylated molecules acting both as an acceptor of acetate (a carbohydrate-equivalent i.e. (H₂CO)₂) and as an emitter of molecular CO₂ and reducing H, thus bifurcating carbohydrate level redox potential into reduced and oxidized components.

The linkage to nucleotide coenzymes such as NAD would have served to create a bifurcation of redox potential in the molecular milieu contributing to the diversity of reacting species. The cycle may have been hypercyclic (Eigen et. al. 1981) or chaotic, consisting of a population of molecules undergoing various generic transformations with net inflow of carboxylic acids and net emission of CO_2 and transfer of H, due to generic transformations as illustrated in fig 21(b). Isomerization would have been catalysed by Fe²⁺. Several steps may have been driven by sunlight photolysis (Waddell et. al. 1989).

The probability that the the central structures of molecular biology existed in the RNA era is consistent with their being chemical stability structures utilized by catalytic RNAs. The small genomes during the RNA era and limited catalytic capacity of RNAs by comparison with protein makes it likely that the emerging RNA-based system had to capitalize on existing chemical stability structures becase it lacked enzyme-based biosynthetic pathways. Genetic takeover also places these stability structures in a category determined by the cosmological milieu, thus giving evolutionary biology a cosmological foundation.



Fig 22: Modern stromatolites (left), structures built of cyanobacteria (blue-green algae) grace Shark Bay, Australia. J. William Schopf has found remnants of 3.6 billion-year-old stromatolites lying near fossils of 3.5 billion-year-old cells that resemble modern cyanobacteria, resembling strings of microscopic cells (right). Life thus arose within the first billion years of earth's formation from the planetary disc (Scientific American Feb 1991).

10. The Last Universal Common Ancestor

Recent research suggests that the last universal common ancestor (LUCA) of all life on the planet may have arisen from a phase interface between alkaline hydrogen-emitting undersea vents and the archaic acidified iron-rich ocean (Martin and Russel 2003), giving rise to an active iron-sulphur reaction phase still present in living cells and associated with electron transport and some of the most ancent proteins, such as ferredoxin, in which differential dynamics in membranous micropores in the vents managed to concentrate polypeptides and polynucleotides to biologically sustainable levels (Baaske et. al. 2007, Budin et. al. 2009), giving rise to the RNA era, while at the same time providing a free energy source based on proton transport across membranous microcellular interfaces resulting from fatty acids also being concentrated above their critical aggregate concentration.



Fig 1a: Proposed scheme for the universal common ancestor (Martin and Russel 2003)

The universal common ancestor of the <u>three domains of life</u> may have thus been a proton-pumping membranous interface from which archaea and bacteria emerged as free-living adaptions. This is suggested by fundemantal differences in their cell walls and other details of evolutionary relationships among some of the oldest genes.

- 1. <u>Biocosmology</u> An overview of how the origin of life may arise from cosmic symmetry-breaking.
- 2. <u>Chemist Shows How RNA Can Be the Starting Point for Life May 14, 2009 A pivotal article</u> showing how nucleotides can be synthesized from simple molecules.
- 3. <u>First Cells, Proton-Pumping and Undersea Rock Pores</u> (Lane 2009 with abstracts pdf password "model") Oct 19, 2009 A breakthrough in understanding how the first living cells could have been created at an undersea rock-pore interface.

It has also been proposed, on the basis of the highly-conserved commonality of transcription and translation proteins to all life, but the apparently independent emergence of distinct DNA replication enzymes in archaea/eucaryotes and eubacteria, that the last universal common ancestor had a mixed RNA-DNA metabolism based on reverse transcriptase, pinpointing it to the latter phases of the RNA era (Leipe et. al. 1999).



Fig 1b: Hypothetical branching and evolution of RNA and DNA replication machinery (<u>Leipe et. al.</u> 1999).

11. The Precocious Origins of Life on Earth

Far from being an improbable accident taking billions of years to find the right conditions, life appears to have become established on Earth as soon as the conditions permitted a liquid water ocean, suggesting either that Earth was richly bombarded with complex organic molecules which quickly found within the diversity of microclimates on Earth some which were directly conducive to the processes leading the to the genetic epoch, or that life's had already begun in the gas and dust cloud initially forming the solar system. Gustaf Arrhenius, (Mojzsis et. al.) studying tiny apatite grains in the Isua formation of Greenland, has found carbon 12 to 13 ratios consistent with the grains originating from living matter. The Isua rocks date from 3.85 billion years ago. Although indications from zircon crystals indicate a solid crust 4.2 billion years ago, no intact rocks have been discovered older than 3.96 billion years. The moon and probably the Earth likewise was heavily bombarded with meteors up to 3.8 billion years ago, suggesting that life evolved on earth as soon as environmental conditions allowed.

There is continuing debate about whether these chemical and 'fossil' traces, now further studied with Raman spectroscopy to give carbon isotope evidence, really represent early cyanobacterial life, prebiotic 'soup' or volcanic or meteorite material [Schopf et. al. 2002, Brazier et. al. 2002, Mojzsis 2002]. However some researchers contend on the basis of inorganic simulations that these microfossils are purely mineral [Hogan 2003]. Jacques Touret [2003] has found that methane as well as high salt water trapped in pillow lava from Isua suggesting the involvement of hydrothermal vents beside an undersea volcano. However these findings are questioned by David Vanko [Necht 2003]. John Parnell has also suggested radioactivity trapped in oily grains may have had a role [Lawton 2003]. In any case there is consensus agreement that life was under way by 3.5 billion years the age of the fossil stromatolite in fig 22, although the nature of these is also debated. These fossils could be the earliest evidence of life on Earth, yet these relics, with names like Chromoccoceae and Oscdlotorioceoe, are morphologically identical to modern cyanobacteria that cover the globe from Antarctica to the Sahara [Cohen 1996]. In July 2011 Brazier who had questioned the biological nature of the earliest fossils, himself claims to have discovered a genuine biological fossil of sulphur bacteria dating to 3.43 billion years.



a,b,e, Clusters of cells, some showing cell wall rupturing (arrows in a,b), folding or invagination (arrow in e). c,d,h, Chains of cells with cellular divisions (arrows). f., Cells attached to detrital quartz grains, exhibiting cell wall.

• Oldest fossils show early life was a beach August 2011 New Sceintist The oldest compelling fossil evidence for cellular life has been discovered on a 3.43-billion-yearold beach in western

Australia. Its grains of sand provided a home for cells that dined on sulphur in a largely oxygenfree world.

• <u>The First Breath</u> (pdf **password=''model''**) Ongoing debate about the first origins of life-driven oxidation

The origins of the first fossil life forms including the stromatolites in fig 23, likewise lie at the limits of the geological record. At 3.5 billion years old, fossilised bacteria are the earliest evidence of life on Earth, and yet these relics, with names like Chromoccoceae and Oscdlotorioceoe, are identical to the sophisticated modern cyano-bacteria that cover the globe from Antarctica to the Sahara (Let There be Life New Scientist 6 July 96).

The emergence of the eucaryotes that lead to the higher organisms is also almost as ancient as the geological record. Traces of oil extracted from Australian shale have pushed the date for the origin of complex cells back another half a billion years. Compounds in the oil suggest that eucaryotic cells, which make up all life on Earth except for bacteria, had evolved as early as 2.7 billion years ago. It is not until about 2.1 billion years ago that fossil imprints appear in the geological record that are so large that they can only be eucaryotes. A team of researchers in Australia has found steranes, molecules with 26 to 30 carbon atoms arranged in four rings, in droplets of oil extracted from rock 700 metres below the surface in the Pilbara region of north-western Australia. These are produced by the decay of cholesterol and other steroids found in the membranes of eukaryotes, but not bacteria (Brocks et. al.). Genetic analysis of the base of the tree of life indicates the oldest branches of both archaea and (eu)bacteria are thermophilic suggesting a period in hot pools or significant meteoric impact leaving only the thermophiles as survivors.

The Copernican principle asserts that the Earth is a typical rocky planet in a typical planetary system, located in an unexceptional region of a common barred-spiral galaxy, hence it is probable that the universe teems with complex life. This is supported to a reasonable extent by the discovery of an increasing number of planets including some putative "Goldilocks" zone planets where water would be liquid and life as we know it could potentially exist. Set against this, the <u>Rare Earth hypothesis</u> argues that the emergence of complex life requires a host of fortuitous circumstances including a galactic habitable zone, a central star and planetary system having the requisite character, the circumstellar habitable zone, the size of the planet, the advantage of a large satellite, conditions needed to assure the planet has a magnetosphere and plate tectonics, the chemistry of the lithosphere, atmosphere, and oceans, the role of "evolutionary pumps" such as massive glaciation and rare bolide impacts, and whatever led to the still mysterious Cambrian explosion of animal phyla. This might mean that planets able to support a bacterial level of life are not so uncommon, but those supporting complex multicellular life might be.

Bringing this question to a pivotal crux in our context, the emergence of mitochondria as endosymbionts has been proposed to be a critical bottleneck which allowed complex life to evolve only once, because, only in this effectively fractal cellular architecture, can the membrane surface areas necessary to support the chemical reactions enabling the vastly larger number of genes in a complex organism's genome to maintain metabolic stability (Lane and Martin *The energetics of genome complexity* 2010 doi:10.1038/nature09486). Whether such endo-symbiosis is rare. or a common extreme of parasitic relationships would then determine how likely or unlikely complex life might be.

Offset against both the uniqueness of the mitochondrial endo-symbiosis and the closely linked, but independent question of the origin of the nucleus and nuclear envelope, has been the <u>discovery</u> of <u>mimiviruses</u> and <u>mamaviruses</u> infecting amoeba (Raoult et, al. *The 1.2-Mb Genome Sequence of Mimivirus* doi: 10.1126/science.1101485) and related very large aquatic viruses such as <u>CroV</u> infecting single celled plankton species, which despite their recent discovery, appear from ocean gene analyses to be potentially ubiquitous and widespread in the oceans and possibly playing a crucial role in regulating the atmospheric-oceanic pathways, such as carbon sequestration (Fisher, Allen, Wilson and Suttle 2010 *Giant virus with a remarkable complement of genes infects marine zooplankton* PNAS doi: 10.1073/pnas.1007615107). These form an intermediate genetic position between viruses and cells, having the largest genomes, with extensive cellular machinery and larger than the smallest completely autonomous bacterial and archaeal genomes.

Mimiviruses also host parasitic virophages, affectionately named <u>sputnik</u> as viral satellites, which piggy back on the metabolism of the large viral factories set up by these giant viral genomes causing the mimiviruses to sicken, and these virophages also contains genes that are linked to viruses infecting each of the three domains of life Eukarya, Archaea and Bacteria (La Scola et. al. *The virophage as a unique parasite of the giant mimivirus* Nature doi:10.1038/nature07218). It has thus been suggested that they have a primary role in the establishment of cellular life and that they may have been instrumental in the emergence of the nuclear envelope.



Fig 23: A quadratic iteration compared with the interactive effects of inverse quadratic charge interaction. The fractal structures of tissues have features similar to the Mandelbrot set on changes of scale. The fractal effects reach from the molecular (a) in which individual proteins are illustrated embedded in the lipid membrane, through cell organelles (b) to the intercellular structure of whole organs as illustrated by skin (c). Such scale-dependent coherence of structure is possible only because of the highly non-linear nature of the electromagnetic force in quantum charge interactions of fermionic matter (Campbell).