BP 49: Physics of the Genesis of Life - Focus Session organized by Moritz Kreysing and Dieter Braun

Time: Thursday 9:30–13:00 Location: SCH A251

Invited Talk BP 49.1 Thu 9:30 SCH A251

The Origin of Cellular Life — •Jack W Szostak — Dept. of Molecular Biology, Massachusetts General Hospital, Boston, MA 02115 USA

The earliest living cells must have had very simple structures in order to emerge spontaneously from the chemistry and physics of the early earth. We are attempting to synthesize such simple artificial cells in order to discover plausible pathways for the transition from chemistry to biology. Very primitive cells may have consisted of a self-replicating nucleic acid genome, encapsulated by a self-replicating cell membrane. We have described robust pathways for the coupled growth and division of primitive cell membranes composed of fatty acids, which were likely to have been available prebiotically. However, no process for the replication of a nucleic acid genome, independent of evolved enzymatic machinery, has yet been described. I will discuss our recent progress towards the realization of an efficient and accurate system for the chemical replication of RNA. I will also discuss physical constraints on the replication of RNA, and the implications of these constraints for efforts to deduce potential environments that could have nurtured the beginnings of life.

BP 49.2 Thu 10:00 SCH A251

Exploring the emergence of function in microfluidic droplets — •Rebecca Turk MacLeod[1], Andrew Griffiths[2], and Leroy Cronin[1] — [1]University of Glasgow, Glasgow, UK — [2]ESPCI, Paris, France

Metabolism-first theories on the origin of life suggest that there may have been prebiotic systems capable of propagation and Darwinian evolution that were not dependent on nucleotide-based replication. We are testing this idea by observing proposed prebiotic reactions compartmentalized in protocell analogues. Using microfluidics, we generate water-in-oil emulsions that contain prebiotic reactants and/or products, and subsequently observe the behavior of the droplets as a function of their chemistry. Compartmentalized carbohydrate products of the formose reaction affect the osmotic pressure of the droplets, thus driving the droplets to grow at the expense of formaldehyde-containing neighbors. Furthermore, a minority population of efficient formose reaction droplets (those with rates enhanced by reaction products) grow at the expense of less-efficient formose droplets.

This phenomenon of growth correlated with chemical complexity may present a means of selection for metabolizing protocells. Accordingly, we are utilizing the automated chemo-robotic tools developed by the Cronin lab to test the progress and evolution of other prebiotic chemistries compartmentalized in water-in-oil emulsions.

BP 49.3 Thu 10:15 SCH A251

Robustness in supramolecular assemblies far-from-equilbrium — •Job Boekhoven, Marta Tena-Solsona, Benedikt Riess, and Raphael Grötsch — TUM, Chemistry Department, Garching, Germany

We will describe supramolecular assemblies that can only exist far-from-equilibrium driven by a chemical reaction network. As a result of their dissipative nature these assemblies are intrinsically unstable and can only be sustained by constant consumption of energy. We found that these assemblies can exert feedback on the reaction network that drives their own formation or degradation. This feedback can increase the robustness of the assemblies, and thus increase the survival time of the structures, compared to assemblies without this feedback. With this minimalist approach, we aim to study how typically life-like features, like robustness, oscillatory behavior and self-replication can emerge from simple, non-biological components.

BP 49.4 Thu 10:30 SCH A251

Could dividing active droplets provide a model for protocells? — •Rabea Seyboldt[1], David Zwicker[1,2], Christoph A. Weber[1,2], Anthony A. Hyman[3], and Frank Jülicher[1] — [1]Max Planck Institute for the Physics of Complex Systems, 01187 Dresden, Germany — [2]School of Engineering and Applied Sciences, Harvard University, Cambridge, MA 02138, USA — [3]Max Planck Institute of Molecular Cell Biology and Genetics, 01307 Dresden, Germany

Macromolecular aggregation and phase separation into droplets has been proposed as a mechanism to organize chemical reactions that could have been a key precursors at the origins of the first living cells. However, it remains unclear how early protocells could have proliferated and divided. Deformed droplets usually relax towards a spherical shape and do not easily divide. Our theoretical study shows that in the presence of chemical reactions that produce droplet material, a chemically active droplet may undergo a shape instability and subsequently divide into two daughter droplets, which may then grow and divide again. We also find that when considering the effects of hydrodynamics which tend to stabilize spherical droplets, the shape instability can still occur for sufficiently small droplets. Our work suggests that chemically active droplets that divide and propagate could serve as a model for prebiotic protocells.

BP 49.5 Thu 10:45 SCH A251

Thermally driven DNA phase transitions and protein expression — •Christof B. Mast[1], Mara L. Heinlein[1], Matthias Morasch[1], Noel Yeh Martin[2], Sheref Mansy[2], Hannes Mutschler[3], and Dieter Braun[1] — [1]LMU Munich, Amalienstrasse 54, 80799 München, Germany — [2]University of Trento, Via Sommarive 9, 38123 Povo TN, Italy — [3]Max Planck Institute of Biochemistry, Am Klopferspitz 18, 82152 Martinsried, Germany

Energy fluxes are the driving forces that push complex systems out of equilibrium into the living state. While modern organisms predominantly use chemical energy fluxes, we argue that the fundamental flux of heat energy across water filled pores was essential to jump start life four billion years ago: A thermal gradient drives thermal fluid convection and thermophoresis of bio-molecules, resulting in their massive and length selective accumulation. We demonstrate that this process is also selective for sequence and chirality which is essential for the emergence of the first functional, homochiral polymers. Starting from nanomolar concentrations of short and unbound single stranded DNA with a length of 36 bases, thermal trapping cooperatively increases their local concentration and length by hybridization, ultimately leading to the formation of a DNA hydrogel. Single mutations in sequence as well as strands of different chirality are spatially separated and therefore locally amplified during the hydrogel phase transition. We also show that thermal traps are compatible and enhance cell free protein expression, possibly mimicking a later stage during the origin of life.

15 min break

BP 49.6 Thu 11:15 SCH A251

Eutectic phase of water-ice as medium for the early RNA world — •Hannes Mutschler[1] and Phil Holliger[2] — [1]Max Planck Institute for Biochemistry, Martinsried, Germany — [2]MRC Laboratory of Molecular Biology, Cambridge, UK

There is strong evidence for a primordial biology, in which RNA was the central biomolecule responsible information storage and catalysis. One of the key questions of this "RNA world" hypothesis is: Which environment might have been sufficiently benign to allow formation and evolution of inherently instable RNA molecules creating ever more complex catalysts including self-replicating ribozymes? We investigate the crowding environment of the eutectic phase of water-ice as a potential medium hosting the early RNA world. We found that eutectic conditions allow derivatives of primitive, naturally occurring ribozymes to efficiently catalyse entropically disfavoured RNA polymerisation and ligation reactions using only very weakly activated but credible building blocks as substrate. We also find that cyclic freeze-thaw cycling is a potent driver of RNA assembly and critical to unlocking the full functional potential of short RNA ligase modules through an unanticipated RNA chaperone effect.

BP 49.7 Thu 11:30 SCH A251

Temperature gradients assemble RNA rich protocells — •Juan M. Iglesias Artola and Moritz Kreysing — Max Planck Institute of Cell Biology and Genetics, Dresden, Germany

We now know that the several components of life (i.e. peptides, nucleic acids and lipids) were plausibly available at an early stage of Earth's

history [1]. However, concentration and selection of these biomolecules still eludes a fulfilling answer. In general, how could scarce functional biomolecules find each other in order to build in complexity? Temperature gradients as available at hydrothermal vent pores, and elsewhere, have already been shown to be a suitable setting to address these questions. These environments have previously been shown to accumulate nucleic acids and exert a selective pressure on sequence length, promoting molecular complexity [2]. Here we show that by using such an out of equilibrium environment we are able to form protocells from a dilute solution of peptides and functional RNA, and that these micro-droplets are able to sustain RNA enzymatic activity. The observation that these temperature gradients also enhance micro-droplet formation opens a new set of possibilities. Within protocells even higher concentrations are possible, as known to be important for ribozyme activity. Moreover, these liquid micro-droplets could be the basis for competitive growth and selection at the protocellular level.

[1]. PB. H. Patel, et al. Nat. Chem 7, (2015) [2] M. Kreysing, et al. Nat. Chem 7, 203 (2015) [3] T. Z. Jia, et al. Nat. Chem 8, 915 (2016)

BP 49.8 Thu 11:45 SCH A251

ATP as a Biological Hydrotrope — •Avinash Patel[1], Liliana Malinovska[1], Simon Alberti[1], Yamuna Krishnan[2], and Anthony A Hyman[1] — [1]Max Planck Institute of Molecular Cell Biology and Genetics, 01307 Dresden, Germany — [2]Department of Chemistry and Grossman Institute for Neuroscience, Quantitative Biology and Human Behavior, University of Chicago, Illinois-60637

Hydrotropes are small molecules that solubilize hydrophobic molecules in aqueous solutions. Typically, hydrotropes are amphiphilic molecules and differ from classical surfactants in that they have low cooperativity of aggregation and work at molar concentrations. We discovered that ATP has properties of a biological hydrotrope. It can both prevent the formation of and dissolve previously formed protein aggregates. This chemical property is manifested at physiological concentrations between 5 to 10 milimolar. Therefore, in addition to being an energy source for biological reactions, for which micromolar concentrations are sufficient, we propose milimolar concentrations of ATP may act as a biological hydrotrope, preventing proteins from aggregating. This may in part explain why ATP is maintained in such high concentrations in cells. During origin of life, we hypothesize the role of ATP as a biological hydrotrope might have been an advantage for its selection by enzymes as an energy source.

BP 49.9 Thu 12:00 SCH A251

Origin of a folded repeat protein from an intrinsically disordered ancestor — •Hongbo Zhu, Edgardo Sepulveda, Marcus D Hartmann, Manjunatha Kogenaru, Reinhard Albrecht, Jörg Martin, and Andrei N Lupas — Max Planck Institute for Developmental Biology, Tuebingen, Germany

Life today depends entirely on proteins as catalysts, but this activity is dependent on the formation of defined three-dimensional structures (folding). As only few randomly synthesized polypeptide chains have a folded structure, folding was clearly a major obstacle in the evolution of DNA-protein-based lifeforms from simpler precursor forms. We have proposed that folded proteins resulted from the increasing complexity of a preselected, ancestral set of peptides, which supported RNA-based life and required the RNA to assume their active conformation. A dominant mechanism to increase complexity is repetition and we have attempted to recreate experimentally the path from an unstructured precursor to a folded protein by amplification. Specifically we used a fragment of the putatively ancient ribosomal protein S20 (RPS20), which is only structured in the context of the ribosomal RNA, to generate a wide-spread fold in living organisms today, the TPR fold. After computational optimization of the fragment, we obtained a native-like TPR fold with 2-5 point mutations, which were neutral in the parent organism, suggesting that they could have been sampled in the course of evolution. TPRs could thus have plausibly arisen by amplification from an ancestral peptide.

BP 49.10 Thu 12:15 SCH A251

Spontaneous emergence of chemical oscillation of oligomers in a primordial broth — •Sabrina Scherer[1], Eva Wollrab[2], Varun Giri[1], Luca Codutti[3], Teresa Carlomagno[3], and Albrecht Ott[1] — [1]Biologische Experimentalphysik, Universität des Saarlandes, Saarbrücken, Germany — [2]Laboratory of Microbial Morphogenesis and Growth, Institut Pasteur, Paris, France — [3]Centre of Biomolecular Drug Research, Leibniz University, Hannover, Germany

We study the dynamics of a complex chemical system, driven by electric discharge that forms from a gas mixture of methane and ammonia in the presence of water. In the course of a running experiment, a hydrophobic organic layer emerges besides the hydrophilic aqueous phase and the gaseous phase that were initially present. The hydrophilic phase contains at least a few thousands of different molecules, primarily distributed in a range of 50 and 500Da. Using real-time mass spectrometry, we observe the spontaneous emergence and disappearance of oligomeric surfactants. Strong non-linearities are required for the observed aperiodic chemical oscillations. The phenomenon is robust against different gas compositions and concentrations, temperatures and many details of the experimental set-up. In contrast, NMR spectroscopy reveals overall high chemical variability that suggests strong non-linearities due to interdependent, sequential reaction steps. We find that oxidation, or doping with small amounts of an active broth can trigger the production of the oligomers. We suggest that surface active molecules perform phase transfer catalysis in the oil/water mixture and self-organize to a spontaneously emerging autocatalytic network.

BP 49.11 Thu 12:30 SCH A251

Divergent prebiotic synthesis of ribonucleotides — •Matthew Powner — UCL, London, UK

RNA is a leading candidate for the original informational biopolymer of life, however a common prebiotic pathways to both purine and pyrimidine ribonucleotides remain elusive. We recently described a prebiotically plausible synthesis of pyrimidine ribonucleotides, but both purine and pyrimidine nucleotides must be synthesised together to access an information rich biopolymer. A divergent strategy to synthesise pyrimidine and 8-oxo-purine ribonucleotides from prebiotic precursors will demonstrate for the first time generational parity between 8-oxo-purine and pyrimidine heterocycles, allowing stepwise synthesis with regiospecific, stereoselective glycosidation and simultaneous phosphorylation with stereochemical inversion to furnish the β-ribo-stereochemistry found in the biological nucleic acids.

BP 49.12 Thu 12:45 SCH A251

Driving the system out of equilibrium - a key to understand the formamide-based model of the origin of life — •Judit Šponer — Institute of Biophysics, Academy of Sciences of the Czech Republic, Královopolská 135, 612 65 Brno, Czech Republic

Thermodynamic stability of prebiotic building blocks is generally considered to be one of the decisive factors controlling their accumulation in the prebiotic pool. On the other hand higher stability means lower reactivity. How to challenge this apparent paradox in prebiotic chemistry? A simple formamide-based origin model[1], I am going to outline in my talk, provides a tentative answer to this question. This model is based on a strongly non-equilibrium chemistry, in which the stepwise decrease of the temperature of the prebiotic environment drives those chemical transformations which could lead to more and more complex molecular entities. Thus, we suggest that each synthetic step took place at different temperatures, i.e. precursors that formed and accumulated at a higher temperature, become thermodynamically unstable and thus more reactive at a lower temperature.

[1] Šponer JE, Šponer J, Nováková O, Brabec V, Šedo O, Zdráhal Z, Costanzo G, Pino S, Saladino R, Di Mauro E. Emergence of the first catalytic oligonucleotides in a formamide-based origin scenario. Chem. Eur. J. 2016, 22:3572-3586 and Šponer JE, Šponer J, Di Mauro E. New evolutionary insights into the non-enzymatic origin of RNA oligomers. Wiley Interdisciplinary Reviews: RNA 2016: DOI: 10.1002/wrna.1400.