

Biological Robustness and Fragility

Robustness is an important property of many dynamic systems and is particularly prevalent in biological systems. This property allows the system to cope with external or internal disturbances within the system and to maintain certain basic functions. Robustness is also a fundamental organizational principle for the evolution of dynamic systems.¹ Vulnerability means that when a system is subjected to certain specific disturbances, it can become unstable with serious consequences for the system's function, which can lead to fatal damage to the system. Systems with both of these properties are prevalent in nature. This paper will introduce these two properties by looking at human organisms.

The immune system is a tightly controlled homeostatic system of the body that provides various defences against the invasion of foreign pathogens or the growth of self-produced antigens. In healthy individuals who maintain healthy immune homeostasis, interference with exogenous and potentially infectious antigens or self-generated antigens that threaten the health of an organ or organ system will trigger a series of appropriate responses aimed at restoring the body's function. The system consists of three defensive layers, the first of which is made up primarily of the skin and mucous membranes. The second layer is made up of bactericidal substances in the body fluids and phagocytes. The third layer consists mainly of immune organs like the thymus, lymph nodes, and spleen and immune cells, i.e. lymphocytes. When germs, viruses, and other disease-causing organisms enter the body, macrophages first engulf them, break them down into antigens and inform the T-cells of the immune system, which react with the antigens to produce a lymphokine substance that activates the T-cells. The immune system then produces T-lymphocytes, which have the ability to kill, and B-lymphocytes, which produce specific antibodies; the T-lymphocytes attack the target cells directly, while the antibodies produced by the B-lymphocytes bind to the disease-causing microorganisms inside the cells and render them useless, thus restoring the body to health. This shows that the human immune system is a mature and dynamic system that can use a series of positive and negative feedbacks to deal with disturbances and to keep the system functioning properly and is highly robust.

I believe robustness is essential in all systems, especially living organisms. If a living system does not have a mature robust structure, it will be disrupted by internal and external disturbances that arise in a very short time, suffering irreparable damage and subsequently causing a devastating collapse of the system. According to Darwin's doctrine of natural selection, living organisms that are unable to resist external disturbances are quickly eliminated by their environment and lose their vital characteristics, thus making it impossible to perpetuate such non-robust living systems. Robust life forms are better able to withstand external disturbances to survive in the natural world. Such robust life systems are also preserved through the reproduction of the organism and become the dominant life system of the species.

¹ Kitano, H. Biological robustness. *Nat Rev Genet* 5, 826–837 (2004).

Many researchers believe that the robustness of organisms is strongly correlated with their vulnerability. For example, in the Highly Desirable Tolerance (HOT) Theory, Carlson and Doyle state that systems that have evolved to be robust to general perturbations are extremely vulnerable to certain types of rare disturbances.^{2 3} For living organisms, the result of vulnerability is often fatal; once a disturbance against vulnerability occurs, the stability of the living organism will be compromised and the stable system state will shift towards vulnerability, which will then be subject to more disturbances against the new vulnerability. This leads to the collapse of the living system and ultimately to permanent damage or even death. The human system is also vulnerable, for example, to mutations in MYD88, a gene present in the body known as myeloid differentiation factor 88, which when mutated can lead to neoplastic disease or mutations in the gene for the virus that causes lymphoma.⁴ This outcome can interfere with the normal functioning of the body's immune system, causing it to collapse and rendering a robust vital system vulnerable and therefore life-threatening.

I believe that the approach to avoiding vulnerability is twofold. The first is for the system itself to evolve and improve, enhancing the robustness of the system to unexpected disturbances and making the living organism more adaptive to its environment. The second point is to study the system's vulnerability and try to avoid disturbances to the system's vulnerability. The second point is to study the vulnerability of the system, to avoid the disturbance of vulnerability and to find ways of transforming this specific disturbance to reduce the vulnerability of the living organism and to increase its robustness.

² Carlson, J. M. & Doyle, J. Highly optimized tolerance: a mechanism for power laws in designed systems. *Phys. Rev.E* 60, 1412–1427 (1999).

³ Carlson, J. M. & Doyle, J. Complexity and robustness. *Proc. Natl Acad. Sci. USA* 99 (Suppl 1), 2538–2545 (2002). **An introductory article on the highly optimized tolerance (HOT) theory**

⁴ Yu X, Li W, Deng Q, Li L, Hsi ED, Young KH, Zhang M, Li Y. MYD88 L265P Mutation in Lymphoid Malignancies. *Cancer Res.* 2018 May 15;78(10):2457–2462. doi: 10.1158/0008-5472.CAN-18-0215. Epub 2018 Apr 27. PMID: 29703722.