**Title: Discovering the mechanism of Hsp70 conformational cycling**

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The 70 kDa heat shock protein (Hsp70) is a highly conserved, ATP-dependent chaperone present in most organisms. Hsp70 is known to assist in the remodeling of dozens of client proteins to maintain proteostasis. Allosteric changes in the conformations of Hsp70 occur due to interactions with ATP, clients, and various cofactors. The *E. coli* homolog of Hsp70 (DnaK) was previously shown to bind directly to the Hsp40 homolog (DnaJ) and nucleotide exchange factor GrpE. These interactions are integral to the conformational cycling of DnaK that allow client protein remodeling. Recently, structural models of DnaK bound to the J-Domain of DnaJ, and DnaK bound to GrpE have been produced. In this work, we investigated the effect that DnaJ and GrpE have on the conformational cycling that occurs in the DnaK system. We used coarse grain models in which each amino acid residue was reduced to a single bead at the carbon α position and attached via spring to amino acids within 9 Å. Coarse grain models were then perturbed and the vibrations were analyzed using Normal Mode Analysis. Two models were used to study DnaK without cochaperones: DnaK apo-ATP, and DnaK ATP conformation. The vibrational modes for each standalone DnaK model were selected to be compared to the models of DnaK-DnaJ and DnaK-GrpE. By comparing the DnaK conformational shifts to the conformational changes of DnaK combined with cofactors, a pattern appears between the two models that describes the methods of interaction that allows cofactors to activate the ATPase activity of DnaK. When bound to DnaJ, the nucleotide binding domain of DnaK is restricted in motion which could allow closer interaction between DnaK and ATP to increase the ATPase activity that happens in the protein. When GrpE-bound, both the nucleotide binding domain and the substrate binding domain of DnaK are more active which allows for the release of ADP and remodeled protein. We are currently exploring the full effects of these changes in conformational motion that could further explain the mechanism of DnaK cycling.