Reweighted-Probability Enhanced Sampling: a reversed perspective on metadynamics

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Abstract

One of the areas of atomistic simulations that has received more attention in the past years is enhanced sampling. Especially when dealing with biological systems, present computers fall short of what would be needed to simulate phenomena that in the lab take place on macroscopic timescales. Thus a plethora of different methods have been suggested to overcome this difficulty.
Among them, metadynamics has become rather popular in recent years, and with it the idea of building an on-the-fly bias potential capable of adjust itself to the characteristics of the system. This kind of approach has been used not only for exploring phase space or calculating free energies, but also to fit coarse-graining models and to directly enforce knowledge coming from experiments, in order to compensate for the limitations of molecular dynamics force fields. We believe that the two areas are deeply connected and that any improvement in enhanced sampling has the potential to bring new insight to coarse-graining or simulations-experiment bridging.
We propose here a novel perspective on metadynamics which, by shifting the focus from the bias potential to the sampled probability distribution, allows for a much improved convergence rate, and opens up to new possibilities. In particular the new algorithm can greatly outperform standard metadynamics when dealing with suboptimal collective variables, thus in the case some slow degree of freedom is missing in the reduced description of the system.

Keywords: enhanced sampling, metadynamics, free energy, methods

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