

## Robustness and Fragility: Two properties of biological system

Written by Liu Sinuo  
db92311@um.edu.mo

Biological robustness and fragility are two natural and bonding properties of biological systems. They are basic and ubiquitous system-level phenomena and can be widely observed across many species. It is significant to understand the principles of robustness and fragility which will help us to correctly view various biological phenomena.

Biological robustness is a characteristic that allows a system to maintain its functions against external and internal perturbations (Kitano, 2004). It is often misunderstood that the function of the robustness is to remain unchanged regardless of any stimulation or mutations, so that the structure and components of the system are not affected. Actually, robustness refers to keeping the specific functions of the system undisturbed, which usually requires the system to change its mode of operation in a flexible way. One extreme example can be seen in the anhydrobiosis, which almost completely pauses metabolism when extremely dehydrated and goes into a dormant state, surviving for several years (Crowe and Crowe, 2000). This dormancy is achieved by mass production of trehalose, and delayed substances become active again upon rehydration. Slow dehydration under extreme cases reflects the robustness of anorexic organisms. Biological robustness is also of great significance to evolution. Complex systems have evolutionable architecture requirements, which essentially requires the system to be robust against environmental and genetic disturbances.

On the contrary, biological fragility refers to the instability of a biological system to keep its functions when there is an internal or external disturbance. For instance, chromosome fragility occurs in mammalian cells that grow in the presence of specific inducers. Fragile sites show contracted or unstained gaps in chromatin, and chromosome breaks often occur in vitro and in vivo (Usdin, 2006).

It sounds that biological robustness and fragility are opposite characteristics, but both of them are of great significance for maintaining system balance. When the fragility of the system is exposed, the robust system is the most vulnerable. For example, *Diabetes mellitus* can be thought of as an exposed systemic fragility that has gained robustness to a lifestyle near-starvation, high energy demand, and a high risk of infection, but it is unusually perturbed by over-nutrition and low energy demand. As fragility is a by product of robustness, the fragile point of the system must be associated with a mechanism that gives rise to enhanced robustness. For example, chromosome fragility, intracellular feedback loops and host-tumor interactions maintain tumor robustness.(Kitano,2004) It is important to recognize that systems that have evolved to resist certain disturbances are extremely vulnerable to unexpected disturbances. This powerful and fragile trade-off is the basis of complex dynamic systems, which has a direct impact on the understanding of diseases and the design of effective therapy.

Biological robustness is an indispensable part of survival, ranging from the individual to the whole

organism. First, robustness is ubiquitous and essential because proteins, cells, biochemical networks, immune systems, organisms, and natural populations exist within changing and sometimes novel conditions under which the maintenance of satisfactory performance will determine persistence or function (Whitacre, 2012). For example, assuming that people's immune system is not robust, it will be easily destroyed by microbes. And another point of view, as mentioned above, evolution favours robust traits (Kitano, 2004). This means that complex systems have evolutionable architecture requirements, which essentially requires the system to be robust to environmental and genetic disturbances. If the system is not robust to genetic disturbance, it is very likely that it will not be able to form an evolutionable system and then perish.

The consequence of fragility may be insensitivity to external or internal mutation and disturbance, which in turn leads to extinction or ecosystem destruction. For instance, it is reported that over 267 species worldwide are being affected by plastic pollution and 700 species are at risk of becoming extinct (Cooper, 2019). Microplastics were found in dead whales, seals and dolphins, indicating that their ingesting system has fragility facing non-biodegradable substance. One way to avoid the biological fragility is to monitor feedback loops in small network. For relatively small networks, a feedback loop has been considered as an important motif for realizing the robustness (Kwon and Cho, 2008). Research showed that the number of feedback loops is also an indicator of the fragility.

In conclusion, biological robustness and fragility are special features in a system. Biological robustness is of great significance to the survival of organisms, and meanwhile the biological fragility can cause severe consequences.

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