

Accelerated Molecular Simulation: A Convolution Approach

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Abstract : Computational Drug Design is often based on Molecular Dynamics simulations of molecular systems. Molecular Dynamics can be used to simulate, e.g., the binding and unbinding event of a small drug-like molecule with regard to the active site of an enzyme or a receptor. However, the time-scale of the overall binding event is many orders of magnitude longer than the time-scale of simulation. Thus, there is a need to speed-up molecular simulations. In order to speed up simulations, the molecular dynamics trajectories have to be steered out of local minimizers of the potential energy surface – the so-called metastabilities – of the molecular system. Increasing the kinetic energy (temperature) is one possibility to accelerate simulated processes. However, with temperature the entropy of the molecular system increases, too. But this kind of steering is not directed enough to steer the molecule out of the minimum toward the saddle point. In this article, we give a new mathematical idea, how a potential energy surface can be changed in such a way, that entropy is kept under control while the trajectories are still steered out of the metastabilities. In order to compute the unsteered transition behaviour based on a steered simulation, we propose to use extrapolation methods. In the end we mathematically show, that our method accelerates the simulations along the direction, in which the curvature of the potential energy surface changes the most, i.e., from local minimizers towards saddle points.

Keywords : extrapolation, Eyring-Kramers, metastability, multilevel sampling

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