PHYSICAL CHEMISTRY SEMINAR

Wednesday, March 27, 2024
10:30-11:30 a.m. BRWN 4102

"I fluctuate, therefore I am: From chemical identity to Boltzmann ensembles for proteins, RNA and crystals"

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Abstract:

Modern structure prediction tools using Artificial Intelligence (AI) have made great progress in predicting single dominant structures for generic proteins, RNA and crystals. However, chemistry is often more than a single structure, and involves carefully predicting an ensemble of structures with just the right structural/temporal fluctuations and thermodynamic weights. Here I will discuss methods from my group that, through combining generative AI with statistical mechanics and molecular simulations, allow predicting an ensemble of atomic resolution conformations together with correct thermodynamic ranking and fluctuations. The examples I show will likely include protein kinases, human RNA and crystal polymorph nucleation, where we will obtain thermodynamic and dynamic observables such as drug residence times, conformational populations, effect of mutations, and melting curves starting solely from chemical identity and associated force-fields. I will conclude with thoughts on how chemistry, specifically classical thermodynamics and statistical mechanics have much to help design the next generation of AI methods meant for chemistry applications with all its quirks and richness.

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