A Mathematical Model for the Kinetics of Hydrolysis of Bacterial Microcrystalline Cellulose by Cellulase Enzymes

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Experimental studies in the Walker laboratory have identified many mechanistic features of the interactions of several cellulase enzymes with bacterial microcrystalline cellulose (BMCC), an idealized model of lignocellulosic materials. Features particularly important to this study include the following:

(1) Only a fraction of the native material is fully accessible to the catalytic domain of bound enzyme and can be hydrolyzed, at least on a rational time scale. The remaining fraction binds enzyme reversibly but does not hydrolyze.

(2) Enzyme binds from solution and establishes adsorption/desorption equilibrium relatively quickly, but hydrolysis of the substrate by bound enzyme proceeds slowly thereafter.

(3) In a closed reaction system, the sugar product accumulating in the liquid phase can "inhibit" the enzyme by binding to its catalytic domain, which gradually decreases the overall rate of hydrolysis.

We incorporate these mechanistic features into a set of three time-dependent, nonlinearly coupled mass balances that describe the time-varying concentrations of (1) enzyme bound at sites on reactive portions of the substrate, (2) enzyme bound at sites on inert portions of the substrate, and (3) cellobiose product accumulating in the liquid phase. These equations can be scaled and solved analytically with a singular perturbation approach that makes use of the disparity of the time scale for adsorption/desorption vs. that for hydrolysis. We verify the accuracy of the model by comparing it to bound enzyme and cellobiose concentrations measured for hydrolysis of BMCC by the *T. fusca* enzymes Cel5A, Cel6B, and Cel9A, and we discuss its implications for collecting useful kinetic data for other cellulase/cellulose systems.