

## **Biological Robustness and Fragility**

### **The Definition of Biological Robustness and Fragility**

Robustness is a property that allows a system to maintain its functionality in the presence of external and internal perturbations. It is a fundamental and commonly observed system-level phenomenon that could not be understood by looking at individual components. (Kitano, 2004) Stability can be classified as mutational, environmental robustness, and so on, depending on the type of perturbations. (JA, 2011) Robustness is achieved through a combination of many genetic and molecular mechanisms and can evolve through direct or indirect selection. However, there are times when biological networks are very fragile in the face of unexpected mutations. When the robustness in biological networks produces a failure, this phenomenon can be understood as biological fragility. For example, *Drosophila* establishes segmental polarity in its initial values and rate constants for molecular interactions to resist perturbations, which is a manifestation of biological robustness. (NT, 2004) However, while the *Drosophila* segmental polarity gene network exhibits robustness to perturbations under its initial conditions, it shows fragility to significant temporal changes. (Chaves et al., 2005) In addition, to explain biological fragility more clearly, diseases could be considered an expression of the fragility of the biological networks. Furthermore, as in the case of the previously proposed example regarding *Drosophila*, it has been shown in several studies that the robustness and fragility of biological networks are interrelated. Carlson and Doyle's study (2002) found that complex systems are stable to general perturbations but exhibit high fragility to some rare perturbations. (JM & J, 2002) Kitano also suggested that there was an inherent trade-off between the robustness and fragility of biological networks. (Kitano, 2004)

### **The Importance of Biological Robustness and Ways to Avoid Fragility**

Robustness is a property that allows a system to maintain its functionality in the presence of external and internal perturbations. It is a fundamental and commonly observed system-level phenomenon that could not be understood by looking at individual components. (Kitano, 2004) Stability can be classified as mutational, environmental robustness, and so on. Robustness is a pervasive characteristic of biological systems that can facilitate the evolution of complex dynamic systems. Evolution would select a robust feature that could withstand environmental perturbations if given enough time, which relates to the properties of robustness and evolvability. Therefore, this makes robustness ubiquitous in evolved biological systems. Besides, systems must be robust to operate in unstable environments with unreliable components. Consistent with the point made by Kitano (2004), robustness is an essential characteristic of complex evolvable systems. Complex biological systems need to possess traits that can tolerate environmental and genetic perturbations to evolve. (Kitano, 2004) This makes robustness extraordinarily important in survival. If fragility is allowed to develop, it may lead to the gradual demise of the biological system. For instance, in the example mentioned above, the increasing severity of disease symptoms is a case of failure of the systemic intervention in fragility.

Therefore, identifying the underlying architecture of robust systems and the associated trade-offs is critical to understanding their failures and countermeasures. Kitano proposes three options to prevent biological fragility: system control, alternative mechanisms, modularity, and decoupling. (Kitano, 2004) System control includes negative and positive feedback to obtain robust dynamic responses observed in a wide range of regulatory networks. (Kitano, 2004) The rationale for alternative mechanisms is that robustness could be enhanced if there are multiple means to achieve a particular function since one of the failed means can be replaced by the others. This concept incorporates redundancy, functional overlap, and diversity, as there are varying degrees of

similarity across the various available alternative means. (Kitano, 2004) Modularity is a mechanism that reduces the impact on the whole system with local control of perturbations and damage. Modules are widely observed in diverse organisms and work as possible biological design principles as well as fundamental elements in engineering and industry. (Kitano, 2004) Decoupling isolates low-level variation from high-level functionality. (Kitano, 2004)

## Reference

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