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

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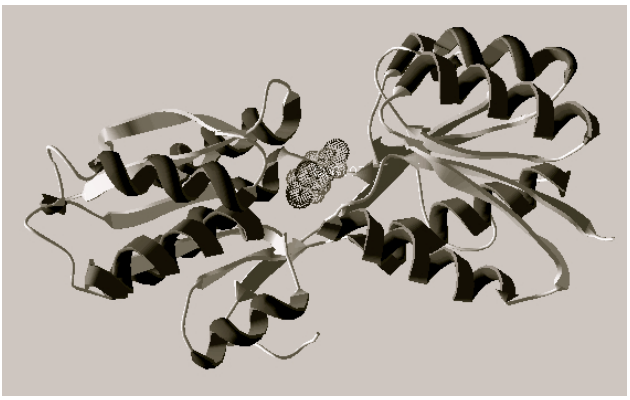
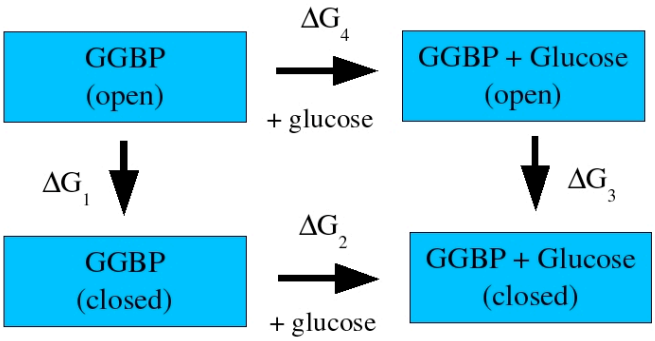
Glucose/galactose binding protein (GGBP), commonly found in bacteria, is responsible for transportation of glucose and galactose sugar molecules into the cell. This protein resembles a Venus Flytrap, where the two halves fold around and bind to the sugar molecule. The goal of this project was to create a free energy profile for GGBP and investigate the energy changes associated with the different conformations of the protein (open/closed and sugar bound). This research used the GROMACS molecular dynamics software to model the protein/sugar system in an explicit water environment (~24,000 water molecules).



One of the ways to generate the free energy profile is to break down the process into mathematically feasible although physically unrealistic steps, shown left.

Free Energy Profile for GGBP



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 efficient drug design. The GGBP system provides reasonable example of a ligand binding to a protein.

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

Besides work with GGBP, a substantial amount of time was spent comparing the performance and scaling factors of different multiprocessor/core computer systems. A 1.6 GHz 28 -processor (single core) Opteron cluster was compared to a MacPro with dual 2.8 GHz Quad-core Intel Xeon processors.