IMPORTANCE SAMPLING AND FREE ENERGY ESTIMATION USING CONTROLLED DIFFUSIVE SYSTEMS

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Diffusive systems on energy landscapes, e.g., systems that satisfy Langevin equations of motion, are often used as models of Hamiltonian systems in contact with a heat bath. This is because the white noise term in a Langevin equation constitutes a reasonable model of the interaction of the system with the heat bath, and because one can in principle compute statistical averages, such as equilibrium free energy differences, by Monte Carlo methods. Unfortunately, rare events such as conformational transitions imply that standard Monte Carlo estimates converge slowly. To reduce the computational cost of simulating many diffusions, one often performs importance sampling. For example, in simulations of single-molecule pulling experiments, one can drive the system out of equilibrium by applying a biasing force, and then use relations between nonequilibrium and equilibrium distributions such as Jarzynski's equality [1].

In this presentation, we consider a method [2] for estimating statistical properties of diffusive systems by efficiently simulating rare events. For a given path functional having the interpretation of work, the idea of the method is to control the diffusive system in an optimal way, such that the biasing force and the free energy estimate together yield an approximation of the free energy landscape after sufficiently many iterations. The focus of our treatment is to use the theory of stochastic processes in order to motivate and extend the method to allow for the simultaneous estimation of equilibrium averages by reweighting nonequilibrium measurements [3]. As proof of principle, we consider the example of committor probability estimation for a model of a conformational transition of solvated alanine dipeptide.

[1] C. Jarzynski, *Phys. Rev. Lett.* **78**, pp. 2690-2693 (1997)
[2] C. Hartmann and C. Schütte, *J. Stat. Mech. Theor. Exp.* pp. P11004 (2012)
[3] H.C. Lie, C. Schütte, and C. Hartmann, submitted to *SIAM J. Sci. Comput.*, preprint available at `http://publications.mi.fu-berlin.de/1476/)`