BP 59: DNA, RNA and Related Enzymes

Time: Thursday 9:30–11:00 Location: H45

Invited Talk BP 59.1 Thu 9:30 H45

RNA-based gene circuits in vitro and in vivo — •Friedrich Simmel — TU München, Garching, Germany

The sequence-progammability of nucleic acids not only allows the design of complex supramolecular structures, but also the realization of dynamically switchable molecular devices. In particular RNA-based switches can be utilized as "rationally designed" genetic regulators, and can thus be used for the realization of artificial gene regulatory circuits. In this talk, a variety of examples of dynamical systems will be described, which can be implemented with such components - either using in vitro gene transcription, cell-free gene expression, or even in vivo.

BP 59.2 Thu 10:00 H45

Knots in DNA and nanopore sequencing — •Stefanie Stalter, Florian Rieger, and Peter Virnau — Institut für Physik, JGU Mainz, Staudingerweg 9, 55128 Mainz

We determine knotting probabilities as a function of salt concentration for DNA strands of up to 150000 base pairs with coarse-grained Monte Carlo simulations. At this size DNA is highly knotted, which has severe implications for the future of nanopore sequencing devices. We also provide evidence for an entropic attraction of knots on the strand and demonstrate how two knots can pass through each other.

BP 59.3 Thu 10:15 H45

Accumulation and Replication in shallow thermal gradients: towards volcanic settings — •Michael Hartmann, Lorenz Keil, and Dieter Braun — Biophysics Department, Ludwig-Maximilians-Universität München, Amalienstraße 54, 80799 München, Germany

The most likely low concentration of molecules in a prebiotic ocean is a central problem for the origin of life. We have argued in the past that focused temperature gradients in hydrothermal, porous systems can thermophoretically accumulate, thermally cycle, and continuously feed the first prebiotic molecules for evolution [Mast, PRL 2010; Mast et al., PNAS 2013; Kreysing et al., Nature Chemistry 2015]. But the applied gradients of $10-100K/mm$ limit the scope of the approach to hydrothermal orifices.

We simulate in silico that a strong molecular accumulation (of nucleotides in particular) more than 10^{20}-fold still takes place in thermal gradients of $0.1K/mm$ ($100K/m$), about $100-1000$ fold more shallow than considered before. Accumulations remain stable under various pore widths and tilt angles. We investigate the stochastic thermal cycling of single molecules by two-dimensional random walk in the convection.

With the findings, more shallow gradients in steam heated, porous volcanic rock can be considered. This is important since wet-dry cycles under UV illumination seem important for the generation of nucleotides [Powner et al., Nature 2009]. To conclude, the study expands the thermal gradient scenario for the onset of molecular evolution towards shallow thermal gradients.

BP 59.4 Thu 10:30 H45

RNAi revised - target mRNA-dependent enhancement of gene silencing — •Simon Dornseifer[1], Sarah Willkomm[1], Rosel Kretschmer-Kazemi Far[1], Janine Libschwager[1], Foteini Beltsiou[1], Kirsten Frank[1], Sandra D. Laufer[1], Thomas Martinetz[2], Georg Sczakiel[1], Jens Christian Claussen[3,2], and Tobias Restle[1] — [1]Inst. Molecular Medicine, Univ. Lübeck — [2]INB, Univ. Lübeck — [3]Comp. Systems Biol., Jacobs Univ. Bremen

The discovery of RNA interference (RNAi) gave rise to the development of new nucleic acid-based technologies as powerful investigational tools and potential therapeutics. Mechanistic key details of RNAi in humans need to be deciphered yet, before such approaches take root in biomedicine and molecular therapy.

We developed and validated an in silico-based model [1] of siRNA-mediated RNAi in human cells in order to link in vitro-derived pre-steady state kinetic data with a quantitative and time-resolved understanding of RNAi on the cellular level. The observation that product release by Argonaute 2 is accelerated in the presence of an excess of target RNA in vitro inspired us to suggest an associative mechanism for the RNA slicer reaction where incoming target mRNAs actively promote dissociation of cleaved mRNA fragments. This novel associative model is compatible with high multiple turnover rates of RNAi-based gene silencing in living cells and accounts for target mRNA concentration-dependent enhancement of the RNAi machinery [1].

[1] S. Dornseifer et al, Nucleic Acids Research (Epub ahead of print 2015) http://dx.doi.org/10.1093/nar/gkv1200

BP 59.5 Thu 10:45 H45

The TASEP with reinitiation before the steady state — David W. Rogers, •Marvin A. Böttcher, Arne Traulsen, and Duncan Greig — Max Planck Institute for Evolutionary Biology, Plön, Germany

The *totally asymmetric simple exclusion process* (TASEP) was initially developed as a stochastic model for mRNA translation. It has subsequently attracted a lot of attention, since it can be applied to a variety of systems, including molecular transport, traffic, or spread of epidemics, and can be solved analytically in multiple cases. However, recent experimental evidence for the translation process shows a negative correlation between transcript length and observables such as ribosome density, protein abundance and codon adaption, which can not be explained with the original TASEP.

We examine the influence of ribosome reinitiation on translation, that is the finishing ribosome directly initiates again without leaving into the ribosome pool, by using an implementation of the TASEP with the Gillespie algorithm. In contrast to previous work we explicitly take the initial phase into account, before steady state is reached. Thereby we demonstrate that reinitation leads to a strong length dependency on both ribosome density on the transcript and protein yield consistent with current experimental evidence, allowing powerful prediction of translational regulation across eukaryotes.