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**Determination of Kinetic Isotope Effects in Yeast Alcohol Dehydrogenase Using Transition Path Sampling** MATTHEW VARGA, STEVEN SCHWARTZ, Univ of Arizona — The experimental determination of kinetic isotope effects in enzymatic systems can be a difficult, time-consuming, and expensive process. In this study, we use the Chandler-Bolhius method for the determination of reaction rates within transition path sampling (rTPS) to determine the primary kinetic isotope effect in yeast alcohol dehydrogenase (YADH). In this study, normal mode centroid molecular dynamics (CMD) was applied to the transferring hydride/deuteride in order to correctly incorporate quantum effects into the molecular simulations. Though previous studies have used rTPS to calculate reaction rate constants in various model and real systems, it has not been applied to a system as large as YADH. Due to the fact that particle transfer is not wholly indicative of the chemical step, this method cannot be used to determine reaction rate constants in YADH. However, it is possible to determine the transition rate constant of the particle transfer, and the kinetic isotope effect of that step. This method provides a set of tools to determine kinetic isotope effects with the atomistic detail of molecular simulations.

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