Allostery in the GroEL subunit

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GroEL is a molecular chaperonin protein that looks like a molecular beaker. The interior of GroEL catalyzes the folding of substrate proteins in E. *coli*. GroEL is made up of two heptameric rings that open up from the T state to R state when ATP is present in the binding pockets of the subunits. When GroEL is in the R state, the substrate protein enters the cavity and a second chaperonin, GroES, binds to the top of GroEL, causing it to open up even further into R´´ state. This also causes ATP to hydrolyze into ADP. The exact mechanism for this allosteric change is an active area of research. We are focusing our efforts on a single GroEL subunit. The subunit has three domains: apical, intermediate, and equatorial. When ATP is present, the majority of any movement is found in the apical domain and the area between the apical and intermediate domain, which acts as a hinge for this molecule. We have studied this mechanism in two ways. First, we performed unbiased molecular dynamics simulations on individual subunits with ATP or ADP in the binding pocket and with an empty biding pocket (apo). At least 20 ns of simulation were performed on each subunit and the angle between the apical, intermediate, and equatorial domain was monitored. Second, we are using umbrella sampling to calculate the potential of mean force for opening/closing the ADP, ATP and apo subunits. Preliminary results are presented and discussed.