Some bacteria use a complex of macromolecular structures that are bound to both the bacterial cell and cell walls of biomass and contain the molecular machinery for digesting biomass and the products, the enzyme-Microbe-Substrate Interface (EMS interface). An understanding of the structure and functioning of the EMS interface enhances our ability to harmoniously tune its components as well as the biomass target. We use our insights to suggest modifications of biomass structure (genetic modifications of plants) and pretreatment processes for optimal conversion of biomass to fuel precursors and modifications of cellulosomal composition and structure for enhanced interaction and degradation of the modified cell walls. We present the Electron Tomography of the EMS interface which produces three-dimensional volume renderings of objects at the 3-5 nanometer scale, appropriate for the macromolecular structures found in the EMS interface and we present the Molecular Modeling of EMS interface components such as cellulases and enzymes and of cell wall components such as cellulose, hemicellulose, and lignin. The modeling contributes to interpretation of tomographic images, testing hypotheses of mechanisms in the EMS interface, and proposing new hypotheses in the same way that the tomography can validate theoretical findings of modeling. Recent successes in our research has brought together the length scales of electron tomography and molecular modeling making new insights into microbial interactions with biomass possible.

**Poster 7-25**

**Towards engineering cellulosomes to diminish product inhibition**

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Product inhibition significantly impacts the efficiency of cellulose deconstruction by cellulase enzymes, but the reported product inhibition constants range over several orders of magnitude depending on the experimental conditions, and there is little consensus on the importance of this phenomenon. To provide insights into cellulase product inhibition, we examine the impact of product binding on both processive and nonprocessive cellulases by calculating the binding free energy of cellobiose to the catalytic domain of representative enzymes from glycoside hydrolase Families 6 and 7 using steered molecular dynamics and alchemical thermodynamics integration methods. Several point mutations on the key binding residues were also made computationally to study the binding free energy changes during the product expulsion process. We aim to engineer the cellulase enzymes to lower the binding free energy of cellobiose, thus accelerating the product expulsion process and improving the efficiency of biomass conversion.

**References**

