Optimizing Parameters in Metadynamics Simulations for Free Energy Calculations

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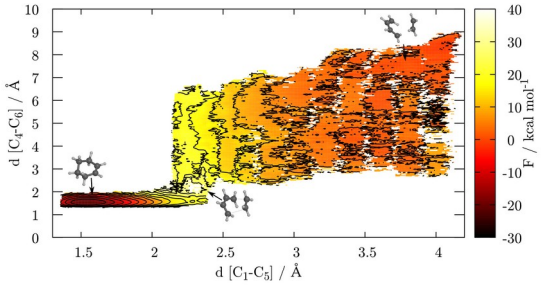

The calculation of free energy surfaces (FES) is essential for understanding chemical reactions. Especially the free energy differences between educts, products and possible transition states, as well as the structure of the latter, allow insight into the nature of the reactions. Well-sliced metadynamics (WS-MTD) [1] is a novel method to calculate FES. It combines umbrella sampling and metadynamics in order to speed up the simulations. However, it employs several fine-tuning parameters whose exact influence on the efficiency and accuracy of the results is not yet well understood.

In this study, the FES of the reaction of 1,3-butadiene and ethylene to cyclohexene, the simplest Diels-Alder reaction, was calculated by WS-MTD. This reaction is well studied, both experimentally and theoretically, and could thus be used to compare the influence of the studied parameters. Using FES calculated with different values of the relevant parameters, the free energy differences between the educts, transition state and products were determined in the form of the activation barrier and reaction energy. These were compared to literature values from experimental and other theoretical studies.

[1] S. Awasthi, V. Kapil, N.N. Nair, *J. Comput. Chem.*, **2016**, *37*, 1413