Biological Robustness and Fragility:

Robustness is a fundamental feature of living systems where its relationship with evolution-trade-offs among robustness, fragility, resource demands, and performance-provides a possible framework for how biological systems have evolved and been organized. It enables to maintain their functioning against external and internal perturbations. Diseases can be considered as a manifestation of fragility of the system. In some cases, such as cancer, the disease state establishes its own robustness against therapeutic interventions. Cited by An integrated in silico-in vitro approach for identifying therapeutic targets against osteoarthritis.

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Robustness facilitates evolvability and robust traits are often selected by evolution. Such a mutually beneficial process is made possible by specific architectural features observed in robust systems. The robust properties can be observed in different biological systems. Escherichia coli is capable of chemotaxis (movement of an organism or entity in response to a chemical stimulus) over a wide range of chemo-attractant concentrations owing to integral intracellular feedback that ensures perfect adaptation and that is independent of ligand concentration7–9.

Biological networks are often fragile against unexpected mutations. For example, the energy control system of our body ensures robustness against common perturbations such as unstable food supply or infections, but the system is fragile against unusual mutations such as high-energy content foods or low-energy utilization lifestyle (Kitano, 2004a). The immune system provides robustness against pathogen threats, but it is fragile against unexpected failures such as dysfunction of MyD88 which is a nonredundant core element. A cancer cell which is robust against a wide range of chemical agents but can be extremely fragile against certain perturbations.

Biological Robustness is integral part of survival. Organisms are constantly exposed to genetic and non-genetic perturbations, robustness is important to ensure the stability of phenotypes. To select for environmental robustness where organisms can function across a wide range of conditions with little change in phenotype or fitness (biology). Some organisms show adaptations to tolerate large changes in temperature, water availability, salinity or food availability.

The nodes involved with a relatively larger number of feedback loops might be more essential in carrying out certain biological functioning. Some examples support this hypothesis. For instance, the Drosophila melanogaster regulatory network for the segment polarity composed of eight genes robustly performs its role only if the initial states of two specific genes are not perturbed (Chaves,2005). The robustness of a biological network is fragile by unexpected mutations. There are two types of such mutations such as a point mutation and a knockout mutation. The fragility caused by a point mutation and the fragility caused by a knockout mutation as the probability with which the robustness of a network is lost by the respective mutation. Robust networks are fragile for mutations at the nodes involving a relatively large number of feedback loops. There are some examples and experimental evidences that partially support this. For instance, the hippocampal CA1 neuronal signalling network includes 137 lethal proteins and 202 nonlethal proteins (Liu *et al.*, 2006).

A network with a larger number of positive feedback loops and a smaller number of negative feedback loops is likely to be more robust against perturbations. This result is partially related with the dynamical roles of feedback loops (Snoussi,1998). A positive feedback loop induces multi stationarity whereas a negative feedback loop generates an oscillatory behaviour. The cause of network fragility is a network acquires robustness as it involves a smaller number of feedback loops for the nodes subject to perturbations while involving a larger number of feedback loops for the nodes under no perturbation. The robustness of a network becomes fragile when unexpected mutations occur at the nodes subject to no perturbation.

This is related to study on the robustness-fragility trade-off system by Kitano (2007) where it is argued that any increase of robustness against a subset of perturbations will be off-set by the decrease of robustness against other perturbations. Robustness and fragility of networks can be measured by examining the underlying coupled feedback loops. This result can also be used for synthetic biological applications when we design or engineer biomolecular regulatory circuits such that robustness and fragility are controlled.