## 90 billion tons of microbial organisms live in the deep biosphere

### *The microcosm in the seafloor*

Biogeoscientists show evidence of 90 billion tons of microbial organisms—expressed in terms of carbon mass—living in the deep biosphere, in a research article published online by Nature, July 20, 2008. This tonnage corresponds to about one-tenth of the amount of carbon stored globally in tropical rainforests. The authors: Kai-Uwe Hinrichs and Julius Lipp of the Center for Marine Environmental Sciences (MARUM) at University of Bremen, Germany; and Fumio Inagaki and Yuki Morono of the Kochi Institute for Core Sample Research at the Japan Agency for Marine-Earth Science and Technology (JAMSTEC) concluded that about 87 percent of the deep biosphere consists of Archaea. This finding is in stark contrast to previous reports, which suggest that Bacteria dominate the subseafloor ecosystem. To reach this conclusion, the researchers investigated sediment cores collected from several hundred meters beneath the seafloor of the Atlantic and Pacific Oceans and the Black Sea. The cored sediments included samples that were the result of research expeditions conducted by the Integrated Ocean Drilling Program (IODP).

According to co-author Prof. Kai-Uwe Hinrichs, a biogeochemist who led the research team, two main objectives were pursued: "We wanted to find out which microorganisms can be found in the seafloor, and how many of them are living down there."

For a long time, scientists believed that extreme conditions such as high pressure, lack of oxygen, and low supply of nutrients and energy would make deep, subseafloor environments inhabitable for any life form. Nonetheless, sea-going investigations have proven the existence of the deep biosphere.

"In general, life below the seafloor is dominated by minute monocellular organisms," explains co-author Julius Lipp, who has just completed his PhD on the subject. "According to our analyses, Bacteria dominate the upper 10 centimeters of the seafloor. Below this level Archaea appear to take over the major fraction of the biomass pool." According to Lipp, Archaea make up at least 87 percent of organisms that colonize the deep biosphere. "These subsurface Archaea can be viewed as starvelings," he continues. "Compared to Bacteria, Archaea appear to be better adapted to the extreme, chronic deficiency of energy that characterizes this habitat – a consequence of the only food being fossil remnants of plants that were pre-digested by generations of other microorganisms."

Next to Bacteria, Archaea represent a distinct domain in the three-domain system of life. Both groups can be identified by fat-like molecules, so-called lipids that make up their cell membranes. To date, estimations of the deep biosphere biomass range from about 60 to 300 billion tons of carbon. Says Prof. Hinrichs, "Our measurements, determined by entirely independent means, are right in this bracket." The authors assume that about 200 million cubic kilometers of mud below the ocean floor are inhabited by microorganisms—a volume that roughly corresponds to a 600 kilometer-long cube.

Drs. Inagaki and Morono, both geomicrobiologists, studied DNA in this project. "Given the strong indication of the Archaea world in the marine subsurface," says Dr. Inagaki, "we intend to study their lifestyle and metabolism, strategy for long-term survival, and ecological roles using subseafloor materials cored by CHIKYU and other drilling platforms." CHIKYU is the world's only riser-equipped research vessel, one of three drilling platforms supported by IODP.

Because all current techniques used to detect biomass in the deep biosphere arrive at different conclusions regarding quantity and composition, Prof. Hinrichs has initiated an international "ring experiment." Currently, he and colleagues in German, European, U.S., and Japanese laboratories investigate standardized sediment samples from the seafloor using varied methods. To gain a more reliable picture of life in the deep biosphere they need to find out whether identical methods applied in different labs lead to dissimilar results. In September, the researchers involved in the ring experiment will present and discuss their findings. The participants hope "this experiment will shed a bit more light on the dark, deep biosphere," says Prof. Hinrichs.

*The Integrated Ocean Drilling Program (IODP) is an international marine research drilling program supported by 23 countries dedicated to advancing scientific understanding of Earth by sampling and monitoring subseafloor environments. Through multiple platforms, preeminent scientists explore IODP's principal research themes: the deep biosphere, environmental change, and solid earth cycles.*

## Epilepsy drug may increase risk of birth defects

ST. PAUL, Minn. – Taking the epilepsy drug topiramate alone or along with other epilepsy drugs during pregnancy may increase the risk of birth defects, according to a study published in the July 22, 2008, issue of Neurology®, the medical journal of the American Academy of Neurology.

Research has shown that many epilepsy drugs increase the risk of birth defects, but little research has been done on topiramate. Studies have shown that topiramate increases the risk of birth defects in animals.

Maintaining effective epilepsy treatment during pregnancy is crucial because seizures may cause harm to the fetus.

For the study, researchers examined women who became pregnant while taking topiramate either on its own or along with other epilepsy drugs. Of 178 babies born, 16 had major birth defects. Three of these were in infants whose mothers were taking only topiramate, and 13 were in those whose mothers were taking topiramate and other epilepsy drugs.

Four of the babies had cleft palates or cleft lips, a rate 11 times higher than that expected if these women were not taking epilepsy drugs. Four male babies had genital birth defects, with two of those classified as major defects, which is 14 times higher than the normal rate for this defect.

“More research needs to be done to confirm these results, especially since it was a small study,” said John Craig, MRCP, of the Royal Group of Hospitals in Belfast, Northern Ireland. “But these results should also get the attention of women with migraine and their doctors, since topiramate is also used for preventing migraine, which is an even more common condition that also occurs frequently in women of childbearing age.”

Craig said the risk of birth defects may be different for women taking the drug for migraine, but that the pregnancies of women exposed to topiramate should be monitored.

This study found that more birth defects occurred in women taking topiramate along with the drug valproate, or valproic acid, than in women taking topiramate and another epilepsy drug. Research has shown that valproate is associated with a high risk of birth defects.

*The study was supported by a research grant from the Epilepsy Research Foundation and by unrestricted educational grants from GlaxoSmithKline, sanofi-aventis, UCB Inc., Janssen-Cilag, Pfizer, and Eisai.*

## New research links International Monetary Fund loans with higher death rates from tuberculosis

International Monetary Fund (IMF) loans were associated with a 16.6% rise in death rates from tuberculosis (TB) in the former Soviet Union and Central and Eastern European countries between 1992 and 2002, finds a study in this week's PLoS Medicine.

The study, by David Stuckler and colleagues from the University of Cambridge, UK, and Yale University, USA, also found that IMF loans were linked with a 13.9% increase in the number of new cases of TB per year and a 13.2% increase per year in the total number of people with the disease.

Between 1992 and 2002, most of the countries studied in this analysis received IMF loans for the first time. As Stuckler and colleagues note, “According to the IMF, the objective of these programs is to achieve macroeconomic stability and economic growth...”, yet a recent report from the Center for Global Development has suggested that countries receiving IMF loans may constrain spending on health and social services. For example, countries receiving IMF loans might need to reduce social spending in order to meet the targets set as a condition of the loan, and do so by placing caps on public wage bills or by privatizing healthcare services. However, previously it has not been clear whether IMF loans are actually linked to any changes in measurable health outcomes.

For their analysis, Stuckler and colleagues used data on health outcomes from the World Health Organization (WHO), and IMF data from the World Bank's World Development Indicators. They set up models to test whether entry to, and exit from, IMF programs was linked with changes in TB outcomes in these countries, while controlling for other factors that might have had an effect (such as the level of economic development, financial desperation, HIV/AIDS, and so on). The authors also tried to understand what mechanisms might be responsible for the increase in TB death rates that they found. Using a separate set of models, the authors suggest that IMF programs are linked to an 8% drop in government spending, a 7% drop in the number of doctors per head, and lower coverage of TB control using the “directly observed treatment, short course” (DOTS) strategy recommended by the WHO. Together, these findings suggest that countries receiving IMF loans make cutbacks in their TB control infrastructure and that this might be responsible for the increase in TB death rates.

In an expert commentary on the study, Megan Murray and Gary King from Harvard University, USA, who were not involved in the study, discuss the difficulties involved in doing such research and the conclusions that can be drawn from the findings. Despite the key limitations they outline (in particular, the fact that IMF loans are not randomly assigned, but are likely given to countries which are “doing badly” economically), they conclude: “we are convinced that at least the authors went very far in testing assumptions and mitigating uncertainties, and so the study and its conclusions should be taken seriously.”

Before applying these findings directly to policy, it would be important to understand whether IMF spending has an effect on health outcomes other than TB, and also to more clearly understand the possible mechanisms which link these loans to worsened health outcomes.

***Citation**: Stuckler D, King LP, Basu S (2008) International Monetary Fund programs and tuberculosis outcomes in post-communist countries. PLoS Med 5(7): e143. doi:10.1371/journal.pmed.0050143*
*http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.0050143*

## Plants make vaccine for treating type of cancer in Stanford study

STANFORD, Calif. - Plants could act as safe, speedy factories for growing antibodies for personalized treatments against a common form of cancer, according to new findings from the Stanford University School of Medicine. The findings came in the first human tests of an injectable vaccine grown in genetically engineered plants.

The treatments, which would vaccinate cancer patients against their malignant cells, could lead to earlier personalized therapy to tackle follicular B-cell lymphoma, an immune-system malignancy diagnosed in about 16,000 people each year.

Doctors regard follicular B-cell lymphoma as a chronic, incurable disease. The standard treatment, chemotherapy, has such severe side effects that patients often opt for watchful waiting in the early stages of illness. However, plant-grown vaccines, which lack side effects, could allow earlier, more aggressive management of the cancer.

“This would be a way to treat cancer without side effects,” said Ronald Levy, MD, professor of oncology and the Robert K. and Helen K. Summy Professor in the School of Medicine, who is the study's senior author. “The idea is to marshal the body's own immune system to fight cancer.”

The findings will appear July 21 in the advance online issue of the Proceedings of the National Academy of Sciences. The study was a phase-1 trial that showed plant-grown cancer vaccines were safe for patients and could be produced quickly and cheaply. Sixteen newly diagnosed lymphoma patients received the treatment; none experienced any side effects from plant-grown vaccines.

Future studies will test the vaccine's effectiveness.

The cancer vaccines rely on a biological quirk of follicular B-cell lymphoma, which is a type of non-Hodgkin's lymphoma. The cancer starts when a single immune cell multiplies uncontrollably, producing many identical clones of itself. The clones all carry the same antibody on their exterior, a marker that is unique to the cancer and is not found on any of the body's healthy cells. Levy's vaccination strategy is to inject many copies of the cancer-specific antibody into a newly diagnosed lymphoma patient, stimulating the patient's immune system to seek and destroy malignant cells.

Previous trials of this kind of vaccine, produced in animal cells and tested in mice and humans, have had mixed success, and the vaccines are not yet commercially available. Growing cancer vaccines in plants could circumvent some of the hurdles to turning the concept into a real treatment, Levy said.

Because each person's cancer antibody is unique, every patient needs a personalized vaccine. Growing personalized vaccines in animal cells takes months, costs thousands of dollars per patient and comes with the theoretical risk that a patient might inadvertently be infected with an animal virus that contaminated the cells used to grow the vaccine. Personalized vaccines could also be produced with genetically engineered bacteria, but bacteria-grown vaccines aren't ideal, either.

“The plant system has some advantages,” said Levy, who is also a member of the Stanford Cancer Center and a Howard Hughes Medical Institute investigator.

The researchers chose tobacco plants that were genetically engineered to reproduce quantities of the vaccine. To make a tobacco plant churn out a human antibody, scientists isolate the antibody from the patient's tumor and put the antibody gene into a modified version of the tobacco mosaic virus. They infect a tobacco plant with the gene-carrying virus by scratching the virus on its leaves. The virus takes the gene into the plant's cells, which then churn out lots of antibody. After a few days, technicians snip off the plant's leaves, grind them up and purify the antibody. Only a few plants are needed to make enough vaccine for each patient.

“The new manufacturing system allows very rapid production of a vaccine,” said Charles Arntzen, PhD, a professor of plant biology at the Arizona Biodesign Institute at Arizona State University, who was not involved in the research. “I think without the speed, it would be hard to convince a cancer patient to wait for a vaccine to be developed, rather than going on some other therapy.”

“It's pretty cool technology,” Levy said. “And it's really ironic that you would make a treatment for cancer out of tobacco. That appealed to me.” None of the harmful chemicals found in cigarettes end up in the purified vaccines.

Not only is the technology fast, cheap and safe, but Levy said there's reason to expect that the plant-grown antibodies will generate a stronger immune response than those made in animal cells. Both plant and animal cells attach sugars to antibodies and other proteins during biochemical processing, but the plant and animal sugars are different. The difference might prompt a more robust immune response to plant-grown antibodies, Levy said.

The next research step is a phase-2 clinical trial to test the effectiveness of plant-grown vaccines in a larger group of lymphoma patients, Levy said. He's optimistic, adding, “We know that if you get the immune system revved up, it can attack and kill cancer.”

*The research team included scientists from Stanford, Touro University in Vallejo, Calif., and the biotechnology companies Large Scale Biology Corp., CBR International Corp., Bayer HealthCare, Integrated Biomolecule Corp., The Biologics Consulting Group Inc. and Holtz Biopharma Consulting.*

*The study was funded by a grant from the National Institutes of Health and by Large Scale Biology Corp.*

## Memory impairment associated with sound processing disorder

Mild memory impairment may be associated with central auditory processing dysfunction, or difficulty hearing in complex situations with competing noise, such as hearing a single conversation amid several other conversations, according to a report in the July issue of Archives of Otolaryngology–Head & Neck Surgery, one of the JAMA/Archives journals.

“Central auditory processing dysfunction is a general term that is applied to persons whose hearing in quiet settings is normal or near normal yet who have substantial hearing difficulty in the presence of auditory stressors such as competing noise and other difficult listening situations,” the authors write as background information in the article. “Central auditory testing is important in evaluating individuals with hearing difficulty, because poor central auditory ability, per se, is not helped by amplification and requires alternative rehabilitation strategies.” Previous studies have shown that central auditory processing is impaired in individuals with Alzheimer's disease and other types of dementia.

George A. Gates, M.D., of the University of Washington, Seattle, and colleagues assessed 313 individuals (average age 80 years) participating in a dementia surveillance program that began in 1994. These included 17 individuals who had been diagnosed with dementia, 64 with mild memory impairment but without a dementia diagnosis and 232 controls without memory loss.

Participants completed three tests designed to gauge central auditory processing: one in which nonsense sentences are read over the background of an interesting narrative and two in which separate sentences or numbers are read into each ear simultaneously. “These central auditory processing test paradigms evaluate how well an individual manages competing signals, a task that requires adequate short-term memory and the ability to shift attention rapidly,” the authors write.

Average scores on central auditory processing tests were significantly lower in the group with dementia and in the group with mild memory impairment than in the control group without memory problems. The association remained significant following adjustment for age and hearing status.

“Central auditory function was affected by even mild memory impairment,” the authors write. “We recommend that central auditory testing be considered in the evaluation of older persons with hearing complaints as part of a comprehensive, individualized program to assist their needs in both the aural rehabilitative and the cognitive domains.”

*(Arch Otolaryngol Head Neck Surg. 2008;134[7]:771-777. Available pre-embargo to the media at www.jamamedia.org.)*

***Editor's Note:*** *This research project was supported by a grant form the National Institute of Deafness and Other Communication Disorders and by a grant from the National Institute on Aging. Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.*

## Controlling nitrogen pollution will not stop toxic algae blooms, says research

**by Ileiren Poon**

July 22, 2008 - Edmonton - Research from the University of Alberta has confirmed that algae blooms, which can poison lakes and kill fish, can be controlled by limiting phosphorus.

After completing one of the longest running experiments ever done on a lake, researchers from the U of A, the University of Minnesota and the Freshwater Institute, say nitrogen control won't be effective in controlling the growth of blue-green algae and, in fact, may actually increase the problem.

“What we found goes against the practices of the European Union and many scientists around the world. Controlling nitrogen does not correct the polluted lakes, and in fact, may actually aggravate the problem and make it worse,” said David Schindler, professor of ecology at the U of A, and one of the leading water researchers in the world.

The dramatic rise in cultural eutrophication-the addition of nutrients to a body of water due to human activity-has resulted from increased deposits of nutrients to lakes, largely from human sewage and agricultural wastes. Scientists around the world have been looking at limiting nitrogen as a way to control the algae outbreaks that result from this over fertilization, but the new research suggests that might not be the best way to go.

The trick is to focus regulation on phosphorus, says Schindler. “Of the three major elements that algae needs, phosphorus is the only one that it can't get directly from the atmosphere. There's a little bit in geology and little bit in rainfall, but not much. It's basically a rockbound element.”

For 37 years, the researchers have looked at Lake 227, a small lake in the Canadian Shield at the Experimental Lakes Area (ELA) in Ontario, and examined the best ways to control the cultural eutrophication process by varying the levels of phosphorous and nitrogen added to the lake.

"We have kept that lake in a state of eutrophication, even though we stopped adding nitrogen 16 years ago because we couldn't afford it," said Schindler. "The lake has shown absolutely no decline in algal blooms without the added nitrogen."

"These algae blooms are a phenomenon of the last 100 years and largely the last 50 years," said Schindler. "Algae are plants, and we all know what happens when you apply phosphorus and nitrogen to plants in our yards. And while we like lush plants in our years, we don't like it in the water."

A previous study, entitled, "A Survey of the State of the World's Lakes," found that the cultural eutrophication of lakes has had a global effect. The percentage of lakes with cultural eutrophication on each were shown in the study: Asia has 54 per cent; Europe has 53 per cent; North America has 48 per cent; South America has 41 per cent, and Africa has 28 per cent.

"The damage to these lakes is a major concern for virtually every continent," said Schindler.

The impact on human society is immense he says, as cultural eutrophication severely reduces water quality, which not only kills and contaminates fish, shellfish and other animals, but also can become a health-related problem in humans once it begins to interfere with drinking water treatment.

*This study appears in the journal Proceedings of the National Academy of Sciences.*
*Address of this ExpressNews article: http://www.expressnews.ualberta.ca/article.cfm?id=9496*

## Beijing pollution may trigger heart attacks, strokes

### *Dirty air spurs blood clots*

CHICAGO -- Olympic athletes aren't the only ones who need to be concerned about the heavily polluted air in Beijing. The dirty air may trigger serious cardiovascular problems for some spectators.

Two researchers in pulmonary medicine and critical care at Northwestern University's Feinberg School of Medicine warn that for people in certain risk groups, breathing high levels of pollution can cause heart attacks and strokes within 24 hours of exposure and increase the possibility of having blood clots in their legs on the plane home.

The people who are vulnerable include those who already have known cardiovascular disease or risk factors for cardiovascular disease such as high blood pressure, high cholesterol, diabetes, obesity, lung disease, a current smoking habit or a family member diagnosed with heart disease before age 55.

"If the air quality is bad, you are more likely to have serious heart disease related events," said Gokhan Mutlu, MD, assistant professor of medicine at the Northwestern's Feinberg School and a physician at Northwestern Memorial Hospital. "Being exposed to higher levels of pollution may unmask heart disease even if you've never had any symptoms."

**Why Pollution Causes Heart Attacks, Strokes And Blood Clots**

Mutlu published research in 2007 that showed how pollution triggers heart attacks and strokes. He discovered that microscopic air pollution -- particles less than one-tenth of the diameter of a human hair -- makes the blood thicker and sticky. He found when lungs are inflamed by pollution, they secrete a substance, interleukin-6, which causes an increased tendency for blood to clot.

Previous studies have shown that thousands of people in the U.S. die from strokes and heart attacks within 24 hours of a spike in microscopic pollution from the exhaust of diesel trucks, buses and coal-burning factories.

A more recent study has shown that people who live in polluted areas are more likely to have blood clots in their legs. Traveling long distances by car or plane is known to put people at risk for these clots.

"If you spend a few weeks in Beijing, your blood might become thicker and sticky and then when you fly 12 hours back to the U.S. that further increases your risk. If clots migrate into the lungs and cause pulmonary embolism, that can kill you," Mutlu warned.

**How To Protect Yourself At Olympics**

Scott Budinger, M.D., an associate professor of medicine at Northwestern's Feinberg School and a physician at Northwestern Memorial Hospital, offered several ways for people to lower their risk at the Olympics.

1. Men over 40 should take an aspirin each day to prevent their blood from becoming thick and sticky. While the benefits of aspirin are less certain for women, he said it probably wouldn't hurt for them to take one, too.
2. Stay indoors during traffic rush-hour periods. "Indoor air pollution levels are always much lower than outdoor, so staying inside will limit your exposure," Budinger said. He cautioned that Beijing's definition of mild pollution would be a pollution alert day in the U.S.
3. On the plane, especially the return flight, frequently walk up and down the aisles and do leg exercises in your seat to prevent blood from pooling in the legs and clots from forming.

*For information on Dr. Mutlu's and Dr. Budinger's study visit:*
*http://www.northwestern.edu/newscenter/stories/2007/09/mutlu.html*
*AUDIO: http://www.northwestern.edu/newscenter/multimedia/2008/07/beijing.html*

## Scientists figure out how the immune system and brain communicate to control disease

MANHASSET, NY – In a major step in understanding how the nervous system and the immune system interact, scientists at The Feinstein Institute for Medical Research have identified a new anatomical path through which the brain and the spleen communicate. The spleen, once thought to be an unnecessary bit of tissue, is now regarded as an organ where important information from the nervous reaches the immune system. Understanding this process could ultimately lead to treatments that target the spleen to send the right message when fighting human disease.

Mauricio Rosas-Ballina, MD, working with colleagues in the laboratory of Kevin J. Tracey, MD, figured out that macrophages in the spleen were making tumor necrosis factor, a powerful inflammation-producing molecule. When they stimulated the vagus nerve, a long nerve that goes from the base of the brain into thoracic and abdominal organs, tumor necrosis factor (TNF) production in the spleen decreased. This study complements previous research performed in Dr. Tracey's laboratory, which showed that stimulation of the vagus nerve increases survival in laboratory models of sepsis.

The findings were published today in the Proceedings of the National Academy of Sciences. Many laboratories at The Feinstein Institute study the immune system in health and in disease. Every year, about 500,000 people develop severe sepsis, a syndrome triggered when the body's immune system wages an attack on the body that is well beyond its normal response to an invader. Sepsis kills about 225,000 deaths in the United States each year.

A hundred years ago, the spleen (located in the upper quadrant of the abdomen) was thought to be only reservoir for blood. It has only been in recent years that scientists discovered that the spleen is a manufacturing plant for immune cells, and a site where immune cells and nerves interact. The spleen defends the body against infection, particularly encapsulated bacteria that circulate through the blood.

The hope is to modulate other immune functions like antibody production through the spleen (via vagus nerve stimulation) as a way to modify the course of infections and possibly some autoimmune disorders.

Dr. Rosas-Ballina began following the winding path of the vagus nerve to establish the route it follows to reach the spleen. He was trying, without much luck, to find fibers of the vagus nerve in this organ. And then he went a little further south to the splenic nerve, the nerve that innervates the spleen. Their results indicate that the vagus nerve inherently communicates with the splenic nerve to suppress TNF production by macrophages in the spleen.

According to the prevailing paradigm, the autonomic nervous system is anatomically and functionally divided in sympathetic and parasympathetic branches, which act in opposition to regulate organ function. “The division between the parasympathetic and sympathetic nervous systems is not clear cut,” said Dr. Rosas-Ballina, explaining that the vagus nerve (the major parasympathetic nerve) acts through the splenic nerve to modulate immune function. He said that results of this study suggest that there may be two separate ways the brain communicates with the spleen to regulate immune function. This points the way to a possible solution for treating sepsis. It may be more effective to take advantage of the central nervous system to control cells of the spleen. This way, “you know where the treatment is going,” said Dr. Rosas-Ballina.

## Cranberry juice creates energy barrier that keeps bacteria away from cells, study shows

### *Results help explain how cranberry juice can prevent urinary tract infections*

WORCESTER, Mass. – For generations, people have consumed cranberry juice, convinced of its power to ward off urinary tract infections, though the exact mechanism of its action has not been well understood. A new study by researchers at Worcester Polytechnic Institute (WPI) reveals that the juice changes the thermodynamic properties of bacteria in the urinary tract, creating an energy barrier that prevents the microorganisms from getting close enough to latch onto cells and initiate an infection.

The study, published in the journal Colloids and Surfaces: B, was conducted by Terri Camesano, associate professor of chemical engineering at WPI, and a team of graduate students, including PhD candidate Yatao Liu. They exposed two varieties of E. coli bacteria, one with hair-like projections known as fimbriae and one without, to different concentrations of cranberry juice. Fimbriae are present on a number of virulent bacteria, including those that cause urinary tract infections, and are believed to be used by bacteria to form strong bonds with cells.

For the fimbriaed bacteria, they found that even at low concentrations, cranberry juice altered two properties that serve as indicators of the ability of bacteria to attach to cells. The first factor is called Gibbs free energy of attachment, which is a measure of the amount of energy that must be expended before a bacterium can attach to

a cell. Without cranberry juice, this value was a negative number, indicating that energy would be released and attachment was highly likely. With cranberry juice the number was positive and it grew steadily as the concentration of juice increased, making attachment to urinary tract cells increasingly unlikely.

Surface free energy also rose, suggesting that the presence of cranberry juice creates an energy barrier that repels the bacteria. The researchers also placed the bacteria and urinary tract cells together in solution. Without cranberry juice, the fimbriaed bacteria attached readily to the cells. As increasing concentrations of cranberry juice were added to the solution, fewer and fewer attachments were observed.

Cranberry juice had no discernible effect on E. coli bacteria without fimbriae, suggesting that compounds in the juice may act directly on the molecular structure of the fimbriae themselves. This reinforces previous work by the WPI team that showed that exposure to cranberry juice alters the shape of the fimbriae, causing them to become compressed. Using an atomic force microscope as a minute strain gauge, the team also showed that the adhesive force exerted by bacteria on urinary tract cells declined in direct proportion to the concentration of cranberry juice in the solution.

"Our results show that, at least for urinary tract infections, cranberry juice targets the right bacteria—those that cause disease—but has no effect on non-pathogenic organisms, suggesting that cranberry juice will not disrupt bacteria that are part of the normal flora in the gut," Camesano says. "We have also shown that this effect occurs at concentrations of cranberry juice that are comparable to levels we would expect to find in the urinary tract."

Camesano notes that unpublished work has shown that while cranberry juice has potent effects on disease-causing bacteria, those effects are transitory. "When we takes E. coli. bacteria that have been treated with cranberry juice and place them in normal growth media, they regain the ability to adhere to urinary tract cells," she says. "This suggests that to realize the antibacterial benefits of cranberry, one must consume cranberry juice regularly—perhaps daily."

For those watching calories, Camesano says other recent work in her lab has shown that the effects of regular cranberry juice cocktail and diet (sugar-free) cranberry juice are identical. "That's good news for people who do not like to consume a lot of sugary juice," she says.

## Scientists identify how gastric reflux may trigger asthma

DURHAM, N.C. – Researchers at Duke University Medical Center appear to have solved at least a piece of a puzzle that has mystified physicians for years: why so many patients with asthma also suffer from GERD, or gastroesophageal reflux disease.

Clinicians first noted a relationship between the two diseases in the mid-1970s. Since then, studies have shown that anywhere from 50 to 90 percent of patients with asthma experience some aspect of GERD. But can GERD cause asthma, or, is it the other way around? Perhaps there is some shared mechanism at the root of both disorders causing them to arise together. Physicians could make a case for each scenario, but until now, the exact nature of the relationship was not clear.

Working in laboratory experiments with mice, Dr. Shu Lin, an assistant professor of surgery and immunology at Duke, discovered that inhaling tiny amounts of stomach fluid that back up into the esophagus – a hallmark of GERD – produces changes in the immune system that can drive the development of asthma.

In the experiments, researchers inserted miniscule amounts of gastric fluid into the lungs of mice (mimicking the human process of micro-aspiration, or breathing in tiny amounts) over a period of eight weeks. They compared these animals' immune systems with those of mice that were exposed to allergens but not the gastric fluid.

The immune systems of the two sets of mice responded very differently. Those that had the gastric fluid in their lungs developed what researchers call a T-helper type 2 response, a type of immune system reaction characteristic of asthma. The other mice responded in a more balanced manner, mounting an immune reaction consisting of both T-helper type 1 and T-helper type 2 responses.

"This is the first experimental evidence in a controlled, laboratory setting linking these two very common conditions in humans," says Lin, the senior author of the study published online in the European Journal of Clinical Investigation. "These data suggest that chronic micro-aspiration of gastric fluid can drive the immune system toward an asthmatic response."

"This does not mean that everyone with GERD is going to develop asthma, by any means," says William Parker, an assistant professor of surgery at Duke and a co-author of the study. "But it may mean that people with GERD may be more likely to develop asthma. If there is an upside to this, it is that developing GERD is something we can pretty much treat and control."

Parker says poor diet, a lack of exercise and obesity all contribute to the development of GERD, and that rising rates of reflux disease are part of a "perfect storm" of environmental and behavioral factors driving

escalating rates of asthma, particularly in Western cultures. “People should avoid the risk factors for GERD. We strongly believe that the rise in asthma, particularly among adults in the country, is in large measure due to lifestyle choices that can be changed.”

Lin and Parker agree that much more work needs to be done to fully understand the cellular and molecular mechanisms involved in the relationship between reflux disease and asthma, but both feel their study offers new directions for developing additional treatment options for both problems.

Lin says patients who already have GERD can minimize gastric reflux – and thereby lessen their chances of developing asthma – by following a few simple guidelines: Eat smaller meals and eat several hours before going to bed; raise the head of the bed a few inches; maintain a healthy weight; and limit fatty goods, coffee, tea, caffeine and alcohol – they can relax the esophageal sphincter and make reflux more likely.

*Funding for the study came from the Society of American Gastrointestinal Endoscopic Surgeons Research Grant and the Parks Protocol Memorial Fund.*

*Additional co-authors from Duke include lead author Andrew Barbas, Tacy Downing, Keki Balsara, Hung-Enn Tan, Gregory Rubinstein, Zoie Holzknecht, Bradley Collins and R. Duane Davis.*

## Researchers probe geographical ties to ALS cases among 1991 Gulf War veterans

DURHAM, N.C. -- Researchers from Duke University, the University of Cincinnati (UC) and the Durham Veterans Administration Medical Center are hoping to find a geographical pattern to help explain why 1991 Gulf War veterans contracted the fatal neurological disease amyotrophic lateral sclerosis (ALS) at twice the normal rate during the decade after the conflict.

By layering military records of troop locations onto Gulf-area maps, “we've found there were some areas of service where there appears to be an elevated risk,” said Marie Lynn Miranda, an associate professor at Duke's Nicholas School of the Environment whose group uses geographic information systems (GIS) to study environmental health problems.

Also known as Lou Gehrig's Disease because it crippled and ultimately killed that baseball great in 1941, ALS causes cellular degeneration in the central nervous system. Its cause is unknown.

“There are no reports on the occurrence of ALS among veterans of other conflicts,” the researchers wrote. “There is only a single report that suggests ALS may arise from environmental exposures associated with military service, per se.” The cases assessed by Miranda and her colleagues occurred within a group of people who are expected to be at low risk for ALS, because they're mostly under the age of 45.

Miranda is the first author of a report on an initial analysis now published online in the research journal NeuroToxicology. The work was funded by the Department of Veterans Affairs Cooperative Studies Program.

The report's senior author is Ronnie Horner, professor and director of the department of public health at Cincinnati, who led research that first documented twice-normal ALS rates among vets of the first Persian Gulf War in an article published in the September 2003 issue of the journal Neurology.

Horner's group is now assessing possible exposures vets might have had in the Gulf region that could explain the higher ALS rates its 2003 study found.

“As one of the largest contemporary set of cases, it presents a real opportunity to identify clues as to the cause of ALS not only for veterans of the first Gulf War but, perhaps, for ALS generally,” Horner said. UC researchers are coordinating their investigations with those of researchers at the Durham, N.C. Veterans Medical Center and nearby Duke Medical Center.

Another UC-led study, published in the July 2008 issue of the journal Neuroepidemiology, found that the risk for developing ALS has now decreased among 1991 Gulf War vets. That suggests that the cause or causes of the ALS had something to do with their deployment in the region between August 1990 and July 1991.

Of the 135 cases diagnosed among the vets within 11 years after the war, only three had a family history of the disease. The small numbers might indicate that there is an environmental cause for ALS, the authors added.

“In the one-year period of military operations, some deployed military personnel experienced numerous exposures to multiple, potentially neurotoxic agents,” Miranda and coauthors wrote in the new report. “If the array of possible candidate environmental exposures could be reduced, it may be possible to identify or at least focus inquiry on specific potential causative agents.”

To narrow down the possibilities, Miranda and fellow investigators used GIS analysis, which allows researchers to layer different kinds of information onto maps to deduce potential risks.

They began by searching Department of Veterans Affairs and Department of Defense records as well as other sources to identify military personnel diagnosed with ALS after 1991. Department of Defense data also allowed the researchers to identify the military units these veterans with ALS served in during their deployment to the Persian Gulf region.

In a separate analysis, the researchers identified troop units known to have been exposed to emissions from a munitions storage area at Khamisayah, Iraq. Those munitions were destroyed by U.S. forces in March 1991, and a United Nations commission later found many rockets there had been loaded for chemical warfare.

A previous Defense Department modeling study deduced that "some 90,000 veterans may have been exposed to low levels of nerve agent" at Khamisayah, the new report said.

The GIS mapping revealed that "there were some areas where there appeared to be an elevated risk," Miranda said. To narrow down the possibilities, she and co-investigators then used statistical methods that assess the "best guess about the likelihood that space matters" for each grid of Gulf territory, she added.

Applying those statistics, the likelihood of a spatial connection with ALS development "climbed as high as 91 percent" in some grid cells, she said, most notably in a region southeast of Khamisayah. But Miranda cautioned that she will need to do additional analyses that add "time" to "place" before she can be more specific.

For instance, the researchers will want to know whether the ALS victim's units were in the path of emissions from Khamisayah on a specific day. Miranda and her colleagues are also interested in examining environmental exposures that may be associated with smoke plumes from oil well fires.

*Other authors of the new NeuroToxicology report include Miranda's Nicholas School colleagues M. Alicia Overstreet Galeano and Eric Tassone as well as Kelli Allen, a research health scientist at the Durham VA Medical Center and a Duke assistant research professor of medicine*

## Onion washing gets monkeys in a lather

* 15:15 21 July 2008

* NewScientist.com news service

*** Matt Kaplan**

If you wash yourself with raw onion, you might expect some aggression from your friends. Now it seems the same holds true of some primates – but for rather different reasons.

For capuchin monkeys, rubbing themselves with pungent-smelling plants is normally a communal and perhaps even a therapeutic activity.

Wild capuchins are known to get together and rub their fur with plants like citrus and peppers that have antifungal or antiseptic properties.

***Experts thought capuchin monkeys like to rub themselves with plants as simple medicine, but the onion rub changed behaviour*** **(Image: Ruth Woodward)**

Some biologists think that the behaviour is medicinal, and that the monkeys are ridding themselves of parasites with their plant rubs. But until now no-one had looked to see what happens after the communal rubs.

Annika Paukner and Stephen Suomi at the National Institute of Child Health and Human Development in Poolesville, Maryland, observed 15 captive capuchins who liked to rub themselves with yellow onions – which also contain high levels of antifungal or antiseptic compounds.

**Rebellion in the ranks?**

They watched what happened after giving the monkeys either onion or apple as a control, five times a week for five months.

The researchers found that while the capuchins were very social with one another during the onion washing, this polite behavior vanished afterwards, and levels of aggression increased.

Capuchins are thought to signal their relative ranking in the colony by urinating on their hands and feet, so the smell of the onion might be overpowering that signal, says Paukner.

"We think the scent of onions may make detecting the scent of urine difficult or even impossible, which may cross wires in the capuchin social circles and explain the increased aggression," she says.

*Journal Reference: Journal of Primatology (DOI: 10.1002/ajp.20595)*

## Toy rocket inspires variable-speed bullets

* 16:43 21 July 2008

* NewScientist.com news service

*** David Hambling**

A gun that fires variable speed bullets and which can be set to kill, wound or just inflict a bruise is being built by a US toy manufacturer. The weapon is based on technology used to propel toy rockets.

Lund and Company Invention, a toy design studio based near Chicago, makes toy rockets that are powered by burning hydrogen obtained by electrolysing water. Now the company is being funded by the US army to adapt the technology to fire bullets instead.

The US Army are interested in arming soldiers with weapons that can be switched between lethal and non-lethal modes. They asked Company Invention to make a rifle that can fire bullets at various speeds.

**Sniper version**

The new weapon, called the Variable Velocity Weapon System or VWS, lets the soldier to use the same rifle for crowd control and combat, by altering the muzzle velocity. It could be loaded with “rubber bullets” designed only to deliver blunt impacts on a person, full-speed lethal rounds or projectiles somewhere between the two.

Bruce Lund, the company's CEO, says the gun works by mixing a liquid or gaseous fuel with air in a combustion chamber behind the bullet. This determines the explosive capability of the propellant and consequently the velocity of the bullet as it leaves the gun. “Projectile velocity varies from non-lethal at 10 metres, to lethal at 100 metres or more, as desired,” says Lund.

The company says that the weapon produces less heat and light than traditional guns. It can also be made lighter and could have a high power setting for long-range sniping.

Police already fire non-lethal projectiles from standard shotguns. These are known as “beanbag” rounds, bags of lead shot which will knock down a suspect at ranges of up to 10 metres. They are termed “non-lethal”, but can cause bruising or even broken ribs.

**'Handgun to Howitzer'**

Lund says that the new weapon system will use different types of bullet for lethal and non-lethal use. Police forces already use separate shotguns for non-lethal loads – typically marking them with bright orange tape to prevent any confusion – so this shouldn't be an issue.

The existing VWS design is a .50 calibre (12.7 mm) rifle weapon, but Lund says the technology can be scaled to any size, “handgun to Howitzer”.

Steve Wright, a security expert at Leeds Metropolitan University, UK warns of the potential risk of variable lethality.

“In a high-stress, high-personal-risk zone, there will be a real temptation for soldiers to turn the tuneable lethality switch up to 'kill' mode so that all doubt is removed.”

A demonstration version will be ready within six months, and the VWS could go into production within 18 months of approval, according to Lund and Company.

## Plankton turn tropical Atlantic into a huge carbon sink

* 22:00 21 July 2008

* NewScientist.com news service

*** Bob Holmes**

A seasonal bloom of ocean plankton fertilised by the Amazon river pulls much more carbon dioxide out of the atmosphere than researchers had previously supposed.

The unexpected bloom may, in fact, be enough to turn the tropical Atlantic Ocean from a net source of atmospheric carbon into a net sink.

Ajit Subramaniam, an oceanographer at Lamont-Doherty Earth Observatory in Palisades, New York, and his colleagues sampled phytoplankton in the plume of water extending from the mouth of the Amazon into the Atlantic.

To their surprise, they found that for much of the year the offshore waters support a thriving plankton population that converts atmospheric nitrogen into biologically usable forms.

This nitrogen fixation allows the plankton to escape the restrictions of the nitrogen-poor Amazon and thrive on its other nutrients, especially phosphorus and silicon.

The result is a rapid uptake of carbon dioxide by the photosynthetic plankton.

**'Major shift'**

Moreover, much of this carbon ends up in long-term storage instead of being recycled quickly like most carbon in the ocean. That's because the main photosynthesisers are diatoms, single-celled algae that build a heavy silica shell around their bodies.

This glassy shell makes diatoms sink rapidly after they die, removing 20 million tonnes of carbon from the atmosphere each year, the researchers estimate.

That's not much compared to the amount emitted by human activity each year but it represents a major shift in our knowledge of the oceans' carbon balance, says Subramanian. And although the Amazon is the largest of the world's rivers, other major tropical rivers such as the Congo and the Orinoco may have similar effects, he says – a conjecture he is now aiming to test.

“I think the value of this work is not so much in figuring out how we can use it to humankind's advantage, but in figuring out that the major rivers of the world may be helping to balance the CO2 inventory of the planet in ways we haven't realised before,” says David Karl, an oceanographer at the University of Hawaii.

Even so, the Amazon's major contribution suggests that proposals to artificially fertilise the ocean to enhance carbon uptake may pay off surprisingly well in tropical waters, says Subramaniam.

*Journal reference: Proceedings of the National Academy of Sciences (DOI: 10.1073/pnas.0710279105)*

## Minimally invasive treatment improves male fertility

OAK BROOK, Ill. – A minimally invasive treatment for a common cause of male infertility can significantly improve a couple's chances for pregnancy, according to a new study published in the August issue of Radiology. The study, conducted at the University of Bonn in Germany, also found that the level of sperm motility prior to treatment is a key predictor of success.

"Venous embolization, a simple treatment using a catheter through the groin, can help to improve sperm function in infertile men," said lead author Sebastian Flacke, M.D., Ph.D., now an associate professor of radiology at the Tufts University School of Medicine, director of noninvasive cardiovascular imaging and vice chair for research and development in the department of radiology at the Lahey Clinic in Burlington, Mass. "With the patients' improved sperm function, more than one-quarter of their healthy partners were able to become pregnant."

Normally, blood flows to the testicles and returns to the heart via a network of tiny veins that have a series of one-way valves to prevent the blood from flowing backward to the testicles. If the valves that regulate the blood flow from these veins become defective, blood does not properly circulate out of the testicles, causing swelling and a network of tangled blood vessels in the scrotum called a varicocele, or varicose vein.

Varicoceles are relatively common, affecting approximately 10 percent to 15 percent of the adult male population in the U.S. According to the National Institutes of Health, most cases occur in young men between the ages of 15 and 25. Many varicoceles cause no symptoms and are harmless. But sometimes a varicocele can cause pain, shrinkage or fertility problems.

The traditional treatment for problematic varicoceles has been open surgery, but recently varicocele embolization has emerged as a minimally invasive outpatient alternative. In the procedure, an interventional radiologist inserts a small catheter through a nick in the skin at the groin and uses x-ray guidance to steer it into the varicocele. A tiny platinum coil and a few milliliters of an agent to ensure the occlusion of the gonadic vein are then inserted through the catheter. Recovery time is minimal, and patients typically can return to work the next day.

Dr. Flacke and colleagues set out to identify predictors of pregnancy after embolization of varicoceles in infertile men. The study included 223 infertile men, ages 18-50, with at least one varicocele. All of the men had healthy partners with whom they were trying to achieve a pregnancy.

In the study, 226 of the patients' 228 varicoceles were successfully treated with embolization. A semen analysis performed on 173 patients three months after the procedure showed that, on average, sperm motility and sperm count had significantly improved. Six months later, 45 couples, or 26 percent, reported a pregnancy. A high level of sperm motility before the procedure was identified as the only significant pre-treatment factor associated with increasing the odds of successful post-treatment pregnancy.

"Embolization of varicoceles in infertile men may be considered a useful adjunct to in-vitro fertilization," Dr. Flacke said.

*"Embolization of Varicoceles: Pre-treatment Sperm Motility Predicts Later Pregnancy in Partners of Infertile Men." Collaborating with Dr. Flacke were Michael Schuster, M.D., Attila Kovacs, M.D., Marcus von Falkenhausen, M.D., Holger M. Strunk, M.D., Gerhard Haidl, M.D., and Hans Schild, M.D. Journal attribution requested.*

**Personal Health**

## Health 'Facts' You Only Thought You Knew

**By JANE E. BRODY**

In 45 years of writing about medicine and health, I've heard more than my share of myths and misinformation, from the merely nonsensical to the downright dangerous. And until I explored the evidence, I too occasionally fell for a "fact" that turned out to be less than met the eye.

Lately a number of medical writers have taken on these commonplaces and old wives' tales.

Last year, Anahad O'Connor, who does so every week in his "Really?" column for Science Times, published "Never Shower in a Thunderstorm: Surprising Facts and Misleading Myths About Our Health and the World We Live In" (Times Books).

Now, Dr. Nancy L. Snyderman, a surgical oncologist at the University of Pennsylvania and a medical correspondent for NBC News, has a new book, "Medical Myths That Can Kill You — And the 101 Truths That Will Save, Extend, and Improve Your Life" (Crown).

The following myths owe something to both authors, and also to my own research. How well informed are you?

**Drink Eight Glasses Of Water A Day** I had long believed that eight glasses of plain water or caffeine-free beverages a day were important to keep the body hydrated and to prevent constipation. Perhaps the toilet paper manufacturers were behind this notion. Researchers have been unable to find scientific support for it.

The Institute of Medicine recently noted that you can meet your body's need for liquids in many ways, including drinking coffee and tea (with or without caffeine) and eating fruits and vegetables with a high water content. Two clues that you may need to drink more are thirst and the color of your urine, which should be clear like, well, water.

If you are physically very active, especially in hot weather, repeatedly sipping cold water is helpful. But beyond two quarts, you may need to also replace the salts lost in sweat — for example, by drinking a diluted sports drink or eating foods with salt and potassium.

**Poison Ivy Is Contagious** The rash of poison ivy cannot be spread from person to person or even to another part of the body unless the plant's resin is still on your hands or clothes. The rash, a contact dermatitis, may seem to spread because it often develops sequentially, depending on when and where the skin was exposed. Scratching does not spread the rash but can prolong it and cause an infection.

Over-the-counter anti-itch lotions and creams are not helpful, and those containing an antihistamine, like Benadryl, may complicate matters by causing an allergic reaction. The rash is best treated with a steroid, topically with hydrocortisone or, in more severe cases, orally with prednisone. Apply a cool wet wash cloth to oozing blisters to speed drying.

Mango skin contains a less potent form of urushiol, the allergen in poison ivy, and you can develop a rash around the mouth if you eat the flesh off the rind.

Those who think they are immune to poison ivy should know that sensitivity develops through repeated exposure.

**Use Cotton Swabs To Clean Your Ears** Bellybuttons, perhaps, but not ears. My son wishes he had known this years ago, before his 2-year-old son copied his dad and punctured his eardrum with a Q-tip. The hole was so big it needed surgical repair.

Dr. Snyderman points out that a cotton swab can push wax farther into the ear, causing impaction and diminished hearing. I've long supported the medical adage: Put nothing smaller than an elbow in your ear. If accumulated wax is a problem, try ear wax softening drops or have your ears professionally cleaned now and then.

**Don't Swim After Eating** My parents repeatedly warned us to wait an hour after a meal. It might have been good advice if I was planning to race, swim a long distance or battle a stiff current. Strenuous exercise on a full stomach is never a good idea, because it can result in stomach or muscle cramps. But experts find no harm in a gentle plunge or casual play in the water (pool or ocean) soon after eating.

What can be hazardous is swimming after drinking alcohol, because it can impair judgment and encourage undue risk-taking.

**Shaving Makes Hair Grow Back Faster And Coarser** This myth persists even though a study conducted 80 years ago disproved it. Hair that is shaved is dead, and shaving has no effect on the speed of regrowth, which comes from the living hair follicles below the skin's surface. The new growth may appear darker since it hasn't been exposed to the sun or chemicals for very long. Also, it may seem coarser since the ends have not been tapered by wear and tear.

**Colon Cleansing Washes Out Poisons** Colonics, as the practice is called, has no known medical value and risks damage to the rectum or bowel. The bowel is not "dirty" and, unless disease or medication interfere, nature does a fine job of clearing out wastes. If you are concerned about unwholesome substances in your body, drink lots of water to help your body get rid of them.

**Natural Is Safer Than Man-Made** A woman recently asked me if it was safe to take "bioidentical hormone replacements." These, I'm afraid, are estrogens, and there is no reliable evidence to support claims that they are safer than the ones made by chemists that have been linked to an increased risk of cancer and heart disease.

Remember, nature has produced some of the most dangerous substances known, including arsenic and botulinum toxin. And chemists have produced medications that can control or cure many life-threatening ills. Many important medications are derived from natural substances that not only have druglike actions but also druglike side effects.

Only carefully controlled clinical trials can assure the safety of a natural or man-made drug, and few natural substances have been tested in this way.

**Take Painkillers Only For Serious Pain** In a doctor's waiting room the other day, a woman sat groaning for an hour and a half before she finally asked the nurse for an over-the-counter pain pill to relieve her headache.

Although many people see pills as the answer to every ill, others avoid medications at all costs, much to their disadvantage.

Pain medication works best if taken at the first hint of pain, and may not work well at all if you wait too long. Dr. Snyderman says to consider taking it before engaging in an activity, like heavy-duty gardening or chopping wood, that is likely to cause pain later. Before I had my arthritic knees replaced, I downed two ibuprofen tablets before every tennis match.

## Hoping Two Drugs Carry a Side Effect: Longer Life

**By NICHOLAS WADE**

BOSTON, Mass. — One day last month, clad in white plastic garments from head to toe, Dr. David Sinclair showed a visitor around his germ-free mouse room here at Harvard Medical School.

The mice, subjects in studies of health and longevity, are kept in wire baskets under intensive nursing care. A mouse gym holds a miniature exercise machine that tests the rodents' ability to balance on a rotating bar. In a nearby water maze, mice must recall visual cues to swim to safety on a hidden platform, a test of their powers of memory. Those that forget their lessons are rescued as they start to submerge and humanely dried out under a heat lamp, Dr. Sinclair assured his visitor.

**COUNTING CALORIES** ***For a longevity study, this mouse is on a restricted diet.*** **Southern Illinois University School of Medicine**

Dr. Sinclair is a co-founder of Sirtris, a company that itself has been swimming in uncharted waters as it works to develop drugs that may extend the human life span. But it seemed to have found a safe platform last month when it was bought last month by the pharmaceutical giant GlaxoSmithKline for $720 million.

Sirtris has two drugs in clinical trials. One is being tested against Type 2 diabetes, one of the many diseases of aging that the company's scientists hope the drugs will avert. With success against just one such disease, the impact on health "could be possibly transformational," said Dr. Patrick Vallance, head of drug discovery at GlaxoSmithKline.

The new drugs are called sirtuin activators, meaning that they activate an enzyme called sirtuin. The basic theory is that all or most species have an ancient strategy for riding out famines: switch resources from reproduction to tissue maintenance. A healthy diet but with 30 percent fewer calories than usual triggers this reaction in mice and is the one intervention that reliably increases their life span. The mice seem to live longer because they are somehow protected from the usual diseases that kill them.

But most people cannot keep to a diet with a 30 percent cut in calories, so a drug that could activate the famine reflex might be highly desirable. Dr. Leonard Guarente, an M.I.T. biologist who founded the field of sirtuin biology, thinks the famine reflex is mediated through the sirtuin enzymes. Dr. Sinclair, his former student, discovered that sirtuins could be activated by drugs. The most potent activator that emerged from his screens was resveratrol, a natural substance found in red wine, though in amounts probably too low to be significant for health.

The Sirtris drug being tested in diabetic patients is a special formulation of resveratrol that delivers a bloodstream dose five times as high as the chemical alone. This drug, called SRT501, has passed safety tests and, at least in small-scale trials, has reduced the patients' glucose levels.

The other drug is a small synthetic chemical that is a thousand times as potent as resveratrol in activating sirtuin and can be given at a much smaller dose. Safety tests in people have just started, with no adverse effects so far.

The hope is that activating sirtuins in people would, like a calorically restricted diet in mice, avert degenerative diseases of aging like diabetes, heart disease, cancer and Alzheimer's. There is no Food and Drug Administration category for longevity drugs, so if the company is to submit a drug for approval, it needs to be for a specific disease.

Nonetheless, longevity is what has motivated the researchers and what makes the drugs potentially so appealing.

Dr. Christoph Westphal, the chief executive of Sirtris, said of the potential of the drugs, "I think that if we are right, this could extend life span by 5 or 10 percent." He added that his goal was to develop drugs against specific diseases, with the extension of life being "almost a side effect of our medicine."

Sirtris was founded in 2004 after Dr. Westphal, then working at a Boston venture capital firm, approached Dr. Sinclair. Because of widespread interest in the sirtuin activation idea, Dr. Westphal had little difficulty raising money and recruiting distinguished scientists to Sirtris's advisory board.

He later decided to sell the company to GlaxoSmithKline, he said, because it was getting harder to raise money and clinical trials could proceed faster with the larger company's resources. Sirtris was acquired at an 84 percent premium, better than the 50 percent at which most companies are bought, Dr. Westphal said.

The impact of Sirtris's drugs, if successful, could extend beyond the drug industry. Dr. Guarente believes that many people might start taking them in middle age, though after having started a family because they may suppress fertility.

Mice on the drugs generally remain healthy right until the end of their lives and then just drop dead. "If they work in people that way, one would look to an extension of health span, with an extension of life as a possible side effect," Dr. Guarente said. "It would necessitate changing ideas about when people retire and when they stop paying into the system."

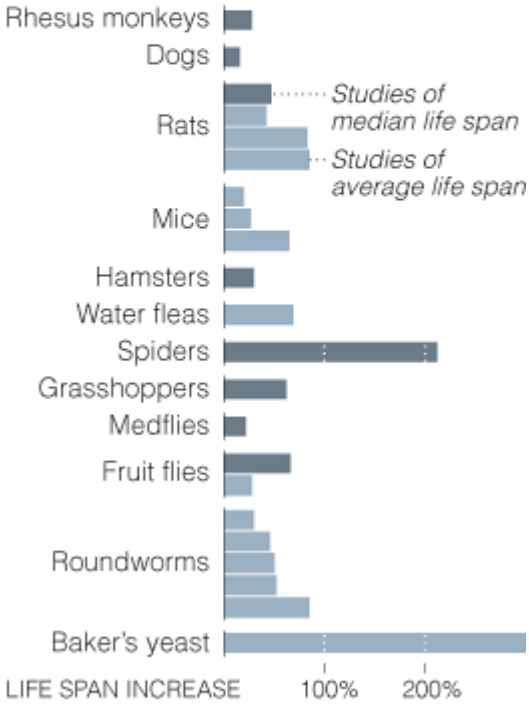
GlaxoSmithKline could put SRT501, its resveratrol formulation, on the market right away, selling it as a natural compound and nutritional pharmaceutical that does not require approval by the F.D.A. "We haven't made any decisions, but that clearly is an option," Dr. Vallance said.

If GlaxoSmithKline decides instead to seek F.D.A. approval, it will need to prove that resveratrol is safe in the large doses required for efficacy. Resveratrol seems to exert many influences on the body, some of which are not exerted through sirtuin. "None of us should be naïve enough to think resveratrol won't have multiple effects, including some you don't want," Dr. Vallance said.

GlaxoSmithKline's purchase of Sirtris has pushed the optimism of sirtuin researchers and others to new heights. "We are all holding our breath," said Dr. Huber Warner, editor of the Journals of Gerontology. But the success of the drugs is far from assured.

**Caloric Restriction**

Most or all species are thought to respond to a prolonged decrease in the number of calories consumed by switching resources from reproduction to tissue maintenance. Below, 22 studies of caloric restriction, using different methods, measured gains in life span in species ranging from monkeys to yeast.




*Source: "Aging and Survival: The Genetics of Life Span Extension by Dietary Restriction," by William Mair and Andrew Dillin* THE NEW YORK TIMES

Most potential drugs fail to make it past clinical trials, and the same may prove true for Sirtris's candidates. The sirtuin-activating chemicals the company has designed could turn out to be toxic. Another uncertainty is that the underlying science is still in flux and debate rages among academic researchers over many details of how caloric restriction works.

Some biologists think that sirtuin is not the only mediator of the famine reflex, and that resveratrol may not work through sirtuin at all in exerting its beneficial effects on mice. "There are data both for and against that hypothesis, though that doesn't dissuade one from pursuing it as a potential benefit," said Dr. Thomas Rando, who studies aging in stem cells at Stanford University.

In initial tests in mice, resveratrol has doubled muscular endurance, lowered the bad form of cholesterol, protected against various bad effects of a high-fat diet and suppressed colon cancer. New reports are confirming some of these benefits, but others are ambiguous or puzzling.

According to a study published on July 3 in the journal Cell Metabolism by Dr. Sinclair and Dr. Rafael de Cabo of the National Institute on Aging, resveratrol given to aging mice reduced their cataracts, strengthened their bones, improved coordination and enhanced their health in several other ways. Yet despite their better health, the mice lived no longer than usual.

"Minimally this calls into question one pillar of the GSK investment," said Dr. Ronald Evans, a leading expert on hormonal responses at the Salk Institute. Dr. Evans said that sirtuin research was promising but unproved, and that he did not agree that sirtuin was the probable mediator of the famine reflex, a concern that "calls into question the second pillar of the GSK investment."

The frontiers of science are often turbulent, and it can take years for clarity to emerge from confusion. Dr. Westphal said the decision to ignore the academic debate about exactly how resveratrol may work was one of two principal reasons for Sirtris's quick success. The other was to focus the company's limited resources on developing just two drugs.

The researchers at Sirtris are no strangers to skepticism. Dr. Guarente and Dr. Sinclair were ridiculed when they first started looking for longevity genes more than 15 years ago, because aging was then considered to be an intractable problem. His colleagues, Dr. Guarente said, "thought I was nuts."

Dr. Sinclair, when he first arrived as a young postdoctoral student in Dr. Guarente's lab to work on longevity, was downcast to learn of the other students' severe doubts. "The view even in Lenny's lab was that this problem was going nowhere, it was a house of cards that would fall down any month now." He called his parents in Australia to tell them he may have made a big mistake. But the research led eventually to the discovery of the sirtuinlike proteins and their role in extending the life span of yeast, worms and flies.

He and Dr. Guarente developed the sirtuin field with the hope of increasing longevity. But because of Sirtris's focus on developing drugs that have the F.D.A.'s approval for specific diseases, both are being less explicit about their hopes of reversing aging. "There's a much greater chance of a drug that can treat disease than of extending life span," Dr. Sinclair said.

"I'm becoming more boring in my old age," he added apologetically.

GlaxoSmithKline's press releases refer to the sirtuins as "enzymes that the company believes control the aging process." But Dr. Vallance is more guarded, saying aging is too hard to measure. The goal is not the extension of human life span; rather, "The prolongation of health is the aim," Dr. Vallance said.

## If You Have a Problem, Ask Everyone

**By CORNELIA DEAN**

John Davis, a chemist in Bloomington, Ill., knows about concrete. For example, he knows that if you keep concrete vibrating it won't set up before you can use it. It will still pour like a liquid.

Now he has applied that knowledge to a seemingly unrelated problem thousands of miles away. He figured out that devices that keep concrete vibrating can be adapted to keep oil in Alaskan storage tanks from freezing. The Oil Spill Recovery Institute of Cordova, Alaska, paid him $20,000 for his idea.

The chemist and the institute came together through InnoCentive, a company that links organizations (seekers) with problems (challenges) to people all over the world (solvers) who win cash prizes for resolving them. The company gets a posting fee and, if the problem is solved, a "finders fee" equal to about 40 percent of the prize.

The process, according to John Seely Brown, a theorist of information technology and former director of the Xerox Palo Alto Research Center, reflects "a huge shift in popular culture, from consuming to participating" enabled by the interactivity so characteristic of the Internet. It is sometimes called open-source science, taking the name from open-source software in which the source code, or original programming, is made public to encourage others to work on improving it.

The approach is catching on. Today, would-be innovators can sign up online to compete for prizes for feats as diverse as landing on the Moon (space.xprize.org/lunar-lander-challenge) and inventing artificial meat (www.peta.org/feat_in_vitro_contest.asp).

This year, researchers at the Howard Hughes Medical Institute and the University of Washington began recruiting computer gamers to an online competition, named Foldit, aimed at unraveling one of the knottiest problems of biology — how proteins fold (fold.it).

And in a report last year, a panel appointed by the National Research Council recommended that the National Science Foundation, the major government financing agency for physical science research, offer prizes of $200,000 to $2 million "in diverse areas" as a first step in a major program "to encourage more complex innovations" addressing economic, social and other challenges. (The report is available at www.nap.edu/catalog.php?record_id=11816).

Senator John McCain of Arizona, the presumptive Republican nominee for president, has proposed that the government offer $300 million to whoever invents a battery compact enough, powerful enough and cheap enough to replace fossil fuels.

Offering prizes for scientific achievements is hardly new. "It has been around for centuries," said Karim R. Lakhani, a professor at Harvard Business School who has studied InnoCentive. One early example was the work of John Harrison, the 18th-century clockmaker who, in response to a prize offered by the British Parliament, solved the problem of determining longitude at sea by inventing a clock that would keep good time even in heavy weather.

But, Dr. Lakhani said, "most laboratories, most R & D endeavors still work on the premise 'we can accumulate and make sense of all the knowledge that is relevant.' The open-source models and a model like InnoCentive show that other approaches can help."

Dwayne Spradlin, president and chief executive of InnoCentive, said in an interview that the company had solved 250 challenges, for prizes typically in the $10,000 to $25,000 range. According to the Web site (www.innocentive.com), the achievements include a compound for skin tanning, a method of preventing snack chip breakage and a mini-extruder in brick-making.

"Odds are one or more products in your home has been innovated in our network," Mr. Spradlin said. "Procter & Gamble has products that were innovated on the InnoCentive network."

InnoCentive began in 2000 as e.Lilly, an in-house innovation "incubator" at the pharmaceutical giant Eli Lilly, Mr. Spradlin said, with the company posting problems that its employees had been unable to solve. From the beginning the results were good, he said. "Most of our companies tell us they have a one-third or better solve rate on their problems and that is more cost-effective than anything they could have done internally."

The company says solvers come from 175 countries. More than a third have doctorates, Mr. Spradlin said, and while motivated by money, they also have a desire to solve "problems that matter."

The company, with offices in Waltham, Mass., has a staff of scientists who work with seekers and solvers, reviewing challenges to make sure they are clear and detailed, and guiding would-be solvers who may have a solution.

That specificity is crucial to InnoCentive's operation, people who have studied the company say. "If you say, 'find me a cure for cancer' it may not work," Dr. Lakhani said. But if problems can be "decomposed" into what he called modular questions, like "find me a biomarker for this condition, these questions may be more tractable."

The idea that solutions can come from anywhere, and from people with seemingly unrelated work, is another key. Dr. Lakhani said his study of InnoCentive found that "the further the problem was from the solver's expertise, the more likely they were to solve it," often by applying specialized knowledge or instruments developed for another purpose.

For example, he said, the brain might be thought of as a biological system, but "certain brain problems may not be solvable by taking a biological approach. You may want to cast it as an electrical engineering approach. An electrical engineer will come in and say, 'Oh, here's the answer for you.' They have not thought of themselves as being neuroscientists but now they can approach the problem from the point of view of electrical engineering."

The oil-flow problem was solved by an outsider, said Scott Pegau, its research program manager. If it could easily have been solved "by people within the industry, it would have been," he said. Instead, Mr. Davis approached it with knowledge he picked up at a friend's concrete business.

One critical element is encouraging organizations to take novel innovation approaches in the first place. That was the task that drew the Rockefeller Foundation to the company, said Maria Blair, an associate vice president there.

Ms. Blair said the foundation was nearing the end of an 18-month pilot program after which the success of the partnership would be assessed. Anecdotal evidence so far suggests the arrangement can be useful, she said, citing as an example a challenge to devise a reliable, durable solar-powered light source that could function as a flashlight and as general room illumination.

"The solver ended up being a scientist from New Zealand," she said, and his light is now being made in China.

"What we want to do," she added, "is connect the nonprofits to the platform, to InnoCentive."

The nonprofits get a break on InnoCentive fees, Mr. Spradlin said, and Ms. Blair said the foundation could subsidize access to innovation platforms. But she said many nonprofit organizations had difficulty dealing with intellectual property rights and related issues.

InnoCentive deals with these issues, in part, by requiring winning solvers to transfer intellectual property rights to the seekers, whose identities are secret, before they can claim an award.

Dr. Lakhani said some companies worried that by posting information about their problems they risk giving valuable information to competitors. Another fear, he said, is that a solver will devise a useful solution, but refuse to turn it over for the prize or even patent it to keep it out of the hands of the organization that originally sought it.

"We have not observed yet any of these kinds of games," Dr. Lakhani said.

By contrast, the Foldit contest is a volunteer effort. It began as Rosetta@home, a project using down-time of computers throughout the world to do the laborious calculations needed to determine the shapes of proteins, strings of amino acid crucial to the cells of every living thing. The way these molecules work depends on how the strings fold, but calculating the folding is, as the Foldit researchers put it, "one of the pre-eminent challenges of biology."

In Foldit, players will compete online to design proteins, and researchers will test designs to see if they are good candidates for use in drugs. The researchers who worked to design it say results will also be interesting because people's intuition for protein folding does not seem necessarily to be tied to formal training or laboratory experience.

"Our ultimate goal is to have ordinary people play the game and eventually be candidates for winning the Nobel Prize," said Zoran Popovic, a computer scientist and engineer at the University of Washington.

Mr. Spradlin's goal for InnoCentive is at least as ambitious. By 2011, he hopes InnoCentive participants will have answered at least 10,000 challenges.

When companies and organizations have a problem, Mr. Spradlin said, "I want us to be the first place they go."

**Basics**

## Mirrors Don't Lie. Mislead? Oh, Yes.

**By NATALIE ANGIER**

For the bubbleheaded young Narcissus of myth, the mirror spun a fatal fantasy, and the beautiful boy chose to die by the side of a reflecting pond rather than leave his "beloved" behind. For the aging narcissist of Shakespeare's 62nd sonnet, the mirror delivered a much-needed whack to his vanity, the sight of a face "beated and chopp'd with tann'd antiquity" underscoring the limits of self-love.

Whether made of highly polished metal or of glass with a coating of metal on the back, mirrors have fascinated people for millennia: ancient Egyptians were often depicted holding hand mirrors. With their capacity to reflect back nearly all incident light upon them and so recapitulate the scene they face, mirrors are like pieces of dreams, their images hyper-real and profoundly fake. Mirrors reveal truths you may not want to see. Give them a little smoke and a house to call their own, and mirrors will tell you nothing but lies.

To scientists, the simultaneous simplicity and complexity of mirrors make them powerful tools for exploring questions about perception and cognition in humans and other neuronally gifted species, and how the brain interprets and acts upon the great tides of sensory information from the external world. They are using mirrors to study how the brain decides what is self and what is other, how it judges distances and trajectories of objects, and how it reconstructs the richly three-dimensional quality of the outside world from what is essentially a two-dimensional snapshot taken by the retina's flat sheet of receptor cells. They are applying mirrors in medicine, to create reflected images of patients' limbs or other body parts and thus trick the brain into healing itself. Mirror therapy has been successful in treating disorders like phantom limb syndrome, chronic pain and post-stroke paralysis.

"In a sense, mirrors are the best 'virtual reality' system that we can build," said Marco Bertamini of the University of Liverpool. "The object 'inside' the mirror is virtual, but as far as our eyes are concerned it exists as much as any other object." Dr. Bertamini and his colleagues have also studied what people believe about the nature of mirrors and mirror images, and have found nearly everybody, even students of physics and math, to be shockingly off the mark.

Other researchers have determined that mirrors can subtly affect human behavior, often in surprisingly positive ways. Subjects tested in a room with a mirror have been found to work harder, to be more helpful and to be less inclined to cheat, compared with control groups performing the same exercises in nonmirrored settings. Reporting in the Journal of Personality and Social Psychology, C. Neil Macrae, Galen V. Bodenhausen and Alan B. Milne found that people in a room with a mirror were comparatively less likely to judge others based on social stereotypes about, for example, sex, race or religion.

"When people are made to be self-aware, they are likelier to stop and think about what they are doing," Dr. Bodenhausen said. "A byproduct of that awareness may be a shift away from acting on autopilot toward more desirable ways of behaving." Physical self-reflection, in other words, encourages philosophical self-reflection, a crash course in the Socratic notion that you cannot know or appreciate others until you know yourself.

The mirror technique does not always keep knees from jerking. When it comes to socially acceptable forms of stereotyping, said Dr. Bodenhausen, like branding all politicians liars or all lawyers crooks, the presence of a mirror may end up augmenting rather than curbing the willingness to pigeonhole.

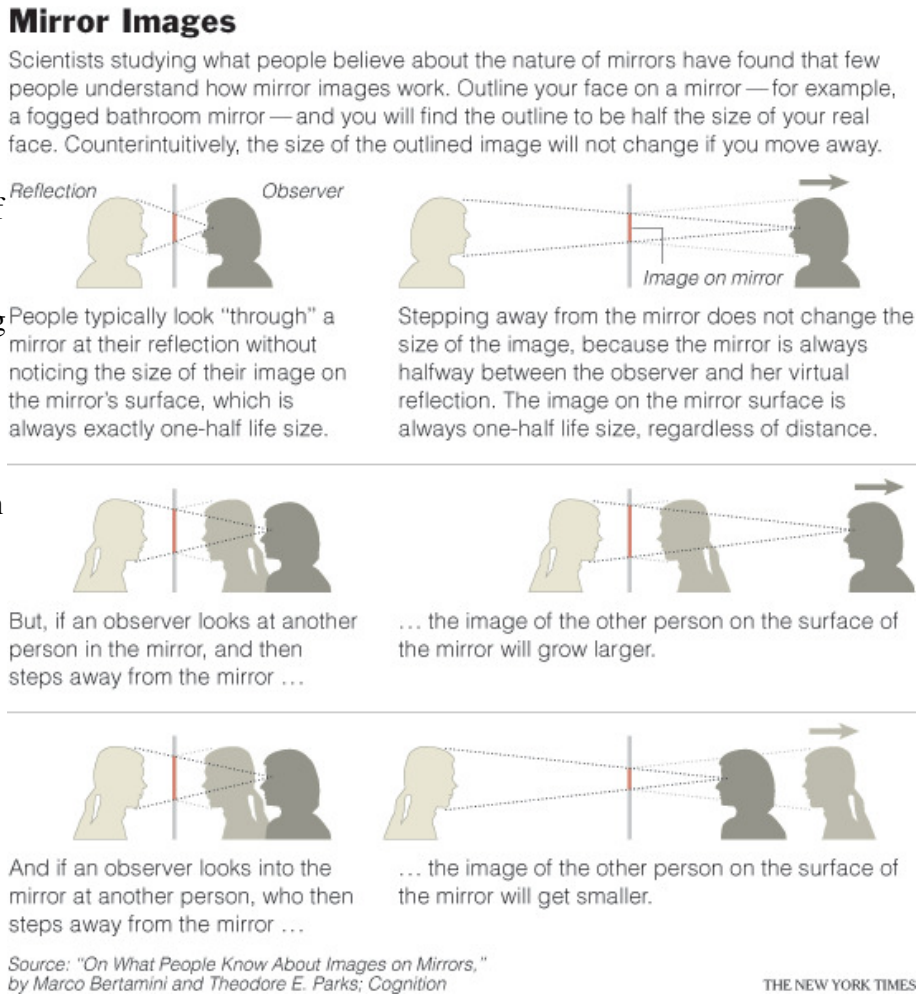
The link between self-awareness and elaborate sociality may help explain why the few nonhuman species that have been found to recognize themselves in a mirror are those with sophisticated social lives. Our gregarious great ape cousins — chimpanzees, bonobos, orangutans and gorillas — along with dolphins and Asian elephants, have passed the famed mirror self-recognition test, which means they will, when given a mirror, scrutinize marks that had been applied to their faces or bodies. The animals also will check up on personal hygiene, inspecting their mouths, nostrils and genitals.

Yet not all members of a certifiably self-reflective species will pass the mirror test. Tellingly, said Diana Reiss, a professor of psychology at Hunter College who has studied mirror self-recognition in elephants and dolphins, "animals raised in isolation do not seem to show mirror self-recognition."

For that matter, humans do not necessarily see the face in the mirror either. In a report titled "Mirror, Mirror on the Wall: Enhancement in Self-Recognition," which appears online in The Personality and Social Psychology Bulletin, Nicholas Epley and Erin Whitchurch described experiments in which people were asked to identify pictures of themselves amid a lineup of distracter faces. Participants identified their personal portraits significantly quicker when their faces were computer enhanced to be 20 percent more attractive. They

were also likelier, when presented with images of themselves made prettier, homelier or left untouched, to call the enhanced image their genuine, unairbrushed face. Such internalized photoshoppery is not simply the result of an all-purpose preference for prettiness: when asked to identify images of strangers in subsequent rounds of testing participants were best at spotting the unenhanced faces.

How can we be so self-delusional when the truth stares back at us? “Although we do indeed see ourselves in the mirror every day, we don’t look exactly the same every time,” explained Dr. Epley, a professor of behavioral science at the University of Chicago Graduate School of Business. There is the scruffy-morning you, the assembled-for-work you, the dressed-for-an-elegant-dinner you. “Which image is you?” he said. “Our research shows that people, on average, resolve that ambiguity in their favor, forming a representation of their image that is more attractive than they actually are.”




When we look in the mirror, our relative beauty is not the only thing we misjudge. In a series of studies, Dr. Bertamini and his colleagues have interviewed scores of people about what they think the mirror shows them. They have asked questions like, Imagine you are standing in front of a bathroom mirror; how big do you think the image of your face is on the surface? And what would happen to the size of that image if you were to step steadily backward, away from the glass?

People overwhelmingly give the same answers. To the first question they say, well, the outline of my face on the mirror would be pretty much the size of my face. As for the second question, that’s obvious: if I move away from the mirror, the size of my image will shrink with each step.

Both answers, it turns out, are wrong. Outline your face on a mirror, and you will find it to be exactly half the size of your real face. Step back as much as you please, and the size of that outlined oval will not change: it will remain half the size of your face (or half the size of whatever part of your body you are looking at), even as the background scene reflected in the mirror steadily changes. Importantly, this half-size rule does not apply to the image of someone else moving about the room. If you sit still by the mirror, and a friend approaches or moves away, the size of the person’s image in the mirror will grow or shrink as our innate sense says it should.

What is it about our reflected self that it plays by such counterintuitive rules? The important point is that no matter how close or far we are from the looking glass, the mirror is always halfway between our physical selves and our projected selves in the virtual world inside the mirror, and so the captured image in the mirror is half our true size.

Rebecca Lawson, who collaborates with Dr. Bertamini at the University of Liverpool, suggests imagining that you had an identical twin, that you were both six feet tall and that you were standing in a room with a movable partition between you. How tall would a window in the partition have to be to allow you to see all six feet of your twin?

The window needs to allow light from the top of your twin’s head and from the bottom of your twin’s feet to reach you, Dr. Lawson said. These two light sources start six feet apart and converge at your eye. If the partition is close to your twin, the upper and lower light points have just begun to converge, so the opening has to be nearly six feet tall to allow you a full-body view. If the partition is close to you, the light has nearly finished converging, so the window can be quite small. If the partition were halfway between you and your twin, the aperture would have to be — three feet tall. Optically, a mirror is similar, Dr. Lawson said, “except that

instead of lighting coming from your twin directly through a window, you see yourself in the mirror with light from your head and your feet being reflected off the mirror into your eye."

This is one partition whose position we cannot change. When we gaze into a mirror, we are all of us Narcissus, tethered eternally to our doppelgänger on the other side.

## Parasitic worm infections increase susceptibility to AIDS viruses

Persons infected with schistosomes, and possibly other parasitic worm infections, may be more likely to become infected with HIV than persons without worm infections, according to a study published July 23rd in the open-access journal PLoS Neglected Tropical Diseases. Researchers at the U.S. Centers for Disease Control and Prevention (Atlanta, United States) and the Dana-Farber Cancer Institute and Harvard Medical School (Boston, United States) found that the infectious dose of an HIV-like virus necessary to infect rhesus macaques was 17-fold lower in animals with acute schistosomiasis than in controls.

The study represents a novel in vivo demonstration that parasitic worms increase a host's susceptibility to becoming infected with an AIDS-causing virus. The macaques co-infected with Schistosoma mansoni also demonstrated higher peak viral loads and higher memory cell concentrations of virus, both predictors of more rapid progression to AIDS. These findings are consistent with the hypothesis that persons living in areas highly endemic for parasitic worms may also have a higher risk of acquiring HIV/AIDS.

Previous studies by this and other research groups have demonstrated that presence of schistosome infections increases viral replication in animal or human hosts with established immunodeficiency virus infections. The earlier findings, combined with the increased susceptibility to AIDS virus transmission shown in this study, may have profound public health implications for areas of the world where both parasitic worms and HIV-1 are endemic.

*http://www.plosntds.org/doi/pntd.0000265 (link will go live on Wednesday, July 23)*

***CITATION**: Chenine A-L, Shai-Kobiler E, Steele LN, Ong H, Augostini P, et al. (2008) Acute Schistosoma mansoni Infection Increases Susceptibility to Systemic SHIV Clade C Infection in Rhesus Macaques after Mucosal Virus Exposure. PLoS Negl Trop Dis 2(7): e265. doi:10.1371/journal.pntd.0000265*

## Age-old magic tricks can provide clues for modern science

Revealing the science behind age-old magic tricks will help us better understand how humans see, think, and act, according to researchers at the University of British Columbia and Durham University in the U.K.

Their study in the current online issue of the journal Trends in Cognitive Sciences concludes that elements of human cognition and perception not yet fully understood by scientists may be clarified by analysing tricks and techniques used by magicians over thousands of years.

The investigators explored several of the key techniques of the magic trade – categorised as "misdirection, illusion and forcing" – which have only recently been formally identified by scientists and taken seriously as a valid research area.

An example of "misdirection" would be the cigarette and lighter trick the researchers used in one of their vision experiments: http://www.dur.ac.uk/gustav.kuhn/Kuhn_et_al_2007/material.htm

For related work on "looking but not seeing" go to: http://www.psych.ubc.ca/~rensink/flicker/

"Although a few attempts have been made in the past to draw links between magic and human cognition, the knowledge obtained by magicians has been largely ignored by modern psychology," says Ronald Rensink, an associate professor who specializes in vision and cognition and teaches in the departments of Psychology and Computer Science at UBC.

Study co-authors are Gustav Kuhn from Durham University's Psychology Department and Alym Amlani, a recent BSc graduate of UBC's Cognitive Systems Program, which integrates computer science, psychology, philosophy and linguistics. Both Kuhn and Amlani are practising magicians who argue that conjurers are "miles ahead" of scientists.

"Imagine someone who makes an object disappear or successfully predicts what you will do next," says Kuhn. "These tricks may seem like they defy the laws of physics and logic, but they are actually created through a combination of skill and a deep knowledge of human psychology."

For example, the vanishing ball illusion indicates that anticipation plays a factor in what we see – our minds tend to fill in the blanks. In this trick, the magician tosses a red ball in the air two times and on the third throw will palm the ball. However, study participants will report seeing the magician toss the ball in the air three times.

The researchers say their work has long-term implications for human-computer interfaces – from online training films and computer graphics to video games and animation. These activities require increasingly sophisticated software capable of grabbing and holding the viewer's attention.

They developed various magic tricks and experiments to test recent findings in vision science, which shows that only a small part of information that enters our eyes actually enters our conscious awareness. One particular finding shows a distinction between where you look and what you see.

This was evident in an experiment that recorded volunteers' eye movements with a tracking device while they watched a video of a “misdirection” trick. The magician goes to light a cigarette, but subtly drops both cigarette and lighter into his lap.

By directing the audience's attention first to his right hand, which is empty, and then to the left hand, also empty, he makes watchers believe both items have simply disappeared.

The researchers asked the volunteers to detect how the magic trick was performed. More than half of the 46 participants did not see the cigarette being dropped although this happened in full view. Further, the eye movement records for this group of volunteers showed that at least two of them were looking directly at the cigarette.

“The critical factor is not where someone directs their eyes, but where they are sending their attention,” explains Rensink. “If they didn't attend to the manipulation behind the trick, they simply weren't able to see how the trick was done.”

*The research team was supported by a Wolfson Research Fellowship from Durham University and the Natural Sciences and Engineering Council of Canada.*

## Biology enters 'The Matrix' through new computer language

**Written by David Cameron.**

BOSTON, Mass. (July 23, 2008)— Ever since the human genome was sequenced less than 10 years ago, researchers have been able to access a dizzying plethora of genomic information with a simple click of a mouse. This digitizing of genomic data—and its public access—is something that would have been unthinkable a generation earlier.

But as molecules go, DNA is pretty straight forward. With its simple composition and linear structure, it easily lends itself to mathematical models. Not so with proteins. In fact, proteins are an order of magnitude more complex than DNA. It is proteins, not DNA, that carry out the cell's heavy lifting. However, with their intricately folded three-dimensional shapes determining a seemingly endless range of possible functions and their manifold interactions with other proteins and with DNA, the leg-work required to mathematically capture the protein universe seems absurd.

And it is.

That is why a team of Harvard Medical School researchers have decided to attack this issue from an entirely new angle. Rather than build a mountain range of proteomic data one grain of dirt at a time, they have developed a computer program that can take on the responsibility of assembling such a gargantuan model.

Enter Little b, a computational language that can penetrate the “mind” of a cell.

“Through incorporating principles of engineering, we've developed a language that can describe biology in the same way a biologist would,” says Jeremy Gunawardena, director of the Virtual Cell Program in Harvard Medical School's department of systems biology. “The potential here is enormous. This opens the door to actually performing discovery science, to look at things like drug interactions, right on the computer.”

These findings will be published in the July 23 issue of Journal of the Royal Society Interface.

Most current computational methods of modeling biological systems are not unlike writing a document with pen and paper. Each new project starts from scratch; there are no facilities for cutting and pasting, for linking to other texts, for including images, etc.—things that come so “naturally” to electronic documents.

Harvard Medical School researcher Jeremy Gunawardena, a mathematician by training, teamed up with Aneil Mallavarapu, a cell biologist and computer scientist, to lead a project that would bypass these limitations.

“We knew that the secret to doing this would be to assimilate fundamental concepts of engineering, concepts like modularity and abstraction, into the biological realm,” says Mallavarapu, who was recently awarded the Merrimack prize by the Council for Systems Biology in Boston for developing this program.

Modularity involves breaking a problem down into separate modules and constructing each module so that it can interact with the others. Abstraction refers to extracting generic biological properties and incorporating them into the modules, so that they can use this abstract information in concrete contexts. Put another way, abstraction means that, unlike the old days of pen and paper, each new model does *not* need to be built from scratch. Models can be built upon each other and their individual modules refined and re-used.

To do this, Mallavarapu used the programming language LISP, a language widely used in artificial intelligence research. LISP is famous among computer scientists due to its ability to write code that, in turn, can write code, enabling a programmer to derive new mini-languages.

“LISP isn't like typical programs, it's more like a conversation,” says Gunawardena. “When we input data into Little b, Little b responds to it and reasons over the data.”

For example, Gunawardena's lab works on kinases, a kind of protein that transfers phosphate chemicals to other proteins in order to regulate their activity. While this property is common to all kinases, there is a great deal of variety in how particular kinases carry this out. Little b, however, understands this basic property of kinases, this abstraction.

Here, the researchers demonstrated how they were able to interact with Little b to build complex models of kinase activity, using Little b as a kind of scientific collaborator, and not simply a passive tool.

On a larger scale, the researchers also used the program to query the development of fruit fly embryos. As a result, they discovered levels of complexity in these embryonic structures that previous research had missed.

“This language is stepping into an unknown universe, when your computer starts building things for you,” says Gunawardena. “Your whole relationship with the computer becomes a different one. You've ceded some control to the machine. The machine is drawing inferences on your behalf and constructing things for you.”

The researchers sometimes admit, half-joking, that Little b sometimes feels a little bit like “The Matrix”—referring, of course, to the film trilogy in which human beings lived in a computer-generated virtual world.

Mallavarapu and Gunawardena have a pretty clear vision for this project: they want every biologist in the world to use it.

But in order to bring the program out from the early adopter community, where it is currently being used by colleagues in the Harvard community, it needs to be more accessible.

“The next step is to create an interface that's easy to use,” says Gunarwardena. “Think of web page development. Lots of people are creating web pages with little or no knowledge of HTML. They use simple interfaces like Dreamweaver. Once we've developed the equivalent, scientists will be able to use our system without having to learn Little b.”

And the more people use it, the smarter it gets. As researchers around the world input their discoveries into Little b, the program will assimilate that information into its language.

The ultimate goal is to have an in silico, virtual cell—a dynamic biological system living in software.

“Sure, it's a long way off,” says Gunawardena, “but we're getting there.”

This research was funded by the National Institutes of Health and Harvard Medical School. The funding and data sources for this study had no role in study design; in the collection, analysis, and interpretation of data; and in the writing of the report.

***Full citation**: Journal of the Royal Society Interface, online publication, July 23, 2008*
*“Programming with models: modularity and abstraction provide powerful capabilities for systems biology”*
*Aneil Mallavarapu, Matthew Thomson, Benjamin Ullian, and Jeremy Gunawardena*
*Department of Systems Biology, Harvard Medical School, Boston MA*

# Head to Head

## Is sun exposure a major cause of melanoma? *Yes*

**Scott W Menzies**, associate professor
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***Every summer we are reminded about the dangers of the sun. Scott Menzies argues that the risks of malignant melanoma are real, but Sam Shuster (doi: 10.1136/bmj.a764) is unconvinced***

Although various phenotypic characteristics enhance or reduce the risk of developing melanoma, sun exposure is the main cause of the disease. This statement is supported by multiple observations.

**Site and sensitivity**

Firstly, anatomical site of low and high sun exposure predicts patterns of melanoma. In general, the relative density of melanoma is highest on body sites receiving more sun exposure in both sexes and lowest on sites receiving little (scalp in women and buttocks in both sexes).1 2 Furthermore, the difference in the patterns of sun exposure between the sexes is consistent with differences in the most common position of melanoma (trunk in men, lower extremities in woman).3

The incidence of melanoma is also much higher in people of races who tend to burn rather than tan.1 The age standardised incidence of melanoma in non-Hispanic white people (populations of mainly European origin) in New Mexico is an order of magnitude greater than that in Hispanic whites, with similar results in non-Hispanic whites versus people of Hispanic, black, and Asian ethnic groups in Los Angeles.1

Within the lightly pigmented populations, studies using skin phototype (colour of non-exposed skin and ability to tan) found a relative risk of melanoma of 3.1 for the lightest quartile and 3.5 for no tanning ability,

which is similar to the risk of people with a history of non-melanoma skin cancer. This is consistent with sun exposure being a strong independent predictor of risk of melanoma.1

**Association with exposure**

Studies looking at melanoma incidence as a function of ambient geographical ultraviolet levels avoid inaccuracies of recall of exposure. When considering race as a variable, ambient ultraviolet index and decreasing latitude were associated with increased incidence of melanoma, but only in non-Hispanic white people in the US and not in other dark skinned races.4 This is consistent with other studies showing incidence of melanoma increasing with decreasing latitude where racial differences (other than populations of mainly European origin) are less observed.5 Such racial differences explain the general increasing incidence of melanoma with decreasing latitudes within countries but not necessarily within continents.6

The increased incidence of melanoma in mid-European countries in people residing in sunny areas, particularly before 10 years of age,7 is consistent with previous migration and geographical residence studies showing that either early exposure or longer exposure in an environment with high ambient solar radiation leads to an increased risk of melanoma.8 Finally, increasing evidence suggests that the incidence of many cancers is inversely related to ambient solar ultraviolet B radiation exposure. However, the pattern for melanoma is reversed, with a positive association between solar ultraviolet B exposure and incidence.9

Case-control studies confirm intermittent sun exposure and sunburn as risk factors for melanoma. Two meta-analyses of case-control studies found that chronic exposure was either negatively associated (odds ratio=0.86)10or not associated.11 In contrast, there were positive associations with intermittent exposure, lifetime sunburn, and childhood sunburn.10 11 Although studies in children are unclear whether total or intermittent exposure conveys risk of melanoma,8 all studies published since the last meta-analysis support the positive association of sun exposure and melanoma risk.12 13 14 15 These studies lack objective measures of exposure, which may reduce the association between personal exposure and melanoma.16 In contrast, studies attempting to measure total sun exposure by cutaneous microtopography show a significant association with melanoma for high grade solar damage, freckling as a child, and history of solar keratoses.1

Epidemiological and mutational analyses strongly support at least two divergent pathways to induce melanoma: those induced by chronic exposure (preferential head and neck site, associated with a history of non-melanoma skin cancer, no mutation in the BRAF gene (which controls the proliferation of melanocytes) and fewer naevus counts) and those induced by intermittent exposure (related to naevus density, BRAF mutation, and a preferential trunk site).17 18 Epidemiological studies may produce confusing results if these divergent pathways are not taken into account.

**Genetic evidence**

In young adults with xeroderma pigmentosum, who have a defect in the repair mechanism of ultraviolet radiation induced thymidine dimers, the incidence of melanoma is 1000 times higher than in controls, although the anatomical distribution is the same.19

Analysis of melanoma mutations found in the suppressor oncogene CDKN2A (P16/INK4a) and ras oncogene family is consistent with induction by ultraviolet radiation.20 Evidence suggests that although ultraviolet radiation is required to induce BRAF mutations found in melanoma and acquired naevi, other factors are also necessary.21 22

**Protection**

Overall, case-control studies have not shown a reduction in the incidence of melanoma with sunscreen use.23 24 However, sunscreens are used to prolong intentional sun exposure,25 they tend to be used by people at higher risk of melanoma, and the studies did not assess the sun protection factor or correct application of sunscreens. Nevertheless, the incidence of melanoma among young adults in Australia fell from 1983 to 1996, coinciding with strong public health messages to use sun protection.1

In white populations of mainly European origin there is evidence of clear associations between sun exposure and melanoma incidence. A comparison of US white people and black people, in which the melanoma incidence of black people was taken as the non-exposed incidence in white people , gave an estimate that 96% of melanoma in men and 92% in women was caused by sun exposure.26 Sun exposure is clearly a major cause of this disease. *Cite this as: BMJ 2008;337:a763*

# Is sun exposure a major cause of melanoma? *No*

**Sam Shuster,** honorary consultant
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***Every summer we are reminded about the dangers of the sun. Scott Menzies (doi: 10.1136/bmj.a763) argues that the risks of malignant melanoma are real, but Sam Shuster is unconvinced***

The list of harmful things grows daily, freshly mined by descriptive epidemiology, a substitute for research that confuses association with cause. Although most disappear under the weight of their own inconsequence, the alleged increase in melanoma from ultraviolet radiation has survived on the life support of regular promotion. I am therefore setting out what is known, which is rather different from what is believed.

**Does ultraviolet light cause melanoma?**

There is solid descriptive, quantitative, and mechanistic proof that ultraviolet rays cause the main skin cancers (basal and squamous). They develop in pale, sun exposed skin,1 are related to degree of exposure and latitude,2 are fewer with avoidance and protection,3 4 are readily produced experimentally,4 and are the overwhelmingly predominant tumour in xeroderma pigmentosum, where DNA repair of ultraviolet light damage is impaired.

None of these is found with melanoma. Variation is more ethnic5 6 7 than pigmentary,8 and 75% occur on relatively unexposed sites,9 especially the feet of dark skinned Africans.6 7 The relation to latitude is small and inconsistent in, for example, Europe10 and the United States11; incidence and mortality fall with greater exposure7 8 9 10 11 12 13 14 15 16 17; incidence is unaffected or increased by use of sunscreens18 ; and the effect of sun bed exposure is small and inconsistent.19 In addition, melanomas are difficult to produce experimentally with ultraviolet 20 light and are far less common than non-melanoma cancers in xeroderma pigmentosum.

Therefore, the effect of ultraviolet light can only be minimal, and the case against a major role is clear. Attempts to relate light exposure to surface area and site are irrelevant, since the cell of origin of melanoma and its distribution are unknown. The suggestion that the poor correlation of melanoma to ultraviolet light is because the causal event is sunburn from intermittent exposure in early life13 14 15 16 17 21 is easily excluded, because the melanomas would then occur at the burn sites; there is no evidence for this, and it is unlikely that any will be found, because sunburn occurs in sun exposed sites, and these are not the sites at which melanomas occur.7 8

There is an association between melanoma and number of naevi,13 22 and naevi increase after exposure to ultraviolet light22 23; but this does not implicate ultraviolet light in the aetiology of melanoma, for the same reasons related to site. The likely explanation of the association is that stimulation of naevus growth by ultraviolet light simply increases the number of visible (and therefore countable) lesions. The associated histological changes can be indistinguishable from melanoma, as is the case with the benign lesions of lentigo maligna in elderly people, sun bed users, and psoriasis patients treated with psoralen and ultraviolet A; benign naevi stimulated by shave excision; and juvenile melanoma. Thus, unlike for squamous and basal cell cancers, there is no proof that ultraviolet light exposure is a significant cause of melanoma.

**Is the reported increase in melanoma real?**

In the past, naevi were left untreated and usually caused no harm. Then, fear of litigation and the search for early lesions led to removal of benign lesions; this introduced an ambiguity into histological classification, which eventually changed the definition of malignancy. Those who observed the process believe misdiagnosis of benign naevi explains the melanoma epidemic.24 This view is supported by the findings of the Eastern region of England that the increase in new “melanomas” during 1991-2004 was entirely due to benign naevi (Levell et al, personal communication); a melanoma mountain in Australia has also been attributed to confusion with a benign disease.25 The relation between incidence of new melanomas and higher social class26 is best explained by removal of benign naevi after health warnings and encouragement to attend “pigmented lesion clinics”—the middle classes are always first on the scene.27

The subjective histopathological criteria used to diagnose melanoma have become too vague for use and are commonly found in benign disease. This problem can be resolved only by research, including a blind re-examination of histological slides used for past and present diagnoses, and a better distinction between benign and malignant changes in naevi.24 27 Meanwhile, it can only be concluded that the reported increase in melanoma is probably an erroneous reclassification of benign naevi. Thus the question of whether ultraviolet light causes melanoma becomes irrelevant, because there is no case to answer.

**Balancing the effects of ultraviolet light**

Of course we know that ultraviolet light causes the common, virtually benign, and mostly trivial skin cancers and that, like smoking, it makes the skin look as if it has been well lived in. But is this enough to justify blanketing the sun when balanced against the possible advantages? We know the sun makes us feel better, although not how28; we need skin synthesis of vitamin D for our bones; ultraviolet light may protect against some forms of cancer29 including melanoma14; and it has important, unexplained immunological effects.30 We need to know much more before we can balance the biological books on ultraviolet radiation, even if we can now close the chapter on melanoma.24 *Competing interests: None declared.*

## Commercial bees spreading disease to wild pollinating bees

Bees provide crucial pollination service to numerous crops and up to a third of the human diet comes from plants pollinated by insects. However, pollinating bees are suffering widespread declines in North America and scientists warn that this could have serious implications for agriculture and food supply. While the cause of these declines has largely been a mystery, new research reveals an alarming spread of disease from commercial bees to wild pollinators.

In a study published in the July 23 issue of the online, open-access journal PLoS ONE, Michael Otterstatter and James Thomson of the University of Toronto present compelling evidence that commercially produced bumble bees used in greenhouses are infecting their wild cousins, and that this is likely contributing to reductions in the natural pollinating bee population.

Otterstatter and Thomson investigated the occurrence of disease in wild bumble bees in southern Ontario, Canada, particularly in areas close to industrial greenhouse operations. In addition, the authors used a combination of laboratory experiments and mathematical modelling to simulate the spread, or 'spillover', of disease from commercial bees to wild populations, and to predict the extent and severity of such spread in the wild.

The researchers found that commercial bumble bees often carry a harmful and highly contagious pathogen, Crithidia bombi, and that these bees regularly escape from greenhouses and interact with wild bees at flowers. Near greenhouses, the rates of infection were startling: up to one half of wild bumble bees were infected with C. bombi, whereas no bees harboured this pathogen at sites away from greenhouses.

Furthermore, the frequency and severity of infections declined with increasing distance from greenhouses, suggesting that these agricultural operations are foci of disease for wild pollinators.

The mathematical model that Otterstatter and Thomson developed confirmed that pathogen spillover from commercial bees would allow disease to invade wild pollinator populations near greenhouses. The model predicts that, although disease may build up slowly at first, given sufficient time, spillover will result in a large-scale epidemic among wild bees.

The commercial bumble bee industry is expanding worldwide. The abundance of disease in commercial bees, and the international trafficking of infected hives, may pose a substantial threat to wild bee pollinators. The authors emphasize that improved management of domestic bees through, for example, greater attention to their diseases and their overlap with wild species, would greatly reduce, or even eliminate, pathogen spillover.

## New Guidelines for Treating Rheumatoid Arthritis

***• Updated rules add new arthritis drugs and combinations***

***• Recommendations not meant to override individualized care***

BIRMINGHAM, Ala. - Proven combinations of medicines and the introduction of new anti-arthritis drugs have significantly improved the treatment of rheumatoid arthritis (RA), according to guidelines issued by the American College of Rheumatology and co-authored by physicians at the University of Alabama at Birmingham (UAB).

Lead author Kenneth Saag, M.D., M.Sc., a professor in the UAB Division of Clinical Immunology and Rheumatology, said the new guidelines update strategies for treating RA with the goal of preventing joint damage and disability.

The new recommendations do not strive to replace individualized medical decisions, Saag said. Instead, they are meant to guide rheumatologists and other health care workers toward the most updated recommendations. The last set of American College of Rheumatology RA treatment guidelines was published in 2002.

“The recommendations developed are not intended to be used in a ‘cookbook' or prescriptive manner, or to limit a physician's clinical judgment,” Saag said. “They provide guidance based on clinical evidence and expert panel input.”

**BIOLOGICS AND DMARDS**

The recommendations focus on several classes of anti-arthritic drugs, including a potent group of agents called disease-modifying anti-rheumatic drugs (DMARDs). Newer genetically engineered DMARDs called biologics often work in combination with earlier therapies.

Many anti-arthritic drugs are designed to stop damaging inflammation, and biologics work to interrupt the chain of events that leads to inflammation.

Newer biologics called anti-TNF agents - adalimumab (Humira), etanercept (Enbrel) and infliximab (Remicade) - prevent the production of an immunity protein that plays a role in inflammation.

Some of the key recommendations include:

* Methotrexate or leflunomide therapy is recommended for most RA patients.

* Anti-TNF agents etanercept, infliximab, or adalimumab along with methotrexate can be used in new or early RA cases with worsening and severe symptoms.

* Doctors should not initiate or resume treatment with methotrexate, leflunomide, or biologics if RA patients have active bacterial infection, shingles (herpes-zoster), hepatitis B, hepatitis C and active or latent tuberculosis.

* Doctors should not prescribe anti-TNF agents to patients with a history of heart failure, lymphoma or multiple sclerosis.

*The full list of RA treatment recommendations is available at www.rheumatology.org by clicking on practice support, then guidelines.*

## Security flaws in online banking sites found to be widespread

ANN ARBOR, Mich.---More than 75 percent of the bank Web sites surveyed in a University of Michigan study had at least one design flaw that could make customers vulnerable to cyber thieves after their money or even their identity.

Atul Prakash, a professor in the Department of Electrical Engineering and Computer Science and doctoral students Laura Falk and Kevin Borders examined the Web sites of 214 financial institutions in 2006. They will present the findings for the first time at the Symposium on Usable Privacy and Security meeting at Carnegie Mellon University July 25.

These design flaws aren't bugs that can be fixed with a patch. They stem from the flow and the layout of these Web sites, according to the study. The flaws include placing log-in boxes and contact information on insecure web pages as well as failing to keep users on the site they initially visited. Prakash said some banks may have taken steps to resolve these problems since this data was gathered, but overall he still sees much need for improvement.

“To our surprise, design flaws that could compromise security were widespread and included some of the largest banks in the country,” Prakash said. “Our focus was on users who try to be careful, but unfortunately some bank sites make it hard for customers to make the right security decisions when doing online banking.”

The flaws leave cracks in security that hackers could exploit to gain access to private information and accounts. The FDIC says computer intrusion, while relatively rare compared with financial crimes like mortgage fraud and check fraud, is a growing problem for banks and their customers.

A recent FDIC Technology Incident Report, compiled from suspicious activity reports banks file quarterly, lists 536 cases of computer intrusion, with an average loss per incident of $30,000. That adds up to a nearly $16-million loss in the second quarter of 2007. Computer intrusions increased by 150 percent between the first quarter of 2007 and the second. In 80 percent of the cases, the source of the intrusion is unknown but it occurred during online banking, the report states.

The design flaws Prakash and his team looked for are:

* Placing secure login boxes on insecure pages: A full 47 percent of banks were guilty of this. A hacker could reroute data entered in the boxes or create a spoof copy of the page to harvest information. In a wireless situation, it's possible to conduct this man-in-the-middle attack without changing the bank URL for the user, so even a vigilant customer could fall victim. To solve this problem, banks should use the standard “secure socket layer” (SSL) protocol on pages that ask for sensitive information, Prakash says. (SSL-protected pages begin with https rather than http.) Most banks use SSL technology for some of their pages, but only a minority secure all their pages this way.

* Putting contact information and security advice on insecure pages: At 55 percent, this was the flaw with the most offenders. An attacker could change an address or phone number and set up his own call center to gather private data from customers who need help. Banks tend to be less cautious with information that's easy to find elsewhere, Prakash says. But customers trust that the information on the bank's site is correct. This problem could be solved by securing these pages with the standard SSL protocol.

* Having a breach in the chain of trust: When the bank redirects customers to a site outside the bank's domain for certain transactions without warning, it has failed to maintain a context for good security decisions, Prakash says. He found this problem in 30 percent of the banks surveyed. Often the look of the site changes, as well as URL and it's hard for the user to know whether to trust this new site. The solution, Prakash says, is to warn users they'll be moving off the bank's site to a trusted new site. Or the bank could house all of its pages on the same server. This problem often arises when banks outsource some security functions.

* Allowing inadequate user IDs and passwords: Researchers looked for sites that use social security numbers or e-mail addresses as user ids. While this information is easy for customers to remember, it's also easy to guess or find out. Researchers also looked for sites that didn't state a policy on passwords or that allowed weak passwords. Twenty-eight percent of sites surveyed had one of these flaws.

* E-mailing security-sensitive information insecurely: The e-mail data path is generally not secure, Prakash says, yet 31 percent of bank Web sites had this flaw. These banks offered to e-mail passwords or statements. In the case of statements, users often weren't told whether they would receive a link, the actual statement, or a notification that the statement was available. A notification isn't a problem, but e-mailing a password, a link or a statement, isn't a good idea, Prakash says.

*Prakash initiated this study after noticing flaws on his own financial institutions' Web sites. The paper is "Analyzing Web sites for user-visible security design flaws." Falk and Borders are students in the Department of Electrical Engineering and Computer Science.*

*For more information on Prakash, visit: http://www.eecs.umich.edu/~aprakash/*

## Viagra could boost orgasms in depressed women

* 20:20 22 July 2008

* NewScientist.com news service

*** Ewen Callaway**

The little blue pill that's reinvigorated the sex lives of millions of men might do the same for women who are feeling blue.

Sildenafil – marketed as Viagra – helps women on antidepressants achieve an orgasm, according to a study funded by the drug's manufacturer, Pfizer.

A previous study found that Viagra boosts clitoral blood flow, but not sexual satisfaction. But anecdotal evidence and a small study hinted that the drug could better the sex lives of women on antidepressants.

Anywhere from 30 to 70% of people taking antidepressants such as Prozac and Zoloft lose some of their sexual appetite. A pill to combat those side effects could keep men and women on their meds, says psychiatrist George Nurnberg of the University of New Mexico, Albuquerque, US, in an upcoming article in the Journal of the American Medical Association.

**More, more**

Nurnberg's team gave Viagra or an identical-looking placebo pill to 98 women, aged 18 to 50, who were already taking antidepressants and who experienced some sexual dysfunction due to their medication. The participants were told to swallow the pill about one or two hours before they expected to have sex.

After two months, three-quarters of the women on the placebo pill still had no sexual appetite compared with just 28% of the women who got the real thing. A further break down, based on questionnaires of sexual satisfaction, suggested that Viagra may have helped women reach orgasm and have better orgasms, compared to the placebo group.

However, Nurnberg's team noticed no major difference between the groups in other areas, such as desire, sexual drive and lubrication. And the women on Viagra were more likely to experience headache, flushing and nasal congestion – known side effects of the drug.

For Pfizer, this is obviously good news. In the face of competition from other impotence drugs, Viagra's sales – while still around $1.7 billion in 2006 – have plateaued, and the drug comes off patent protection in 2011, meaning other companies can make generic forms.

**Staying the course**

If the US Food and Drug Administration ever approved the pill for women on antidepressants – a much larger clinical study would be needed to make that case – this would open up a staggeringly large market.

And even if Viagra isn't approved for depressed women, doctors are free to prescribe the pill "off-label", and a high-profile journal article could lead to more Viagra prescriptions for women.

It is more likely, though, that Pfizer and other drug companies will focus on other drugs that could treat sexual dysfunction in women. One medicine has shown promise in rats, increasing vaginal blood flow.

Nurnberg and his co-authors suggest that Viagra, by improving sex, could help women stay on their antidepressants. About 70% of people stop taking antidepressants in the first months of treatment.

Salvatore Caruso, president of the Italian Federation of Scientific Sexology and a researcher at the University of Catania isn't surprised that Viagra has some effect on women. Increased blood flow – Viagra's mode of action – has a similar effect on the genitals of men and women, he says. *Journal reference: JAMA (vol 300, p 395)*

## Soy foods are associated with lower sperm concentrations

Men who eat an average of half a serving of soy food a day have lower concentrations of sperm than men who do not eat soy foods, according to research published online in Europe's leading reproductive medicine journal, Human Reproduction, today (Thursday 24 July). The association was particularly marked in men who were overweight or obese, the study found.

In the largest study in humans to examine the relationship between semen quality and phytoestrogens (plant compounds that can behave like the hormone, oestrogen), Dr Jorge Chavarro, a research fellow in the department of nutrition at Harvard School of Public Health, Boston, USA, and his colleagues found that men who ate the most soy food had 41 million sperm per millilitre less than men who did not consume soy products. (The "normal" sperm concentration for men ranges between 80-120 million/ml).

Isoflavones (daidzein, genistein and glycitein) are plant-derived compounds with oestrogenic effects that are found mainly in soy beans and soy-derived products. Animal studies have linked the high consumption of isoflavones with infertility in animals, but so far there has been little evidence of their effect in humans.

Dr Chavarro and his colleagues analysed the intake of 15 soy-based foods in 99 men who had attended a fertility clinic with their partners to be evaluated for sub-fertility between 2000 and 2006. They asked them how often and how much they had eaten in the previous three months; the foods included tofu, tempeh, tofu or soy sausages, bacon, burgers and mince, soy milk, cheese, yoghurt and ice cream, and other soy products such as roasted nuts, drinks, powders and energy bars.

Different foods have different levels of isoflavones in them, and so the researchers related the size of the serving to the particular food. For instance, a standard serving of tofu was 115g and for soy milk it was one cup (240 millilitres).

The men were divided into four groups according to their intake of soy foods and isoflavones. After adjusting for factors such as age, abstinence time, body mass index (BMI), alcohol and caffeine intake and smoking, Dr Chavarro found that men in the highest intake category had, on average, 41 million sperm/ml less than men who did not eat soy foods. "Men in the highest intake group had a mean soy food intake of half a serving per day: in terms of their isoflavone content that is comparable to having one cup of soy milk or one serving of tofu, tempeh or soy burgers every other day," he said.

"It is important to highlight that the figure of half a serving a day is the average intake for men in the highest intake group. Some men in this group had intakes of soy foods as high as nearly four servings per day."

The researchers found evidence that the association between soy food intake and sperm concentrations were stronger in men who were overweight or obese (and 72% of them were). They also found the relationship between soy foods and sperm concentration was strongest in men with the higher sperm concentrations. "The implication is that men who have normal or high sperm counts may be more susceptible to soy foods than men with low sperm counts, but this remains to be evaluated," explained Dr Chavarro.

The study does not reveal why soy foods have this effect on sperm, but Dr Chavarro speculates that increased oestrogenic activity may have an adverse effect on the production of sperm by interfering with other hormonal signals. This effect could be strengthened further in overweight and obese men because men with high levels of body fat produce more oestrogen than slimmer men, leading to high overall levels of oestrogen in the body and reproductive organs.

Soy foods are the most important source of phytoestrogens in people in the Western world, and the researchers say they were able to comprehensively assess the men's soy intake. They did not assess intake of isoflavones from other sources, such as bakery products made with soy flour. "However, the most likely effect of not assessing intake of these foods is that the associations reported in this study are attenuated," said Dr Chavarro.

The researchers say that the clinical significance of their research remains to be determined, and further randomised trials are needed.

*[1] Soy food and isoflavone intake in relation to semen quality parameters among men from an infertility clinic. Human Reproduction. Published online under advance access. doi:10.1093/humrep/den243.*

## Biofilms use chemical weapons

***Researcher at the Helmholtz Center for Infection Research discovers defense strategies used by biofilm bacteria***

Bacteria rarely come as loners; more often they grow in crowds and squat on surfaces where they form a community together. These so-called biofilms develop on any surface that bacteria can attach themselves to. The dilemma we face is that neither disinfectants and antibiotics, nor phagocytes and our immune system can destroy these biofilms. This is a particular problem in hospitals if these bacteria form a community on a catheter or implant where they could potentially cause a serious infection. Scientists at the Helmholtz Centre for Infection Research in Braunschweig have now identified one of the fundamental mechanisms used by the bacteria in biofilms to protect themselves against the attacking phagocytes. The scientists are now publishing their findings in the renowned specialist publication PLoS ONE, together with colleagues from Australia, Great Britain and the USA – the discovery being that biofilm bacteria use chemical weapons to defend themselves.

Until now, scientists have been unable to understand the root of the biofilm problem – the inability of phagocytes to destroy these biofilms. Dr. Carsten Matz decided to investigate this problem. As a model for his investigation, this Braunschweig-based researcher decided to look at marine bacteria. They face constant threats in their habitat from environmental phagocytes, the amoebae, which behave in a similar way in the sea as the immune cells in our body: they seek out and feed on the bacteria. So long as bacteria are swimming freely and separately in the water, they are easy pickings for these predators. However, if they become attached to a surface and socialize with other bacteria, the amoebae can no longer successfully attack them. “The surprising thing was that the amoebae attacking the biofilms were de-activated or even killed. The bacteria are clearly not just building a fortress, they are also fighting back,” says Carsten Matz.

The bacteria utilise chemical weapons to achieve this. A widespread and highly effective molecule used by marine bacteria is the pigment violacein. Once the defence system is ready, the biofilm shimmers a soft purple colour. If the attackers consume just a single cell of the biofilm – and the pigment they contain – this paralyses the attackers momentarily and the violacein triggers a suicide mechanism in the amoebae.

“I feel that these results could offer a change of perspective,” says Carsten Matz. “Biofilms may no longer be seen just as a problem; they may also be a source of new bioactive agents. When organized in biofilms, bacteria produce highly effective substances which individual bacteria alone cannot produce.” And the scientists hope to use these molecules to combat a specific group of pathogens: Human parasites that cause devastating infections such as sleeping illness and malaria. Amoeba are ancient relatives of these pathogens and thus biofilm-derived weapons may provide an excellent basis for the design of new parasiticidal drugs.

## Licking your wounds: Scientists isolate compound in human saliva that speeds wound healing

***New research in the FASEB Journal raises expectorations for people with chronic wounds***

A report by scientists from The Netherlands published online in The FASEB Journal (http://www.fasebj.org) identifies a compound in human saliva that greatly speeds wound healing. This research may offer hope to people suffering from chronic wounds related to diabetes and other disorders, as well as traumatic injuries and burns. In addition, because the compounds can be mass produced, they have the potential to become as common as antibiotic creams and rubbing alcohol.

“We hope our finding is ultimately beneficial for people who suffer from non-healing wounds, such as foot ulcers and diabetic ulcers, as well as for treatment of trauma-induced wounds like burns,” said Menno Oudhoff, first author of the report.

Specifically, scientists found that histatin, a small protein in saliva previously only believed to kill bacteria was responsible for the healing. To come to this conclusion, the researchers used epithelial cells that line the inner cheek, and cultured in dishes until the surfaces were completely covered with cells. Then they made an artificial wound in the cell layer in each dish, by scratching a small piece of the cells away. In one dish, cells were bathed in an isotonic fluid without any additions. In the other dish, cells were bathed in human saliva. After 16 hours the scientists noticed that the saliva treated “wound” was almost completely closed. In the dish with the untreated “wound,” a substantial part of the “wound” was still open. This proved that human saliva contains a factor which accelerates wound closure of oral cells. Because saliva is a complex liquid with many components, the next step was to identify which component was responsible for wound healing. Using various techniques the researchers split the saliva into its individual components, tested each in their wound model, and finally determined that histatin was responsible.

“This study not only answers the biological question of why animals lick their wounds,” said Gerald Weissmann, MD, Editor-in-Chief of The FASEB Journal, “it also explains why wounds in the mouth, like those

of a tooth extraction, heal much faster than comparable wounds of the skin and bone. It also directs us to begin looking at saliva as a source for new drugs."

## Autism's social struggles due to disrupted communication networks in brain

### *Faulty brain connections conceal intentions of others in autism*

Picking up on innuendo and social cues is a central component of engaging in conversation, but people with autism often struggle to determine another person's intentions in a social interaction. New research from Carnegie Mellon University sheds light on the neural mechanisms that are responsible for such social difficulties in autism, and on the workings of these social brain mechanisms in all of us.

According to the study, which is available on the Web site of the journal Social Neuroscience, inefficient pathways for transmitting information between certain brain regions are to blame. The research implicates abnormalities in the brain's inter-regional communication system, which connects the gray matter's computing centers.

"The communication between the frontal and posterior areas of the social brain network is impaired in autism, making it difficult to understand the intentions of others" said the study's senior author, Marcel Just, the D.O. Hebb Professor of Psychology at Carnegie Mellon.

The study is the first to measure the synchronization between the brain areas that make up the Theory of Mind (ToM) network, which is responsible for processing the intentions and thoughts of others. It is the first to provide such concrete evidence of faulty social network connections.

To measure the ToM network's effectiveness, the researchers asked 12 high-functioning autistic adults and 12 control participants to view animations of interacting geometric figures, an example of which can be viewed at www.ccbi.cmu.edu/reprints/reprints.htm.

Participants then were asked to select the word from several choices that best described the interaction. For example, a large triangle would nudge a small triangle to move outside its enclosure, and the correct word choice would be "persuading." The control subjects were consistently better at inferring the intention from the action than the participants with autism were.

While the study participants were performing the task, the researchers used functional magnetic resonance imaging (fMRI) to measure activation levels in all of the cortical areas that compose the ToM network. Specifically, they simultaneously examined activation levels in several frontal and posterior brain regions to determine the synchronization levels in the network. The synchronization was reliably lower in the group with autism.

Furthermore, the autistic participants' brains showed much lower activation levels than their counterparts in the frontal regions. These measures of brain activity in autism, such as the activation level in the posterior part of the ToM network (located approximately behind one's right ear), were correlated with how well each autism participant performed in the Happe's Strange Story Test — a pencil-and-paper assessment of an individual's understanding of non-literal statements, such as figures of speech.

"This study offers compelling evidence that a lack of synchronization in the Theory of Mind network is largely responsible for social challenges in autism," said Just, director of Carnegie Mellon's Center for Cognitive Brain Imaging. "That evidence can provide the foundation for therapies that are more useful than current approaches."

The findings have the potential to guide the development of theoretically based interventions for autism that could target this particular shortfall, for example, by focusing on games and activities that would strengthen the connections. Eventually, it might be possible to tailor autism therapies to the brain communication deficit on a case-by-case basis. Measuring the connectivity before and after an intervention also could be used to determine effectiveness.

*The research was supported by a Collaborative Program of Excellence in Autism grant from NICHD and the Cure Autism Now grant awarded to the study's lead author, Rajesh K. Kana, now an Assistant Professor of Psychology at the University of Alabama at Birmingham.*

*Additional study co-authors include Timothy Keller, Ph.D. and Vladimir Cherkassky, Ph.D. of Carnegie Mellon and Nancy J. Minshew, M.D. of the University of Pittsburgh School of Medicine.*

## Want a reason to love your lower belly fat? It's rich in stem cells

### *ASPS study finds some areas of the body have greater concentrations of stem cells*

ARLINGTON HEIGHTS, Ill. – Fat removed from the lower abdomen and inner thigh through liposuction was found to be an excellent source of stem cells, with higher stem cell concentrations than other areas of the body, reports a Brazilian-based study in August's Plastic and Reconstructive Surgery®, the official medical journal of the American Society of Plastic Surgeons (ASPS). This is the first study of its kind to examine whether fat tissues from different areas of the body vary in stem cell concentration.

“Adult stem cells, derived from our own tissues, hold strong promise for improved clinical therapies,” said J. Peter Rubin, MD, a member of the ASPS Fat Grafting Task Force who is involved in pre-clinical trial work on stem cells taken from fat. “The potential for healing and repairing injury or disease through stem cells, including conditions like breast cancer and reconstruction, heart failure, spinal injuries, diabetes and Parkinson's disease are incredible. We may be able to more permanently and naturally get rid of pesky wrinkles or augment breasts with stem cell enriched fat in the future as well. Knowing more about the biology of stem cells will be of great value when we are ready for clinical trials in this country.”

In the study, 23 female patients having liposuction in at least four different body areas agreed to have their fat isolated for adult stem cells and analyzed to determine stem cell concentrations. The body areas that were liposuctioned were: lower abdomen, upper abdomen, inner knee, inner thigh, flank and hips.

The study results found a significant difference in stem cell concentrations in different areas of the body. A major finding was that the concentration of stem cells was greatest in the lower abdomen and inner thighs. Interestingly, stem cell concentration in the lower abdomen was five times greater than in the upper abdomen.

“The value of stem cells harvested through fat is the ready and ample supply available,” said ASPS President Richard D'Amico, MD. “Using stem cells will some day have very practical applications to the specialty of plastic surgery. That we may be able to generate new tissue or bone that can be used in many of the reconstructive and cosmetic procedures we do every day is a tremendous.”

Stem cells are unspecialized cells that have not yet developed a specific function. Not only are they capable of self renewal, stem cells can divide and produce others that become specialized cells. Scientists and doctors theorize that stem cells will be able to repair or replace damaged or diseased cells. Clinical trials researching the potential of stem cells from fat are ongoing in Europe and Asia. In the U.S., there are many investigators doing pre-clinical trial work to meet the stringent safety guidelines the FDA sets for clinical trials.

According to ASPS statistics, more than 301,000 liposuction procedures were performed in 2007.

## Toxic chemicals found in common scented laundry products, air fresheners

A University of Washington study of top-selling laundry products and air fresheners found the products emitted dozens of different chemicals. All six products tested gave off at least one chemical regulated as toxic or hazardous under federal laws, but none of those chemicals was listed on the product labels.

“I first got interested in this topic because people were telling me that the air fresheners in public restrooms and the scent from laundry products vented outdoors were making them sick,” said Anne Steinemann, a UW professor of civil and environmental engineering and of public affairs. “And I wanted to know, 'What's in these products that is causing these effects?'“

She analyzed the products to discover the chemicals' identity.

“I was surprised by both the number and the potential toxicity of the chemicals that were found,” Steinemann said. Chemicals included acetone, the active ingredient in paint thinner and nail-polish remover; limonene, a molecule with a citrus scent; and acetaldehyde, chloromethane and 1,4-dioxane.

“Nearly 100 volatile organic compounds were emitted from these six products, and none were listed on any product label. Plus, five of the six products emitted one or more carcinogenic 'hazardous air pollutants,' which are considered by the Environmental Protection Agency to have no safe exposure level,” Steinemann said.

Her study was published online today by the journal Environmental Impact Assessment Review. Steinemann chose not to disclose the brand names of the six products she tested. In a larger study of 25 cleaners, personal care products, air fresheners and laundry products, now submitted for publication, she found that many other brands contained similar chemicals.

Because manufacturers of consumer products are not required to disclose the ingredients, Steinemann analyzed the products to discover their contents. She studied three common air fresheners (a solid deodorizer disk, a liquid spray and a plug-in oil) and three laundry products (a dryer sheet, fabric softener and a detergent), selecting a top seller in each category. She bought household items at a grocery store and asked companies for samples of industrial products.

In the laboratory, each product was placed in an isolated space at room temperature and the surrounding air was analyzed for volatile organic compounds, small molecules that evaporate from the product's surface into the air.

Results showed 58 different volatile organic compounds above a concentration of 300 micrograms per cubic meter, many of which were present in more than one of the six products. For instance, a plug-in air freshener contained more than 20 different volatile organic compounds. Of these, seven are regulated as toxic or hazardous under federal laws. The product label lists no ingredients, and information on the Material Safety Data Sheet, required for workplace handling of chemicals, lists the contents as “mixture of perfume oils.”

This study does not address links between exposure to chemicals and health effects. However, two national surveys published by Steinemann and a colleague in 2004 and 2005 found that about 20 percent of the

population reported adverse health effects from air fresheners, and about 10 percent complained of adverse effects from laundry products vented to the outdoors. Among asthmatics such complaints were roughly twice as common.

Manufacturers are not required to list the ingredients used in laundry products and air fresheners. Personal-care products and cleaners often contain similar fragrance chemicals, Steinemann said. And although cosmetics are required by the Food and Drug Administration to list ingredients, no law requires products of any kind to list chemicals used in fragrances.

"Fragrance chemicals are of particular interest because of the potential for involuntary exposure, or second-hand scents," Steinemann said.

"Be careful if you buy products with fragrance, because you really don't know what's in them," she added. "I'd like to see better labeling. In the meantime, I'd recommend that instead of air fresheners people use ventilation, and with laundry products, choose fragrance-free versions."

The European Union recently enacted legislation requiring products to list 26 fragrance chemicals when they are present above a certain concentration in cosmetic products and detergents. No similar laws exist in the United States.

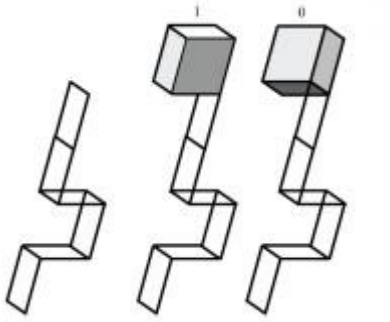
"I hope this study will raise public awareness, and reduce exposures to potentially hazardous chemicals," said Steinemann. *For more information, contact Steinemann at (206) 616-2661 or acstein@u.washington.edu.*

## Study suggests human visual system could make powerful computer

Troy, N.Y. – Since the idea of using DNA to create faster, smaller, and more powerful computers originated in 1994, scientists have been scrambling to develop successful ways to use genetic code for computation. Now, new research from a professor at Rensselaer Polytechnic Institute suggests that if we want to carry out artificial computations, all we have to do is literally look around.

Assistant Professor of Cognitive Science Mark Changizi has begun to develop a technique to turn our eyes and visual system into a programmable computer. His findings are reported in the latest issue of the journal Perception.

Harnessing the computing power of our visual system, according to Changizi, requires visually representing a computer program in such a way that when an individual views the representation, the visual system naturally carries out the computation and generates a perception.



***To actually get your visual system to carry out this computation requires "perceptually walking through the circuit" from the inputs downward to the output.*** **Rensselaer/Changizi**

Ideally, we would be able to glance at a complex visual stimulus (the software program), and our visual system (the hardware) would automatically and effortlessly generate a perception, which would inform us of the output of the computation, Changizi said.

Changizi has begun successfully applying his approach by developing visual representations of digital circuits. A large and important class of computations used in calculators, computers, phones, and most of today's electronic products, digital circuits are constructed from assemblies of logic gates, and always have an output value of zero or one.

"A digital circuit needs wire in order to transmit signals to different parts of the circuit. The 'wire' in a visual representation of a digital circuit is part of the drawing itself, which can be perceived only in two ways," said Changizi, who created visual stimuli to elicit perceptions of an object tilted toward (an output of one) or away (an output of zero) from the viewer. "An input to a digital circuit is a zero or one. Similarly, an input to a visual version of the circuit is an unambiguous cue to the tilt at that part of the circuit."

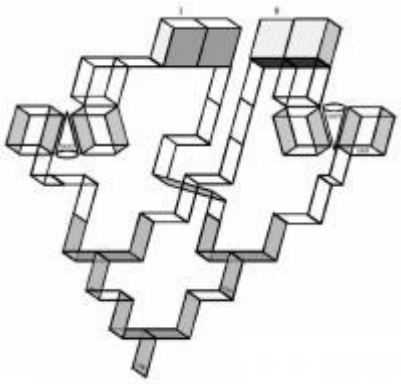
Changizi used simple drawings of unambiguous boxes as inputs for his visually represented digital circuits. The positioning and shading of each box indicates which direction the image is tilted.

He also created visual representations of the logic gates NOT, which flips a circuit's state from 0 to 1 or vice versa; OR, which outputs 1 if one or both inputs are 1; and AND, which outputs 1 only if both inputs are 1.

"Visually represented NOT gates flip a box's perceived tilt as you work through a circuit, and OR gates are designed with transparency cues so that the elicited perception is always that the box is tilted toward you, unless overridden," Changizi said. "The AND gate is similarly designed with transparency cues, but contrary to the OR gate, it will always favor the perception that it is tilted away from you."

By perceptually walking through Changizi's visual representation of a digital circuit, from the inputs downward to the output, our visual system will naturally carry out the computation so that the "output" of the circuit is the way we perceive the final box to tilt, and thus a one or zero.

"Not only may our visual system one day give DNA computation a run for its money, but visual circuits have many potential advantages for teaching logic," Changizi said. "People are notoriously poor logical reasoners — someday visual circuits may enable logic-poor individuals to 'see their way' through complex logical formulae."



Although Changizi's visual stimuli are successful at eliciting viewer perception, he says there are still serious difficulties to overcome. The visual logic gates do not always transmit the appropriate perception at the output, and it can be difficult to perceive one's way through these visual circuits, although Changizi argues we may have to train our visual system to work through them, similar to the way we need to be taught to read.

***Examples of visual wire alone; and with inputs one, to indicate a tilt toward the viewer; and 0, to indicate a tilt away.*** **Rensselaer/Changizi**

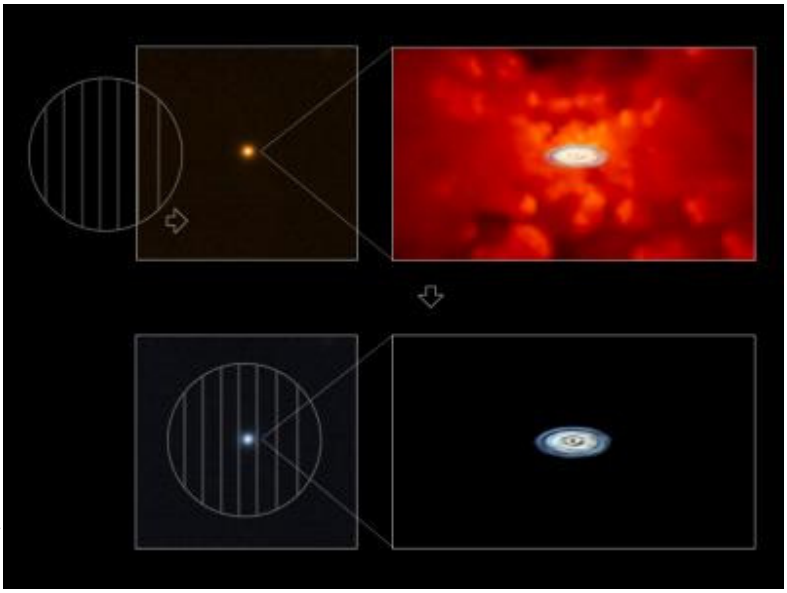
Additionally, building larger circuits will require smaller or more specialized visual circuit components.

"My hope is that other perception and illusion experts will think of novel visual components which serve to mimic some digital circuit component, thereby enriching the powers of visual circuits," Changizi said.

## Polarizing filter allows astronomers to see disks surrounding black holes

(Santa Barbara, Calif.) - For the first time, a team of international researchers has found a way to view the accretion disks surrounding black holes and verify that their true electromagnetic spectra match what astronomers have long predicted they would be. Their work will be published in the July 24 issue of the science journal Nature.

A black hole and its bright accretion disk have been thought to form a quasar, the powerful light source at the center of some distant galaxies. Using a polarizing filter, the research team, which included Robert Antonucci and Omer Blaes, professors of physics at the University of California, Santa Barbara, isolated the light emitted by the accretion disk from that produced by other matter in the vicinity of the black hole.



"This work has greatly strengthened the evidence for the accepted explanation of quasars," said Antonucci.

According to Antonucci, the physical process that astronomers find most appealing to explain a quasar's energy source and light production involves matter falling toward a supermassive black hole and swirling around in a disk as it makes its way to the event horizon - the spherical surface that marks the boundary of the black hole. In the process, friction causes the matter to heat up such that it produces light in all wavelengths of the spectrum, including infrared, visible, and ultraviolet. Finally, the matter falls into the black hole and thereby increases the black hole's mass.

***A polarizing filter attached to a telescope suppresses the light emitted by dust particles and ionized gas clouds around the quasar so its true electromagnetic spectrum can be revealed.*** **Makoto Kishimoto, with cloud image by Schartmann.**

"If that's true, we can predict from the laws of physics what the electromagnetic spectrum of the quasar should be," said Antonucci. But testing the prediction has been impossible until now because astronomers have not been able to distinguish between the light emanating from the accretion disk and that of dust particle and ionized gas clouds in the area of the black hole.

By attaching a polarizing filter to the United Kingdom Infrared Telescope (UKIRT) on Mauna Kea in Hawaii, the research team, led by Makoto Kishimoto, an astronomer with the Max-Plank Institute for Radio Astronomy in Bonn, and a former postdoctoral fellow at UCSB, eliminated the extraneous light and was able to measure the spectrum of the accretion disk. Doing so, they demonstrated that the spectrum matches what previously had been predicted. The researchers also used extensive data gathered from the polarization analyzer of the Very Large Telescope, an observatory in Chile that is operated by the European Space Observatory.

What makes the polarizing filter able to perform its magic is the fact that direct light is not polarized - that is, it has no preference in terms of the directional alignment of its electrical field. The accretion disk emanates

direct light, as do the dust particles and ionized gas. However, a small amount of light from the accretion disk, which is the exact light the researchers want to study, reflects off gas located very close to the black hole. This light is polarized.

"So if we plot only polarized light, it's as if the additional light isn't there and we can see the true spectrum of the accretion disk," Antonucci said. "With this knowledge we have a better understanding of how black holes consume matter and expand."

Studying the spectrum of a glowing object such as a quasar provides astronomers with an incredible amount of valuable information about its properties and processes, Antonucci noted. "Our understanding of the physical processes in the disk is still rather poor, but now at least we are confident of the overall picture," he said.

## Scientists Suspect Omega-3 Fatty Acids Could Slow Acute Wound Healing

Columbus, Ohio – A recent study shows that popular fish oil supplements have an effect on the healing process of small, acute wounds in human skin. But whether that effect is detrimental, as researchers initially suspected, remains a mystery.

The omega-3 fatty acids found in fish oils are widely considered to benefit cardiovascular health and other diseases related to chronic inflammation because of their anti-inflammatory properties. But insufficient inflammation during the initial stage of wound healing may delay the advancement of later stages.

In the study, blister wounds on the arms of people taking fish oil supplements were compared to the wounds of people taking a placebo. The wounds healed in about the same amount of time – but at the local cellular level, something unexpected happened. The levels of proteins associated with initiating and sustaining inflammation were higher in the blister fluid in people who had taken the active fish oil supplements. The researchers had expected those proteins to be lowered by the increased systemic presence of omega-3 fatty acids in the blood.

"That finding was hard to explain," said Jodi McDaniel, lead author of the study and an assistant professor of nursing at Ohio State University. "These proteins may have other functions that we don't yet fully understand. And our results also suggested there could be a difference between men and women in the amount of inflammatory proteins that are produced, because on average, women had lower levels of one of the proteins."

If the polyunsaturated fatty acids in the fish oils do indeed delay acute wound healing, then they probably should be discontinued for awhile by patients scheduled for surgery, McDaniel said. They appear to have enough of an effect that patients should at least inform their doctors if they're taking a fish oil supplement, she added.

But there could still be a bright side to the supplements' ability to alter those proteins and other molecular substances that control inflammation locally. Fish oil's systemic anti-inflammatory power, which has been illustrated in previous studies, still might assist in the healing of chronic wounds at the local level. Chronic wounds are essentially stuck in an inflammatory stage that slows or prevents transition to the later stages needed for complete healing. That mechanism needs to be explored further, McDaniel said.

"There's so much information out there now about omega-3s and they clearly have lots of potential," McDaniel said. "We're just trying to figure out how to evaluate what they do and how to advise people to take these supplements. Our goal isn't to stop supplement use but to fill in the picture of what conditions they help and what they might hurt."

The research is published in a recent issue of the journal Wound Repair and Regeneration.

Study participants were divided into two groups of 15 healthy adults each. One group took a placebo, and the other took an active supplement containing 1.6 grams of eicosapentaenoic acid (EPA) and 1.1 grams of docosahexaenoic acid (DHA) daily for four weeks. EPA and DHA are the polyunsaturated fatty acids obtained primarily from fish oil that serve as the basis of most standard omega-3 supplements.

Previous research has suggested that these fatty acids affect the production of proteins called proinflammatory cytokines, which signal biological processes during the inflammatory stage of wound healing. The primary cytokines in the process are interleukin-1 beta (IL-1b), interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-a).

But research had not yet addressed how the interaction between fatty acids and these cytokines might affect human wounds.

McDaniel and colleagues expected to find that research participants taking the fish oil supplements – and therefore being affected by their anti-inflammatory properties – would have significantly lower levels of the cytokines in their blister wounds during the initial stage of inflammation, resulting in a slower healing process.

Instead, the group taking the fish oil had significantly higher levels of IL-1b in their blister wounds than did the placebo group 24 hours after the wounds were created. The active group also had higher levels of IL-6 and TNF-a cytokines in their blisters over time than did the placebo group, but those differences in levels were not

significant. The blisters took an average of 10.7 days to completely heal in the active supplement group and an average of 9.8 days in the placebo group, but the difference was not significant.

The results suggest that the function of these cytokines still isn't completely understood, McDaniel said. And the scientists were also surprised to find that gender appeared to make a difference in cytokine production. Men were more likely than women among the active supplement group to have higher levels of the IL-1b cytokine in their wounds. McDaniel said that some studies have suggested that estrogen plays a role in inhibiting the production of this particular protein during the inflammatory stage of wound healing, but more research is needed.

McDaniel and colleagues are following up with a similar study in which they are adding a low-dose aspirin to both the fish oil supplement and placebo groups. Some research has shown that aspirin can facilitate the anti-inflammatory properties of omega-3 fatty acids, and low-dose aspirin is commonly included in the medication regimen of patients with cardiovascular disease.

The researchers also will look at different biological markers in blister wounds to see if the combination of fish oil and aspirin produces compounds that function as what McDaniel called "stop and go switches" in controlling inflammation.

"If we find that the fish oil can work in an anti-inflammatory fashion at the local level of wound sites, we would consider moving on to the chronic wound population," McDaniel said. "Even if we find that there are times when omega-3 fatty acids should not be taken in advance of creating an acute wound, such as in elective surgery, we still have high hopes that fish oil might be beneficial for chronic wounds in certain situations."

*This research was supported by the National Institutes of Health/National Institute of Nursing Research Predoctoral National Research Service Award Fellowship program; Sigma Theta Tau International, Epsilon Chapter; and Ohio State University Alumni Grants for Graduate Research & Scholarship.*

*Co-authors on the study were Martha Belury of Ohio State's College of Education and Human Ecology and Karen Ahijevych and Wendy Blakely of Ohio State's College of Nursing.*

## Plant steroids offer new paradigm for how hormones work

Stanford, CA—Steroids bulk up plants just as they do human athletes, but the playbook of molecular signals that tell the genes to boost growth and development in plant cells is far more complicated than in human and animal cells. A new study by plant biologists at the Carnegie Institution used an emerging molecular approach called proteomics to identify key links in the steroid signaling chain. Understanding how these plant hormones activate genes could lead not only to enhanced harvests but also to new insights into how steroids regulate growth in both plant and animal cells.

The study by Zhi-Yong Wang and Wenqinag Tang of the Carnegie Institution's Department of Plant Biology with seven co-authors* is published in the July 25 issue of Science magazine.

Plant steroids, called brassinosteroids, are key hormones throughout the plant kingdom. They regulate many aspects of growth and development, and mutants deficient in brassinosteroids are often extremely stunted and infertile. Brassinosteroids are similar in many respects to animal steroids, but appear to function very differently at the cellular level. Animal cells respond to steroids using internal receptor molecules within the cells nucleus, whereas in plants the receptors are anchored to the outside surface of the cell membranes. A challenge for researchers has been to piece together the steps by which the hormonal signal is transmitted from the cell surface receptor to its action in the nucleus, where genes are the targets of regulation. Traditionally, genetic methods have been used to identify several components of the BR signaling pathway. However, genetic approach cannot identify all the components of a signaling pathway largely because of genetic redundancy (many genes play the same role in the cell).

To identify the links in the signal transduction chain, the researchers used the techniques of proteomics. "Proteomics is analogous to genomics," says Wang. "In genomics, we aim for a comprehensive survey of all the genes in genome. In proteomics, we're mapping the proteins." Because there can be hundreds of thousands of different proteins in a single organism, proteomics requires techniques, such as 2-dimensional gel electrophoresis, which can process and segregate thousands of proteins at a time based on differences in their size and charge.

But even with these methods, isolating the low-abundance signaling proteins was a daunting task. "Earlier attempts to identify these molecules failed, because the analyses were swamped by the more abundant proteins," says Wang. "But because we knew the proteins would be associated with the cell membrane, we tried separating the membranes from the rest of the cell material and just analyzed that fraction. And that worked."

The study targeted a class of proteins called kinases, which transmit signals by exchanging phosphate ions. The electrophoresis analyses identified a group of kinases that responded to the presence of brassinosteroids.

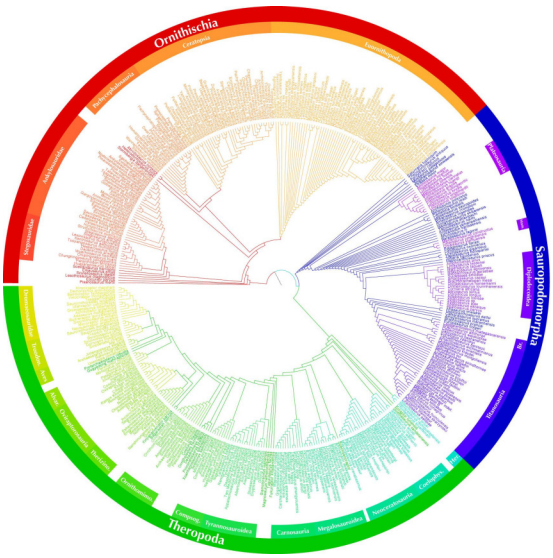
The researchers called these proteins BSKs (brassinosteroid signaling kinases). Follow-up analyses confirmed their crucial function in brassinosteroid signaling.

"BSKs are the first major signaling component to be identified by a quantitative proteomics approach in plants." says Wang. "Finding them fills a major gap in the brassinosteroid signal pathway and may have major implications for our understanding of other signaling processes in plants as well. The plant genome codes for many hundreds of receptors at the cell surface, but a major missing link is their connection to the intracellular signaling cascades. Plant cells also contain quite a number of proteins that are similar to BSK, so it is tempting to speculate that they represent these missing connections". Wang's findings have not only helped establish the connections of the steroid signaling pathway, but possibly offers a paradigm for both kinase signaling in plants and for steroid signaling by cell-surface receptors in general. More importantly, the success of the proteomic methods demonstrated by Wang's study will have a major impact on studies of other signal transduction pathways.

*Tae-Wuk Kim, Yu Sun, Zhiping Deng, Shengwei Zhu, and Ruiju Wang of the Carnegie Institution; Juan A Oses-Prieto and Alma L. Burlingame of the University of California, San Francisco.*

## Dinosaur evolutionary tree unveiled

* 18:00 23 July 2008
* NewScientist.com news service
* **Colin Barras**
* **Michael Marshall**




Dinosaurs may have been the largest land animals of the Cretaceous period, but a new study suggests that they were conspicuously absent from the 'terrestrial revolution' of that time, in which the number of land species rose rapidly.

Graeme Lloyd at the University of Bristol, UK, and his team studied all of the existing dinosaur taxonomic literature to produce a 'supertree' of dinosaur species. The new supertree, which includes 440 of the 600 known dinosaur species, shows that the dinosaurs evolved rapidly during their first 50 million years. By the Middle to Late Jurassic, a period famous for its giant dinosaurs including Diplodocus and Allosaurus, dinosaur evolution had slowed to a crawl.

It remained at that low level throughout the following Cretaceous period, a time of plenty in Earth's terrestrial history in which flowering plants, lizards, snakes, birds and mammals all became much more numerous. Dinosaurs apparently did not take advantage of the abundant food supply that emerged during the Cretaceous Terrestrial Revolution.

"Our supertree allows us to look for unusual patterns across the whole of dinosaurs for the first time," says Lloyd. "It is the most comprehensive picture ever produced of how dinosaurs evolved."

*Journal reference: Proceedings of the Royal Society B, DOI: 10.1098/rspb.2008.0715*

## Overactive bladders play with the mind

* 23 July 2008
* **Bob Holmes**

THE urge to pee too frequently might literally mess with your mind. Experiments in rats show that an overactive bladder changes brain activity. If the same is true in humans, it could in part explain the disrupted sleep, reduced ability to concentrate and confusion that often accompany ageing.

"If you have an overactive bladder, you don't just have a bladder problem. It has neurobehavioural consequences," says Rita Valentino, a neuroscientist at the Children's Hospital of Philadelphia in Pennsylvania.

As much as 17 per cent of the US population is affected by the disorder, which is characterised by uncontrolled bladder contractions, leading to frequent urination. It is often caused by a partial obstruction of the urethra, such as in men with enlarged prostates. Valentino and her colleagues mimicked this in rats by surgically constricting the outlet from the bladder.

When the team scanned the rats' brains they found increased activation of a region of the brainstem called the locus coeruleus, which helps control alertness. In normal mammals, this region is activated only when the bladder is full, and helps the animal to disengage from other activities. In rats with overactive bladders, however, activation seems to occur continually. An overactive locus coeruleus triggered increased and disordered activity in the forebrain, which controls higher brain function (Proceedings of the National Academy

of Sciences, DOI: 10.1073/pnas.0800969105). In people, this is likely to lead to anxiety, disrupted sleep and other behavioural problems.

The study is the first to show that a bladder disorder can have a direct effect on brain function. "This helps complete the puzzle of why overactive bladder symptoms are so disruptive to quality of life," says Craig Comiter, a urologist at Stanford University School of Medicine in California.

Bowel disorders such as irritable bowel syndrome may also overactivate the locus coeruleus, which would help explain the psychiatric disorders that often accompany IBS, Valentino says.

## Prevailing theory of aging challenged in Stanford worm study

STANFORD, Calif. - Age may not be rust after all. Specific genetic instructions drive aging in worms, report researchers at the Stanford University School of Medicine. Their discovery contradicts the prevailing theory that aging is a buildup of tissue damage akin to rust, and implies science might eventually halt or even reverse the ravages of age.

"We were really surprised," said Stuart Kim, PhD, professor of developmental biology and of genetics, who is the senior author of the research.

Kim's lab examined the regulation of aging in C. elegans, a millimeter-long nematode worm whose simple body and small number of genes make it a useful tool for biologists. The worms age rapidly: their maximum life span is about two weeks.

Comparing young worms to old worms, Kim's team discovered age-related shifts in levels of three transcription factors, the molecular switches that turn genes on and off. These shifts trigger genetic pathways that transform young worms into geezers. The findings will appear in the July 24 issue of the journal Cell.

The question of what causes aging has spawned competing schools of thought. One side says inborn genetic programs make organisms grow old. This theory has had trouble gaining traction because it implies that aging evolved, that natural selection pushed older organisms down a path of deterioration. However, natural selection works by favoring genes that help organisms produce lots of offspring. After reproduction ends, genes are beyond natural selection's reach, so scientists argued that aging couldn't be genetically programmed.

The alternate theory holds that aging is an inevitable consequence of accumulated wear and tear: Toxins, free-radical molecules, DNA-damaging radiation, disease and stress ravage the body to the point it can't rebound. So far, this theory has dominated aging research.

But the Stanford team's findings told a different story. "Our data just didn't fit the current model of damage accumulation, and so we had to consider the alternative model of developmental drift," Kim said.

The scientists used microarrays - silicon chips that detect changes in gene expression - to hunt for genes that were turned on differently in young and old worms. They found hundreds of age-regulated genes switched on and off by a single transcription factor called elt-3, which becomes more abundant with age. Two other transcription factors that regulate elt-3 also changed with age.

To see whether these signal molecules were part of a wear-and-tear aging mechanism, the researchers exposed worms to stresses thought to cause aging, such as heat (a known stressor for nematode worms), free-radical oxidation, radiation and disease. But none of the stressors affected the genes that make the worms get old.

So it looked as though worm aging wasn't a storm of chemical damage. Instead, Kim said, key regulatory pathways optimized for youth have drifted off track in older animals. Natural selection can't fix problems that arise late in the animals' life spans, so the genetic pathways for aging become entrenched by mistake. Kim's team refers to this slide as "developmental drift."

"We found a normal developmental program that works in young animals, but becomes unbalanced as the worm gets older," he said. "It accounts for the lion's share of molecular differences between young and old worms."

Kim can't say for sure whether the same process of drift happens in humans, but said scientists can begin searching for this new aging mechanism now that it has been discovered in a model organism. And he said developmental drift makes a lot of sense as a reason why creatures get old.

"Everyone has assumed we age by rust," Kim said. "But then how do you explain animals that don't age?"

Some tortoises lay eggs at the age of 100, he points out. There are whales that live to be 200, and clams that make it past 400. Those species use the same building blocks for their DNA, proteins and fats as humans, mice and nematode worms. The chemistry of the wear-and-tear process, including damage from oxygen free-radicals, should be the same in all cells, which makes it hard to explain why species have dramatically different life spans.

"A free radical doesn't care if it's in a human cell or a worm cell," Kim said.

If aging is not a cost of unavoidable chemistry but is instead driven by changes in regulatory genes, the aging process may not be inevitable. It is at least theoretically possible to slow down or stop developmental drift.

"The take-home message is that aging can be slowed and managed by manipulating signaling circuits within cells," said Marc Tatar, PhD, a professor of biology and medicine at Brown University who was not involved in the research. "This is a new and potentially powerful circuit that has just been discovered for doing that."

Kim added, "It's a new way to think about how to slow the aging process."

Stanford co-authors on the study included postdoctoral scholar Yelena Budovskaya, PhD; doctoral student *Lucinda Southworth; Kendall Wu, PhD, a former Stanford postdoctoral scholar now working at Affymetrix Inc., and Min Jiang, a former Stanford lab technician. The Stanford team collaborated with Patricia Tedesco and Thomas Johnson of the University of Colorado-Boulder.*

*The research was supported by grants from the National Institutes of Health, the Ellison Medical Foundation and the Larry L. Hillblom Foundation.*

## Material May Help Autos Turn Heat Into Electricity

COLUMBUS, Ohio -- Researchers have invented a new material that will make cars even more efficient, by converting heat wasted through engine exhaust into electricity.

In the current issue of the journal Science, they describe a material with twice the efficiency of anything currently on the market. The same technology could work in power generators and heat pumps, said project leader Joseph Heremans, Ohio Eminent Scholar in Nanotechnology at Ohio State University.

Scientists call such materials thermoelectric materials, and they rate the materials' efficiency based on how much heat they can convert into electricity at a given temperature.

Previously, the most efficient material used commercially in thermoelectric power generators was an alloy called sodium-doped lead telluride, which had a rating of 0.71. The new material, thallium-doped lead telluride, has a rating of 1.5 -- more than twice that of the previous leader.

What's more important to Heremans is that the new material is most effective between 450 and 950 degrees Fahrenheit -- a typical temperature range for power systems such as automobile engines.

Some experts argue that only about 25 percent of the energy produced by a typical gasoline engine is used to move a car or power its accessories, and nearly 60 percent is lost through waste heat -- much of which escapes in engine exhaust.

A thermoelectric (TE) device can capture some of that waste heat, Heremans said. It would also make a practical addition to an automobile, because it has no moving parts to wear out or break down.

"The material does all the work. It produces electrical power just like conventional heat engines -- steam engines, gas or diesel engines -- that are coupled to electrical generators, but it uses electrons as the working fluids instead of water or gases, and makes electricity directly." "Thermoelectrics are also very small," he added. "I like to say that TE converters compare to other heat engines like the transistor compares to the vacuum tube."

The engineers took a unique strategy to design this new material. To maximize the amount of electricity produced by a TE material, engineers would normally try to limit the amount of heat that can pass through it without being captured and converted to electricity. So the typical strategy for making a good thermoelectric material is to lower its thermal conductivity.

In Heremans' lab, he used to work to lower the thermal conductivity by building nanometer-sized structures such as nanowires into materials. A nanometer is one billionth of a meter.

Those nanostructured materials are not very stable, are very difficult to make in large quantities, and are difficult to connect with conventional electronic circuits and external heat sources.

For this new material, he and his colleagues took a different strategy: they left out the fancy nanostructures, and instead focused on how to convert the maximum amount of heat that was trapped in the material naturally.

To do this, they took advantage of some new ideas in quantum mechanics.

Heremans pointed to a 2006 paper published by other researchers in the journal Physical Review Letters, which suggested that elements such as thallium and tellurium could interact on a quantum-mechanical level to create a resonance between the thallium electrons and those in the host lead telluride thermoelectric material, depending on the bonds between the atoms.

"It comes down to a peculiar behavior of an electron in a thallium atom when it has tellurium neighbors," he said. "We'd been working for 10 years to engineer this kind of behavior using different kinds of nanostructured materials, but with limited success. Then I saw this paper, and I knew we could do the same thing we'd been trying to do with nanostructures, but with this bulk semiconductor instead."

Heremans designed the new material with Vladimir Jovovic, who did this work for his doctoral thesis in the Department of Mechanical Engineering at Ohio State. Researchers at Osaka University -- Ken Kurosaki, Anek Charoenphakdee, and Shinsuke Yamanaka -- created samples of the material for testing. Then researchers at the California Institute of Technology -- G. Jeffrey Snyder, Eric S. Toberer, and Ali Saramat -- tested the material at high temperatures. Heremans and Jovovic tested it at low temperatures and provided experimental proof that the physical mechanism they postulated was indeed at work.

The team found that near 450 degrees Fahrenheit, the material converted heat to electricity with an efficiency rating of about 0.75 -- close to that of sodium doped telluride. But as the temperature rose, so did the efficiency of the new material. It peaked at 950 degrees Fahrenheit, with a rating of 1.5.

Heremans' team is continuing to work on this patent-pending technology. "We hope to go much further. I think it should be quite possible to apply other lessons learned from thermoelectric nanotechnology to boost the rating by another factor of two -- that's what we're shooting for now," he said.

*This research was funded by the BSST Corporation; the State of Ohio Department of Development's Center for Photovoltaic Innovation and Commercialization at Ohio State University; the Beckman Institute; the Swedish Bengt Lundqvist Minne Foundation; and NASA's Jet Propulsion Laboratory.*

## The quiet explosion

### *Object intermediate between normal supernovae and gamma-ray bursts found*

A European-led team of astronomers are providing hints that a recent supernova may not be as normal as initially thought. Instead, the star that exploded is now understood to have collapsed into a black hole, producing a weak jet, typical of much more violent events, the so-called gamma-ray bursts. The object, SN 2008D, is thus probably among the weakest explosions that produce very fast moving jets. This discovery represents a crucial milestone in the understanding of the most violent phenomena observed in the Universe.

These striking results, partly based on observations with ESO's Very Large Telescope, will appear tomorrow in Science Express, the online version of Science.

Stars that were at birth more massive than about 8 times the mass of our Sun end their relatively short life in a cosmic, cataclysmic firework lighting up the Universe. The outcome is the formation of the densest objects that exist, neutron stars and black holes. When exploding, some of the most massive stars emit a short cry of agony, in the form of a burst of very energetic light, X- or gamma-rays.

In the early afternoon (in Europe) of 9 January 2008, the NASA/STFC/ASI Swift telescope discovered serendipitously a 5-minute long burst of X-rays coming from within the spiral galaxy NGC 2770, located 90 million light-years away towards the Lynx constellation. The Swift satellite was studying a supernova that had exploded the previous year in the same galaxy, but the burst of X-rays came from another location, and was soon shown to arise from a different supernova, named SN 2008D.

Researchers at the Italian National Institute for Astrophysics (INAF), the Max-Planck Institute for Astrophysics (MPA), and at various other institutions have observed the supernova at great length. The team is led by Paolo Mazzali of INAF's Padova Observatory and MPA.

"What made this event very interesting," says Mazzali, "is that the X-ray signal was very weak and 'soft' [1], very different from a gamma-ray burst and more in line with what is expected from a normal supernova."

So, after the supernova was discovered, the team rapidly observed it from the Asiago Observatory in Northern Italy and established that it was a Type Ic supernova.

"These are supernovae produced by stars that have lost their hydrogen and helium-rich outermost layers before exploding, and are the only type of supernovae which are associated with (long) gamma-ray bursts," explains Mazzali. "The object thus became even more interesting!"

Earlier this year, an independent team of astronomers reported in the journal Nature that SN 2008D is a rather normal supernova. The fact that X-rays were detected was, they said, because for the first time, astronomers were lucky enough to catch the star in the act of exploding.

Mazzali and his team think otherwise. "Our observations and modeling show this to be a rather unusual event, to be better understood in terms of an object lying at the boundary between normal supernovae and gamma-ray bursts."

The team set up an observational campaign to monitor the evolution of the supernova using both ESO and national telescopes, collecting a large quantity of data. The early behaviour of the supernova indicated that it was a highly energetic event, although not quite as powerful as a gamma-ray burst. After a few days, however, the spectra of the supernova began to change. In particular Helium lines appeared, showing that the progenitor star was not stripped as deeply as supernovae associated with gamma-ray bursts.

Over the years, Mazzali and his group have developed theoretical models to analyse the properties of supernovae. When applied to SN2008D, their models indicated that the progenitor star was at birth as massive

as 30 times the Sun, but had lost so much mass that at the time of the explosion the star had a mass of only 8-10 solar masses. The likely result of the collapse of such a massive star is a black hole.

"Since the masses and energies involved are smaller than in every known gamma-ray burst related supernova, we think that the collapse of the star gave rise to a weak jet, and that the presence of the Helium layer made it even more difficult for the jet to remain collimated, so that when it emerged from the stellar surface the signal was weak," says Massimo Della Valle, co-author.

"The scenario we propose implies that gamma-ray burst-like inner engine activity exists in all supernovae that form a black hole," adds co-author Stefano Valenti.

"As our X-ray and gamma-ray instruments become more advanced, we are slowly uncovering the very diverse properties of stellar explosions," explains Guido Chincarini, co-author and the Principal Investigator of the Italian research on gamma-ray bursts. "The bright gamma-ray bursts were the easiest to discover, and now we are seeing variations on a theme that link these special events to more normal ones."

These are however very important discoveries, as they continue to paint a picture of how massive star end their lives, producing dense objects, and injecting new chemical elements back into the gas from which new stars will be formed.

***More information***

*The metamorphosis of Supernova SN 2008D/XRF 080109: a link between Supernovae and GRBs/Hypernovae, by Paolo Mazzali et al., Science Express, 24 July 2008.*

*[1] Astronomers classify X-rays as soft when the relative amount of high-energy X-rays is smaller than that of lower-energy ones.*

## Study shows emergency physicians have good first instincts in diagnosing heart attacks

WINSTON-SALEM, N.C. – A study out of Wake Forest University Baptist Medical Center demonstrates emergency room doctors are correctly identifying patients who are having a heart attack, even when laboratory tests haven't yet confirmed it.

The study used data from a registry called i*trACS, and analyzed patients with heart attack symptoms who were admitted to emergency departments (EDs) in eight participating U.S. centers.

The findings were released today in the Emergency Medicine Journal.

"One of the most common complaints we see in the Emergency Department is chest pain," said Chadwick Miller, M.D., lead author and assistant professor of emergency medicine at Wake Forest Baptist. "That's why it is so important to figure out if we're doing a good job of diagnosing and treating heart attacks, or if there's a better way to do it."

The patients in the registry were divided into three groups: no myocardial infarction (No MI), non-ST segment elevation myocardial infarction (NSTEMI), or evolving myocardial infarction (EMI).

The groups were determined by a blood test that measured levels of the protein troponin, which increases when the heart muscle is damaged from a heart attack.

Patients classified as No MI may have had symptoms but, according to the troponin levels throughout their hospital stay, did not actually have a heart attack. Patients classified as NSTEMI showed elevated troponin levels when first admitted, usually because their heart attack happened several hours or even days before coming to the ED. Patients classified as EMI did not initially show elevated troponin levels when presenting to the ED, but showed evidence of heart damage up to 12 hours later.

The study focused primarily on EMI patients. When a patient was admitted into the ED with heart attack symptoms, doctors at centers participating in the i*trACS registry would record their initial impressions of the symptoms exhibited by the patient. According to the results, the initial impression of the physicians showed that a higher percentage of them assigned a higher risk of heart attack to the EMI (76 percent) and NSTEMI (71 percent) patients, than the No MI (52 percent) group. As a result, the EMI patients were triaged to higher levels of care than the no MI group, despite the initial negative troponin results.

"There has been a lot of concern that clinicians either aren't spending enough time getting clinical history from patients or are not using the information they obtain," said Miller. "Patients with EMI are at particular risk for being evaluated less aggressively because their initial troponin result is normal, even though they have had a heart attack. This study suggests that although we are relying on better medical technology to diagnose patients, the clinical impression is still very important."

"It is reassuring to see that the admission patterns among the EMI patients were more aggressive than with the No MI patients, even though in both groups the patients' troponin results were not elevated. This suggests that clinicians are not allowing the non-elevated troponin results to overshadow their clinical impression."

The i*trACS registry was compiled over a period of 26 months. More than 17,000 patients were enrolled. However, only 4,136 of those patients were included in the analysis, primarily because patients had to have two

troponin results within 12 hours to be included. Patients were also excluded from the i*trACS registry if they were pregnant, or under 18 years old.

*The i*trACS registry was supported by an educational grant from Millenium Pharmaceuticals and Schering-Plough Pharmaceuticals.*

*Co-investigators were James Hoekstra, M.D., also of Wake Forest; Gregory Fermann, M.D., Christopher Lindsell, Ph.D., and Brian Gibler, M.D., all from University of Cincinnati; Kenneth Mahaffey, M.D., Duke Clinical Research Institute; Frank Peacock, M.D., Cleveland Clinic Foundation; Charles Pollack, M.A., M.D., and Judd Hollander, M.D., University of Pennsylvania; and Deborah B. Diercks, M.D., University of California, Davis Medical Center.*

## Hyperactive immune resistance brings blindness in old age

### *Recent discoveries regarding the origins of senile blindness*

Age-dependent macular degeneration (AMD) is the commonest cause of blindness in the western industrialised nations. Hereditary changes in the regulation of the immune system influence the risk of contracting AMD. Opthalmologists at the University Clinic in Bonn, working in co-operation with researchers from Göttingen, Regensburg and Great Britain, have now, for the first time, demonstrated that in cases of senile blindness the patient's immune resistance is hyperactive throughout his entire body.

An Anglo-German research team embracing immunologists from Göttingen University has added a further important aspect to our current knowledge of the processes leading to senile blindness. For the first time, they have been able to show that in the case of patients with AMD their entire immune system is hyperactive. It had not previously been known whether such an immune reaction affecting the entire body played any role in this eye disease.

The investigation was conducted by scientists from Bonn, Göttingen, Regensburg and Oxford under the leadership of Privatdozent Dr. Hendrik Scholl of Bonn University's Eye Clinic. The results achieved by this research team have now been published in the current edition of the PLoS ONE: http://www.plosone.org/article/info:doi/10.1371/journal.pone.0002593

**Faults in the (immune) System**

The Anglo-German research team worked on the hypothesis that one cause of the appearance of senile blindness, AMD, might be faulty regulation of the so-called complement system. This system is an important element in our hereditary immune resistance, and is involved where inflammatory reactions occur. Previously, it had only been known that changes in genes containing the hereditary information for proteins in the complement system increase the risk of contracting AMD. Some of these proteins activate, others inhibit, the complement system.

The team examined the blood of a total of 112 AMD-patients and 67 healthy control persons for signs of faults in the regulation of their complement systems. They sought out changes in protein concentration which would indicate activation of the complement system. The experiments were conducted in Göttingen University's Department for Cellular and Molecular Immunology under the leadership of Professor Dr. Martin Oppermann. The investigations of the patients´ blood did, indeed, reveal clear changes in the concentrations of a number of complement proteins which, moreover, correlated closely to the previously identified hereditary factors.

**Dormant inflammatory Situation of the Body**

"Our study has revealed for the first time that in the case of AMD patients the complement system is hyperactive over the entire body", Dr. Hendrik Scholl declares. The typical substances indicating a permanent inflammatory reaction circulate in the blood. "These results infer that senile blindness may arise from a permanent state of inflammation in the body. This can obviously lie dormant for decades, then in advanced old age can lead to the appearance of symptoms of the disease. According to Dr. Scholl, the point of most acute vision, at the centre of the retina, appears to be the susceptible point.

In Germany, an estimated 4.5 million people suffer from age-dependent macular degeneration (AMD). With this disease, the point of most acute vision on the retina (macula) becomes subject to progressive deterioration. The patient can no longer read, and he or she loses the ability to lead an independent existence. Opthalmologists had hitherto known comparatively little about the causes of this disease, except that hereditary factors were involved, and also other easily influenced factors, such as smoking.

## Many little parasites add up to one big biomass

* 10:45 24 July 2008

* NewScientist.com news service

*** Catherine Brahic**

Parasites are small, but they punch above their weight in terms of their effects on other life forms. Now it turns out that the amount of parasites in an ecosystem physically weighs more than the top predators.

It was previously thought parasites did not contribute much biomass when put against that of other animals and plants. To check this, Armand Kuris of the University of California, Santa Barbara, and colleagues painstakingly estimated the biomass of animals, plants and parasites in three estuaries in California and Baja California.

They sampled 23 random sites in each estuary and estimated the biomass of all life-forms in each of those sites, from tiny parasites up to birds – the local top predators.

**'Castration' effect**

Put together, the parasites in each estuary weighed as much as the local fish and between 3 and 9 times more than the local birds. Parasites that "castrate" their hosts – prevent them from reproducing – had the greatest cumulative biomass and on their own weighed as much as the local winter birds.

For Andrew Dobson of Princeton University, one of Kuris's collaborators, this shows that that castration is the most effective way for parasites to survive. Castration allows parasites to keep the hosts alive while preventing them from spending any energy on their own reproduction.

"All free-living organisms host one or more parasites," says Peter Olson of the Natural History Museum in London. For this reason, it has long been thought that parasites are likely to be the most common life-form on Earth in terms of numbers of species, and possibly numbers of individuals.

"However, in terms of biomass, parasitologists and non-parasitologists alike have generally assumed parasite biomass to be negligible in comparison with free-living organisms," Olsen says. "Kuris and colleagues' finding is surprising."

Dobson says he has work in press showing that parasites contain between 10 and 1000 times more pollutants than their hosts. He suggests parasites might play an important role in cleaning up the animals they inhabit.

*Journal reference: Nature(DOI: 10.1038/nature06970)*

## Mate or hibernate? That's the question worm pheromones answer

GAINESVILLE, Fla. — If worms could talk, they might tell potential suitors, "I like the way you wriggle," complete with that telltale come slither look. But worms send their valentines via signals known as pheromones, a complex chemical code researchers are now cracking, according to a study published Wednesday (July 23) in the journal Nature.

Scientists from the University of Florida, Cornell University, the California Institute of Technology and the U.S. Department of Agriculture have discovered the first mating pheromone in one of science's most well-studied research subjects, the tiny worm Caenorhabditis elegans. But perhaps even more interesting is what the newly discovered pheromone also directs worms to do — hibernate.

At lower levels, the pheromone signals the male C. elegans to mate with its partner. But when the worm population grows and the food supply dwindles, the chemical signal increases and the cue changes from mate to hibernate. This discovery could help researchers find ways to combat more harmful worms that destroy crops and provide clues for scientists studying similar parasite worms, said Arthur Edison, Ph.D., a UF associate professor of biochemistry and molecular biology in the College of Medicine and one of the study's senior authors.

"Even though it's the same compound, it affects different behaviors," said Fatma Kaplan, Ph.D., a postdoctoral associate in Edison's lab and one of the study's lead authors. "It's two different life traits converging."

In 2002, Cal Tech researcher Paul Sternberg, Ph.D., discovered that male C. elegans were attracted to a signal the opposite sex was sending out, but scientists weren't sure exactly what it was.

"C. elegans is one of the best-studied organisms on earth," Edison said. "The entire cell lineage of the animal is known from fertilized egg to adult animal. Every single cell division had been mapped out. But until now, its small-molecule signaling has been poorly understood. We wanted to understand how C. elegans talk to each other, basically."

About four out of every five animals on the planet is the same type of organism as C. elegans — a nematode, said Edison. Although the C. elegans worm, which is about 1 millimeter in length, is harmless to humans, many nematodes destroy crops or act as parasites in humans and animals, such as the large human intestinal parasite Ascaris lumbricoides. Because it is easy to grow and manipulate in the laboratory, C. elegans is a model for understanding the basic biology of humans, animals and other worms that threaten human health.

C. elegans worms are either male or hermaphrodite — meaning they feature both male and female reproductive organs — and to pinpoint how they communicate, UF researchers and their collaborators isolated the chemicals the hermaphrodites secrete and tested them on male worms.

Initial tests proved the males were attracted to the secretions when the hermaphrodites were fertile. Using mass spectroscopy and nuclear magnetic resonance spectroscopy — including a UF- and National High Magnetic Field Laboratory-developed NMR probe that allows researchers to test extremely small amounts — researchers isolated the three chemicals in these secretions that are responsible for the mating signal.

When tested individually, the chemicals produced little to no response. But the chemicals strongly attracted male worms when they worked in synergy with each other, said Edison, who also serves as director of the McKnight Brain Institute's Advanced Magnetic Resonance Imaging and Spectroscopy facility and co-principal investigator of the National High Magnetic Field Laboratory.

But it was a chance collaboration with Cornell researcher Frank Schroeder, Ph.D., that led to the paper's biggest finding, Edison said. Schroeder had recently discovered what's known as a dauer pheromone. These chemicals signal worms to enter a hibernation phase when the food supply is low. Schroeder's hibernation pheromone and the UF-discovered mating pheromone were almost identical. Tests in worms revealed that mating pheromones also act as a dauer pheromones at high concentrations.

"It's like a bell-shaped curve," Edison said. "If (the pheromone level is) too low, it doesn't work. If you add more, you get a nice mating response. If it gets high, the mating response stops and they go into hibernation mode.

"It makes nice ecological sense that (one compound) could be doing both jobs," he added. "But before this work, nobody in the whole history of C. elegans research had associated dauer formation with mating. Now these small molecules link the two behaviors."

Researchers have been trying to find C. elegans mating pheromones for a long time, said Piali Sengupta, Ph.D., a professor of biology at Brandeis University, who agreed that it makes sense that the mating pheromone has a dual role in causing hibernation.

"This opens up the field," Sengupta said. "This is just the beginning. There is going to be a lot more (research) coming out related to this."

*Edison and Kaplan's collaborators include: Sternberg, Schroeder, Cal Tech researcher Jagan Srinivasan, UF researchers Ramadan Ajredini and Cherian Zachariah, Cornell researcher Rabia U. Malik and USDA researchers Hans Alborn and Peter Teal.*

*The research was funded by the Human Frontiers Science Program, the National Institutes of Health and the Howard Hughes Medical Institute.*

## Mustard – hot stuff for natural pest control

***Modern science will put a centuries-old farming practice under the microscope at the Third International Biofumigation Symposium in Canberra from 21 – 25 July 2008.***

Researchers, growers and Industry specialists from 22 countries will share the latest research into the use of Brassica species, such as mustard, radish, or rapeseed, to manage soil-borne pests and weeds – a technique known as biofumigation.

“Brassica plants naturally release compounds that suppress pests and pathogens, principally isothiocyanates (ITCs), which most people would recognise as the ‘hot’ flavour in mustard or horseradish,” says CSIRO’s Dr John Kirkegaard, the conference convenor.

“When ITCs are released in soil by green-manuring, soil-borne pests and pathogens can be suppressed and the yields of solanaceous vegetables such as potatoes, tomatoes and eggplants can be increased by up to 40 per cent in some cases.

“The technique is relevant to developed countries seeking alternatives to banned synthetic pesticides such as methyl-bromide, as well as poor farmers in developing countries who often have few alternatives for controlling serious diseases in their crops,” Dr Kirkegaard says.

“It can provide economic and social benefits, as improved crop yields lead to increased incomes, as well as a range of environmental and health benefits from a reduced reliance on fumigants and pesticides.”

Using brassicas to manage soil-borne pests is not new, but modern science is providing new insights and techniques to enhance the reliability of the effect as part of an integrated pest control strategy. Brassicas can also provide other benefits to the soil as green manures.

Australian scientists are at the forefront of this area of research, in projects on tropical vegetable production systems in north Queensland and the Philippines, supported by the Australian Centre for International Agricultural Research (ACIAR), and on temperate southern Australian vegetable production, supported by

Horticulture Australia Limited (HAL) using voluntary contributions from industry and matched funding from the Australian Government.

The Symposium will consist of three days of scientific and Industry presentations designed to stimulate discussions about the underpinning science, as well as the practical application of biofumigation technology in Australia and worldwide. "The Symposium is an excellent opportunity to draw together the latest research on the subject from around the globe," Dr Kirkegaard says.

## Advice to drop condom use is HIV 'disaster'

* 00:01 25 July 2008

* NewScientist.com news service

*** Rachel Nowak**

The Swiss Federal Commission for HIV/AIDS raised eyebrows earlier this year when it effectively said that HIV-infected people could safely not use condoms.

The reasoning is that if you have HIV, but have been effectively treated with antiretroviral drugs, and have no genital infections, then you are "sexually non-infectious" and cannot transmit HIV to uninfected partners.

But now a computer analysis of rates of HIV transmission from individuals with different levels of the virus in their blood has shown that infection can still occur and that condoms are still essential.

If groups of couples that include one healthy partner, and one partner with an HIV infection that is controlled by drugs, stop using condoms, the incidence of HIV will increase four-fold among the couples in just 10 years.

The analysis was conducted by David Wilson of the National Centre in HIV Epidemiology and Clinical Research, at the University of New South Wales in Sydney, Australia.

**Condoms essential**

Wilson ran the computer simulation to find out what would happen if people with 10 copies of HIV per millilitre of blood – a level that indicates that antiretroviral therapy has effectively controlled the infection – had unprotected sex 100 times each year.

The results showed that over the 10 years, there would be 3524 new male-to-male HIV infections in a population of 10000 couples, 425 new male-to-female transmissions in a population of 10000, and 215 new female-to-male transmissions.

"Those are four-fold increases compared to the incidence with current condom use," says Wilson.

"Antiretroviral drugs can augment condom use, but this study shows that it would be a disaster if they replaced them as the key preventative strategy," says Jonathan Anderson, a general practitioner with a special interest in HIV at the Carlton Clinic in Melbourne, Australia, and president of the Australasian Society of HIV Medicine.

**Cumulative effect**

Although infections are rare when a person is on effective antiretroviral therapy, the Swiss organisation made a mistake in equating an improbable event with an impossible event, says Wilson. It also failed to take into account the cumulative effect of taking a very small risk a large number of times.

"The Swiss statement was not sensible at the public health level," he says. "The logical consequence would be that people would stop using condoms – our study shows that that would increase the risk of HIV transmission substantially, especially among men who have sex with men."

In the past decade, several western countries including Australia and the UK have seen large increases in HIV transmission rates, despite the widespread use of antiretroviral drugs.

A contributing factor is thought to be a fall in the use of condoms, as HIV infection is increasingly seen as a disease that can be managed with drugs, rather than a death sentence.

*Journal reference: The Lancet, vol 372, p 314 (pdf format)*

## Life from Venus blown to Earth?

***Life on Venus could be blown to Earth by powerful winds, scientists claim.***

Previous research has considered the possibility of micro organisms existing in Venus's atmosphere despite extreme temperatures on its surface.

But two scientists at the Cardiff Centre for Astrobiology say microbes from Venus could actually be blown into the Earth's atmosphere by solar winds.

Their findings follow analysis of data from the European Space Agency's Venus Express probe, launched in 2005.

Prof Chandra Wickramasinghe and Dr Janaki Wickramasinghe claim Venus's clouds contain chemicals that are consistent with the presence of micro organisms.

They suggest that under certain conditions, these microbes from high in Venus's atmosphere could be blown into the Earth's atmosphere.

This process would only take days or weeks.

But the Sun, Earth and Venus must be suitably aligned, which last happened in 2004 and will not happen again until 2012.

Prof Wickramasinghe said: "Venus and Earth have often been referred to as sisters because of their geological similarities.

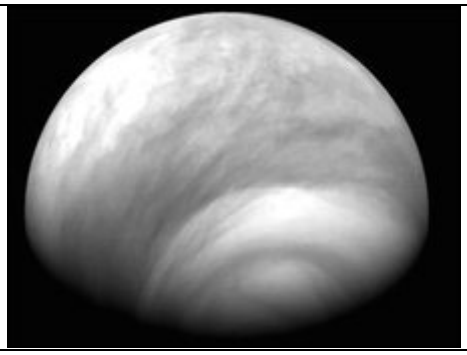
"Our research proposes that the two sisters may be biologically interconnected as well."

The work has been published online in a new paper in the Astrophysics and Space Science journal.

But Prof Fred Taylor, a planetary scientist at Oxford University, said he was sceptical about the research.

"The idea of life on Venus, particularly the clouds where the temperature and pressure are similar to the Earth, has been floated around for a while but is not really very likely," he said.

He added that it was "most unlikely" anyway that microbes from Venus could be transferred to the Earth's atmosphere by solar winds.



***Temperatures on the surface of Venus can reach 464C (867F)***

**VENUS FACTS**

***Distance from Sun: 108,200,000km***
***Diameter: 12,103km***
***Year length: 224.7 Earth days***
***Atmosphere: 96% carbon dioxide, 3% nitrogen***
***Moons: 0***
***Missions: Between 1961 and 1989 the US and USSR launched more than 30 spacecraft towards Venus***
***Brightness: Venus is the brightest object in the sky apart from the Sun and Moon***

The Venus Express probe, launched in November 2005, is orbiting the planet to study its atmosphere.

Scientists hope to learn how Venus, which is similar to Earth in size, mass and composition, evolved so differently over the last 4.6 billion years.

The mission was the first to be sent to the planet in 15 years.