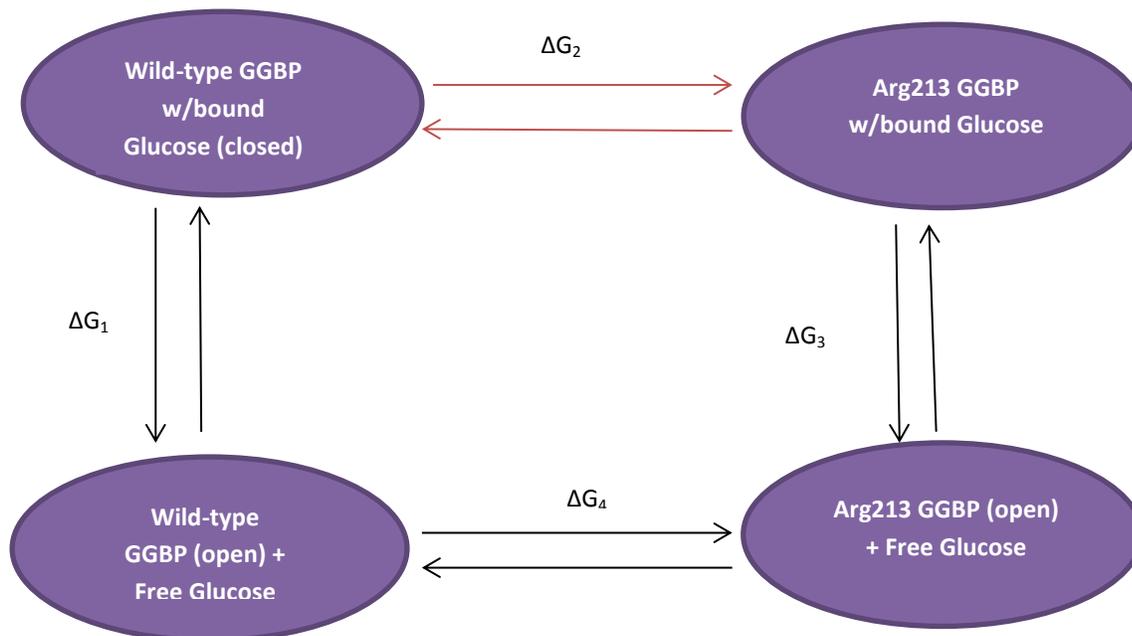


# Measuring the Free Energy Change of the Glucose/Galactose Binding Protein Utilizing Molecular Dynamic Simulations

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Glucose/Galactose Binding Protein (GGBP) is an  $\alpha/\beta$  protein found in bacteria that mediates chemotaxis and is involved in the active transport of glucose and galactose. The binding of the sugar to the protein occurs through hydrogen bonding with the OH groups on these sugars. The formation of these bonds is important in determining the binding energy of the sugar to the protein. Utilizing Molecular Dynamic simulations, a thermodynamic cycle is being performed to determine the difference in binding affinity for the wild type and a mutant form of GGBP (Ala213 to Arg213) of glucose. The cycle is broken down into four steps and four  $\Delta G$  calculations (illustrated below). The focus of this research is to test the  $\Delta G$  of mutation between the wild type and mutated form ( $\Delta G_2$  on illustration). Gromacs-4.6.5 is being used to run the Molecular Dynamic simulations and a double annihilation. “Dummy” atoms were added in the wild GGBP which were then replaced by the mutated residue topology (Arg213). The change in free energy will be calculated using the Weighted Histogram Analysis Method (WHAM) to extract the Potential of Mean Force (PMF) and thus to calculate the  $\Delta G_{\text{Mutation}}$  ( $\Delta G_2$ ). The  $\Delta\Delta G_{\text{binding}}$  can be calculated by  $\Delta G_1 - \Delta G_3$  which is equal to  $\Delta G_2 - \Delta G_4$ , collecting three of the four  $\Delta G$ 's we can calculate the missing  $\Delta G$  and  $\Delta\Delta G$ , since  $\Delta G_1 + \Delta G_4 - \Delta G_3 - \Delta G_2 = 0$  (Fig.1).



**Figure 1. Thermodynamic Cycle of the Wild-Type GGBP/Mutated GGBP binding with glucose with the red arrows indicating the  $\Delta G$  being measured in this research.**