ASU Department of Physics
Arizona State University

COLLOQUIUM

Thursday, August 17, 2023

Refreshments at 3:15pm outside PSF 101
Colloquium from 3:30pm - 4:30pm in PSF 101

From the Wiggling of Atoms to Fundamental Biological processes via Multiscale Modeling

Professor Oliver Beckstein

Arizona State University

Abstract:

Biological systems offer fascinating opportunities to explore non-equilibrium physics at the molecular scale, spanning time scales from sub-nanoseconds to seconds. The energy scale of biology, is, however, quite narrow around a few kT (the energy of a thermal fluctuation) and thus such biological processes always compete against random thermal motion. In other words, even though all atoms wiggle seemingly randomly due to their thermal energy, these systems can nevertheless function as molecular machines that turn free energy into useful work. Part of the explanation is that biomolecules such as proteins evolved into specific three-dimensional shapes ("structures") that can alternate between a handful of well-defined states. The transitions between these states can be driven by external free energy gradients to generate directed cyclical reactions that, on average, perform work. Thus the function of a protein is fully encoded in its structure and hence a fundamental problem in biophysics has been to model the function of proteins starting from their structures. In this colloquium I will describe a multiscale approach grounded in statistical physics to predict "protein function from structure". We infer microscopic quantities such as free energies and rates from atomic scale molecular dynamics (MD) simulations and use these quantities to parameterize kinetic network models of the biological process. Solving the associated master equation under non-equilibrium conditions yields macroscopic observables. As an example I will show in molecular detail how a so-called secondary active transporter, a protein located in the cell membrane, moves sodium ions out of a cell against an electrochemical sodium gradient by consuming the free energy stored in a proton gradient. Using only the experimental structures of the transporter, we are able to compute the catalytic turnover (the number of transport events per second) as a function of membrane potential, pH and sodium concentrations, thus demonstrating how we can use computational methods to model fundamental biological processes in a bottom-up approach.

Biography:

Oliver Beckstein is an Associate Professor in the Department of Physics and Center for Biological Physics at Arizona State University https://becksteinlab.physics.asu.edu. He uses and develops computational methods to better understand the molecular mechanisms of biological processes. A special focus is on the quantitative prediction of the function and activity of proteins from the knowledge of their structures alone. He is a co-founder and core developer of the widely used open source MDAnalysis library for the analysis of biomolecular simulations https://www.mdanalysis.org/.

He obtained his undergraduate degree in Physics from the Universität Erlangen-Nürnberg, Germany and his doctoral degree in Biochemistry from the University of Oxford, UK. He held a Junior Research Fellowship at Merton College, Oxford and postdoctoral positions at Johns Hopkins University and the University of Oxford.

Host: Prof. Douglas Shepherd
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