BP 21: Poster IIIb

Computational Biophysics, Protein Structure and Dynamics, Synthetic Life-like Systems and Origins of Life

Time: Wednesday 11:00–14:30 Location: Poster C

BP 21.1 Wed 11:00 Poster C

Contact Maps in RNA Structure Prediction — •Christian Faber, Utkarsh Upadhyay, Benjamin Kotton, and Alexander Schug — Forschungszentrum Jülich, Jülich, Germany

Predicting the spatial structure of non-coding RNA (*ncRNA*) is an important task for understanding fundamental processes in living nature. Physical force fields are used to infer the structure from a sequence using simulations on high-performance computers. However, the best results are obtained by incorporating evolutionary data via a binary mapping of contacts. The same phenomenon can be seen in protein structure prediction, where the groundbreaking *AlphaFold2* also incorporates this step. Much work has been done in the past to optimise the algorithms for simulations, but what are good contacts and why are these contacts important in the first place is an unsolved puzzle. To find answers, we tried different contact map topologies on a well-defined test set of *ncRNA*s. We also looked at using fewer, but wisely chosen contacts and how this can improve prediction. To obtain our results, we ran many simulations for comparison on the high performance cluster *JUWELS* with the RNA folding software *SimRNA* and used convolutional neural networks (*CNN*) to select contacts. Our results suggest that it is important to pay more attention to the selection of contacts, especially when developing machine learning algorithms. Furthermore, good contacts not only ensure faster folding in the simulation, they are actually essential for correct folding. It seems that it is the additional constraints that bring the physical force field into the more correct form.

BP 21.2 Wed 11:00 Poster C

Expanding the scope of bulk experiments by ensemble signal decomposition — •Nadin Haase, Simon Christ, and Sophia Rudorf — Institute of Cell Biology and Biophysics, Leibniz University Hannover, Germany

Compared to single-molecule experiments, ensemble or bulk methods are relatively time- and cost-efficient, and signal decomposition can help to expand their scope. Previously, we developed a detailed Markov model that incorporates the most central aspects of mRNA translation. Recently, we used our Markov model of translation to decompose fluorescent signatures of translating ribosomes in in-vitro ensemble experiments, revealing hidden kinetic information on the early phase of mRNA translation. Here, we investigate the limits of this method in terms of translation rates and the number of consecutive elongation cycles. Specifically, we show that the decomposition of a noisy ensemble signal generated by ribosomes translating mRNAs with more than just 5 codons represents already an ill-posed problem. We demonstrate that this problem can be treated with regularization to obtain translation state-specific information. Our results may aid in the extraction of information from bulk experiments to study the dynamics not only of translating ribosomes but also of other processive enzymes.

BP 21.3 Wed 11:00 Poster C

Implementation and Implications of a Lattice Model for the Understanding of Lipid Rafts in Membranes — •Simon Kellers, Fabian Keller, and Andreas Heuer — Institute of Physical Chemistry, University of Münster, Corrensstrasse 28/30, 48149 Münster, Germany

Based on comprehensive and extensive MD simulations of lipid bilayers, consisting of unsaturated, saturated lipids and CHOL [1], an existing lattice model [2][3] has been extended to incorporate the effects of CHOL on lipid ordering, relevant for the formation of lipid rafts. The MD simulation results suggest that interactions strongly depend on local CHOL concentrations. Furthermore, both lipids and CHOL are surrounded by four neighbors each, implying a square lattice model with a subgrid for CHOL.

The model relies solely on the enthalpic data from simulations and requires no phenomenological input. Additionally, as key variable it takes the order parameter of the lipids into account. The entropic contributions of the individual chains are adjusted through an iterative Boltzmann procedure, allowing for a clear separation and investigation of enthalpic and entropic effects. Due to the coarse-grained nature of the model, extensive and prolonged simulations of large systems will be feasible, allowing for the investigation of, e.g., the emergence of phase separation or phase transitions. [1] Keller, F; Heuer, A; *Soft Matter* **2021**, 25, 17 [2] Hakobyan, D; Heuer, A; *J. Chem. Phys.* **2017**, 6, 142 [3] Hakobyan, D; Heuer, A; *J. Chem. Theory Comput.* **2019**, 11, 15

BP 21.4 Wed 11:00 Poster C

Reversible formation of von willebrand factor platelet aggregates in blood flow — •Alper Topuz, Gerhard Gompper, and Dmitry A. Fedosov — Theoretical Physics of Living Matter, Institute of Biological Information Processing (IBI-5), Forschungszentrum Jülich, 52425, Jülich, Germany

Blood is a complex fluid that comprises of red blood cells, platelets, and various proteins suspended in plasma. Platelets and von Willebrand factor (vWF) proteins play a pivotal role in hemostasis (blood clotting). At high shear stresses, vWF molecules can stretch and become adhesive, so that they form bonds with encountered platelets, resulting in the formation of vWF-platelet aggregates. We employ hydrodynamic simulations together with explicit deformable cells and stretchable vWF polymers to model this aggregation-disaggregation process in blood flow. The aggregate formation is found to primarily occur near walls due to large wall-shear stresses. After reaching a critical size, the aggregates migrate away from the walls toward the vessel center. Under healthy conditions, vWF-platelet aggregates are reversible, as they dissociate again when the surrounding shear stresses become small. We explore different binding properties between vWF and platelets, which affect the reversibility of the aggregates and investigate the corresponding formation and disassociation characteristics of the aggregates. Understanding the aggregation process in blood flow is crucial in several pathologies such as thrombi formation and possible vessel blockage.

BP 21.5 Wed 11:00 Poster C

Modeling contraction of heart muscle tissue — •Michael Würriehausen[1], Volker Walhorn[1], Andreas Dendorfer[2], Hendrik Milting[3], and Dario Anselmetti[1] — [1]Bielefeld Univsersity — [2]Ludwig-Maximilians-University Munich — [3]Heart- and Diabetes Center Bad Oeynhausen

Computational modeling of heart muscle contractions is crucial for a better understanding of mechanical and electrical signals involved rhythmic dynamic of cardiac muscle dynamics. Two major groups of muscle models exist -the Hill-type and the Huxley-type muscle models, both of which are presented in this work. Hill-type models primarily use mechanical analogies such as an active force generating actuators, passive spring-like elements and passive viscous-damping elements to describe the whole muscle as a monolithic system. In contrast, Huxley models consider biophysical processes at the cellular level based on the actin myosin cross-bridge kinetics.

In the Huxley model we have designed, the muscle is divided into segments consisting of individual muscle cells, each of which has its own set of elements for reproducing muscle contraction. Both, Huxley and Hills models include the cardiac action potential and intracellular calcium concentration as key factors for a new approach in the muscle activation dynamics. The models can provide information about the relationship between heart muscle diseases and physiological parameters that are used in the numerical calculation to simulate muscle contraction.

BP 21.6 Wed 11:00 Poster C

Red blood cells adhesion and its Influence on capillary Flow in-vivo Microvasculature: A Simulation Study — •Mohammed Bendaoud[1,2], Alexis Darras[1], Yazdan Rashidi[1], Christian Wagner[1], and Chaouqi Misbah[2] — [1]Department of Experimental Physics, Saarland University, Saarbruecken 66123, Germany — [2]Université Grenoble Alpes, CNRS, LIPhy, F-38000 Grenoble, France

Red blood cells (RBCs) can aggregate and disassociate reversibly under normal physiological conditions. Cardiovascular diseases like hypercholesterolemia and diabetes have been associated with increased RBC aggregation. Fibrinogen is the main cause of this aggregation.

The normal range for human fibrinogen levels is 1.8 - 4 mg/ml. Diabetes can cause stable aggregates to form, leading to vessel blockages. This study aims to investigate the influence of adhesion between red blood cells and between RBCs and vessel walls on their behaviour in blood vessel networks. This encompasses RBC and plasma distribution, blood flow rate, and RBC lingering. Studying adhesion's impact on RBC behaviour is crucial for comprehending the intricate dynamics of blood flow in microvessels. We employ the lattice Boltzmann method in 2D to simulate RBCs behaviour with adhesion in a complex vascular network.

BP 21.7 Wed 11:00 Poster C

Simulating tumor-induced angiogenesis using Cells in Silico — •Eric Behle[1], Julian Herold[2], and Alexander Schug[1] — [1]NIC Research Group Computational Structural Biology, Jülich Supercomputing Centre, Jülich Research Center, Jülich, Germany — [2]Steinbuch Centre for Computing, KIT, Karlsruhe

Cancer remains an inadequately understood ailment affecting humanity. Its treatment poses a challenge due to tumor variability and a tumor's impact on the surrounding environment. Tumor-induced angiogenesis is a concerning aspect of the disease. Here, a hypoxic tumor secretes growth factors, which prompts nearby blood vessel branching and successive growth toward the tumor. To study this process on a computational level, we turned to Cells in Silico (CiS), a high performance framework for large-scale tissue simulation previously developed by us. Combining a cellular Potts model and an agent-based layer, CiS is capable of simulating tissues composed of tens of millions of cells, while accurately representing many physical and biological properties. Our ultimate objective is to construct a cellular digital twin of a tumor, and integrating a realistically evolving nutrient environment is crucial. Hence, we have implemented tumor-induced blood vessel growth into CiS, and have studied the behavior of tumors placed in different environments. With this we aim to explore questions regarding hot spots for tumor growth within the body.

BP 21.8 Wed 11:00 Poster C

Developing coarse graining RNA force fields via Machine Learning — •Anton Dorn[1] and Alexander Schug[1,2] — [1]Jülich Supercomputing Centre, Jülich, Germany — [2]Steinbruch Centre for Computing, Karlsruhe, Germany

In Protein structure prediction there have been massive improvements recently due to deep learning driven exploration of the rich experimental data. A direct transfer, however, of these methods to RNA structure prediction is impossible due to much sparser experimental data for RNA. Still, the combination of molecular force fields with constraints derived from statistical analysis of genomic data such as direct coupling analysis can lead to good quality structure predictions also for RNA. Here, we want to optimize the accuracy of the employed coarse-grained RNA force field for the molecular simulations by employing machine learning techniques. The data sparsity can here be alleviated by building on established atomistic RNA force fields. In a first step we show the viability of this approach by focusing on small RNA molecules in Molecular Dynamics simulations. We explore different bead numbers for the coarse graining to determine the best approximation.

BP 21.9 Wed 11:00 Poster C

Flexible patchy particles for modelling biomolecular condensates — •Alena Taskina[1,2], Simon Dannenberg[1], and Stefan Klumpp[1,2] — [1]Georg August Universität, Göttingen, Germany — [2]Max Planck School Matter to Life

Biomolecular condensates play a pivotal role in the spatial organization within cells. They form by liquid-liquid phase separation (LLPS), based on multivalent, non-specific interactions among proteins. The patchy particle model, comprising cores with isotropic repulsive potential and patches with attractive potential, captures the process of LLPS. In our study, we modify the current model by allowing patches to move laterally around the core. This refinement mimics the flexibility of protein domains. We investigated the phase behavior, connectivity, dynamics, and structural characteristics of the condensates. Increasing flexibility leads to a lower critical temperature, in gas-liquid coexistence curves, and thus a decreased stability of the condensate. The reason behind this decreased stability appears to be the dynamic nature of the bonds between patches, which results in fewer bonds being formed at certain temperatures. Furthermore, we observed that these more dynamic bonds contribute to an increased diffusivity of the condensates. Despite their reduced stability, condensates with more flexible patches were found to have a higher density that can be attributed to a less pronounced local ordering within the system, allowing for a more efficient packing of particles.

BP 21.10 Wed 11:00 Poster C

Free energy calculations of drug permeation through the bacterial outer membranes — •Vasily Unguryan and Jochen Hub — Saarland university, Saarbrücken, Germany

The development of bacterial resistance to antibiotics requires ongoing efforts to find new drugs. For the class of Gram-negative bacteria, their complex outer membrane represents a first and highly selective barrier on the cell-entering pathway for potential drug molecules. The outer leaflet of the membrane is mainly composed of lipopolysaccharides, whose chemical complexity leads to slow lateral diffusion and tight packing compared to phospholipid membranes, thus imposing poor uptake of many drug candidates.

Molecular dynamics simulations may, in principle, rationalize the low permeability of the outer membrane, for instance, by computing the free energy profile for drug permeation along the membrane permeation pathway. Unfortunately, common umbrella sampling simulations, widely used to compute free energy profiles, converge poorly for complex systems such as outer membrane models. In this project, we combine different enhanced sampling techniques to overcome such challenges, with the aim of deriving both free energy and diffusivity profiles for the permeation of bulky drug-like molecules across the outer membrane.

BP 21.11 Wed 11:00 Poster C

Dynamical and kinetic assessment of nucleic acid systems by CG simulations — •Lorenzo Petrolli, Manuel Micheloni, and Giovanni Mattiotti — Physics Department, University of Trento - via Sommarive, 14 I-38123 Trento, Italy

The in silico characterisation of nucleic acids at the molecular scale by Molecular Dynamics (MD) techniques has been extremely insightful in depicting the essential dynamics underlying a variety of biological activities. To relieve the numerical overhead associated with MD simulations of nucleic acids at the atomistic scale, coarse-grained (CG) force fields have been developed, such as oxDNA [1], that capture the global behaviour of nucleic acids, while keeping an appropriate level of resolution accounting for sequence-specific thermodynamic properties.

Here, we leverage the oxDNA force field and address two significant biological scenarios. On one hand, we characterise the equilibrium dynamics of a viral RNA fragment - and the evolution of the secondary and tertiary motifs thereof. On the other hand, we assess the kinetics of the DNA disruption by double strand breaks on circular DNA molecules, expanding on an earlier work [2], and describe the implications on the experimental characterization of the effects from cell irradiation.

[1] Snodin et al., J. Chem. Phys. 2015; [2] Micheloni et al., Biophys. J. 2023

BP 21.12 Wed 11:00 Poster C

A Bio-inspired Agent-based Model for Collective Shepherding — •yating zheng[1,2] and pawel romanczuk[1,2] — [1]Humboldt-Universität zu Berlin — [2]Research Cluster of Excellence 'Science of Intelligence'

Collective shepherding is a general control method for a swarm of intelligent agents to control other self-organized moving agents. The shepherding behaviour resembles prosperous animal behaviours, such as prey and predator, collective foraging and flocking behaviour and integrates their intrinsic qualities. However, most shepherding algorithms ignore the natural features of animal interactions and are limited to using one single shepherd. We propose an agent-based model to solve the shepherding problem with multiple shepherds. We first explore and compare different communication networks among sheep. Then we investigate the emerging coordination mechanism among shepherds and the related factors. Our model provides a potential method to control a heterogeneous swarm of robots.

BP 21.13 Wed 11:00 Poster C

Application of similarity measures to MD simulation data — •Fabian Schuhmann[1], Leonie Ryvkin[2], James D. McLaren[3], Luca Gerhards[3], and Ilia A. Solov'yov[3] — [1]University of Copenhagen, Copenhagen, Denmark — [2]Technische Universiteit Eindhoven, Eindhoven, Netherlands — [3]Carl von Ossietzky Universität Oldenburg, Oldenburg, Germany

Biological processes involve movements across all measurable scales, which must be analyzed and understood to derive Nature's reasoning and understand the studied object's potential function. Especially in molecular dynamics simulations, considerable resources are allocated to get a picture of the motion of a protein.

While one can easily compare a protein structure to a reference employing tools like the Root Mean Square Deviation, methods need to become more involved to compare two whole trajectories. In a stop-motion movie, how does one spot the difference among thousands of atoms, all wiggling and moving?

We have gathered eight different similarity measures in an easy-to-use Python package called SiMBols. SiMBols includes the Hausdorff distance, the (weak) Fréchet distance, dynamic time warping, Longest Common Subsequence, a difference distance matrix approach, Wasserstein distance, and Kullback-Leibler divergence and combines them in a unified way.

Employing a case study, we will use the measures. We will find that the different similarity measures differ in their computation time and the research question they might answer.

BP 21.14 Wed 11:00 Poster C

Computational Approaches to Liquid-Liquid Phase Separation of Partially Disordered RS-Proteins — •Yannick Witzky[1], Arash Nikoubashman[1,2,3], and Friederike Schmid[1] — [1]Institute of Physics, JGU Mainz, Germany — [2]Leibniz-Institut für Polymerforschung, Dresden, Germany — [3]Institut für Theoretische Physik, TU Dresden, Germany

RS-proteins are RNA binding proteins that shape photomorphogenesis in plants by regulating alternative splicing events. Their light dependent appearance within nuclear speckles connects this alternative splicing function to their likely ability to induce or take part in liquid-liquid phase separation (LLPS). These divergent tasks of specific RNA binding and LLPS are reflected by the dual composition of RS proteins: folded domains, that contain the functionally important RNA binding sites, are complemented by intrinsically disordered regions (IDRs) which are common players in LLPS. To study the influence of the highly charged IDRs and the post translational phosphorylation of their amino acids on LLPS, we use replica exchange molecular dynamics with common IDP models [1,2] for enhanced sampling.

[1] Tesei et al. (2022) Open Research Europe, 2(94), 94. [2] Rizuan et al. (2022) J Chem Inf Model 62(18), 4474-4485.

BP 21.15 Wed 11:00 Poster C

Novel DNA-based nano force sensor to measure the clustering force of membrane-proteins — •Neda Rahmani and Weria Pezeshkian — Niels Bohr International Academy, Niels Bohr Institute, University of Copenhagen, Copenhagen, Denmark

Membrane-mediated clustering forces contribute to biological processes on cellular membranes, such as intracellular trafficking and signaling; they have their origin in a protein's ability to physically perturb the membrane's relaxed state. Clustering of extracellular ligands and proteins on the plasma membrane is required to perform specific cellular functions, such as signaling and endocytosis. Attractive forces that originate in perturbations of the membrane*s physical properties contribute to this clustering. The bacterial Shiga toxin (STxB) interacts with its cellular receptor, the glycosphingolipid globotriaosylceramide (Gb3 or CD77), as a first step to entering target cells. Previous studies have shown that toxin molecules cluster on the plasma membrane, despite the apparent lack of direct interactions between them. A membrane fluctuation-induced force generates an effective attractive force at separations around 1 nm, remains strong at distances up to the size of toxin molecules (several nanometers), and persists even beyond. This force is predicted to operate between manufactured nanoparticles providing they are sufficiently rigid and tightly bound to the membrane. In this project, we are going to design a nano force sensor to detect and calculate the clustering force between STxB bounded to a bilayer through GB3, and the suggested device is a DNA-based tweezer.

BP 21.16 Wed 11:00 Poster C

Using molecular dynamics simulation as a microscope of the peptide's translocation process through an aerolysin nanopore — •Michel Mom[1], Kumar Sarthak[2], Aleksei Aksimentiev[2], and Christian Holm[1] — [1]Institute for Computational Physics, University of Stuttgart, Stuttgart, Germany — [2]Beckman Institute for Advanced Science and Technology and Department of Physics, University of Illinois at Urbana- Champaign, Urbana, United-States

In recent years, a cost-effective method was developed to sequence DNA and RNA with high precision at the single-molecule level. This research project aims to extend this sequencing method to proteins and peptides which is still in the early stages. The method involves placing the analyte in an electrolyte solution separated by a lipid membrane which contains an implemented biological nanopore. An applied electrical voltage drives ion and analyte transport through the nanopore. The presence of the analyte in the nanopore results in a temporary reduction of the open-pore current, from which one can draw valuable conclusions about the structure of the investigated protein. To understand the effects of the analyte transport on the ionic flow at the atomic level, we conduct molecular dynamics simulations. Our results offer valuable insights into the translocation process of the peptide, revealing regions of resistance and predicting the residual ionic current. This poster demonstrates our application of molecular dynamics simulations to translocate peptides through a novel aerolysin nanopore variant, showcasing a proof of concept for future studies.

BP 21.17 Wed 11:00 Poster C

Reaction-diffusion models for growing skin patterns in cuttlefish — •Sigrid Trägenap, Feron Basoeki, and Matthias Kaschube — Frankfurt Institute for Advanced Studies

Cuttlefish exhibit unparalleled camouflage abilities supported by an array of chromatophores on their skin. These abilities persist throughout their lifespan, despite an at least 100-fold increase in body size and and chromatophore numbers. Recent advances (Reiter et al., Nature, 2018) allowed the identification and tracking of the chromatophore array over months. Their analysis revealed a typical distance between nearest neighbour chromatophores with unique local irregularities and that new chromatophores arise in gaps in the existing array. However, how this local irregularity arises and what local features predict chromatophore insertion remain unclear. Here, we address these questions by describing the development of the chromatophore array as an activator-inhibitor reaction-diffusion model on a growing domain. This can account for the experimentally observed distribution in distances between chromatophores, suggesting that a regular steady state is not reached due to the continuous growth. We find that chromatophores are inserted at the global inhibitor minima, predicting insertion locations for nonuniform growth. Additionally, such a model predicts an increased distance to the nearest neighbor chromatophore with development, explained by the overlapping ranges of Turing instabilities. This minimal model offers experimentally testable predictions and facilitates the identification of additional components necessary to fully describe chromatophore array development.

BP 21.18 Wed 11:00 Poster C

An order-disorder transition in cortical development — •Lorenzo Butti[1], Nathaniel Powell[2], Bettina Hein[1], Deyue Kong[1], Jonas Elpelt[1], Haleigh Mulholland[2], Matthias Kaschube[1], and Gordon Smith.[2] — [1]FIAS, Frankfurt am Main, Germany. — [2]University of Minnesota, Minneapolis, USA

How neural activity in cortex is shaped by the underlying neural circuitry remains poorly understood. Recent experiments in ferrets have shown that at an early stage in development, spontaneous activity exhibits a modular correlation structure that is similar to a quantitative degree across multiple cortical areas (including both sensory and higher association areas) [1].

In this work, we investigate how this correlation structure evolves over the course of development in different cortical areas. In all areas we observed a transition from an ordered, modular organization to a more fine-scaled, disordered organization.

To explain these results, we study a linear recurrent neural network model.* Assuming the recurrent interactions follow a local excitation and lateral inhibition (LELI) scheme, the model is able to reproduce the modular structure of spontaneous activity we observe in the early cortex[2]. We then analyse different scenarios of possible network changes and we find that an effective weakening of recurrent connections over development is a major factor affecting the degree of modularity and how it changes across development.

[1]https://www.world-wide.org/cosyne-22/universality-modular-correlated-networks-5a1134a0 [2]Smith et al., 2018

BP 21.19 Wed 11:00 Poster C

Stability of the Pore Structure of α-Latrotoxin and the Unusual Ion Transport Mechanism through a Synaptic Membrane — •Azadeh Alavizargar and Andreas Heuer — Institute

of Physical Chemistry, University of Muenster, Corrensstr. 28/30, 48149 Muenster, Germany

Latrotoxins (LaTXs) are presynaptic pore-forming neurotoxins found in the venom of Latrodectus spiders, known as black widows. Through the binding of LaTXs to specific receptors on the surface of neuronal cells, neurotransmitters are released by the formation of Ca2+-conducting tetrameric pores inside the membrane. The cryo-electron microscopy pre-pore and the pore structure of the α-LaTX has been resolved by the group of Christos Gastogiannis. However, the structure of the membrane part has not been characterized so far. Thus, the mechanism of ion transport through the membrane is still unclear.

Therefore, in this work we study the pore structure of α-LaTX, starting from the AlphaFold prediction, via molecular dynamics (MD) simulations also using Metadynamics. It turns out that the N-terminal is composed of a stable coiled-coiled bundle and a complex membrane-protein part. Specifically, we study the ion transport of Na+ and Ca2+ ions across the membrane. Surprisingly, the coiled-coiled region is not involved in the ion transport and the ions are attracted and finally crossed only through its membrane part. These results provide crucial insights towards the understanding of the mechanism of the LaTX family of neurotoxins.

BP 21.20 Wed 11:00 Poster C

Modelling contrast-variation SAXS experiments by explicit-solvent molecular dynamics — •Noora Aho and Jochen Hub — Theoretical Physics and Center for Biophysics, Saarland University, Saarbrücken, Germany

Small angle X-ray scattering (SAXS) has established its role in structural biology during the last decades, providing information on the shape, interactions and large-scale conformational transitions of biomolecules in solution. In addition, so called contrast-variation SAXS, where the scattering data is recorder at multiple solvent electron densities, adds the possibility to measure electron densities of biomolecular assemblies enabling the visualisation of distinct biomolecules. The interpretation of experimental SAXS data requires the accurate calculation of SAXS curves from structural models. To achieve this, explicit-solvent molecular dynamics (MD) is a powerful method, taking into account both the atomistic accuracy and correct thermal fluctuations in the scattering curve calculations.

In this work, our aim is to expand the application of explicit-solvent MD simulations from conventional SAXS to contrast-variation SAXS experiments. We model the ferrichrome membrane transporter protein FhuA in the presence of lanthanide contrast agents in explicit solvent and calculate corresponding SAXS curves using MD simulations. In addition to supplementing experimental SAXS data for the specific protein, our simulations serve as an example of the possibilities of explicit-solvent MD in interpretation of advanced SAXS experiments.

BP 21.21 Wed 11:00 Poster C

Machine Learning Guided RNA Structure Prediction — •Utkarsh Upadhyay[1], Oskar Taubert[2], and Alexander Schug[1] — [1]Jülich Supercomputing Centre, Germany — [2]Karlsruher Institut für Technologie, Germany

For around 50 years, the primary focus of genomic research has been the development of efficient and accurate methods to predict the structure of proteins, which led to the birth of better sequencing techniques and databases. About 98% of the human genome(RNA, DNA) during this action was overlooked. However, In the past few years, studies have revealed the existence of many non-coding RNAs which catalyse various biological processes; to understand these roles better, we require the appropriate structure of RNAs. Recent years have led to breakthroughs in protein structure prediction via Deep Learning. The scarcity of RNA structures, however, makes a direct transfer of these methods impossible. Here, we present machine-learning techniques that can work with limited training data. We predict contact maps as a proxy to understand and predict RNA structure, they provide a minimal representation of the structure. We have worked on methods that took accuracy from 47%(DCA)[1] to 77%(CoCoNet)[2] and now to 87%(Barnacle)[3] i.e. doubling accuracy while reducing false positives by five-fold. Further, we are working on developing language models that can make use of large sequence databases and provide more structural insights. We are confident that this remarkable progress will reduce the sequence-structure gap for RNA.

BP 21.22 Wed 11:00 Poster C

A NAP-XPS-study on X-ray radiation damage: Chemical changes to Gene-V Protein — •Dorothea C. Hallier[1,2,3], Jörg Radnik[2], Paul M. Dietrich[4], Harald Seitz[1,3], and Marc Benjamin Hahn[2] — [1]Fraunhofer Insitute for Cell Therapy and Immunology, Branch Bioanalytics and Bioprocesses, Potsdam, Germany — [2]Federal Insitute for Materials Research and Testing BAM Berlin, Berlin, Germany — [3]Univerity of Potsdam, Institute for Biochemistry and Biology, Potsdam Germany — [4]SPECS Surface Nano Analysis GmbH, Berlin, Germany

Single-stranded DNA-binding proteins such as Gene-V Protein (G5P/GVP) are involved in maintaining the DNA metabolism in cells. This is essential for cell viability, especially after exposure to ionizing radiation, i.e. after radiation therapy in cancer treatment. X-ray photoelectron spectroscopy (XPS) was used to analyze the chemical damage of ionizing radiation to G5P itself. Direct and indirect damage was detected through combined vacuum XPS and near-ambient pressure (NAP) XPS measurements under water atmosphere. A strong increase of protein damage was observed in water as compared to vacuum.

BP 21.23 Wed 11:00 Poster C

Length Scale Selection Through Mechano-Chemical Coupling — •Antonia Winter[1], Yuhao Liu[1], Alexander Ziepke[1], George Dadunashvili[1], and Erwin Frey[1,2] — [1]Arnold Sommerfeld Center for Theoretical Physics and Center for NanoSciences, Ludwig-Maximilians-Universität München, Theresienstraße 37, 80333 Munich, Germany — [2]Max Planck School Matter to Life, Hofgartenstraße 8, 80539 München, Germany

The formation of spatial and temporal patterns is an essential part of being a living organism. Control of the length scales of patterns is a key aspect of the robust and reproducible biological function of the organisms, which leads to the question of how this pattern length scale can be controlled. One possible mechanism is mechano-chemical coupling between curvature-inducing proteins and the deformation of membranes. We investigate a minimal system combining geometric membrane-mediated coupling and protein-protein interactions. In our theoretical framework, the dynamics of proteins are characterized by a Flory-Huggins energy capturing their interactions on a membrane manifold, while the fluid-elastic membrane is described by a Canham-Helfrich energy wherein proteins induce spontaneous curvature of the membrane. As a result, we obtain three different phases: A fully phase-separated system, a spatially homogenous regime, where the geometry suppresses the protein aggregation, and an interrupted coarsening regime, where the length scale of the resulting pattern is determined by the balance between the cost of protein mixing and the membrane curvature in the free energy.

BP 21.24 Wed 11:00 Poster C

Dramatic differences between the structural susceptibility of the S1 pre- and the S2 postfusion states of the SARS-CoV-2 spike protein to external electric fields revealed by molecular dynamics simulations — •Alexander Lipskij — Theoretical Physics and Center of Interdisciplinary Nanostructure Science and Technology, FB10

In its prefusion state, the SARS-CoV-2 Spike protein (S) is metastable, which is considered to be an important feature for optimizing or regulating their functions. Binding of its S1 subunit (S1) with the ACE2 receptor causes dramatic conformational change in the S protein where S1 splits from the S2 subunit, which then penetrates the membrane of the host cell, promoting the fusion of the viral and cell membranes resulting in the infection of the host cell. In a previous work, we showed using large scale molecular dynamics simulations that the application of external electric fields (EF) induce drastic changes and damage in the receptor-binding domain (RBD) of the wild type S protein, as well of the Alpha, Beta and Gamma variants, leaving a structure which cannot be recognized any more by ACE2. In this work we extend the study to Delta and Omicron and confirm the high sensitivity and extreme vulnerability of S to moderate EF, and we show that, in contrast, the postfusion state of the S protein does not suffer structural damage even if electric field intensities four orders of magnitude higher applied. As a consequence, these results provide a solid scientific basis for confirming the metastability roots of the SARS-CoV-2 S protein, which is susceptible to damage by EF, in the prefusion state.

BP 21.25 Wed 11:00 Poster C

Finding (Un)binding Pathways in Protein-Ligand Systems — •Miriam Jäger and Steffen Wolf — Biomolecular Dynamics, Institute of Physics, University of Freiburg, Hermann-Herder-Str. 3, 79104 Freiburg, Germany

Understanding dynamics and free energy landscapes of ligand association and dissociation from proteins is hampered by the slow timescales of these transitions. To enhance transition sampling we enforce ligand unbinding from a protein by applying dissipation-corrected targeted MD (dcTMD) simulations, which enforce a moving distance constraint along a pre-chosen reaction coordinate. Using a naive biasing coordinate, ligand unbinding occurs via different pathways, which need to be identified to carry out a dissipation correction. However, uncovering the different pathways along complex reaction coordinates presents a challenge. To address this challenge, we utilize the Streptavidin-biotin complex as test system. Employing various distance measures as input features to cluster similar unbinding trajectories, we aim to reconstruct unbinding pathways and connecting these pathways to internal coordinates.

BP 21.26 Wed 11:00 Poster C

AlphaFold-driven modeling of cytochrome bd-I: A structural approach to antibiotic design — •Noah Rickermann, Jonathan Hungerland, and Ilia A. Solov'yov — University Oldenburg, Department of Physics, Carl-von-Ossietzky-Str. 9-11, 26129 Oldenburg, Germany

In the pursuit of novel antibiotics, targeting proteins involved in the metabolic pathways of pathogens has emerged as a promising strategy. The terminal oxidase cytochrome bd-I, found exclusively in bacteria (e.g. E. Coli or M. tuberculosis), serves as a promising target for antibiotics. However, incomplete structural data due to limitations of electron microscopy hinders a comprehensive understanding of the protein's function. This study introduces a computational model of the cytochrome bd-I complex, reconstructed using the AlphaFold protein structure prediction program, in combination with experimental information for placement of the prosthetic groups. Model validation incorporated the mutation study of Mogi et al. [1], who examined substrate binding properties in cytochrome bd-I. To assess the accuracy of the derived protein model free energy perturbation simulations were employed. Additionally, efforts were carried out to identify potential inhibitors for Cytochrome bd-I, yielding promising drug candidates in the early stages of the investigation [2-3].

[1] Mogi et al. Biochem. 45.25 (2006) [2] Jacobsen et al. "Introducing the Automated Ligand Searcher". J. Chem. Inf. Model. (2023) [3] Korol et al. "Introducing VIKING: A novel misc platform for multiscale modeling". ACS Omega 5.2 (2020)

BP 21.27 Wed 11:00 Poster C

Binding Study of Beta-2-Glycoprotein I and Integrin-Containing Artificial Lipid Membranes — •Emma Weilbeer[1], Una Janke[1], Thomas McDonnell[2], and Mihaela Delcea[1] — [1]Biophysical Chemistry Department, Institute of Biochemistry, University of Greifswald — [2]Division of Medicine/ Biochemical Engineering, University College London, UK

Beta-2-glycoprotein I (β2GPI) is a highly glycosylated plasma protein and the most important antigenic target for autoantibodies in antiphospholipid syndrome. β2GPI circulates as a closed form but opens up under specific conditions. Although β2GPI has been found in blood clots, its physiological role is not yet fully understood. Therefore, it is of great importance to investigate the function and the dynamics of β2GPI in the coagulation cascade using for example, biophysical methods. Imaging of fluorescently labeled protein suggests that β2GPI binds to human embryonic kidney cells expressing αIIbβ3 integrin (i.e. the main platelet receptor essential for platelet aggregation and undergoing conformational dynamics). We have investigated the interaction of open and closed β2GPI with activated and non-activated integrin αIIbβ3-containing lipid bilayers mimicking the outer leaflet of platelet membranes. A combination of various biophysical methods (e.g. dynamic light scattering, circular dichroism spectroscopy, atomic force microscopy, surface plasmon resonance) have been used for protein characterization and protein-protein interactions. Our biomimetic model enables the specific analysis of disease relevant protein-protein interactions involving protein conformational dynamics.

BP 21.28 Wed 11:00 Poster C

Coarse-grained simulations of peptide Lge1(1-80) — •Agaya Johnson[1], Anton Polyansky[2], Sofia Kantorovich[1], and Bojan Zagrovic[2] — [1]Computational and Soft Matter Physics, University of Vienna, Kolingasse 14-16, 1090 Vienna, Austria — [2]Department of Structural and Computational Biology, Campus-Vienna-Biocenter 5, 1030 Vienna

Biomolecular condensates in cells such as p-bodies, nucleoli and stress granules play an important role in regulating biological processes like transcription, ribonucleic acid(RNA) metabolism and ribosome biogenesis. Studying of such biomolecular condensates will give insight into the molecular basis of diseases, like neurodegenerative diseases, cancer and diabetes. The main purpose of this study is to understand the main phenomenon, which leads to the formation of these bimolecular condensates such that we get a conclusion, whether is it phase separation, self assemble or an aggregation. We use Lge1(1-80) peptide as a model for study because Lge1(1-80) is mostly disordered, prone to form many cation-pi and pi-pi interaction(R, G and R rich sequence) and because of its alternating net charge which are the prerequisites for the phase separation. Due to the limitation of high-resolution experimental techniques, we are using molecular dynamics simulation with coarse-grained approaches, with the help of software ESPResSo. Our goal is to develop a coarse-grained model for the proteins that exhibit structural transitions and to understand the fundamental mechanisms under those transitions.

BP 21.29 Wed 11:00 Poster C

Non-Markovian friction dependence on intra-molecular reaction coordinates in protein folding — •Jonathan Remmert, Benjamin A. Dalton, and Roland R. Netz — Freie Universität Berlin, Berlin

Protein folding is commonly described using one-dimensional reaction coordinates. The dynamics of these coordinates depend on the free energy profile and on the effective friction. Experimental techniques to measure protein folding, such as FRET experiments, use distances between residues in the amino acid chain as reaction coordinates, which are known to exhibit strongly non-Markovian dynamics.

By applying novel methods to extract non-Markovian friction kernels from simulation data, we describe the dynamics of intra-molecular distance reaction coordinates by the Generalised Langevin Equation. We explore the dependence of the non-Markovian friction on the specific distance coordinate chosen, thereby enabling a detailed theoretical description and understanding of FRET experiments.

BP 21.30 Wed 11:00 Poster C

Electric field susceptibility of metastable proteins and implications for controlling viral propagation — •Claudia Arbeitman[1,2,3], Pablo Rojas[1], Alexander Lipskij[1], Pedro Ojeda-May[4], and Martin Garcia[1] — [1]Theoretical Physics, University of Kassel, Kassel, Germany — [2]GIBIO-UTN, Buenos Aires, Argentina — [3]CONICET, Buenos Aires, Argentina — [4]Umeå University, Umeå, Sweden

The internal motion and configuration of proteins are intimately related to their ability to perform functions. Their conformational changes and stability properties determine the molecular recognition capabilities and, ultimately, the set of interactions with other molecules. The thermodynamic stability and kinetic barriers that limit the kinetic accessibility of the conformational landscape of proteins are, though, not the same for all families of proteins.

In this work, we use molecular dynamics simulations to show that metastable proteins, such as the SARS-CoV-2 spike protein in the prefusion conformation, are susceptible to irreversible changes in their secondary and tertiary structures when exposed to moderate electric fields, orders of magnitude weaker than those reported for other proteins and for the same protein in the post-fusion conformation. Simulations of the docking with the host cell receptor ACE2 reveal that changes in the structure lead to impaired recognition. We explain the implications of these findings for the future study of metastable proteins and the development of inactivation technologies.

BP 21.31 Wed 11:00 Poster C

Role of Phase Separation in RNA co-evolution — •Samuel Santhosh Gomez, Gaetano Granatelli, and Christoph Weber — University of Augsburg, Augsburg, Germany

The PhD project, called 'Client Scaffold Model for Compartmentalized RNA Evolution', aims to create a theoretical framework that can account for RNA strand replication. From which, to then to study how compartments formed by scaffold phase-separation may be able to play a role in providing micro environments that might allow for the possibility for co-evolution of RNA replicators with RNA replicator parasites. The motivation for such a theoretical model comes from host-parasite RNA replicator experiments that suggested that droplet compartments might be able to provide an environment for co-evolution which is not possible in the well mixed homogeneous case.

BP 21.32 Wed 11:00 Poster C

Controlling transport for RNA enrichment in 2D-alkaline chimneys — •Mona Byberg Michelsen and Karen Alim — School of Natural Sciences, Technical University of Munich, Germany

Alkaline vents at the prebiotic ocean floor are hypothesized as a setting for the emergence of life. These alkaline vents (AVs) produce chimneys with intricate hierarchical architectures and steep pH gradients. Under these conditions, intricate flow networks facilitate complex transport of organic molecules and other compounds. For the emergence of life, the enrichment and synthesis of organic molecules, in particular nucleic acids, need to be facilitated. Yet, the location within the AV chimneys and the necessary flow conditions to overcome the concentration problem are still unknown.

Our recently established microfluidic two-dimensional (2D) model of alkaline chimneys allows us to directly observe chimney architecture, fluid flow, and molecule transport and enrichment. By combining optical tracking with numerical methods, we aim to establish a quantitative model of transport through the AV chimney. Experimental 2D chimneys will be optimized using predictions from the quantitative model and tested for enrichment of organic compounds. Finally, the effects of a dynamic chimney environment will be probed by periodically changing inflow salt concentration and tracking the impact on denaturation and hybridization of nucleic acids. Through this combination of experiments and quantitative modeling, we aim to uncover the physical prerequisites for the enrichment of nucleic acids and the creation of dynamic environments facilitating replication at the origin of life.

BP 21.33 Wed 11:00 Poster C

Theory of RNA evolution in phase-separated systems — •Gaetano Granatelli, Samuel Santhosh Gomez, and Christoph Weber — Faculty of Mathematics, Natural Sciences, and Materials Engineering: Institute of Physics, University of Augsburg, Germany

Evolution is due to the error-prone replication processes of genetic material, DNA or RNA, performed by replication machinery translated from the same genetic material.

The aim of the project is to develop a theoretical framework that can account for RNA replication with and without a phase-separated droplet, to investigate how phase coexistence could play a role in providing spatially confined micro-environments which allow for the co-evolution with parasitic RNA replicators. We build our model upon a client-scaffold theoretical framework that decouples phase separation of scaffold molecules from the reaction kinetics of dilute clients.

The motivation for such a model comes from theoretical and experimental work on translation-coupled RNA replication systems within cell-like compartments, where the evolution of host and parasitic RNA species is analysed: hosts have the ability to translate a self-encoded RNA replicase, whereas parasites do not (having lost their replicase encoding region due to mutations). These studies suggest that compartmentalization might be necessary for co-evolution of host and parasite replicators, which instead is not observed in bulk conditions.

BP 21.34 Wed 11:00 Poster C

Cell-Free Gene Expression in Bioprinted Fluidic Networks — •Alexandra Bienau and Friedrich C. Simmel — Technical University Munich, Germany

Cell-free protein expression is a valuable tool to produce specific proteins in vitro without the need for a host organism. The reduced metabolic background activity enables high product concentrations and precisely controlled reaction conditions for prototyping genetic circuitry. Microfluidic devices instead of closed reactors were used in previous works to enable longer reaction times and out-of-equilibrium behavior.

In this work, we create fluidic networks in a diffusible hydrogel environment using extrusion-based bioprinting as a fast production tool. We print sacrificial structures of Pluronics F-127 and cast agarose around them to build channels within the hydrogel, mimicking natural fluid distribution networks. The channels can be filled with customized liquids, such as the cell-free reaction mixture, and the reactions are not limited to the channels but can extend into the surrounding gel by diffusion. The behavior of fluorescent protein production within the agarose hydrogels is investigated using an E. coli-based cell extract.

Implementing gene circuitry by cell-free reactions allows for adding another design layer using bottom-up self-organization. In the future, we aim to use this design strategy to create more complex, tissue-like objects. We envision the construction of biohybrid structures combining artificial and natural cells to develop smart soft-robotic materials.