BP 19: Poster VII

Computational Biophysics (BP 17.1 – BP 17.11); Protein Structure & Dynamics (BP 17.12 – BP 17.17); Single Molecule Biophysics (BP 17.18 – BP 17 .25); Statistical Physics of Biological Systems (BP 17.26 – BP 17.32)

Time: Tuesday 14:00–16:00 Location: P2/3OG

BP 19.1 Tue 14:00 P2/3OG

How to Pare a Pair: Topology Control and Pruning in Intertwined Complex Networks. — •Felix Kramer[1,2] and Carl Modes[1,2] — [1]Center for Systems Biology Dresden (CSBD), Dresden, Germany — [2]Max Planck Institut for Molecular Cell Biology and Genetics (MPI-CBG), Dresden, Germany

Recent work on self-organized remodelling of vasculature in slimemold, leaf venation systems or vessel systems in vertebrates has provided a plethora of potential adaptation mechanisms. All these have in common the underlying hypothesis of a flow driven machinery, meant to prune primary plexi in order to optimize the system's dissipation, flow uniformity or more, with different versions of constraints. Nevertheless, the long-term dynamics of adapting networks whose architecture and function is particularly dependent of their respective environment have not been properly understood. Therefore, interwoven capillary systems such as found in the liver, kidney and pancreas, present a novel challenge regarding the field of coupled distribution networks. We here present an advanced version of the discrete Hu-Cai model, coupling two spatial networks in 3D. We show that spatial coupling of two flow adapting networks can control the onset of topological complexity given the system is exposed to short-term flow fluctuations. Further, our approach results in an alternative form of Murray's law, which incorporates the local vessel interactions and flow fluctuations.

BP 19.2 Tue 14:00 P2/3OG

Foamlike network of bundled semiflexible polymers — •Tobias A. Kampmann and Jan Kierfeld — TU Dortmund University, Germany

We applied the EC algorithm to a system of many (semiflexible) harmonic chains, where the simulation efficiency is comparable to optimized molecular dynamics simulations, while still incorporating the essential features of the actual dynamics. This algorithm allows the simulation of polymer melts, where reptation can be clearly observed. When the polymers interact via a short range, attractive square well potential bundled structures are assembled. We analyse time series of quasi-two-dimensional systems, where foam-like structures arise. This can be linked to the attractive interaction which leads to a minimization of the overall bundle length similar to surface tension in the case of foams. The low mobility and the bending stiffness of polymers lead to structural differences in comparison to soap foams.

BP 19.3 Tue 14:00 P2/3OG

Morpheus: A user-friendly modeling and simulation framework for multicellular systems — Jörn Starruss, Diego Jahn, Robert Müller, Walter de Back, Andreas Deutsch, and •Lutz Brusch — Center for Information Services and High Performance Computing (ZIH), Technische Universität Dresden, Germany

Computational modeling and simulation become increasingly important to analyze tissue morphogenesis. Existing software for multicellular models require scientists to encode their models in an imperative programming language. Morpheus (1,2), on the other hand, is an extensible open-source software framework that is entirely based on declarative modeling. It uses the domain-specific language MorpheusML to define multicellular models through a user-friendly GUI and has since proven applicable by a much broader community, including experimentalists. We here present how MorpheusML enables advanced scientific workflows (3) and cross-software exchange of multicellular models (4). MorpheusML can represent the spatial and mechanical aspects of interacting cells. A numerical simulation is then composed by automatic scheduling of predefined components in the simulator. Moreover, Morpheus supports simulations based on experimental data, e.g. segmented cell configurations, and offers a broad set of analysis tools to extract features right during simulation.

(1) Starruß et al. Bioinformatics 30, 1331, 2014. (2) Morpheus homepage: https://morpheus.gitlab.io (3) Parameter estimation workflow: https://fitmulticell.gitlab.io (4) Model standardization: https://multicellml.org

BP 19.4 Tue 14:00 P2/3OG

Personalized numerical modeling for stent implantation in the aorta — •Dandan Ma[1,3], Yong Wang[2,3], Michael Steinmetz[1], and Martin Uecker[1,3] — [1]University Medical Center Göttingen, 37075 Göttingen, Germany — [2]MPI for Dynamics and Self-Organization, 37077 Göttingen, Germany — [3]German Center for Cardiovascular Research (DZHK), Partner Site Göttingen, Germany

The coarctation of the aorta (CoA) accounts for 7% of all congenital heart defects. Stent implanted is a recommended therapy to reduce the pressure gradient and restore blood flow. Computational fluid dynamic (CFD) can provide valuable insight for flows in a patient-specific model, and thereby predict therapy outcome. In this study, the flow within an aorta, reconstructed from magnitude resonance imaging (MRI) data, was numerically modeled firstly, using lattice Boltzmann method. Both large eddy simulation (LES) and direct numerical simulation (DNS) were adopted to resolve the turbulent blood flow, with boundary condition extracted from phase-contrast MRI (PC-MRI) measurement. Numerical results such as flow velocity, pressure drop and wall shear stress (WSS) were obtained. By comparing the results from LES, DNS and PC-MRI, we conclude that the LES is capable of obtaining accurate aortic flow within acceptable simulation time. In silico stent implantation for a child with CoA was then performed, by predicting the deformed geometry after implantation and modeling the flow therein with LES. It is shown from the numerical results that both pressure drop and maximum WSS are reduced. Such methodology will be used to optimize patient-specific therapy.

BP 19.5 Tue 14:00 P2/3OG

AI Developer: a general tool for deep-learning image classification in life science and beyond — Martin Kräter[1,2], Shada Abuhattum[1,2], Despina Soteriou[1], Jochen Guck[1,2], and •Maik Herbig[1,2] — [1]Max Planck Institute for the Science of Light, Erlangen — [2]Biotechnology Center of the TU Dresden, Dresden

The publication record on artificial intelligence (AI) -based image analysis has increased drastically over the last years. However, all application cases consist of individual solutions with high specificity for a particular use. Here, we present an easy-to-use, adaptable, open source software, called AIDeveloper (AID) to train neural nets (NN) for image classification without the need for programming. The software provides a variety of NN-architectures that can be simply selected for training. AID allows the user to apply trained models on new data, obtain metrics for classification performance, and export final models to different formats. The working principles of AID are first illustrated by training a convolutional neural net (CNN) on a large standard dataset consisting of images of different objects (CIFAR-10). We further demonstrate the range of possible applications on selected biophysical and biomedical problems, such as distinguishing differentiated and non-differentiated stem cells, performing a whole blood cell count, and classifying B- and T-cells, all based on cell images alone. Thus, AID can empower anyone to develop, train, and apply NNs for image classification. Moreover, models can be generated by non-programmers, exported, and used on different devices, which allows for an interdisciplinary use.

BP 19.6 Tue 14:00 P2/3OG

Parallel Network-Based Biocomputation using molecular motors- Solving Exact cover — •Pradheebha Surendiran[1], Aseem Salhotra[2], Till Korten[3], Alf Månsson[2], and Heiner Linke[1] — [1]Nanolund and Solid state physics, Lund university, Lund, Sweden — [2]Department of chemistry and biomedical sciences, Linnaeus university, Kalmar, Sweden — [3]B-cube, Centre for molecular bioengineering, Technische universität Dresden, Dresden, Germany

Computational problems of a combinatorial nature requires exponential time to explore the solution, making traditional serial computation intractable, and parallel computation a necessity. The subset sum problem was recently solved [1] encoding them into a graphical network of channels ingrained onto a nanofabricated device which was then explored by molecular motors to find all possible solutions to the

problem. This approach of network based parallel-computation (NBC) could be potentially used to solve other problems by scaling in an energy efficient manner compared to that of the conventional computer. In this work, we focus on solving Exact Cover(ExCov) which is a decision problem applying the same strategy. We fabricate the problem encoded nanodevice with upscaled network of channels and observe the motility of molecular motors using fluorescence microscopy. Thus scaling of these devices has led to the interest of developing different architectural elements and also employ methods such as deep learning for the automatic evaluation of the huge amount of data obtained. [1] Nicolau et al, PNAS 113 (10), 2591-2596 (2016) Funding: EC-H2020 Bio4Comp Grant-No. 732482

BP 19.7 Tue 14:00 P2/3OG

Morphogenesis in Viscoelastic Tissues via Planar Deformations — •Abhijeet Krishna[1,2], Jana Fuhrmann[1], Joris Paijmans[1,2,3], Suzanne Eaton[1,2,3], Frank Jülicher[1,2], Natalie Dye[1], and Carl Modes[1,2] — [1]Max Planck Institute of Cell Biology and Genetics, Dresden, Germany — [2]Center for Systems Biology Dresden, Dresden, Germany — [3]Max Planck Institute of Physics of Complex Systems, Dresden, Germany

The mechanisms by which tissue surfaces develop to form complex 3D morphologies is an interesting question from the perspective of developmental biology. A model system for answering this question is the Drosophila wing imaginal disc which is a flat epithelial tissue that everts out of the plane to form a surface with non-zero Gaussian curvature. We are interested in understanding the mechanics of this eversion. It has been shown that before eversion, the cells in the wing disc elongate anisotropically and orient themselves in concentric circles around the central region of the tissue. Our hypothesis is that during eversion, cells lose their anisotropic characters which would lead to inhomogeneous and patterned planar deformations. Such inhomogeneous planar deformations can lead to change in the Gaussian curvature of the tissue. We build a spring-dashpot lattice model to simulate a viscoelastic and thick epithelial tissue. Using our model, we try to explain the robustness of the event of eversion. We also propose a mechanism by which eversion could be temporally controlled by the tissue.

BP 19.8 Tue 14:00 P2/3OG

mRNA secondary structure on cationic lipid membrane surfaces — •Mohd Ibrahim and Nadine Schwierz — Department of Theoritical Biophysics, Max Planck Insitute of Biophysics,Max-von-Laue-Str. 3, 60438 Frankfurt, Germany

RNA based therapeutics have emerged as promising candidates for treating currently untreatable diseases like cancer or diabetes. Since RNA is highly charged and degradable it needs a carrier to be transported into the cells. Lipid nanoparticles (LNPs) hold great promise and have been extensively studied for such purposes. However, the delivery efficiency of existing LNPs is very low and the structure of RNA-LNP systems remains poorly understood. A powerful technique to elucidate the structure of nanoparticles are scattering experiments (SAXS and SANS). However, interpreting scattering intensities for a complex systems like LNP is non-trivial. Molecular dynamic simulations in conjunction with scattering experiments can serve as a powerful method to overcome this hurdle. In this work, we use coarse-grained MD simulations to elucidate the conformations of mRNA on the cationic lipid membrane surface. Using existing secondary prediction tools to model mRNA structures, we show that SAXS intensities can be used to differentiate between different RNA conformations on cationic lipid membrane surfaces. By comparing our scattering intensities with experiments we will be able to identify the most probable RNA conformation on the lipid membrane surface or inside lipid nanoparticle thus aiding our understanding of RNA loaded LNP structures.

BP 19.9 Tue 14:00 P2/3OG

Uncertainty quantification for electromagnetic models of biological cells based on dielectric spectroscopy data — •Julius Zimmermann[1], Fukun Shi[2,3], Jürgen Kolb[2,3], and Ursula van Rienen[1,4] — [1]Institut für allgemeine Elektrotechnik, Universität Rostock, 18051 Rostock — [2]Institut für Physik, Universität Rostock, 18059 Rostock — [3]Leibniz-Institut für Plasmaforschung und Technologie (INP), 17489 Greifswald — [4]Department Life, Light & Matter, Universität Rostock, 18051 Rostock

Developing reliable models to understand the interaction between electromagnetic fields and biological cells is a challenging task due to a lack of precise data. We present an approach to estimate the induced transmembrane potential. The approach is based on the electroquasistatic formulation of Maxwell's equations and requires knowledge of the conductivity and relative permittivity of the different constituents of the system under investigation (that is cell membrane, cytoplasm and extracellular medium). We estimate the required parameters from dielectric spectroscopy data. Based on the estimate's uncertainty, the uncertainty of the model output is estimated in a mathematically rigorous fashion.

Acknowledgement: This research was supported by the German Research Foundation (Deutsche Forschungsgemeinschaft, DFG) within the Collaborative Research Centre 1270 ELAINE.

BP 19.10 Tue 14:00 P2/3OG

Physical Analysis of One-Component Signalling in Bacteria — •Linda Martini and Ulrich Gerland — Physics of Complex Biosystems, Technical University of Munich, Garching, Germany

Adaptation to changing environments is of vital importance to bacterial cells and is enabled by sophisticated signal transduction systems. While classical two-component signalling is well studied, the mechanisms of one-component systems, where a single protein implements both sensing and response regulation, are mostly uncharacterized. One such one-component system is the membrane-integrated protein CadC, which is part of the pH-stress response system in E. Coli. As it directly binds to the genomic DNA to regulate transcription, it faces a target search problem the dynamics of which are still to be understood. Using kinetic Monte Carlo simulations of a lattice model, we focus on a characterization of the coupled stochastic dynamics of the DNA and the proteins, and its dependence on the system parameters. Understanding the kinetics of membrane-localized proteins specifically binding to a dynamic DNA will be important to interpret corresponding in vitro experiments and more generally to understand the biophysics of one-component signal transduction.

BP 19.11 Tue 14:00 P2/3OG

Metaheuristic Optimization of Biomolecular Simulation Parameters — •Marie Weiel[1], Markus Götz[1], and Alexander Schug[2] — [1]Karlsruhe Institute of Technology, Karlsruhe, Germany — [2]Jülich Supercomputing Centre, Jülich, Germany

Owing to the structure-function paradigm, a wealth of structural information on proteins has been accumulated. Experimental data might be ambiguous and have to be interpreted to access their actual content. A common way is to integrate them into molecular simulations via an energetic bias favoring conformations concordant with the data. Data-assisted simulations often rely on parameters, the choice of which is far from trivial but crucial for performance. A central question is how to weight experimental information with respect to prior knowledge in the underlying physical model. We propose a metaheuristic particle-swarm based optimization method. In our setup, a particle corresponds to a simulation using a particular combination of parameters to be optimized. To assess simulation outcome, the ensemble's physicality and its agreement with the data are considered. We use Rosetta and bias energy, respectively, out of which the objective function is constructed. To assign equal importance, each contribution has to be rescaled to the same order of magnitude. As the related objective function hyperparameters are a priori unknown but have a critical impact on the search-space topology, they are refined on the fly while the algorithm proceeds. The better different contribution ranges are known from complete simulations, the more accurate values can be chosen, improving optimization efficiency and thus simulation quality.

BP 19.12 Tue 14:00 P2/3OG

Markov Modeling of an Allosteric Transition — •Georg Diez, Daniel Nagel, Benjamin Lickert, and Gerhard Stock — Albert-Ludwigs-Universität Freiburg, 79104 Freiburg, Germany

Allostery plays a fundamental role in regulatory biological processes, in which a functional change of a protein is triggered at one site by the binding of a ligand to another, distant site. It yet remains unclear what forces drive the underlying mechanisms, especially if they are of structural or dynamical nature. In order to investigate allostery, here we study molecular dynamics data of a PDZ domain, in which the binding of a ligand causing an allosteric transition is mimicked by an azobenzene photoswitch.

Markov State Models are a powerful tool for accessing the full dynamics of a system since they only require locally converged trajectories instead of one single long trajectory. This allows us to analyze an ensemble of equilibrium and non-equilibrium trajectories which in

total cover more than 400 μs [1].

The chances to make predictions about the dynamical and conformational change of the system will be illustrated. At the same time, the virtues and shortcomings of constructing a Markov State Model will be addressed.

[1] S. Buchenberg, F. Sittel, and G. Stock, "Time-resolved observation of protein allosteric communication," Proc. Natl. Acad. Sci. U.S.A. 114,E6804 (2017)

BP 19.13 Tue 14:00 P2/3OG

Finding Pathways of Markov State Models — Daniel Nagel and •Gerhard Stock — Albert-Ludwigs-Universität Freiburg, 79104 Freiburg, Germany

In numerous fields of research, the population dynamics of states is described in terms of a master equation or a Markov state model (MSM). Given Markovian dynamics, we can define a transition matrix T_{ij} for a certain lagtime τ_{lag} which determines completely the time evolution of the system. Often we are interested in the pathways of the MSM, that lead from an initial to a final state. E.g., the in protein folding these paths account for the mechanism the molecular reaction evolves. These paths naturally arise in a Markov chain Monte Carlo simulation, where we draw random numbers which determine the next step depending on the transition matrix T_{ij}. The catch is the slow convergence. As a remedy, Vanden Eijnden and co-workers have proposed transition path theory. However, this method is designed to only give the most important pathways correctly. In systems of biological interest, e.g. protein folding, allostery etc., many pathways may arise and may also be important to understand the mechanism. To cope with these problems, we suggest a new method which directly considers the path probabilities. In contrast to Markov chain Monte Carlo, it samples the path space more efficiently and gives a well-defined error. We demonstrate the performance and discuss the insights revealed by adopting the folding of villin headpiece.

BP 19.14 Tue 14:00 P2/3OG

Quantitative analysis of protein binding curves — •Lukas Refisch and Clemens Kreutz — Institute of Medical Biometry and Statistics, Faculty of Medicine and Medical Center - University of Freiburg, Germany

New measurement techniques for the quantification of reaction rate constants are continuously emerging. Usually, densely sampled time courses of labeled or unlabeled protein intensities are measured to observe a change from one equilibrium state which relaxes to another one. Traditional analysis approaches commonly assume simplifications of the underlying effects and select subsets of measured data to perform the analysis on. Instead, we propose using comprehensive ordinary differential equation (ODE) models that describe the entire protein binding process and can therefore be fitted to the full time series of obtained data.

We present advances for the analyses of two different experimental settings (i) microscale thermophoresis and (ii) reflectometric interferometry utilizing ODE models. They explicitly incorporate assumptions about the underlying processes and are fitted directly to the experimental data. These models contain several parameters that are estimated from data, some of them specifying time points at which experimental conditions change. The parameter estimates also contain information about spatial effects, like e.g. the flow of a solution across a microarray which is estimated from time course data. Our approach finds reliable characterization of binding curves and automates the data analysis, thus increasing the rate of data analysis considerably.

BP 19.15 Tue 14:00 P2/3OG

Targeted Molecular Dynamics Calculations of Free Energy Profiles of Gramicidin A Using a Nonequilibrium Friction Correction — •Miriam Jäger, Gerhard Stock, and Steffen Wolf — Albert-Ludwigs- Universität Freiburg

Standard unbiased molecular dynamics (MD) simulations are impractical to sample rare events due to their high computational costs. An economic approach to simulate such processes are biased MD simulations. We here use targeted MD simulations, which apply a moving distance constraint along some prechosen reaction coordinate to enforce rare transitions. Free energy profiles can be calculated on the fly from such simulations by dissipation-corrected targeted MD, which combines a second-order cumulant expansion of Jarzynski's equality with an interpretation within the framework of Langevin equations of motion [1]. We here applied dissipation-corrected targeted MD to potassium diffusion through ion channels, using the Gramicidin A channel as a test system. Performing a non-equilibrium principal component analysis on backbone dihedral angles to separate different protein conformations appearing during the transfer, we find that the dissipation-corrected free energy profiles correspond well to barriers predicted by other methods. Further, the friction profiles give insight into ion-protein and ion-water molecule interactions.

[1] S. Wolf and G. Stock, Targeted molecular dynamics calculations of free energy profiles using a nonequilibrium friction correction, J. Chem. Theory Comput. 14, 6175 (2018).

BP 19.16 Tue 14:00 P2/3OG

Optimizing aerodynamic-lens-stack geometries for nanoparticle injection — Lena Worbs[1,3], •Jannik Lübke[1,2,3], Armando Estillore[1], Amit Kumar Samanta[1], and Jochen Küpper[1,2,3] — [1]Center for Free-Electron Laser Science, Deutsches Elektronen-Synchrotron (DESY), Hamburg, Germany — [2]Center for Ultrafast Imaging, Universität Hamburg, Germany — [3]Department of Physics, Universität Hamburg, Germany

Single-particle imaging (SPI) experiments at x-ray free-electron lasers (XFELs) promise high-resolution-imaging of the structure and dynamics of nanoparticles. By guiding isolated sample molecules to the focus of an XFEL, diffraction patterns of individual particles can be collected. Sufficient amounts of patterns of identical nanoparticles are needed to overcome the inherently small signal-to-noise ratio and reconstruct the underlying 3D structure [1]. To achieve atomic resolution, a beam of identical particles needs to be delivered into the XFEL focus, which necessitates sample-control methods. We develop various control techniques, such as particle beam focusing using fluid dynamics [2], temperature control [3], charge state selectivity using electric fields, and further methods. Here, we present theoretical and experimental studies for improving of aerodynamic-lens geometries [3] to create high-density particle beams for SPI experiments.

[1] M. M. Seibert et al., *Nature* **470**, 78 (2011)
[2] N. Roth et al., *J. Aerosol Sci.* **124**, 17 (2018)
[3] A. K. Samanta et al., *arXiv*:1910.12606 (2019)

BP 19.17 Tue 14:00 P2/3OG

Domain Swapping in Crystallin Proteins Can Drive Early Stages of Cataract Formation — •Govardhan Reddy Patluri and Balaka Mondal — Indian Institute of Science, Bangalore, India

Crystallins (Crys) are densely packed, long-lived eye lens proteins responsible for the ocular functions of the lens. Physicochemical perturbations in the cellular environment disrupt the native state stability of Cry proteins and populate aggregation prone misfolded states. These misfolded states gradually accumulate to produce high molecular weight amorphous aggregates, which scatter visible light resulting in lens opacity or cataract. The molecular mechanism of cataract formation or structure of these aggregation prone precursors remain elusive to date. Using molecular dynamics simulations and coarse-grained protein model of human γC and γD Crys, we identified the aggregation prone misfolded states present in the unfolding pathways of these proteins. We further show that these partially misfolded conformations readily undergo dimerization by domain swapping revealing the early stages of aggregation leading to cataract formation.

BP 19.18 Tue 14:00 P2/3OG

High-yield fabrication of DNA and RNA constructs for single molecule force and torque spectroscopy experiments. — •Flavia Stal Papini, Mona Seifert, and David Dulin — Junior Research Group 2, Interdisciplinary Center for Clinical Research, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Cauerstraße 4, 91058 Erlangen, Germany

Single molecule biophysics experiments have enabled the observation of biomolecules with a great deal of precision in space and time, e.g. nucleic acids mechanical properties and protein*nucleic acid interactions using force and torque spectroscopy techniques. The success of these experiments strongly depends on the efficient design and fabrication of complex nucleic acid structures, as the outcome of the experiment strongly depends on the high quality of the final construct. Though the molecular biology techniques involved are well known, the fabrication of nucleic acid constructs for single molecule experiments still remains a difficult task. We developed new protocols to generate high-yield and high-quality coilable double-stranded DNA and RNA constructs, as well as DNA and RNA hairpins with *500*1000 bp long stems (Papini et al., NAR 2019). A new approach based on single-stranded DNA annealing is presented and its efficiency in the fabrication of complex DNA constructs is shown in magnetic tweezers assays. Our protocols

enable the design of a large range of nucleic acid constructs for single molecule biophysics experiments.

BP 19.19 Tue 14:00 P2/3OG

Temperature controlled high-throughput magnetic tweezers assay for viral RNA-dependent RNA polymerase study — •Mona Seifert[1], Pauline van Nies[1], Flávia Stal Papini[1], Jamie Arnold[2], Minna Poranen[3], Craig Cameron[2], Martin Depken[4], and David Dulin[1] — [1]IZKF, FAU Erlangen-Nürnberg — [2]The University of North Carolina Chapel Hill — [3]University of Helsinki — [4]TU Delft

The viral RNA-dependent RNA polymerase (RdRp) is an essential factor for the virus to establish a successful infection as it generates all viral RNA. As enzymatic kinetic processes follow the Arrhenius law, polymerase nucleotide addition rate is expected to be temperature sensitive. We previously introduced high-throughput magnetic tweezers to study RdRp kinetics using kilobases long templates, i.e. a length similar to the viral genome, with near single base resolution. To perform experiments at in vivo temperature, we developed a temperature controlling system for our magnetic tweezers assay and performed in situ temperature calibration by leveraging the temperature dependence of DNA twist. We applied the temperature controlled setup to study the elongation kinetics of different RdRps at several temperatures and we observed that the increase in temperature correlates with a higher nucleotide addition rate and short pause exit rate, confirming the catalytic nature of these pauses. Non-catalytic backtrack pauses however are temperature insensitive. The assay we present here simultaneously provides high throughput and temperature control, which will be essential for future studies of complex viral replicases.

BP 19.20 Tue 14:00 P2/3OG

Probing Nucleosome Dynamics in Magnetic Tweezers — •Yi-Yun Lin[1], Willem Vanderlinden[1], Lori Van de Cauter[1], Tine Brouns[1,2], and Jan Lipfert[1] — [1]Department of Physics, Nanosystems Initiative Munich, Center for NanoScience, LMU Munich, Amalienstrasse 54, 80799, Munich, Germany — [2]KU Leuven, Division of Molecular Imaging and Photonics, Celestijnenlaan 200F, 3001, Leuven, Belgium

Nucleosomes are the fundamental unit of chromatin. They control eukaryotic genome accessibility and can regulate expression, replication and repair of the genome by organizing chromatin. Multiple factors affect chromatin dynamics and control the unwrapping and assembly of nucleosomes. Lens epithelium-derived growth factor (LEDGF) p75 is a co-activator of general transcription. In vivo LEDGF/p75 can recognize transcriptionally active genomic regions by specific binding of its PWWP domain to tri-methylated histone H3 lysine 36 (H3K36me3). To investigate how LEDGF/p75 affects chromatin structure, we applied single molecule magnetic tweezers. Our results suggest that LEDGF/p75 alters nucleosome unwrapping and inter-nucleosome interactions, and help us understand the cellular mechanisms of LEDGF/p75 as a transcriptional co-activator.

BP 19.21 Tue 14:00 P2/3OG

Deep Learning for DNA Reads through 2D Solid-state Nanopores — •Angel Diaz Carral[1], Chandra Shekar Sarap[1], Ke Liu[2], Aleksandra Radenovic[2], Maria Fyta[1], and Elka Radoslavova[3] — [1]Institute for Computational Physics, Universität Stuttgart, Germany — [2]Laboratory of Nanoscale Biology, Institute of Bioengineering, School of Engineering, EPFL, Switzerland — [3]Fundamental Physics Department, Faculty of Science UNED, Spain

DNA molecules can electrophoretically be driven through nanopores giving rise to measurable electronic current blockades important for DNA sensing. In this work, experimental ionic traces from 2D molybdenum disulfide nanopores DNA translocations are used to train a Deep Learning model for interpreting the DNA events and improving the identification of different nucleotides threading the nanopore. We propose a methodological approach to train a Clustering model for identifying molecular events related to different conformations of DNA nucleotides threading the nanopore. This approach has revealed the efficiency of using the height of the ionic blockade as the training feature. This can lead to a clear clustering of the nanopore events over the use of the traditionally used dwell time. In order to eventually predict the type of molecule threading the pore, the features selected in the clustering analysis are used to train a Convolutional Neural Network capable of optimizing and accelerating the nanopore read-out. Our approach allows for a deep insight into characteristic molecular features in 2D nanopores and provides a feedback mechanism to tune these materials and interpret the experimentally measured signals.

BP 19.22 Tue 14:00 P2/3OG

Avidity of multivalent DNA binding to DNA origami — •Maximilian Voggenthaler[1], Ricarda Berger[1], Joachim Rädler[1], Ralf Jungmann[2], Florian Schüder[2], Alexander Auer[2], Eugene Petrov[1], and Tim Liedl[1] — [1]Department of Physics and Center for Nanoscience, Ludwig Maximillian University, Munich, Germany — [2]Max Planck Institute of Biochemistry, Martinsried, Germany

Multivalent binding is a frequently occurring theme in biological recognition that enables both tight binding and high specificity. DNA nanotechnology employs this concept when higher order assemblies are designed by multivalent hybridization sites. However, the effective binding affinity of multiple linkages with both steric as well as electrostatic constraints has not been studied in a quantitative manner. Here, we study the binding affinity of a double stranded DNA helix with two single stranded overhangs to a DNA origami block equipped with two complementary strands as multivalent receptor. We use fluorescence correlation spectroscopy, thermophoresis, total internal reflection fluorescence microscopy and gel electrophoresis to study avidity as a function of spacing and salt concentration. Our findings are important for better engineering of super selective linkages in origami self-assembly and medical nanoagents.

BP 19.23 Tue 14:00 P2/3OG

In situ magnetic tweezers force calibration for all tether length — •Eugeniu Ostrofet, Flavia Stal-Papini, and David Dulin — FAU, Erlangen, Germany

Magnetic tweezers are a powerful technique to perform high-throughput and high-resolution force spectroscopy measurements at single-molecule level. The camera-based detection of magnetic tweezers enables the observation of hundreds of magnetic beads in parallel, and therefore the characterization of the mechanochemical behavior of hundreds of nucleic acids and enzymes. The accuracy of force spectroscopy measurements relies on a precise force calibration. In magnetic tweezers, the forces are quantified from the lateral fluctuations of the tethered magnetic bead. Such measurements are difficult to perform on short tethers, i.e. less than 4 kbp DNA, and therefore often rely on calibration tables, i.e. magnetic force versus magnets distance, performed using long DNA molecules, i.e. ~8 kbp and longer. However, the bead-to-bead variation in magnetic content leads to force dispersion, which biases the force spectroscopy measurement. To solve this issue, we present a new and simple strategy to perform in situ force calibration for hundreds of tethered magnetic beads simultaneously, for any tether length, and for the whole accessible force range for a given magnets-magnetic bead configuration. We illustrate the usefulness of our approach by characterizing the force dependence of protein-DNA interactions using a DNA hairpin-based force jump assay.

BP 19.24 Tue 14:00 P2/3OG

Optical tweezers and multimodality imaging: a platform for dynamic single-molecule analysis — •Ann Mukhortava, Baerbel Lorenz, Philipp Rauch, and Andrea Candelli — LUMICKS B.V. Amsterdam, Pilotenstraat 51, 1059CH Amsterdam, The Netherlands

The possibility to investigate molecular interactions, structure, and dynamics using single-molecule fluorescence- and force spectroscopy-based methods has led to many new insights over the past decades. Here, we present our efforts in establishing the easy and reliable experimental workflow for further enabling discoveries in the field of biology and biophysics using both the combination of optical tweezers with single-molecule fluorescence microscopy (C-Trap). As a proof of concept, we will discuss an overview of the experimental designs and the workflow for combining FRET with an ultra-stable optical trap for studying binding and colocalization dynamics of histones and a helper protein on DNA and observing protein/DNA hairpin folding dynamics. These experiments show that the technological advances in hybrid single-molecule methods can be turned into an easy-to-use and stable instrument that opens up new venues in many research areas.

BP 19.25 Tue 14:00 P2/3OG

A proof-of-principle set-up linking ion channel conformation and function by combining single-molecule FRET and single-channel recording — •Steven Vanuytsel, Christopher Parperis, and Mark Wallace — Department of Chemistry, King's College London, London, UK

Building a bridge between static high-resolution membrane protein structures and the kinetic information obtained via patch-clamping remains challenging due to significant incompatibilities in the experimental conditions required to measure these two signals. Nevertheless, when successful, such a method would provide a plethora of information by allowing the construction of a molecular movie that links function to conformation.

Optical single-channel recording (oSCR) shifts the measurement of ionic current from an electrical to an optical readout, allowing parallel interrogation of multiple channels simultaneously. Furthermore, shifting from an electrical to an optical set-up allows a straightforward route to measure function and conformation in parallel by interrogating the latter using single-molecule Förster Resonance Energy Transfer (smFRET).

Here, we report on our recent work to establish parallelized smFRET and oSCR recordings in a proof-of-principle set-up that allows control over single-molecule *gating* kinetics of a protein nanopore that stochastically senses fluorescently labelled DNA, thereby allowing us to record well-controlled simultaneous events.

BP 19.26 Tue 14:00 P2/3OG

Modeling meiotic chromosomes - random walk bridges in a confinement — •Tim Klingberg[1,2], Meng Wang[1,2], Xingyu Zhang[1,2], Hui-Shun Kuan[1,2], and Vasily Zaburdaev[1,2] — [1]Friedrich-Alexander-Universität Erlangen-Nürnberg — [2]Max-Planck-Zentrum für Physik und Medizin

The alignment and correct pairing of homologous chromosomes is a crucial step during meiosis. In its early stages, the chromosomes are tethered with their telomeres to the nuclear envelope. Telomers may interact with the cytoskeleton while the fluctuations of chromosomes in the nucleus are affected by the physical properties of the chromatin and the state of the nucleoplasm. Overall, it is largely not understood how the homologous chromosomes manage to align and pair with the exquisite precision and in a short period of time. Our goal is to understand physical limitations of the pairing and homologous search process. To this end, we focus on quantifying possible configurations of tethered chromosomes in the confinement of the nucleus. We use the bead-rod polymer model for numerical simulations and the theory of random walk bridges for analytical calculations. We show that a smaller persistence length leads to smaller polymer fluctuations but also to a higher entropic force acting on tethered ends. We argue that such an optimization problem may determine physical properties of chromosomes in meiosis.

BP 19.27 Tue 14:00 P2/3OG

Bayesian gradient-sensing in the presence of noise — •Maja Novak and Benjamin M. Friedrich — TU Dresden (CFAED, PoL), Dresden, Germany

Chemotaxis, the navigation of biological cells in external concentration fields, guides foraging bacteria to food patches, immune cells to inflammation sites, or sperm cells to the egg. Chemotaxis strategies must be adapted to sensing and motility noise, inevitable at the microscopic scales of cells, by optimal filtering of chemosensorial input and choice of chemotaxis strategy. A key question is: how to combine most recent and previous sensory input?

We present an information-theoretic framework of optimal gradient-sensing and chemotactic navigation, based on Bayesian sequential estimation. Remarkably, the Bayesian strategy optimally combines "temporal comparison" and "spatial comparison", two distinct gradient sensing strategies employed by biological cells. The width of likelihood estimates of individual agents provides a reliable proxy for the dispersion of direction angles of an ensemble, reflecting the consistency of our approach.

We investigate a search strategy that maximizes the expected information gain in each time step, generalizing the previously proposed "infotaxis" strategy [1] to the case of multiple sensors. We find that agents move slower at locations with low local signal-to-noise ratio to increase the fidelity of gradient measurements.

[1] Vergassola et al. 2007

BP 19.28 Tue 14:00 P2/3OG

Pitfalls in statistical data analysis — •Thomas John and Christian Wagner — Experimentalphysik, Universität Saarland

During your studies, you learned various ways of evaluating and displaying data. We would like to introduce some further statistical evaluation methods. After the presentation, you may no longer generate histograms with bars and you will never again try to fit a Gaussian curve to an empirical probability distribution. Even if both methods are intuitively clear, it delivers less precise results as more indirect methods. As keywords, we would mention: kernel density estimators and fitting to empirical cumulative distribution functions.

[1] D. W. Scott, Multivariate Density Estimation: Theory, Practice and Visualization, Wiley Series in Probability and Statistics 2015.

BP 19.29 Tue 14:00 P2/3OG

Tracing non-equilibrium signatures in time series obtained from biological systems — •Samuel Salinas-Almaguer, Florian Rehfeldt, and Matthias Weiss — Experimentalphysik I, Universität Bayreuth

Revealing whether a stationary time series originated from an out-of-equilibrium system is, in general, a non-trivial task. While living biological systems surely are far away from thermal equilibrium, this might not be directly visible in a given experimentally acquired time series of some accessible observables. Therefore, probing whether time reversibility and detailed balance are broken in such time series, and quantifying a putative net entropy production is mandatory in the analysis. Using analytical and numerical toy systems as well as experimental data acquired in living cells, we compare different methods to uncover and quantify the non-equilibrium nature of time series.

BP 19.30 Tue 14:00 P2/3OG

Theory of Active Transport by DNA-relaying — •Christian Hanauer[1,2], Silke Bergeler[1], Erwin Frey[1], and Chase Broedersz[1] — [1]Arnold Sommerfeld Center for Theoretical Physics and Center for NanoScience, Ludwig-Maximilians-Universität, 80333 Munich, Germany — [2]Max Planck Institute for the Physics of Complex Systems, 01187 Dresden, Germany

Robust and faithful segregation of chromosomes is essential for the replication of bacterial cells. In recent years, experiments have identified the biochemical and mechanical properties of the chromosome as key ingredients for active transport in bacterial cells. Intracellular cargos, such as chromosomal ori, are thought to use chromosome fluctuations to transport themselves along a guiding concentration gradient of DNA-binding ATPases. However, a theory for this DNA-relaying is still lacking. Here, we present a theoretical framework that allows us to calculate the relaying force on the cargo. We test our predictions by Brownian Dynamics simulations. Our analytical model provides insight into how the system parameters determine this active transport mechanism.

BP 19.31 Tue 14:00 P2/3OG

Maximum entropy model for the spatial organization of the E. coli chromosome — •Lucas Tröger, Joris Messelink, and Chase Broedersz — LMU, Munich, Germany

Bacterial chromosomes lack many proteins that are central for the spatial structuring of eukaryotic DNA. Despite this, bacterial chromosomes are not just randomly folded within the cells; recent Hi-C experiments that quantify spatial interactions between pairs of regions of the chromosome reveal a high degree of organization. However, extracting a 3D model from such data remains a major challenge. To address this problem, we use a statistical mechanics approach. Specifically, we infer a least-biased 3D representation of the chromosome of Escherichia coli by developing a maximum entropy model based on Hi-C data. This allows us to derive the full joint probability distribution of spatial chromosome configurations in E. coli. From this, novel organizational features can be extracted.

BP 19.32 Tue 14:00 P2/3OG

Reconciliation of controversial death pattern of starved cells — •Hamid Seyed-Allaei, Elena Biselli, Zara Gough, Felix Fleschhut, and Ulrich Gerland — Department of Physics, Technical University, Munich, Germany

During carbon starvation of isothermal batch culture of E. Coli, viability of the cells as a function of time decreases exponentially for approximately 10 days. This behavior is the result of a collective behavior where living starved cells use the leaked nutrients from dead cells and can be explained by the balance of the nutrient flux of the leaking dead cells and the maintenance of the living starved cells. The single cell level study of isolated starved cells, however, indicates that the death rate of the cells follow the Gompertz law of mortality which relates the death rate to the age. The greater the time since a cell has received nutrients, the higher its death rate. The observation of Gompertz law of mortality in isolated starved cells with increasing death

rate over time seems controversial with the observation of exponential decay with a constant death rate in isothermal batch culture. In this study we reconcile these two seemingly controversial results by the help of theoretical modeling.