BP 37: Systems Biology, Evolution and Neural Networks I

Time: Thursday 15:00–17:30 Location: ZEU 250

Invited Talk BP 37.1 Thu 15:00 ZEU 250

Growth, death, and adaptation of bacterial cells: a quantitative analysis — •Ulrich Gerland — TUM, Munich, Germany

Bacteria such as *Escherichia Coli* serve as model systems to study basic principles of evolving living systems. For physicists seeking a quantitative understanding of such systems there are essentially two complementary approaches: One can consider a functionally defined subsystem and seek to understand how its function emerges from the interplay between the constituent molecules. If an entire cell is taken as a functional unit (arguably the smallest unit of life), this bottom-up approach is currently intractable. Alternatively, one can analyze the behavior of a functional unit, and extract quantitative phenomenological laws that reflect either fundamental trade-offs or evolved strategies. Importantly, this approach is applicable also to entire cells. It can form both the starting point and the guiding principle for a systematic top-down analysis of living systems. I will illustrate this increasingly popular approach with our own work (partially unpublished) on the growth, death, and interdependence between growth and death of *Escherichia Coli* cells. In particular, I will also discuss a trade-off in the apparent survival strategy of these bacteria and its evolutionary implications.

BP 37.2 Thu 15:30 ZEU 250

Ruggedness and accessibilioty in tradeoff induced landscapes — •Suman Das and Joachim Krug — University of Cologne, Cologne, Germany

Evolutionary fitness landscapes depend on environmental parameters. Contrary to the widespread attention given to fitness landscapes at fixed environments, the effect of environmental changes on gene-gene interactions has not been studied systematically. We study the case of environment dependent landscapes where the fitness effects of mutations exhibit adaptational tradeoffs, i.e mutations which are beneficial in one parameter regime become deleterious in another. We find that such landscapes have predictable properties that are largely independent of the precise details of individual parameter values in the system. In particular, we find that high ruggedness and high accessibility of fitness maxima coexist in these systems, making them distinct from the commonly studied random landscape models. We discuss the relevance of such landscapes in the context of antibiotic resistance.

BP 37.3 Thu 15:45 ZEU 250

Sequence selection of oligonucleotides under a ligation chain reaction — •Patrick Kudella and Dieter Braun — Systems Biophysics, Ludwig-Maximilians-Universität München

Replication of information on oligonucleotides such as RNA or DNA is essential for the emergence of life. Previous studies focus on the replication of single sequences, but we believe it is the key to monitor selection dynamics and replication starting in an already completely random pool of sequences.

We expect a nonlinear ligation dynamic had set in, once polymerization was able to create oligomers long enough for hybridization and thus capable of structure formation and templated ligation. We study if certain sequences could have been selected at this onset of replication that potentially lead to interesting non-linear and frequency-dependent behavior.

By using adenine-thymine-only 12mers long random-sequence strands as starting material, the sequence space for the first ligation stage creating 24mers can still be completely sampled. We obtained more than 12 million individual strands by Next Generation Sequencing (NGS), showing a significant selection of sequences undergoing this elongation dynamic. Utilizing a self-written LabView code we can study starting sequence pool biases, short- and long- range correlation in sequence space, base-fraction evolution as a function of product length as well as the driving selection mechanics as a function of product length. In addition, we show temperature, concentration and sequence-space dependent dynamics of this system by PAGE.

BP 37.4 Thu 16:00 ZEU 250

Ligation Chain Reactions in Non-Equilibrium Convection Compartments with Microscale pH Cycles — •Annalena Salditt and Dieter Braun — Ludwig-Maximilians-Universität

Early replication mechanisms for the origin of life rely on periodic strand separation to start new rounds of replication necessary to stabilize and accumulate information of long nucleic acids. Especially for catalytically active RNAs, high temperatures required for strand separation promote their hydrolysis, leading to a loss of information. Therefore, a geophysical non-equilibrium environment on early Earth would have required means to separate hybridized strands after replication and to localize long, potentially functional molecules against diffusion while protecting them from hydrolysis. We perform ligation extension experiments in moderate temperature gradients across micrometer thick, water-filled chambers with a water-CO2 interface to induce a miniaturized water cycle while maintaining thermophoretic trapping conditions. In addition to more realistic early atmospheric conditions of the Earth, the CO2-water interface causes periodic pH changes, that induce the hybridization of double strands. We expect this to be a promising autonomous setting for ligation chain reactions starting from a random or semi-random oligomer pool.

15 min. coffee break

BP 37.5 Thu 16:30 ZEU 250

Collective dynamics shape drug resistance evolution in dense cellular populations — •Jona Kayser[1,2], Carl Schreck[3], and Oskar Hallatschek[3] — [1]Max-Planck-Institute for the Science of Light, Erlangen — [2]Zentrum für Physik und Medizin, Erlangen — [3]University of California, Berkeley

The principle factor limiting curative cancer treatment is the evolution of drug resistance. Recent work has yielded substantial progress in our understanding of the molecular and biochemical mechanisms of resistance while studies of well-mixed microbial cultures have shed light on the ensuing evolutionary dynamics in disperse populations. Yet, how the mechanical interactions between cells in dense populations, including solid tutors, shape evolutionary trajectories is not well understood.

Here, using a genetically tailored model system of neoplastic growth, based on microbial colonies, I show that the physical cell-cell interaction inherent to dense cellular populations can induce collective phenomena that reshape evolutionary outcomes and may boost drug resistance evolution. In addition, I present new results advocating for an intricate interplay between such an emergent mechano-cooperation and multi-step adaptation. The uncovered mechanisms lay the foundation for a new conceptual framework of intratumoral evolutionary dynamic as an emergent phenomenon, which might crucially inform novel treatment strategies, such as adaptive therapy.

BP 37.6 Thu 16:45 ZEU 250

The effects of cross-species gene transfer on genome dynamics — •Mona Förster[1], Isabel Rathmann[1], Jeffrey Power[2], Viera Kovacova[1], Michael Lässig[1], and Berenike Maier[1] — [1]Universität zu Köln, Deutschland — [2]Universität Tübingen, Deutschland

Phylogenetic studies have provided strong evidence that gene transfer happens frequently and acts across species. However, the rate at which gene transfer occurs and its short-term effect on genome dynamics are poorly understood. To address the effect of intra- and interspecies gene transfer on genome dynamics we developed an evolution experiment and analysis method to detect horizontal gene transfer. To investigate mechanistic contributions to gene transfer probability, we ensured minimal selection by not allowing for population dynamics. We were able to detect a remarkably high gene transfer rate of 0.4 $\%h^{-1}$ across subspecies of *Bacillus subtilis*. This rate was lower by 125 times when gene transfer was probed between *B. subtilis* and *Bacillus atrophaeus*. Interestingly, the average sequence divergence of integrated segments is comparable between both donors with a mean of 6.7 %. In both experiments, gene transfer increased the number of mutations depending on replacement quantity. The fact that the fraction of replaced genome increases linearly throughout the 40 h of DNA uptake suggests that transfer of genes is not yet saturated. In future long term evolutionary experiments, it will be interesting to relate the rate of gene transfer across donor and recipient with the pattern of sequence divergence to better understand what sets species apart.

BP 37.7 Thu 17:00 ZEU 250

Genetically engineered control of phenotypic structure in microbial colonies — •Philip Bittihn[1,4], Andriy Didovyk[1,5], Lev S. Tsimring[1], and Jeff Hasty[1,2,3] — [1]BioCircuits Institute — [2]Department of Bioengineering — [3]Molecular Biology Section, Division of Biological Sciences, University of California, San Diego, La Jolla, CA, USA — [4]Current address: Department of Living Matter Physics, Max Planck Institute for Dynamics and Self-Organization, Göttingen, Germany — [5]Current address: Vertex Pharmaceuticals, San Diego, California, USA

Many essential biological behaviors originate from an entanglement of biological (cellular) and physical processes. This is a challenge not only for traditional biology and physics methodology, but also for synthetic biology, where such interactions severely limit the ability to engineer desired behavior with artificial gene regulatory networks. We show how to achieve control of phenotypic structure in bacterial microcolonies by simultaneously exploiting internal gene expression and metabolism, as well as physical coordination through signal diffusion and growth, which leads to self-generated nutrient gradients and a heterogeneous population consisting of both dividing and dormant cells. In microfluidic experiments and a mathematical model, we show that gene circuits which sense and control growth can create a spatio-temporal feedback loop via nutrient transport and generate sustained growth oscillations, while a phenotype-specific lysis circuit can selectively eliminate dormant cells. Our results demonstrate how to understand and control multicellular substrates as complex active physical systems.

BP 37.8 Thu 17:15 ZEU 250

Gene Expression Dynamics Determine Toxin Driven Bacterial Competition — •Alexandra Götz, Anna Weiss, Benedikt von Bronk, Andreas Mader, and Madeleine Opitz — Ludwig-Maximilians-Universität, München, Germany

Microbial community composition is greatly influenced by stochastic and deterministic bacterial interactions on the single cell level, determining stability and fate of mixed bacterial populations in a given habitat. Here, we study bacterial competition that is driven by production and release of the toxic bacteriocin ColicinE2 of Escherichia coli. In this model system, a complex regulatory network controls the expression of the toxin from the ColicinE2 operon. Using fluorescence time-lapse microscopy, we investigated how the regulatory system controls the time-point and amount of toxin released into the environment and disentangled the components responsible for toxin expression dynamics and release. Investigating several mutant strains, we determined how different regulatory modules affect gene expression noise. In a next step, we investigated the impact of noise and toxin expression dynamics on the competition of the toxin-producing bacterium with a bacterium sensitive towards the toxin. Finally, theoretical simulations allowed us to analyze the role of toxin release times and toxin amounts with regard to the bacterial competition over a broad parameter range.