

## Measuring the $\Delta G$ of Binding of Glucose to Mutant GGBP via Molecular Dynamics and Umbrella Sampling

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The Glucose/Galactose Binding Protein (GGBP) is responsible for the transport of sugars, and the mediation of chemotaxis in many bacterial species. The protein is composed of two domains that enclose the sugar molecule and binds with hydrogen bonds and Van der Waals forces. This research focuses on how the free energy of binding of glucose to GGBP is altered when the binding pocket is altered by alchemical mutagenesis. By mutating Phe 16 to Leu a large portion of the complimentary surface was destroyed due to the comparative lack of surface area for the Leu sidechain as compared to Phe. The free energy of binding was calculated using molecular dynamics simulations (GROMACS 4.6.5) via the umbrella sampling method. Glucose was pulled out of the protein to a distance of 5 nm and data was sampled at every 0.2 nm (5 ns production runs at each pull increment). This data was then analyzed with the Weighted Histogram Analysis Method (WHAM) to extract the Potential of Mean Force (PMF) for each sample point. This information was then used to calculate the  $\Delta G_{\text{Binding}}$  for the wild type (Phe-16) and the mutant (Leu-16).

