

Abstract Submitted
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Controlling allosteric networks in proteins NIKOLAY DOKHOLYAN, University of North Carolina at Chapel Hill — We present a novel methodology based on graph theory and discrete molecular dynamics simulations for delineating allosteric pathways in proteins. We use this methodology to uncover the structural mechanisms responsible for coupling of distal sites on proteins and utilize it for allosteric modulation of proteins. We will present examples where inference of allosteric networks and its rewiring allows us to “rescue” cystic fibrosis transmembrane conductance regulator (CFTR), a protein associated with fatal genetic disease cystic fibrosis. We also use our methodology to control protein function allosterically. We design a novel protein domain that can be inserted into identified allosteric site of target protein. Using a drug that binds to our domain, we alter the function of the target protein. We successfully tested this methodology *in vitro*, in living cells and in zebrafish. We further demonstrate transferability of our allosteric modulation methodology to other systems and extend it to become light-activatable.

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