Accelerated Molecular dynamics simulations combining MELD and GaMD.

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Even with the recent advances in machine learning, the accuracy offered by molecular dynamics simulations is still highly valued and required in most cases. However, its slowness and computational cost are too high. To improve these parameters, we have incorporated a new feature into our in-house method Modeling Employing Limited Data (MELD) with coarse physical insights [1] that allow the inclusion of Gaussian accelerated Molecular Dynamics (GaMD) [2]. MELD resolves protein structures by a Bayesian inference approach combining physical models with experimental semi-reliable data. To enhance sampling, MELD uses Hamiltonian and temperature Replica Exchange Molecular Dynamics (H-REMD). The top replicas have a high temperature and weak restraints, which allow the system to sample broadly. The bottom replicas are at room temperature with strong restraints, focusing sampling on low-free-energy regions. MELD uses the GPU-accelerated OpenMM library [3] to achieve good performance. GaMD is a computational method for unconstrained enhanced sampling that works by adding a harmonic boost potential to smooth the biomolecular potential energy surface and reduce energy barriers. Preliminary analyzes for protein folding with implicit solvent showed that the simulations combining MELD and GaMD needed up to 3 times fewer replicas than the simulations using MELD alone. In addition, MELD with GaMD needed less simulation time to show superior results when identifying the low-free-energy regions by clustering and comparing them to experimental structures.

References

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