

## Overcoming the rare-event sampling problem in biological systems with infinite swapping

Nuria Plattner, Universität Basel

Infinite swapping (INS) is a recently developed method to overcome the rare-event sampling problem.[1] The method is based on a mathematical analysis of parallel tempering (PT) by large deviation theory.[2] An expanded computational ensemble composed of a number of replicas at different temperatures is used for PT and for INS, but while the basic concept of PT is to sample various replicas of the system at different temperatures and exchange information between the replicas occasionally, INS uses the symmetrized distribution of configurations in temperature space, which corresponds to the infinite swapping limit of PT. INS is a general method and therefore potentially useful for various application areas.

In biological systems, rare-event sampling problems arise due to the different timescales on which biological processes occur and a number of challenges needs to be addressed due to the specific properties of functional free energy surfaces characterizing biological macromolecules. The application of INS to biological problems is discussed for two biological systems, the alanine dipeptide, which is a small system and therefore optimal to evaluate sampling efficiency quantitatively and the Villin headpiece, which is used as a test case for the protein folding process.

(1) N. Plattner, J. D. Doll, P. Dupuis, H. Wang, Y. Liu, and J. E. Gubernatis, *J. Chem. Phys.*, **135**, 134111, (2011)

(2) P. Dupuis, Y. Liu, N. Plattner, and J. D. Doll, *SIAM J. Multiscale Model. Simul.*, **10**, 986, (2012)