Day 3, Thursday, 1.9.2022

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Talks

KEYNOTE

Life as a matter of function

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Compared to physics and chemistry, biology has always been lacking something like a simplified model system such as the hydrogen atom that would allow to formulate and scrutinize first principles and laws required for a fundamental understanding of the phenomenon of life. The reason is that biology's study object is a moving target, as life ever since its origin on earth several billions of years ago has been complexifying through evolution, and although there is the conceptual agreement that the cell should be considered the basic unit of life, nothing is "basic" about this unit, the smallest representations of which still are incomprehensively complicated chemical reaction systems with more than thousands of genes alone. Our hypothesis is that if one ever wants to have in hands and under the microscope a truly minimal living system, one will have to build it from scratch. In contrast to origin-of-life research, however, we do not focus too strongly on the actual molecules nor aim to reproduce the plausible series of events that presumably led to the life we find on earth today. Instead, we understand life as a organizational form of matter that is primarily distinguished by a set of key functions, which can however be abstracted from their specific representatives in various organisms. In the past years, it has been our ambition to identify such a set of key functions for one of life's most central features, self-division. Our experimental work focuses on the reconstitution of a dramatically reduced number of elements of the bacterial cell division system, which however appear to emerge basic features of division in protocell compartments. From our work so far that I will present in my talk, we feel encouraged to believe that the complex cellular division machineries may indeed be deduced to a very limited set of general functional elements, and that some of these rudimentary functions may even still be partly conserved in "modern", highly specialized, proteins.

10:55 – 11:15

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Biogenesis: evaluating fundamental timescales

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How long does it take for the first viable living cells to emerge on a planet? Recent experiments in prebiotic chemistry and their overlap with insights from the geochemical records of early Earth and Mars allow for evaluation of some fundamental timescales. Many questions remain open, but new experiments are underway.

11:15 – 11:35

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Prebiotic Peptide Synthesis and Spontaneous Amyloid Formation Inside a Proto-Cellular Compartment

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Cellular life requires a high degree of molecular complexity and self-organization, some of which must have originated in a prebiotic context. Here, we demonstrate how both of these features can emerge in a plausibly prebiotic system. We found that chemical gradients in simple mixtures of activated amino acids and fatty acids can lead to the formation of amyloid-like peptide fibrils that are localized inside of a proto-cellular compartment. In this process, the fatty acid or lipid vesicles act both as a filter, allowing the selective passage of activated amino acids, and as a barrier, blocking the diffusion of the amyloidogenic peptides that form spontaneously inside the vesicles. This synergy between two distinct building blocks of life induces a significant increase in molecular complexity and spatial order thereby providing a route for the early molecular evolution that could give rise to a living cell.

11:35 – 11:55

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Membraneless Biocondensate Hypothesis prior to Protocells near the Origins of Life, The Evolution of Evolutionary Processes over 3.8 Billion Years towards Feedback-Driven Actively Accelerated Organismal and Real-Time Cancer Evolution

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The origins of life under driven non-equilibrium conditions require evolvable information-storage macromolecules, either membrane-bound vesicles or protocells, or alternatively membraneless biocondensates generated by liquid-liquid phase separations (LLPS), soon followed by energy metabolism.

The evolution of early life and of contemporary viruses has been driven in significant part by random genetic mutations, while modern unicellular and organismal evolution primarily leverages evolved, efficient and active cell biology processes for adaptive changes prior to selection. Random mutations are often buffered by cell homeostasis, or they have a negative role, e.g., by causing death or monogenic diseases, or by triggering real-time cancer evolution. Accordingly, the Modern Synthesis theory no longer adequately describes the efficient, often punctuated and at times directionally adaptive natural genetic engineering (NGE) processes deduced from the DNA record of evolution.

Early life and advanced life organismal evolution has many parallels with real-time cancer evolution in a host, and they can inform each other. The somatic mutation theory (SMT) of cancer describes driver mutations that can trigger oncogenesis, and passenger mutations characteristic of periods of genetic microevolution in cancer. At the precancerous stage, most somatic mutations are repaired or buffered in the cell, aberrant cells are removed, or organismal bioelectric tissue signals or other physiological functional networks maintain control of rogue, mutated cells. However, the SMT is not sufficient to describe the observed punctuated macroevolution of cancer-cell genes, chromosomes, karyotypes and epigenomes, nor of expressed cancer-cell transcriptomes, proteomes and epiproteomes, which include non-DNA-templated posttranslational modifications, protein-protein interactions and metabolites. Moreover, punctuated cancer cell macroevolution often culminates in macro-effects, which include epithelial-mesenchymal transitions (EMT), cancer cell polyploidies and even giant multinucleated cancer cells that drive cancer progression, therapy resistance and metastasis. All of this cancer-cell evolution competes in a molecular and cellular arms race with host immune cells and antibodies, as well as with the host tumor microenvironment.

Empirically observed punctuated, multilevel and multiclonal cancer macroevolution, and the concomitant, rapid co-development of the host immune system and tumor micro- environment, can occur with the efficiency, speed and lethality of cancer that is enabled by evolved, active natural genetic engineering (NGE) mechanisms. NGE affects both vertical cancer-cell genomic inheritance and evolution towards therapy resistance and metastasis, as well as viral or cancer-cell exosome vector-driven horizontal gene transfers that contributes to cancer cell cooperation, or to transforming previously noncancerous somatic cells into destabilized cancer cells during metastasis.
In addition, externally driven, irreversible and transferable (EDIT) adaptations are exemplified by mitotically heritable, non-templated cancer cell epigenetics, and by mitotically heritable cancer-cell surface protein and lipid glycosylation, as important examples of fast time-scale molecular evolution
mechanisms in which genes are followers, similar to evo-devo processes in organismal evolution.

Poster

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Arts and Humanities Scholarship in Origin and Prevalence of Life Research

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The origin and prevalence of life in the universe are topics of great significance for the arts and humanities, as well as for the natural sciences. One can easily appreciate that scholars in the arts and humanities who have an interest in these themes ought to attend to research and theories put forward by scientists: in thinking about these matters, they should to be up-to-date with the state of scientific knowledge. The exchange can also run in the other direction, however, with the arts and humanities offering resources for the community of natural scientists working on the origin and distribution of life. Centuries of thinking in the humanities about the nature of life are likely to offer fresh perspectives for the necessarily creative work of interpretation involved in thinking about processes of life beyond our own experience. This poster will present some of the fruits of thought about the place of arts and humanities perspectives in this field that has gone into the foundation of the Leverhulme Centre for Life in the Universe at the University of Cambridge. Particular emphasis will be placed on the potential for philosophical exploration of core concepts that animate this work – ideas such as 'origin', 'pathway', or 'matter' – to offer new perspectives. It will also point to the capacity for philosophy to serve as a bridge between scientific questions and some useful, and more philosophical, areas of mathematics, such as game theory and the exploration of complexity. It is hoped that this poster will serve as a bridge between the work convened in and around Zürich and the burgeoning arts and humanities dimensions to work in Cambridge.