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Title: Decomposition of Neutron Scattering Spectra with Molecular Dynamics Simulations on Dynamics of Cytochrome P450cam

Name: Miao, Yinglong

Affiliation: University of Tennessee/Oak Ridge National Laboratory Center for Molecular Biophysics

Cytochrome P450s are essential hemoprotein monooxygenases which catalyze a variety of biochemical processes including carcinogenesis, drug metabolism, lipid and steroid biosynthesis and degradation of pollutants. As an enzyme from Pseudomonas putida that catalyzes the regio- and stereo-specific hydroxylation of camphor in its active site, Cytochrome P450cam (CYP101) has long served as a model system for studying P450s. Neutron scattering experiments combined with molecular dynamics simulations have been performed to investigate the structural flexibility of substrate-free and camphor-bound CYP101. Quasielastic neutron scattering spectra measured at three different energy resolutions (i.e., 1 μeV, 3.5 μeV and 25 μeV) show that substrate-free CYP101 undergoes internal motions distributed over similar relaxation times as camphor-bound CYP101 but with larger amplitudes, indicating substrate-free CYP101 possesses increased dynamics than the latter on ps-ns timescales. MD simulations performed in parallel are in good agreement with the neutron scattering spectra and used to decompose the later in details. Flexible regions are identified surrounding the substrate access site in the protein and they are found to contribute to the higher flexibility of substrate-free CYP101 compared with the camphor-bound form.