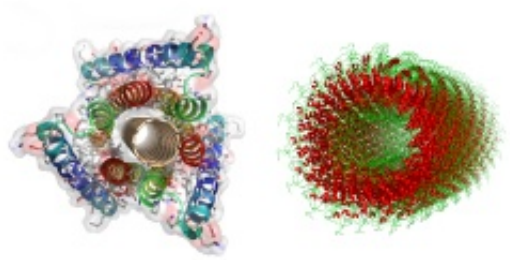
Penn researchers help nanoscale engineers choose self-assembling proteins

May 30 2011, By Evan Lerner



The researchers' structure, left, was inspired by tobacco mosaic virus, right.

Engineering structures on the smallest possible scales -- using molecules and individual atoms as building blocks -- is both physically and conceptually challenging. An interdisciplinary team of researchers at the University of Pennsylvania has now developed a method of computationally selecting the best of these blocks, drawing inspiration from the similar behavior of proteins in making biological structures.

The team was led by postdoctoral student Gevorg Grigoryan and professor William DeGrado of the Department of Biochemistry and Biophysics in Penn's Perelman School of Medicine, as well as graduate student Yong Ho Kim of the Department of Chemistry in Penn's School of Arts and Sciences. Their colleagues included members of the Department of Physics and Astronomy in SAS.

Their research was published in the journal Science last week.

The team set out to design proteins that could wrap around single-walled carbon nanotubes. Consisting of a cylindrical pattern of carbon atoms tens of thousands of times thinner than a human hair, nanotubes are enticing to nanoengineers as they are extraordinarily strong and could be useful as platform for other nano-structures.

“We wanted to achieve a specific geometric pattern of the atoms that these proteins are composed of on the surface of the nanotube,” Grigoryan said. “If you know the underlying atomic lattice, it means that you know how to further build around it, how to attach things to it. It's like scaffolding for future building.”

The hurdle in making such scaffolds isn’t a lack of information, but a surfeit of it: researchers have compiled databases that list hundreds of thousands of actual and potential protein structures in atomic detail. Picking the building materials for a particular structure from this vast array and assuring that they self-assemble into the desired shape was beyond the abilities of powerful computers, much less humans.

“There's just an enormous space of structural possibilities to weed through trying to figure out which are feasible,” Grigoryan said. “To have a process that can do that quickly, that can look at a structure and say ‘that's not reasonable, that can't be built out of common units,’ would solve that problem.”

The researchers’ algorithm works in three steps, which, given the parameters of the desired scaffolding, successively eliminate proteins that will not produce the right shape. The elimination criteria were based on traits like symmetry, periodicity of binding sites and similarity to protein “motifs” found in nature.

After separating the wheat from the chaff, the result is a list of thousands of candidate proteins. While still a daunting amount, the algorithm makes the protein selection process merely difficult, rather than impossible.

The research team tested their algorithm by designing a protein that would not only stably wrap around a nanotube in a helix but also provide a regular pattern on its exterior to which gold particles could be attached.

“You could use this to build a gold nanowire, for instance, or modulate the optical properties of the underlying tube in desired ways” Grigoryan said.

Next steps will include applying this algorithm for designing proteins that can attach to graphene, which is essentially an unrolled nanotube. Being able to make scaffolds out of customizable array of proteins in a variety of shapes could lead to advances in everything from miniaturization of circuitry to drug delivery.

Engineering these materials in the lab requires a tremendous amount of precision and computational power, but such efforts are essentially mimicking a phenomenon found in even the simplest forms of life.

“The kind of packing that certain viruses have in their viral envelope is similar to what we have here in that they self-assemble. They have protein units that, on their own, form their complicated structures with features that are far beyond the size of any single protein,” Grigoryan said. “Each protein doesn’t know what the final structure is going to be, but it still helps form it. We were inspired by that.”

Provided by University of Pennsylvania