F. Schmid
friederike.schmid@uni-mainz.de

P. Virnau
virnau@uni-mainz.de

L. Stelzl
lstelzl@uni-mainz.de

JOHANNES GUTENBERG UNIVERSITÄT MAINZ

Seminar über Theorie der kondensierten Materie / TRR146 Seminar

Feb. 9, 2023 at 3 p.m.
Minkowski Room, 05-119, Staudingerweg 7,

Roberto Covino
Frankfurt Institute for Advanced Studies

Investigating mechanisms of biomolecular self-organization by integrating physics-based simulations and AI

Molecular self-organization driven by concerted many-body interactions produces the ordered structures that define both inanimate and living matter. Understanding the physical mechanisms that govern the formation of molecular complexes is key to controlling the assembly of nanomachines and new materials.
Molecular dynamics simulations and single-molecule experiments offer the unprecedented possibility to reveal mechanisms of molecular self-organization in high resolution. However, outstanding limitations hinder their success. Machine learning and artificial intelligence promise to empower both approaches to overcome fundamental challenges.
In the first part of my talk, I will present an autonomous AI that learns molecular mechanisms from computer simulations. The AI agent simulates infrequent and stochastic molecular reorganizations and progressively learns how to predict their outcome. Using symbolic regression, we distill simplified quantitative models that reveal mechanistic insight in a human-understandable form. Our innovative AI enables sampling rare events by autonomously driving many parallel simulations with minimal human intervention and aids their mechanistic interpretation. I will present applications on nucleation processes, the assembly of membrane proteins in lipid bilayers, and polymer and protein folding.
In the second part of my talk, I will discuss how integrating physical modeling

and AI helps extract mechanistic understanding from single-molecule force spectroscopy. While these experiments offer the possibility of measuring fundamental quantities like free energies, these measurements are often incomplete and indirect. In practice, we measure a few order parameters that are the outcome of the coupled dynamics of the molecule and the mesoscopic experimental apparatus, which could lead to estimation artifacts. I will discuss this problem as Bayesian inference and illustrate how simulation-based inference provides a powerful solution. Coupling a simulator that encodes the physics of the measuring process with density estimation using neural networks leads to accurate estimates of molecular free energies.

In conclusion, integrating physics-based models and AI provides a powerful way to extract accurate quantitative information from simulations and biophysical experiments.

Contact:
Lukas Stelzl
lstelzl@uni-mainz.de