Calculation of Free Energy for the Binding and Conversion of Gulose and Galactose to the Glucose/Galactose Binding Protein Using Computational Alchemy

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Molecular dynamics free energy simulations were used to model the conversion of the sugar gulose to galactose when bond to a protein and also for the sugars alone using the GROMACS software package. Initially, gulose was placed in a box of water using GROMACS. The free energy change for the epimerization reaction, resulting in the conversion of gulose to galactose, was calculated using a computer alchemy approach by rotating the hydroxyl group bound to carbon three. Simulations were also performed to model the binding of gulose to the glucose/galactose binding protein (GGBP) while calculating the free energy difference between GGBP being bound or unbound to gulose. The free energies were then determined for individual steps and right hand and left hand approximations were used to find the total free energy. Free energy changes were also calculated using the Bennett Acceptance Ratio method. Gulose was found to be less stable in water than galactose (at a value of ΔG_6= -0.042 ±0.36 KJ/mol) and that gulose is more stably bound to GGBP than galactose (at a value of ΔG_5=0.399 ±1.32 KJ/mol).

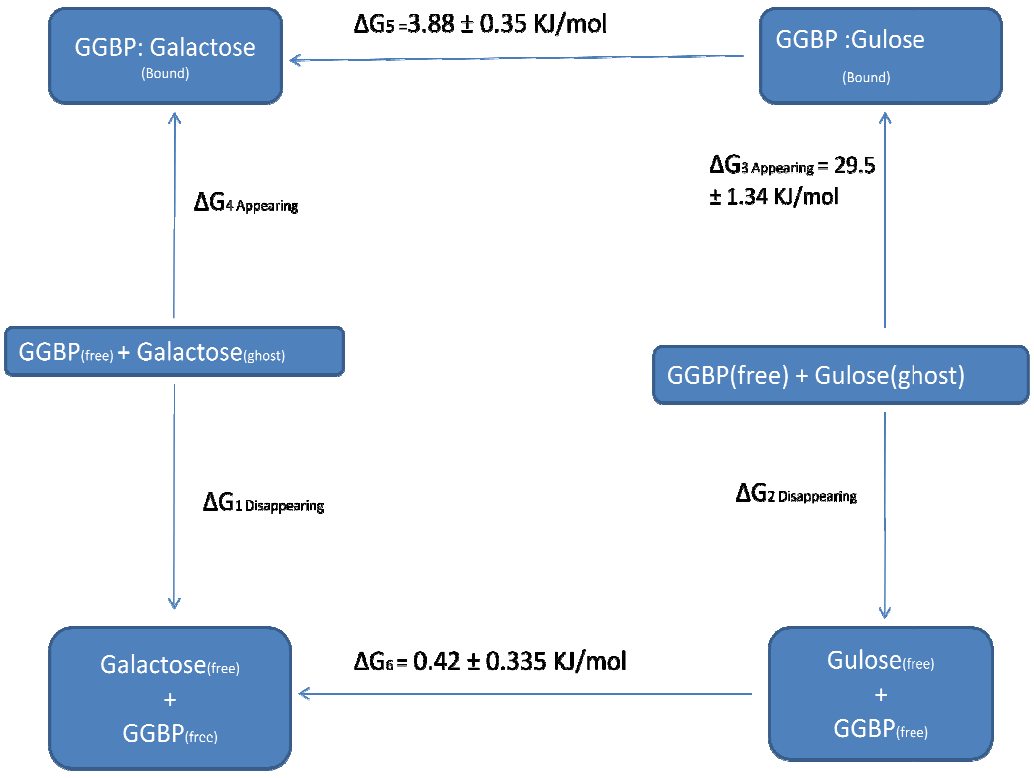

Figure 1: Thermodynamic cycle with the conversion of gulose to galactose when in the presence of GGBP.