Computer simulation of rare events in material science and biophysics

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Abstract:

The realistic simulation of complex systems in biophysics and condensed matter is one of the biggest challenges in computational chemistry. We recently introduced a method that seems to provide a manner to cope with the complexity of these systems [1- 6], greatly enhancing the possibility to observe rare events in a short computational time. In this approach the finite temperature dynamics of one or more collective variables (Cvs) is biased by a history-dependent potential constructed as sum of Gaussians centered on the trajectory of the CVs. After a transient period, the free energy dependence on the CVs can be estimated as the negative of the bias potential.

We will discuss a recent extension of the method that allows a free energy reconstruction in a very large number of variables, and we will present some application of the methodology to crystal structure prediction and protein folding.

1. A. Laio and M. Parrinello, *Escaping free energy minima*, Proc Natl. Acad. Sci. *USA*, **99**,12562 (2002).
2. R. Martonak *et al*, *Predicting crystal structures: The Parrinello-Rahman method revisited*, Phys. Rev. Lett. **90**, 75503 (2003).
3. M. Iannuzzi *et al*, *Efficient exploration of reactive potential energy surfaces using Car-Parrinello molecular dynamics*, Phys. Rev. Lett. **90**, 238302 (2003).
4. C. Micheletti *et al*, *Reconstructing the density of states by history-dependent metadynamics*, Phys. Rev. Lett. **92**, 170601 (2004).
5. F. Gervasio *et al*, *Flexible docking in solution using metadynamics*, J. Am. Chem. Soc. **127**, 2600 (2005).
6. G. Bussi *et al*, *Equilibrium free energies from non-equilibrium metadynamics*, Phys. Rev. Lett. **96**, 090601 (2006).