

Tracking ATP binding by adenylate kinase using time-resolved X-ray solution scattering

Content

Adenylate kinase (ADK) is a phosphotransferase that maintains energy homeostasis in cells by catalyzing the reversible transfer of a phosphoryl group from ATP to AMP to produce two ADPs. The protein consists of highly flexible ATP- and AMP-binding domains that undergo large conformational changes relative to the more static core domain during catalysis. The ADK protein has proven an excellent model system for both experimental and computational methods, but the coupling between conformation change and substrate binding and the timing of these events are not fully understood. We performed time-resolved X-ray solution scattering experiments using externally laser-triggered caged-ATP substrate to track ADK functional dynamics. The time-resolved X-ray data identified a kinetic state with a rise-time of 5.3 ms that upon computer simulation-driven structural refinement was shown to display significant closure of the ATP-binding domain, but with a fully open AMP-binding domain. Hence, this study shows unequivocally that upon exposure to ATP, the initial response by the protein is starting to close its ATP-binding domain, while keeping the structural change in the AMP-binding domain on hold. The methodology holds great promise to study relative order and timing of structural events in protein functional dynamics.

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