

## **Biological Robustness and fragility**

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Robustness and fragility are important features in engineering, biology, economic and computer science. In this essay, biological robustness and fragility will be focused, examples of robustness and fragility in biological system will be given and their significances and consequences will be analyzed.

Biological robustness is a feature that found in biological system, its function is maintaining the phenotype stability of biological system when it subjected to uncertain disturbances such as environmental changes, random events, or genetic variation (Kitano, 2004). Robustness is also involved in evolution of biological system, after a certain time, evolution could be select a robust trait that is tolerant against uncertain disturbances like environmental perturbations, which facilitates the evolvability of complex systems (Kitano, 2004). On the contrary, when the biological system is in the quality or state of being easily broken or destroyed under uncertain disturbances, the fragility of system is exposed.

From aspects of physiology, humans' body show their robustness by maintaining the homeostasis through a self-regulating process while adjusting to changing external conditions (Billman, 2020). For example, renin and angiotensin II play roles in Renin-Angiotensin System (RAS) to correct a drop in blood pressure may be caused by external influences like injury and hemorrhage to maintain homeostasis state of humans' body and show its robustness (Silverthorn et al., 2019). While diseases can be thought as one of the elements to expose fragility of human's body (Kitano, 2004). For example, HIV will hijack the robust immune-response mechanism and expose body's fragility by infecting CD4-positive T cells and replicating when the cell activates its anti-virus responses (Kitano, 2004).

Also, robustness and fragility of biological systems are correlated with each other. According to Kitano (2004), cancer is an example of robustness and fragility trade-offs. The tumor still proliferates, metastasizes, and relapses despite administering many therapies and anti-cancer drugs due to its intrinsic mechanisms for robustness (a fail-safe formed by high level of genetic heterogeneity, and multiple feedback loops in the cellular and the tumor-host environment) (Kitano, 2004). But cancer cells can be extremely fragile against certain perturbations, so, control of the tumor's robustness and find out the point of fragility of the

robust system is possible clinical strategies against cancer (Kitano, 2004). Similarly, robustness and fragility trade-offs are found in biological network, the research did by Kwon & Cho (2008) shows that a biological network acquires robustness since perturbations are only subjected to a small number of feedback loops for the nodes but not for a large number of feedback loop for the nodes. When unexpected mutations occur at the nodes of no perturbation, the robustness of the biological network becomes fragile (Kwon & Cho, 2008).

Apparently, robustness is integral part of survival within biological system. From a macro perspective like ecosystem, robustness is significant since it can maintain the biological equilibrium from being disturbed by external factors. For example, when a fire occurs in the forest, although some trees will be burned, the inorganic nutrients in the soil will increase and promote growing of new plants under conditions of sufficient sunlight and germination of seeds. From a micro perspective like DNA, robustness is important since it can ensure DNA within cells does its job properly. For example, five major DNA repair pathway like base excision repair (BER) are active throughout different stages of the cell cycle and allowing cells to repair its DNA damage (Chatterjee & Walker, 2017) to maintain normal operations of cells.

On the contrary, exposing of fragility may cause severe consequences to biological system. For example, cell cycle plays a regulatory role on cell division and proliferation, when some transcription factors within the cell cycle like p53 is inactivated, its fragility will be exposed, transformed cells will divide and survive uncontrollably, and caused cancer. To avoid the severe consequence, it is necessary to control the robustness of biological system and reduce uncertain disturbances to avoid exposing their point of fragility. In the previous example, reducing risk factors may be a solution to reduce the risk of cancer. Specifically, smoking cessation could reduce the risk of lung cancer since as a risk factor of lung cancer, smoking is an external disturbances to respiratory system, and lung cancer may be avoided by limiting influences of such uncertain disturbances on the point of fragility.

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