Nano World: Nanotubes may unfold proteins

April 25 2006

Bottling proteins in nanotubes may cause them to unfold, which may drive researchers exploring nanotubes as drug-delivery vehicles to rethink their strategies, experts told UPI's Nano World.

These findings could have greater implications when it comes to our understanding of how proteins are assembled by nature's own nanotechnology, the organic machinery that synthesizes and folds proteins, added researcher Vijay Pande, a biophysical chemist and structural biologist at Stanford University in California. This could in turn help understand how antibiotics work or how diseases lead to misfolded proteins.

Scientists worldwide are experimenting with nanotubes and other hollow nanoparticles as packages to carry drugs into cells. The hope is such encapsulation can protect drugs from the ravages of the body and, if adorned with the right molecules as guides, deliver them into the cells where they are most needed.

The elegant properties that proteins exhibit often depend on how the molecules are folded. Many times protein folds are held in place by so-called hydrogen bonds. While scientists have for decades advanced their knowledge on how proteins fold under a variety of conditions in test tubes, Pande and his colleagues wanted to investigate how proteins behaved in situations more like those they might encounter in the body, such as within capsules.

The researchers employed the resources of the distributed computing

project known as Folding@Home, which relies on the computing power donated by some 200,000 volunteered computers over the Internet. They simulated how a simple protein made of 23 amino acids behaved within single-walled carbon nanotubes some 1.5 to 3 nanometers or billionths of a meter wide.

Pande and his colleagues discovered confining proteins in nanotubes altered the way they interacted with the water they were dissolved in. Essentially, the proteins gain hydrogen bonds with the water, but lose the hydrogen bonds that keep their folds in place, he explained.

Instead of ruling out nanotubes and other hollow nanoparticles as drug delivery vehicles, Pande stresses these findings could help improve them, by for instance coating nanotube interiors with molecules that keep proteins properly folded, or even use this unfolding effect "to control the protein in a way not obvious before," he said.

Researchers may also wish to examine perforated nanotubes, said biophysicist Devarajan Thirumalai at the University of Maryland in College Park. He cautioned that proteins may spontaneously fold back into their original shapes outside the nanotubes, and that further research was necessary into how proteins behaved in confined spaces.

Pande noted that ribosomes, the organic machinery cells use to synthesize proteins, eject their products out tunnels roughly 1.5 nanometers wide. These findings could help understand how the body folds its proteins. Moreover, roughly a third of all antibiotics target bacterial ribosomes, with important ones such as orthomycin actually attacking the ribosome exit tunnel, and further research could help understand how these antibiotics work, perhaps yielding insights that could improve such drugs.

Pande and his colleagues reported their findings in the *Journal of the*

American Chemical Society.