

Robustness is a property of a biological system to maintain certain functions or traits under external and internal perturbations. It is a systems-level property that cannot be comprehended by examining the individual components. Mechanisms guarantee robustness including system control, alternative mechanisms, modularity, and decoupling. System control involves negative and positive feedback, the former is the primary mechanism of control that provides a robust response, and the latter increases the stimuli to make the simulated state more distinguishable from the non-stimulated state. Alternative mechanisms refer to several means to carry out a certain function able to rescue each other if one of them fails. Modularity is the mechanism for containing perturbations and damage locally to minimize the effects on the whole system. Decoupling separates low-level variance from high-level capabilities, and by providing a buffer, it contributes to robustness (Kitano, 2004).

According to the definition of robustness, understanding it requires figuring out two questions, what are the functions or traits of interest, and what are the perturbations faced? For instance, in the yeast research from Costanzo et al, the trait of interest is the global yeast genetic interaction network and the perturbation is the environmental perturbation. There is a global genetic interaction network under specific conditions for budding yeast which reveals thousands of linkages that frequently exist between functionally related genes. The researchers mapped gene-gene interactions under 14 environmental conditions to better understand the effect of the gene's interaction with other genes, the environment, or them both on the phenotype. Through the analysis of these interactions, they suggest that between 5 and 24% of genetic interactions found in a reference genetic network can be modified in a different environment. Combined with other validation, they draw the conclusion that the yeast genetic interaction network is very robust to environmental perturbation. The robustness may be due to the majority of links on the global genetic interaction network staying constant or unaltered in a new environment (2021).

Robustness is very pervasive and widely observed in many species. It is also fundamental to species survival since it ensures the stability of function and traits that are regularly exposed to perturbations. Moreover, robustness allows for the accumulation of cryptic genetic variation. New adaptations and evolutionary novelties may arise as a result of this variation (Félix & Wagner, 2006).

Fragility is an intrinsic trade-off of robustness that acts as a counterbalance to enhanced robustness to some perturbation. In other words, complex systems that have evolved to be robust to general disturbances can be quite fragile to some sort of rare perturbations (Kitano, 2004). The disease can be seen as the exposed fragility of systems that are both robust and fragile. For instance, the energy regulation system in our bodies ensures resistance to frequent perturbations like diseases or unstable food supply, but the system is vulnerable to unexpected alternations like high-energy content diets or low-energy consumption lifestyles. Diabetes mellitus is a typical example of this kind of system failing, necessitating deliberate interventions to keep

an epidemic state under control (Kitano et al., 2004). As the opposite of robustness, fragility limits the performance of complex dynamic systems. It has an adverse effect on the adaptation and development of species. When a system exhibits fragility, that is, when it loses its stability and normal function or traits in response to disturbance, survival is affected.

Fragility is also ubiquitous, with natural, biological, social, and technological networks all having fragility. But there is still a lack of convincing theories to explain why natural evolution and human design fail to optimize networks and avoid fragility (Pasqualetti et al., 2020). Quantifying fragility, combined with its correlation with robustness, may provide a basis for how to avoid fragility. In research from Kwon and Cho, through a large number of computational experiments based on feedback dynamics, researchers have quantitatively analyzed the robustness and fragility of biological networks. They found that networks are likely to be more robust to perturbation if they have more positive feedback loops and fewer negative feedback loops. They also discovered that the nodes of a robust network that are typically sensitive to perturbations are primarily involved with fewer feedback loops than the other nodes. The robust network eventually becomes fragile to unexpected mutations at nodes that were not previously exposed to perturbations due to this topological property (2008). Combining the above discovery, the number of positive and negative feedback loops may be enlightening for achieving enhanced robustness and avoiding fragility.

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