Question 1

Biological robustness is a system property to keep a stability of live-body structure and function as uncertainty factor from external and internal variety disturbs it [1]. However, robustness is often misunderstood to mean staying unchanged regardless of stimuli or mutations, so that the structure and components of the system, and therefore the mode of operation, is unaffected. robustness is the maintenance of specific functionalities of the system against perturbations, and it often requires the system to change its mode of operation in a flexible way. In other words, robustness allows changes in the structure and components of the system owing to perturbations, but specific functions are maintained. System control, alternative (or fail-safe) mechanisms, modularity and decoupling are the underlying mechanisms that produce robustness, and the robustness of a system can manifest itself in one of two ways: the system returns to its current ATTRACTOR or moves to a new attractor that maintains the system's functions [2].

Biological robustness has been widely observed across many species, from the level of gene transcription to the level of systemic homeostasis. For instance, *Escherichia coli* is capable of chemotaxis over a wide range of chemo-attractant concentrations owing to integral intracellular feedback that ensures perfect adaptation and that is independent of ligand concentration [3].

Robustness is an inherent property of evolving, complex dynamic systems and it enables the system to maintain its functionalities against external and internal perturbations [2], so a system must be robust to function in unpredictable environments using unreliable components. For complex biological systems, they must be robust against environmental and genetic perturbations to be evolvable. At the same time, evolution often selects traits that might enhance robustness of the organism [2]. In other word, various mechanisms incurring robustness of organisms actually facilitate evolution, and evolution favors robust traits, which means that requirements for robustness and evolvability are similar. Therefore, for complex biological systems, there are architectural requirements to be evolvable, which essentially requires the system to be robust against environmental and genetic perturbations, with the result that biological robustness becomes an integral part of survival.

Robustness and fragility of biological networks are correlated with each other. Systems designed or evolved to be robust against common or known perturbations can often be fragile to new perturbations [4]. Therefore, biological fragility can be explained as the property that biological networks are often fragile against unexpected mutations [5].

The phenomenon of biological fragility is not uncommon. For example, 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 [6].

For the consequences of fragility, fragility limits performance in complex networks, and robust systems are most vulnerable when the system's fragility is exposed [2]. For example, Diabetes mellitus can be thought of as an exposed fragility of the system that has acquired robustness against near-starvation, a high energy-demand lifestyle and high risk of infection, but it is unusually perturbed by over-nutrition and a low energy-demand lifestyle [7].

To avoid the fragility of biological systems, there may be some ways to refer to it. First, improving the robustness of the system may be a good idea to avoid fragility. With better robustness, the system may be able to handle more perturbations including those which may seem to be new and unexpected in the past. System control, alternative mechanisms, modularity and decoupling, which are the underlying mechanisms that produce robustness, would be ideal entry points to improve. In addition, associated literature shows that 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, and 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 [5]. Therefore, examining potential coupling feedback loops in biological systems, adding positive feedback loops and reducing negative feedback loops may also help avoid fragility.

References

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