Demystifying molecular dynamics: from classical simulations to enhanced sampling methods

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Molecular dynamics (MD) simulations, often described as a form of computational microscopy, have the ability to reveal biomolecular mechanisms at incredibly high spatial and temporal resolutions beyond the reach of many experimental techniques. With the increasing availability of high-performance computing, they have become integral in biomolecular investigations spanning rational molecular design, deciphering molecular mechanisms, and uncovering structural bases of human diseases. However, the effectiveness of MD simulations often hinges on the ability to sufficiently sample all relevant metastable states of a system, a challenge that frequently demands prohibitively long simulation times for classical MD methods. To overcome this, various enhanced sampling methods have been developed in recent years to accelerate the exploration of the conformational space and enhance the sampling of rare events.

This talk will provide an approachable overview of the utility and evolution of MD simulation techniques, beginning with a case study demonstrating how classical MD can motivate and guide experimental work in designing glycosylated insulin with improved properties for oral delivery. Following this, the discussion will highlight the diverse strategies adopted by popular enhanced sampling methods such as metadynamics and replica exchange, along with a brief introduction to recent innovations in the field. Lastly, the presentation will conclude by discussing ongoing efforts in the field, especially in the wake of machine learning. From fundamentals to recent advancements, this presentation seeks to demystify common MD simulation techniques, offering insights for both newcomers and experienced researchers in the field, as well as potential collaborators with experimental backgrounds.