When we talk about biological robustness and fragility, these concepts are usually used in system biology to estimate the interconnected interactions that regulate the functions of living things. Biological robustness is the ability of organisms to keep a stable condition or have specific functions when they are exposed to some particular factors[1]. Fragility is the opposite of robustness, meaning the phenotype is sensitive to changes in the cell and environment.

Robustness can be shown in the negative autoregulation. Negative autoregulation is when the level of gene product is high, a regulatory gene depresses its transcription as well as the transcription of other genes, so the gene can produce a steady-state level of protein despite the noise of the system. λ repressor is the protein that has negative autoregulation and can keep robustness until the molecule induce the lytic cycle of bacteria[2]. λ repressor can activate the expression of cI gene, which encodes λ repressor. When the concentration of it rises highly, it will bind to the operator called OR3; OR3 is located in the sequence of PRM and block RNA polymerase binding to it. The gene near PRM is cI and can not be transcripted. The robustness of λ repressor would help bacteria keep itself lysogenic, and this condition also has robustness and usually will not switch to lytic condition.

Robustness is an integral part of survival because in the same population of cells, they usually have different levels of gene expression, and these factors that cause this condition are called noise, including intrinsic and extrinsic noise. However, if cells respond to every change, cells do not have the resource to grow. Robustness is indispensable for these cells to have similar physiology and stay in a steady stage, so they can have normal biological reactions and keep consuming energy and reproducing, which can help them survive. Taking the example of λ bacteriophage, the robustness of λ repressor can keep bacteria lysogenic, so the bacteria can split and copy more sequences of λ bacteriophage. If the robustness disappear, bacteria may be released quickly and there are not time for λ bacteriophage to produce protein, which hinder reproduction of itself.

Robustness is common in organisms but fragility is also an important character of physiology. Fragility usually means this part can be easily changed and usually have a large influence in the phenotype or survival of cell, and it has a bad influence in the survival of cell because fragility means the structure is easily broken, so the biological function of this structure can not be realized.

For fragility, we usually say that the pathway have fragility, or we usually use this word to describe some biological structure or phenotype of cell, such as DNA fragility and chromosomal fragility. The common fragile sites in DNA are some gaps and breaks on metaphase chromosome of cells, and they can represent a large proportion of DNA damage. Fragile X chromosome is X chromosome having fragility site. The causes of it is the unusual number of repeat CGG in FMP1. There are more than 50 neurodegenerative diseases in human connected with Fragile X chromosome.

To avoid the bad influence of DNA fragility, cells have evolved many ways to deal with it, such as recombination repair and NHEJ. Recombination repair can help the new strand of DNA, which have the damaged template, reform a complete strand and fill the gap. NHEJ usually help cell survive but do not consider the preciseness of DNA because there is much damage in DNA, and it has stopped a cell's normal life.

However, fragility is not useless. For cancer, finding the fragility can help us find new methods to repress or kill cancer cell[3].

When we want to judge robustness and fragility in system biology, we usually focus on if the upstream input(the changes) changes the downstream phenotype. Robustness is that the average keep stable, but variance change. Fragility is that the curve of phenotype change largely. By building the mathematical model of the cell to study the system of life, robustness and fragility are important characteristics of this model to show the physiology in data. However, the data of organisms is so large that scientists must use informatics to process data and can get a more precise network of macromolecules.

References

1. Félix, M. A. & Barkoulas, M. Pervasive robustness in biological systems. *Nature Reviews Genetics* vol. 16 483–496 Preprint at https://doi.org/10.1038/nrg3949 (2015).
2. Santillá, M. & Mackey, M. C. *Why the Lysogenic State of Phage l Is So Stable: A Mathematical Modeling Approach*. *Biophysical Journal* vol. 86 (2004).
3. Radisavljevic, Z. Locus of fragility in robust breast cancer system. *Journal of Cellular Biochemistry* vol. 92 1020–1024 Preprint at https://doi.org/10.1002/jcb.20141 (2004).