World Academy of Science, Engineering and Technology
International Journal of Mathematical and Computational Sciences
Vol:11, No:05, 2017

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 ”steared” 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 ”stearing” is not directed enough to stear 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 steared out of the metastabilities. In order to compute the unsteared transition behaviour based on a steared 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
Conference Title : ICMCM 2017 : International Conference on Mathematical and Computational Medicine
Conference Location : Amsterdam, Netherlands
Conference Dates : May 14-15, 2017