Metadynamics Simulations of Chemical Reactions in Solution

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The energy barrier is an important parameter in describing and understanding chemical reactions. However, its calculation - especially in the case of the free energy barrier - is a difficult task, since it cannot be easily obtained from molecular dynamics (MD) simulations.

Different methods have been proposed in order to reconstruct the free energy surface (FES) from MDs, such as Umbrella Sampling (US), Metadynamics (MTD) or the recently proposed Well-Sliced Metadynamics (WS-MTD) approach developed by Awasthi *et al*.[1], which is a combination of US and MTD.

In this work, four important chemical reactions have been investigated via standard MTD and WS-MTD in order to estimate the free energy barrier. The chosen reactions cover a range of different types and mechanisms, consisting of a Diels-Alder reaction, an aromatic decarboxylation, an aromatic Claisen rearrangement and the base-catalyzed hydrolysis of formamide. This selection thus includes a cycloaddition, an elimination, an intermolecular rearrangement as well as an OH^--addition.

Utilizing the CPMD code it was possible to obtain many ps long trajectories of the reactions in the gas phase as well as in an explicitly included solvent. From those trajectories, the FES were reconstructed using the WHAM code.

[1] S. Awasthi *et al*., *J. Comput. Chem.*, **2016**, *37*, 1413-1421