Investigating Free Energy and Conformational Changes in Glucose/Galactose Binding Protein Using Molecular Dynamics Simulations

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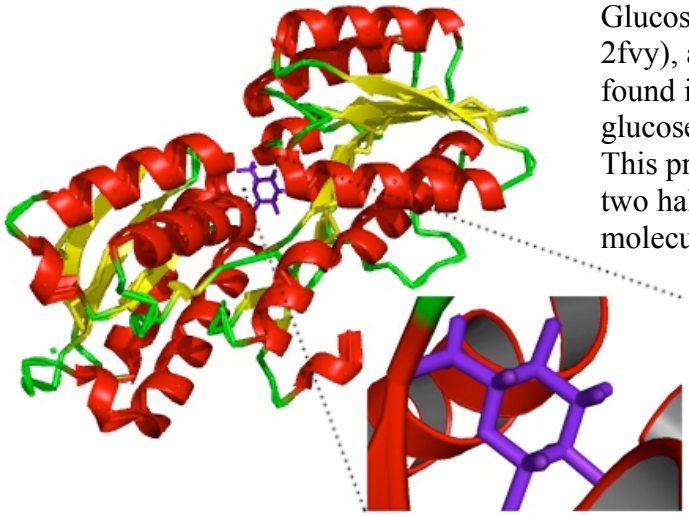
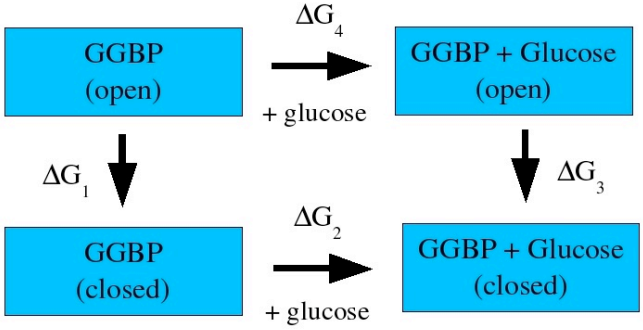


Glucose/galactose binding protein (GGBP, PDB ID 2fvy), a monomeric two-domain protein, commonly found in bacteria, is responsible for transportation of glucose and galactose sugar molecules into the cell. This protein resembles a Venus Flytrap, where the two halves fold around and bind to the sugar molecule.

The ultimate goal of the project is to create a free energy profile for GGBP and investigate free energy changes associated with different conformations (open/closed and sugar bound).

One of the ways to generate the free energy profile is to break down the process into mathematically feasible although physically unrealistic steps, shown below. Determining the value of each of the individual steps will help us understand which step - binding of the sugar molecule or the conformational change (open to close) of the protein - makes the greatest contribution to the energy change. Understanding the relative importance of these contributions is vital to computational drug design.

Free Energy Profile for GGBP



$$\Delta G_1 + \Delta G_2 = \Delta G_4 + \Delta G_3$$

In this part of the project we developed a model of a closed unbound form of the *E. Coli* GGBP. We developed the model using homology modeling server Swiss-Model Server and used a closed unbound form of *S. Typhimurium* GGBP (PDB ID 1gcg) as a template. After the model was developed, it is being used to calculate the free energy changes due to conformational change of the protein.

The other part of the project is to calculate the energy change due to glucose binding to the protein using the "slow growth" method of GROMACS molecular dynamics software.