

Mechanistic insights into substrate-assisted glycoside hydrolases

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Glycoside hydrolases (GHs) catalyze the hydrolysis of glycosidic bonds in carbohydrates and glycoconjugates. They generally exhibit a catalytic dyad of two acidic residues (acid/base and general base).^{1,2} Some of them perform hydrolysis via a *substrate-assisted* mechanism in which the reactive sugar reacts with itself, forming a bicyclic intermediate, which has been described in the literature as an oxazoline or an oxazolinium ion depending on the enzyme family and often with controversy even within the same family. Here we elucidated the reaction mechanism of family GH18 *Serratia marcescens* chitinase B (*SmChiB*) by means of QM/MM metadynamics, using Density Functional Theory to describe the QM atoms. The computed mechanism shows a well-defined hydrogen bond network that controls catalysis by protonating/deprotonating the oxazoline intermediate,³ clarifying previous work. We compare these results with the “expected” mechanism for other substrate-assisted GH enzymes.

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