

**COMPUTATIONAL STUDIES ON ENZYMATIC PHOSPHATE
HYDROLYSIS**

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Among other phosphate hydrolysis enzymes, GTP-binding proteins can be considered as signal switch molecules that cycle between the GTP-bound ON-state and the GDP-bound OFF-state. These proteins are usually switched ON by the action of activated guanine-exchange-factors (GEFs) that catalyze the exchange of protein bound GDP by GTP. In the GTP-bound ON conformation, these GTP-binding proteins interact specifically with an appropriate effector molecule and thus transmit the corresponding signal to the next downstream component in the signaling cascade. All known GTP-binding proteins exhibit a GTPase activity that recycles the protein back to its inactive GDP-bound form. This process is regulated by GTPase activating proteins (GAPs). The rate of this reaction is crucial for the corresponding timing of the regulated process: the longer a GTP-binding protein remains in its active GTP-bound state, the longer it will transmit and also amplify a certain signal. Hence, the rate of GTP hydrolysis is of great importance for the right timing of many processes in a cell and in this process binding of the nucleotide, protein-protein interactions and enzyme reactivity share the main roles in the play. In this talk we will present several examples and pose many questions on these challenging studies by computational methods, including flexible protein-protein docking and empirical valence bond (EVB) studies of the chemical process of phosphate hydrolysis.