Ergodic sampling in biomolecular simulations using collective variable biases

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Although biology has shifted from macroscopic to mainly molecular approaches, the atomic detail of living systems is still inaccessible to the most powerful microscope, warranting the use of molecular simulation as a "computational microscope". Yet biomolecular simulations are subject to difficult trade-offs between model resolution, size, and time scale. In practice, in our simulations, biologically meaningful processes are rare events. One type of approach to enhance the observation of such rare events is based on "collective variables" that function as transition coordinates, and may thus be used to bias the simulations. In particular, algorithms of the Adaptive Biasing Force family can accelerate transitions while computing free energy profiles, under near-equilibrium conditions. We will discuss such algorithms, their design, practical considerations, limitations, and future perspectives.