International Conference on Molecular Systems Biology 2009

Hysteretic and graded responses in bacterial two-component signal transduction

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In bacteria, two component systems (TCS) are the key signal transduction networks regulating global responses to environmental change. Environmental signals may modulate the phosphorylation state of sensor kinases (SK). The phosphorylated sensor kinase transfers the phosphate to its cognate response regulator (RR), which will cause some physiological response to the signal. In many instances, the SK is bifunctional and, when unphosphorylated, it is also capable of dephosphorylating the RR. The phosphatase activity may also be modulated by environmental signals. In this talk the steady state and kinetic properties of the network are analyzed using in silico methods. Mathematical modeling reveals that the TCS can show bistable behavior for a given parameter range if unphosphorylated SK and RR form a dead-end complex that prevents SK autophosphorylation. Additionally, for bistability to exist the major flux channel for the dephosphorylation of the RR must not depend on the unphosphorylated SK. Structural modeling and published affinity studies suggest that unphosphorylated kinase EnvZ and unphosphorylated response regulator OmpR form a dead-end complex. However, the bistability is not possible because the dephosphorylation of OmpR~P is mainly done by unphosphorylated EnvZ. The implications of this potential bistability in the design of two component systems are discussed.