Towards a judicious choice of degrees of freedom to sample reaction paths of enzymatic reactions

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Modeling enzymatic reaction pathways is a challenging and also computationally demanding task. The numerous degrees of freedom in an enzymatic system, out of which many can be relevant for the reaction and its energetic profile, at least indirectly, render the notion of “the reaction mechanism”, read a single reaction pathway, naïve. One promising approach to tackle this issue is by using the transition network. Our system of interest, Carboxypeptidase A (CPA), which contains a divalent zinc ion in its active site, is an important exopeptidase secreted by the pancreas for digesting intake proteins in the metabolism cycle. It catalyzes the elimination of the C-terminal amino acid via hydrolysis, with a preference for residues with hydrophobic side chains.

Our goal: Develop a method to automatically sample the reaction pathways and find the most probable route by an automated choice of degrees of freedom for the sampling.

[1] F. Noe, D. Krachtus, J. C. Smith, S. Fischer, *Journal of Chemical Theory and Computation,* **2006**, 2, 840-857

[2] D. Xu, H Guo, Q. Cui. J. Phys. Chem. A , 111, **2007**, 5630–5636