High-throughput all-atom molecular dynamics simulations using distributed computing

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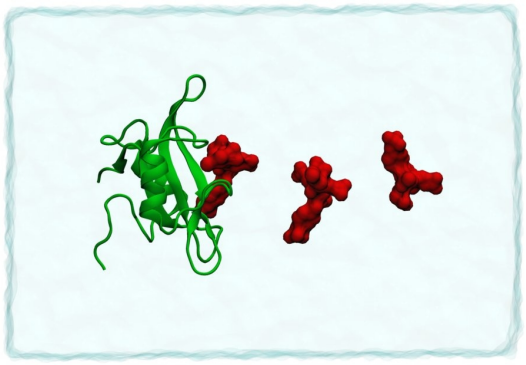

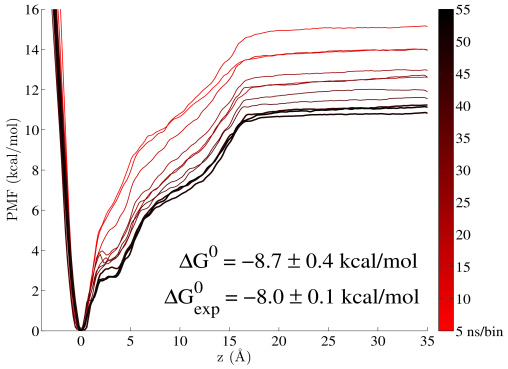

Although molecular dynamics simulation methods are useful in the modeling of macromolecular systems, they remain computationally expensive, with production work requiring costly high-performance computing (HPC) resources. We review recent innovations in accelerating molecular dynamics on graphics processing units (GPUs), and we describe GPUGRID, a volunteer computing project that uses the GPU resources of non-dedicated desktop and workstation computers. In particular, we demonstrate the capability of simulating thousands of all-atom molecular trajectories generated at an average of 20 ns/day each (for systems of ~30,000-80,000 atoms). In conjunction with a potential of mean force (PMF) protocol for computing binding free energies [1], we recently demonstrated the use of GPUGRID in the computation of accurate binding affinities of the Src SH2 domain-pYEEI ligand complex by reconstructing the PMF over 20.5 μs of umbrella sampling data. We obtain a standard free energy of binding of −8.7 ± 0.4 kcal/mol within 0.7 kcal/mol from experimental results [2].

We are now working on an optimized version of the protocol to make the system suitable for routine high-throughput protein-ligand accurate binding affinity prediction s.

[1] S. Doudou, N.A. Burton, R. H. Henchman, *J. Chem. Theory Comput.,* 2009, 5, 909–918.
[2] I. Buch, M.J. Harvey, T. Giorgino, D.P. Anderson and G. De Fabritiis, *J Chem Inf Mod*, 2010, *In press*.