



# **Innovations Report**

## **Mar 2006 Part II**

- **ICT**
- **Microelectr. & Nanotech**
- **Life Sciences**

# Table of Contents

- **ICT**

- New network architecture delivers super-broadband wired & wireless service simultaneously
- Laser chips could power petaflop computers
- GA Tech develops ultra-efficient embedded architectures based on probabilistic technology
- Light at the end of the channel
- New process builds electronic function into optical fiber
- RFID worm created in the lab

- **Microelectr. & Nanotech**

- Nanotube circuit could boost chip speeds
- Beyond Silicon
- Rice University researchers create 'nanorice'
- Penn researchers create the first reliable method for making gaps for nanotech apps
- Virus used to make nanoparticles

- **Life sciences**

- Brain-Healing Nanotechnology
- Supercomputer builds a virus
- New Tools Developed For Studying Neurodegenerative Brain Disorders
- A One-Two Punch for Alzheimer's
- Comprehensive strategy to identify structural variation in human genome

**ICT**

## **New network architecture delivers super-broadband wired & wireless service simultaneously**

### **Optical-wireless convergence**

Telecommunications researchers have demonstrated a novel communications network design that would provide both ultra-high-speed wireless and wired access services from the same signals carried on a single optical fiber.

The new hybrid system could allow dual wired/wireless transmission of the same content such as high-definition television, data and voice up to 100 times faster than current networks. The new architecture would reduce the cost of providing dramatically improved service to conference centers, airports, hotels, shopping malls – and ultimately to homes and small offices.

Today, telecommunications providers generally supply services that are either all-wireless, through cellular telephones or similar devices, or all-wired – through DSL, cable or optical access network. As wireless providers seek to provide new bandwidth-intensive services such as video, music and high-speed Internet access, however, the bandwidth needs of wired and wireless services are converging.

The optical-wireless access network envisioned by Gee-kung Chang at Georgia Tech would connect to existing optical fiber networks that already serve much of the nation. But before entering a building, signals on the optical fiber would be optically up-converted in the central office from their normal infrared wavelengths to the millimeter-wave spectrum.

Using a new technique, wireless and baseband signals carried by multiple wavelengths would be converted onto the millimeter-wave carrier simultaneously. The conversion would be done using one of several all-optical techniques. The resulting signal would be split into two components and carried by passive optical network (PON) infrastructure installed throughout a building.

One component of the signal would be detected by high-speed receivers built into the ceilings of rooms, then amplified for short-range wireless transmission at frequencies of 40 to 60 gigahertz. The other signal component – carrying identical information – would be accessed through standard wall outlet throughout the building using a low-cost receiver and optical filter.

Either way, users could receive signals at data rates of up to 2.5 gigabits per second, significantly faster than service provided by most Wi-Fi or WiMax systems used at Internet hot-spots and other service areas.

Because the capacity of optical fiber is so high, this optical-wireless network could use wavelength division multiplexing (WDM) to carry as many as 32 different channels, each providing 2.5 gigabit-per-second service. That would allow users within buildings to subscribe to services from many different providers, each with their own content.

A key issue will be reducing the cost of the components. Another issue will be antenna designs for delivering high-speed wireless to specific areas of a building without interfering with service in adjoining spaces.

Companies such as NEC and BellSouth are already working on components integration and systems requirements needed for the hybrid optical-wireless communications network.

Integrating the system components may be the most challenging part of the implementation and network deployment.

## **Laser chips could power petaflop computers**

Laser communications chips capable of pumping data through the veins of gargantuan "petaflop" supercomputers have been demonstrated by NEC in Japan.

The communications chips can transfer information through optical fibres at a blistering 25 gigabits per second (a gigabit is a billion bits). This is a record for such components, according to NEC, and is many times faster than the purely electronic interconnects used in today's supercomputers.

Communications chips can convert electronic signals into optical ones. Using optical fibres to relay data between the chips is what may give this type of supercomputer the edge over previous ones using processors connected electronically.

NEC used a type of semiconducting laser diode called a Vertical-Cavity Surface Emitting Laser (VCSEL) which generates laser pulses in response to an electrical current. Researchers at the company created more efficient VCSEL devices by making the diodes from a blend of gallium arsenide and indium gallium arsenide - they used indium instead of the more conventional aluminium. This made it possible to transfer laser pulses more rapidly through optical fibre.

The new VCSEL chips could be used to make supercomputers of unprecedented power by routing data more efficiently between thousands of individual computer processors. NEC believes the chips could prove crucial to the development of the first petaflop class supercomputer - a machine capable of carrying out a thousand trillion mathematical calculations every second.

"Petaflop-class performance can be achieved in the next-generation supercomputer installed with the new VCSEL, in about 2010,"

## Light at the end of the channel

If photonic circuits are ever to compete with their electronic counterparts, strong confinement of light waves coupled with low propagation losses is needed. A new class of waveguides offers both. Miniaturized circuits that use light to carry digital information would be inherently faster than conventional electronic circuits, and have a capacity thousands of times greater. But there's a snag: the development of practical, small photonic components is impeded by the diffraction limit — the fact that light will spread out on passing through any region narrower than its wavelength.

On Nature 440, Bozhevolnyi et al. flag a new route around this obstacle. They present the first components that guide and manipulate light in the form of so-called channel plasmon–polaritons. These guide the light along the bottom of sub-wavelength V-shaped grooves, milled in a metal film, without high propagation losses.

Channel plasmon–polaritons are young members of an extended family known as the surface plasmons. These are electromagnetic waves that originate in the collective excitation of free electrons at the interface of a metal and an insulating dielectric, such as air. Surface plasmons remain tightly bound to the interface: a plasmon of an optical wavelength — between about 400 and 750 nanometres — penetrates around 10 nm into the metal and decays over a few hundred nanometres in the dielectric. Surface plasmons thus concentrate light in a volume less than its wavelength across. They can also be used to transmit electromagnetic signals: for the near-infrared wavelengths around 1.5 micrometres, typically used in telecommunications, the propagation length of a plasmon at a planar gold–air interface is about a millimetre, and therefore long enough to connect two devices on a chip optically. The use of surface plasmons is also compatible with available planar electronics technology, also offering the possibility of transporting optical signals and electrical current on the same substrate.

But to create miniature photonic circuits, surface plasmons have to be confined not just in the direction perpendicular to the interface, but also in the plane of the interface, so that they can propagate efficiently through narrow metal strips. This has proved problematic: when a propagating plasmon is squeezed from the sides, its propagation length is severely reduced. The several strategies deployed to circumvent this problem all represented an imperfect trade-off between sub-wavelength lateral confinement and propagation length.

In short, a new actor was needed: enter the channel plasmon–polariton (CPP). The fundamental idea of guiding light along the bottom of milled V-grooves in a planar metal surface results in low propagation loss. Extensive numerical simulations have confirmed this.

On the experimental side, too, things have begun to evolve rapidly. Just eight months ago, Bozhevolnyi and colleagues reported the experimental achievement of CPP propagation along a straight, V-groove waveguide drilled in a gold film using focused ion-beam milling.

In their latest contribution, Bozhevolnyi et al. fabricate the first CPP-based optical components. The first of these is a 'Y-splitter', a junction in which two straight waveguides are connected to a third over a distance of only 5  $\mu\text{m}$ , just over three times the light's wavelength. This feature is of paramount importance for the implementation of miniature optical circuits on a chip.

The fabrication process exploits current planar technology: milling grooves onto a metal film with a focused ion beam is similar to drawing lines on a paper with a pencil. The possibilities for such techniques are huge, but there are still some problems. Nevertheless, the successes already achieved in a very short period of experimental research using channel plasmons to mould the flow of light hint at bright prospects ahead.

## **GA Tech develops ultra-efficient embedded architectures based on probabilistic technology**

### **Probabilistic system on chip technology reduces energy consumption by a factor of more than 500 for some applications**

Researchers at the Georgia Institute of Technology announce energy savings by a factor of more than 500 in simulations with their ultra energy efficient embedded architecture based on Probabilistic CMOS (PCMOS). The research team's PCMOS devices take advantage of noise, currently fabricated at the quarter-micron (0.25 micron) level, and uses probability to extract great energy savings. The findings will be presented at the Design, Automation and Test In Europe (DATE) Conference, the leading peer-reviewed European electronic systems design meeting, on March 9 in Munich, Germany.

The research team led by Dr. Krishna Palem, a joint professor in the Georgia Tech College of Computing and the School of Electrical and Computer Engineering and founding director of the Center for Research in Embedded Systems & Technology, has confirmed that architectural and application gains to be reported at DATE are as high as a factor of 560 when compared to comparable CMOS based architectures. As traditional CMOS semiconductor technology approaches the nanoscale, coping with noise and energy savings are increasingly important. PCMOS harnesses the inherent instability of noise and uses it as a resource to achieve energy efficient architectures. In the architectures, noise induces distortion in the application. However, given the human ability to average this routinely such as in voice when using cell phones, or in images when they are streamed to hand held devices, the user does not often notice the distortion as significant and is willing to pay the price for significant energy savings. A demonstration showing this effect in the context of video decompression used in modern DVD images is available for viewing at <http://www.crest.gatech.edu/palempbitscurrent/demo.html>

"Probabilistic architectures extend PCMOS to computing substrates beyond devices," says Palem. "By mixing chip measurements and simulations, gains have been shown using this technology for such applications as Hyper-encryption as applied to computer security, and through cognitive applications such as speech recognition and pattern recognition as well as image decompression. The gains ranged from a factor of 10 to a factor of more than 500 over conventional architectural approaches."

Beyond such architectural objectives, when applications need random sources, historically pseudo-random numbers generators were used. The Georgia Tech research team used the National Institute of Standards and Technology (NIST) recommended tests to quantify and measure the quality of randomness of PCMOS within this limited context of being viewed as a source of random bits, beyond complete Probabilistic System on Chip (PSoC) architectures. PCMOS outperformed CMOS in the quality of random sequences generated.

## New process builds electronic function into optical fiber

**Optical fiber helped bring us the Internet, and silicon/germanium devices brought us microelectronics. Now, a joint team from Penn State University and the University of Southampton has developed a new way to combine these technologies. The team has made semiconductor devices, including a transistor, inside microstructured optical fibers. The resulting ability to generate and manipulate signals inside optical fibers could have applications in fields as diverse as medicine, computing, and remote sensing devices.**

Optical fiber has proved to be the ideal medium for transmitting signals based on light, while crystalline semiconductors are the best way to manipulate electrons. One of the greatest current technological challenges is exchanging information between optics and electronics rapidly and efficiently. This new technique may provide the tools to cross the divide. The results of this research will be published in the 17 March edition of the journal Science.

"This advance is the basis for a technology that could build a large range of devices inside an optical fiber," said John Badding, associate professor of chemistry at Penn State University. While the optical fiber transmits data, a semiconductor device allows active manipulation of the light, including generating and detecting, amplifying signals, and controlling wavelengths. "If the signal never leaves the fiber, then it is faster, cheaper and more efficient," said Badding. "

"This fusion of two separate technologies opens the possibility of true optoelectronic devices that do not require conversion between optical and electronic signals," said Pier Sazio, senior research fellow in the Optoelectronics Research Centre at the University of Southampton (UK). "If you think of the fiber as a water main, this structure places the pumping station inside the pipe. The glass fiber provides the transmission and the semiconductor provides the function."

Beyond telecommunications, optical fibers are used in a wide range of technologies that employ light. "For example, in endoscopic surgery, by building a laser inside the fiber you might be able to deliver a wavelength that could not otherwise be used," said Badding.

The key breakthrough was the ability to form crystalline semiconductors that nearly fill the entire inside diameter, or pore, of very narrow glass capillaries. These capillaries are optical fibers--long, clear tubes that can carry light signals in many wavelengths simultaneously. When the tube is filled with a crystalline semiconductor, such as germanium, the semiconductor forms a wire inside the optical fiber. The combination of optical and electrical capabilities provides the platform for development of new optoelectronic devices.



These photos show a glass fiber with a bundle of semiconductor wires emanating from it. Each wire is just 2 microns in diameter--20 times smaller than a human hair. The glass fiber is glowing from blue laser light. One of the images shows the wire-packed glass fiber passing through the eye of a needle. Credit: Neil Baril, Penn State.



## RFID worm created in the lab

Researchers have discovered a way to infect Radio Frequency Identification (RFID) tags with a computer worm, raising the disturbing prospect that products, ID cards, and even pets could be used to spread malicious code.

RFID tags provides a simple and efficient method of short-range identification and are increasingly being used to track products, make automatic payments and control access to buildings and public transport. They can be implanted into pets, cattle, and even humans for identification purposes. But researchers from Vrije Universiteit in Amsterdam, led by Andrew Tanenbaum, have found that RFID tags can also be used to spread dangerous computer code. They demonstrated techniques for creating malicious tags at the Fourth Annual IEEE International Conference on Pervasive Computing and Communications in Pisa, Italy,

Roughly the size of a grain of rice, an RFID tag contains a miniaturised computer chip and radio transmitter capable of sending a unique identification code over a short distance to a receiver and a connected computer. The tags are powered inductively, by the signal from the external reading device, which means they can operate indefinitely without a battery.

RFID tags are already viewed with some suspicion by privacy groups because they offer a way to increase surveillance of individuals. But, until now, it has been assumed they are unsuitable for spreading computer worms or viruses because each tag has a limited memory, typically less than 1024 bits.

The Vrije Universiteit team found that compact malicious code could be written to RFID tags after all. By replacing a tag's normal identification code with a carefully written message, the researchers found they could exploit bugs in a computer connected to an RFID reader. This made it possible to spread a self-replicating computer worm capable of infecting other compatible, and rewritable, RFID tags. "It's a very interesting idea," says Burt Kaliski, vice president of research at US company RSA Security. "RFID introduces data into a system, and if that system's data processing is not properly designed then many types of attack may be possible." But Kaliski also notes that simple RFID tags, which cannot be overwritten, should be far more difficult to exploit.

### **Airport Infections**

A tag infected with a worm and attached, for example, to a piece of luggage could rapidly infect other luggage in an airport, the Dutch researchers say. "On arrival at other airports, these cases will be scanned again and within 24 hours, hundreds of airports throughout the world could be infected," they said in a statement issued by the university. The Dutch researchers add that a malicious RFID tags could also bypass physical security measures by fooling a computer into thinking it has just received a different identification code. In the hypothetical airport example, this would provide "the perfect solution for smugglers and terrorists wanting to send suspicious luggage across the world without being noticed,"

# **Microelectronics & Nanotech**

## **Nanotube circuit could boost chip speeds**

A single-molecule logic circuit has shown that using carbon nanotubes instead of silicon pathways could someday soup up integrated circuits to near-terahertz processing, up from today's low-gigahertz range.

Researchers at IBM Research Center used techniques similar to conventional chip-making technology to create field effect transistors along a carbon nanotube that had been deposited onto a silicon wafer. Unlike shrunken conventional silicon circuits, the resulting logic circuit yielded virtually no electron flow impedance, meaning current flowed faster.

“This isn't about making the circuits smaller, it's about making them faster,” said Joerg Appenzeller, one of the circuit's developers in Science latest issue. “Nanotubes fit the characteristics we need to advance high-end processing.”

The components of today's computer chips are made by doping tracts of a silicon substrate with metals of different electronic properties. While this technique was the breakthrough technology behind the integrated circuit, it becomes increasingly problematic in the race for smaller and smaller components.

Moore's Law, coined in 1965, predicted that with the speed of technological development, the number of transistors in a chip and therefore a chip's speed would double roughly every 18 months. The problem is that as electrical paths shrink, electrical resistance increases proportionally. Also, the process of doping – adding impurities to the silicon to alter its electrical properties – means that the impurities left behind scatter electron flow, which becomes more of a problem at smaller scales. The major reason behind the resistance, however, is an odd phenomenon known as plasmonic resonance, in which an electron's path is hindered when it becomes coupled with vibrations in the surrounding lattice structure. But because the carbon nanotube is a single molecule with electrons passing along the tube, this problem is averted and resistance minimised, even at tiny scales. Additionally, smaller silicon pathways make it easier for electrons to "jump tract" and leech into other nearby components. But in a nanotube circuit, this would be highly improbable as electrons would be carried down the molecular tract of the nanotube. These properties will allow the manufacture of smaller transistors with electrons flowing faster through their wires, making for faster processing.

“There is still a long way to go” Appenzeller adds “and development goes beyond simply optimising transistor sizes or design architecture Current nanotube production methods are not yet able to produce tubes with the exact shapes or consistent sizes that would be needed to build even one chip, let alone mass manufacturing them”

## Beyond Silicon

Chip-maker Intel has just announced a transistor made from a material called indium antimonide (InSb) that had some impressive stats: it was clocked at 1.5 times the speed of silicon-based transistors and used one-tenth the power.

According to Intel's director of technology strategy, Paolo Gargini, a shift from silicon might be crucial for the chip-making industry, so it can build smaller devices over the next couple of decades. As transistors made of silicon keep shrinking, the material's limitations are becoming more apparent. "Silicon is not the best semiconductor," Gargini says.

But of course silicon is both highly prevalent and relatively inexpensive, and its manufacturing process has been honed for 30 years. What makes so-called "compound semiconductors" — those made out of more than one element, such as indium antimonide — so attractive is their special electrical and optical properties.

Electrons can pass through an indium antimonide crystal 50 times faster than through a silicon crystal, Gargini says. As a result, not only are electronic operations significantly faster, but less power is needed to push the electrons.

Compound semiconductors also have optical properties that could help speed up communication between transistors on a chip and multiple chips within a device. These materials easily emit and detect light — a characteristic that has been studied and improved for decades, says David Hodges, at the University of California, Berkeley. Therefore, he says, light emitters and detectors made of compound materials could potentially replace copper wires, which are a major "impediment of speed."

Compound materials also have their disadvantages, though. Currently, hundreds of billions of transistors are manufactured at a time on top of silicon wafers that can be as large as 12 inches in diameter. The crystals of compound materials, such as indium antimonide (InSb), gallium arsenide (GaAs), indium arsenide (InAs), and indium gallium arsenide (InGaAs), however, tend to break apart easily, and so can't be made into such large wafers, says Gargini. This means that compound materials could never completely replace silicon as the wafer base for electrical devices, he says. Instead, "islands" of InSb transistors must be deposited on the large-diameter silicon substrate.

Finding the best buffer for the InSb "islands" on the silicon wafer and finding the right the insulating layer, the "gate dielectric," on top of the transistor, which is crucial to the electrical operations of the device, are still huge challenges before InSB could be considered a real substitute for Silicon. According to electrical engineers at MIT, however, such hurdles will be overcome as the field matures

## Rice University researchers create 'nanorice'

### Nanoparticle's shape could improve chemical sensing, biological imaging

Who better to invent "nanorice" than researchers at Rice University? But marketing and whimsy weren't what motivated the team of engineers, physicists and chemists from Rice's Laboratory for Nanophotonics (LANP) to make rice-shaped particles of gold and iron oxide.



Nanorice is made of non-conducting iron oxide called hematite that's covered with gold. The core size and shell thickness vary slightly but the particles are about 20 times smaller than a red blood cell.

"On the nanoscale, the shape of a particle plays a critical role in how it interacts with light," said LANP Director Naomi Halas. "We were looking for a new shape that would combine the best properties of the two most optically useful shapes – spheres and rods. It's just a coincidence that that shape turned out to look exactly like a grain of rice."

Nanoparticles like nanorice can be used to focus light on small regions of space. Rice's scientists plan to capitalize on this by attaching grains of nanorice to scanning probe microscopes. By moving the grains next to proteins and unmapped features on the surfaces of cells, they hope to get a far clearer picture than what's available with current technology.

The nanorice research will appear in the April 12 issue of Nano Letters

In form, nanorice is similar to nanoshells, a spherical nanoparticle Halas invented in 1998 that is currently being examined for possible applications in molecular imaging, cancer treatment, medical diagnostics and chemical sensing. Both nanorice and nanoshells are made of a non-conducting core that is covered by a metallic shell.

Halas' investigations find that nanorice possesses far greater structural tunability than nanoshells and another commonly studied optical nanoparticle, the nanorod. In fact, tests indicate that nanorice is the most sensitive surface plasmon resonance (SPR) nanosensor yet devised.

Research over the past decade has shown that nanoscale objects can amplify and focus light in ways scientists never imagined. The "how" of this involves plasmons, ripples of waves in the ocean of electrons that flow constantly across the surfaces of metals. When light of a specific frequency strikes a plasmon that oscillates at a compatible frequency, the energy from the light is converted into electrical energy that propagates, as plasmons, through the nanostructure.

Changing the shape of a metal at the nanoscale allows engineers and scientists to modify the properties of these plasmon waves, controlling the way that the metal nanostructure responds to light. Because of this, metal nanostructures can have beautiful, vivid colors that depend on their shape. Some nanoscale structures -- like nanorice and nanoshells -- act as superlenses that can amplify light waves and focus them to spot sizes far smaller than a wavelength of light.

"The distinct advantage of the nanorice particle over nanoparticle dimers is that the electric field enhancements occur on open-ended surfaces of the particle that are much more accessible," said Halas. "For Surface-enhanced Raman Scattering (SERS) and SPR applications, we believe nanorice may have the field intensities needed to characterize biomolecules -- like proteins and DNA --that adsorb on the particle."

## **Penn researchers create the first reliable method for making gaps for nanotech apps**

### **Mind the Nanogaps: Penn Researchers Create the First Reliable Method for Making Gaps for Nanotech Apps**

Researchers at the University of Pennsylvania have announced that they have bridged a major obstruction in the creation of nanoscale electronics by developing a simple, reliable and observable method of creating tiny, tiny gaps between electrodes.

Such "nanogaps" will make it possible to make electrical contact to structures on the nanoscale billionths of a meter. In a recent edition of the journal *Applied Physics Letters*, online now, physicists Marija Drndic and Michael Fischbein describe the creation of nanogaps, which could have applications ranging from ultra fast electronics to quantum computing to high-speed gene reading.

"A number of people have proposed nanoelectronic devices that use nanogaps, but nobody has been able to create nanogaps reliably in practice," said Marija Drndic, an assistant professor in Penn's Department of Physics and Astronomy in the School of Arts and Sciences. "For the first time, we were able to make the world's smallest and cleanest nanometer gaps that can be imaged directly with atomic resolution. These nanogaps can be used to electrically connect small objects, such as an individual molecule."

The ability to hook individual molecules -whether they are the product of nanotechnology or biotechnology -to electronic circuits is the goal of many researchers. Such systems will have applications in medicine, robotics, materials science and even security. In addition, electronics on the nanoscale will be used to create denser, faster storage devices and microprocessor chips.

To create these gaps, Drndic and graduate student Michael Fischbein used electron beam lithography, a common nanotechnology tool that uses electrons to create patterns on a surface. Their research succeeded where previous efforts failed because of the type of surface they used, thin layers of silicon nitride.

"Electron beam lithography works on small scale, but it is limited down to about 10 nanometers," Drndic said. "It is not like drawing a line on a page; as an electron beam hits a material the electrons tend to scatter forward and backward, which makes it difficult to create tiny lines."

While other researchers focused on breaking small wires to create nanogaps, similar to how a fuse can be popped open, the Penn researchers went the opposite route, making the gaps directly.

"Contrary to many expectations, the thin layer of silicon nitride, which we used instead of the usual oxide on silicon, helped minimize the amount of electron scattering to the point where we could make clean gaps," Fischbein said.

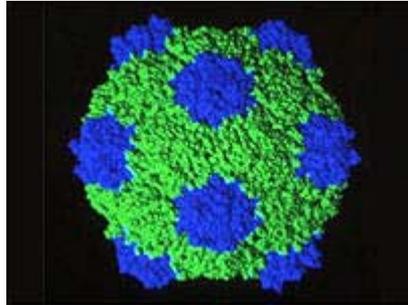
Just as important, these nanogaps are compatible with high-resolution transmission electron microscopy, or HRTEM. Because nanogaps are created on thin films, it is easy to study the structure through HRTEM and assess their quality.

Already, the researchers have used nanogaps to measure electrical charge through several coupled nanocrystals, which are also referred to as quantum dots. Previous researchers have demonstrated that quantum dots can be manipulated to change their physical properties, particularly their optical properties. In fact, the blue laser, which will soon be put into use in commercial products, was a result of early research in changing the colors of quantum dots.

## **Virus used to make nanoparticles**

UK scientists from Norwich have used a plant virus to create nanotechnology building blocks. The virus, which infects black-eyed peas, was employed as a "scaffold" on to which other chemicals were attached.

The virus is spherical and has a diameter of 30 nanometres



By linking iron-containing compounds to the virus's surface, the John Innes Centre team was able to create electronically active nanoparticles. The researchers tell the journal *Small* that their work could be used in the future to make tiny electrical devices.

The work is yet another example of how scientists are now trying to engineer objects on the scale of atoms and molecules. At the nanoscale, materials can be "tuned" to display unusual properties that could be exploited to build faster, lighter, stronger and more efficient devices and systems.

# **Life Sciences**

## **Brain-Healing Nanotechnology**

A ground-breaking treatment could restore lost abilities to stroke victims and others.

Although victims of stroke and traumatic brain and spinal cord injuries sometimes recover through rehabilitation, they often have permanent disabilities, in part, because scar tissue and regulatory chemicals in the brain slow nerve growth, preventing nerve tissue from repairing itself. Now a treatment that has restored lost vision in lab animals appears to overcome these obstacles, allowing a mass of nerve cells to regrow after being cut.

"We think this is the basis of reconstructive brain surgery -- which is something nobody has ever heard of before," says Rutledge Ellis-Behnke, a brain and cognitive sciences researcher at MIT.

The treatment, described in the Proceedings of the National Academy of Sciences and performed at MIT, Hong Kong University, and Fourth Military Medical University in China, may be available to humans in trials in as little as three years if all goes well in large-animal studies, the researchers say.

In their experiments, the researchers first cut into a brain structure that conveys signals for vision, causing the small lab animals to be blinded in one eye. They then injected a clear fluid containing chains of amino acids into the damaged area. Once in the environment of the brain, these chains, called peptides, bind to one another, assembling into nano-scale fibers that bridge the gap left by the damage. The mesh of fibers prevents scar tissue from forming and may also encourage cell growth (the researchers are still investigating the mechanisms involved). As a result, nerve cells restored severed connections, allowing 75 percent of the animals to see well enough to detect and turn toward food. The treatment restored around 30,000 nerve connections, compared with 25-30 connections made possible in other experimental treatments, Ellis-Behnke says.

Because the treatment overcomes key obstacles to the healing of nerve tissue in stroke and traumatic brain and spinal cord injury, the researchers, as well as other experts in the field, believe it could prove to be an effective treatment for these types of nervous system damage.

## Supercomputer builds a virus

### Vast simulation captures molecules in motion.

One of the world's most powerful supercomputers has conjured a fleeting moment in the life of a virus. The researchers say the simulation is the first to capture a whole biological organism in such intricate molecular detail.

The simulation pushes today's computing power to the limit. But it is only a first step. In future researchers hope that bigger, longer simulations will reveal details about how viruses invade cells and cause disease.

Klaus Schulten at the University of Illinois, Urbana, and his colleagues built a computer model of the satellite tobacco mosaic virus, a tiny spherical package of RNA.

Their success depended on the latest version of a computer program called NAMD, which Schulten and his colleagues have built over the past decade to simulate biological molecules. The program allows the several hundred different processors within a supercomputer to work in parallel on the same problem.

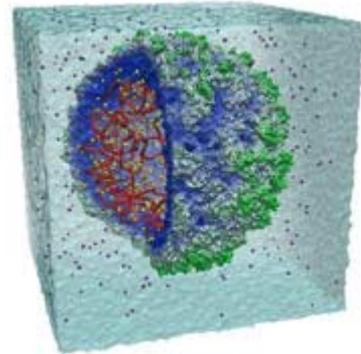
Running on a machine at the National Center for Supercomputing Applications, Urbana, the program calculated how each of the million or so atoms in the virus and a surrounding drop of salt water was interacting with almost every other atom every femtosecond, or millionth of a billionth of a second.

The team managed to model the entire virus in action for 50 billionths of a second. Such a task would take a desktop computer around 35 years, says Schulten. "This is just a first glimpse," he says. "But it looks gorgeous."

### In, out

The fleeting simulation, published in this month's *Structure*, reveals that although the virus looks symmetrical it pulses in and out asymmetrically, as if it were breathing. The model also shows that the virus coat collapses without its genetic material. This suggests that, when reproducing, the virus builds its coat around the genetic material rather than inserting the genetic material into a complete coat. "We saw something that is truly revolutionary," Schulten says.

Computer scientists have simulated viruses before, but they often had to limit themselves to one part of a virus and assume that the rest behaves in the same way.

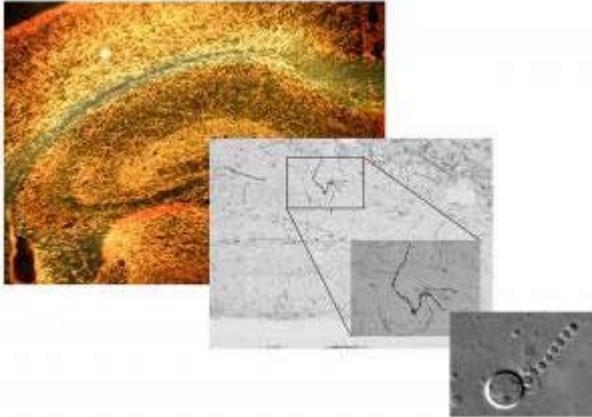


The model shows one million atoms over 50 billionths of a second.

*Credit: University of Illinois / NCSA*

## New Tools Developed For Studying Neurodegenerative Brain Disorders

Penn State researchers have created an elegantly simple model of an axon--the extension of a neuron that communicates with other neurons--and have used this model to reproduce a change in the axon's shape that is characteristic of neurodegenerative disorders such as Alzheimer's and Parkinson's diseases. This achievement is the first of its kind in a highly simplified biophysical model system. The model provides a novel avenue for investigating the specific mechanisms that contribute to complex brain diseases. It also provides a means of discovering new kinds of drugs for the treatment of these disorders. The research appears in the April 2006 issue of the Proceedings of the National Academy of Science.



*A simple biophysical model of an axon was used to study the catastrophic consequences of oxidative [stress](#) to neurons. The result was that the protruding microtubule cytoskeleton collapsed into a deformed structure resembling a string of beads (right panel). This is the same morphology observed during the degeneration of actual neurons in the brain as seen in the center panel.*

This model, produced in the laboratory of Paul S. Weiss, at Penn State, has the essential features of an axon, including a lipid membrane that encloses a "cytoskeleton" scaffolding, which produces the axon's shape. The outer membrane was prepared to contain a very small amount of dye molecules that are sensitive to ultraviolet light. Shining light on the artificial axons initiated a photochemical reaction that produced highly reactive "free radicals" and triggered a catastrophic oxidative-stress reaction. The result was that the previously protruding microtubule cytoskeleton collapsed into a constricted and deformed structure resembling a string of beads--the same morphology observed during the degeneration of actual neurons. Surprisingly, the model reproduced this highly characteristic "beading" or "pearling" even though it does not include proteins that were previously thought to be essential for causing this kind of axon destruction. "One of the beauties of a simplified model is that it allows you to ask very simple questions, which sometimes are difficult to answer in a complex living system, and sometimes to get surprising answers," Weiss said. "What makes this model so exciting is that it generates many more questions than it answers," Weiss said. "It will allow us to test hypotheses of how damage occurs, and importantly, how we might prevent it. There is a real opportunity to come up with novel therapeutic treatments."

"There is tremendous urgency right now to determine which processes cause the destructive mechanisms that we see in neurodegenerative diseases," said coauthor Anne Milasincic Andrews. "Our study shows that oxidative stress, whatever its origin, is capable of causing the cytoskeleton of this artificial system to collapse in the same way that it does in diseased or aging brains."

## **A One-Two Punch for Alzheimer's**

**An enzyme has been identified that can target both major markers of Alzheimer's, providing a new venue for drug development.**

Alzheimer's disease has two hallmarks: protein clumps, called plaques, that cluster outside of neurons, and twisted protein fibers, called tangles, that build up inside neurons. In the vast majority of Alzheimer's cases, scientists don't know what triggers build-up of these proteins, and they have been arguing heatedly for years about whether plaques or tangles are the true culprit behind the devastating cognitive decline caused by the disease.

Now scientists at Harvard have identified an enzyme that can block build-up of both plaques and tangles in cellular models -- a finding that could help link these two perplexing neurological problems and provide a new avenue for drug development.

"[The enzyme] could be a universal regulator of AD pathology...With one molecule you might be able to target and correct two major problems of the disease," experts not involved in the research are commenting. "Whether it will do that, time will tell...but I think the findings will trigger a lot more work on [this enzyme,] so at the end of day we'll know if it represents a good drug target."

Both plaques and tangles are caused by the abnormal build-up of proteins. Tangles are made up of a protein called tau, while plaques are made up of fragments of a protein called amyloid precursor protein (APP). In Alzheimer's patients, both those proteins undergo chemical changes that make them more likely to clump together.

In a previous research, Kun Ping Lu, from Harvard Medical School, found that an enzyme called Pin1 reverts the tau protein back to its healthy conformation, thereby preventing the formation of tangles. In the current paper, published in *Nature* 440, Lu showed that Pin1 could also restore the APP protein to its normal shape, preventing the build-up of the toxic fragment that accumulates in plaques. "Pin1 is like the oil in a car engine. You need oil to keep it running smoothly; without it, things begin to break down. If you don't have Pin1, proteins become misshapen and aggregate into tangles or plaques," says Lu.

The findings could aid the ongoing quest in Alzheimer's biology to find a single chemical, biological, or genetic change that might lead to both plaques and tangles, says Sam Gandy, chair of the Alzheimer's Association Medical and Scientific Advisory Council "This is a good candidate for looking for that final common pathway. Pin1 provides a single molecule that could interact and potentially cause both features of pathology,"

## **Comprehensive strategy to identify structural variation in human genome**

The National Human Genome Research Institute (NHGRI), one of the National Institutes of Health (NIH), today announced its latest round of sequencing targets, with an emphasis on enhancing the understanding of how human genes function and how genomic differences between individuals influence the risk of health and disease.

The plan given the highest priority is a project to identify structural variations in the human genome, which will characterize the most common types of structural variation in human DNA. The effort will use 48 human DNA samples donated for the recently completed International HapMap Project, which produced a comprehensive catalog of human genetic variation, or haplotypes, designed to speed the search for genes involved in common diseases. The HapMap identified neighborhoods of tiny changes in DNA -- known as single nucleotide polymorphisms (SNPs) -- that can be involved in human disease. The structural variation effort will seek to identify instances where larger segments of DNA have been deleted, duplicated or rearranged -- all of which can cause disease by disrupting the structure and function of genes.

A recent analysis has shown that these large-scale structural variations are much more common than previously appreciated. In fact, the genomes of any two humans are thought to differ by several hundred insertions, deletions and inversions.

The second plan will add DNA sequence to existing draft sequences of a number of primate species and add additional sequence information in regions of high biological interest within those genomes. The increased coverage -- a high-density genome sequence -- will allow for an even better understanding of the factors contributing to the evolution of the human genome.

The third plan includes sequencing the genomes of eight new mammals. NHGRI will base the choice of the eight mammals to be sequenced on the availability of high-quality DNA samples, the organisms' promise as biomedical models, and the presence of unique, innovative biological processes that may have contributed to the human genome over the course of evolution. Such comparisons between mammalian genomes represent one of the most effective ways to pinpoint the roughly 5 percent of the 3-billion base pair human genome that is most obviously functional. According to computer modeling results, it is expected that comparisons among the 24 genome sequences will allow conserved sequences as small as six base pairs to be identified reliably. Six base pairs is roughly the size of a transcription factor binding site: a small DNA sequence occurring near a gene that is involved in switching the gene on or off.