BP 29: Statistical Physics of Biological Systems II (joint session BP/DY)

Time: Thursday 9:30–12:00 Location: H 1028

BP 29.1 Thu 9:30 H 1028

Coarsening model explains cross-species universality of crossover interference — •Marcel Ernst[1], Raphael Mercier[2], and David Zwicker[1] — [1]Max Planck Institute for Dynamics and Self-Organization, Am Faßberg 17, 37077 Göttingen, Germany — [2]Max Planck Institute for Plant Breeding Research, Carl-von-Linné-Weg 10, 50829 Cologne, Germany

During meiosis, crossovers between female and male chromosomes mix genetic information. Experimental observations consistently produce two important results: First, the number of crossovers per chromosome is at least one and usually small, ranging from one to three. Second, there is crossover interference, which prevents nearby crossovers on a single chromosome. In this talk, I will present a novel quantification of crossover interference, which reveals a universal behavior across multiple species. This behavior is consistent with a recently proposed model, where biomolecular condensates that coarsen by exchanging material along chromosomes determine crossover positions. This process is disrupted in mutants lacking the axial structure connecting chromosome pairs, leading to strongly reduced interference. To explain that behavior, I will also present an extension of the coarsening model, which includes material exchange with the surrounding nucleoplasm. The modified coarsening dynamics provide a more detailed description of all experimental data and unveil the physical mechanism of crossover interference.

BP 29.2 Thu 9:45 H 1028

Designing phase coexistence in multicomponent mixtures: surface tensions and the Gibbs' rule — •Filipe Thewes and Peter Sollich — Institut für Theoretische Physik, Georg-August-Universität Göttingen, Göttingen, Germany

Gibbs' phase rule constrains the maximum number of phases that can coexist in multicomponent mixtures. It relates the maximum number of phases to the number of components and the degrees of freedom. The phases formed in equilibrium depend directly on the interactions between the different components, opening the possibility for the inverse problem of designing a set of interactions that recover a desired phase behavior. This perspective has been explored recently in relation to phase separation in biological systems as a mechanism for cells to control their internal structure and function. Interestingly, recent approaches for such interactions design are able to retrieve in the grand-canonical setting a number of phases that is larger than predicted by a naive application of Gibbs' phase rule. In this talk, I will first revisit Gibbs' rule in the *grandcanonical* ensemble and show that designed interactions act as new degrees of freedom that do increase the number of possible phases. I then show that in a canonical setting the number of phases is determined by interfacial tensions; above the naive Gibbs limit we find long-lived metastable states in numerical simulations. In the second part, I will discuss which conditions on the interfacial tensions result in "super-Gibbs" canonical phase splits. These conditions lead to a second step in the design problem of multicomponent mixtures, namely that of controlling the interfacial properties.

BP 29.3 Thu 10:00 H 1028

Microscopic model for aging of RNA condensates — •Hugo Le Roy — EPFL, Lausanne, Switzerland

Biomolecular condensates are membrane-less comparments in the cell that are involved in a wide diversity of biological processes. These liquid-liquid phase-separated droplets exhibit a viscoelastic mechanical response. This behavior is rationalized by modeling the complex molecules that make up a condensate as stickers and spacers that can assemble into a network-like structure. The proper functioning of biocondensates requires precise control over their composition, size, and mechanical response. For example, several neurodegenerative diseases are associated with dysfunctional condensates that solidify over a long period of time (days) until they become solid. A phenomenon usually described as aging. The emergence of such a long timescale of evolution from microscopic events, as well as the structural reorganization that leads to aging remains mostly an open question. To explore the connection between the mechanical properties of the condensates and their structure, we use a simplified description of the condensates. In our framework, a condensate is considered as an associative gel made of polymers (RNA) and linkers (DEAD-box proteins), whose response time is related to the interaction time between the constituents. We show that the interaction between linkers and long polymers results in an attractive Casimir force between linkers. As a consequence, linkers tend to cluster over equilibration of the network. Such a clustering does not make the material stiffer but leads to an exponential increase of the relaxation timescale in agreement with experimental observations.

BP 29.4 Thu 10:15 H 1028

Are phases an appropriate description for cells? — •Martin Girard — Max-Planck-Institute für Polymerforschung

Phase separation has emerged as an important topic for cellular function. From lipid rafts to liquid-liquid phase separation, our current understanding is that it is crucial for organization. We putatively expect that rules extracted from simple systems, two component mixtures, extend to multicomponent systems. While this is true in the thermodynamic limit, I will discuss here the thermodynamic limit for multicomponent systems. Using a toy model, I will show that what we consider "large systems" is largely subjective and dependent on details in multicomponent systems. For "small" systems, rules are very different, and the system is dominated by fluctuations. Usual assumptions, such as equivalence of thermodynamic ensembles, are broken. Still, the system can be driven to exhibit behavior that is similar to a phase transition, for instance by changing the statistical ensemble. Practically, this means that observed phase behavior may be largely dependent on system preparation. This naturally leads to a fundamental question: is the traditional phase behavior an appropriate description for cellular behavior?

15 min. break

BP 29.5 Thu 10:45 H 1028

Complex and 3-dimensional RNA random walks: comparison and application to sequence data across biological taxa — •Jack Mortimer and Jens Christian Claussen — School of Computer Science, University of Birmingham, UK

The DNA random walk is a classical attempt to grasp long-range features of DNA (or RNA) sequences by mapping pairs of amino acids to ± 1 steps of a random walk, and interpret the resulting "time series" by scaling analysis [1]. But as four letters C,G,A,T comprise the DNA alphabet it is a straightforward idea to utilize complex numbers to exploit this information (rather than ignoring it). This direction has been investigated also elsewhere [2] but different definitions were used, and it is not yet conclusive how far biological data can be differentiated.

In this contribution, we attempt a comparison of different complex RW definitions together with a 3D RW, discuss their relations between each other, and apply them to a wide range of DNA sequences. While the various DNA RW's seem not to be directly disciminatory for each species, we find that they provide a wide spread across the datasets. In conclusion, complex and higher-dimensional DNA random walks are a promising tool to extract long-range features from DNA, although the biological interpretation of this method remains to be investigated.

[1] Peng, Buldyrev, Goldberger et al., Nature 356,168 (1992)
[2] Cattani, in: Bioinf Res Dev, Springer, p. 528 (2008)

BP 29.6 Thu 11:00 H 1028

Trajectory mutual information in biochemical systems: Gaussian vs. Poissonian fluctuations — •Anne-Lena Moor[1,2], Christoph Zechner[1,2], and Pieter Rein ten Wolde[3] — [1]Max Planck Institute of Molecular Cell Biology and Genetics — [2]Center for Systems Biology Dresden — [3]AMOLF Amsterdam

Signal processing in biochemical networks relies on dynamic information transmission between time-trajectories of the respective molecular components. From a mathematical point of view, the transferred information can be described via the mutual information. Traditionally, this has been calculated using a Gaussian approximation. Our recent work suggests that this method is not always suitable for every biochemical networks which can lead to quantitative and qualitative mismatches to the exact solution. In this work, we explain the origin of these discrepancies and present a modified version of the Gaussian framework that aligns better with the characteristics of stochastic biochemical networks.

BP 29.7 Thu 11:15 H 1028

Geometry and epigenetic memory during ageing — •Matteo Ciarchi[1], Steffen Rulands[2], and Benjamin Simons[3] — [1]Max Planck Institute for the Physics of Complex Systems, Dresden — [2]Ludwig-Maximilians-Universität, München — [3]Department of Applied Mathematics and Theoretical Physics, Cambridge

Ageing is the decline of the physiological function of an organism over time. This process has been shown to be tightly correlated to changes in epigenetic modifications of the DNA. But how does the slow process of ageing over decades emerge from the fast molecular changes in the epigenome? Here, we show that the interplay between fluctuations and DNA geometry gives rise to memory that translates short-term molecular changes to a slow drift on the time-scales of aging. We draw on sequencing experiments that compare DNA methylation on the time scales of few cell divisions to longitudinal measurements over the much longer time scales of aging. We find that the drift of DNA methylation over time in both cases is highly nonlinear and cannot be explained by known biochemical processes. In order to understand these observations, we derive a field-theoretic framework that couples epigenetic processes along the DNA sequence with dynamic geometrical changes of the DNA in three-dimensional space. Using this theory, we show that the conformational changes in three-dimensional space allow for memory to form along the DNA sequence. Taken together, our work shows that epigenetic ageing is the accumulation of fast, intrinsic molecular processes over long time scales.

BP 29.8 Thu 11:30 H 1028

Exploring tumor karyotype evolution using the Macro-Karyotype concept — •Lucija Tomašić[1], Thomas van Ravesteyn[2,3], Geert J. P. L. Kops[2,3], and Nenad Pavin[1] — [1]Faculty of Science, University of Zagreb, Croatia — [2]Hubrecht Institute and University Medical Centre Utrecht, Utrecht, The Netherlands — [3]Oncode Institute, Utrecht, The Netherlands

Most tumors exhibit abnormal chromosome content (karyotype) resulting from errors in mitotic division. While tumors tend to manifest diverse karyotype aberrations, typically with gains of specific chromosomes, understanding the dynamics leading to these configurations is challenging due to the dimensionality of the karyotype space. To address this complexity, we introduce the 'Macro-Karyotype' concept,a novel framework for comprehensively exploring tumor chromosomal evolution. Combining in vitro organoid evolution with mathematical modeling, our study demonstrates that premalignant human organoids spontaneously undergo chromosome copy number alterations related to cancer. A gradual gain of specific chromosomes over time is observed, propelled by the enhanced fitness of these karyotypes. Additionally, some karyotypes undergo dramatic changes through whole-genome duplication and multipolar divisions, followed by normalization over time through the selection of karyotypes with lower mitotic error rates. Our findings uncover the selection of homogeneous karyotypes driven by cellular fitness, significantly constraining the available karyotype space. Our study deepens understanding of tumor karyotype evolution and informs factors influencing cancer related chromosomal changes.

BP 29.9 Thu 11:45 H 1028

How do particles with complex interactions self-assemble ? — •Lara Koehler[1], Martin Lenz[2], and Pierre Ronceray[3] — [1]Max Planck Institute for the Physics of Complex Systems — [2]Université Paris Saclay — [3]Aix Marseille Université

In living cells, proteins self-assemble into large functional structures based on specific interactions between molecularly complex patches. Due to this complexity, protein self-assembly results from a competition between a large number of distinct interaction energies, of the order of one per pair of patches. Current self-assembly models however typically ignore this aspect, and the principles by which it determines the large-scale structure of protein assemblies are largely unknown. Here, we use Monte-Carlo simulations and machine learning to start to unravel these principles. We observe that despite widespread geometrical frustration, aggregates of particles with complex interactions fall within only a few categories that often display high degrees of spatial order, including crystals, fibers, and micelles. We then successfully identify the most relevant aspect of the interaction complexity in predicting these outcomes, namely the particles' ability to form periodic structures. Our results provide a first characterization of the rich design space associated with identical particles with complex interactions, and could inspire engineered self-assembling nanoobjects as well as help understand the emergence of robust functional protein structures.