Tuning the Catalytic Activity of the Synthetic Enzyme KE15 with DNA

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Comparing to natural enzymes, synthetic enzymes can be stable under non-physiological reaction conditions and broaden the range of reaction that could be catalyzed. With this ability to overcome the limitations of natural enzymes, synthetic enzymes therefore provide a promising route to develop catalysts for industrial purposes. However, in most cases the protein scaffold of synthetic enzymes is not optimized and does not contribute to the catalytic performance. In this talk, I will present a novel approach to tune the activity of synthetic enzymes, which relies on regulating electrostatic interactions in the enzyme active site. More specifically, I will show how DNA, a highly polar molecule, can be utilized as an environmental factor to induce electrostatic effects in the active site. I will present molecular dynamics simulations of the Kemp Eliminase KE15, performed with the AMOEBA polarizable force field. This method allows the computation of intrinsic electric fields in the active site, which probe and quantify the enzymatic activity. With this approach, I will show how a DNA fragment placed around the enzyme can stabilize the transition state, lowering the activation energy of the reaction. This demonstration of principle is a fundamental milestone in the development of DNA origamis as structural and functional scaffolds for enzymatic regulation.

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