Prediction of Allosteric switch involved in the regulation of Copper(I) in *Mtb* CsoR

Abhigna Polavarapu and Mu-Hyun Baik*
Department of Chemistry
Indiana University

CsoR(Copper sensitive operon Repressor) in *Mycobacterium tuberculosis*(*Mtb*) is a protein involved in the *in vivo* regulation of copper concentration. *Mtb* engineered CsoR to sense excess Cu^{I} in the cytosol which negatively represses the transcription of copper exporter gene. In its apo form CsoR is bound to the operator region of *cso* operon on DNA. Cu^{I} is speculated to bind in an unusual trigonal planar fashion with two cysteines and one histidine based on crystal structure analysis. When CsoR binds to copper it undergoes an overall structural change (allostery) and looses its affinity to DNA activating the transcription of metal exporter CtpV. In the current computational exploration we focus on the binding mode of Cu^{I} and identify different protonation states of copper bound cysteines. We performed MD simulations on the apo and copper bound form with an initial guess from a QM/MM calculation to predict the **Structural Switch** involved in the **Allosteric regulation**.