1SA-01 Theoretical and experimental approaches to analyze the mechanism of rotational switching in bacterial flagellar motor

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ABSTRACT

The switch that controls the direction of flagellar rotation during bacterial chemotaxis has a highly cooperative response. This has previously been understood in terms of the classic two-state, concerted model of allosteric regulation. Here, we used high-resolution optical microscopy to observe switching of single motors and uncover the stochastic multiscale nature of our switch. Our observations are in detailed quantitative agreement with a recent general model of allosteric cooperativity that exhibits conformational spread, namely the stochastic growth and shrinkage of domains formed by neighboring subunits sharing a particular conformational state. By incorporating a torque-dependent flapping rate, we extended the conformational spread model to explain the latest experimental observation: flagellar motor switch responds to external load as well as chemoattractant signal. Our recent experiment observed a large group of single E. coli flagellar motors switching in the physiological regime. We showed that motor switching has stable individuality. Two properties of motor switching the switching bias and mean switching duration vary significantly from cell to cell. We propose such individuality may allow populations of cells to better survive in rapidly changing environments by “hedging their bets”.

1SA-02 Bacterial chemotaxis reveals complexity in cellular organisation and mechanisms for decision making

Judith Armitage (OCISRS, Department of Biochemistry, University of Oxford)

The Escherichia coli chemosensory pathway is one of the best understood sensory systems in biology, with transmembrane chemoreceptors regulating the activity of a histidine kinase protein. This HPK phosphotransfers to a small diffusible CheY protein that binds the flagellar motor to cause direction changing, and a methyl esterase, CheB that resets the signalling state of the receptors. This simple feedback sensory pathway allows E. coli to respond to environmental changes over 5-6 orders of magnitude background concentration. However, most bacterial species have more than one chemosensory pathway, and how these regulate swimming is unclear. Rhodobacter sphaeroides encodes 3 complete chemosensory pathways, with two being expressed under normal laboratory conditions. Using fluorescent fusions to the different chemosensory proteins, we showed that the two pathways are physically separate in the cell, one pathway localising with transmembrane receptors at the poles, the other localising with soluble receptors at the midcell. In the seminar I will show (i) how specificity is determined in the phosphotransfer reactions of the two pathways, (ii) how the cytoplasmic chemosensory cluster is localised and segregated, ensuring each daughter cell has a complete pathway and (iii) how combining the biochemical parameters and response kinetics with mathematical modelling predicts communication between the two pathways, allowing responses to be tuned to the metabolic requirement of the cell.

1SA-03 The regulatory network controlling flagellar assembly dynamics

Christopher V Rao (University of Illinois at Urbana-Champaign)

Bacteria such as Escherichia coli and Salmonella enterica are able to swim in liquids and swarm over surfaces using flagella. Briefly, flagella are long helical filaments attached to rotary motors embedded within the membrane. Over fifty genes are involved in assembling functional flagella. The expression of these genes is tightly controlled by a number of regulatory feedback loops that couple gene expression to the assembly process. Over the past few years, we in collaboration with Philip Aldridge have experimentally characterized how these feedback loops govern gene expression dynamics. In this talk, I will discuss our recent efforts developing an integrated computational model of flagellar regulatory network. A key insight derived from developing this model is that bacteria actively count and control the number of flagella that they build. When viewed from this perspective, I will demonstrate how the structure of the flagellar networks logically evolved to mediate this control objective.

1SA-04 酵母細胞システムのロバストネス解析

Hisa Moriya (R.C.S, Okayama University)

Robustness analysis of the yeast cellular system

In the cell, intracellular parameters such as gene expression levels are fluctuated due to the effect of environmental changes, mutations, and noise in biochemical reactions. It has been recognized that biological systems are robustly designed so that they can maintain their functions despite the perturbations of these parameters. However, we barely know the robustness of real cells, because we have not had any suitable experimental technology to access cellular robustness. One way to access robustness is to measure the limits of internal parameters to maintain cellular function. We thus have developed a genetic method designated genetic Tug-Of-War (gTOW) by which we can measure the limit of overexpression of a target gene, as the gene copy number. With gTOW, we have studied the robustness of the cell cycle regulatory systems of the budding and the fission yeast. Through comparison of the gTOW data with mathematical models developed Novak-Tyson group, we discovered that stoichiometric imbalance causes cellular fragility, and a novel molecular mechanism to make cellular system robust. We have recently measured the limits of all 6,000 genes in the budding yeast genome. We finally show the possibility that imbalances in stoichiometric regulations create cellular fragility in general, and a hypothesis that a network created with gene dosage balances constrains the composition of the genome.

1SA-05 生体分子ネットワークの構造とダイナミクス：既知から未知を予測する

Structure of regulatory networks and dynamics of biomolecules: Predicting unknown from known


Regulatory relations between biological molecules constitute complex network systems, and realize diverse biological functions through the dynamics of molecular activities. However, we understand very little of the dynamics of biological systems because regulatory networks just give us the information of linkages, not that of regulatory functions. In this study we introduce a new theory, named “linkage logic”, to analyze the dynamics of complex systems only from the regulatory networks. By the method, we can restrict dynamical behaviors of a given network system from the knowledge of regulatory linkages alone. We formalize two aspects of the linkage logic: the “Principle of Compatibility” determines the upper limit of the diversity of attractors of the dynamics; the “Principle of Dependency” determines the possible combinations of steady states of the system. By combining these two aspects, (i) for a given network, we can identify a cluster of nodes that gives an alternative representation of the attractors of the whole system, (ii) we can reduce a given complex network into a smaller one without losing the dynamical property for the diversity of steady states, (iii) we can examine the consistency between the structure of network and observed set of steady states, and (iv) sometimes we can predict unknown states or unknown regulations from an observed set of steady states alone. We illustrate the method by several applications to an experimentally determined regulatory network for biological functions.

1SA-06 Feedback and feed-forward controls of cell cycle transitions

Attila Csikasz-Nagy (The Microsoft Research-University of Trento)

DNA replication, mitosis and mitotic exit are critical transitions of the cell cycle which should occur only once per cycle. The importance of various positive feedback and feed-forward loops in the irreversibility of these transitions has been investigated recently. A picture arises, where the key cell cycle regulator Cdk is controlled by positive feedback loops and Cdk enforces its downstream targets through feed-forward regulation. We will show the dynamical features of such regulatory loops and discuss how these are used at cell cycle transitions. Furthermore we will show how transcriptional regulation of activators and inhibitors of cell cycle transitions can influence the robustness of the transitions.

References

