SINGLE-MOLECULE DATA DRIVEN THEORY FOR DETECTING SHORT-LIVED STATES IN F1-ATPASE ROTATION

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A data-driven modeling method of the molecular machine F1-ATPase is presented. On the one hand, our theory is built to treat a variety of different type of single-molecule and ensemble experiments used to probe the F1-ATPase. On the other hand, the model is applied to different F-ATPase species, in particular the Thermophilic Bacillus and Paracoccus Denitrificans, since their a_3b_3 ring structure is highly conserved and hence the mechano-chemistry is presumably similar, even though their stepping kinetics vary.

An elastic molecular transfer theory provides a framework for a multi-state model which includes the probe used in single-molecule imaging and magnetic manipulation. When applied to unconstrained rotation of single F1-ATPase, the model is able to enhance the resolution of the single-molecule imaging. In the rotation of the F1-ATPase, the use of the angular jumps ("secant velocities") provides a tool for the detection of fast states of microsecond life time which are hidden by the fluctuations of the imaging probe.

Ultimately, the motivation is to gain mechanistic insight into the chemo-mechanics that leads to biological function: our model-based method was used to predict the life time and angular position of the intermediate during the correlated behaviour in F-ATPase. The release of nucleotides would be a bottleneck process, but the binding of another nucleotide to another site acts to accelerate the release by 5-6 orders of magnitude. The correlated behavior is captured in our model via the angle-dependent rate constants of the individual substeps. We propose that the allosteric mechanism is universally found in all F-ATPase species and may be present in other members of the AAA+ ring proteins.