Team develops artificial cells to study molecular crowding and gene expression

July 14 2013

The interior of a living cell is a crowded place, with proteins and other macromolecules packed tightly together. A team of scientists at Carnegie Mellon University has approximated this molecular crowding in an artificial cellular system and found that tight quarters help the process of gene expression, especially when other conditions are less than ideal.

As the researchers report in an advance online publication by the journal *Nature Nanotechnology*, these findings may help explain how cells have adapted to the phenomenon of molecular crowding, which has been preserved through evolution. And this understanding may guide synthetic biologists as they develop artificial cells that might someday be used for drug delivery, biofuel production and biosensors.

"These are baby steps we're taking in learning how to make artificial cells," said Cheemeng Tan, a Lane Postdoctoral Fellow and a Branco-Weiss Fellow in the Lane Center for Computational Biology, who led the study. Most studies of synthetic biological systems today employ solution-based chemistry, which does not involve molecular crowding. The findings of the CMU study and the lessons of evolution suggest that bioengineers will need to build crowding into artificial cells if synthetic genetic circuits are to function as they would in real cells.

The research team, which included Russell Schwartz, professor of biological sciences; Philip LeDuc, professor of mechanical engineering and biological sciences; Marcel Bruchez, professor of chemistry; and Saumya Saurabh, a Ph.D. student in chemistry, developed their artificial

cellular system using molecular components from bacteriophage T7, a virus that infects bacteria that is often used as a model in synthetic biology.

To mimic the crowded intracellular environment, the researchers used various amounts of inert polymers to gauge the effects of different density levels.

Crowding in a cell isn't so different from a crowd of people, Tan said. If only a few people are in a room, it's easy for people to mingle, or even to become isolated. But in a crowded room where it's hard to move around, individuals will often tend to stay close to each other for extended periods. The same thing happens in a cell. If the intracellular space is crowded, binding between molecules increases.

Notably, the researchers found that the dense environments also made gene transcription less sensitive to environmental changes. When the researchers altered concentrations of magnesium, ammonium and spermidine – chemicals that modulate the stability and binding of macromolecules – they found higher perturbations of gene expression in low density environments than in high density environments.

"Artificial cellular systems have tremendous potential for applications in drug delivery, bioremediation and cellular computing," Tan said. "Our findings underscore how scientists could harness functioning mechanisms of natural cells to their advantage to control these synthetic cellular systems, as well as in hybrid systems that combine synthetic materials and natural cells."

More information: Molecular crowding shapes gene expression in synthetic cellular nanosystems, *Nature Nanotechnology*, DOI: 10.1038/nnano.2013.132

Provided by Carnegie Mellon University