SCIENCE NEWS

Jupiter's Icy Moon: Window into Europa's Ocean Lies Right at the Surface

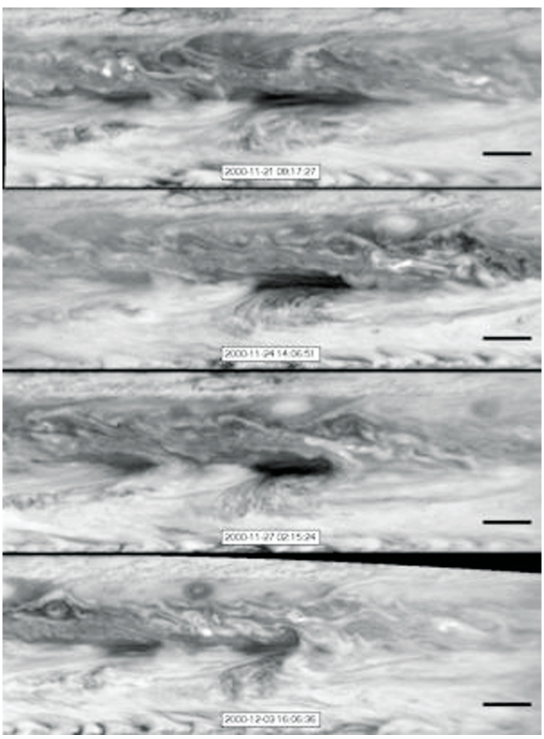
If you could lick the surface of Jupiter's icy moon Europa, you would actually be sampling a bit of the ocean beneath. So says Mike Brown, an astronomer at the California Institute of Technology (Caltech). Brown — known as the Pluto killer for discovering a Kuiper-belt object that led to the demotion of Pluto from planetary status — and Kevin Hand from the Jet Propulsion Laboratory (JPL) have found the strongest evidence yet that salty water from the vast liquid ocean beneath Europa's frozen exterior actually makes its way to the surface.

The finding, based on some of the first data of its kind since NASA's Galileo mission (1989-2003) to study Jupiter and its moons, suggests that there is a chemical exchange between the ocean and surface, making the ocean a richer chemical environment, and implies that learning more about the ocean could be as simple as analysing the moon's surface. The work is described in a paper that has been accepted for publication in the *Astronomical Journal*.

"We now have evidence that Europa's ocean is not isolated — that the ocean and the surface talk to each other and exchange chemicals," says Brown, the Richard and Barbara Rosenberg Professor and Professor of planetary astronomy at Caltech. "That means that energy might be going into the ocean, which is important in terms of the possibilities for life there. It also means that if you'd like to know what's in the ocean, you can just go to the surface and scrape some off."

"The surface ice is providing us a window into that potentially habitable ocean below," says Hand, Deputy Chief Scientist for solar system exploration at JPL.

Since the days of the Galileo mission, when the spacecraft showed that Europa was covered with an icy shell, scientists have debated the composition of Europa's surface. The infrared spectrometre aboard Galileo was not capable of providing the detail needed to definitively identify some of the materials present on the surface. Now, using current technology on ground-based telescopes, Brown and Hand have identified a spectroscopic feature on Europa's surface that indicates the presence of a magnesium sulfate salt, a mineral called epsomite, that could only originate from the ocean below.



In this series of images from NASA's Cassini spacecraft, a dark, rectangular hot spot (top) interacts with a line of vortices that approaches from on the upper-right side (second panel). The interaction distorts the shape of the hot spot (third panel), leaving it diminished (bottom). (Credit: NASA/JPL-Caltech/SSI/GSFC)

"Magnesium should not be on the surface of Europa unless it's coming from the ocean," Brown says. "So that means ocean water gets onto the surface, and stuff on the surface presumably gets into the ocean water."

Europa's ocean is thought to be 100 kilometres deep and covers the entire globe. The moon remains locked in relation to Jupiter, with the same hemisphere always leading and the other trailing in its orbit. The leading hemisphere has a yellowish appearance, while the trailing hemisphere seems to be splattered and streaked with a red material.

The spectroscopic data from that red side has been a cause of scientific debate for 15 years. It is thought that one of Jupiter's largest moons, Io, spews volcanic sulfur from its atmosphere, and Jupiter's strong magnetic field sends some of that sulfur hurtling toward the trailing hemisphere of Europa, where it sticks. It is also clear from Galileo's data that there is something other than pure water ice on the trailing hemisphere's surface. The debate has focused on what that other something is — i.e., what has caused the spectroscopic data to deviate from the signature of pure water ice.

"From Galileo's spectra, people knew something was there besides water. They argued for years over what it might be — sodium sulfate, hydrogen sulfate, sodium hydrogen carbonate, all these things that look more or less similar in this range of the spectrum," says Brown. "But the really difficult thing was that the spectrometre on the Galileo spacecraft was just too coarse."

Brown and Hand decided that the latest spectrometres on ground-based telescopes could improve the data pertaining to Europa, even from a distance of about 400 million miles. Using the Keck II telescope on Mauna Kea — which is outfitted with adaptive optics to adjust for the blurring effect of Earth's atmosphere — and its OH-Suppressing Infrared Integral Field Spectrograph (OSIRIS), they first mapped the distribution of pure water ice versus anything else on the moon. The spectra showed that even Europa's leading hemisphere contains significant amounts of nonwater ice. Then, at low latitudes on the trailing hemisphere — the area with the greatest concentration of the nonwater ice material — they found a tiny dip in the spectrum that had never been detected before.

"We now have the best spectrum of this thing in the world," Brown says. "Nobody knew there was this little dip in the spectrum because no one had the resolution to zoom in on it before."

The two researchers racked their brains to come up with materials that might explain the new spectroscopic feature, and then tested everything from sodium chloride to Drano in Hand's lab at JPL, where he tries to simulate the environments found on various icy worlds. "We tried to think outside the box to consider all sorts of other possibilities, but at the end of the day, the magnesium sulfate persisted," Hand says.

Some scientists had long suspected that magnesium sulfate was on the surface of Europa. But, Brown says, "the interesting twist is that it doesn't look like the magnesium sulfate is coming from the ocean." Since the mineral he and Hand found is only on the trailing side, where the moon is being bombarded with sulfur from Io, they believe that there is a magnesium-bearing mineral everywhere on Europa that produces magnesium sulfate in combination with sulfur. The pervasive magnesium-bearing mineral might also be what makes up the nonwater ice detected on the leading hemisphere's surface.

Brown and Hand believe that this mystery magnesium-bearing mineral is magnesium chloride. But magnesium is not the only unexpected element on the surface of Europa. Fifteen years ago, Brown showed that Europa is surrounded by an atmosphere of atomic sodium and potassium, presumably originating from the surface. The researchers reason that the sodium and potassium chlorides are actually the dominant salts on the surface of Europa, but that they are not detectable because they have no clear spectral features.

The scientists combined this information with the fact that Europa's ocean can only be one of two types — either sulfate-rich or chlorine-rich. Having ruled out the sulfate-rich version since magnesium sulfate was found only on the trailing side, Brown and Hand hypothesise that the ocean is chlorine-rich and that the sodium and potassium must be present as chlorides.

Therefore, Brown says, they believe the composition of Europa's sea closely resembles the salty ocean of Earth. "If you could go swim down in the ocean of Europa and taste it, it would just taste like normal old salt," he says.

Hand emphasises that, from an astrobiology standpoint, Europa is considered a premier target in the search for life beyond Earth; a NASA-funded study team led by JPL and the Johns Hopkins University Applied Physics Laboratory have been working with the scientific community to identify options to explore Europa further. "If we've learned anything about life on Earth, it's that where there's liquid water, there's generally life," Hand says. "And of course our ocean is a nice salty ocean. Perhaps Europa's salty ocean is also a wonderful place for life."

The *Astronomical Journal* paper is titled "Salts and Radiation Products on the Surface of Europa." The work was supported, in part, by the NASA Astrobiology Institute through the Astrobiology of Icy Worlds node at JPL.

Source: *Science Daily Online*

New Cancer Diagnostic Technique Debuts

Cancer cells break down sugars and produce the metabolic acid lactate at a much higher rate than normal cells. This phenomenon provides a telltale sign that cancer is present, via diagnostics such as PET scans, and possibly offers an avenue for novel cancer therapies. Now a team of Chilean researchers at the Centro de Estudios Científicos (CECs), with the collaboration of Carnegie's Wolf Frommer, has devised a molecular sensor that can detect levels of lactate in individual cells in real time.

Prior to this advance, no other measurement method could non-invasively detect lactate in real time at the single-cell level. The work, published in the open access journal *PLOS ONE*, is a boon to understanding how different types of cells go awry when cancer hits.

"Over the last decade, the Frommer lab at Carnegie has pioneered the use of Förster Resonance Energy Transfer, or FRET, sensors to measure the concentration and flow of sugars in individual cells with a simple fluorescent colour change. This has started to revolutionise the field of cell metabolism," explained CECs researcher Alejandro San Martín, lead author of the article. "Using the same underlying physical principle and inspired by the sugar sensors, we have now invented a new type of sensor based on a transcriptional factor. A molecule that normally helps bacteria to adapt to its environment has now been tricked into measuring lactate for us."

Lactate shuttles between cells and inside cells as part of the normal metabolic process. But it is also involved in diseases that include inflammation, inadequate oxygen supply to cells, restricted blood supply to tissues, and neurological degradation, in addition to cancer.

"Standard methods to measure lactate are based on reactions among enzymes, which require a large number of cells in complex cell mixtures," explained Felipe Barros, leader of the project. "This makes it difficult or even impossible to see how different types of cells are acting when cancerous. Our new technique lets us measure the metabolism of individual cells, giving us a new window for understanding how different cancers operate. An important advantage of this technique is that it may be used in high-throughput format, as required for drug development."

This work used a bacterial transcription factor — a protein that binds to specific DNA sequences to control the flow of genetic information from DNA to mRNA — as a means to produce and insert the lactate sensor. They turned the sensor on in three cell types: normal brain cells, tumor brain cells, and human embryonic cells. The sensor was able to quantify very low concentrations of lactate, providing an unprecedented sensitivity and range of detection.

The researchers found that the tumor cells produced lactate 3-5 times faster than the non-tumor cells. "The high rate of lactate production in the cancer cell is the hallmark of cancer metabolism," remarked Frommer. "This result paves the way for understanding the nuances of cancer metabolism in different types of cancer and for developing new techniques for combatting this scourge."

In addition, the biosensors promise to solve an old controversy. While some studies have suggested the glucose provides the fuel for the brain, recent research has provided evidence that lactate feeds energy metabolism in neurons. Oxidation of lactate can be used to produce large amount of ATP — the coenzyme that carries energy in cells. The Barros and Frommer teams are excited about the solving this enigma with the use of their new sensors, together with the previously developed glucose sensors. Recently, a collaboration between the two labs led to the patenting of the first method capable of measuring the rate of glucose consumption in single cells.

Source: *Science Daily Online*

Creating your Own Animated 3-D Characters and Scenes for the Web

To show spatial animations on websites, developers so far have had only two options: to use special software or to implement it from scratch. Computer scientists at Saarland University have developed a declarative markup language which facilitates the creation of distinct spatial animations and ensures their smooth replay in the web browser.

The researchers will show their results at the trade fair Cebit in Hannover starting on 5 March (Hall 9, booth F34).

Computer scientists from Saarland University enable web developers to shape the Internet in its third dimension in an easier way. (Credit: Image courtesy of University Saarland)

It could be a grotto. Light is glowing up from below and gives the moving waves a glance of an opal under the sunlight. "This computer graphic was written with our new description language by a school boy in not more than two hours after a briefly reading of the instructions," explains Felix Klein, doctoral candidate at the chair of Computer Graphics at Saarland University. As Klein is moving three slide switches with the mouse which are placed under the wave graphic on the display, the water is transforming. Now, the waves are spreading circularly from the center point, as if someone had thrown a pebble into the middle of the water.

"Xflow" is the name of the new description language developed by Klein and his colleagues. It makes it not only possible to describe such three-dimensional appearing animations more easily but also manages it that the required data is efficiently processed by the central processing unit and the graphics processor. Hence, the animation is running in the browser fluidly. "Up till now, this has not been that easy," explains Philipp Slusallek, Professor for Computer Graphics at Saarland University. "Meanwhile, even a mobile phone has enough computing power to play spatial data content from the internet. But the web technologies, necessary for using 3D content on the web, and the machine-orientated programming of graphic hardware have not found a common ground yet," so Slusallek, who also works as the Scientific Director of the German Research Center for Artificial Intelligence and as Director of Research of the Intel Visual Computing Institute (IVCI) in Saarbrücken.

Xflow shall help to fill this gap. It's declarative. What means in this case, that the developers rather describe which pattern synthesis effects shall get constructed, than to wrack their brains about how these can be computed in detail. In its appearance, Xflow resembles to the languages HTML and Javascript. With Javascript, it is indeed possible to describe three-dimensional data contents; however the data, which is needed for that, cannot be computed offhand in a parallel and thus efficient way. Xflow allows the so-called parallelisation automatically due to its structure. Neither, the programmers need to worry about this, nor about the allocation of disk space. Other software systems can also accomplish this, but with them only a limited number of shifts, textures and pattern effects can be described.

Xflow offers an alternative by defining a multiplicity of small components, so-called operators, of which complex animations can be created easily. In doing so, it uses the service of the HTML-upgrading XML3D, which allows the easy embedding of spatial data contents on websites. It was also developed by Philipp Slusallek and his team. He is confident: "After XML3D we took the next step forward to present three-dimensional contents on the internet in such an easy way as it's already the case with embedded Youtube videos." The development of Xflow has been supported by the IVCI of Saarland University and by the German Research Center for Artificial Intelligence (DFKI).

Source: ***Science Daily Online***

In Greenland and Antarctic Tests, Yeti Helps Conquer Some 'Abominable' Polar Hazards

A century after Western explorers first crossed the dangerous landscapes of the Arctic and Antarctic, researchers funded by the National Science Foundation (NSF) have successfully deployed a self-guided robot that uses ground-penetrating radar to map deadly crevasses hidden in ice-covered terrains.

Deployment of the robot—dubbed Yeti—could make Arctic and Antarctic explorations safer by revealing unseen fissures buried beneath ice and snow that could potentially claim human lives and expensive equipment.

Researchers say Yeti opens the door to making polar travel safer for crews that supply remote scientific research stations. Attempts have been made by researchers in the polar regions to use robots for tasks such as searching for meteorites in Antarctica. However, researchers who have worked with Yeti say it is probably the first robot to successfully deploy in the field that is able to identify hazards lurking under the thin cover of snow.

These findings are based on deployments of Yeti in Greenland's Inland Traverse, an over-ice supply train from Thule in the north of Greenland to NSF's Summit Station on the ice cap, and in NSF's South Pole Traverse, a 1,031-mile, over-ice trek from McMurdo Station in Antarctica to the South Pole.

A team of researchers from the US Army's Cold Regions Research and Engineering Laboratory (CRREL) and the Thayer School of Engineering at Dartmouth College, along with a student at Stanford University's neuroscience programme, recently published their findings in the *Journal of Field Robotics*.

"Polar exploration is not unlike space missions; we put people into the field where it is expensive and it is dangerous to do science," said CRREL's James Lever.

Using Yeti—and potential follow-on devices that Lever expects may be developed in the future by improving on the Yeti template—has value not only in reducing some of the danger to human beings working in polar environments. Deploying Yeti and machines like it also plays to the strength of robots, which are well suited for learning and performing repetitive tasks more efficiently than humans.

Lever added that robots like Yeti not only improve safety; they also have the potential to reduce the costs of logistical support of science in the remote polar regions and extend the capabilities of researchers.

Yeti was developed with funding from the National Aeronautics and Space Administration's Jet Propulsion Laboratory.

Students of Lever and Laura Ray, at Dartmouth, also a principal investigator on the Yeti project and a co-author of the paper, designed and created a predecessor to Yeti—called Cool Robot— that was funded by NSF's Division of Polar Programmes to conduct work in Antarctica.

Under a separate NSF grant, researchers plan to deploy Cool Robot this summer to circumnavigate NSF's Summit Station on the Greenland ice sheet, taking atmospheric samples as it goes. The solar-powered, four-wheel-drive Cool Robot led to Yeti's success, while helping the researchers meet NSF's goal of integrating research and education.

"Our focus with Yeti is on improving operational efficiency," Lever said. "But more generally, robotics has the potential to produce more science with more spatial and temporal coverage for less money. We're not gong to replace the scientists. But what we can do is extend their reach and add to the science mission."

Yeti is an 81-kilogram (180-pound) battery powered, four-wheel drive vehicle, about a metre across, that is capable of operating in temperatures as low as -30 Celsius (-20 Fahrenheit). Yeti uses Global Positioning System coordinates to navigate and to plot the position of under-ice hazards.

That work—and the accompanying risks—in the past has fallen exclusively to human crews using ground-penetrating radar to map the under-ice features.

Crevasses often can span widths of 9 metres (30 feet) or more and reach depths of up to 60 metres (200 feet). Snow often accumulates in such a way that it forms unstable bridges over the crevasse, obscuring them from view.

Prior to the development of Yeti, a vehicle pushing a GPR unit would move ahead of a traverse to attempt to detect crevasses. Although the radar was pushed ahead of the vehicle, giving some margin of advanced warning and safety, the system is none-the-less dangerous and stressful for the crews, especially when traversing long distances.

In addition to having the potential to greatly reduce the danger to humans, the Yeti project also has helped advance research into how robots learn, as the research team uses the data gathered by Yeti during hundreds of crevasse encounters to refine algorithms that will allow machines in future to automatically map and avoid crevasses on their own.

Yeti has also proven itself adept at tasks that were not originally envisioned for it.

During the 2012-13 Antarctic research season, Yeti was used to map ice caves on the slopes of Mount Erebus, the world's southernmost active volcano.

The ice caves are attracting increasingly more scientific attention. Volcanologists are interested in the volcano's chemical outgassing through fissures on its flanks, and biologists are interested in what sort of microbial life might exist in these discrete environments, which are much warmer and far more humid than the frigid, wind-sculpted surface.

In a deployment that coincided with the 100th anniversary of the arrival of the first explorers at the geographic South Pole in the 2011-2012 research season, Yeti repeatedly and uniformly executed closely spaced survey grids to find known, but inaccurately mapped, buried hazards.

The robot mapped out the long-abandoned original South Pole research station, built in the late 1950s and subsequently buried under the Antarctic ice sheet by years of snowfall and drift. A previous, less refined survey of the site by a human crew had only generally identified the outline of the major buildings. The Yeti-based survey generated a map detailed enough to allow crews to directly access the corners of structures near the ice surface in order to safely demolish them.

Source: ***Science Daily Online***

Making Fuel from Bacteria

In the search for the fuels of tomorrow, Swedish researchers are finding inspiration in the sea. Not in offshore oil wells, but in the water where blue-green algae thrive.

The building blocks of blue-green algae – sunlight, carbon dioxide and bacteria – are being used by researchers at KTH Royal Institute of Technology in Stockholm to produce butanol, a hydrocarbon-like fuel for motor vehicles.

The advantage of butanol is that the raw materials are abundant and renewable, and production has the potential to be 20 times more efficient than making ethanol from corn and sugar cane.

Using genetically-modified cyanobacteria, the team linked butanol production to the algae's natural metabolism, says Paul Hudson, a researcher at the School of Biotechnology at KTH who leads the research. "With relevant genes integrated in the right place in cyanobacteria's genome, we have tricked the cells to produce butanol instead of fulfilling their normal function," he says.

The team demonstrated that it can control butanol production by changing the conditions in the surrounding environment. This opens up other opportunities for control, such as producing butanol during specific times of day, Hudson says.

Paul Hudson, a researcher at the School of Biotechnology at KTH, shows the algae used to make fuel. (Credit: Image courtesy of KTH The Royal Institute of Technology)

Hudson says that it could be a decade before production of biofuel from cyanobacteria is a commercial reality.

"We are very excited that we are now able to produce biofuel from cyanobacteria. At the same time we must remember that the manufacturing process is very different from today's biofuels," he says. "We need to improve the production hundredfold before it becomes commercially viable.

Already, there is a demonstrator facility in New Mexico, US for producing biodiesel from algae, which is a more advanced process, Hudson says.

One of Sweden's leading biotechnology researchers, Professor Mathias Uhlén at KTH, has overall responsibility for the project. He says that the use of engineering methods to build genomes of microorganisms is a relatively new area.

A bacterium that produces cheap fuel by sunlight and carbon dioxide could change the world.

Hudson agrees. "One of the problems with biofuels we have today, that is, corn ethanol, is that the price of corn rises slowly while jumping up and down all the time and it is quite unpredictable," he says. "In addition, there is limited arable land and corn ethanol production is also influenced by the price of oil, since corn requires transport.

"Fuel based on cyanobacteria requires very little ground space to be prepared. And the availability of raw materials - sunlight, carbon dioxide and seawater - is in principle infinite," Hudson says.

He adds that some cyanobacteria also able to extract nitrogen from the air and thus do not need any fertiliser.

The next step in the research is to ensure that cyanobacteria produce butanol in larger quantities without it dying of exhaustion or butanol, which they cannot withstand particularly well. After that, more genes will have to be modified so that the end product becomes longer hydrocarbons that can fully function as a substitute for gasoline. And finally, the process must be executed outside of the lab and scaled up to work in industry.

There are also plans to develop fuel from cyanobacteria that are more energetic and therefore particularly suitable for aircraft engines.

The project is formally called Forma Center for Metabolic Engineering, and it involves researchers Chalmers University in Sweden. It has received about EUR 3 million from the nonprofit Council Formas.

Source: ***Science Daily Online***

Fungi may be Able to Replace Plastics One Day

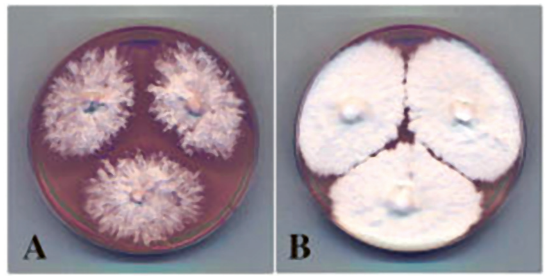
Fungi, with the exception of shitake and certain other mushrooms, tend to be something we associate with moldy bread or dank-smelling mildew. But they really deserve more respect. Fungi have fantastic capabilities and can be grown, under certain circumstances, in almost any shape and be totally biodegradable. And, if this weren't enough, they might have the potential to replace plastics one day. The secret is in the mycelia.

Union College Biology Professor Steve Horton likens this mostly underground portion of fungi (the mushrooms that pop up are the reproductive structures) to a tiny biological chain of tubular cells.

"It's this linked chain of cells that's able to communicate with the outside world, to sense what's there in terms of food and light and moisture," he said. "Mycelia can take in nutrients from available organic materials like wood and use them as food, and the fungus is able to grow as a result."

"When you think of fungi and their mycelia, their function — ecologically — is really vital in degrading and breaking things down," Horton added. "Without fungi, and bacteria, we'd be I don't know how many meters deep in waste, both plant matter and animal tissue."

Looking something like extremely delicate, white dental floss, mycelia grow in, through and around just about any organic substrate. Whether it's leaves or mulch, mycelia digest these natural materials and can also bind everything together in a cohesive mat. And these mats can be grown in molds, such as those that might make a packing carton.



Fungi have fantastic capabilities and can be grown, under certain circumstances, in almost any shape and be totally biodegradable. And, if this weren't enough, they might have the potential to replace plastics one day. (Credit: Union College)

Ecovative Design, in Green Island, N.Y., is harnessing this particular mycological power and is being helped by Horton, and another Union researcher, Ronald Bucinell, Associate Professor of mechanical engineering.

Ecovative uses several species of fungi to manufacture environmentally-friendly products. The process starts with farming byproducts, like cotton gin waste; seed hulls from rice, buckwheat and oats; hemp or other plant materials. These are sterilised, mixed with nutrients and chilled. Then the mycelia spawn are added and are so good at proliferating that every cubic inch of material soon contains millions of tiny fungal fibers.

This compact matrix is then grown in a mould the shape of whatever item Ecovative is making. Once the desired texture, rigidity and other characteristics of the product are achieved, it's popped from its mold and heated and dried to kill the mycelia and stop its growth.

The all-natural products, the creation of which can take less than 5 days, have no allergy concerns and are completely non-toxic. More impressive is the fact that they're also impervious to fire (to a point), and just as water resistant as Styrofoam, but they won't sit around taking up space in a landfill. They are also more UV-stable than foam since they are not petrochemical based, and won't emit volatile organic compounds. When exposed to the right microbes, they will break down in 180 days in any landfill or backyard.

Mycelium is comparatively inexpensive too as it can grow on farm waste that can't be fed to animals or burned for fuel. Better yet, the fungi can be propagated without sunlight or much human oversight in simple trays at room temperature — no immense greenhouses with costly temperature-control systems needed. It also means a smaller carbon footprint and Ecovative is hoping to the point where they can displace all plastics and foams in the market.

And this is where Union professors and researchers, Steve Horton and Ronald Bucinell, are aiding them in this effort. In Horton's lab, he and his students are tinkering with a species of fungus Ecovative uses in its manufacturing.

"We manipulate one strain in various ways to see if we can make versions of the fungus to suit certain applications the company has in mind," Horton said. "For example, it might be helpful if Ecovative has certain versions that grow faster."

Associate Professor of Mechanical Engineering Ronald Bucinell and his students also offer critical support to Ecovative's research and development pipeline. Bucinell's particular expertise is in experimental mechanics and the mechanics of reinforced materials and is tasked with seeing how strong sample material is under different parameters. This includes determining whether mycelia bind better to one plant material or another; and does the way it's treated — with heat or something else — make it stronger or weaker.

Whether it is packaging or PCR (a genetics tool), the Ecovative founders are grateful for their higher-ed partners.

"Steve is unique because his research over the last 28 years has focused on the effect of genetic pathways on fungal physiology, which factors greatly into what we can do with mycelia," Ecovative co-founder Gavin McIntyre said. "And Ron is one of the foremost experts in composites design. To have these two scientists so close to our facilities in Green Island is highly valuable."

"This is a brand new field in materials, and collaboration allows us to learn a lot, and quickly," McIntyre continued. "That's really important when you're trying to replace plastics."

The project is supported through funding from NSF and NYSERDA.

Source: Science Daily Online

'Monster' Starburst Galaxies Discovered in Early Universe

Astronomers using the Atacama Large Millimeter/submillimeter Array (ALMA) telescope have discovered starburst galaxies earlier in the Universe's history than they were previously thought to have existed. These newly discovered galaxies represent what today's most massive galaxies looked like in their energetic, star-forming youth.

The results, published in a set of papers to appear in the journal *Nature* and in the *Astrophysical*

Journal, will help astronomers better understand when and how the earliest massive galaxies formed.

The most intense bursts of star birth are thought to have occurred in the early Universe in massive, bright galaxies. These starburst galaxies converted vast reservoirs of gas and dust into new stars at a furious pace — many thousands of times faster than stately spiral galaxies like our own Milky Way.

The international team of researchers first discovered these distant starburst galaxies with the National Science Foundation's 10-metre South Pole Telescope. Though dim in visible light, they were glowing brightly in millimeter wavelength light, a portion of the electromagnetic spectrum that the new ALMA telescope was designed to explore.

Using only 16 of ALMA's eventual full complement of 66 antennas, the researchers were able to precisely determine the distance to 18 of these galaxies, revealing that they were among the most distant starburst galaxies ever detected, seen when the Universe was only one to three billion years old. These results were surprising because very few similar galaxies had previously been discovered at similar distances, and it wasn't clear how galaxies that early in the history of the Universe could produce stars at such a prodigious rate.

"The more distant the galaxy, the further back in time one is looking, so by measuring their distances we can piece together a timeline of how vigorously the Universe was making new stars at different stages of its 13.7 billion-year history," said Joaquin Vieira a postdoctoral scholar at Caltech who led the team and is lead author of the *Nature* paper.

In fact, two of these galaxies are the most distant starburst galaxies published to date — so distant that their light began its journey when the Universe was only one billion years old. Intriguingly, emission from water molecules was detected in one of these record-breakers, making it the most distant detection of water in the Universe published to date.

"ALMA's sensitivity and wide wavelength range mean we could make our measurements in just a few minutes per galaxy — about one hundred times faster than before," said Axel Weiss of the Max-Planck-Institute for Radioastronomy in Bonn, Germany, who led the work to measure the distances to the galaxies. "Previously, a measurement like this would be a laborious process of combining data from both visible-light and radio telescopes."

The galaxies found in this study have relatives in the local Universe, but the intensity of star formation in these distant objects is unlike anything seen nearby. "Our most extreme galactic neighbors are not forming stars nearly as energetically as the galaxies we observed with ALMA," said Vieira. "These are monstrous bursts of star formation."

The new results indicate these galaxies are forming 1,000 stars per year, compared to just 1 per year for our Milky Way galaxy.

This unprecedented measurement was made possible by gravitational lensing, in which the light from a distant galaxy is distorted and magnified by the gravitational force of a nearer foreground galaxy. "These beautiful pictures from ALMA show the background galaxies warped into arcs of light known as Einstein rings, which encircle the foreground galaxies," said Yashar Hezaveh of McGill University in Montreal, Canada, who led the study of the gravitational lensing. "The dark matter surrounding galaxies half-way across the Universe effectively provides us with cosmic telescopes that make the very distant galaxies appear bigger and brighter."

Analysis of this gravitational distortion reveals that some of the distant star-forming galaxies are as bright as 40 trillion Suns, and that gravitational lensing has magnified this light by up to 22 times. Future observations with ALMA using gravitational lensing can take a more detailed look at the distribution of dark matter surrounding galaxies.

"This is an amazing example of astronomers from around the world collaborating to make an exciting discovery with this new facility," said Daniel Marrone with the University of Arizona, principal investigator of the ALMA gravitational lensing study. "This is just the beginning for ALMA and for the study of these starburst galaxies. Our next step is to study these objects in greater detail and figure out exactly how and why they are forming stars at such prodigious rates."

ALMA, an international astronomy facility, is a partnership of Europe, North America and East Asia in cooperation with the Republic of Chile. ALMA construction and operations are led on behalf of Europe by ESO, on behalf of North America by the National Radio Astronomy Observatory (NRAO), and on behalf of East Asia by the National Astronomical Observatory of Japan (NAOJ). The Joint ALMA Observatory (JAO) provides the unified leadership and management of the construction, commissioning and operation of ALMA.

The National Radio Astronomy Observatory is a facility of the National Science Foundation, operated under cooperative agreement by Associated Universities, Inc.

Source: ***Science Daily Online***

'Hot Spots' Ride a Merry-Go-Round On Jupiter

In the swirling canopy of Jupiter's atmosphere, cloudless patches are so exceptional that the big ones get the special name "hot spots." Exactly how these clearings form and why they're only found near the planet's equator have long been mysteries. Now, using images from NASA's Cassini spacecraft, scientists have found new evidence that hot spots in Jupiter's atmosphere are created by a Rossby wave, a pattern also seen in Earth's atmosphere and oceans. The team found the wave responsible for the hot spots glides up and down through layers of the atmosphere like a carousel horse on a merry-go-round.

"This is the first time anybody has closely tracked the shape of multiple hot spots over a period of time, which is the best way to appreciate the dynamic nature of these features," said the study's lead author, David Choi, a NASA Postdoctoral Fellow working at NASA's Goddard Space Flight Center in Greenbelt, Md. The paper is published online in the April issue of the journal *Icarus.*

Choi and his colleagues made time-lapse movies from hundreds of observations taken by Cassini during its flyby of Jupiter in late 2000, when the spacecraft made its closest approach to the planet. The movies zoom in on a line of hot spots between one of Jupiter's dark belts and bright white zones, roughly 7 degrees north of the equator. Covering about two months (in Earth time), the study examines the daily and weekly changes in the sizes and shapes of the hot spots, each of which covers more area than North America, on average.

Much of what scientists know about hot spots came from NASA's Galileo mission, which released an atmospheric probe that descended into a hot spot in 1995. This was the first, and so far only, in-situ investigation of Jupiter's atmosphere.

"Galileo's probe data and a handful of orbiter images hinted at the complex winds swirling around and through these hot spots, and raised questions about whether they fundamentally were waves, cyclones or something in between," said Ashwin Vasavada, a paper co-author who is based at NASA's Jet Propulsion Laboratory in Pasadena, Calif., and who was a member of the Cassini imaging team during the Jupiter flyby. "Cassini's fantastic movies now show the entire life cycle and evolution of hot spots in great detail."

Because hot spots are breaks in the clouds, they provide windows into a normally unseen layer of Jupiter's atmosphere, possibly all the way down to the level where water clouds can form. In pictures, hot spots appear shadowy, but because the deeper layers are warmer, hot spots are very bright at the infrared wavelengths where heat is sensed; in fact, this is how they got their name.

One hypothesis is that hot spots occur when big drafts of air sink in the atmosphere and get heated or dried out in the process. But the surprising regularity of hot spots has led some researchers to suspect there is an atmospheric wave involved. Typically, eight to 10 hot spots line up, roughly evenly spaced, with dense white plumes of cloud in between. This pattern could be explained by a wave that pushes cold air down, breaking up any clouds, and then carries warm air up, causing the heavy cloud cover seen in the plumes. Computer modeling has strengthened this line of reasoning.

From the Cassini movies, the researchers mapped the winds in and around each hot spot and plume, and examined interactions with vortices that pass by, in addition to wind gyres, or spiraling vortices, that merge with the hot spots. To separate these motions from the jet stream in which the hot spots reside, the scientists also tracked the movements of small "scooter" clouds, similar to cirrus clouds on Earth. This provided what may be the first direct measurement of the true wind speed of the jet stream, which was clocked at about 300 to 450 mph (500 to 720 kilometres per hour) — much faster than anyone previously thought. The hot spots amble at the more leisurely pace of about 225 mph (362 kilometres per hour).

By teasing out these individual movements, the researchers saw that the motions of the hot spots fit the pattern of a Rossby wave in the atmosphere. On Earth, Rossby waves play a major role in weather. For example, when a blast of frigid Arctic air suddenly dips down and freezes Florida's crops, a Rossby wave is interacting with the polar jet stream and sending it off its typical course. The wave travels around our planet but periodically wanders north and south as it goes.

The wave responsible for the hot spots also circles the planet west to east, but instead of wandering north and south, it glides up and down in the atmosphere. The researchers estimate this wave may rise and fall 15 to 30 miles (24 to 50 kilometres) in altitude.

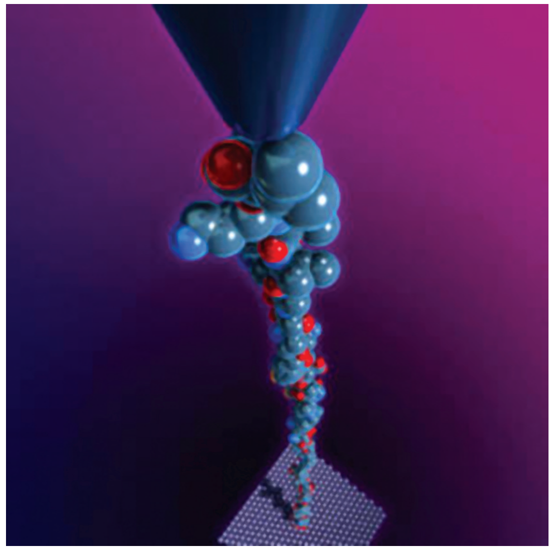
The new findings should help researchers understand how well the observations returned by the Galileo probe extend to the rest of Jupiter's atmosphere. "And that is another step in answering more of the questions that still surround hot spots on Jupiter," said Choi.

Source: ***Science Daily Online***

Stressed Proteins can Cause Blood Clots for Hours

New research from Rice University, Baylor College of Medicine (BCM) and the Puget Sound Blood Center (PSBC) has revealed how stresses of flow in the small blood vessels of the heart and brain could cause a common protein to change shape and form dangerous blood clots. The scientists were surprised to find that the proteins could remain in the dangerous, clot-initiating shape for up to five hours before returning to their normal, healthy shape.

The study — the first of its kind — focused on a protein called von Willebrand factor, or VWF, a key player in clot formation. A team led by Rice physicist Ching-Hwa Kiang found that "shear" forces, like those found in small arteries of patients with atherosclerosis, cause snippets of nonclotting VWF to change into a clot-forming shape for hours at a time. The finding appears online this week in *Physical Review Letters.*



Rice University researchers in the lab of Ching-Hwa Kiang use the bobbing needle from an atomic force microscope to grab and pull individual protein molecules. By stretching the proteins, Kiang's team can measure the precise physical forces that shape them. (Credit: C. Kiang/Rice University)

"When I first heard what Dr Kiang's team had found, I was shocked," said blood platelet expert Dr Joel Moake, a study co-author who holds joint appointments at Rice and BCM. Moake, whose research group was the first to describe how high shear stress could cause platelets to stick to VWF, said, "I had thought that the condition might last for such a short time that it would be unmeasurable. No one expected to find that this condition would persist for hours. This has profound clinical implications."

Kiang, Associate Professor of physics and astronomy and of bioengineering, studies the forces involved in protein folding. Proteins are the workhorses of biology. Tens of thousands are produced each second in every living cell, and each of these folds into a characteristic shape within moments of its creation. Despite its ubiquity, protein folding is an immensely complex process that is shrouded in mystery.

Kiang is a pioneer in the use of atomic force microscopes (AFM) to shed light on the fundamental physical processes involved in protein folding. The AFM has a tiny needle with a tip measuring just a few atoms across. The needle is suspended from a tiny arm that bobs up and down over a surface. Kiang's team uses the bobbing needle to grab and pull apart individual protein molecules. By stretching these like rubber bands, her team has shown it can measure the precise physical forces that hold them in their folded shape.

"In this study, we did more than just measure the forces; we used those measurements to see what state the molecule was in," Kiang said. "In this way, we were able to study the dynamics of the molecule, to see how it changed over a period of time."

Moake, a senior research scientist in bioengineering at Rice and professor of medicine at BCM, said the work is vitally important because it helps explain the workings of VWF.

"VWF is synthesised in the cells that line the walls of blood vessels, and it's stored there until the cells get signals that the vessels are in danger of injury," Moake said. "In response to those stimuli, the cell secretes VWF. It's a long protein, and one end remains anchored to the cell while the rest unfurls from the wall like a streamer."

The act of unfurling makes VWF sticky for platelets, and that begins the process of hemostasis, which prevents people from bleeding to death when blood vessels are damaged by cuts and wounds.

"The body recognises when clotting must stop — when there are too many strings, too much sticking, too many platelet clumps — and it uses an enzyme to clip the long VWF strings," Moake explained. "First, it makes large, soluble versions of the strings that remain somewhat sticky, and then these large soluble portions of VWF are reduced into smaller subunits of VWF that circulate in the plasma."

Under normal conditions, these circulating subunits, which are called PVWF, fold into compact shapes and cease to be sticky to platelets. However, previous research had shown that a type of physical stress called "shear" — which can arise in partially occluded arterial blood vessels with high flow rates — could cause PVWF to become sticky to platelets.

"That's all we knew," Moake said. "We didn't know how the conformation of the PVWF protein changed. That is why Dr Kiang's research is so important and makes it more likely that therapeutic interventions can be more rationally designed."

To study the problem, Kiang's lab worked closely with Moake's team at Rice's BioScience Research Collaborative and with researchers from the laboratory of co-author Jing-fei Dong, formerly of BCM and now at PSBC in Seattle. Moake's and Dong's groups prepared samples of PVWF, subjecting some to the shear stresses known to induce clot formation. Kiang's team used AFMs to test the samples. Through a combination of experiments and deductive reasoning, her team determined exactly which portion of PVWF changed its conformation during shear stress. They also determined how long the protein remained partially unfurled before relaxing into its natural shape.

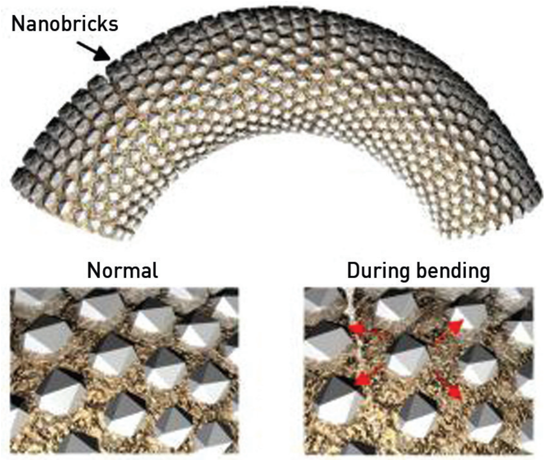
"The next step will be to design new experiments that allow us to monitor the proteins as they bind to platelets and initiate clot formation," Kiang said. "That will tell us even more about the physical properties of the proteins and provide more clues about potential therapies."

The research was supported by the National Institutes of Health, the National Science Foundation, the Alliance for NanoHealth, the Welch Foundation, the Mary R. Gibson Foundation and the Everett Hinkson Fund. Study co-authors include Rice graduate students Sithara Wijeratne and Eric Frey, former Rice graduate student Eric Botello, BCM researchers Hui-Chun Yeh and Angela Bergeron, Rice undergraduate Jay Patel, PSBC's Zhou Zhou and Rice senior research technicians Leticia Nolasco and Nancy Turner.

Source: ***Science Daily Online***

Inspired by Deep Sea Sponges: Creating Flexible Minerals

Scientists at Johannes Gutenberg University Mainz (JGU) and the Max Planck Institute for Polymer Research (MPI-P) in Germany have created a new synthetic hybrid material with a mineral content of almost 90 per cent, yet extremely flexible. They imitated the structural elements found in most sea sponges and recreated the sponge spicules using the natural mineral calcium carbonate and a protein of the sponge. Natural minerals are usually very hard and prickly, as fragile as porcelain.



The nanometer size of the calcite bricks facilitates bending of the synthetic spicules. The radius of curvature upon bending is very large compared to the size of the individual particles. This prevents a fracture of the brittle mineral bricks. (Credit: Tremel work group, JGU)

Amazingly, the synthetic spicules are superior to their natural counterparts in terms of flexibility, exhibiting a rubber-like flexibility. The synthetic spicules can, for example, easily be U-shaped without breaking or showing any signs of fracture This highly unusual characteristic, described by the German researchers in the current issue of *Science,* is mainly due to the part of organic substances in the new hybrid material. It is about ten times as much as in natural spicules.

Spicules are structural elements found in most sea sponges. They provide structural support and deter predators. They are very hard, prickly, and even quite difficult to cut with a knife. The spicules of sponges thus offer a perfect example of a lightweight, tough, and impenetrable defense system, which may inspire engineers to create body armours of the future.

The researchers led by Wolfgang Tremel, Professor at Johannes Gutenberg University Mainz, and Hans-Jürgen Butt, Director at the Max Planck Institute for Polymer Research in Mainz, used these natural sponge spicules as a model to cultivate them in the lab. The synthetic spicules were made from calcite ($CaCO3$) and silicatein-á. The latter is a protein from siliceous sponges that, in nature, catalyses the formation of silica, which forms the natural silica spicules of sponges. Silicatein-á was used in the lab setting to control the self-organisation of the calcite spicules. The synthetic material was self-assembled from an amorphous calcium carbonate intermediate and silicatein and subsequently aged to the final crystalline material. After six months, the synthetic spicules consisted of calcite nanocrystals aligned in a brick wall fashion with the protein embedded like cement in the boundaries between the calcite nanocrystals. The spicules were of 10 to 300 micrometres in length with a diametre of 5 to 10 micrometres.

As the scientists, among them chemists, polymer researchers, and the molecular biologist Professor Werner E. G. Müller from the Mainz University Medical Center, also write in their *Science*publication, the synthetic spicules have yet another special characteristic, i.e., they are able to transmit light waves even when they are bent.

Source: ***Science Daily Online***

Statistical Physics Offers a New Way to Look at Climate

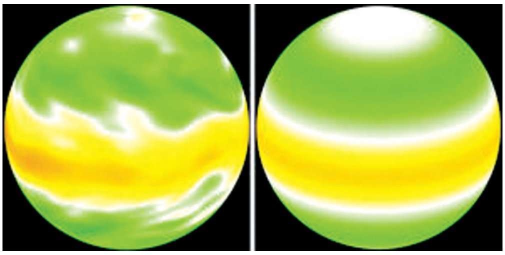
Statistical physics offers an approach to studying climate change that could dramatically reduce the time and brute-force computing that current simulation techniques require. The new approach focuses on fundamental forces that drive climate rather than on "following every little swirl" of water or air.

Scientists are using ever more complex models running on ever more powerful computers to simulate Earth's climate. But new research suggests that basic physics could offer a simpler and more meaningful way to model key elements of climate.

The research, published in the journal *Physical Review Letters*, shows that a technique called direct statistical simulation does a good job of modeling fluid jets, fast-moving flows that form naturally in oceans and in the atmosphere. Brad Marston, Professor of physics at Brown University and one of the authors of the paper, says the findings are a key step toward bringing powerful statistical models rooted in basic physics to bear on climate science.

The method of simulation used in climate science now is useful but cumbersome, Marston said. The method, known as direct numerical simulation, amounts to taking a modified weather model and running it through long periods of time. Moment-to-moment weather — rainfall, temperatures, wind speeds at a given moment, and other variables — is averaged over time to arrive at the climate statistics of interest. Because the simulations need to account for every weather event along the way, they are mind-bogglingly complex, take a long time run, and require the world's most powerful computers.

One practical advantage of the new approach: the ability to model climate conditions from millions of years ago without having to reconstruct the world's entire weather history. Direct statistical



Two views, two approaches to simulation. Computer-generated images of a planet's "zonal velocity" (the west-to-east component of wind) use direct numerical simulation (the traditional approach, left) and direct statistical simulation. The latter has limits, but its development is at a very early stage. (Credit: Marston lab/Brown University)

simulation, on the other hand, is a new way of looking at climate. "The approach we're investigating," Marston said, "is the idea that one can directly find the statistics without having to do these lengthy time integrations."

It's a bit like the approach physicists use to describe the behavior of gases.

"Say you wanted to describe the air in a room," Marston said. "One way to do it would be to run a giant supercomputer simulation of all the positions of all of the molecules bouncing off of each other. But another way would be to develop statistical mechanics and find that the gas actually obeys simple laws you can write down on a piece of paper: PV=nRT, the gas equation. That's a much more useful description, and that's the approach we're trying to take with the climate."

Conceptually, the technique focuses attention on fundamental forces driving climate, instead of "following every little swirl," Marston said. A practical advantage would be the ability to model climate conditions from millions of years ago without having to reconstruct the world's entire weather history in the process.

The theoretical basis for direct statistical simulation has been around for nearly 50 years. The problem, however, is that the mathematical and computational tools to apply the idea to climate systems aren't fully developed. That is what Marston and his collaborators have been working on for the last few years, and the results in this new paper show their techniques have good potential.

The paper, which Marston wrote with University of Leeds mathematician Steve Tobias, investigates whether direct statistical simulation is useful in describing the formation and characteristics of fluid jets, narrow bands of fast-moving fluid that move in one direction. Jets form naturally in all kinds of moving fluids, including atmospheres and oceans. On Earth, atmospheric jet streams are major drivers of storm tracks.

For their study, Marston and Tobias simulated the jets that form as a fluid moves on a hypothetical spinning sphere. They modeled the fluid using both the traditional numerical technique and their statistical technique, and then compared the output of the two models. They found that the models generally arrived at similar values for the number of jets that would form and the strength of the airflow, demonstrating that statistical simulation can indeed be used to model jets.

There were limits, however, to what the statistical model could do. The study found that as pace of adding and removing energy to the fluid system increased, the statistical model started to break down. Marston and Tobias are currently working on an expansion of their technique to deal with that problem.

Despite the limitation, Marston is upbeat about the potential for the technique. "We're very pleased that it works as well as it did here," he said.

Since completing the study, Marston has integrated the method into a computer program called "GCM" that he has made easily available via Apple's Mac App Store for other researchers to download. The programme allows users to build their own simulations, comparing numerical and statistical models. Marston expects that researchers who are interested in this field will download it and play with the technique on their own, providing new insights along the way. "I'm hoping that citizen-scientists will also explore climate modeling with it as well, and perhaps make a discovery or two," he said.

There's much more work to be done on this, Marston stresses, both in solving the energy problem and in scaling the technique to model more realistic climate systems. At this point, the simulations have only been applied to hypothetical atmospheres with one or two layers. Earth's atmosphere is a bit more complex than that.

"The research is at a very early stage," Marston said, "but it's picking up steam."

Source: ***Science Daily Online***

Playing Action Video games Improves Visual Search

Researchers at the University of Toronto have shown that playing shooting or driving video games, even for a relatively short time, improves the ability to search for a target hidden among irrelevant distractions in complex scenes.

"Recent studies in different labs, including here at the University of Toronto, have shown that playing first-person shooter video games can enhance other aspects of visual attention," says psychology professor Ian Spence. "But no one has previously demonstrated that visual search is also improved."

Searching efficiently and accurately is essential for many tasks. "It's necessary for baggage screening, reading X rays or MRIs, interpreting satellite images, defeating camouflage or even just locating a friend's face in a crowd," says Spence.

In the first experiment, the researchers compared action videogame players and non-players on three visual search tasks and found that the experienced players were better.

"But this difference could be a result of a pre-existing superiority in experienced gamers compared to those who avoid them, says Sijing Wu, a PhD candidate in Spence's lab in U of T's Department of Psychology and lead author of the study. "A training experiment was necessary to establish whether playing an action game could actually improve search skills."

In the second experiment, 60 participants — who had not previously played videogames — played for a total of 10 hours in one to two hour sessions. Twenty participants were randomly assigned to play the first-person shooter game, Medal of Honor, 20 to a driving-racing game, Need for Speed and 20 to a three-dimensional puzzle game, Ballance as a control.

Researchers at the University of Toronto have shown that playing shooting or driving videogames, even for a relatively short time, improves the ability to search for a target hidden among irrelevant distractions in complex scenes. (Credit: © tomispin / Fotolia)

"After playing either the shooter or driving game for only 10 hours, participants were faster and more accurate on the three visual search tasks," says Wu. "However, the control participants — who played the puzzle game — did not improve."

"We have shown that playing a driving-racing game can produce the same benefits as a shooter game," says Wu. "This could be very important in situations where we wish to train visual search skills. Driving games are likely to be more acceptable than shooting games because of the lower levels of violence."

Source: Science Daily Online

New Vaccine-Design Approach Targets Viruses Such as HIV

A team led by scientists from The Scripps Research Institute (TSRI) and the International AIDS Vaccine Initiative (IAVI) has unveiled a new technique for vaccine design that could be particularly useful against HIV and other fast-changing viruses.

The report, which appears 28 March 2013, in *Science Express*, the early online edition of the journal *Science*, offers a step toward solving what has been one of the central problems of modern vaccine design: how to stimulate the immune system to produce the right kind of antibody response to protect against a wide range of viral strains. The researchers demonstrated their new technique by engineering an immunogen (substance that induces immunity) that has promise to reliably initiate an otherwise rare response effective against many types of HIV.

"We're hoping to test this immunogen soon in mice engineered to produce human antibodies, and eventually in humans," said team leader William R. Schief, who is an Associate Professor of immunology and member of the IAVI Neutralising Antibody Center at TSRI.

Seeking a Better Way

For highly variable viruses such as HIV and influenza, vaccine researchers want to elicit antibodies that protect against most or all viral strains — not just a few strains, as seasonal flu vaccines currently on the market. Vaccine researchers have identified several of these broadly neutralising antibodies from long-term HIV-positive survivors, harvesting antibody-producing B cells from blood samples and then sifting through them to identify those that produce antibodies capable of neutralising multiple strains of HIV. Such broadly neutralising antibodies typically work by blocking crucial functional sites on a virus that are conserved among different strains despite high mutation elsewhere.

However, even with these powerful broadly neutralising antibodies in hand, scientists need to find a way to elicit their production in the body through a vaccine. "For example, to elicit broadly neutralising antibodies called VRC01-class antibodies that neutralize 90 per cent of known HIV strains, you could try using the HIV envelope protein as your immunogen," said Schief, "but you run into the problem that the envelope protein doesn't bind with any detectable affinity to the B cells needed to launch a broadly neutralising antibody response."

To reliably initiate that VRC01-class antibody response, Schief and his colleagues therefore sought to develop a new method for designing vaccine immunogens.

From Weak to Strong

Joseph Jardine, a TSRI graduate student in the Schief laboratory, evaluated the genes of VRC01-producing B cells in order to deduce the identities of the less mature B cells — known as germline B cells — from which they originate. Germline B cells are major targets of modern viral vaccines, because it is the initial stimulation of these B cells and their antibodies that leads to a long-term antibody response.

In response to vaccination, germline B cells could, in principle, mature into the desired VRC01-producing B cells — but natural HIV proteins fail to bind or stimulate these germline B cells so they cannot get the process started. The team thus set out to design an artificial immunogen that would be successful at achieving this.

The researchers demonstrated their new technique by engineering a compound that has promise to initiate an otherwise rare immune response against many types of HIV. Here, the germline-targeting immunogen eOD-GT6 (red) is shown bound to its target, the germline VRC01 antibody (magenta and yellow). (Credit: Photo courtesy of The Scripps Research Institute.)

Jardine used a protein modeling software suite called Rosetta to improve the binding of VRC01 germline B cell antibodies to HIV's envelope protein. "We asked Rosetta to look for mutations on the side of the HIV envelope protein that would help it bind tightly to our germline antibodies," he said.

Rosetta identified dozens of mutations that could help improve binding to germline antibodies. Jardine then generated libraries that contained all possible combinations of beneficial mutations, resulting in millions of mutants, and screened them using techniques called yeast surface display and FACS. This combination of computational prediction and directed evolution successfully produced a few mutant envelope proteins with high affinity for germline VRC01-class antibodies.

Jardine then focused on making a minimal immunogen — much smaller than HIV envelope — and so continued development using the "engineered outer domain (eOD)" previously developed by Po-Ssu Huang in the Schief lab while Schief was at the University of Washington. Several iterative rounds of design and selection using a panel of germline antibodies produced a final, optimised immunogen — a construct they called eOD-GT6.

A Closer Look

To get a better look at eOD-GT6 and its interaction with germline antibodies, the team turned to the laboratory of Ian A. Wilson, chair of the Department of Integrative Structural and Computational Biology and a member of the IAVI Neutralising Antibody Center at TSRI.

Jean-Philippe Julien, a senior research associate in the Wilson laboratory, determined the 3D atomic structure of the designed immunogen using X-ray crystallography — and, in an unusual feat, also determined the crystal structure of a germline VRC01 antibody, plus the structure of the immunogen and antibody bound together.

"We wanted to know whether eOD-GT6 looked the way we anticipated and whether it bound to the antibody in the way that we predicted — and in both cases the answer was 'yes'," said Julien. "We also were able to identify the key mutations that conferred its reactivity with germline VRC01 antibodies."

Mimicking a Virus

Vaccine researchers know that such an immunogen typically does better at stimulating an antibody response when it is presented not as a single copy but in a closely spaced cluster of multiple copies, and with only its antibody-binding end exposed. "We wanted it to look like a virus," said Sergey Menis, a visiting graduate student in the Schief laboratory.

Menis therefore devised a tiny virus-mimicking particle made from 60 copies of an obscure bacterial enzyme and coated it with 60 copies of eOD-GT6. The particle worked well at activating VRC01 germline B cells and even mature B cells in the lab dish, whereas single-copy eOD-GT6 did not.

"Essentially it's a self-assembling nanoparticle that presents the immunogen in a properly oriented way," Menis said. "We're hoping that this approach can be used not just for an HIV vaccine but for many other vaccines, too."

The next step for the eOD-GT6 immunogen project, said Schief, is to test its ability to stimulate an antibody response in lab animals that are themselves engineered to produce human germline antibodies. The difficulty with testing immunogens that target human germline antibodies is that animals typically used for vaccine testing cannot make those same antibodies. So the team is collaborating with other researchers who are engineering mice to produce human germline antibodies. After that, he hopes to learn how to drive the response, from the activation of the germline B cells all the way to the production of mature, broadly neutralising VRC01-class antibodies, using a series of designed immunogens.

Schief also hopes they will be able to test their germline-targeting approach in humans sooner rather than later, noting "it will be really important to find out if this works in a human being."

The first authors of the paper, "Rational HIV immunogen design to target specific germline B cell receptors," were Jardine, Julien and Menis. Co-authors were Takayuki Ota and Devin Sok of the Nemazee and Burton laboratories at TSRI, respectively; Travis Nieusma of the Ward laboratory at TSRI; John Mathison of the Ulevitch laboratory at TSRI; Oleksandr Kalyuzhniy and Skye MacPherson, researchers in the Schief laboratory from IAVI and TSRI, respectively; Po-Ssu Huang and David Baker of the University of Washington, Seattle; Andrew McGuire and Leonidas Stamatatos of the Seattle Biomedical Research Institute; and TSRI principal investigators Andrew B. Ward, David Nemazee, Ian A. Wilson, and Dennis R. Burton, who is also head of the IAVI Neutralizing Center at TSRI.

The project was funded in part by IAVI; the National Institutes of Health (AI84817, AI081625 and AI33292); and the Ragon Institute.

Source: Science Daily Online

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