Simulating carbon-cycling enzymes

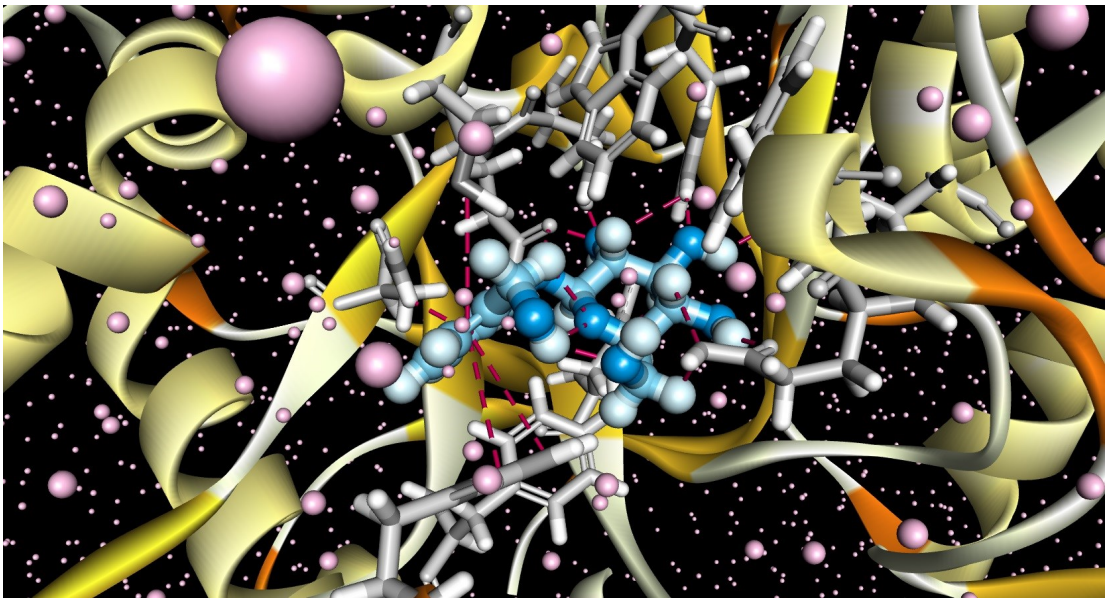
CAC

Project description

Cellulose is the most abundant source of renewable carbon and energy on earth. However, the efficient conversion of cellulose to useful sugars and biofuels by natural microbial enzymes remains a challenge. To address this challenge, the Aristilde Research Group at the Cornell University College of Agriculture and Life Sciences performed the first study of its kind that employs a fully-computational approach to evaluate how different environmental conditions disrupt the activity of carbon-cycling extracellular enzymes. Two such enzymes—one from a fungus and one from a bacterium—were simulated in an explicit fully-solvated environment at different protonation states.

CLIENT
Aristilde Research Group

SERVICES
- Red Cloud
- Cloud Consulting
- Programming



Molecular dynamics close-up snapshot of substrate (shades of blue) in the active site of a beta-glucosidase with H-bond networks (dark pink dotted lines) between amino acid residues (gray) and the substrate. The simulations were conducted in a fully-hydrated system with explicit water molecules; water oxygen atoms are shown as light pink spheres. The peptide backbone of the enzyme is shown in ribbon-style (shades of yellow and orange).

CAC services

CAC consultants created a Red Cloud image with BIOVIA Materials Studio and Discovery Studio; resolved license, installation, and security issues; and, took a snapshot of the cloud image that booted up with all server software running correctly. CAC also created a set of test procedures to determine that the cloud instances ran correctly and provided instructions on how to manage instances. Subsequently, we experimented with the GROMACS molecular dynamics package on TACC's Stampede, created a job submission script, and analyzed scaling behaviors based on simulation length.

Results

The major findings were (1) while amino acid residues on the surface of the enzyme undergo substantial changes in protonation states, the residues in the active site remain the same and are protected against external stimuli, and (2) the chemical changes outside of the immediate active site lead to disruption in the favorable conformations needed for optimal substrate binding. Therefore, the chemical susceptibility of the outer surface of these enzymes may dictate their response to external environmental changes even when the active site chemistry is quite robust. To learn more, read "Short-time dynamics of pH-dependent conformation and substrate binding in the active site of beta-glucosidases: A computational study" by David Flannelly, Thalia Aoki, and Ludmilla Aristilde in the *Journal of Structural Biology*. This research was supported by two National Science Foundation Graduate Fellowships and start-up funds from Cornell University.

"CAC consultants and the Red Cloud platform were instrumental in facilitating the development of our preliminary model analysis. We then used a job submission script and scaling tests written by CAC to make longer runs on an XSEDE supercomputer. The resulting data analysis was performed on Red Cloud."

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