Allostery and function of the chaperonin GroEL nano-machine

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Chaperonins are nano-machines that are built of two back-to-back stacked heptameric rings. They assist protein folding by undergoing large conformational changes that are controlled by ATP binding and hydrolysis. In the first part of the talk, I will describe the impact of encapsulation on the stability of protein substrates. Confining compartments are ubiquitous in biology, but there have been few experimental studies on the thermodynamics of protein folding in such environments. We found that the stability of a model protein substrate in the GroEL/ES chaperonin cage is reduced by more than 5 kcal mol^{-1} compared to that in bulk solution and that this destabilization is caused, at least in part, by a diminished hydrophobic effect in the GroEL/ES cavity. This reduced hydrophobic effect is probably caused by water ordering due to the small number of hydration shells between the cavity and protein substrate surfaces. Hence, encapsulated protein substrates can undergo a process akin to cold denaturation. In the second part of the talk, I will describe new approaches for elucidating allosteric mechanisms. Using these approaches, it has been possible to show that GroEL undergoes concerted intra-ring conformational changes.