Title:	Force-activated catalytic pathway accelerates bacterial adhesion against flow
Authors:	Hazra, J.P. (/jspui/browse?type=author&value=Hazra%2C+J.P.) Arora, N. (/jspui/browse?type=author&value=Arora%2C+N.) Sagar, A. (/jspui/browse?type=author&value=Sagar%2C+A.) Srinivasan, S. (/jspui/browse?type=author&value=Srinivasan%2C+S.) Chaudhuri, A. (/jspui/browse?type=author&value=Chaudhuri%2C+A.) Rakshit, S. (/jspui/browse?type=author&value=Rakshit%2C+S.)
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Abstract:	Mechanical cues often influence the factors affecting the transition states of catalytic reactions and alter the activation pathway. However, tracking the real-time dynamics of such activation pathways is limited. Using single-molecule trapping of reaction intermediates, we developed a method that enabled us to perform one reaction at one site and simultaneously study the real-time dynamics of the catalytic pathway. Using this, we showed single-molecule calligraphy at nanometer resolution and deciphered the mechanism of the sortase A enzymatic reaction that, counter-intuitively, accelerates bacterial adhesion under shear tension. Our method captured a force-induced dissociation of the enzyme–substrate bond that accelerates the forward reaction 100×, proposing a new mechano-activated catalytic pathway. In corroboration, our molecular dynamics simulations in the presence of force identified a force-induced conformational switch in the enzyme that accelerates proton transfer between CYS184 (acceptor) and HIS120 (donor) catalytic dyads by reducing the inter-residue distances. Overall, the present study opens up the possibility of studying the influence of factors affecting transition states in real time and paves the way for the rational design of enzymes with enhanced efficiency.
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