

In general, robustness is a property that allows a system to maintain its functions against internal and external perturbations(Alderson & Doyle, 2010). The definition can be adapted in many fields, ranging from biology, ecology, and medicine to network-centric technologies.

On the one hand, Robustness is one of the fundamental characteristics of biological systems. Many biological systems have an intrinsic capacity to maintain specific functions or traits when exposed to particular perturbations and have thus been described as being robust(Whitacre, 2012). Thus, robustness is a key property of biological networks that are able to maintain their functioning under external and internal perturbations. On the other hand, complexity arises in highly evolved biological and technological systems primarily to provide mechanisms to create robustness, but systems that are robust involve intrinsic trade-offs(Kitano, 2004). Enhanced robustness against certain perturbations has to be balanced by extreme fragility elsewhere, leading to “robust yet fragile” tradeoffs in system design.

Life is capable of withstanding internal and external fluctuations such as genetic mutations, such as genetic mutations, loss of structural integrity, infectious diseases, and endogenous threats such as cancer, temperature fluctuations. Therefore, biological robustness is integral part of survival and it involves in various biological processes, including protein folding, gene expression, metabolic flux, organism survival, and ecological resilience in single cells, differentiating cells, animals, etc. (Kitano, 2007).

There are many examples of biological robustness and fragility. For instance, *Drosophila* establishes segmental polarity against perturbations in its initial values and rate constants of molecular interactions. This stability is due to the positive feedback of the gene product on its own expression, which induces individual cells in the model compartment to adopt different stable expression states that correspond to different cell types in the compartment polarity structure.(Ingolia, 2004). However, it has also been reported that biological networks are often fragile against unexpected mutations. For

example, the immune system provides organisms with robustness against pathogen threats, yet it also often adversely affects the organism as in autoimmune diseases, which means that it is fragile against unexpected failures such as dysfunction of MyD88 which is a nonredundant core element (Kitano & Oda, 2006).

Tumors are highly robust and maintain their proliferative potential across a wide range of anticancer therapies. Fragility is a by-product of robustness and sometimes we can exploit systemic fragility to address enhanced robustness and vice versa. For example, tumor robustness is maintained by chromosomal instability, intracellular feedback loops, and host-tumor interactions. Possible therapeutic approaches include cell cycle control by combining several drugs, using RNAi, disruption or stabilization of unstable chromosomes, delivery of engineered genes to re-establish control of host-tumor interactions, or introduction of genetic circuits for conditional expression of tumor suppressor genes (Bingle et al., 2002; Hasty et al., 2002).

In conclusion, the perspective on biological robustness and fragility would provide effective guiding principles for understanding many biological phenomena, and for therapy design.

## Reference

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