

Electron Transfer-Induced Conformational Changes in NRH:Quinone Oxidoreductase

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Abstract

NRH:quinone oxidoreductase is a flavoenzyme that catalyzes the one-step reduction of quinones to hydroquinones using its cofactor, flavin adenine dinucleotide (FAD). The enzyme kinetics goes through a 'ping-pong' mechanism, in which changes in the flavin redox state regulate binding and release of substrates. In the reductive half-cycle, the first substrate binds and transfers electrons to the flavin inducing a conformational change of the active site that favors the subsequent release of the substrate. In the next step, the second substrate binds the empty active site and accepts electrons from the flavin, thus completing the redox cycle. The redistribution of charges at the active site causes a reversion to the initial conformation, and thus, the cycle repeats. In previous molecular dynamics simulation study,¹ the observed changes (near the flavin) were in the pico – nanosecond time-scale and cannot account for the large-scale oscillatory movements associated with the binding and release of alternate substrates. Herein, we are studying the slower dynamics of the subunit interface (surrounding the active site) using Normal Mode Analysis and examining how it is- related to the faster local motions triggered by electron/proton transfers. The role of coevolving residues on the dynamics² is also being examined using Statistical Coevolution Analysis.

Bibliography.

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