Engineering PET-degrading enzymes – targeting the energy barrier for PET binding

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In view of the worsening climate crisis and increasing plastic waste pollution, scientific interest in the development of an environmentally friendly enzymatic degradation mechanism for plastics is growing. However, the bottleneck in the industrial application of enzymes for plastic waste recycling is their insufficient activity and partial lack of stability under industrial conditions. [1]

To this end, we investigated the binding behavior of highly active PET-degrading enzymes to polyethylene terephthalate (PET). Adsorption to the PET surface could be captured by classical molecular dynamics (MD) simulations. However, the entry of PET into the active site associated with the formation of productive binding poses was presumably hindered by an energy barrier limiting the activity of the enzyme. Using Hamiltonian Replica Exchange MD (HREMD) simulations, we were able to overcome this barrier and investigate entry pathways leading to productive conformations. In addition to hindering intramolecular PET interactions, we identified amino acids that potentially hinder entry into the binding site based on free energy surface profiles of amino acid-PET interaction. These residues serve as promising mutation sites to enhance PET degradation activity, which will be investigated *in vitro* in the future.

[1] R. P. Magalhaes, J. M. Cunha, S. F. Sousa, *Int J Mol Sci*, **2021**, *22*, 11257.