Program for ILASOL 2006

January 4th 2007 at the Weizmann Institute of Science, Botnar Auditorium (Belfer Building).

9:00-9:05 Doron Lancet (WIS) Opening Remarks

Session 1 - Evolution

9:05-9:35 Eva Jablonka (TAU) **Epigenetic inheritance in early evolution**.

9:35-9:55 Emmanuel Tannenbaum (BGU) **Selective advantage for sexual reproduction.**

9:55-10:15 Irit Davidson (Kimron Veterinary Institute) **Generation of diversity in viruses due to molecular recombination between animal viruses and between plant and animal viruses: lessons to be learned from the avian world.**

Session 2 – Plenary

10:30-11:30 Eörs Szathmáry (Collegium Budapest) **Metabolists, Geneticists, Compartmentalists, Unite!!!**

Session 3: Astrobiology

11:30-12:10 Akiva Bar-Nun (TAU) **a. How good is our understanding of comets. b. Titan's Chemistry**.

12:10 -12:35 Joe Gale (HUJI) **Problems of teaching multidisciplinary Astrobiology**.

12:35 -13:00 Iris Fry (Technion) **Stanley Miller's life and work - Reflections on the state of a scientific discipline.**

Session 4: Early Genes

14:00-14:25 Ohad Carny (TAU) **Molecular co-evolution and the emergence of LUCA.**

14:25- 14:50 Idan Gabdank (BGU) **Duplex nature of the earliest mini-genes.**

Session 5: Thermodynamics

14:50 -15:10 Avshalom Elitzur and Goren Gordon (WIS) **The Ski-Lift: A Ubiquitous Biological Pathway between Thermodynamic States.**

15:10 - 15:30 Ora Kedem (BGU,WIS) **Primordial active transport.**

15:30 - 15:45 **Discussion on thermodynamic principles**.

15:45 - 16:00 Oleg Kupervasser (Technion) **What is life?**

Session 5: Lipid World

16:15-16:35 Tony Futerman (WIS) **The Lipid World model for the origin of life: Sticky questions about sticky problems.**

16:35-16:50 Barak Shenhav, Aia Oz and Doron Lancet (WIS) **Lipid World – Responses and discussion.**

Session 6: Closing

16:50-17:20 Malcolm E. Schrader (HUJI) **Evolution and the Bible: The Non-Traditional Approach.**

Epigenetic inheritance in early evolution.

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I start my lecture from a consideration of Gánti's chemoton model, which is a model of a minimal biological system comprised of several different autocatalytic systems. I argue that non-nucleic acid inheritance systems were not only an important part of early living organisms, but that such systems constrained and guided nucleic acid-based evolution. Moreover, the evolution of the different inheritance systems was crucial for early evolutionary transitions.

Selective advantage for sexual reproduction.

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This talk develops a simplified model for sexual reproduction within the quasispecies formalism. The model assumes a diploid genome consisting of two chromosomes, where the fitness is determined by the number of chromosomes that are identical to a given master sequence. We also assume that there is a cost to sexual reproduction, given by a characteristic time tau_*seek* during which haploid cells seek out a mate with which to recombine. If the mating strategy is such that only viable haploids can mate, then when tau_*seek*=0, it is possible to show that sexual reproduction will always out compete asexual reproduction. However, as tau_*seek* increases, sexual reproduction only becomes advantageous at progressively higher mutation rates. Once the time cost for sex reaches a critical threshold, the selective advantage for sexual reproduction disappears entirely. The results of this paper suggest that sexual reproduction is not advantageous in small populations per se, but rather in populations with low replication rates. In this regime, the cost for sex is sufficiently low that the selective advantage obtained through recombination leads to the dominance of the strategy. In fact, at a given replication rate and for a fixed environment volume, sexual reproduction is selected for in high populations because of the reduced time spent finding a reproductive partner.

Creation of diversity in the animal virus world by inter-species and intra-species recombination: lessons learned from poultry viruses

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Both humans and animals harbor infections caused by DNA (herpes and pox) and retroviruses. The two virus types can infect the same organism and the same cell. As the initial retrovirus requirement for replication is integration into dsDNA following by reverse transcription, it can integrate into the cellular or the viral genomes. That molecular recombination can cause the DNA virus to alter its biology (tropism, spread, virulence, antigenicity) and to impact virus evolution.

Chickens have a distinct advantage for study of virus diversity, because they are the natural host, therefore the study reflects real natural and not artifactual events and because multiple infections can be reproduced experimentally.

First example for creation of viral diversity through molecular recombinations between two virus families are the five avian oncogenic viruses, that belong to both herpes and retroviruses, and are economically important in veterinary virology. We analysed naturally-acquired mixed infection, experimentally infected chickens and embryonated eggs.

The second example of recombination between two virus families in poultry is the fowlpox virus (FPV), which contains various inserts of the retrovirus, reticuloendotheliosis virus (REV), for which we studied the collection of Israeli isolates from commercial flocks.

The third example is the Circoviruses, whose virus origin represent an unusual transfer from plants to vertebrates; A plant virus belonging to the nanovirus family recombined probably with a vertebrate-infecting virus, a calicivirus, which is a RNA virus and a step of reverse transcription facilitated by a retrovirus or a retrotransposon must have contributed a reverse transcriptase for the recombination to take place. Circoviruses are circular single-stranded small DNA viruses with host specificity for bacteria, animals, humans and plants. The poultry Circovirus, chicken infectious anemia virus (CIAV) is being studied by us, since its effects are both symptomatic or asymptomatic, causing immunosuppression. The significance of circoviruses in many animals, including humans, is mostly under-estimated and veiled, and more studies are needed. However, the mechanism of diversity creation of viruses, as exemplified by the three examples of avian viruses, might contribute to the variety of life on earth.

METABOLISTS, GENETICISTS, COMPARTMENTALISTS, UNITE!!

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I shall give my perspective on the origin of life research. In my view structural studies must be complemented by dynamical ones, and a systems chemical approach is inevitable. I shall discuss the main difficulties in the (re)construction of various (infra) biological chemical systems, and shall attempt to outline some tasks for the future.

How good is our understanding of Titan's atmosphere and comets

Akiva Bar-Nun, with Diana Laufer, Gila Notesco, Ronen Jacovi and Igal Pat-El (TAU)
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Titan's atmospheric chemistry was suggested to be similar to that of Earth's primitive atmosphere. Apparently it is not. Moreover, the lack of liquid water on Titan prevents further chemical evolution. We shall describe the very nice agreement between our experimental findings on Titan's atmospheric chemistry and the finding of the Cassini and Huygens spacecraft on Titan.

Comets are considered as major contributions of water and organics to Earth's primitive oceans and atmosphere, during the late heavy bombardment period, ending ~3.8×10^9 y ago, hence their extensive studies. We shall describe the very nice agreement between our experimental findings and the findings of the Stardust and Deep-Impact space missions.

A brief account will be given to the new analyses of the Stardust materials brought back to Earth.

A few words will be added on liquid water on Mars up to ~3.8×10^9 y ago.

Problems of Teaching Multidisciplinary Astrobiology

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Astrobiology employs many disciplines, including Astronomy, Earth Sciences and Biology. If taught by a number of specialist lecturers the professional level tends to be high, but the resulting course is often disjointed and lacking of a central theme.

At the H.U. we have developed an elective, third year workshop which addresses the above and attracts a steady number (15-30) of participants. There is one leader/lecturer and some 4-5 invited specialist speakers. However, most of the work centers on student papers, prepared in writing and as oral presentations. The latter take the form of workshop discussions, based on the papers. The papers are first edited by the lecturer at private tutorial sessions and are then distributed, ahead of the class discussion.

Students come mainly from Biology and Earth Sciences, but also from Astronomy and Physics, with occasional M.D. or Teaching Studies majors. The present course centers on just one aspect of Astrobiology: the "Astrobiology of Planet Earth".

The organization and main themes of the workshop will be described.

Stanley Miller's Life and Work – Reflections on the State of a Scientific Discipline

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Miller's personal and scientific biography, from his memorable experiments with Urey at the University of Chicago in the early 1950s until this very day, can be conceived as a reflection of the development of the scientific field devoted to origin-of-life research.

The significance of Miller's achievement in the 1950s has to be evaluated in its historical context. His contributions during the last decades have to be examined as part of the major controversies characterizing the field. Appreciation of these controversies, and Miller's active role in them, can be gained by taking into account the various facets of the scientific enterprise - empirical, theoretical, philosophical, political and personal. Trying to understand these aspects could help in answering the basic questions raised by both friends and foes of science: Is the as-yet lack of solution to the origin-of-life problem a cause for despair? Does it reflect on the scientific status of origin-of-life research?

Molecular co-evolution and the emergence of LUCA

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One of the basic questions regarding the development of the last universal common ancestor (LUCA) is how did biological organization evolve from an abiotic supply of small organic molecules? The most prevalent paradigm, regarding the primordial soup, points at RNA molecules as chief candidates for the development of a self-replicating system. However, this ‘RNA world’ hypothesis suffers from a main Achilles heel – the instability of the RNA molecules in the primordial earth conditions.

It was recently demonstrated by our group that peptide molecules as simple as dipeptides can self-assemble into well-ordered tubular, fibrilar, and closed-cage structures. In addition, we have confirmed the ability of such assemblies to bind nucleotide bases. In light of these examples, regarding the self-assembly propensity of short peptides and their ability to bind and recognize RNA, we examine the possible role of self-assembled peptide structures in RNA stabilization and early chemical catalysis. These features lay the grounds for molecular co-evolution of short peptide and RNA sequences in the emergence of LUCA.

Duplex nature of the earliest mini-genes.

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Reconstruction of the evolutionary history of the triplet code on the basis of amino acid chronology [1], suggests that the earliest mRNAs existed in the form of duplexes encoding the proteins in both strands. This has been recently confirmed by tracing the earliest hairpins of mRNA [2]. The "complementary" heptapeptides corresponding to the hairpins, expressed in binary alphabet of *A*, amino acids encoded by pyrimidine-central codons, and *G*, amino acids encoded by purine-central codons, have been found in modern proteins in nearly equal amounts. Such an alphabet is chosen in correspondence with the observed universal conservation of the central purines and central pyrimidines of the codons, as it follows from the amino acid substitution matrices [2]. Thus, at least the "hairpin" peptides appear to have been encoded in the duplexes. Analysis of all 128 binary heptapeptides shows the same complementary parity in corresponding scores for complete proteomes of 13 phylogenetically diverse prokaryotes. This demonstrates, that the hypothesized duplex coding at the beginning of Life can be still detected in modern sequences, due to conservation of the middle bases of the codons.

[1] Trifonov E.N. The triplet code from first principles. *J Biomol Str Dyn*, Vol. 22, pp. 1-11, 2004.
[2] Gabdank I., Barash D., Trifonov E.N. Tracing ancient mRNA hairpins. *J Biomol Str Dyn*, Vol. 24, pp. 163-170, 2006.

The Ski-Lift: An Ubiquitous Biological Pathway between Thermodynamic States

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"The Ski-Lift: A Ubiquitous Biological Pathway between Thermodynamic States" A.C. Elitzur & G. Gordon Whereas the transitions between low- and high-entropy states have been thoroughly studied in thermodynamics, no attention has been given to transitions between states that differ widely with respect to their microstates yet have nearly the same entropy. Another neglected passage is the one from high entropy to a state whose entropy is lower, namely, a complex state, yet not the lowest. We study both transitions, using exact analytical expressions, and ask what is the most efficient path for them. Surprisingly, the best path turns out to be a "zigzag," going first to a very high-order state first and then "gliding" down the entropy scale to the desired state. We then show that this is the path taken by organisms when facing the need for transitions of the above two kinds. We give a mathematical proof for the efficiency of this path and point out several examples, both quantitative and qualitative, in which life takes it.

Energetics of Active Transport

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A simple model for the accumulation of one type of molecules, S, in a liposome is described. The first step in the process of accumulation is the binding of S to a photo-activated species, and its transfer to a group on the surface of the liposome. From there, A is transferred into the liposome spontaneously until a certain limiting concentration is reached.
The affinity of the binding reaction is the source of free energy for the accumulation. It is shown that the maximal "uphill" flow, the increased chemical potential of S, is determined by the affinity of the binding reaction. Active transport, accumulation driven by chemical reaction, is an energy converter, a kind of machine.
The thermodynamic efficiency of a machine is defined by the ratio between output and input of free energy. The general factors limiting efficiency and the efficiency of modern active transport will be discussed.
Conclusion: accumulation of a given species can take place with lipids and simple molecules. The complex molecules by which modern active transport is carried out, are essential for high thermodynamic efficiency of the process.

The Lipid World model for the origin of life: Sticky questions about sticky problems.

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The first cell is believed to be composed of a single vesicle that partitions components and avoids dilution within the primordial sea; such closed membranes are proposed to be essential for the first self-reproducing cell to arise [see Koch and Silver, Adv. Microb. Physiol. 2005;50:227-59]. However, little attention has been paid to the origin of the lipids that would be essential components of the vesicle membrane. In this discussion, I will suggest that our current understanding of prebiotic chemistry, together with the complexity of lipid biochemistry, does not provide an adequate explanation for lipid evolution *per se*, or for the role that lipids might have played in the formation of the prebiotic cell.

Evolution and the Bible: The Non-Traditional Approach.

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It is shown that the historical origin of the idea of biological evolution occurs in the Bible in the first account of “creation” in the first chapter of Genesis. The second account, found in the second chapter, which is the legend of Adam and Eve in the Garden of Eden, is not evolutionary. The “objectively” estimated date of the first account is given as roughly 700 BCE on the basis of strong arguments by Y. Kaufmann, in *The Religion of Israel, From its Beginnings to the Babylonian Exile* (Moshe Greenberg, 1960). Previous “objective” estimates assigned the date of approximately 400 BCE. Historians of evolution have often credited the Greek philosopher Empedocles (495-435 BCE) with first proposing the idea of evolution. There is little substance behind this claim however, either in terms of the date proposed or its content. Empedocles makes no suggestion of the appearance of a succession of real biological forms starting from the simple and proceeding to the complex.