Computational studies of substrate binding modes of PET44

Alena Endres[1], Holger Gohlke[1,2]

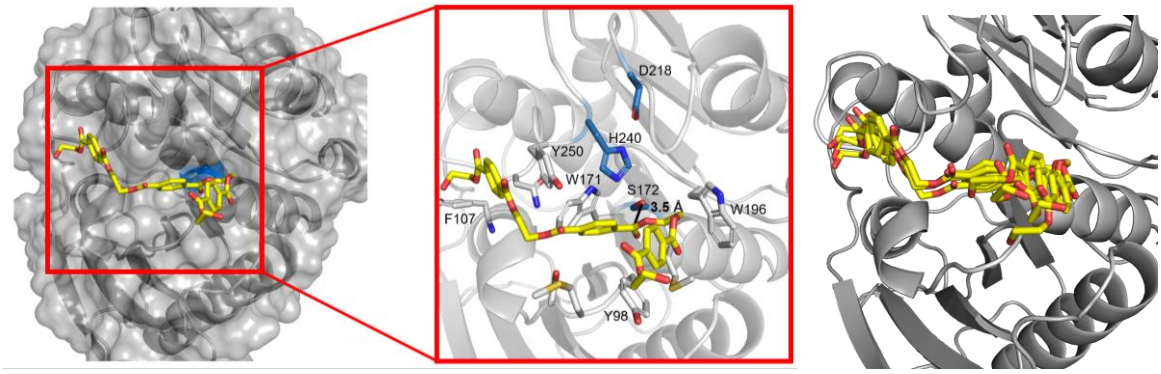
[1]*Institute for Pharmaceutical and Medicinal Chemistry, Heinrich-Heine-Universität Düsseldorf, 40225 Düsseldorf, Germany*

[2]*Institute of Bio- and Geosciences (IBG-4: Bioinformatics), Forschungszentrum Jülich, 52425 Jülich, Germany*

Each year around 400 million tons of plastic waste is produced, increasing yearly[1]. Degradation of these synthetic polymers can take up to 1000 years, and less than 10% of the plastic waste is recycled[2-3]. None of the current recycling methods is feasible for industrial applications[3], they are either leading to poor-quality plastic, air pollution, are energetically inefficient, or need to use harsh chemicals leading to toxic waste[2]. Polyethylene terephthalate (PET) is, with a production of around 33 million tons yearly, within the top five most produced synthetic polymers[1]. Because of its ester bonds, it can be biocatalytically degraded representing an environmentally friendly solution. However, currently known enzymes capable of cleaving PET (PETases) show low enzymatic activity, especially towards PET with high crystallinity as is the case in PET bottles, making those enzymes not available to use with postconsumer plastics[2-3]. Extending previous work on esterases[4] and petases[5], we here investigate the novel PETase PET44.

PET44 is a PETase identified, characterized, and crystallized by our collaborators. The PETase shows the typical fold of an α-/β-hydrolase with a catalytic groove containing the catalytic triad consisting of Ser-His-Asp. Computational studies were carried out investigating the possible binding modes of a PET-trimer, a PET-dimer and two dodecalactones via molecular docking consistent with the proposed catalytic mechanism as well as their robustness through molecular dynamics simulations as done in previous studies[5].

We show that all model substrates bind in the catalytic groove, mostly interacting with hydrophobic amino acids. The binding mode for the PET trimer, shown in the figure, places a central subunit located near the active site, leaving part of the last PET subunit to protrude outside the catalytic groove, near a tryptophane residue, which limits the accessible surface of the catalytic groove to one side. The central subunit close to the catalytic triad of the PET trimer shows low variability during the simulations indicating strong interactions, whereas the ends, especially the one protruding outside, show different confirmations due to the lack of interactions with the enzyme. This knowledge can help, combined with experimental validations, to redesign the catalytic groove of PETases to enhance their activity and therefore make them viable for industrial applications.



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