Cells are like robust computational systems

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Gene regulatory networks in cell nuclei are similar to cloud computing networks, such as Google or Yahoo!, researchers report today in the online journal *Molecular Systems Biology*. The similarity is that each system keeps working despite the failure of individual components, whether they are master genes or computer processors.

This finding by an international team led by Carnegie Mellon University computational biologist Ziv Bar-Joseph helps explain not only the robustness of cells, but also some seemingly incongruent experimental results that have puzzled biologists.

"Similarities in the sequences of certain master genes allow them to back up each other to a degree we hadn't appreciated," said Bar-Joseph, an assistant professor of computer science and machine learning and a member of Carnegie Mellon's Ray and Stephanie Lane Center for Computational Biology.

Between 5 and 10 percent of the genes in all living species are master genes that produce proteins called transcription factors that turn all other genes on or off. Many diseases are associated with mutations in one or several of these transcription factors. However, as the new study shows, if one of these genes is lost, other "parallel" master genes with similar sequences, called paralogs, often can replace it by turning on the same set of genes.

That would explain the curious results of some experiments in organisms ranging from yeast to humans, in which researchers have recently

identified the genes controlled by several master genes. Researchers have been surprised to find that when they remove one master gene at a time, almost none of the genes controlled by that master gene are de-activated.

In the current work, the Carnegie Mellon researchers and their colleagues in Israel and Spain identified the most probable backup for each master gene. They found that removing the master genes that had very similar backups had almost no noticeable effect, but when they removed master genes with less similar backups, the effect was significant. Additional experiments showed that when both the master gene and its immediate backup were removed, the effects became very noticeable, even for those genes with a similar backup gene. In one example, when the gene Pdr1 was removed, researchers found almost no decrease in activation among the genes it controls; when Pdr1 and its paralog were removed, however, 19 percent of the genes Pdr1 controls failed to activate.

"It's extremely rare in nature that a cell would lose both a master gene and its backup, so for the most part cells are very robust machines," said Anthony Gitter, a graduate student in Carnegie Mellon's Computer Science Department and lead author of the Nature MSB article. "We now have reason to think of cells as robust computational devices, employing redundancy in the same way that enables large computing systems, such as Amazon, to keep operating despite the fact that servers routinely fail."

Source: Carnegie Mellon University (news : web)