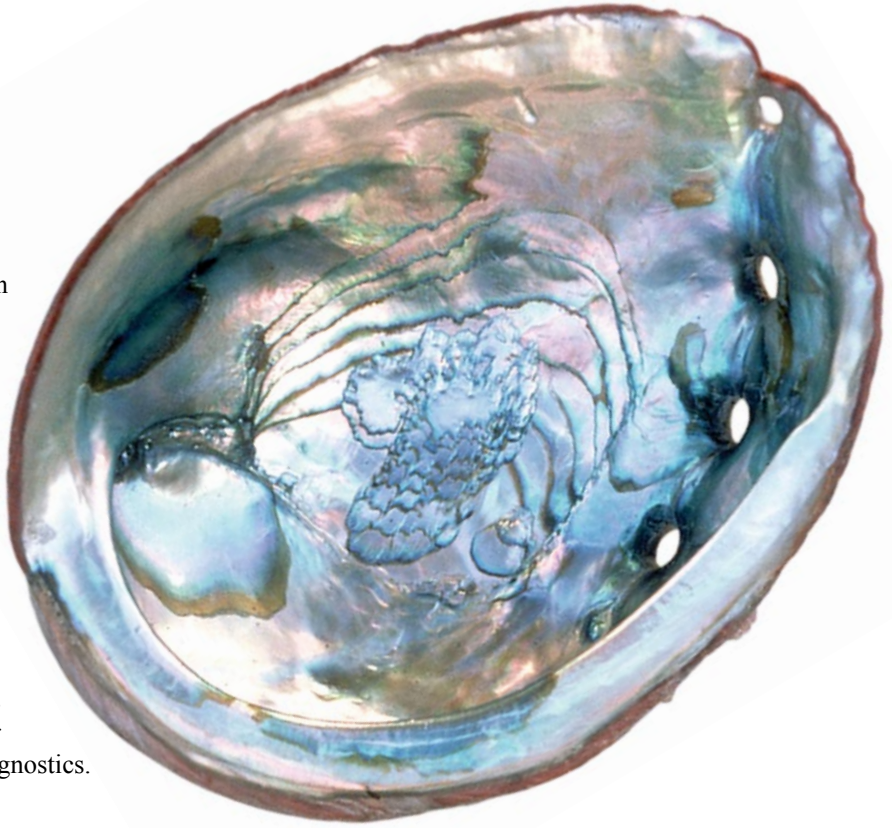
Wired on the Nanoscale

IF you think viruses are only good (or not good) for causing the common cold, flu, and other ailments, then you're in for a surprise.

Scientist Yu Huang, a Lawrence fellow at Livermore, spent a year and a half at the Massachusetts Institute of Technology learning a technique for creating metallic and semiconducting nanostructures using genetically engineered viruses. Among the structures she has created are tiny gold nanowires that may be used to make single-molecule devices. The technique allows the scientist the final word in determining the size and shape of the structures at a level that has been difficult to control with other techniques. Future applications for single-molecule devices include light-emitting displays, optical detectors and lasers, fast interconnects, nanometer-scale computer components, magnetic storage, sensors, and medical diagnostics.



An abalone shell is an example of a structure found in nature that is created by an organism binding to and assembling inorganic materials in its environment.

Building with Viruses

As the sizes of electronic devices continue to shrink, the need for control over minutely small dimensions—even down to single molecules and atoms—increases. Huang and other researchers are following nature's lead to solve this technological problem. "Our goal is to build structures at the molecular level from the bottom up, just as nature does," says Huang.

In nature, some organisms have evolved the ability to bind to and assemble inorganic materials with nearly perfect alignment, orientation, and shape, in a complex yet beautifully controlled fashion. The proteins expressed from particular genes in living bone, shells, diatoms, and certain bacteria can bind to inorganic materials creating elegant structures with great precision on scales from the nanoscopic to macroscopic. An abalone shell is one example of this process in nature.

For the past few years, Huang and other scientists have been researching the process, using bacteria, viruses, and other organisms as the first building blocks for generating devices on the nanoscale. Whereas organisms in nature must make do with their own genes and proteins and whatever materials are accessible in their environments, scientists can turn to special protein libraries called peptide combinatorial libraries and splice in genes that express specific proteins. This technique allows the researchers to choose which proteins will coat the surface of a given organism and, in turn, which inorganic materials will bind to the organism. The use of specific genes and proteins allows the possibility of controlling the self-assembly of multiple electronic components on a single device.

A Golden Opportunity

Huang has been using the M13 bacteriophage, a virus that infects bacteria. M13 is a circular single-stranded DNA molecule encased in a flexible cylinder that is coated with the protein pVIII. In addition, at one end of the M13 virus are five copies of the protein pIII, and at the other end of the virus are five copies of two other proteins.

Huang uses the M13 bacteriophage virus to create one-dimensional (1D) nanostructures, such as gold nanowires, and more complex

2D and 3D structures. In addition, she has taken the process a step further by connecting such structures to each other. Using viruses as "scaffolds" from which to build these structures allows scientists to take advantage of the growth process perfected by nature.

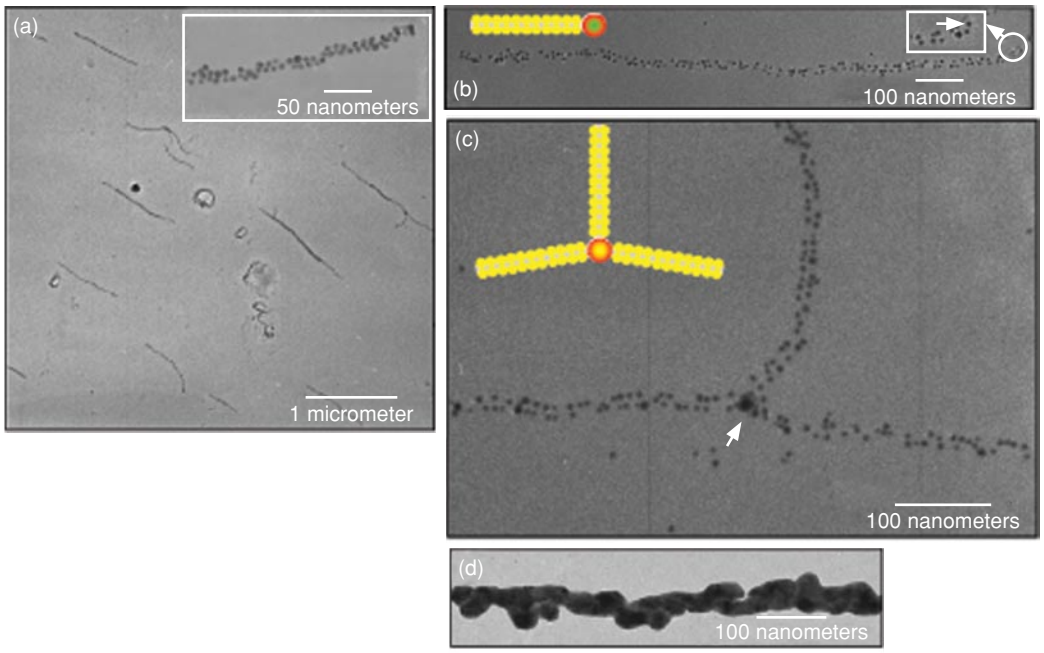
Huang began by modifying two genes (gIII and gVIII) in the genome of the M13 bacteriophage. The modified gVIII gene expresses a modified pVIII protein that has a high affinity for binding to gold. The modified gIII gene expresses a modified pIII protein that binds well to streptavidin (a protein routinely used to purify DNA binding proteins). The modified pVIII protein coats the length of the genetically engineered bacteriophage clone, and the modified pIII protein expresses at just one end of the clone.

Huang then used the modified virus as a building block on which to bind and assemble 1D gold nanocrystal arrays. Solutions containing the genetically modified bacteriophage virus were mixed with a suspension that held gold nanoparticles. Images taken with a transmission electron microscope (TEM) showed that the gold nanoparticles had assembled around the modified bacteriophages (called 8–3 bacteriophages because of their modified proteins pVIII and pIII) into wirelike structures. A closer look revealed that the gold nanoparticles were actually arranged in an ordered 1D array on the pVIII proteins along the axis of the virus.

Huang then assembled a more complex structure using the modified pIII proteins at one end of the bacteriophage to bind to gold particles coated with streptavidin. TEM images showed that an array of 5-nanometer-diameter gold particles had formed on the modified pVIII proteins, and streptavidin-coated 15-nanometer-diameter gold particles had bound to the pIII proteins on the end.

"We can easily extend this process to other materials and structures," notes Huang. For example, when the streptavidin-coated gold was replaced with streptavidin-conjugated cadmium selenide quantum dots, the result was arrays with quantum dots bound to the modified pIII proteins and gold nanoparticle arrays bound to the modified pVIII proteins. "We can connect more than one bacteriophage to a quantum dot and create complex structures," says Huang.

She also created continuous metallic nanowires—originally 1D arrays of separate gold nanocrystals—with average diameters of 40 nanometers and lengths of 100 nanometers. The process involved using electroless deposition to coat the existing gold nanoparticle arrays with additional gold. Huang conducted studies of these wires to evaluate their capability to transmit electricity. Measurements indicated that the wires, indeed, can act as conductors for considerable amounts of electrical current at the nanoscale. "These experiments indicated that a wire built on modified pVIII proteins could be used to transmit electricity to another nanostructure, such as a quantum dot built on the pIII proteins at the end of the virus," she explained. "The approach is one solution to the interconnection problem found in studies of quantum objects." Other studies are under way to thoroughly



Transmission electron microscopy images of a genetically engineered 8–3 bacteriophage virus show the formation of nanostructures. (a) Distinct wirelike structures are self-assembled into one-dimensional arrays along the axis of the virus. (b, c) More complex structures are created from gold nanoparticles and streptavidin-coated gold particles and quantum dots, using the modified virus as a starting building block. White indicates the virus structure, yellow dots are gold nanoparticles, the green dot is a quantum dot, and red indicates the streptavidin coating. (d) This continuous metallic nanowire began as one-dimensional arrays of gold nanoparticles bound to the genetically engineered virus. After 5 minutes of electroless deposition, enough additional gold particles were deposited to thicken the wire to the point where it could transmit a small electric current.

characterize the bacteriophage-based wires and detail their electrical performance.

From Livermore to Beyond

Huang came to Livermore from Harvard's Department of Chemistry as part of a prestigious postdoctoral program called the Lawrence Fellowship Program. The purpose of the fellowship is to pursue cutting-edge science and stimulate cross-fertilization of ideas. Lawrence fellows have the freedom to pursue research with ample resources to support their efforts. (See *S&TR*, November 2002, pp. 12–18.) "One thing I found very attractive about the Laboratory is that many opportunities exist to exchange ideas and work with scientists of different disciplines," Huang notes.

Huang has recently completed her three-year fellowship and is preparing to move on to an assistant professorship position at the University of California at Los Angeles (UCLA). Harry Radousky, deputy director of Livermore's University Relations Program, views Huang's appointment as a success for the Laboratory both now and in the future. "The program attracts some of the brightest scientists to the Lab and promotes university collaborations," he says. "We see situations such as Huang's as a success story—our hope being that our fellows will find a place either here at the Laboratory or at prestigious universities, where they will strengthen collaborative ties between the Laboratory and their institution."

Huang is indeed planning future collaborations with her Livermore colleagues. They plan to genetically engineer viruses to produce precise nanostructures and better understand the pathogenesis of kidney-stone formation. She intends to establish a research program at UCLA that focuses on developing complex material structures with molecular precision through genetic control of biological scaffolds. The program will investigate these structures' fundamental properties and explore their use as functional nanosystems for various applications such as molecular electronics and drug delivery.

—Ann Parker

Yu Huang's research, conducted at Lawrence Livermore and at the Massachusetts Institute of Technology as a Lawrence fellow, will continue when she takes on a new position at the University of California at Los Angeles.

Key Words: bacteriophage, biological scaffolds, DNA, genetic engineering, Lawrence Fellowship Program, nanosystems, nanotechnology, nanowires, quantum dots, virus.

For further information contact Yu Huang (925) 424-4831 (huang20@llnl.gov).