Contribution ID: **14** Type: **not specified**

Neural Thermodynamic Integration: Free Energies from Energy-based Diffusion Models

Wednesday, 23 October 2024 09:20 (40 minutes)

Thermodynamic integration (TI) offers a rigorous method for estimating free-energy differences by integrating over a sequence of interpolating conformational ensembles. However, TI calculations are computationally expensive and typically limited to coupling a small number of degrees of freedom due to the need to sample numerous intermediate ensembles with sufficient conformational-space overlap. In this work, we propose to perform TI along an alchemical pathway represented by a trainable neural network, which we term Neural TI. Critically, we parametrize a time-dependent Hamiltonian interpolating between the interacting and non-interacting systems, and optimize its gradient using a denoising-diffusion objective. The ability of the resulting energy-based diffusion model to sample all intermediate ensembles allows us to perform TI from a single reference calculation. We apply our method to Lennard-Jones fluids, where we report accurate calculations of the excess chemical potential, demonstrating that Neural TI is capable of coupling hundreds of degrees of freedom at once.

Presenter: Prof. BEREAU, Tristan