BP 4: Computational Biophysics I

Time: Monday 15:00–18:00 Location: H 0112

BP 4.1 Mon 15:00 H 0112

Efficient radial-shell model for 3D tumor spheroid dynamics with radiotherapy — •Florian Franke[1], Soňa Michlíková[2,3], Sebastian Aland[1,4,5], Leoni A. Kunz-Schughart[2,6], Anja Voss-Böhme[1], and Steffen Lange[1,2] — [1]HTW Dresden - University of Applied Sciences — [2]OncoRay, Natl. Center for Radiation Research in Oncology, TU Dresden — [3]Helmholtz-Zentrum Dresden - Rossendorf, Germany — [4]TU Bergakademie Freiberg — [5]Center for Systems Biology, Dresden — [6]Natl. Center for Tumor Diseases, Dresden, Germany

Approximately 50% of patients diagnosed with cancer receive radiotherapy at least once during their disease. Experiments with sophisticated in-cellulo assays to improve radiotherapeutic outcomes are still challenging, and some critical details of tumor cell dynamics still need to be explored. To enhance the informative value of such approaches and support future therapeutic study designs, we developed an efficient mathematical model for three-dimensional multicellular tumor spheroids, which reflect microregions within a large tumor or avascular micrometastases and which are an auspicious experimental framework to pre-assess the curative effect of radio(chemo)therapy. We validate our mathematical model using experimental tumor spheroid growth data of several cell lines with and without radiotherapy and observe equal or better performance than previous models. Moreover, our model allows for efficient parameter calibration within previously reported and/or physiologically reasonable ranges. Based on this data-driven approach, we can explain the mechanism of the characteristic dynamics at small tumor volumes.

BP 4.2 Mon 15:15 H 0112

Leveraging Point Cloud Transformers and Simulation-based Inference for Enhanced Parameter Inference in Tumor Growth Modeling — •Julian Herold[1], Eric Behle[2], and Alexander Schug[2] — [1]Kalrsruhe Institut für Technologie (KIT), Karlsruhe, Germany — [2]Jülich Supercomputing Centre (JSC), Jülich, Germany

Computational modeling serves as a cornerstone in unraveling the intricate dynamics of living tissues. However, the challenge of deriving quantitatively meaningful parameters from experimental data persists. Conventional methods, such as ABC, rely on summary statistics, introducing inherent limitations in the selection of relevant metrics. To address these challenges, we advocate for the adoption of Simulation-based Inference (SBI), harnessing the capabilities of deep learning techniques to navigate the complexities associated with parameter inference. In this study, we present utilizing point cloud transformers directly on positional data extracted from in-vitro spheroids, circumventing the reliance on summary statistics and thus overcoming the limitations of traditional methods. Our methodology integrates the training of neural networks into the parameter inference pipeline of CellsInSilico (CiS), a high-performance framework designed for large-scale tissue simulations. Not only does this yield superior results in terms of inference accuracy, but it also enhances computational efficiency compared to conventional methodologies, empowering researchers to explore critical biological questions. Demonstrated utility includes investigating the interplay between the extracellular matrix and tumor invasion.

BP 4.3 Mon 15:30 H 0112

Modeling and simulation of red blood cells aggregation in cardiovascular networks — •Fouzia Imharken[1,2], Chaouqi Misbah[1], and Hamid Ez-zahraouy[2] — [1]Interdisciplinary Laboratory of Physics (LIPhy)-UGA-Grenoble- French — [2]Laboratory of Condensed Matter and Interdisciplinary Sciences-Mohamed 5 University-Morocco

Cardiovascular dysfunctions due to undesirable adhesion among blood elements (like red blood cells-RBCs) are the main causes of mortality in the world. In our study, we intend to develop simple models to better understand the perfusion of blood in microcirculation by considering a complex geometry under several conditions (shear, confinement, pressure, etc.) in the presence of adhesion among RBCs using an immersed boundary-lattice Boltzmann method. Our primary results show that the aggregation of RBCs and their mechanical properties has a strong impact on their distribution in the network. For stiff RBCs (due to a disease) a weak adhesion leads to super diffusion instead of ballistic transport, as compared to the case without adhesion.

BP 4.4 Mon 15:45 H 0112

Validating the Protein Hydration Shell against Small-angle Scattering Data - Effects of Water Models, Force Fields, and Surface Composition — •Johanna-Barbara Linse and Jochen S. Hub — Theoretical Physics and Center for Biophysics, Saarland University, Saarbrücken, 66123, Germany

The proteins hydration shell plays key roles in protein stability and function. So far, it remained unclear whether hydration shells predicted by explicit-solvent molecular dynamics (MD) simulations match experimental conditions, as precise experimental data on hydration shell structures were limited. Small-angle scattering (SAS) experiments provide insight into hydration shell properties, because the detected radius of gyration (R_g) and zero-angle scattering (I_0) depend on the contrast between the hydration shell and the solvent. Using explicit-solvent MD simulations and SAS calculations, we calculated R_g values for five proteins, evaluating 18 combinations of protein force fields and water models. Validation of the results against consensus data from a round-robin benchmark project revealed remarkable agreement between MD simulations and experiments, depending on the choice of force field and water model. Furthermore, we investigated the influence of amino acid surface composition of proteins on the hydration shell contrast, providing contrast scores for 20 amino acids. Our studies show that explicit-solvent SAS calculations and consensus SAS data provide a novel routes for scrutinizing the proteins hydration shell and for predicting the amino acid effects on the hydration shell structure.

BP 4.5 Mon 16:00 H 0112

Chromatic medium under active perturbation — •Rakesh Das — Max Planck Institute for the Physics of Complex Systems, Nöthnitzer Strasse 38, 01187 Dresden, Germany — Mechanobiology Institute, National University of Singapore, Singapore 117411

Chromatin organization inside a cell nucleus and its coordination with subnuclear compartments (SNCs) play crucial roles in genome regulation. However, numerous enzymes act inside the nucleus that actively perturb the medium. We investigated the effect of such active perturbations (AP) on the compartmentalization of chromatin into eu- and hetero-chromatin phases and the SNC-dynamics embedded therein. We use a polymer physics framework, where the chromatin is perturbed through a non-localized active mechanism mimicking the action of TopoisomeraseII enzyme. Computer simulations show the emergence of characteristic phase separation morphologies, viz., wall-like organization of euchromatin with negative nematic ordering of the euchromatic segments due to such active perturbations. A simplified equilibrium model can catch the essence of the phase separation but fails to explain such emergent features. This highlights the critical role of AP in chromatin organization. Using a similar computational setting, we show that the SNC-dynamics in such a complex medium can be described as a combination of three modes linked with different physical aspects of the embedding medium. Under AP, mainly a slow mode associated with remodeling of chromatic meshes enhances SNC-dynamics. This may provide an insight into the role of global AP on regulating the target-searching processes in the chromatic medium.

BP 4.6 Mon 16:15 H 0112

Kinetics of radiation-induced DNA double-strand breaks through coarse-grained simulations — •Manuel Micheloni[1,2], Lorenzo Petrolli[1,2], Gianluca Lattanzi[1,2], and Raffaello Potestio[1,2] — [1]Physics Department, University of Trento, via Sommarive, 14 I-38123 Trento, Italy — [2]INFN-TIFPA, Trento Institute for Fundamental Physics and Applications, I-38123 Trento, Italy

Double-strand breaks (DSBs), the covalent cut of the DNA backbone over both strands, are a detrimental outcome of cell irradiation. The earliest stages of the irradiation of DNA feature fast and localized processes, hardly characterizable by conventional experimental techniques, but viable for *in silico* assessments; mean-field descriptions have been extremely insightful at correlating irradiation regimes and macroscopic observables (i.e. cell survival), albeit neglecting structural, mechanical and kinetic implications associated with lesioned DNA molecules. In fact, in spite of their biological significance, the dynamical evolution of DSBs is still largely uncertain. *Via* coarse-grained molecular dynamics simulations, we have addressed the mechanical rupture of a DNA

molecule by diverse DSB motifs, i.e., within a range of distances between strand breaks (DSB distance). We have shown the cooperative nature of the process, characterized by an abrupt transition driven by the disruption of the residual interactions between DNA moieties, governed by Poisson statistics. Moreover, we have accessed the timescales of the rupturing process, inferring an exponential dependence of the characteristic rupture times on the DSB distances, typically associated with an Arrhenius-like law of thermally-activated processes.

15 min. break

BP 4.7 Mon 16:45 H 0112

Computational design of graphene nanopores for amino-acid detection — •Longlong Li and Maria Fyta — Computational Biotechnology, RWTH Aachen University, Germany

Nanometer-sized pores, the nanopores, opened in two-dimensional (2D) materials have been shown to enhance biosensing due to their atomic-layer resolution. Using density-functional theory and the non-equilibrium Green's functions approach, we perform systematic simulations to investigate the electronic and transport properties of graphene nanopores in which single amino acids are placed. The simulations aim to gain an in-depth understanding of the interaction between these biomolecules and graphene nanopores and reveal amino-acid specific characteristics. The results indicate the significant role of these biomolecules, their structure and properties in modulating the electronic structure and transport of the pristine nanopores. Our research provides valuable insights into designing graphene nanopore-based biosensing devices, with precise control over their electronic and transport properties.

BP 4.8 Mon 17:00 H 0112

Tensile strength of water with organic impurities — •Marin Šako and Matej Kanduč — Jožef Stefan Institute, Ljubljana, Slovenia

The stability of water is a long-standing problem in physics, studied since the 17th century and continuing to be a subject of investigation today. There is a notable discrepancy between experimental findings and theoretical predictions, as well as inconsistency in measurements across different experiments. While theory predicts that water should be remarkably stable against cavitation, experiments show quite the opposite. In this talk, I will present our work on the conditions that lead to catastrophic cavitation events in decane and water. Additionally, I will discuss how the tensile strength of water is influenced by hydrocarbon impurities, such as oil droplets. We use a framework that combines classical nucleation theory with molecular dynamics simulations. We find that while pure bulk water is exceptionally stable against cavitation, the presence of even tiniest amounts of decane is enough to destabilize water and reduce its tensile strength to experimentally measured lower values. Using our numerical analysis, we find that a decane droplet of a radius of around 1 nm in a macroscopic volume of water is enough to destabilize the system. This is the reason why even in ultra-pure water, the measured tensile strength is significantly lower compared to theoretical predictions. We also find that the curvature correction of surface tension is important to take into account when studying cavitation, nanodroplets, or nanobubbles.

BP 4.9 Mon 17:15 H 0112

Introducing the Automated Ligand Searcher — Luise Jacobsen[1], Jonathan Hungerland[2], •Vladimir Bačić[2], Luca Gerhards[2], Fabian Schuhmann[3], and Ilia A. Solov'yov[2] — [1]Department of Physics, Chemistry and Pharmacy, University of Southern Denmark, 5230 Odense M, Denmark — [2]Institute of Physics, Carl von Ossietzky Universität, 26129 Oldenburg, Germany — [3]Niels Bohr International Academy, Niels Bohr Institute, University of Copenhagen, 2100 Copenhagen, Denmark

The Automated Ligand Searcher (ALISE) is designed as an automated computational drug discovery tool. To approximate the binding free energy of ligands to a receptor, ALISE includes a three-stage workflow, with each stage involving an increasingly sophisticated computational method: molecular docking, molecular dynamics, and free energy perturbation, respectively. To narrow the number of potential ligands, poorly performing ligands are gradually segregated out. The performance and usability of ALISE are benchmarked for a case study containing known active ligands and decoys for the HIV protease. The example illustrates that ALISE filters the decoys successfully and demonstrates that the automation, comprehensiveness, and user-friendliness of the software make it a valuable tool for improved and faster drug development workflows.

BP 4.10 Mon 17:30 H 0112

Radial dependence of X-ray induced ionization clusters around a gold nanoparticle — •Leo Thomas[1,2], Hans Rabus[1], and Miriam Schwarze[1] — [1]National Metrology Insititute, Berlin Germany — [2]Dept. II, Technical University of Berlin, Germany

One strategy to improve the efficacy of radiotherapy for cancer is increasing the tumor*s sensitivity to irradiation, e.g., by introducing gold nanoparticles (GNPs) into cancer cells [1].

This work explores the enhancement of ionization clusters around a GNP, which are considered to be indicative of the induction of DNA lesions [2], a potential trigger for cell-death-inducing damage [3].

Monte Carlo track structure simulations were performed in a two-step-approach. The produced ionizations were scored using Associated Volume Clustering [4] to obtain the radial profile of ionization clusters frequency.

The influence of the GNP on the electron fluence spectrum is relatively small and occurs mainly at energies below 10 keV. Accordingly, increased ionization clustering is limited to a range up to about 200 nm. Here, smaller GNPs (radii up to 10 nm) cause noticeable peaks in the frequency ionization clusters upon occurrence of a photon interaction at distances around 50 nm from the GNP surface.

[1] J. Hainfeld et al.,Nanomedicine (Lond), 8 (2013) 1601-9 [2] A. Rucinski et al., Phys Med Biol, 66 (2021) 24TR01 [3] M. Lomax et al., Clin Oncol, 25 (2013) 578-85. [4] K. R. Kase et al., The dosimetry of ionizing radiation Vol 1 (1985) Chap. 2

BP 4.11 Mon 17:45 H 0112

Cationic and anionic lipid mixing favors the lamellar-to-hexagonal phase transition in coarse-grained molecular dynamics simulations — •David Noel Zimmer[1,2], Friederike Schmid[1], and Giovanni Settanni[1,2] — [1]Physics Department Johannes Gutenberg University Mainz — [2]Faculty of Physics and Astronomy Ruhr University Bochum

Lipid-based nanoparticles (LNPs) are used as delivery vehicles for RNA-therapeutics, a potentially broad class of drugs including COVID-19 vaccines as well as drugs against genetically inherited diseases and cancer. LNPs are produced by rapid mixing the cargo RNA at low pH with a lipid formulation containing ionizable cationic lipids, helper and PEGylated lipids. The lipid formulation helps to compact the RNA, to screen it from degradation and to deliver it to the target cell. LNPs' mechanisms of action is not yet well understood. Here, we use coarse-grained molecular dynamics simulation to investigate the effect of the fusion process between the LNP and the endosomal membrane following cellular uptake of the LNP. The simulations show that the mixing of the anionic lipids of the endosome with the cationic lipids of the LNP leads to a stabilization of the hexagonal phase versus the lamellar phase. Analysis of the hexagonal phase shows that cationic lipids tend to accumulate in the space between three adjacent tubules, while anionic lipids distribute more uniformly around the tubules, indicating a lack of correlation in the position of the two oppositely charged lipids.