

Elucidating KcsA structural dynamics using time-resolved X-ray solution scattering and molecular dynamics simulations

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Potassium channels are ubiquitous membrane proteins that enable selective K⁺ ion permeation. The study of membrane proteins at atomistic resolution has become possible using different experimental and computational techniques and has led to increasing scrutiny of K⁺ channels as drug targets. We are interested in exploring the structural response of the pH-sensitive bacterial potassium channel KcsA upon a pH-change using time-resolved X-ray solution scattering in concert with guided Molecular dynamics (MD) simulations.

Time-resolved X-ray solution scattering was conducted to shed light on KcsA structural dynamics in the μ s to ms range. Upon UV-light activation, a photo-sensitive compound is triggered to release protons. The subsequent drop in pH (pH 7 to pH 4), leads to structural shifts in KcsA from inactive to active conformations. As a next step, MD simulations are required to fit time-resolved X-ray solution scattering data. In brief, MD simulations can be employed to sample inactive and active candidate conformations extracted from known structures. From these MD simulations, difference X-ray scattering curves can be calculated and compared against experimental data.

Using time-resolved X-ray solution scattering, we successfully observed structural perturbations in the pH sensitive ion channel KcsA. Initial results indicate two potential movements. The experimental data has been decomposed into basis spectra with corresponding time evolution. Optimized fits to the experimental data allow for subsequent analyses of protein conformational and pore size changes, corresponding to different KcsA activation states. This fundamental research may lead to the development of new technologies to study time-resolved protein perturbations.