Biological Robustness and Fragility

Robustness is an important property of the biological system. It enables the system to maintain functionality against internal and external perturbations (Kitano, 2004a). Robustness does not mean the unchanged of the system; it allows the changes in the mode of operations and structures to fit the situations caused by mutations in order to keep its functions (Kitano, 2004a). For example, bacteria can change to a new status under the pressure of antibiotics while still maintaining their sensitivity (Balaban, 2004).

Robustness exists extensively in biological systems, from keeping the stability of genetics in evolution to the ability of a population to survive infectious diseases. One example of robustness is cancer in the human body to survive and proliferate under the pressure of anti-cancer therapies. The robustness exploits functional redundancy and feedback control of cancer cells (Kitano, 2004b). Cancer as a system consists of different kinds of cells, which contains large cellular heterogeneity and redundancy (Kitano, 2003). Heterogeneous redundancy means different components with similar functions (Kitano, 2004b). Under external perturbations such as anti-cancer drugs, redundancy provides a larger chance for the whole cancer system to survive. The total cancer system can survive if some of the cells are not recognized and killed. Feedback-control system also reflects the robustness of the cancer system against chemotherapy at the cellular level (Kitano, 2004b). One negative feedback control by tumor cells is the overexpression of MDM2. It decreases the level of tumor cell apoptosis by suppressing the p53 protein, a tumor suppressor protein that controls the cell cycle in normal cells. Moreover, the cell cycle contains a variety of feedback-control loops that keep the proliferation potential of tumor cells, making the tumor cell more robust against stimuli (Morohashi, 2002).

Biological robustness is essential for survival. The robustness of the system keeps the system from being affected by perturbations. For the immune system of individuals, the perturbations could be the attack of the pathogen. If the system is not robust, which means that it cannot recognize and take response, the individuals may get infected easily or even die. As for the cancer system, if there is less heterogeneity, all the cancer cells could be targeted and killed by specific anti-cancer drugs. Also, the robustness of the system facilitates evolution, and evolution favours robust traits (Kitano, 2004a). The robust traits that have positive functions for the population will be kept against perturbations and passed to the next generation, which is required by evolution.

Robustness and fragility are correlated with each other. Even though the biological system is robust against general perturbations, it is also fragile when affected by unexpected mutations. Fragility means that the system cannot maintain its functions against some extreme stimuli. The human immune system is robust against most kinds of pathogens by the bow-tie structure of the adaptive immune subsystem

(Kitano, 2006). Antigen-presenting cells recognize the external pathogen and transmit signals to CD4+ T cells, which promote CD4+ T cells' differentiation and further promote other immune responses with the co-stimulation of cytokines (Kitano, 2006). However, the immune system is also fragile because of the CD4+ T cell, which is the core component of the bow-tie structure. When infected with HIV, the level of CD4+ T cells decreases, and the whole immune system will eventually lose function (McCune, 2001).

Fragility will cause potential risks for biological systems. If certain perturbation happens to the system, it cannot recover. As discussed before, the cancer system is robust to most kinds of stimuli because of the redundancy of components while fragile to certain recognition. Likewise, the immune system is also robust to most pathogen infections while fragile because of the non-redundant elements. It indicates that if the heterogeneity of the system increase and there is always redundancy for the same function, the system will be more robust and have less chance to be influenced by particular stimuli. Another situation that causes system fragility happens when inappropriate components cannot be found and removed (Kitano, 2004a), such as the HIV-infected CD4+ T cells. If the abnormity could be found in time, the fragility could be avoided.

Reference

1. Kitano H. (2004a). Biological robustness. Nature reviews. Genetics, 5(11), 826–837. https://doi.org/10.1038/nrg1471

2. Balaban, N. Q., Merrin, J., Chait, R., Kowalik, L., & Leibler, S. (2004). Bacterial persistence as a phenotypic switch. Science (New York, N.Y.), 305(5690), 1622–1625. https://doi.org/10.1126/science.1099390

3. Kitano H. (2004b). Cancer as a robust system: implications for anticancer therapy. Nature reviews. Cancer, 4(3), 227–235. https://doi.org/10.1038/nrc1300

4. Kitano, Hiroaki, Oda, Kanae. (2006). Robustness trade-offs and host–microbial symbiosis in the immune system. Molecular Systems Biology, 2. 2006.0022. https://doi.org/10.1038/msb4100039

5. Kitano, H. (2003). Cancer robustness: Tumour tactics. Nature 426, 125. https://doi.org/10.1038/426125a

6. Morohashi, M., Winn, A. E., Borisuk, M. T., Bolouri, H., Doyle, J., & Kitano, H. (2002). Robustness as a measure of plausibility in models of biochemical networks. Journal of theoretical biology, 216(1), 19–30. https://doi.org/10.1006/jtbi.2002.2537

7. McCune J. M. (2001). The dynamics of CD4+ T-cell depletion in HIV disease. Nature, 410(6831), 974–979. https://doi.org/10.1038/35073648