

ILASOL 24th meeting – talks (updated 16/11/2010)

1. Design and Analysis of Synthetic Carbon Fixation Pathways

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Carbon fixation is the process by which carbon dioxide is incorporated into organic compounds. In modern agriculture where water, light and nutrients can be abundant, carbon fixation could become a significant growth limiting factor. Hence, increasing the fixation rate is of major importance in the road toward sustainability in food and energy production. There have been recent attempts to improve the rate and specificity of Rubisco, the carboxylating enzyme operating in the Calvin-Benson cycle; however, they have achieved only limited success. Nature employs several alternative carbon fixation pathways, which prompted us to ask whether more efficient novel synthetic cycles could be devised. Using the entire repertoire of ~5000 metabolic enzymes known to occur in nature, we computationally identified alternative carbon fixation pathways which combine existing metabolic building blocks from various organisms. We compared the natural and synthetic pathways based on physicochemical criteria that include kinetics, energetics and topology. Our study suggests that some of the proposed synthetic pathways could have significant quantitative advantages over their natural counterparts, such as the overall kinetic rate. One such cycle, which is predicted to be 2-3 times faster than the Calvin-Benson cycle, employs the most effective carboxylating enzyme, PEP carboxylase, utilizing the core of the naturally evolved C4 cycle. While implementing such alternative cycles presents daunting challenges related to expression levels, activity, stability, localization and regulation we believe that our findings suggest exciting avenues of exploration in the grand challenge of enhancing food and renewable fuel production via metabolic engineering and synthetic biology.

2. Synthetic Cellular Compartments on a Surface

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3. Riboswitches and Their Biological Function

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4. Maxwell's Demon: Implications for Evolution and Biogenesis

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Maxwell's paradox points out an apparent contradiction to the Second Law, by which entropy can be reduced without energy dispersal. The paradox has been resolved only in the 20th century, when it was shown that the Demon's feat requires information, the energetic cost of which fully accords with the Second Law. The relevance of this issue to evolution and biogenesis is evident. I discuss the degree to which real evolution is analogous to the ideal version of the Demon case, and derive some possible lessons for models of life's origin.

5. What is Life

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Following Delbruck's genes as "atomic associations" (Atomverbände), Schrodinger's oxymoron aperiodic crystal.

Watson & Crick uphold not only molecular biology's methodological reductionism but also the triumph of the reductionist conception of Life. The need for a top-down conception of life resurfaced from within the bottom-up molecular biological science.

Organization of matter and function is that which provided life its unique meaning.

Lamarck and Buffon pointed out that biological systems are physical systems constrained by their history.

The Cartesian approach of defining necessary and sufficient properties for life versus the Aristotelian approach of defining life as we experience it. Following Kant, Leibowitz, the

Believer-scientist, defined the phenomenon of life as belonging into the metaphysical sphere.

Darwinian Theory conceives life as the outcome of innumerable processes that evolved as sequences of (random) trials and (selective) errors over space and millennia.

Life depended on the evolution of a Program, a system of physico-chemical reactions that would allow the repeated reinvention of the system.

Bedau's model of life's characteristic hallmarks: the Program-Metabolism-Container (PMC) model. An Aristotelian definition of life as the one that survived the "struggle for existence."

Gardner's "Strange events permit themselves the luxury of occurring," considering the time span and the number of celestial bodies, "will undoubtedly occur, with no less and no more than its appropriate frequency, however surprised we may be that it should occur to us" (R. A. Fisher).

Ruma Falk: we always view events that occurred to us as more surprising than similar events that occurred to others.

6. The Importance of Being Translatable

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RNA splicing is a regulatory process by which eukaryotic pre-messenger RNAs, transcribed by RNA polymerase II, are cleaved and ligated to produce mature messenger RNAs suitable to function as templates for protein synthesis. The chemical transformations involved in RNA splicing occur within the supraspliceosome – a huge (21 mega Dalton) nuclear ribonucleoprotein complex. A substantial volume of studies have suggested that the spliceosome is an RNA-centric enzyme and that the splicing reactions are actually catalyzed by the spliceosomal uridine-rich small nuclear RNAs. Recent evidence from our group suggest a current functional role for the initiator tRNA in the regulation of alternative splicing, by helping establish an open reading frame that is recognized by the spliceosome. This new evidence implies a connection between tRNA, a molecule is considered to be one of the more ancient relics from the RNA world, and the splicing machinery. A connection at the borderline of the transition from an RNA

based world to the protein world - the maintenance of the correct open reading frame of the mature mRNA.

7. Everlasting Triplet Expansions: From the Origin of Triplet Code to Modern Genomes

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Analysis of occurrence of simple amino acid repeats in large ensemble of prokaryotic and eukaryotic sequences reveals that nearly all amino acids found in the repeats belong to those which have in their codon repertoires aggressively expanding triplets, all of three known pathologically expanding classes GCU (GCU, CUG, UGC, AGC, GCA, CAG), GCC (GCC, CCG, CGC, GGC, GCG, CGG) and AAG (AAG, AGA, GAA, CTT, TTC, TCT). This is observed especially clear in the first exons of proteins of higher eukaryotes. The data are interpreted as manifestation of everlasting triplet expansions, starting from the very origin of the triplet code. The spontaneous expansions continued to occur all the way during evolution, leaving their footprints in the protein-coding sequences as still visible simple amino acid repeats, as preferred triplets encoding the repeats, and as preferred codons in the codon usage tables. One way to look at it is constantly reemerging life that selfishly inflates the genomes, being subject of either elimination or mutational assimilation.

8. High Self-Catalysis Reduces Evolvability

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It is widely accepted that self-catalysis (SC), or self-replication, is required for a living (or living-like) entity to prevail in its environment, but just how potent SC should be and

what happens when it is too potent? This goes back to Eigen's hypercycle, which stressed the balance between self-replicating RNAs and catalyzing enzymes.

Using the GARD (graded autocatalytic replication domain) model for evolution of molecular assemblies, it is suggested that only a minimal level of SC is required for faithful assembly reproduction, and above minimal SC reduces the computational diversity of assemblies and an evolution-related score, in a buffered GARD micro environment.

9. Physical and Evolutionary Insights from Infection Cycles of Giant Viruses

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10. Simulation of Early Embryonal Development Dynamics

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In the history of theoretical biology Alexander Oparin provided a plausible theory for the advent of the first cell membrane in his discovery that lipids form a spherical bilayer. The Miller-Urey experiment demonstrated the synthesis of life chemicals from simple atmospheric components. While evolutionary biology provides plausible theories for the evolution of the fully developed forms which appeared suddenly in the Cambrian era, the origin of the phyletic bodyplans remains an unsolved mystery.

This paper presents a causative, graphically illustrated theory of the origin of the form of the vertebrate skeleton. It provides a demonstration to support the premise that the form of the vertebrate skeleton is encoded in the surface of the egg membrane rather than in the nucleus or the cytoplasm. The premise presumes an idealized hypothetical construction of the egg cell membrane as a spherical surface composed of rows and columns of lipid molecules which subdivide the surface into trapezoidal quadrilaterals formed by longitudinally segmented circumferential bands, the whole surmounted by polar caps. The paper demonstrates that the configuration of the skeleton and the shapes of the bones result as each of the quadrilateral segments fold, or roll up, axially during the

process of internally-directed gastrulation in mechanically predictable, epigenetic events. The process is presumed to be energized by the potential energy stored in the membrane as it is placed under tension by the internal inflation of the egg during oogenesis, and released in the recoil of the membrane upon puncture.

The plausibility of the premise is established by the observation that the structural form of the bones of the tetrapod rib cage and limbs consists of flat rectangular elements partially folded or rolled axially. As a corollary, the paper offers a demonstration in which forms representing the axial and appendicular skeletal bones, when unfolded and unrolled, can reconstitute a sphere.

The model presumes that the genes supply the materials of construction of the body in precise quantities at timed intervals, thus maintaining and occasionally changing the proportions of the otherwise immutable phyletic form over generations, without participating in its formative organization.

11. Chemical Evolution of RNA World: a Living Theory

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Eulogies of the Oparin-Urey-Miller approach to origin of life may be premature. If the details involving a strongly reducing atmosphere and electric excitation are replaced by a near neutral atmosphere, ultra-violet excitation, and an unknown local methane source, the OUMZ (Oparin-Urey-Miller-Zahnle) version is workable. Further modifications introduced here involving land based substrate instead of ocean soup, and newly found methane local sources, yield RNA world with automatic pentose sugar component. The entire process yields plausible enthalpic thermodynamics.

12. Modeling Catalytic Networks: Relevance to the Origin of Life

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Catalytic reaction networks, consisting of synthetic molecular arrays interconnected by autocatalytic and cross catalytic pathways among reactants and templates, are studied in order to unravel complex systems behavior and model scenarios related to the origin of life and early molecular evolution [1]. Here we show several examples of such modeling. Using theoretical studies and simulations, we can use such networks to design several emergent phenomena, including molecular logic gates, arithmetic units and network motifs [2]. Then, by analyzing the symmetry constraints of such networks, we show how higher catalytic order is required for their construction, suggesting that early molecular evolution proceeded via higher order reactions [3]. By applying the concept of catalytic networks to the quasispecies model, we show how second order systems lead to discontinuous phase transitions – unlike standard first order quasispecies that yield continuous transitions – a result with potential implications for understanding RNA virus evolution [4]. Furthermore, in a kinetic analysis and simulation of two competing replicators, one non-metabolic and the other metabolic, we've demonstrated how metabolism may emerge in resource-poor environments [5].

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13. Extraterrestrial Intelligence? The Fermi Paradox in the SETI Era

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