New evidence on the robustness of metabolic networks

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Biological systems are constantly evolving in ways that increase their fitness for survival amidst environmental fluctuations and internal errors. Now, in a study of cell metabolism, a Northwestern University research team has found new evidence that evolution has produced cell metabolisms that are especially well suited to handle potentially harmful changes like gene deletions and mutations.

The results, published online this week in the journal *PNAS*, could be useful in areas where researchers want to manipulate metabolic network structure, such as in bioengineering and medicine, and in the design of robust synthetic networks for use in energy production and distribution networks and in critical infrastructures, such as transportation networks.

The research was led by Julio M. Ottino, dean of the McCormick School of Engineering and Applied Science and Walter P. Murphy Professor of Chemical and Biological Engineering. Other authors of the paper, titled "Cascading failure and robustness in metabolic networks," are Luís A. Nunes Amaral, associate professor of chemical and biological engineering, and lead author Ashley Smart, who recently received his doctoral degree from Northwestern and is now a postdoctoral fellow at the California Institute of Technology.

Cell metabolism is essentially a large network of reactions whose purpose is to convert nutrients into products and energy. Because the network is highly interconnected, it is possible for a single reaction failure (which may be precipitated by a gene deletion or mutation) to initiate a cascade that affects several other reactions in the system. This event could be likened to disturbing a small area of snow that may trigger a large avalanche or the failure of a single transmission line in an electric power grid that may cause a widespread blackout.

By measuring the size of these "cascade" events in simulated metabolic networks, the Northwestern researchers were able to develop a quantitative measure of metabolic robustness: the more robust the network, the less the probability that small disturbances produce large cascades.

They found that the likelihood of large failure cascades in a metabolic network is unusually small, compared to what they would expect from comparable, randomly structured networks.

In other words, these metabolic networks have evolved to be exceptionally robust, adopting organizational structures that help minimize the potentially harmful impacts of gene deletions and mutations. Ottino and his colleagues developed a mathematical model describing the cascading failure phenomenon as a percolation-like process.

The cascading failure model opens up new possibilities for developing math- and statistics-based descriptions of how network structure affects metabolic function in biological systems. The relationship between metabolic structure and function is an important, lingering question for researchers in areas such as bioengineering and disease treatment in medicine, where one goal is to manipulate metabolic network structure in order to obtain desired behaviors.

The Northwestern team concludes it is possible that nature, in this case, is the best teacher: improved understanding of how cell metabolisms have evolved to handle failure cascades may provide clues as to how one might design synthetic networks for similar robustness.

Source: Northwestern University

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