A Unified Catalytic Mechanism of Adenosine Triphosphate Hydrolysis in ATPase Enzymes

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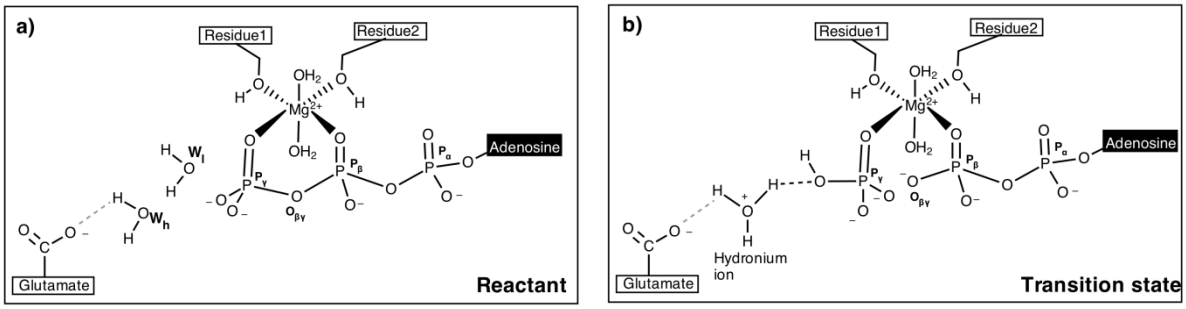
Adenosine triphosphate (ATP) hydrolysis plays vital role in living organisms. The ATPase enzymes (e.g, myosin [1], kinesin [2] and F1-ATPase [3]) utilize the chemical energy generated by the ATP hydrolysis to carry out mechanical tasks (e.g., muscle contraction, cytokinesis and rotary motion) in living cells. The detailed mechanism of ATP hydrolysis catalyzed by ATPase enzymes is still not fully understood. However, based on the recently reported hybrid QM/MM simulations of the catalytic ATP hydrolysis reaction in ATPase enzymes, common mechanistic features of the catalytic reaction are emerging. Although these ATPase enzymes are involved in a variety of biological functions, catalytic reaction of ATP hydrolysis occurs through noticeably common mechanism. Here, a comparative review of the computational (QM and QM/MM) studies of the catalytic mechanism of ATP hydrolysis in Mg^{2+}-ATP bound ATPase enzymes is presented. Simulations indicate that hydrolysis mechanism in ATPases is initiated by the cleavage of P_γ–$O_{\beta\gamma}$ bond of ATP (dissociative mechanism) that produces ADP and trigonal planar metaphosphate moiety. A glutamate residue situated in the vicinity of terminal γ-phosphate serves as a general base (see Scheme 1), that assists one helping water molecule (W_h) to abstract proton from the lytic water molecule (W_l) to generate hydronium ion and hydroxyl nucleophile. The nucleophilic attack of hydroxyl group on the metaphosphate results in the ADP·P_i hydrolysis product, while hydronium proton is transferred to the glutamate residue.



Scheme 1: Reactant a) and Transition state b) of ATP in ATPases.

References

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