**Israel Society for Astrobiology and the Study of the Origin of Life (ILASOL) 26th meeting**

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<http://www.ilasol.org.il>

1. **The origins of protein divergence and the expansion of sequence space**

Alon Wellner

Department of Biological Chemistry, Weizmann Institute of Science, Rehovot 76100, Israel

Alon.Wellner@weizmann.ac.il

When a protein’s function, structure and sequence are conserved throughout all life kingdoms, it can be traced back to the last universal common ancestor (LUCA). By definition, the evolution of such proteins is very slow. Other proteins have diverged from LUCA beyond recognition, and cannot be assigned as orthologs. What restricts the evolutionary rate of LUCA proteins? In our study we focus on an ancient divergence event that occurred within phosphoglycerate kinase (PGK), an essential and ubiquitous glycolytic enzyme. We exchanged lysine 219, a conserved and essential active-site residue in human phosphoglycerate kinase (PGK), to serine which is found only in archaeal PGKs. This exchange, and the reciprocal Ser219Lys exchange in an archaeal PGK, resulted in loss of function. Iterative rounds of mutagenesis and selection led to a gradual gain of function with 219Ser that traded-off with the 219Lys activity. These findings demonstrate how such exchanges are restricted by complex networks of epistatic interactions that shape the rugged fitness landscape proteins have to navigate as they evolve. Nevertheless, our study predicts that any residue, even the most conserved ones will eventually change, given the appropriate sequence composition.

1. **How frequent are biotic worlds?**

Amri Wandel

HUJI

amri@huji.ac.il

After two years of Kepler data we know a lot more on the frequency of small planets, in particular that terrestrial-size planets are quite common, and many of them may reside within the Habitable Zone of their sun. With this input one may estimate the space density of biotic worlds, which may be much larger than thought earlier. Such estimates are nevertheless subject to the unknown prior of the evolution of life one an Earthlike planet.

1. **Where does calcium come from? the hellium supernova connection**

Avishay Gal-Yam

WIS

Avishay.Gal-yam@weizmann.ac.il

1. **GARD realities: true lipids, open-endedness and ecology**

Doron Lancet

Department of Molecular Genetics, Weizmann Institute of Science

Doron.lancet@weizmann.ac.il

1. **Possible role for proteins in the origin of life**

Gonen Ashkenasy

BGU

gonenash@bgu.ac.il

1. **Is metaphysics a four-letter word and why is this relevant to origin-of-life researchers?**

Iris Fry

Dept. of Humanities and Arts, Technion

fryiris@gmail.com

Science is not neutral metaphysically. Its empirical and theoretical core presupposes a natural reality in which processes and events are caused naturally, are not divinely designed and do not serve divine purposes. This metaphysical view cannot be proved or disproved. In this sense it is comparable to a theistic metaphysics. Yet, the claim that naturalism and theism are of the same status and that the theory of evolution and creationism are both "a religion" is wrong. Unlike theistic metaphysics, naturalism is a metaphysical view that developed historically on the basis of the empirical and theoretical achievements of science. There is an intricate feedback loop among scientific research, its accumulating results and the underlying, guiding assumptions of this research. The scientific status of the study of the origin of life and its persistent search after a solution of the problem cannot be explained without taking into account also the metaphysical aspect of science.

1. **The transition from photosynthesis to chemosynthesis in natural environments: how an energetic supercharge transforms biology**

Jason Raymond

Arizona State University

jason.raymond@asu.edu

Our research studies 1. the evolution of life (and metabolism) and 2. the interplay between life and environment in complex, natural ecosystems. These two interests merge in hydrothermal ecosystems where the upper temperature limit for photosynthesis is exceeded. Though physical and geochemical factors can shift the actual temperature at which this temperature limit – and concomitant transition from chemotrophy to phototrophy – occurs, one constant is that this transition underpins an utter transition in biological complexity.
This presentation will focus on our recent discoveries in modern environments that are shaping how we think the evolution of photosynthesis supercharged ancient life and heralded a new era in biological evolution.

1. **The "Rare Earth" hypothesis revisited**

Joseph Gale

Inst. Life Sciences, HU

gale.joe@mail.huji.ac.il

Some 15 years ago Ward and Brownlee published their Rare Earth hypothesis, which argued that it is extremely unlikely that complex, certainly intelligent life exists elsewhere in the Universe.
A better appreciation of the sheer size of the universe, a number of errors in Ward and Brownlee's assumptions, and the discovery of planets, including those with calculated surface temperatures which could support liquid water, around some 15% of all stars, appear to counter their conclusions. However, the extremely demanding requirements of complex life as we know it still make their claim basically sound. Moreover, without an unexpected breakthrough in physics, the vast distance from Earth to the nearest stars, the slow speed of light (or any radiation) and the short human lifespan together make it extremely unlikely that we could communicate with any intelligent beings which may be found.

1. **Traces of primordial eukaryotic mechanisms: the regulatory roles of the minor spliceosome**

Liran Carmel

Department of Genetics, The Institute of Life Sciences, The Hebrew University of Jerusalem

liran.carmel@carmelab.com

DNA of eukaryotic life forms harbors fragmented genes, whereby coding segments – the exons – are separated by noncoding ones – the introns. Upon transcription, the introns are excised and the exons are joined together by a cellular machine known as the spliceosome. The spliceosome is among the most complex cellular machines, comprising small RNA molecules and, in human, over 150 proteins. Given the apparent cellular cost of maintaining this huge machine, the evolutionary path that led to its development has remained obscure. Even more surprisingly, a small subset of introns is excised by another cellular machine, called the minor spliceosome. It is probably as ancient as the major spliceosome, but there is evidence for a gradual decline in its usage. One would expect a complete loss of this machine, but recent findings show that the position of the minor introns is generally more conserved than that of the major type, suggesting some evolutionary pressure to preserve the minor spliceosome. Based on molecular evidence, we hypothesize that minor introns lead to decrease in the expression level of their host genes, possibly due to slower splicing reaction. Indeed, analysis of microarray data in human show that genes that harbor minor introns have a significantly lower expression level.

1. **A vestige of a prebiotic bonding entity is functioning within the contemporary ribosome**

Miri Krupkin

Department of Structural Biology, Weizmann Institute of Science

Miri.Krupkin@weizmann.ac.il

A universal semi-symmetrical region identified within all contemporary ribosomes is suggested to originate from an entity that we named the “proto-ribosome”. The proto-ribosome is a prebiotic pocket-like entity capable to accommodate substrates whose stereochemistry enables the creation of peptide bonds. This proto-ribosome could have evolved from an earlier catalytic entity we named the “pre-proto-ribosome”. This pre-proto-ribosome was a molecular machine capable of performing essential tasks in the RNA world, which was later snatched by the amino acids invaders for producing proteins.

1. **Looking for Life elsewhere: Review of the Present and Future Life-related Space Missions**

Oded Avraham

School of Education Tel-Aviv University Te-Aviv

odedavr1@post.tau.ac.il

The search for life and life-supporting environments in the solar system is vital for understanding the origin of life. Current Life-Related missions are reviewed, as well as future mission designs and future mission concepts as they are mirrored in official budget reports, decadal surveys, and personal interviews with researchers. Emphasis is made on the necessity of each mission, chances of success, repercussions of discovery, and its role in public engagement with respect to science education.

1. **Evolutionary dynamics of RNA replicator systems at high mutation rates**

Paulien Hogeweg

Bioinformatics group, Utrecht University, the Netherlands

P.Hogeweg@uu.nl

We study how RNA-like replicators cope with high mutation rates. We discuss evolution of the genotype-phenotype mapping, and the resulting shape of the quasispecies, and eco-evolutionary interaction structure, and spatio-temporal patterns. We show that the spatial patterns act as higher level Darwinian entities, which determine the evolutionary dynamics of the replicators. We show that an RNA world of self-catalysing RNA replicators can evolve
into a DNA-RNA world where RNA catalyses DNA replication and transcription, as well as RNA replication, whereas reversed transcription is minimal. The ensuing division of labor, DNA for information storage, RNA for catalysis, evolves despite the longer (and therefore slower) replication cycle. This is because it prevents evolutionary deteorating towards minimal catalysis.
We conclude that not only short term functional properties but also the evolutionary properties of evolving entities determine the outcome of evolution.

1. **From cyanide and water to RNA sensors of stress in human cytokine genes**

Raymond Keampfer

Department of Biochemistry and Molecular Biology, Institute of Medical Research Israel-Canada, The Hebrew University-Hadassah Medical School, Jerusalem, 91120 Israel

kaempfer@hebrew.edu

Cyanide and water will condense readily to formamide which can serve as the basis for all compounds needed to create RNA spontaneously, argue Saladino et al. (2012). The plasticity of RNA is illustrated not only by its catalytic properties and its ability to sense small molecules. RNA can serve also as an active sensor of stress signaling, as exemplified by RNA elements within the human genes encoding tumor necrosis factor and interferon-gamma, inflammatory cytokines key to our survival. These short RNA structures fold into pseudoknots that activate the RNA-dependent protein kinase PKR central to the integrated cellular stress response, and control thereby splicing of tumor of necrosis factor mRNA and translation of interferon-gamma mRNA. Regulatory and template functions of RNA in modern organisms lend strong support to a scenario of kick-starting life through RNA.

1. **Cell-free protein synthesis and assembly on a biochip**

Roy Bar-Ziv

WIS

roy.bar-ziv@weizmann.ac.il

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