DY 45: Statistical Physics in Biological Systems (joint session DY/BP)

Time: Wednesday 10:00–13:30 Location: BH-N 333

DY 45.1 Wed 10:00 BH-N 333

Fluctuation effects in single-molecule dynamics: From subergodic time-scales to the kinetics in the few-encounter limit — Alessio Lapolla, David Hartich, and •Aljaz Godec — Mathematical Biophysics Group, Max-Planck-Institute for Biophysical Chemistry (Göttingen)

Single-molecule (SM) dynamics evade the confines of traditional ensemble statistical mechanics. A correct theoretical description of SM dynamics requires a time-average statistical mechanics – the explicit consideration of trajectory-to-trajectory fluctuations over finite observation times. Similarly, a new paradigm emerges when considering molecular reaction kinetics in the few-encounter limit occurring, e.g. in transcription regulation or in diseases triggered by protein misfolding, where already the first reactive event is 'catastrophic'.

We will review our recent theoretical results on a rigorous formulation of occupation-time statistical mechanics, and a first passage time theory of few-encounter kinetics. We will discuss why our results are relevant for explaining quantitatively emerging biophysical phenomena at low-copy numbers.

DY 45.2 Wed 10:15 BH-N 333

Extreme value statistics of mutation accumulation in renewing cell populations — •Philip Greulich[1,2] and Benjamin D. Simons[3,4] — [1]Mathematical Sciences, University of Southampton, UK — [2]Institute for Life Sciences, University of Southampton, UK — [3]Cavendish Laboratory, University of Cambridge, UK — [4]Gurdon Institute, University of Cambridge, UK

The emergence of a predominant phenotype within a cell population is often triggered by a rare accumulation of DNA mutations in a single cell. For example, tumors may be initiated by a single cell in which multiple mutations cooperate to bypass a cell's defense mechanisms. The risk of such an event is thus determined by the extremal accumulation of mutations across tissue cells. To address this risk, we studied the statistics of the maximum mutation numbers in a Moran process, as a model for a renewing cell population. By drawing an analogy between the genealogy of a cell population and the theory of branching random walks, I will present new analytical estimates for the probability of exceeding a threshold number of mutations, and show how the statistical distribution of maximum mutation numbers scales with age and cell population size.

DY 45.3 Wed 10:30 BH-N 333

The rate of recombination and its effect on mutational robustness — •Alexander Klug and Joachim Krug — Institut für Theoretische Physik, Universität zu Köln, Germany

Mutational robustness refers to the effect of mutations on the fitness of a population. In case of high mutational robustness most mutations do not change the fitness or have only a minor effect on it. Hence from the point of view of fitness landscapes, mutational robustness describes the occurrence of clusters of genotypes of almost equal fitness. Using a deterministic population model with selection and mutation it can be shown that the population slightly favours genotypes inside such clusters which therefore results in increased mutational robustness[1]. We show that this effect is strongly enhanced by the introduction of recombination on the basis of analytical results for a two-locus landscape and numerical results for different neutral landscape models with multiple loci.

[1] E. van Nimwegen, J. P. Crutchfield, M. Huynen, PNAS 96:9716-9720 (1999)

DY 45.4 Wed 10:45 BH-N 333

Accelerating Evolution With Dynamic Fitness Landscapes — •Alexander Leonard[1,2] and Sebastian Ahnert[1,2] — [1]Cavendish Laboratory, Univeristy of Cambridge — [2]Sainsbury Laborary, University of Cambridge

Using a tractable lattice self assembly model to produce polyomino phenotypes from numeric genotypes, along with genetic algorithms and fitness proportional selection, allows abstract evolutionary behaviour to be probed in great detail. Comparing a static fitness landscape with a landscape with periodically changing fitness sub goals yields novel behaviour that can be approached analytically. In particular, we find dynamic landscapes, despite only selecting for subsets of goals at any given time, on average solve the total fitness goal faster than static landscapes.

The genotype space, and hence the genotype to phenotype mapping, is unchanged between the static and dynamic cases. As such, the distinct evolutionary behaviour must originate from the paths through the landscape populations take to reach global fitness peaks. Considering purely information-theoretic quantities like the genotype robustness, upper and lower bounds can be found for the oscillation period yielding optimal solving discovery rates.

Additionally, landscapes with longer oscillation periods typically use more genotype coding to produce an equivalent phenotype, indicating that more rapidly oscillating landscapes yield more modular genotypes in response to the more dynamic environment. Such findings are widely applicable to genetic algorithms with complex fitness landscapes.

DY 45.5 Wed 11:00 BH-N 333

Active textiles with Janus filaments — •Len Pismen and Andrei Zakharov — Technion - Israel Institute of Technology

We describe reshaping of active textiles actuated by bending of Janus filaments comprising both active and passive components. A great variety of shapes, determined by minimising the overall energy of the fabric, can be produced by varying bending directions determined by the orientation of Janus filaments. Under certain conditions, alternative equilibrium states, one absolutely stable and the other metastable coexist, and their relative energy may flip its sign as system parameters, such as the extension upon actuation, change. A snap-through reshaping in a specially structured textile reproduces the Venus flytrap effect.

DY 45.6 Wed 11:15 BH-N 333

Local weather driven model for the potential West Nile Virus spread in Germany — •Suman Bhowmick[1,3], Hartmut H. K. Lentz[1], Philipp Lorentz[2], Philipp Lorentz Hövel[2], and Igor Sokolov[3] — [1]Institut für Epidemiologie, Friedrich Loeffler Institut, Germany — [2]Institut für Theoretische Physik, TU Berlin, Germany — [3]Institut für Physik, HU Berlin, Germany

We endeavoured to explore the possible role of the migratory birds in the potential spread of West Nile Virus (WNV) in Germany through a compartment based, mechanistic model. It is of SEIR (susceptible-exposed-infected-removed) type to decipher the intricacy of the spreading dynamics of the WNV. The parameters associated with the model are temperature driven. In addition to that we have considered the seasonal appearance and disappearance of the migratory birds. As results, we will present the numerical solutions of the local infection model as well as an analytical expression for the basic reproduction number R0 and its dependence on the temperature. The phase plots demonstrate two very different kinds of dynamics in Germany. In the north where the temperature is quite low, the phase portrait shows the stable nontrivial equilibrium where as in the south due to the warmer weather, we have found stable limit cyclic behaviour. Potential risk map of the spread of WNV shall be investigated through the coupling of local ODE model with the constructed migratory birds network. Keywords Epidemiological model, Bird migration, Network, Sensitivity analysis, Vector borne disease

15 min. break

DY 45.7 Wed 11:45 BH-N 333

Nonlinear Dynamics of Calcium Cycling in Cardiomyocytes — •Filippo G. Cosi[1], Stefan Luther[1,2,3,4,5], and Ulrich Parlitz[1,2,4] — [1]Max Planck Institute for Dynamics and Self-Organization, Göttingen, Germany — [2]Georg-August-Universität Göttingen, Institute for Nonlinear Dynamics, Göttingen, Germany — [3]University Medical Center Göttingen, Institute of Pharmacology and Toxicology, Göttingen, Germany — [4]DZHK (German Center for Cardiovascular Research), partnersite Göttingen, Germany — [5]Department of Physics and Department of Bioengineering, Northeastern University, Boston, USA

Delayed or early after depolarisations and Calcium alternans inside single cardiomyocytes are known to alterate the sane dynamics of the muscle cell leading to heart defects and even failure on a greater scale.

Defects in the subcellular components, like Rynodine Receptors

(RyR) or Sodium-Calcium Exchangers (NCX) are believed to be the cause of these depolarisations and alternans. In our project, we therefore investigate how these defects are influencing the Calcium and membrane potential dynamics on a cellular scale. A mathematical model including both, the stochastic nature of the cellular components and the whole cell Calcium dynamics, is developed.

Calcium waves, showing a sequential and spontaneous activation of the cell, are presented as results of the model together with the main structure of the algorithm. Diffusive Calcium waves are assumed to be one of the symptoms of diseased ventricular cardiomyocytes causing Calcium alternans and delayed after depolarisations.

DY 45.8 Wed 12:00 BH-N 333

A minimal model to study pH-dependent phase separation — •Omar Adame-Arana[1], Christoph A. Weber[1,2], Vasily Zaburdaev[1], Jacques Prost[3], and Frank Jülicher[1] — [1]Max Planck Institute for the Physics of Complex Systems, Nöthnitzer Str. 38, 01187 Dresden, Germany — [2]Paulson School of Engineering and Applied Sciences, Harvard University, Pierce Hall 412, 28 Oxford Street Cambridge, MA 02138, USA — [3]Institut Curie, 26 rue d'Ulm, 75248 Paris Cedex 05, France

Liquid phase separation is ubiquitous in nature. There is an increasing interest in studying the role of the formation of liquid like droplets as an organizer of the cell cytoplasm. pH influences the charge state of macromolecules such as proteins and can therefore affect phase separation. We propose a minimal model to study how pH can influence the phase separation of a solution composed of macroions of different charge states. We couple a phase separating system to chemical reactions associated with pH. Using this model we first construct the corresponding phase diagrams at the isoelectric point and study the effects of different interaction parameters on the phase diagrams. We then study the effects of changes of pH on phase diagrams. We find that phase separation is most pronounced near the isoelectric point.

DY 45.9 Wed 12:15 BH-N 333

Nonequilibrium force-velocity relation for single polymerization motor — •Thomas Niedermayer[1,2] and Reinhard Lipowsky[2] — [1]Physikalisch-Technische Bundesanstalt (PTB), Berlin — [2]Max-Planck-Institut für Kolloid- und Grenzflächenforschung, Potsdam

In biological cells, the force generating assembly of cytoskeletal filaments is a nonequilibrium process which is coupled to the hydrolysis of bound nucleotides. This complex phenomenon may be captured by a stochastic process involving the association, aging, and dissociation of subunits. Necessarily, aging increases the shrinkage velocity of filaments under load and decreases the stall force. A recently proposed recursive solution for the stochastic process enables us to calculate the force-velocity relation for single cytoskeletal filaments in agreement with extensive stochastic simulations. Both for actin filaments and microtubules, we predict the onset of fast depolymerization slightly above the stall force. This effect involves strong correlations of the subunit states, underlining the failure of mean field calculations.

DY 45.10 Wed 12:30 BH-N 333

Dynamics and Thermodynamics of Chemical Reaction Networks — •Riccardo Rao and Massimiliano Esposito — Complex Systems and Statistical Mechanics, Physics and Materials Science Research Unit, University of Luxembourg, L-1511 Luxembourg, G.D. Luxembourg

Chemical Networks (CN) are large sets of coupled chemical reactions where some of the species are externally controlled. Cell metabolism and biochemical signal transduction networks are notable examples of CN. We present a rigorous nonequilibrium thermodynamic description of CN in terms of deterministic rate equations. Our description is inspired by Stochastic Thermodynamics and is based on Chemical Reaction Network Theory. The energy and entropy balances of CN are derived and a nonequilibrium Gibbs free energy is introduced. This latter is related to the chemical work necessary to sustain nonequilibrium steady states and to the driving work necessary to control the network far from equilibrium. We finally discuss these different forms of work in the stochastic framework.

[1] R. Rao and M. Esposito, Nonequilibrium Thermodynamics of Chemical Reaction Networks: Wisdom from Stochastic Thermodynamics, Phys. Rev. X, 2016, 6, 041064.

DY 45.11 Wed 12:45 BH-N 333

Thermodynamically Consistent Coarse Graining of Biocatalysts beyond Michaelis–Menten — •Artur Wachtel, Riccardo Rao, and Massimiliano Esposito — Physics and Materials Science Research Unit, University of Luxembourg, Luxembourg

Virtually all processes in living cells involve catalytic molecules to enhance chemical reactions: various enzymes process metabolites and signaling molecules, catalytically active membrane proteins serve as transporters or receptors for chemical signals.

In this talk we start from the detailed catalytic mechanism of a single biocatalyst and we provide a coarse-graining procedure which, by construction, is thermodynamically consistent even out of equilibrium: This procedure provides stoichiometries, reaction fluxes (kinetic rate laws), and reaction forces (Gibbs energies of reaction) for the coarse-grained level. It can treat active transporters and molecular machines, and thus extends the applicability of ideas that originated in enzyme kinetics. We thus identify the conditions under which a relation between one-way fluxes and forces holds at the coarse-grained level as it holds at the detailed level. In doing so, we clarify the speculations and broad claims made in the literature about such a general flux–force relation. As a further consequence we show that, in contrast to common belief, the second law of thermodynamics does not require the currents and the forces of biochemical reaction networks to be always aligned.

[1] A. Wachtel, R. Rao and M. Esposito, arXiv:1709.06045 (2017)

DY 45.12 Wed 13:00 BH-N 333

Entropic Allostery of Protein Binding and 'Allosteron' Networks — •Alice C. von der Heydt and Tom C.B. McLeish — Dept of Physics, Durham University, Durham, DH1 3LE, UK

Proteins form an essential part of all living organisms. Effector-binding and self-assembly are vital to their biological function. Allostery, *i.e.*, non-local signal transduction and co-operativity among distant sites of a protein, does not imply binding to cause major structural changes. Entropic allostery, instead, rests upon a subtle tuning of the amplitudes and the spectrum of thermal fluctuation modes, to enable binding co-operativity. This mechanism (Cooper and Dryden, 1984) may provide the main part of the allosteric free energy if collective, long-wavelength modes dominate the density of thermally accessible states, and thus, coarse-grained models apply. In an effort to establish a theory of entropic allostery and to elucidate the range of applications, we construct and analyse a basic toy-model unit, the 'allosteron', and its association into networks akin to protein complexes. An allosteron is equipped with both internal and coupling, harmonic degrees of freedom whose interaction strengths can be modified through binding of ligands. Physical interaction strengths derive from a class of Lennard-Jones potentials defined via the balance of attractive and repulsive (entropic) forces. The impact of entropic allostery is demonstrated and discussed for the binding of proteins and their assemblies, such as ring oligomers, that are suitably modelled by coupled allosterons.

DY 45.13 Wed 13:15 BH-N 333

Estimation of the infinitesimal generator by square-root approximation — •Luca Donati[1], Martin Heida[2], Bettina Keller[1], and Marcus Weber[3] — [1]Freie Universität Berlin, Berlin, Germany — [2]WIAS, Berlin, Germany — [3]ZIB, Berlin, Germany

The dynamics of molecular systems can be represented by a continuous operator, called Propagator, that propagates probability densities with time. Associated to the Propagator, there exists another operator, called infinitesimal Generator, that defines the Fokker-Planck equation and provides information about the dynamics of the system in terms of transition rates between states. We have studied a method to obtain the discretized version of the Generator.

The method considers a Voronoi tasselleation of the conformational space and exploits the Gauss theorem to write the instantaneous rate between adjacent cells in terms of the Boltzmann weight of the intersecting surface. This quantity can be approximated by the geometric average of the Boltzmann weights of the cells.

We also show that there exists a direct correlation between the Generator and the potential energy function of the system. The method can be used to study the effect on dynamics of the system of small thermodynamic changes or perturbations of the potential energy function. We present results for 2d diffusion process and Alanine dipeptide.