Innovations Report
Jan 2006

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ICT

IST Results

Riding the ultra wideband communications wave

Europe is helping to push forward the boundaries of current radio technology looking at the next generation of radio devices. A whole new Ultra WideBand (UWB) communications industry is emerging and once all phases of a major European research effort into UWB are complete, Europe will be in a stronger position to exploit this new technology.

Ultra wideband usually refers to a radio communications technique based on transmitting very-short-duration pulses, down to nanoseconds (billionths of a second) or picoseconds (trillionths). The occupied bandwidth can take up very large frequency ranges.

This allows UWB to deliver data rates up to 1 gigabit over short distances. With further development UWB may even exceed that speed. It uses little power and can operate in the same bands as existing communications without producing significant interference. The implications and potential applications are enormous, and the market could become a multi-billion business by 2010.

The PULSERS project is massive. In the first phase, the project had 30 partners and phase II, starting in January 2006, will have 36 partners. The total budget is €37 million for the first two phases in total. A third phase is envisaged. For the first phase, the project aimed at defining the systems, developing new components and taking part in defining rules and standards for the radio technology. The second phase includes the development of further components and the demonstration of very high transfer rates. In the last phase the team will integrate UWB with other networks and trial specific system applications. The project's already considerable positive role in the regulation and standardisation of UWB will be even intensified in the PULSERS Phase II, says Zeisberg.

There is a huge number of potential applications for the technology. Obvious markets are Personal Area Networks (PAN) to link one person's devices together, or local area networks (LAN), to link devices in a room. This will mean that devices like DVD players, TVs, stereos and speakers can be linked together without wires.

"Besides wireless short range communications ...UWB technology enables precise real-time location tracking inherently due to its unique feature of ultra-wide radio frequency band allocation," says Dr Sven Zeisberg, PULSERS project manager at German firm GWT.

"Widespread application of this new wireless technology will facilitate growth of a number of new market segments -all different, but all enabled by the unique features of UWB radio being highly scalable with regard to complexity, range, costs and data rate as well as location precision accuracy," he says.

Data rates range from a kilobit per second with a robust, low cost, low complexity, and low power devices, up to a gigabit per second with a high performance and low power devices. Thus, PULSERS currently is working on two systems, a High or Very High Data Rate (HDR, VHDR) system, and a Low Data Rate/Location Tracking (LDR/LT) system.

The regulator estimated that the profits associated with UWB PAN applications would outweigh the costs by 2010, a year after PULSERS completes its final phase. These figures are conservatively estimated for PAN applications alone, they don't account for any other UWB application or the potential market in other EU states. UWB will probably be huge. "There is a huge potential of creating a new set of applications based on wireless technology," says Zeisberg. "This could boost European economies."

Weitere Informationen finden Sie im WWW:

- http://istresults.cordis.lu/

CSC - Finnish IT Centre for Science

European and American supercomputing infrastructures linked through a common wide-area global file system

DEISA, the European supercomputing grid infrastructure, and TeraGrid, the US supercomputing cyberinfrastructure, and have been linked, for the purposes of a technology demonstration, by a common, scalable, wide-area global file system spanning two continents.

The bridging of communities in the old and the new world were showcased during the Supercomputing Conference SC05 at Seattle. It was shown that any scientist, accessing TeraGrid from any of the participating sites in the US, or accessing DEISA from any of the DEISA sites in France, Germany or Italy, can directly and transparently create or access collaborative data stored in the now linked grid-wide global file systems of TeraGrid and DEISA with one common file address space. The even more important aspect is that the same is true for applications which, executed at any of the participating sites, transparently access data in the common file address space.

High performance wide-area global file systems as GPFS from IBM open totally new modes of operation within grid infrastructures, especially in supercomputing grids with a fairly limited number of participating sites. A common data repository with fast access, transparently accessible both by applications running anywhere in the grid, and by scientists working at any partner site as entry point to the grid, greatly facilitates cooperative scientific work at the continually increasing geographically distributed scientific communities.

Both DEISA and TeraGrid have begun using the high performance wide-area global file system GPFS from IBM in production mode. For the technology demonstration, the dedicated DEISA and TeraGrid networks were interconnected with the help of specialists from GEANT, Abilene/Internet2, and the national research networks from France, Germany, and Italy (RENATER, DFN, GARR). They established a two continent spanning high performance network between TeraGrid sites at The San Diego Supercomputer Center (SDSC), Chicago, and Indiana, and DEISA sites in several European countries (France, Germany, Italy). Over this dedicated connection, DEISA and TeraGrid global file systems were merged into one common global file system. This network connection between the two infrastructures is expected to become persistent at some time in the future.

The demonstration featured the execution of supercomputing applications of various scientific disciplines which were carried out both as TeraGrid and as DEISA applications. Single site applications transparently wrote their results to the intercontinental global file system, ready for transparent further processing from other access grid access points.

Featured applications for the demo included a Protein Structure Prediction and a Cosmological Simulation carried out at SDSC, US (www.sdsc.edu) and a Gyrokinetic Turbulence Simulation and also a Cosmological Simulation carried out at Garching Computing Centre of the Max Planck Society (RZG), Germany.

Weitere Informationen finden Sie im WWW:

- http://www.deisa.org
- http://www.teragrid.org
- http://www.rzg.mpg.de

Elhuyar Fundazioa

Cheaper mobile phones or GPS and with enhanced performance

In his PhD thesis the Pamplona engineer, Francisco Falcone Lanas, has put forward various structures based on what are known as left-handed metamaterials, materials that can be used to make smaller mobile phones, aerials or GPS and which have better specifications and performance. This is the first PhD defended in the world on applications of left-handed metamaterials.

Photonic crystal devices

The research undertaken by Francisco Falcone in his PhD involved analysing the application of metamaterial structures in conventional high-frequency planar technology.

For his thesis Francisco Falcone analysed two types of structure. One with photonic crystals which have good control of the signal but are not greatly efficient with respect to size. These are known as Electromagnetic Bandgap (EBG) structures. Taking these as a basis, Francisco Falcone put forward a number of microstrip technology devices, etching a periodic pattern on their planar surfaces. This is the most significant difference in these proposed, smaller and more compact unidimensional structures, compared to the previous, bidimensional ones. Moreover, they have experimented with the introduction of a resonator in planar technology.

First worldwide

It is, nevertheless, it is with the second type of structure where the results of the research team at the Public University of Navarre are more spectacular. What are known as left-handed metamaterials involve materials which have curious electromagnetic properties and which are not found naturally, i.e. they are artificially generated media.

In this part of the research Francisco Falcone synthesised left-handed materials in planar technology by using Split Ring Resonators (SRR) together with a medium of fine metallic wires. In this respect we can say that we have achieved the very first implementation worldwide of a low loss LHM metamaterial. An evolution of this device was the use of a new particle therein - which we call complementary SSR - in which the role of paper and metal is interchanged.

In this way and applying classical metamaterial concepts, we obtained devices with extremely low losses. Our proposal was based on the introduction of particles in planar technology, i.e. their integration into the circuit. In fact, we have managed to obtain the devices with the lowest losses ever obtained worldwide. We were the first to propose this phenomenon and the discovery received recognition on being published in the prestigious scientific magazine, Physical Review Letters.

The advantage of its use is that it enables the making of a series of circuits that otherwise would be impossible and, moreover, these give quite an optimal response in that they have few and very low losses.

This PhD puts forward the potential use of these kinds of structures for devices such as filters, couplings and aerials for 2nd, 3rd and 4th generations mobile communications systems such as satellite systems and WLAN. But, above all, they are low cost structures and very easy to manufacture.

Weitere Informationen finden Sie im WWW:

- http://www.basqueresearch.com

Breakthrough for quantum measurement

22 November 2005

Two teams of physicists have measured the capacitance of a Josephson junction for the first time. The methods developed by the two teams could be used to measure the state of quantum bits in a quantum computer without disturbing the state.

A Josephson junction consists of two superconducting layers separated by a thin insulating layer. Brian Josephson of Cambridge University won the Nobel prize in 1973 for predicting, while he was still a PhD student, that the Cooper pairs in the superconducting layers would be able to tunnel through the insulating layer without losing their superconducting properties. Josephson junctions are widely used in many electronic devices, including logic circuits, memory cells and amplifiers. Superconducting quantum interference devices (SQUIDs), also rely on the junctions to measure extremely small magnetic fields.

Figure 1

In the classical regime, the junction behaves like an inductance. In the 1980s, however, theorists predicted that a Josephson junction would behave like a capacitor if it was small enough. Now, Per Delsing and colleagues at Chalmers University of Technology in Sweden, and independently, Pertti Hakonen and co-workers at Helsinki University of Technology and the Landau Institute of Theoretical Physics in Moscow have observed this effect in experiments for the first time.

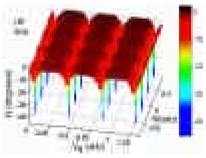


Figure 2

The Sweden team measured the effect in a Cooper-pair transistor, a device that contains two Josephson junctions in series (*Phys. Rev. Lett.* **95** 206806). The Helsinki-Moscow group saw the effect in a Cooper-pair box, which contains one junction (*Phys. Rev. Lett.* **95** 206807).

Delsing and colleagues at Chalmers University began by embedding their Cooper-pair transistor in a resonant circuit. Next, they cooled the device down to millikelvin temperatures and measured how the phase of a radio-frequency signal changed when it was reflected from the circuit. Based on these measurements, the team was able to show that the device behaved like a quantum capacitor. Hakonen and co-workers in Helsinki and Moscow group employed a similar technique. Both teams found that the devices behaved as predicted by theory.

The effect could be used to read out quantum bits (qubits) in a reliable way because the quantum capacitance of the excited state of the qubit has the opposite sign to the ground state. These states could be used as the "1s" and "0s" in a quantum computer. Indeed Hakonen and colleagues have already used this approach to read the value of a qubit without changing its value -- which is almost always a problem when measuring the quantum state of any system.

"In the future, the Josephson capacitance could be used for operations in a large-scale quantum computer," says Mika Sillanpaa of Helsinki University. "The Josephson inductance and Josephson capacitance together would also allow us to build new types of quantum 'band engineered' electronic devices, such as low-noise parametric amplifiers."

About the author

Belle Dumé is science writer at *PhysicsWeb*

University of Pittsburgh

Toward a quantum computer, one dot at a time

Pitt researchers develop nanoscale semiconductor islands small enough to hold single electrons

Researchers at the University of Pittsburgh have developed a way to create semiconductor islands smaller than 10 nanometers in scale, known as quantum dots. The islands, made from germanium and placed on the surface of silicon with two-nanometer precision, are capable of confining single electrons.

"We believe this development moves us closer to our goal of constructing a quantum computer," said Jeremy Levy, Pitt professor of physics and astronomy and director of the Pittsburgh-based Center for Oxide-Semiconductor Materials for Quantum Computation. Levy and colleagues reported on the advance in a paper published in October 2005 in the journal Applied Physics Letters.

Quantum computers do not yet exist, but it is known that they can bypass all known encryption schemes used today on the Internet. Quantum computers also are capable of efficiently solving the most important equation in quantum physics: the Schrödinger equation, which describes the time-dependence of quantum mechanical systems. Hence, if quantum computers can be built, they likely will have as large an impact on technology as the transistor.

Electrons have a property known as "spin," which can take one of two directions--clockwise and counter-clockwise. Because of their quantum-mechanical nature, electrons can spin in both directions at once. That bizarre property allows the spin to be used as a "quantum bit" in a quantum computer. The ability to confine individual electrons, as opposed to "puddles" of electrons used in conventional computer technology, is essential for the working of a quantum computer.

The next step, said Levy, is to perform electronic and optical measurements on these materials to prove that there is indeed one electron on each quantum dot and to probe the coupling between the spins of neighbor electrons. "We can do that now because we have this control over the spacing and the size," he said.

The results achieved by Levy and colleagues are an example of "essentially nano" research, which involves manipulating properties at the smallest scales--from one to 20 nanometers.

Pitt has invested heavily in nanoscale research, beginning with the establishment of its Institute for NanoScience and Engineering (INSE), and continuing with the NanoScale Fabrication and Characterization Facility, which contains core technology such as electron-beam lithography, transmission electron microscopes, and a state-of-the-art cleanroom environment. The INSE is an integrated, multidisciplinary organization that brings coherence to the University's research efforts and resources in the fields of nanoscale science and engineering. For more information, visit www.nano.pitt.edu.

Other researchers on the study were John T. Yates Jr., R.K. Mellon Professor of Chemistry and Physics at Pitt; former Pitt chemistry graduate student Olivier Guise; Joachim Ahner of Pittsburgh-based Seagate Technology; and Venugopalan Vaithyanathan and Darrell G. Schlom of Pennsylvania State University.

Weitere Informationen finden Sie im WWW:

- http://www.pitt.edu
- http://www.nano.pitt.edu

Ohio State University

A new way to help computers recognize patterns

Researchers at Ohio State University have found a way to boost the development of pattern recognition software by taking a different approach from that used by most experts in the field.

This work may impact research in areas as diverse as genetics, economics, climate modeling, and neuroscience.

Aleix Martinez, assistant professor of electrical and computer engineering at Ohio State, explained what all these areas of research have in common: pattern recognition.

He designs computer algorithms to replicate human vision, so he studies the patterns in shape and color that help us recognize objects, from apples to friendly faces. But much of today's research in other areas comes down to finding patterns in data -- identifying the common factors among people who develop a certain disease, for example.

In fact, the majority of pattern recognition algorithms in science and engineering today are derived from the same basic equation and employ the same methods, collectively called linear feature extraction, Martinez said.

But the typical methods don't always give researchers the answers they want. That's why Martinez has developed a fast and easy test to find out in advance which algorithms are best in a particular circumstance.

"You can spend hours or weeks exploring a particular method, just to find out that it doesn't work," he said. "Or you could use our test and find out right away if you shouldn't waste your time with a particular approach."

The research grew out of the frustration that Martinez and his colleagues felt in the university's Computational Biology and Cognitive Science Laboratory, when linear algorithms worked well in some applications, but not others.

In the journal IEEE Transactions on Pattern Analysis and Machine Intelligence, he and doctoral student Manil Zhu described the test they developed, which rates how well a particular pattern recognition algorithm will work for a given application.

Along the way, they discovered what happens to scientific data when researchers use a less-than-ideal algorithm: They don't necessarily get the wrong answer, but they do get unnecessary information along with the answer, which adds to the problem.

He gave an example.

"Let's say you are trying to understand why some patients have a disease. And you have certain variables, which could be the type of food they eat, what they drink, amount of exercise they take, and where they live. And you want to find out which variables are most important to their developing that disease. You may run an algorithm and find that two variables -- say, the amount of exercise and where they live -- most influence whether they get the disease. But it may turn out that one of those variables is not necessary. So your answer isn't totally wrong, but a smaller set of variables would have worked better," he said. "The problem is that such errors may contribute to the incorrect classification of future observations."

Microelectronics & Nanotech

DOE/Argonne National Laboratory

Magnetic spin details may lead to new devices

An unusual pool of scientific talent at the U.S. Department of Energy's Argonne National Laboratory, combined with new nanofabrication and nanocharacterization instruments, is helping to open a new frontier in electronics, to be made up of very small and very fast devices.

SPIN RESEARCH – Argonne researcher Sam Bader with a new instrument to measure spin resonance frequencies, developed by Argonne senior scientist Frank

A new discovery by this group opens a path to new computer technologies and related devices, and could drive entire industries into the future, the researchers say.

The researchers learned that swirling spin structures called magnetic vortices, when trapped within lithographically patterned ferromagnetic structures, behave in novel ways. In a nickel-iron alloy, the two vortices swirl in opposite directions, one clockwise and the other counterclockwise. However, the researchers discovered that the magnetic polarity of the central core of the vortices, like the eye of a hurricane, controlled the time-evolution of the magnetic properties, not the swirling direction.

The material being studied is about one micron in size, and the area of the vortex core is about 10 nanometers in size. For comparison, the period at the end of this sentence is about 100 microns or 100,000 nanometers in diameter.

Group leader Sam Bader, an Argonne scientist for more than 30 years, explained that the work could lead to the next generation of electronic devices. "When the first computer hard disk was introduced 50 years ago, it required a rather large size to store each bit of digital information. On today's computer disks, the corresponding size is about one-50-millionth of that needed in the original disks. We are now moving well into the nanoscale range, and nanomagnetism is one of the real drivers of the nanotechnology field."

The beauty of nanoscience, Bader said, is that researchers can take conventional materials, such as the nickel-iron alloy, reduce them to the nanoscale and create whole new properties. "Thinking far into the future, for example, we can envision circuits where the flow of spin, not the flow of electrical charge, will operate computers and other electronic devices while saving wasted heat energy that is generated in present-day devices."

As with other materials at the nanoscale, Bader said, nanomagnets take on new properties, some of them unpredictable.

Understanding that unpredictability and underlying physics is important to researchers developing the new technology, said Argonne scientist Val Novosad. "With this very small array of spins, where each atom has a magnetic moment, the vortex core responds to stimuli by traveling in spiral trajectories."

The researchers created the material in the form of an array of elliptical pancakes, each holding two vortex cores, stimulated the material with a magnetic pulse and watched the subsequent behavior.

“This first-ever reported experiment revealing unique dynamic behavior of two interacting magnetic vortices required a considerable assist from technology,” Novosad said.

Argonne senior scientist Marcos Grimsditch provided the inspiration for the novel magnetic configuration of the samples, which were fabricated using a new electron beam lithography facility to be housed at Argonne’s Center for Nanoscale Materials, scheduled to open later this year. The tiny process could be monitored using a new instrument to measure spin resonance frequencies, developed by Argonne senior scientist Frank Fradin. And the interpretation of the experimental data was assisted by numerical modeling from Argonne post-doctoral student Kristen Buchanan, winner of a fellowship from Canada’s Natural Science and Engineering Research Council, and the analytical theory expertise of visiting theorist Konstantin Guslienko at Argonne’s Theory Institute.

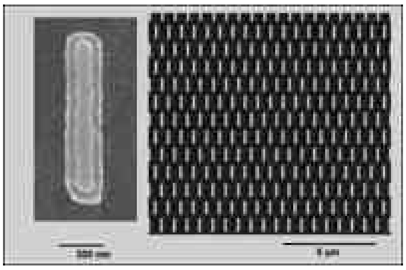
“Every step along the way was state of the art,” Bader said, “from the fabrication of the material to the measurement of the spin to the creation of software to illustrate the data through a movie.”

The research was reported in the new peer-reviewed journal,Nature Physics. The six Argonne researchers are co-authors of the article, along with Pierre Roy of Uppsala University in Sweden , a graduate student in residence at Argonne as part of his thesis research experience.

The nation’s first national laboratory, Argonne National Laboratory conducts basic and applied scientific research across a wide spectrum of disciplines, ranging from high-energy physics to climatology and biotechnology. Since 1990, Argonne has worked with more than 600 companies and numerous federal agencies and other organizations to help advance America’s scientific leadership and prepare the nation for the future. Argonne is managed by the University of Chicago for the U.S. Department of Energy’s Office of Science.

Purdue 'metamaterial' could lead to better optics, communications

Engineers at Purdue University are the first researchers to create a material that has a "negative index of refraction" in the wavelength of light used for telecommunications, a step that could lead to better communications and imaging technologies.



This image, taken with a field-emission scanning electron microscope, shows tiny parallel "nanorods" of gold that represent the first material that has a "negative index of refraction" in the wavelength of light used for telecommunications, a step that could lead to better communications and imaging technologies. The material, created by Purdue engineers, conducts clouds of electrons called "plasmons" with a frequency of light referred to as the near-infrared, the same wavelength used for fiberoptic communications. Each of the rods is about as wide as 100 nanometers, or 100 billionths of a meter, and 700 nanometers long. (Purdue University School of Electrical and Computer Engineering)
Click here for a high resolution photograph.

"This work represents a milestone because it demonstrates that it is possible to have a negative refractive index in the optical range, which increases the likelihood of harnessing this phenomenon for optics and communications," said Vladimir Shalaev, the Robert and Anne Burnett Professor of Electrical and Computer Engineering.

The material consists of tiny parallel "nanorods" of gold that conduct clouds of electrons called "plasmons" with a frequency of light referred to as the near-infrared. The wavelength size of this near-infrared light is 1.5 microns, or millionths of a meter, the same wavelength used for fiberoptic communications.

"This is the most important wavelength for communications," Shalaev said.

Findings are detailed in a paper appearing Dec. 15 in the journal Optics Letters, published by the Optical Society of America. The paper was written by Shalaev, his graduate research assistants Wenshan Cai and Uday K. Chettiar, doctoral student Hsiao-Kuan Yuan, senior research scientists Andrey K. Sarychev and Vladimir P. Drachev, and principal research scientist Alexander V. Kildishev.

The nanorods are an example of materials that are able to reverse a phenomenon called refraction, which occurs as electromagnetic waves, including light, bend when passing from one material into another and is caused by a change in the speed of light as it passes from one medium into another. Scientists measure this bending of radiation by its "index of refraction." Refraction causes the bent-stick-in-water effect, which occurs when a stick placed in a glass of water appears bent when viewed from the outside. Each material has its own refraction index, which describes how much light will bend in that particular material and defines how much the speed of light slows down while passing through a material. All natural materials, such as glass, air and water, have positive refractive indices.

In the late 1960s, researchers hypothesized what would happen if a material had a negative refractive index, causing it to bend light in the opposite direction from ordinary materials. In 2000, researcher John Pendry at the Imperial College London theorized that slabs of such material might be used to create a "superlens" that would drastically improve the quality of medical diagnostic imaging and other technologies. Such lenses theoretically could compensate for the loss of a portion of the light transmitting an image as it passes through a lens. Lenses and imaging systems could be improved if this lost light, which scientists call "evanescent light," could be restored. An imaging system that used a combination of positive and negative refraction might restore the lost evanescent light.

Harnessing materials that have a negative index of refraction could make it possible to take optical images of objects that are smaller than the wavelength of visible light, including molecules such as DNA, for research and medical imaging; the development of "photo-nanolithography," which would make it possible to etch smaller electronic devices and circuits, resulting in more powerful computers; new types of antennas, computer components and consumer electronics such as cell phones that use light instead of electricity for carrying signals and processing information, resulting in faster communications.

A major obstacle now hindering development of opto-electronic devices is that wavelengths of light are too large to fit into the tiny features needed for miniature circuits and components. "Plasmonic nanomaterials," however, could make it possible to squeeze light waves into much smaller spaces, Shalaev said.

Various research groups have fabricated "metamaterials" made of tiny metal rings and rods, which have a negative index of refraction. No metamaterials have yet been created that have negative refraction indices for visible light, but now the Purdue researchers have created the first metamaterial with a negative refractive index in the near-infrared portion of the spectrum. This is just beyond the range of visible light, demonstrating the feasibility of applying the concept to communications and computers.

"The challenge was to fabricate a structure that would have not only an electrical response, but also a magnetic response in the near-infrared range," Shalaev said.

The gold nanorods conduct clouds of electrons, all moving in unison as if they were a single object instead of millions of individual electrons. These groups of electrons are known collectively as plasmons. Light from a laser or other source was shined onto the nanorods, inducing an "electro-optical current" in the tiny circuit. Each of the rods is about as wide as 100 nanometers, or 100 billionths of a meter, and 700 nanometers long.

"These rods basically conduct current because they are a metal, producing an effect we call optical inductance, while a material between the rods produces another effect called optical capacitance," Shalaev said. "The result is the formation of a very small electromagnetic circuit, but this circuit works in higher frequencies than normal circuits, in a portion of the spectrum we call optical frequencies, which includes the near-infrared. So we have created a structure that works as kind of an optical circuit and interacts effectively with both of the field components of light: electrical and magnetic."

The research has been funded by the U.S. Army Research Office and the National Science Foundation and is affiliated with Purdue's Birck Nanotechnology Center at Discovery Park, the university's hub for interdisciplinary research.

"Although many researchers are skeptical about developing materials with a negative index of refraction in optical wavelengths and then using them in practical technologies, I think the challenges are mainly engineering problems that could eventually be overcome," Shalaev said. "There is no fundamental law of physics that would prevent this from happening."

Johns Hopkins University

Memory design breakthrough can lead to faster computers

Team improves infinitesimal rings for speedy, reliable, efficient magnetic memory

Imagine a computer that doesn't lose data even in a sudden power outage, or a coin-sized hard drive that could store 100 or more movies.

Magnetic random-access memory, or MRAM, could make these possible, and would also offer numerous other advantages. It would, for instance, operate at much faster than the speed of ordinary memory but consume 99 percent less energy.

The current challenge, however, is the design of a fast, reliable and inexpensive way to build stable and densely packed magnetic memory cells.

A team of researchers at The Johns Hopkins University, writing in the Jan. 13 issue of Physical Review Letters, has come up with one possible answer: tiny, irregularly shaped cobalt or nickel rings that can serve as memory cells. These "nanorings" can store a great quantity of information. They also are immune to the problem of "stray" magnetic fields, which are fields that "leak" from other kinds of magnets and can thus interfere with magnets next to them.

"It's the asymmetrical design that's the breakthrough, but we are also very excited about the fast, efficient and inexpensive method we came up with for making them," said paper co-author Frank Q. Zhu, a doctoral candidate in the Henry A. Rowland Department of Physics and Astronomy in the Krieger School of Arts and Sciences at Johns Hopkins.

The nanorings are extremely small, with a diameter of about 100 nanometers. A single nanometer is one billionth of a meter. A single strand of human hair can hold 1 million rings of this size, Zhu says.

The asymmetrical design allows more of the nanorings to end up in a so-called "vortex state," meaning they have no stray field at all. With no stray field to contend with, Zhu's team's nanorings act like quiet neighbors who don't bother each other and, thus, can be packed together extremely densely. As a result, the amount of information that can be stored in a given area is greatly increased.

Fabrication of the nanorings is a multistep procedure involving self-assembly, thin film deposition and dry etching. The key to creating the irregular rings, Zhu said, is to -- while etching the rings with an argon ion beam at the end of the process -- tilt the substrate on which the rings are formed.

"In our previous study, we found that 100 nanometer symmetric nanorings have only about a 40 percent chance to get vortex state," Zhu said. "But the asymmetric nanorings have between a 40 percent and 100 percent chance to get vortex state. This chance can be controlled on-demand by utilizing the direction of magnetic field."

Yale University

Yale engineers make standardized bulk synthesis of nanowires possible

A team of Yale scientists have demonstrated a method to understand effective synthesis of semiconductor nanowires (NWs) for both their quality and quantity, according to a report published in the journal Nanotechnology.

Graduate student Eric Stern in the department of biomedical engineering along with his colleague Guosheng Cheng, associate research scientist in electrical engineering systematically varied and tested parameters for producing GaN NWs using an optical lithographic method as a template for testing characteristics of the NWs.

A nanowire is an ultra-miniaturized cylindrical semiconductor, as small as 1 to 100 nanometers in diameter, and extending as long as a millimeter -- or 10,000 times its thickness. One nanometer is approximately a 25-millionth of an inch. GaN was chosen for these experiments as a material commonly employed in synthesis of semiconductors.

Development of reliable NW fabrication will allow the exploration of the next steps in semiconductor miniaturization. This reported technology produces ten-times the number of NWs as previous technology and sets parameters for standardization of NWs.

"This brings nanowires to an interface with the rest of the world of semiconductor research," said Stern. "Until this point, the greatest hurdle for the technology has been the inability to produce more than individual nanowires and to have statistically reproducible synthesis so that the properties of nanowires can be explored."

Their study also demonstrated the proof-of-principle that the NWs act as scaled FETs (field effect transistors), the technology commonly used in microelectronics.

Rensselaer Polytechnic Institute

Nanotube foams flex and rebound with super compressibility

Carbon nanotubes have enticed researchers since their discovery in 1991, offering an impressive combination of high strength and low weight. Now a new study suggests that they also act like super-compressible springs, opening the door to foam-like materials for just about any application where strength and flexibility are needed, from disposable coffee cups to the exterior of the space shuttle.

Buckled carbon nanotubes under compression. Credit: Cao/RPI

The research, which is reported in the Nov. 25 issue of the journal Science, shows that films of aligned multiwalled carbon nanotubes can act like a layer of mattress springs, flexing and rebounding in response to a force. But unlike a mattress, which can sag and lose its springiness, these nanotube foams maintain their resilience even after thousands of compression cycles.

In foams that exist today, strength and flexibility are opposing properties: as one goes up, the other must go down. With carbon nanotubes, no such tradeoff exists.

"Carbon nanotubes display an exceptional combination of strength, flexibility, and low density, making them attractive and interesting materials for producing strong, ultra-light foam-like structures," says Pulickel Ajayan, the Henry Burlage Professor of Materials Science and Engineering at Rensselaer Polytechnic Institute and coauthor of the paper.

Carbon nanotubes are made from graphite-like carbon, where the atoms are arranged like a rolled-up tube of chicken wire. Ajayan and a team of researchers at the University of Hawaii at Manoa and the University of Florida subjected films of vertically aligned nanotubes to a battery of tests, demonstrating their impressive strength and resilience.

"These nanotubes can be squeezed to less than 15 percent of their normal lengths by buckling and folding themselves like springs," says lead author Anyuan Cao, who did much of the work as a postdoctoral researcher in AjayanâTMs lab and is now assistant professor of mechanical engineering at the University of Hawaii at Manoa. After every cycle of compression, the nanotubes unfold and recover, producing a strong cushioning effect.

The thickness of the nanotube foams decreased slightly after several hundred cycles, but then quickly stabilized and remained constant, even up to 10,000 cycles. When compared with conventional foams designed to sustain large strains, nanotube foams recovered very quickly and exhibited higher compressive strength, according to the researchers. Throughout the entire experiments, the foams did not fracture, tear, or collapse.

And their intriguing properties do not end there. Nanotubes also are stable in the face of extreme chemical environments, high temperatures, and humidity all of which adds up to a number of possible applications, from flexible electromechanical systems to coatings for absorbing energy.

The foams are just the latest in a long line of nanotube-based materials that have been produced through collaborations with AjayanTMs lab, all of which have exhibited tantalizing properties. Ajayan and his colleagues from the University of Hawaii at Manoa recently developed tiny brushes with bristles made from carbon nanotubes, which could be used for tasks that range from cleaning microscopic surfaces to serving as electrical contacts. And in collaboration with researchers from the University of Akron, Ajayan and his team created artificial gecko feet with 200 times the sticking power of the real thing.

Stengthening the glow of nanotube luminescence

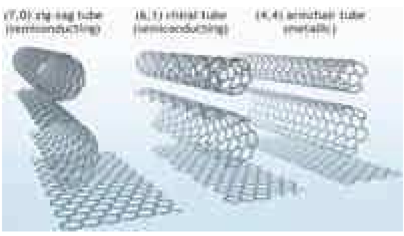
Latest study shows surprising variations in individual nanotube efficiency

Nanotubes are the poster children of the nanotechnology revolution. These tiny carbon tubes – less than 1/50,000 the diameter of a human hair – possess novel properties that have researchers excitedly exploring dozens of potential applications ranging from transistors to space elevators.

Tobias Hertel in the lab.
Click here for a high resolution photograph.

Nanotubes also produce light with a number of interesting properties, which have led researchers to propose various optical applications. One of the most promising is to use the tiny tubes as fluorescent markers to study biological systems, a role pioneered by fluorescent proteins. But there has been one primary problem: Nanotubes have proven to be very inefficient phosphors, absorbing a thousand photons for every photon that they emit (a ratio called quantum efficiency).

Now, however, the latest research into nanotube luminescence has found that there is substantial room for increasing the efficiency of these infinitesimal light sources: The study, which is the first to measure the luminescence of single nanotubes, was published in the Nov. 4 issue of Physical Review Letters and reports that there is a surprising amount of variation between the quantum efficiencies of the 15 individual nanotubes that were examined.



Nanotubes have different properties depending on slight differences in the way that carbon atoms are arranged.

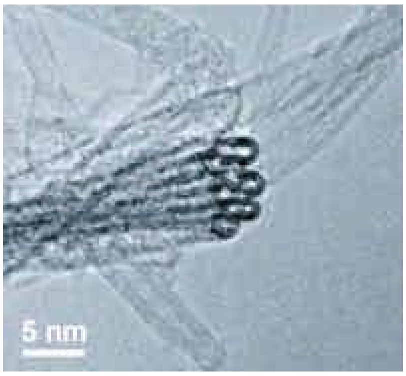
"We were expecting to see individual differences of only a few percent, so we were very surprised to find that some nanotubes are a 1,000 percent more efficient than others," says Tobias Hertel, associate professor of physics at Vanderbilt University, who conducted the study with two German research groups.

Nanotubes are members of the fullerene family along with buckyballs, carbon molecules shaped like soccer balls. Nanotubes, which are also called buckytubes, are seamless cylinders made of carbon atoms and capped on at least one end with a buckyball hemisphere. Nanotubes come in two basic forms: single-walled and multi-walled, which have two or more concentric shells. Slight differences in the geometric arrangement of carbon atoms produces nanotubes with different electrical properties, either metallic or semiconductor. Semiconducting nanotubes are the variety that produces light.

Since nanotubes were discovered in 1991, scientists have determined that they are relatively easy to make and have developed several methods for doing so.

The original process that was used is called the arc-discharge technique. Large amounts of current are passed through two graphite rods in a container filled with high-pressure helium gas. As the rods are brought together, an electrical arc is formed and the carbon in the smaller rod is transformed into a tubular structure filled with nanotubes. This produces a mixture of different types of nanotubes, including single-walled and multiple walled, semiconductor and metallic varieties in the form of black, sooty powder.

A more recent process uses a laser to vaporize carbon by scanning repeated across a flat slab made from a mixture of graphite and metal. This approach is noted for its ability to make a large proportion of single-walled tubes. In addition, a chemical vapor deposition process has been developed that is most suitable for producing nanotubes in commercial quantities.



An electron microscope image shows a bundle of nanotubes.
Click here for a high resolution image.

"Our analysis pinpoints structural defects as the source for most of the energy drain that reduces nanotubes' quantum efficiency as a light source. It should be possible to plug these energy sinks and improve their overall efficiency by a factor of five or so by improvements in the synthesis processes," Hertel says.

Although he doesn't know exactly what these improvements will be, Hertel is confident that they will happen. Improving nanotube synthesis is a big business. "There are hundreds of research groups around the world who are working full time to improve nanotube synthesis," he reports. As a result, improvements in the various synthesis processes are reported regularly.

Even if improving the nanotube's quantum efficiency proves unexpectedly difficult, there are likely to be work-arounds. For example, another way to brighten nanotubes is to simply make them longer, the physicist points out.

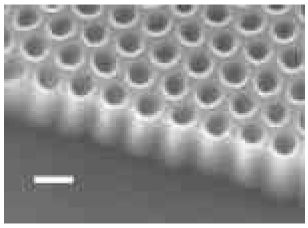
Other research groups are already experimenting with the use of nanotubes as a replacement for fluorescent proteins in the study of biological systems. In this application, they are competing with another nanotechnology called quantum dots, which are tiny fluorescent beads often made of cadmium selenide. According to Hertel, nanotubes have several inherent advantages over quantum dots for this application. Nanotubes are not known to be toxic to living cells, unlike the cadmium found in quantum dots. They produce a narrower, more precise beam of light, which makes them easier to detect. Finally, they are more stable and continue producing light long after quantum dots have faded.

Hertel's co-authors on the study are Mathias Steiner, Huihong Qian and Achim Hartschuh from the University of Tuebingen, Alfred Meixner from the University of Siegen, Markus Raschke and Christoph Lienau from the Max Born Institute and Axel Hagen from the Fritz Haber Institute of the Max Planck Society.

Nanostructured silicon emits laser light

6 December 2005

Scientists in the US claim to have observed lasing from a nanostructured piece of silicon for the first time (*Nature Materials* 4 887 2005). The news follows demonstrations earlier this year of silicon lasers that relied on either the Raman effect or rare-earth doping to achieve optical gain.



Nanostructured silicon

The team from Brown University took an electronic grade silicon-on-insulator (SOI) wafer and used refractive ion etching and a nanopore mask to etch billions of tiny (60 nm wide) pores into its surface. They then cooled the wafer to cryogenic temperatures (10 K) and pumped it with up to 1.5 W of green light from an Argon Ion laser.

As the pump power was increased, Jimmy Xu and his colleagues Sylvain Cloutier and Pavel Kossyrev observed the telltale signs of lasing in the infrared - optical gain followed by linewidth narrowing and the generation of a sharp emission peak at a wavelength of 1278 nm.

Although the exact mechanism behind the lasing is not clear, Xu's team believes that it is due to the creation of A-centre defect states in the silicon. These defect energy states are located just below the conduction band and allow trapped electrons and free holes to recombine and emit light.

Currently, the emitted laser light is very weak, with an estimated output power of 30 nW and an external efficiency of about 0.0001% (1×10^{-6}) and Xu says that his team did well to spot it. That said, the researchers are confident that by optimizing the design it can be scaled to higher powers.

"Even though the external efficiency may seem to be very low, it is comparable to the optically pumped solid-state lasers in their early days and conventional noble gas lasers," said the researchers in their paper. "Although only observed at cryogenic temperatures so far, we hope that this report will help generate broad interest and stimulate further investigations."

About the author

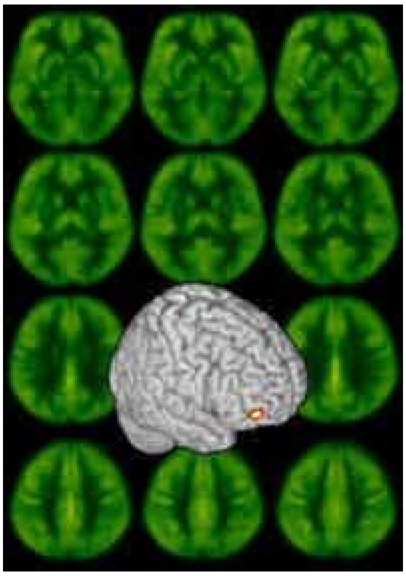
Oliver Graydon is editor of *Optics.org* and *Opto & Laser Europe* magazine.

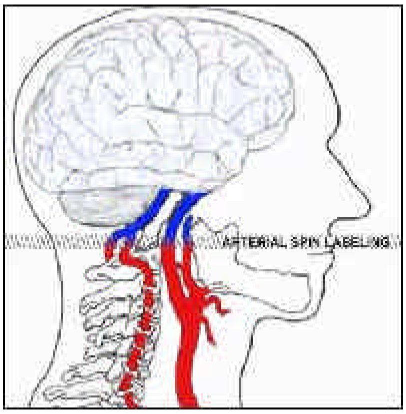
Life Sciences

University of Pennsylvania School of Medicine

Penn research permits first-ever visualization of psychological stress in the human brain

New application of fMRI technique may help physicians better diagnose and treat the effects of stress





Using a novel application of an fMRI (functional magnetic resonance imaging) technique, researchers at the University of Pennsylvania School of Medicine have, for the first time, visualized the effects of everyday psychological stress in a healthy human brain. Their work, performed at Penn's Center for Functional Neuroimaging, provides a neuro-imaging marker of psychological stress -- which will pave the way for the development of improved strategies for preventing or correcting the long-term health consequences of chronic stress. The researchers' study appears in the November 21 online edition of Proceedings of the National Academy of Sciences.

In the Penn study, researchers induced stress on healthy subjects by asking them to quickly tackle challenging mental exercises while being monitored for performance. During the fMRI scans, the researchers also recorded subjects' emotional responses -- such as stress, anxiety, and frustration -- and measured the corresponding changes in stress hormone and heart rate. Many subjects described themselves as being "flustered, distracted, rushed and upset" by the stress task.

The results showed increased cerebral blood-flow during the "stress test" in the right anterior portion of the brain (prefrontal cortex) -- an area long associated with anxiety and depression. More interestingly, the increased cerebral blood-flow persisted even when the testing was complete. These results suggest a strong link between psychological stress and negative emotions. On the other hand, the prefrontal cortex is also associated with the ability to perform executive functions -- such as working memory and goal-oriented behavior -- that permit humans to adapt to environmental challenges and threats. "The message from this study is that while stress may be useful in increasing focus, chronic stress could also be detrimental to mental health," concludes Jiongjiong Wang, PhD, Assistant Professor of Radiology and principal investigator of the study.

"How the brain reacts under psychological stress is an untouched subject for cognitive neuroscientists, but it is certainly a critical piece of the puzzle in understanding the health effects of stress," adds Wang. "Our findings should help significantly advance our understanding of this process."

To date, most fMRI studies have indirectly measured changes in cerebral blood-flow and metabolism induced by neural activation, using a technique that is sensitive to the oxygenation levels in blood. "The fMRI technique employed in our study – arterial spin labeling – can measure cerebral flood-flow directly," states John A. Detre, MD, Associate Professor of Neurology and Radiology, and senior author of the study. "This technique is very similar to PET (positron emission tomography) scanning, except that it's entirely non-invasive – without the need for injections or radioactivity. In this elegant technique, water molecules in subjects' own blood are 'tagged' by the magnet and used as the natural contrast agent to measure cerebral blood-flow." Researchers at Penn's Center for

Functional Neuroimaging have been at the forefront of the development of this technique, and its applications to imaging brain-function during cognitive and emotional processes.

The study was sponsored by grants from the National Science Foundation, the National Institutes of Health, and the U.S. Air Force. In addition to Drs. Wang and Detre, the team of investigators included Penn researchers Hengyi Rao, Gabriel S. Wetmore, Patricia M. Furlan, Marc Korczykowski, and David F. Dinges.

About PENN Medicine:

PENN Medicine is a $2.7 billion enterprise dedicated to the related missions of medical education, biomedical research, and high-quality patient care. PENN Medicine consists of the University of Pennsylvania School of Medicine (founded in 1765 as the nation's first medical school) and the University of Pennsylvania Health System.

Penn's School of Medicine is ranked #2 in the nation for receipt of NIH research funds; and ranked #4 in the nation in U.S. News & World Report's most recent ranking of top research-oriented medical schools. Supporting 1,400 fulltime faculty and 700 students, the School of Medicine is recognized worldwide for its superior education and training of the next generation of physician-scientists and leaders of academic medicine.

The University of Pennsylvania Health System includes three hospitals [Hospital of the University of Pennsylvania, which is consistently ranked one of the nation's few "Honor Roll" hospitals by U.S. News & World Report; Pennsylvania Hospital, the nation's first hospital; and Penn Presbyterian Medical Center]; a faculty practice plan; a primary-care provider network; two multispecialty satellite facilities; and home care and hospice.

Weitere Informationen finden Sie im WWW:

- http://www.cfn.upenn.edu
- http://www.uphs.upenn.edu

Radiological Society of North America

New Technology May Help Radiologists Find More Breast Cancers

Digital tomosynthesis shows promise over conventional film mammography as a more specific breast screening technique and a more accurate diagnostic technology, according to a study presented today at the annual meeting of the Radiological Society of North America (RSNA).

"The results of our preliminary trial suggest that tomosynthesis may decrease false-positive screening mammography findings by half, thereby reducing the number of women who are recalled after screening mammography for a second, more thorough exam," said lead author Steven Poplack, M.D., associate professor of diagnostic radiology and obstetrics and gynecology at the Dartmouth Hitchcock Medical Center/Dartmouth Medical School in Lebanon, N.H.

A patient's experience is much the same for tomosynthesis as it is for a standard mammography exam. Tomosynthesis obtains digital data that can be manipulated and displayed in a variety of ways, including paging through or cine display of thin (one millimeter) sections or slices of breast tissue, which eliminates the problem of overlying tissue that might be mistaken for lesions or that may hide small cancers.

To evaluate the role of tomosynthesis in breast cancer screening and diagnosis, Dr. Poplack and colleagues studied 98 women who were recalled for diagnostic imaging following abnormal screening mammograms. The initial screening mammography exams showed 112 findings in the women.

When the researchers compared the exams and took into account findings seen with tomosynthesis only, they found that approximately 40 percent of the patients would not have been recalled had they originally been screened using tomosynthesis. As a diagnostic imaging technique for follow-up of a potential abnormality in the breast, tomosynthesis was as good if not better than diagnostic mammography in 88 percent of patients.

Dr. Poplack is optimistic about the ability of tomosynthesis to improve the overall accuracy of diagnosing breast disease. "Tomosynthesis is going to reduce the number of false-positive screening exams and will probably allow us to find more early breast cancers," he said.

He pointed to a number of reasons this technology is appealing. "The similarity of tomosynthesis to mammography allows us to build on the current foundation of mammography while improving interpretation," he said. "It is both an evolution of mammography technology and revolutionary new technology."

Dr. Poplack expects that tomosynthesis, which is currently in the research phase, will be routinely be used in both screening and diagnostic mammography at major medical centers in the next several years.

Dr. Poplack's co-authors are Christine Kogel, R.N., Helene Nagy, M.D., and Tor Tosteson, Sc.D.

Weitere Informationen finden Sie im WWW:

- http://www.rsna.org

Magnetic probe successfully tracks implanted cells in cancer patients

Technique shows that injection accuracy is critical, but not perfect

By using MRI to detect magnetic probes of tiny iron oxide particles, an international research team for the first time has successfully tracked immune-stimulating cells implanted into cancer patients for treatment purposes.

"In four of the eight patients, MRI revealed that the implanted cells weren't where they needed to be to be effective for treatment," says Jeff Bulte, Ph.D., an associate professor of radiology at Hopkins' Institute for Cell Engineering who developed methods to optimally label cells with the clinically approved iron oxide particles.

This new application of the probes -- already clinically approved for MRI scanning of the liver -- could dramatically improve efforts to test and use cellular therapies such as vaccines to treat cancer or prevent its recurrence or stem cells to repair damaged organs, say the researchers.

Bulte and a team of Dutch researchers used MRI and a magnetic probe approved by both European and U.S. agencies to locate therapeutic cells injected into eight melanoma patients.

"Our results show that the MRI-based technique was more accurate than tracking the cells using radioactivity and that ultrasound failed to accurately guide injection of the cells into lymph nodes in half of the patients," says Bulte, an author on the report, which appears in the November issue of Nature Biotechnology.

The cells used in the current study, so-called dendritic cells, are the immune system's own "most wanted posters" because they take up and display foreign proteins that tell the immune system's fighters what cells to look for and destroy.

Since the mid-1990s, clinical trials have been testing dendritic cells to see whether they can stimulate the immune system to kill cancer cells. In these trials, dendritic cells from patients are exposed to proteins from the patients' cancer cells and then returned to the patients.

However, some of the clinical trials of such "cancer vaccines" have been disappointing, with some patients responding very well but others not at all. A critical issue behind each patient's success on the treatment, however, is whether the cells get to the lymph nodes, where the immune system's fighters are normally "trained" by dendritic cells. Until now, there's been no accurate way to know where the cells end up.

It's thought, but not proven, that the best way to get the cells where they need to be is to inject them directly into the lymph nodes that drain the area containing a tumor. Currently, doctors use ultrasound to guide the needle, and dendritic cells carrying a radioactive tag are sometimes used to try to double-check the cells' final resting place.

However, in this study, the Dutch team discovered that using MRI and iron oxide particles was able to track the cells' location much more accurately than the radioactive tracking method and provided anatomic detail simultaneously -- structural detail not possible by tracking radioactivity.

"On the MR images, we can see the lymph nodes, and we can see the magnetically labeled dendritic cells, and we can tell very clearly whether they are in the same place," says the study's first author, Jolanda de Vries, an assistant professor at the Nijmegen Center for the Molecular Life Sciences (NCMLS) of the Radboud University Nijmegen Medical Center in The Netherlands. "The cells can't get from the fat into the lymph nodes by themselves, so injecting them properly is very important."

Bulte says he, Dara Kraitchman, Ph.D., D.V.M., and colleagues at Hopkins are already testing magnetically labeled stem cells with MRI-compatible injection systems to allow MRI guidance of injection in large animals.

The current clinical trial builds on Bulte's earlier work tracking magnetically labeled cells in animals. Four years ago, he and colleagues reported that stem cells containing so-called magnetodendrimers could be followed by MRI.

But to advance to clinical trials, the research team switched from the experimental magnetic tags to formulations of iron oxide already approved for clinical use in Europe (as Endorem) and the United States (as Feridex). Because immature dendritic cells naturally take up materials around them, they simply absorbed, or ingested, the iron oxide particles when exposed to them in the lab. The magnetically labeled, cancer-primed cells were then returned to the patients, all of whom had stage III melanoma.

"Although dendritic cell therapy is used in clinical trials to treat patients with melanoma, in this study we wanted to see whether the magnetically labeled cells could be tracked by MRI, to study their migratory behavior in more detail," says Carl Figdor, principal investigator of the study, of the NCMLS. "We were very pleased that they showed up clearly. With the anatomic information from the MRI, we could see precisely where they were -- inside or outside of the lymph nodes."

Source: **University of Pittsburgh Medical Center**
Date: 2006-01-17
URL: http://www.sciencedaily.com/releases/2006/01/060117023837.htm

Two Pathways Found That Lead To Alzheimer's Disease

Mild cognitive impairment (MCI), a transitional stage between normal cognition and Alzheimer's disease, exists in two different forms, according to a study published today by researchers from the University of Pittsburgh School of Medicine and the University of California, Los Angeles in the Archives of Neurology.

Using a new imaging procedure that creates 3-D maps of the brain, researchers determined specific areas that had degenerated in people with MCI. Depending on the person's symptoms, more tissue was lost in the hippocampus, a brain area critical for memory and one of the earliest to change in Alzheimer's disease, indicating two different paths of progression to Alzheimer's disease. The finding could lead to better diagnosis and treatment of patients with MCI, perhaps delaying or preventing the onset of dementia.

MCI is categorized into two sub-types -- currently distinguished based solely on symptoms. Those with MCI, amnesic subtype (MCI-A) have memory impairments only, while those with MCI, multiple cognitive domain subtype (MCI-MCD) have other types of mild impairments, such as in judgment or language, but also have either mild or no memory loss. Both sub-types progress to Alzheimer's disease at the same rate. Until now it was not known if the pathologies of the two types of MCI were different, or if MCI-MCD was just a more advanced form of MCI-A.

Researchers found that the hippocampus of the patients with MCI-A was 14 percent smaller than that of the healthy subjects, nearly as great as the 23 percent shrinkage seen in Alzheimer's disease. But, the hippocampus of those with MCI-MCD most resembled that of the controls, showing only 5 percent shrinkage.

Using highly accurate Magnetic Resonance Imaging (MRI) data from six patients with MCI-A, 20 with MCI-MCD and 20 with Alzheimer's disease who were seen at the University of Pittsburgh's Alzheimer Disease Research Center and 20 healthy controls, researchers created 3-D mesh reconstructions of each participant's hippocampus that allowed them to see where the hippocampus had deteriorated. This study is the first to use such modeling technology to visualize changes in the brains of people with MCI. Prior studies have only been able to measure the volume of the hippocampus and estimate atrophy through noticeable volume loss.

"These vibrant images produced by 3-D modeling have proven what we suspected -- there are at least two transitional states that lead to Alzheimer's disease," said James T. Becker, Ph.D., a neuropsychologist and professor of psychiatry, neurology and psychology, at the University of Pittsburgh School of Medicine and lead author of the study. "Now we can investigate these pathways and develop treatments that, we hope, may slow or stop the progression of Alzheimer's."

Alzheimer's disease affects as many as 10 percent of people older than 65, and delaying or preventing the onset of dementia is an important medical priority. "We can now see the pattern of brain damage in people with MCI and we can use these new types of images to monitor how different therapies may be working," said Paul M. Thompson, Ph.D., associate professor of neurology, at the University of California, Los Angeles. "By imaging the brain like this, we can explore the progression of diseases, and see if therapies are protecting the brain."

NIH/National Institute of Neurological Disorders and Stroke

Study links Alzheimer’s disease to abnormal cell division

A new study in mice suggests that Alzheimer’s disease (AD) may be triggered when adult neurons try to divide. The finding helps researchers understand what goes wrong in the disease and may lead to new ways of treating it. The study was funded in part by the National Institute of Neurological Disorders and Stroke (NINDS), part of the National Institutes of Health, and appears in the January 18, 2006 issue of The Journal of Neuroscience.*

For unknown reasons, nerve cells (neurons) affected by AD and many other neurodegenerative diseases often start to divide before they die. The new study shows that, in animal models of AD, this abnormal cell division starts long before amyloid plaques or other markers of the disease appear. Cell division occurs through a process called the cell cycle. "If you could stop cell cycling, you might be able to stop neurons from dying prematurely. This could be a fresh approach to therapy for Alzheimer’s and other diseases, including stroke, amyotrophic lateral sclerosis [also known as Lou Gehrig’s disease], and HIV dementia," says Karl Herrup, Ph.D., of Case Western Reserve University in Cleveland, who led the study.

The researchers compared the brains of three different mouse models of AD to brains from normal mice, looking specifically for markers of cell cycling. They found that, in the AD mouse models, cell cycle-related proteins appeared in neurons 6 months before the first amyloid plaques or disease-related immune reactions developed in the brain. Many of the neurons also had increased numbers of chromosomes, which is typical of cells that have begun to divide. These changes were not seen in normal mice. The regions of the brain most affected by the neuronal cell cycling were the cortex and the hippocampus – the same regions most affected in AD. The cortex is important for thought and reasoning, while the hippocampus plays a key role in learning and memory. Some parts of the brainstem also showed evidence of cell cycling.

While the cell cycling appeared to be necessary for neurons to die, it was not an immediate cause of cell death in the mouse models of AD. Instead, the affected neurons appeared to live for many months in a near-functional state, with the mice showing only mild behavioral changes during that time. This suggests that another type of cellular problem, still unidentified, must damage the neurons in order for them to die.

The findings shed new light on the theory that the accumulation of amyloid beta in the brain causes the neuron death in AD. Because the abnormal cell cycling begins months before the formation of amyloid plaques, it is unlikely that the plaques themselves trigger the disease process. However, tiny clumps made up of several amyloid beta molecules (called micro-molecular aggregates) form before the plaques and may trigger the disease. Since the three mouse models tested in this study all had mutations in the gene that codes for amyloid precursor protein, the similarity between affected brain regions in these mice and in people with AD also supports the amyloid hypothesis.

While previous studies have linked AD to abnormal cell cycling, this is the first study to examine the link using standard mouse models of AD. The results indicate that the mice, which do not develop neurofibrillary tangles or the severe behavioral symptoms of AD, are accurate models of the early cellular processes that lead to the disease. "The cell cycle markers mimic the human situation rather well," says Dr. Herrup. "This opens a range of new experimental possibilities using the cell cycle events as indicators of neuronal distress."

Dr. Herrup and his colleagues are now trying to determine if feeding the mouse models the drug ibuprofen can stop abnormal cell cycling in neurons and halt neurodegeneration. Ibuprofen is an anti-inflammatory drug that reduces production of amyloid beta, and some studies have suggested that it may reduce the risk of AD. The researchers are also planning additional studies to identify why neurons start to divide when they are diseased and why entering the cell cycle appears to trigger cell death.

Source: **Northwestern University**
Date: 2006-01-19
URL: http://www.sciencedaily.com/releases/2006/01/060118210714.htm

Gene Therapy 'Turns Off' Mutation Linked To Parkinson's Disease

A group of Northwestern University researchers is developing a novel gene therapy aimed at selectively turning off one of the genes involved in the development of Parkinson's disease.

The gene therapy, described in the January online issue of the journal Experimental Neurology, was designed by Martha Bohn and her laboratory group at Northwestern University Feinberg School of Medicine.

Bohn is Medical Research Council Professor and director of the neurobiology program at Children's Memorial Research Center and professor of pediatrics and of molecular pharmacology and biological chemistry at the Feinberg School. The gene technique the Bohn lab developed removes a protein known as alpha-synuclein from the diseased dopamine-producing neurons that die in Parkinson's disease. Alpha-synuclein is abundant in structures known as Lewy bodies -- a diagnostic hallmark of Parkinson's disease.

Research has shown that mutant forms of the alpha-synuclein gene, as well as too much alpha-synuclein protein, are involved in the development Parkinson's disease in some families.

For this research, the Bohn lab combined a recently developed technology called "RNA interference" with gene therapy to turn off alpha-synuclein in dopamine neurons. RNA interference is a sophisticated method to selectively turn off one gene in a cell, leaving others unaffected.

By placing the RNA interference into a crippled, non-disease-causing virus, scientists in the Bohn lab have been able to deliver the RNA interference tool to the brain of rats and turn off the alpha-synuclein protein in neurons. "This is the first step in developing a new therapy for Parkinson's disease based on molecular knowledge of the disease," said Mohan K. Sapru, research assistant professor of pediatrics, who is first author on the study and co-inventor of the gene therapy technology.

"It may also be useful for other diseases of the brain, such as dementia with Lewy bodies, a disease also characterized by Lewy bodies in the brain," Sapru said.

The Bohn lab will subsequently test this gene therapy in mouse models of the disease. If the RNA interference approach works in the mouse, a gene therapy based on silencing the _alpha-synuclein gene will be developed for clinical trials for Parkinson's patients.

European Molecular Biology Laboratory

The closest look ever at the cell’s machines

The first genome-wide screen for protein complexes is completed

Today researchers in Germany announce they have finished the first complete analysis of the "molecular machines" in one of biology’s most important model organisms: S. cerevisiae (baker’s yeast). The study from the biotechnology company Cellzome, in collaboration with the European Molecular Biology Laboratory (EMBL), appears in this week’s online edition of Nature.

"To carry out their tasks, most proteins work in dynamic complexes that may contain dozens of molecules," says Giulio Superti-Furga, who launched the large-scale project at Cellzome four years ago. "If you think of the cell as a factory floor, up to now, we’ve known some of the components of a fraction of the machines. That has seriously limited what we know about how cells work. This study gives us a nearly complete parts list of all the machines, and it goes beyond that to tell us how they populate the cell and partition tasks among themselves."

The study combined a method of extracting complete protein complexes from cells (tandem affinity purification, developed in 2001 by Bertrand Séraphin at EMBL), mass spectrometry and bioinformatics to investigate the entire protein household of yeast, turning up 257 machines that had never been observed. It also revealed new components of nearly every complex already known.

In the course of the work, new computational techniques were developed at EMBL that gave new insights into the dynamic nature of protein complexes. In contrast to most man-made factories, cells continually dismantle and reassemble their machines at different stages of the cell cycle and in response to environmental challenges, such as infections.

"This would be a logistical nightmare if the cell had to build every machine from scratch any time it needed to do something," says Anne-Claude Gavin, former Director of Molecular and Cell Biology at Cellzome and currently a team leader at EMBL. "We’ve discovered that the reality is different. Cells use a mixed strategy of prefabricating core elements of machines and then synthesizing additional, snap-on molecules that give each machine a precise function. That provides an economic way to diversify biological processes and also to control them."

Thus if the cell needs to respond quickly, such as in a disease or another emergency, it may only need to produce few parts to switch on or tune the machine. On the other hand, if something shouldn’t happen, it may only need to block the production of a few molecules.

Patrick Aloy and Rob Russell at EMBL used sophisticated computer techniques to reveal the modular organisation of these cellular machines. "This is the most complete set of protein complexes available and probably the set with the highest quality," Aloy says. "Most proteomics studies in the past have shown whether molecules interact or not, in a ’yes/no’ way. The completeness of this data lets us see how likely any particular molecule is to bind to another. By combining such measurements for all the proteins in the cell, we discovered new complexes and revealed their modular nature."

"Investigating protein complexes has always posed a tricky problem – they’re too small to be studied by microscopes, and generally too large to be studied by techniques like X-ray crystallography," says Russell. "But they play such a crucial role in the cell that we need to fill in this gap. There’s still a huge amount to be learned from this data and from the methods we are developing to combine computational and biochemical investigations of the cell."

"This is an important milestone towards a more global and systems-wide understanding of the cells of organisms ranging from yeast to humans," says Peer Bork, Head of the Structural and Computational Biology Unit at EMBL, and one of the authors of the paper. "Ultimately we hope to achieve a ’molecular anatomy’ that takes us from the level of the entire cell to the much deeper level of all the molecules and atoms that make it up."

Baker’s yeast is evolutionary related to the cells of animals and humans, which means that the findings will be more widely applicable. "The same principles discovered here in yeast apply to human cells," says Gitte Neubauer, Vice President at Cellzome. "Drug targets and pathologically relevant proteins are parts of machines and pathways."

The collaboration between Cellzome and EMBL has been very successful, she says, producing fundamental new insights in how molecules are organised and contributing to Cellzome’s success in complex and pathway analysis.