BP 21: Systems Biology III

Time: Tuesday 14:00–16:00 Location: BPa

Invited Talk BP 21.1 Tue 14:00 BPa

Predicting Protein and RNA Structures: from statistical physics to machine learning — •Alexander Schug — John von Neumann Institute for Computing, Jülich Supercomputer Centre, Forschungszentrum Jülich — Faculty of Biology, University of Duisburg-Essen

On the molecular level, life is orchestrated through an interplay of many biomolecules. To gain any detailed understanding of biomolecular function, one needs to know their structure. Yet the structural characterization of many important biomolecules and their complexes - typically preceding any detailed mechanistic exploration of their function- remains experimentally challenging. Tools rooted in statistical physics such as Direct Coupling Analysis (DCA) but also increasingly Machine Learning driven approaches take advantage of the explosive growth of sequence databases and infer residue co-evolution to guide structure prediction methods via spatial constraints. For proteins, systematic large-scale studies of >1000 protein families are already possible. Additional information, such as low-resolution experimental information (e.g. SAXS or FRET) can be used as further constraints in simulations. For RNA there are significantly less data available, which hinders in particular ML based approaches. Still, DCA combined with ML can improve prediction quality.

BP 21.2 Tue 14:30 BPa

Rational optimization of drug-membrane selectivity by computational screening — •Bernadette Mohr and Tristan Bereau — Max Planck Institute for Polymer Research, Mainz, Germany

Success rates of drug discovery are non-satisfactory considering the high cost in time and resources. This leads to an increased demand for development of improved screening methods. In our work, we explore the capabilities of using a coarse-grained (CG) model to efficiently find candidate structures with desired properties. The Martini CG force field is a physics-based model that incorporates both the essential chemical features with a robust treatment of statistical mechanics. Martini simplifies the molecular representation through a small set of bead types that encode a variety of functional groups present in organic chemistry. This offers two advantages: (i) many molecules map to the same CG representation and (ii) screening boils down to systematically varying among the set of CG bead types available. The combination of these two aspects makes Martini a remarkably efficient candidate for high-throughput screening. We apply this approach to the selective binding of drugs between Cardiolipin and phosphoglycerols in mitochondrial membranes. A systematic screening starting from an already-reported compound will be presented. We identify clear design rules for improved selectivity, and rationalize them on a physical basis. As an outlook, we explore prospects of further boosting screening at higher throughput by means of connecting the CG simulations within a deep-learning framework.

BP 21.3 Tue 14:50 BPa

Morphology of spherical epithelial monolayers — •Aboutaleb Amiri[1], Charlie Duclut[2,3], Carl Modes[2,3], and Frank Jülicher[1,3] — [1]Max Planck Institute for the Physics of Complex Systems, 01187 Dresden, Germany — [2]Max Plack Institute for Molecular Cell Biology and Genetics, 01037 Dresden, Germany — [3]Center for Systems Biology Dresden, 01307 Dresden, Germany

We develop a generalised vertex model off the mechanics of epithelial cell monolayers to study morphogenesis in three dimensions. In this approach, a cell is represented by a polyhedron which is characterised by the location of its vertices in 3D space. We take into account apical, basal, and lateral cell surface tension, as well as pressure differences between outside and inside the cells. We consider an epithelium with spherical topology enclosing a lumen and investigate mechanisms that can generate different morphologies. In particular, we are interested in the roles of mechanical feedback on cell behaviours for the morphogenesis of closed epithelial monolayers.

BP 21.4 Tue 15:10 BPa

Load distribution among the main structures of a passively flexed lumbar spine — •Julia M. Riede[1], Falk Mörl[2], Michael Günther[1], Maria Hammer[1], and Syn Schmitt[1] — [1]Computational Biophysics&Biorobotics, IMSB/Simtech, University of Stuttgart, Germany — [2]Biomechanics&Ergonomics, FSA mbH Erfurt, Germany

Mechanical loads may induce degeneration of spinal structures. It is still unknown how the load during spine motion is distributed among the spine's main structures: muscles, vertebrae and facet joints, ligaments, and intervertebral discs. Currently, there are no measurements that capture the load on all spinal structures at once. Therefore, computer simulations are the method of choice to overcome the lack of knowledge about the biophysical properties and processes determining spinal in vivo dynamics.

For predicting the load distribution of spinal structures, we combined experimental and simulation methods. In experiments, we determined the overall stiffness for forward-flexing rotations between the lumbar vertebrae L5 and L4 of subjects lying in sideways position and being bent by a machine, without active muscle resistance. Forward dynamics simulations of this experiment using our detailed musculoskeletal multibody model of the human allowed for a structural resolution of the loads in the L4|5 region. The results indicated that stiffness values of particularly ligaments and passive muscle tissue put in from literature resources were too high. With now corrected values, our model has gained validity for future investigations on human movement dynamics and modelling applications like e.g. exoskeletons.

30 min. Meet the Speaker