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Learning Reaction Mechanisms from Molecular Dynamics: Isomerization in Retinal and p–Coumaric Acid

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Accurate reaction coordinates are essential for understanding chemical reactions, yet identifying them remains a longstanding challenge. While free–energy landscapes and minimum–energy paths are widely used for this purpose, they need not coincide with the pathways actually followed by reactive trajectories. The committor provides a rigorous, dynamics–based reaction coordinate because it directly measures the probability of reaching products before reactants. For molecular reactions, the committor is difficult to determine and even harder to represent in terms of physically interpretable molecular coordinates. Recent developments combining transition–path sampling with machine–learned committors now make it possible to characterize reactive trajectories directly and to identify the molecular motions that control their dynamics.
In this talk, I will present an analysis of the thermal *cis–trans* isomerizations of retinal and p–coumaric acid using "Artificial Intelligence for Molecular Mechanism Discovery" (AIMMD). In these apparently simple double–bond rotations one might expect the central torsion and the free–energy landscape to largely determine the reaction pathway. Instead, the transition–path ensembles reveal strongly curved, stepwise S–shaped pathways involving the coupled motion of four dihedral angles around the reactive bond. This S–shape is absent from the minimum–free–energy path: it arises from the dynamics of the short transition events combined with the mass asymmetry between heavy–atom and hydrogen–bearing dihedrals. These results highlight that reaction pathways cannot be inferred from the potential or free–energy surface alone but require an explicit description of the underlying dynamics and that committor–learning and transition–path techniques allow us to move beyond a static description of reaction pathways.

References

[1] K. Töpfer, G. Lazzeri, V. Ossanna, F. Renner, G. Lattanzi, R. Covino, B. G. Keller, *arXiv preprint arXiv:2604.24245* **2026**.