

## Biological Robustness and Fragility

Biological robustness is a ubiquitous feature of biological systems. It ensures that the specific function of the system is maintained in the face of external and internal disturbances<sup>[1]</sup>. System control, alternative (or fail-safe) mechanisms, modularity and decoupling are the basic mechanisms that generate robustness. However, biological fragility is characterized by a reduction in the physiological reserve required for an individual to respond to endogenous and exogenous stressors.

Robustness enables the system to maintain its functionalities against external and internal perturbations. This property has been widely observed across many species, from the level of gene transcription to the level of systemic homeostasis. For example, fate decision of  $\lambda$  phage — the result of which is the activation of either LYSIS or LYSOGENY pathways — was once considered the result of fine tuning of the binding affinity of promoters to corresponding regulatory factors. On the other hand, it has also been reported that biological networks are often fragile against unexpected mutations. For example, the energy control system of our body ensures robustness against common perturbations such as unstable food supply or infections, but the system is fragile against unusual mutations such as high-energy content foods or low-energy utilization lifestyle<sup>[2]</sup>. The immune system provides robustness against pathogen threats, but it is fragile against unexpected failures such as dysfunction of MyD88 which is a nonredundant core element. The segment polarity gene network of *Drosophila* shows robustness against perturbations in its initial condition but shows fragility against a large temporal variability.

Biological robustness is a property that allows a system to maintain its functions despite external and internal perturbations. It is one of the fundamental and ubiquitously observed systems-level phenomena that cannot be understood by looking at the individual components. A system must be robust to function in unpredictable environments using unreliable components. Understanding the origin and principles of robustness in biological systems will help us to put various biological phenomena into perspective; it will also catalyze the formation of principles at the systems level. I argue that robustness is a fundamental feature of evolvable complex systems. Complex biological systems must be robust against environmental and genetic perturbations to be evolvable. Evolution often selects traits that might enhance robustness of the organism. Robustness is, therefore, ubiquitous in living organisms that have evolved. However, systems that are robust face fragility and performance setback as an inherent

trade-off. Identification of the basic architecture for a robust system and the associated trade-offs is essential for understanding their faults and countermeasures — diseases and therapies, respectively.

Robustness is often misunderstood to mean staying unchanged regardless of stimuli or mutations, so that the structure and components of the system, and therefore the mode of operation, is unaffected. In fact, robustness is the maintenance of specific functionalities of the system against perturbations, and it often requires the system to change its mode of operation in a flexible way. In other words, robustness allows changes in the structure and components of the system owing to perturbations, but specific functions are maintained. At present, it has been found that biological robustness is universal in the whole biological system, organs, cells, molecules and other levels, such as bacterial chemotaxis, cell cycle, cell signal communication, gene mutation, biological development, gene network, etc. Understanding biological robustness is of great significance for the occurrence, development and treatment of cancer, AIDS, diabetes and other diseases.

In my opinion, biological vulnerability leads to similar results to AIDS. When an organism's immune system is weakened, a variety of bacteria and viruses invade the organism and produce a series of reactions. Due to biological vulnerability, the body does not respond to this disturbance, resulting in some serious diseases and even complications. In view of this phenomenon, it is important to understand the architectural characteristics of robust and evolutionable systems as well as the inherent nature of robustness and vulnerability, because they determine the mode of system failure and effective countermeasures. If we can effectively contact them, we will avoid this problem

## **citations**

- [1] Kitano, H. Biological robustness. *Nat Rev Genet* 5, 826–837 (2004). <https://doi.org/10.1038/nrg1471>
- [2] Yung-Keun Kwon, Kwang-Hyun Cho, Quantitative analysis of robustness and fragility in biological networks based on feedback dynamics, *Bioinformatics*, Volume 24, Issue 7, 1 April 2008, Pages 987 - 994, <https://doi.org/10.1093/bioinformatics/btn060>