Measuring the Change in Free Energy of Mutated Glucose/Galactose Binding Protein Using Molecular Dynamics Simulations

Ross R. Cirincione, Christopher L. McCoy, Kathleen J. Jedreski, and Amil A. Anderson

Department of Chemistry | Wittenberg University | Springfield, Ohio

GGBP is found in the bacteria *Escherichia coli* where it is in the periplasmic space and is used for chemotaxis. As the binding of glucose to this protein can be directly related the amount of glucose in an environment, the use of GGBP as a biosensor in humans has been proposed. In this research, molecular dynamics were used to determine the binding affinity of glucose to mutants of the glucose galactose binding protein. With the binding of the sugar to the protein, the two protein domains close around the sugar in a hinge-like manner, leading to the closed conformation of the protein. GROMACS software was used to simulate interactions using the umbrella sampling method, where the glucose molecule was pulled from the binding pocket of GGBP. Values for the potential of mean force were calculated using weighted histogram analysis method, and differences from the resulting plot were used to determine the change in the binding free energy, and then the difference of binding affinity of the sugar to GGBP and its mutant. A thermodynamic cycle (Figure 1) is being investigated to contribute to a better profile of the sugar-protein system. A lowered binding affinity is favored as human physiological levels of glucose would saturate the wild-type GGBP. Lower binding affinity can be achieved through mutagenesis of residues located near the ligand binding pocket of GGBP; in this case, Alanine 213 was mutated to Arginine 213 (A213R).

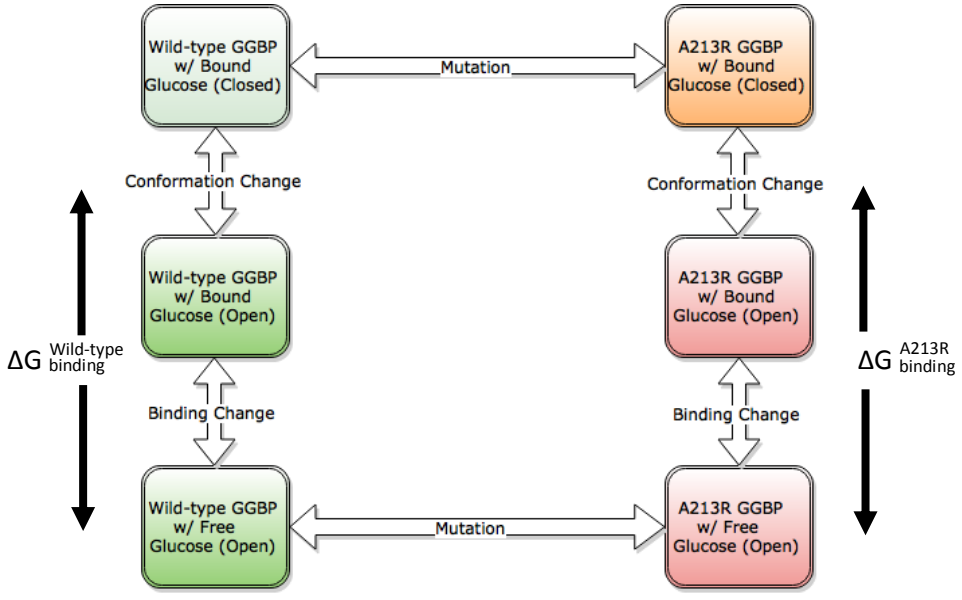

Figure 1. Thermodynamic cycle of GGBP. The change in free energy for binding is the difference in energy between any two corners of the same side in the diagram (ΔG).