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https://github.com/Zealous0/Test-Question.git

Biological Robustness and Fragility

Robustness of biological systems, also known as biological or genetic robustness[1], is common in biological evolution and refers to the fact that when a system is perturbed or under uncertain conditions, certain specific functions in the system will maintain against the perturbation to keep the specific function able to operate correctly. According to the kind of perturbation involved, robustness can be classified as mutational, environmental, recombinational, or behavioral robustness, etc[2][3][4]. Mechanisms to ensure system robustness are system control, substitution (or fail-safe) mechanisms, modularity, and decoupling[1]. On the other hand, it has also been reported that systems that have evolved to be robust to general perturbations are often fragile to certain types of rare mutations[5]. Biological fragility is manifested by the introduction of various control feedback loops that can lead to system instability when unexpected perturbations are encountered, resulting in catastrophic failures[1].

Bacterial chemotaxis ensures system robustness through mechanisms of system control. Bacterial chemotaxis is a directional mode of movement of bacteria, a fundamental property of their survival by adapting to changes in their environment, which gives them the ability to find food sources and escape from toxic environments, giving them a competitive survival advantage. Bacteria can adapt to changes in chemical inducers over a wide range of concentrations and always regulate their behavior in response to changes in chemical inducer concentrations. This process is achieved by a closed-loop feedback loop shown in Figure 1. This feedback mechanism capable of adapting to changes in ligand concentration has been demonstrated experimentally and by simulation. In particular, the average activation level, measured by frequency, converges rapidly to a stable value during sudden changes in ligand concentration. This means that the system determines its frequency only by sensing drastic changes in ligand concentration, but it is insensitive to the absolute value of ligand concentration. Thus, regardless of the absolute value of the concentration, the system can always sense and control its movement toward the region of high inducer concentration as long as it does not saturate its sensory system. Similarly, diabetes can be used to illustrate the biological fragility of a system[6]. Diabetes has acquired robustness to a near-starvation, high-energy-demand lifestyle, and high risk of infection, but it is abnormally disrupted by a lifestyle of excessive nutrition and low energy requirements. Both biological and engineered systems are most vulnerable when their fragilities are exposed.

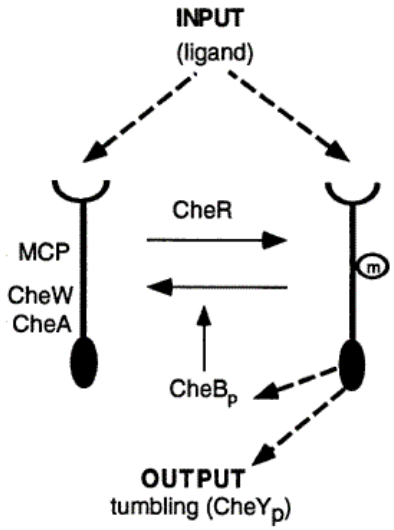

Fig1. Chemotaxis system of *E.coli*. The chemotactic ligand binds to the specific receptor MCP to form a stable complex consisting of the proteins CheA and CheW, which are phosphorylated regulatory factor enzymes, CheY, which binds to the flagellar motor and generates changes, and the ligand bound to the receptor, which is modified by the kinase of CheA. The two proteins are methylation of CheR and demethylation of CheB during the adaptive process, and the feedback mechanism of CheA indirect CheB phosphorylation facilitates demethylation[7].

Robustness is a universal property of biological systems. It is considered an essential feature of complex evolutionary systems and is an integral part of survival. First, robustness benifits evolution. The environment and genes are forever changing, so complex biological systems must be robust to environmental and genetic perturbations to evolve, and the specific architectural features observed in robust systems make such a reciprocal process possible. Robust features are thus often selected by evolution, and evolution typically selects those features that enhance the robustness of the organism. Second, a deeper understanding of the inherent properties of robust systems will provide guiding principles for a better understanding of complex diseases (e.g., diabetes and cancer) and treatment design.

The foundation of complex dynamic systems includes an inherent trade-off where robust systems face fragilities and performance setbacks, where increasing robustness leads to increased fragility, and where biological systems become unstable when encountering rare surprises leading to failures and reduced performance. The tradeoff among robustness, vulnerability, and performance can be observed in biological systems at different levels. For example, bacteria should be able to swim faster without negative feedback, but this would be at the expense of their accuracy in following chemical gradients: Using negative feedback improves the ability of bacteria to follow chemical gradients but at the cost of reduced swimming speed. Another example: in electronic circuit design, the use of negative feedback control improves fidelity or amplification over a certain input range by reducing the overall gain of the amplifier. Thus, the use of negative feedback control achieves robustness over a range of inputs at the cost of some aspects of performance and creates fragility elsewhere[1]. This fragility cannot be completely avoided, and if the fragility is reduced, losses are incurred elsewhere as well, depending on the tradeoff.

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