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"Past-future Information Bottleneck Framework for Sampling Molecular Reaction Coordinate, Thermodynamics and Kinetics."

Abstract: The ability to rapidly learn from high-dimensional data to make reliable bets about future outcomes is crucial in many contexts. This could be a fly avoiding predators, or the retina processing gigabytes of data almost instantaneously to guide complex human actions. In this work we draw parallels between such tasks, and the efficient sampling of complex biomolecules with hundreds of thousands of atoms. For this we use the Predictive Information Bottleneck (PIB) framework developed and used for the first two classes of problems, and re-formulate it for the sampling of biomolecular structure and dynamics, especially when plagued with rare events [1-3]. Our method considers a given biomolecular trajectory expressed in terms of order parameters or basis functions, and uses a deep neural network to learn the minimally complex yet most predictive aspects of this trajectory, viz the PIB. This information is used to perform iterative rounds of biased simulations that enhance the sampling along the PIB to gradually improve its accuracy, directly obtaining associated thermodynamic and kinetic information. We demonstrate the method on different test-pieces, including benzene dissociation from the protein lysozyme, where we calculate the dissociation pathway and timescales slower than milliseconds. Finally, by performing an analysis of residues contributing to the PIB, we predict the critical mutations in the system which would be most impactful on the stability of the crucial but ephemeral transition state. We believe this work marks a big step forward in the use of predictive artificial intelligence ideas for the sampling of biomolecules.