THE OFF-PATH SIMULATION METHOD: A NEW TECHNIQUE THAT MIXES CHAIN-OF-REPLICA METHODS WITH UMBRELLA SAMPLING-LIKE APPROACHES

Justin K. White,1 Milan Hodoscek,2 Bernard R. Brooks,3 H. Lee Woodcock,1*

1. University of South Florida, Department of Chemistry, Tampa, FL
2. National Institutes of Chemistry, Center for Moleculer Modeling, Ljubjana, Slovenia
3. National Institutes of Health, NHLBI, Laboratory of Computational Biology, Bethesda, MD

Free energy is typically referred to as the most important quantity in chemistry, with computational approaches offering unique insight into the effects that govern chemical and biochemical processes. In this work, we introduce a new chain-of-replica method that uses an umbrella sampling-like approach to determine the potential of mean force (PMF) and present examples. The Off-Path Simulation method (OPS) uses multiple distance restraints to sample orthogonal directions of a discretized reference energy pathway. Further, we have interfaced this methodology in a fully distributed parallel scheme that loosely couples replicas; this facilitates the study of larger systems with near perfect scalability. We applied the OPS methodology to calculate the torsional free energy of butane, and the dissaccharide maltose (vacuum and solvated). OPS calculated values are compared to published theoretical work to verify the validity of this new approach.