SUMMER SEMESTER 2025

RTG 2756 CYTAC SEMINAR SERIES

TUESDAY, JULY 8
17:00 IN HS5

CYTAC
RTG 2756

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INVESTIGATING BIOMOLECULAR SELF-ORGANIZATION WITH SIMULATION INTELLIGENCE

Biomolecules are incredibly dynamic, constantly shifting between various conformations within a network connected by infrequent structural intermediates. This collection of structures, known as their conformational ensemble, including these rare intermediate structures, dictates how biomolecules function within a cell. However, comprehensively mapping these ensembles remains a significant challenge for both computational and experimental methods. Computer simulations, enhanced by machine learning, offer a promising solution to these challenges in biomolecular sciences.

In the first part of my talk, I'll showcase our work on integrating path sampling with machine learning. This empowers us to simulate rare conformational transitions more effectively. Our algorithm provides efficient sampling and delivers crucial mechanistic, thermodynamic, and kinetic insights into these rare molecular events, all at a moderate computational cost.

The second part of my talk will focus on using simulation-based inference to identify biomolecular conformations in cryo-electron microscopy (cryo-EM) data. Cryo-EM is a powerful tool for characterizing protein conformational ensembles. Even though a frozen sample contains information about the entire ensemble, accurately identifying rare or disordered molecular conformations from a single cryo-EM image is still difficult. To address this, we developed the cryo-EM simulation-based inference (cryoSBI) framework by integrating physics-based simulations, Bayesian inference, and deep learning. This framework allows us to infer molecular conformations and their associated uncertainties directly from individual cryo-EM images. We've validated cryoSBI using both synthetic and experimental data. This approach opens new avenues for characterizing entire conformational ensembles using experimental data.