EXPLORING MULTIPLE-STEP MULTIPLE-COORDINATE ENZYMATIC REACTIONS: ON-THE-PATH RANDOM WALK SAMPLING FOR FREE ENERGY PATH OPTIMIZATION. Wei Yang, Department of Chemistry and Biochemistry, Florida State University, Institute of Molecular Biophysics, Tallahassee, FL 32306

Commonly, enzymatic reactions are studied via free energy simulations along one or two reaction coordinates, in particular in a stepwise fashion. This classical approach has greatly limited the robustness and the reliability of computational understanding of complex enzymatic reactions. In this talk, we are presenting the first generalized ensemble sampling method for free energy path optimization: on-the-path random walk method. Two challenging systems: the pseudo-uridination reaction catalyzed by pseudo-uridinase and the deamination reaction catalyzed by GMPR are studied via the novel method.