

Measuring the Free Energy Change of Binding of Glucose to Glucose-Galactose Binding Protein

Natalie Nguyen '17, Sabrina Davis '18, Amil Anderson

Wittenberg University, Springfield, OH

The glucose-galactose binding protein (GGBP) is one of several enzymes being utilized to develop a fluorescence-based glucose sensor for monitoring glucose levels *in vivo*.¹ This research focuses on using molecular dynamics to measure the binding free energy of glucose to a wild type GGBP. The process is represented by the thermodynamic cycle below (Figure 1) where the free energy of binding can be evaluated by simulating glucose annihilation from the binding pocket with the addition of harmonic restraints to prevent the ghost ligand molecule from drifting. Each indicated transition in the figure was simulated using Gromacs 5.1.2 and thermodynamic integration simulation method. The free energy of binding was estimated to be 7.9 ± 0.4 kcal/mol which is close to experimental results of 9.1 kcal/mol.² The methods used to measure these values can be applied to similar systems such as mutated versions of GGBP for future studies.

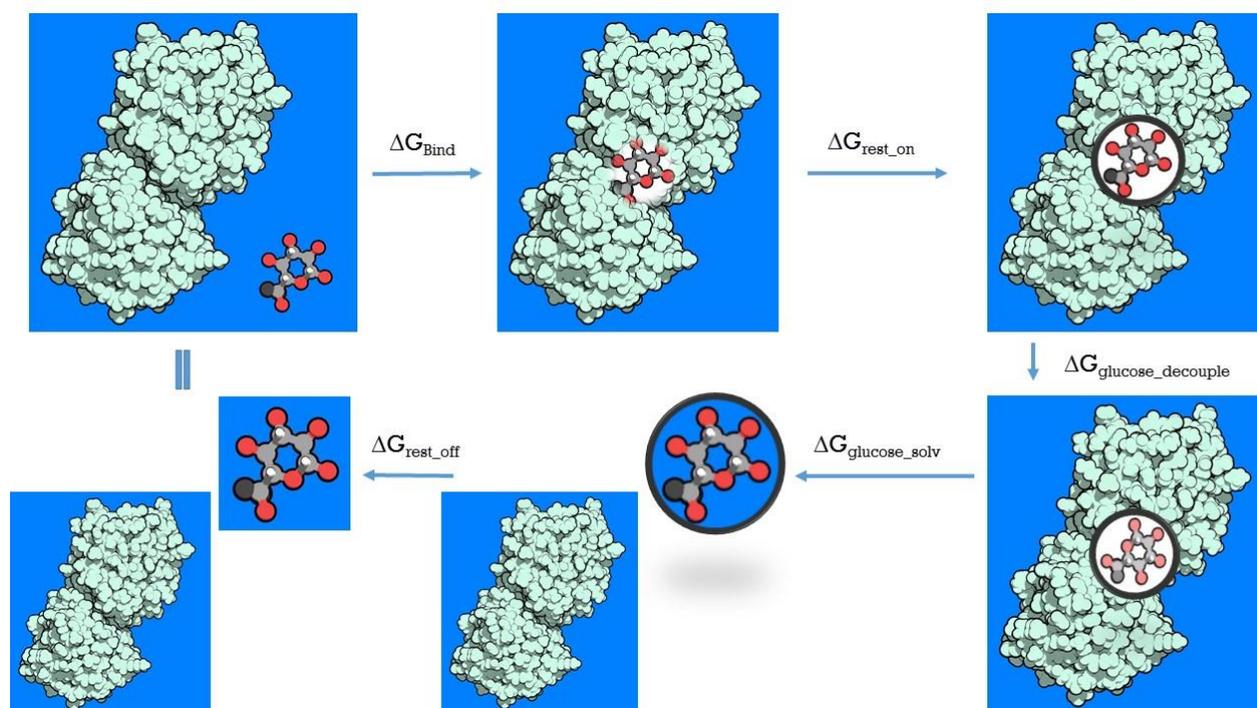


Figure 1. Depiction of the thermodynamic cycle used to evaluate the free energy of binding of glucose to GGBP, ΔG_{Bind} . $\Delta G_{\text{rest_on}}$ and $\Delta G_{\text{rest_off}}$ are the free energies associated with the application and removal of harmonic restraints that are used to restrain the glucose during the process to prevent drifting during the simulations; the restraints are modeled as a grey ring around glucose in the figure. $\Delta G_{\text{glucose_decouple}}$ is the result of removing glucose from the binding site of GGBP by disabling intermolecular forces between the two molecules. $\Delta G_{\text{glucose_solv}}$ is the free energy of glucose solvation. The last transition is the transportation of glucose to the same box with GGBP which has no associated free energy change.

¹ Pickup, J. C.; Hussain, F.; Evans, N.D.; Rolinski, O.J.; Birch, D. J. S. *Fluorescence-based glucose sensors*. **2004**, *20*, 2555-2565; *Biosensors and Bioelectronics*, *Science Direct*. **2005**.

² Zukin, R. S.; Strange P.G.; Heavey L. R.; Koshland, D.E. Jr. *Properties of the Galactose Binding Protein of Salmonella typhimurium and Escherichia coli*. **1977**, *16*, 3, 381-386; *Biochemistry*.