Gaussian accelerated Molecular Dynamics (GaMD) and Deep Learning

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Gaussian accelerated molecular dynamics (GaMD) is an enhanced sampling technique that works by applying a harmonic boost potential to reduce system energy barriers and accelerate molecular simulations by orders of magnitude. It does not require predefined collective variables, being advantageous for unconstrained enhanced sampling of complex biological systems. Because the boost potential usually exhibits a near Gaussian distribution, free energy profiles of large biomolecules can be properly recovered through cumulant expansion to the second order. GaMD has been implemented in the widely used AMBER, NAMD, Open-MM, GENESIS and Tinker-HP simulation packages. Since original publication in 2015, GaMD has received >500 citations in the field. Applications of GaMD have revealed mechanisms of protein folding and conformational changes, allostery, ligand binding, protein-protein/membrane/nucleic acid interactions and carbohydrate dynamics. Based on GaMD, we have recently developed selective Ligand GaMD (LiGaMD)[1], Peptide GaMD (Pep-GaMD)[2] and Protein-Protein Interaction GaMD (PPI- GaMD)[3]. These new algorithms, *for the first time*, enabled *microsecond* atomic simulations to capture repetitive dissociation and binding of small-molecule ligands, highly flexible peptides and proteins, thereby allowing for highly efficient and accurate calculations of ligand/peptide/protein binding free energies and kinetics. These calculations will greatly facilitate therapeutic design of drugs, peptides and antibodies. Furthermore, we have developed the GaMD, Deep Learning and free energy prOfiling Workflow (GLOW), which provides a systematic approach to predicting molecular determinants and mapping free energy profiles of biomolecules[4]. In this talk, I will present these recent efforts in our development of new GaMD algorithms and integration of GaMD with Deep Learning to explore binding thermodynamics, kinetics and free energy profiles of biomolecules[5].

References:

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