NANOBIOTECHNOLOGY CENTER NBTC

SMALL WORLD, BIG SCIENCE

The dream of developing tools and processes to interact with biosystems on the scale of individual cells and biomolecules is being realized by researchers at the Nanobiotechnology Center (NBTC).

"We're studying the ways cells communicate with their environment at the molecular level," says center director Harold Craighead, professor of applied and engineering physics at Cornell University and the Charles W. Lake, Jr. Professor of Engineering. "We're developing new devices to allow us to investigate these properties at the finest level of detail, approaching single-molecule responses." Toward this end, the center fosters a close collaboration between life scientists, physical scientists, and engineers.

Center researchers have developed cell cultures "on a chip," that is, cultures in a laboratory system that can more accurately model the response of humans to pathogens or therapeutic drugs, for example. These systems integrate different types of human cell tissue in a biological test platform that may significantly reduce the amount of animal testing involved in early-stage screening of new drugs.

Another group is working on a laboratory model of the blood-brain barrier, which protects the brain from exposure to harmful substances in the blood stream. NBTC associate director Graham Kerslick explains that the researcher team can grow the required cell types on a sort of scaffold—a micropatterned polymer membrane—and can model how the barrier works when presented with various biomolecules, toxins, or drugs.

NBTC research by Kelvin Lee and colleagues on techniques to detect a suite of compounds associated with neurodegenerative diseases such as Alzheimer's may yield a rapid diagnostic test for the disease. Currently, there is no definitive way to diagnose the condition in humans while still alive. The researchers are developing methods to detect a set of proteins in spinal fluid as a signature of the disease.

Biological imaging technology has gained a boost from the development of a new kind of nanoparticle called Cornell dots, or CU dots for short. These silica nanoparticles may be used in displays, biological imaging, optical computing, and sensors. CU dots offer many advantages over the previous technologies for imaging: not only are they many times brighter than single fluorescent dye molecules, they don't fade as much as the alternative, called quantum dots. They provide a more constant light source and are less expensive and more inert than quantum dots.

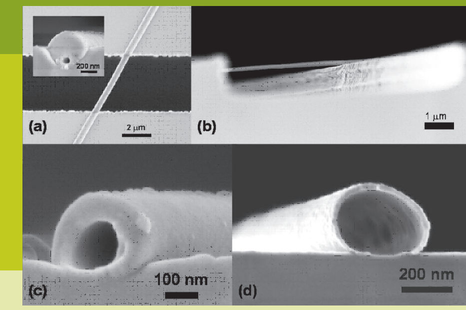
The brightly glowing particles contain fluorescent dye molecules surrounded by a protective silica shell, forming a package of about 25 nanometers in diameter. The surface may be coated with ligands to allow the particles to attach to species of interest. Center co-director Harvey Hoch, chair of plant pathology at Cornell, Geneva, N.Y., notes this development is a "significant contribution. It will provide a good marker for cell studies—it's a nice tool for microscopists and cell biologists." Hoch is a leader in using micro- and nanofabrication technologies to address questions in biology.

Kerslick notes the CU dot technology has been licensed by Cornell to a startup company called Hybrid Silicon Technologies, Ithaca, which is looking to commercialize the capabilities of fluorescent silica nanoparticles for biological imaging applications.

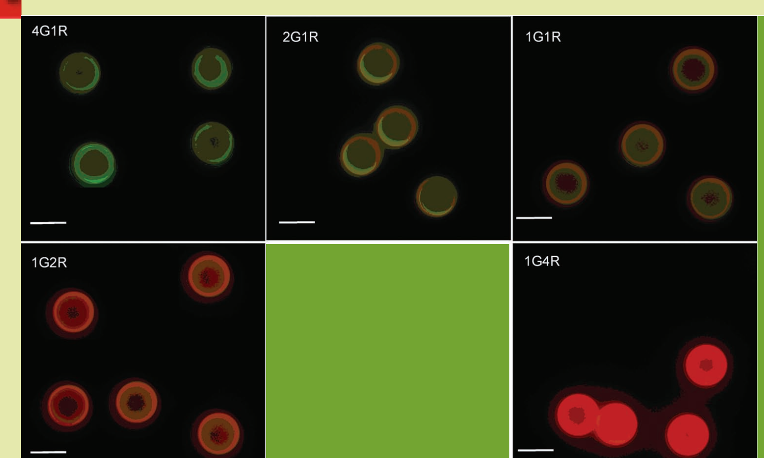
On another front, a group led by Dan Luo of Cornell has created "nanobarcodes" that can be used to rapidly identify genes, pathogens, drugs, and other chemicals. The technique uses multicolor fluorescent tags made out of synthetic DNA that attach to the target species. Under UV light, the tags produce a combination of colors unique to the species of interest, and can be read by a computer scanner or microscope. The method has been shown to distinguish several different pathogens simultaneously.

Luo, a professor of biological and environmental engineering, has utilized short strands of DNA molecules that can self-assemble into unusual shapes. By linking these DNA structures to polystyrene molecules, he created tiny geodesic spheres about 400 nm in diameter that could carry drugs into cells, among other potential applications. DNA buckyballs created by Luo were selected by *R&D Magazine* as one of the 25 "most innovative products of 2006" in the Inaugural MicroNano 25 competition. The winners were featured the August 2006 issue of *R&D.*

Luo's research on using DNA to construct new materials and nanodevices is being commercialized by an Ithaca startup company called DNANO Systems. The company recently won second place at the 7th Cornell BR Ventures Business Idea Competition. The company has also received funding from NYSTAR (New York Office of Science, Technology & Academic Research), which supports technology development and commercialization in New York State.



Electrospun polymer nanofibers were used as templates for creating nanochannels in a variety of materials. (a) Top-down view of suspended sputtered glass nanochannel, with cross-section on bare silicon. (b) Side view of suspended glass nanochannel . (c) Cross section of chemical vapor deposited glass nanochannel. (d) Cross section of evaporated aluminum nanochannel. *Image: NBTC, BDA2*



Merged fluorescent colors (pseudocolors) of nanobarcodes from individual polystyrene microbeads under a fluorescent microscope. Note that only two colors were used in the barcodes. (from *Nature Biotechnology,* 23, p. 883, 2005) *Photo: NBTC, BDA7*

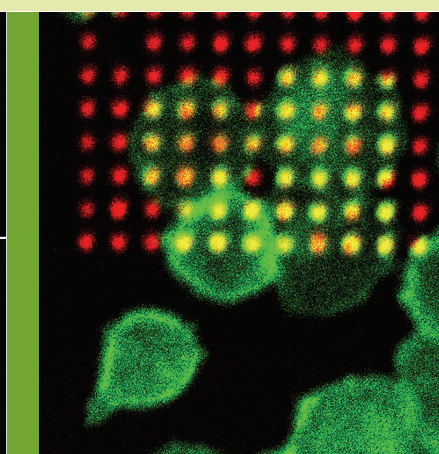
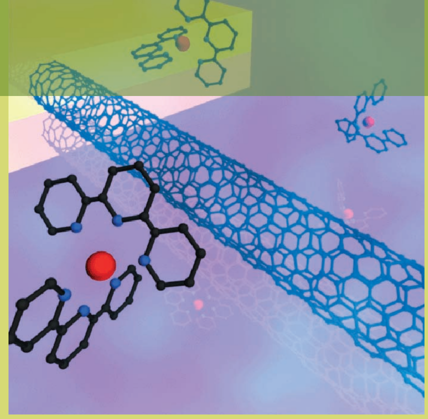
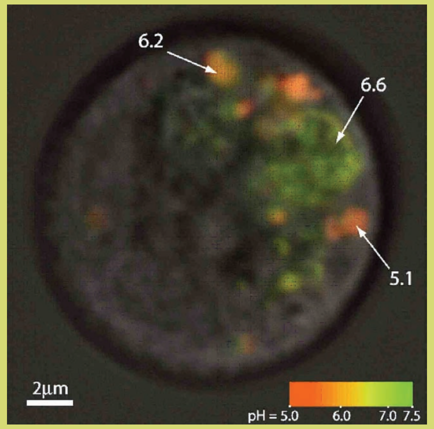


Image shows cell receptors that mount on a cell's surface and detect foreign bodies like allergens. Patterned "nano-keys" allow receptors to cluster in a way that activates the cell's inner machinery. *Photo: Wu, Holowka, Craighead, and Baird*

Nanobiotechnology Center co-director Harvey Hoch, chair of plant pathology at Cornell, Geneva, N.Y.





CU dots. Preliminary imaging data showing pH measurements made on RBL mast cells using 70 nm CU dot-based sensors. *Image: NBTC, NCB1*

VIEWPOINT

FROM THE DIRECTOR

Harold Craighead

Harold Craighead has a unique vantage point on the evolution of an NSF Science and Technology Center. He was the original director of the Nanobiotechnology Center when it was founded in 2000, then left to become interim dean of engineering, returned as center codirector, and now is director again.

He reflects on the changes since the founding of the center. "We were just 'wishful thinking' back then. Now, we're part of a brand new nanotechnology building, we have facilities and dozens of investigators and staff. We have people collaborating who didn't even know each other before. Now, students take for granted they will work in an interdisciplinary setting—they're going to combine cell biology, mechanical engineering or physics, immunology. A generation of students has gone through now, and it's just understood."

"Our students are highly sought after, getting jobs in government labs, industry, and academic settings," says Craighead. "We're producing a type of student that didn't really exist when we started. Students are in the vanguard leading a transformation of the academic environment. We publish papers, but the influence goes on much longer in the students that go out into the workforce," he emphasizes.

"My main mission is to keep the organization functioning so people can do their work. My motivation is to facilitate a broader range of work than I could do as an individual."

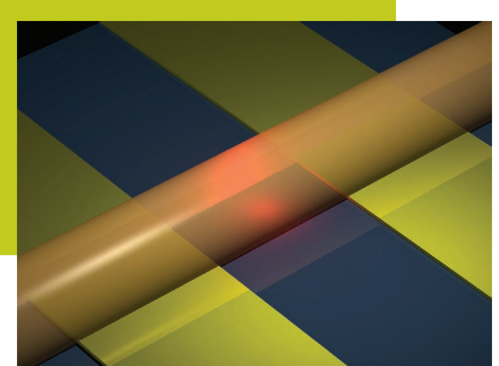
"The reality is, it takes a lot of diverse skills and efforts to make this happen," says Craighead. "Energy, negotiation, communication, motivation, intellectual curiosity, and commitment are the ingredients."

NEWS WATCH

NANOLAMPS LIGHT THE WAY TO NEW FLEXIBLE ELECTRONICS DEVICES

Center researchers have produced microscopic "nanolamps"–light-emitting nanofibers about the size of a virus or bacterium. It's one of the smallest organic light-emitting devices to date, made of fibers just 200 nanometers wide. Potential applications include sensing, microscopy, and flat-panel displays. The work was published in the February 2007 issue of *Nano Letters*.

At right: An illustrated closeup of an electrospun fiber. During experimentation the organic devices gave off an orange glow. *Photo: Jose M. Moran-Mirabal*



NANOBIOTECHNOLOGY

"IT'S A NANO WORLD" TRAVELING EXHIBITION

What if you could shrink to the size of a cell and zip through a blood vessel, or see what skin and hair are made of at the molecular level?

Thanks to an exhibit developed with the help of the Nanobiotechnology Center at Cornell University, you almost can. Working with the Sciencenter, Ithaca, N.Y., and its contractors, including Painted Universe Inc., also of Ithaca the team created a traveling 3,000 square-foot hands-on interactive museum exhibition that introduces children and their families around the country to the biological wonders of the very tiny.

"It's a Nano World" exhibition has traveled the U.S., even making a stop at Innoventions at Epcot in Lake Buena Vista, Fla., in 2004. The target audience for this traveling exhibition is 5 to 8 year-old children (K-3).

At one station in the exhibit, visitors can view highly magnified photographs of familiar objects like a penny or a bee and uncover photos with decreasing levels of magnification until an easily recognizable photo of the item is revealed. At another station, visitors can stick their hands into a glove box and use special tools to separate out different "cells" based on physical properties. The "Scope on a Rope" station has flexible projection microscopes to let visitors look at their own skin, hair, and clothing, magnified either 30 or 200 times.

The exhibition began touring in Winter 2003, and has been seen by more than 1 million visitors at museums throughout the U.S. The project is primarily funded by the Nanobiotechnology Center (NBTC) at Cornell University through a grant from the National Science Foundation.

"It's a Nano World" will be in Casper, Wyo., at The Science Zone during summer 2007. During fall 2007 it travels to the Austin Children's Museum, and during the first half of 2008, it is scheduled to be at Mobius Kids, Spokane, Wash.

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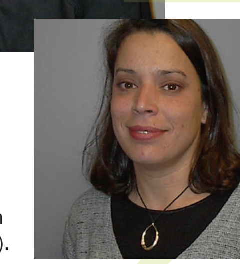
EDUCATION AT NBTC

Graduate education has received a boost at the center through a graduate-level nanobiotechnology course that is videoconferenced to NBTC partner institutions. The course covers biology basics as well as the principles and practice of microfabrication techniques, with a focus on applications in biomedical and biological research. Students participate in a team design project that stresses interdisciplinary communication and problem solving.

The Nanobiotechnology Center also plays a key role in transferring research to K12 audiences and museums, notes education director Jennifer Weil. "Just giving the raw research materials isn't enough—we need to help researchers to translate these materials and to design effective and appropriate ways to help teachers use them."

Weil has a staff of three dedicated to this mission. One of the programs they lead is a high school internship program over the summer. Ten juniors and seniors come to the center for four weeks in the summer to work on a research theme. Last year, they designed and built a micofluidics device to regulate mixing of chemicals. This summer, plans call for students to model the vascular system of a plant using microfluidics systems.

The center's Science Kit lending library is a source of science experiments and equipment that K12 teachers may borrow at low cost—only the price of shipping the materials back to the library. During the 2005-06 academic year, these materials reached 108 teachers and 3,036 students in 73 school districts across 16 states, says Weil. For more information, visit http://www.nbtc.cornell.edu/education.htm



The Nanobiotechnology Center plays a key role in transferring research to K12 audiences and museums, notes education director Jennifer Weil (right).