Using Molecular Modeling to Understand Enzymatic Cellulose Hydrolysis

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Cellobiohydrolase I (CBH 1) from *Trichoderma reesei* is one of the most active enzymes in the hydrolyzation of cellulose. CBH 1 is a multi-domain enzyme, consisting of a large catalytic module containing an active site tunnel and a small cellulose binding module joined to one another by a 27 residue linker peptide. As an exoglucanase CBH 1 hydrolyzes cellulose in a "processive" manner; the exact mechanism of is not fully understood. As part of an ongoing effort to better understand the hydrolysis process, molecular dynamics simulations that focus on determining the function of the linker peptide have been performed. Although the sequence of the linker peptide is known and it has been shown that the linker is important for enzymatic activity, the role of the linker is yet to be determined. Results from molecular dynamics simulations in which the motion and conformation of the linker adsorbed on a cellulose surface in an aqueous environment will be presented and our simulation data compared with the hypothesis that the linker behaves like a spring, which helps the enzyme to move along a cellulose chain. Since this spring-like motion is a key element in the processive depolymerization of cellulose by Cel7A, our efforts to understand this mechanism, and thus in the future to engineer more capable cellobiohydrolases, is a key element in making the conversion of biomass to biofuels more efficient.