

Thermodynamic Free Energy Calculations for Determining the Free Energy Difference in Sugar Binding for the Glucose/Galactose Binding Protein

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The glucose/galactose binding protein (GGBP) mediates chemotaxis in bacteria but also transports sugars, mainly glucose and galactose, through the membranes of cells via an integral membrane protein. It binds around the sugar using a “hinge feature” connecting two domains (Figure 1). The free energy change for the binding of either glucose or galactose to GGBP was studied by free energy molecular dynamic simulations. To convert glucose into galactose, naturally, requires an epimerization reaction, but computationally we switched the position of the hydroxyl group, by mutating from one configuration to the other. The difference in the free energy change between the bindings of the two sugars shows that glucose is preferred over galactose with a free energy change of $30(\pm 2)$ kJ/mol (Figure 2). It is also more energetically favorable for the protein to be bound to a sugar rather than open and free of the sugar ($-27(\pm 3)$ kJ/mol).

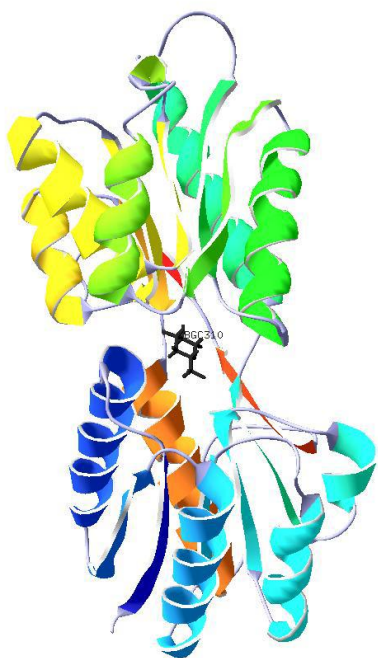


Figure 1: GGBP with Beta-D-glucose bound in the center between the alpha and beta domain.

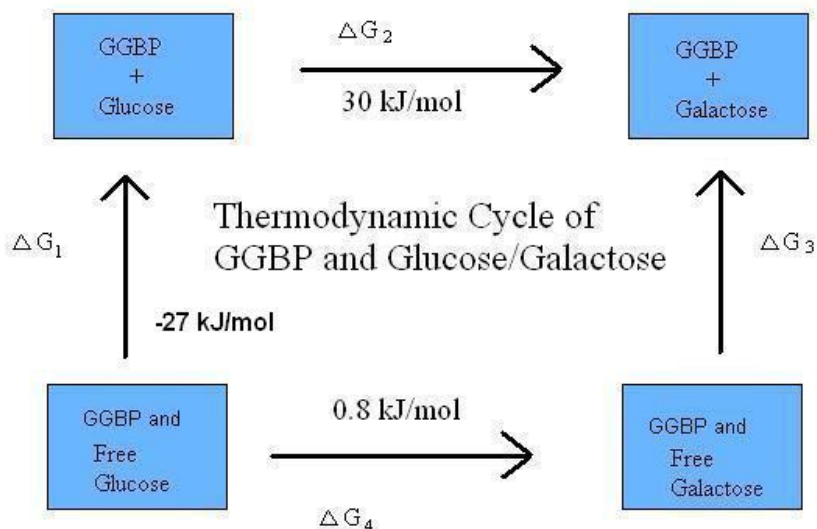


Figure 2: The thermodynamic free energy cycle of the conversion of glucose to galactose.