

Measuring the Free Energy Change of the Glucose/Galactose Binding Protein using Molecular Dynamics and Umbrella Sampling with Limited Position Restraints

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The Glucose/Galactose Binding Protein (GGBP) plays a significant role in bacterial chemotaxis towards glucose and galactose. There are two distinct conformations for GGBP; the open-state and the closed-state when either glucose or galactose is bound between the two domains. GGBP has recently been evaluated as a possible biosensor to non-invasively measure glucose levels in diabetes mellitus patients. The binding free energy of GGBP and glucose can be calculated computationally with umbrella sampling. This research attempts to calculate the $\Delta G_{\text{binding}}$ of GGBP and glucose using the umbrella sampling pull method with a single positional restraint on GGBP. Previous research has performed the umbrella sampling pull method for GGBP and glucose using a more involved six degrees of freedom restraint on the protein/glucose system during simulations. This research will contribute to a larger project in creating a thermodynamic cycle for the mutation of residue Ala-213 to Arg in GGBP to measure $\Delta\Delta G_{\text{binding}}$. These simulations also help us determine if a two-step process (Closed GGBP with bound glucose to open GGBP with bound glucose to open GGBP with free glucose) is required to calculate the $\Delta G_{\text{binding}}$.

