

Artificial Allosteric Control of Maltose Binding Protein.

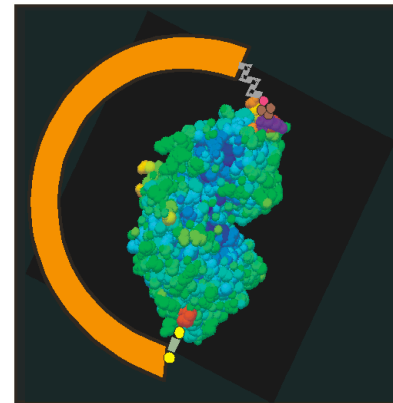
Brian Choi

Allosteric control is the mechanism whereby a control molecule binds to a site on a protein, inducing a conformational change at a distant site, which affects the function of the protein. It is the fundamental molecular control mechanism in the cell, the basis of many steps in the signaling pathways, including regulation of gene expression.

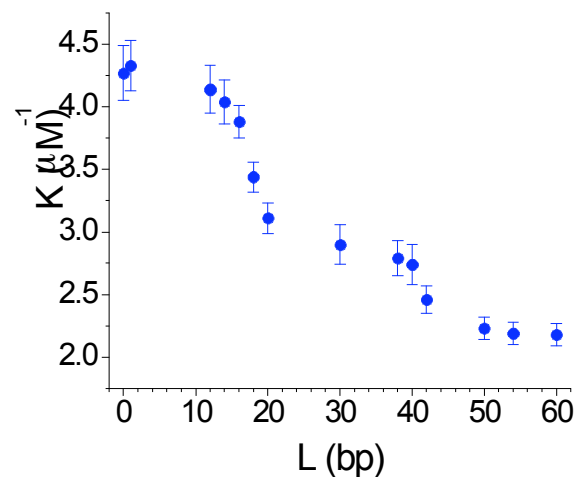
We are building artificial allosteric control modules on different proteins, based on a new molecular engineering approach, which allows to exert a mechanical tension on the protein, externally controlled. The fundamental question we address is the physical nature of allosteric control (what does it take to make the protein change conformation?). Biotechnology applications we foresee for the new molecules include a new generation of amplified molecular probes, and “smart drugs”.

In the case of the Maltose Binding Protein (MBP), we show that a mechanical stress which favors the “open” conformation of the molecule, applied by means of a molecular spring attached as shown below, lowers the binding affinity for maltose. In fact, the binding affinity can be modulated by varying the mechanical stress.

Tension in the DNA “molecular spring” favors the open conformation of the protein, lowering the binding affinity for the substrate.



Mechanical modulation of the binding affinity of MBP for maltose. As the stiffness of the molecular spring is increased (increasing L = length of the complementary strand hybridized to the ss DNA of the chimera above), the binding affinity K decreases.



- B. Choi, G. Zocchi, S. Canale, Y. Wu, S. Chan, L. Jeanne Perry, “Artificial allosteric control of Maltose Binding Protein”, *Phys. Rev. Lett.* **94**, 038103 (2005).