



Spintronics Just Got Faster

In a tremendous boost for spintronic technologies, EPFL scientists have shown that electrons can jump through spins much faster than previously thought.

Electrons spin around atoms, but also spin around themselves, and can cross over from one spin state to another, a property which can be exploited for the next-generation hard drives. However, 'spin crossover' has been considered too slow to be efficient. Using ultrafast measurements, EPFL scientists have now shown for the first time that electrons can cross spins at least 1,00,000 times faster than previously thought. Apart from its enormous implications for fundamental physics, the finding can also propel the field of spintronics forward. The study is published in *Nature Chemistry*.

The rules of spin

Although difficult to describe in everyday terms, electron spin can be loosely compared to the rotation of a planet or a top spinning around its axis. Electrons can spin in different manners

referred to as 'spin states' and designated by the numbers 0, 1/2, 1, 3/2, 2, etc. During chemical reactions, electrons can cross from one spin state to another, e.g., from 0 to 1 or 1/2 to 3/2.

Spin crossover is already used in many technologies, e.g., optical light-emitting devices (OLED), energy conversion systems and cancer phototherapy. Most prominently, spin crossover is the basis of the fledgling field of spintronics. The problem is that spin crossover has been thought to be too slow to be efficient enough in circuits.

Spin crossover is extremely fast

The lab of Majed Chergui at EPFL has now demonstrated that spin crossover is considerably faster than previously thought. Using the highest time-resolution technology in the world, the lab was able to 'see' electrons crossing through four spin states within 50 quadrillionths of a second or 50 femtoseconds.

"Time resolution has always been a limitation," says Chergui. "Over the years, labs have used techniques that could only measure spin changes to a billionth to a millionth of a second.

So they thought that spin crossover happened in this timeframe."

Chergui's lab focussed on materials that show much promise in spintronics applications. In these materials, electrons jump through four spin-states: from 0 to 1 to 2. In 2009, Chergui's lab pushed the boundaries of time resolution to show that this 0–2 'jump' can happen within 150 femtoseconds — suggesting that it was a direct event. Despite this, the community still maintained that such spin crossovers go through intermediate steps.

But Chergui had his doubts. Working with his postdoc Gerald Auböck, they used the lab's world-recognised expertise in ultrafast spectroscopy to 'crank up' the time resolution. Briefly, a laser shines on the material sample under investigation, causing its electrons to move. Another laser measures their spin changes over time in the ultraviolet light range.

The finding essentially demolishes the notion of intermediate steps between spin jumps, as it does not allow enough time for them: only 50 quadrillionths of a second to go from the '0' to the '2' spin state. This is the first study to ever push time resolution to this limit in the ultraviolet domain. "This probably means that it's even faster," says Chergui. "But, more importantly, that it is a direct process."

From observation to explanation

With profound implications for both technology and fundamental physics and chemistry, the study is an observation without an explanation. Chergui believes that the key is electrons shuttling back-and-forth between the iron atom at the center of the material's molecules and its surrounding elements. "When the laser light shines on the atom, it changes the electron's spin angle, affecting the entire spin dynamics in the molecule."

It is now up to theoreticians to develop a new model for ultrafast spin changes. On the experimental side of things, Chergui's lab is now focussing on actually observing electrons shuttling inside the molecules. This will require even more sophisticated approaches, such as core-level spectroscopy. Nonetheless, the study challenges ideas about spin crossover, and might offer long-awaited solutions to the limitations of spintronics.

Peppermint Oil and Cinnamon could Help Treat and Heal Chronic Wounds

Infectious colonies of bacteria called biofilms that develop on chronic wounds and medical devices can cause serious health problems and are tough to treat. But now scientists have found a way to package antimicrobial compounds from peppermint and cinnamon in tiny capsules that can both kill biofilms and actively promote healing. The researchers say that the new material, reported in the journal *ACS Nano*, could be used as a topical antibacterial treatment and disinfectant.

Many bacteria clump together in sticky plaques in a way that makes it difficult to eliminate them with traditional antibiotics. Doctors sometimes recommend cutting out infected tissues. This approach is costly, however, and because it's invasive, many patients opt out of the treatment altogether. Essential oils and other natural compounds have emerged recently as alternative substances that can get rid of pathogenic bacteria, but researchers have had a hard time translating their antibacterial activity into treatments. Vincent M. Rotello and colleagues wanted to address this challenge. The researchers packaged peppermint oil and cinnamaldehyde, the compound in cinnamon responsible for its flavour and aroma, into silica

nanoparticles. The microcapsule treatment was effective against four different types of bacteria, including one antibiotic-resistant strain. It also promoted the growth of fibroblasts, a cell type that is important in wound healing.

Mammoths Killed by Abrupt Climate Change

New research has revealed that abrupt warming, that closely resembles the rapid human-made warming occurring today, has repeatedly played a key role in mass extinction events of large animals, the megafauna, in earth's past.

Using advances in analysing ancient DNA, radiocarbon dating and other geologic records, an international team led by researchers from the University of Adelaide and the University of New South Wales (Australia) have revealed that short, rapid warming events, known as interstadials, recorded during the last ice age or Pleistocene (60,000–12,000 years ago) coincided with major extinction events even before the appearance of man.

Published earlier in *Science*, the researchers report extreme cold periods, such as the last glacial maximum, do not appear to correspond with these extinctions.

"This abrupt warming had a profound impact on climate that caused marked shifts in global rainfall and vegetation patterns," said University of Adelaide lead author and Director of the Australian Centre for Ancient DNA, Professor Alan Cooper.

"Even without the presence of humans we saw mass extinctions. When you add the modern addition of human pressures and fragmenting of the environment to the rapid changes brought by

global warming, it raises serious concerns about the future of our environment."

The researchers came to their conclusions after detecting a pattern, 10 years ago, in ancient DNA studies suggesting the rapid disappearance of large species. At first the researchers thought these were related to intense cold snaps.

However, as more fossil-DNA became available from museum specimen collections and through improvements in carbon dating and temperature records that showed better resolution through time, they were surprised to find the opposite. It became increasingly clear that rapid warming, not sudden cold snaps, was the cause of the extinctions during the last glacial maximum.

The research helps explain further the sudden disappearance of mammoths and giant sloths that became extinct around 11,000 years ago at the end of the last ice age.

"It is important to recognise that man still plays an important role in the disappearance of the major mega fauna species," said fellow author Professor Chris Turney from the University of New South Wales.

The abrupt warming of the climate caused massive changes to the environment that set the extinction events in motion, but the rise of humans applied the coup de grace to a population that was already under stress.

In addition to the finding, the new statistical methods used to interrogate the datasets (led by Adelaide co-author, Professor Corey Bradshaw) and the new data itself has created an extraordinarily precise record of climate change and species movement over the Pleistocene.

This new dataset will allow future researchers a better understanding of this important period than has ever been possible before.

High-pressure Oxygen can Effectively Treat Fibromyalgia

Fibromyalgia is almost impossible to diagnose. The chronic pain syndrome strikes an estimated 1 in 70 Americans, most of them women. The disorder is often triggered by head trauma, a neurological infection, or severe emotional stress, and is characterised by symptoms such as musculoskeletal pain, fatigue, memory loss and mood swings. Fibromyalgia is often mistaken for other culprits and most patients suffer months, even years, of unrelenting pain before being properly diagnosed. And once diagnosed, patients enjoy little respite because few therapies have been found to be effective in assuaging its symptoms.

A new study published in *PLoS One* by Tel Aviv University researchers may turn the tide. The research found that women with fibromyalgia were able to drastically reduce, or even eliminate, their use of pain medication following hyperbaric oxygen treatment. The study was led by the late Prof. Eshel Ben-Jacob of TAU's School of Physics and Astronomy and Rice University's Center for Theoretical Biological Physics, Dr. Shai Efrati of TAU's Sagol School of Neuroscience and Assaf Harofeh Medical Center and Prof. Dan Buskila from Soroka Medical Center, and was conducted by a team of scientists from TAU, Rice University, Assaf Harofeh Medical Center, Ben-Gurion University, and Tel Aviv Sourasky Medical Center.

The TAU researchers believe that they have also identified the primary factor causing fibromyalgia: the disruption of the brain mechanism for processing pain. "As a physician, the most important finding for me is that 70 per cent of the patients could recover from their fibromyalgia symptoms," said Dr. Efrati.

"The most exciting finding for the world of research, however, is that we were able to map the malfunctioning brain regions responsible for the syndrome."

A high-pressure solution

Hyperbaric oxygen chambers expose patients to pure oxygen at higher-than-atmospheric pressures and are commonly used to treat patients with embolisms, burns, carbon monoxide poisoning and decompression sickness.

The clinical trial, which exposed participants to two months of hyperbaric oxygen therapy, found significant changes in the brain activity and symptoms of 70 per cent of participants. The trial involved 60 women who had been diagnosed with fibromyalgia at least two years earlier. Half of the 48 patients who completed the therapy received 40 hyperbaric oxygen treatments—90-minute treatments exposing patients to pure oxygen at twice the atmospheric pressure, five days a week over the course of two months.

The successful treatment enabled patients to drastically reduce or even eliminate their use of pain medications. "The intake of the drugs eased the pain but did not reverse the condition. But hyperbaric oxygen treatments did reverse the condition," said Dr. Efrati, who added that the findings warrant further study.

Getting to the root of the problem

"The results are of significant importance," Dr. Efrati said. "Hyperbaric oxygen treatments are designed to address the actual cause of fibromyalgia — the brain pathology responsible for the syndrome. It means that brain repair, including neuronal regeneration, is possible even for chronic, long-lasting pain syndromes, and we can and should aim for that in any future treatment development."

The researchers did find some discrepancies among patients with different fibromyalgia catalysts. When fibromyalgia was triggered by a traumatic brain injury, for example, they witnessed a complete resolution without any need for further treatment. But when the trigger was attributed to other causes, such as fever-related diseases, patients required periodic maintenance therapy.

The researchers are continuing to conduct comprehensive studies on the renewal of brain tissue under hyperbaric conditions.

Eyeing Up Earth-like Planets

Almost 2,000 exoplanets have been discovered to date, ranging from rocky Earth-like planets to hot-Jupiters, and orbiting every type of star. But how many of these distant worlds are habitable? Today's technology means that we currently have very little information about what exoplanets are like beyond their presence, size and distance from star. With the launch of the James Webb Space Telescope (JWST), we may have our first glimpses into atmospheres of Earth-like exoplanets, according to the results of a study by Dr Joanna Barstow presented at the National Astronomy Meeting in Llandudno.

"A planet's atmosphere provides a good guide to likely conditions on the surface," said Barstow, of the University of Oxford. "The Earth's atmosphere contains significant amounts of nitrogen, oxygen, ozone and water. By contrast, its inhospitable 'evil twin', Venus, has an atmosphere made mostly of carbon dioxide, which drives its surface temperature to a blistering 450°C."

A successor to the Hubble Space Telescope, JWST is due for launch in 2018 and will study the Universe in infrared wavelengths. Barstow's study shows that JWST may be able

to differentiate between a planet with a clement, Earth-like atmosphere, and one with more hostile conditions, such as those that are found on our neighbouring planet Venus. JWST will have the capability to detect key markers that could indicate the presence of a climate like our own when looking at Earth-sized planets around stars that are smaller and redder than Sun.

Different gases have already been identified successfully in the atmospheres of several large, hot, Jupiter-sized planets by studying tiny variations in the starlight that passes through their atmospheres when they cross in front of their parent stars. However, these variations are miniscule: the light filtered through the exoplanet's atmosphere is one ten-thousandth of the total starlight detected. Studying planets the size of the Earth is an even greater challenge. Although JWST would struggle with analysing a Solar System exactly like our own, it would be capable of studying Earth-like planets around cooler stars — if such a system were to be found.

"If we took the Earth and Venus, and placed them in orbit around a cool, red star that's not too far away, our study shows that JWST could tell them apart. Earth's ozone layer, 10 kilometres above the surface, is produced when light from the Sun interacts with molecules of oxygen in the atmosphere, and it produces an unmistakable signal that could be detected by JWST. Venus, without a substantial ozone layer, would look very different," said Barstow. "That's assuming that planets starting out like Earth and Venus would evolve in the same way around a cool star!"

However, JWST will be used for a wide range of astronomical applications, not just detecting exoplanets, and securing time on the telescope will be highly competitive. To make these detections, astronomers would need to observe the exoplanets at least 30 times, taking valuable telescope time.

"Future telescopes that are dedicated to observing the atmospheres of many rocky planets around different stars will be required to fully resolve the question of habitability on exoplanets. In the meantime, JWST will observe many other weird and wonderful planets in unprecedented detail," said Barstow.

Rhythm of Cells: Daily Changes in Human Cells

Life is subject to natural rhythms, such as the light and dark cycle or seasonal variation in temperature. A recent study by researchers at the Vetmeduni Vienna, shows that the composition of human cell membranes varies depending on the time of day. These cyclical changes in cell membranes could have a significant impact on health and disease. The results were published in the *Journal of Biological Rhythms*. Fatty acids are important components of cell membranes. They have signalling functions within the cells and play a role in controlling metabolic processes in the entire body. Thomas Ruf and Walter Arnold of the Research Institute of Wildlife Ecology at the University of Veterinary Medicine, Vienna, investigated these cyclic fluctuations in human cells.

"Nearly all physiological processes in humans and animals, such as body temperature or heart rate, undergo daily rhythms, and many even exhibit annual fluctuations. We wanted to find out if these rhythms are related to changes in cell membranes," explains first author Thomas Ruf.

The researchers investigated buccal mucosa cells in 20 subjects over a period of one year. Study participants collected their cells on a predetermined day every month at three-hour intervals by intensively rinsing their mouths with water and then freezing the samples in special flasks.

The composition of fatty acid changes during the course of the day

The analysis of the cell membranes revealed significant daily rhythms in 11 fatty acids. Several fatty acids were present in higher concentrations at night, others during the daytime. "The cellular changes have one thing in common: they always occurred at about the same time in all participants. This shows that a clear rhythm is present," Ruf explains.

"From animal physiology, we know that the fatty acid composition in cell membranes can be remodelled in response to environmental conditions. Fatty acid composition is especially subject to seasonal fluctuations. However, while the participants of our study all showed daily fluctuations, seasonal changes occurred only in individual cases."

In contrast to wildlife, no clear annual rhythm could be seen in the fatty acid patterns of the study participants. Around one half of the subjects showed yearly rhythms, but these were not synchronous. Some participants exhibited a peak in spring or in summer, while in others the same fatty acid had higher concentrations in autumn or in the winter. "In western countries, seasons are having an increasingly smaller impact on the body. This is due to the prevalence of artificial light, which makes for longer days, and the long heating season, which minimises temperature fluctuations. Annual rhythms still exist, but these are no longer synchronised with the seasons," says Ruf.

Certain diseases occur in seasonal rhythms

This remodelling of human cell membranes could be of medical importance. It is known that certain fatty acids, such as omega-3 fatty acids offer protection against certain diseases, while

others, if taken up in excess, can have negative effects. The composition of the fatty acids in cell membranes may therefore have a variety of different health consequences.

"This may also explain why certain diseases and even death occur at specific times of day. Statistically speaking, heart attacks occur more often in the morning than in the evening. Blood pressure usually rises before noon. We currently do not know exactly what causes the changes in the composition of the cell membranes. The type of food eaten and the time of food intake may also play a role. These questions must still be researched," Ruf points out.

In addition to consuming sufficient quantities of important healthy fatty acids, such as omega-3 fatty acids in fish oil or oleic acids in olive oil, it may also be important to choose the right time for intake.

Climate Change

Global Sea Levels

Global sea levels have risen six metres or more with just slight global warming.

A new review analysing three decades of research on the historic effects of melting polar ice sheets found that global sea levels have risen at least six metres, or about 20 feet, above present levels on multiple occasions over the past three million years.

What is most concerning, scientists say, is that the amount of melting was caused by an increase of only 1–2 degrees (Celsius) in global mean temperatures.

Results of the study have been published earlier in the journal *Science*.

"Studies have shown that both the Greenland and Antarctic ice sheets contributed significantly to this sea level rise above modern levels," said Anders Carlson, an Oregon State University glacial geologist and paleoclimatologist, and co-author of the study. "Modern atmospheric carbon dioxide (CO₂) levels are today equivalent to those about three million years ago, when sea level was at least six metres higher because the ice sheets were greatly reduced."

"It takes time for the warming to whittle down the ice sheets," added Carlson, who is in OSU's College of Earth, Ocean and Atmospheric Sciences, "but it doesn't take forever. There is evidence that we are likely seeing that transformation begin to take place now."

Co-author Peter Clark, an OSU paleoclimatologist, said that because current CO₂ levels are as high as they were three million years ago, "we are already committed to a certain amount of sea level rise."

"The ominous aspect to this is that CO₂ levels are continuing to rise, so we are entering uncharted territory," Clark said. "What is not as certain is the time frame, which is less well-constrained. We could be talking many centuries to a few millennia to see the full impact of melting ice sheets."

The review, which was led by Andrea Dutton of the University of Florida, summarised more than 30 years of research on past changes in ice sheets and sea level. It shows that changes in Earth's climate and sea level are closely linked, with only small amounts of warming needed to have a significant effect on sea levels. Those impacts can be significant.

Six metres (or about 20 feet) of sea level rise does not sound like a lot. However, coastal cities worldwide have experienced enormous growth in population and infrastructure over the past couple of centuries — and a global mean sea

level rise of 10 to 20 feet could be catastrophic to the hundreds of millions of people living in these coastal zones.

Much of the state of Florida, for example, has an elevation of 50 feet or less, and the city of Miami has an average elevation of six feet. Parts of New Orleans and other areas of Louisiana were overcome by Hurricane Katrina — by a surging Gulf of Mexico that could be 10 to 20 feet higher in the future. Dhaka in Bangladesh is one of the world's 10 most populous cities with 14.4 million inhabitants, all living in low-lying areas. Tokyo and Singapore also have been singled out as extremely vulnerable to sea level rise.

"The influence of rising oceans is even greater than the overall amount of sea level rise because of storm surge, erosion and inundation," said Carlson, who studies the interaction of ice sheets, oceans and the climate system on centennial time scales. "The impact could be enormous."

The Science review is part of the larger Past Global Changes, or PAGES, international science team. A working group known as PALSEA2 (Paleo constraints on sea level rise) used past records of local change in sea level and converted them to a global mean sea level by predicting how the surface of the Earth deforms due to changes in ice-ocean loading of the crust, along with changes in gravitational attraction on the ocean surface.

Independently, Greenland and Antarctic ice sheet volumes were estimated by observations from adjacent ocean sediment records and by ice sheet models.

"The two approaches are independent of one another, giving us high confidence in the estimates of past changes in sea level," Carlson said. The past climates that forced these changes in ice volume and sea level were reconstructed mainly from temperature-

sensitive measurements in ocean cores from around the globe, and from ice cores.

The National Science Foundation supported the research.

Promising Progress for New Treatment of Type 1 Diabetes

New research from Uppsala University shows promising progress in the use of anti-inflammatory cytokine for treatment of Type 1 diabetes (T1D). The study, published in the open access journal *Scientific Reports* (Nature Publishing Group), reveals that administration of interleukin-35 (a protein made by immune cells) to mice with Type 1 diabetes, reverses or cures the disease by maintaining a normal blood glucose level and the immune tolerance.

T1D is a chronic disease, which for the patients leads to a life-long dependence of daily injections of insulin. In Sweden, approximately two new cases of the disease are diagnosed everyday. Insulin is a hormone, which is produced by the beta cells in the pancreas. Insulin is required to prevent a harmful rise in the blood glucose level.

The exact cause of T1D is not yet known, however, it is considered as an auto-immune disease. A condition that occurs when our own immune system by mistake attacks and destroys healthy cells. In T1D, an infection and/or unknown factors probably trigger(s) the immune cell attack, which ultimately leads to an insufficient insulin production.

In the new study, Dr. Kailash Singh, a Ph.D. student in Professor Stellan Sandler's research group at the Department of Medical Cell Biology at Uppsala University, studied the so-called immune regulatory T cells' actions in T1D mouse models. The study shows that the immune regulatory T cells alter their function by producing pro-inflammatory

destructive proteins instead of protective anti-inflammatory proteins, such as interleukin-35 (IL-35) under T1D conditions.

"This suggests that the good guys have gone bad in early development of Type 1 diabetes and therefore our immune cells destroy the beta cell," says Dr. Kailash Singh.

Furthermore, the concentration of IL-35 was lower in T1D patients compared to healthy individuals. These findings may suggest that IL-35 could play a crucial role in human T1D. In addition, the researchers have found a novel mechanism that explains how the immune regulatory T cells are changing their destiny under a T1D condition.

Professor Sandler's research team tested whether or not IL-35 could also suppress development of T1D and reverse established T1D. To induce T1D in mice they injected a chemical compound called streptozotocin. These mice developed signs of T1D and increasing blood glucose levels similar as in human T1D. IL-35 injections given after disease induction prevented from development of T1D. Strikingly, IL-35 injections to mice, which were diabetic for two consecutive days, normalised blood glucose concentrations.

The research team also successfully investigated IL-35 in another model of T1D called non-obese diabetic mouse (NOD). The interruption of IL-35 treatment did not result in return of diabetes in any of the mouse models.

The findings encourage further research on the use of IL-35 for treatment of T1D and offer new clues as to why immune regulatory T cells fail in counteracting T1D.

"To the best of our knowledge, we are the first to show that IL-35 can reverse established Type 1 diabetes in two different mouse models and that the concentration of the particular cytokine is

lower in Type 1 diabetes patients than in healthy individuals. Also, we are providing an insight into a novel mechanism: how immune regulatory T cells change their fate under autoimmune conditions," says Dr. Kailash Singh.

Managing Mining of the Deep Seabed

Thousands of feet below the ocean's surface lies a hidden world of undiscovered species and unique seabed habitats—as well as a vast untapped store of natural resources including valuable metals and rare-earth minerals. Technology and infrastructure development worldwide is dramatically increasing demand for these resources, which are key components in everything from cars and modern buildings to computers and smartphones. This demand has catalysed interest in mining huge areas of the deep-sea floor.

In a paper published in *Science*, researchers from the Center for Ocean Solutions and co-authors from leading institutions around the world proposed a strategy for balancing commercial extraction of deep-sea resources with protection of diverse seabed habitats. The paper is intended to inform upcoming discussions by the International Seabed Authority (ISA) that will set the groundwork for future deep-sea environmental protection and mining regulations.

"Our purpose is to point out that the ISA has an important opportunity to create networks of no-mining Marine Protected Areas (MPAs) as part of the regulatory framework they are considering in their July meeting," says lead author Lisa Wedding, an early career science fellow at the Center for Ocean Solutions. "The establishment of regional MPA networks in the deep sea could potentially benefit both mining and biodiversity

interests by providing more economic certainty and ecosystem protection."

The ISA is charged with managing the seabed and its resources outside of national jurisdictions for the benefit of humankind. According to the United Nations Convention on the Law of the Sea (UNCLOS), the deep seabed is legally a part of the 'common heritage of humankind,' meaning that it belongs to each and every human on the planet.

"The ISA is the only body with the legal standing and responsibility to manage mining beyond national jurisdiction," said Kristina Gjerde, an international high-seas lawyer and co-author of the *Science* paper.

Since 2001, the ISA has granted 26 mining exploration contracts covering more than one million square kilometers of seabed, with 18 of these contracts granted in the last four years. Researchers recommend that the ISA, as part of its strategic plans to protect deep-seabed habitats and manage mining impacts, take a precautionary approach and set up networks of MPAs before additional large claim areas are granted for deep seabed mining.

"Given our paltry understanding of deep-sea environments, regional networks of MPAs that designate significant portions of the deep seabed as off-limits to mining would provide key insurance against unanticipated environmental impacts," said co-author Steven Gaines, Dean of the Bren School of Environmental Science & Management at the University of California at Santa Barbara.

Mining impacts could affect important environmental benefits that the deep sea provides to human beings. For example, the deep sea is a key player in our planet's carbon cycle, capturing a substantial amount of human-emitted carbon which impacts both

weather and climate. Mining activities could disturb these deep-sea carbon sinks, releasing excess carbon back into the atmosphere. The deep sea also sustains economically important fisheries, and harbors micro organisms which have proven valuable in a number of pharmaceutical, medical and industrial applications.

"Deep-sea areas targeted by mining claims frequently harbor high biodiversity and fragile habitats, and may have very slow rates of recovery from physical disturbance," said Craig Smith, a co-author and professor of oceanography at the University of Hawaii at Manoa. Smith and a team of scientists, helped the ISA pioneer the deep sea's first regional environmental management plan in 2012. Located in an area of the Pacific Ocean known as the Clarion-Clipperton Zone (CCZ), the plan honoured existing mining exploration claims while protecting delicate habitats by creating a network of MPAs. The CCZ serves as a model for how future deep-sea ecosystem management could unfold.

"This kind of precautionary approach achieves a balance of economic interests and conservation benefits," said Sarah Reiter, a co-author and former early career law and policy fellow at the Center for Ocean Solutions, and ocean policy analyst at the Monterey Bay Aquarium.

The upcoming ISA session on July 15th represents a critical juncture for defining the future of deep-sea mining and protection.

"The time is now to protect this important part of the planet for current and future generations," said Larry Crowder, a co-author and science director at the Center for Ocean Solutions and senior fellow at the Stanford Woods Institute for the Environment. "Decisions that affect us all will be made by the ISA this summer."

Don't look now, but the pronoun 'I' is becoming obsolete.

Recent microbiological research has shown that thinking of plants and animals, including humans, as autonomous individuals is a serious over-simplification.

A series of groundbreaking studies have revealed that what we have always thought of as individuals are actually 'biomolecular networks' that consist of visible hosts plus millions of invisible microbes that have a significant effect on how the host develops, the diseases it catches, how it behaves and possibly even its social interactions.

"It's a case of the whole being greater than the sum of its parts," said Seth Bordenstein, associate professor of biological sciences at Vanderbilt University, who has contributed to the body of scientific knowledge that is pointing to the conclusion that symbiotic microbes play a fundamental role in virtually all aspects of plant and animal biology, including the origin of new species.

In this case, the parts are the host and its genome plus the thousands of different species of bacteria living in or on the host, along with all their genomes, collectively known as the microbiome. (The host is something like the tip of the iceberg while the bacteria are like the part of the iceberg that is underwater: Nine out of every 10 cells in plant and animal bodies are bacterial. But bacterial cells are so much smaller than host cells that they are generally unnoticed.)

Microbiologists have coined new terms for these collective entities — holobiont — and for their genomes — hologenome. "These terms are needed to define the assemblage of organisms

that make up the so-called individual," said Bordenstein.

In the article 'Host Biology in Light of the Microbiome: Ten Principles of Holobionts and Hologenomes' published online on 18 August in the open access journal *PLoS Biology*, Bordenstein and his colleague Kevin Theis from the University of Michigan take the general concepts involved in this new paradigm and break them down into underlying principles that apply to the entire field of biology.

They make specific and refutable predictions based on these principles and call for other biologists to test them theoretically and experimentally.

"One of the basic expectations from this conceptual framework is that animal and plant experiments that do not account for what is happening at the microbiological level will be incomplete and, in some cases, will be misleading as well," said Bordenstein.

The first principle they advance is that holobionts and hologenomes are fundamental units of biological organisation.

Another is that evolutionary forces, such as natural selection and drift may act on the hologenome, not just on the genome. So mutations in the microbiome that affect the fitness of a holobiont are just as important as mutations in the host's genome. However, they argue that this does not change the basic rules of evolution but simply upgrades the types of biological units that the rules may act upon.

Although it does not change the basic rules of evolution, holobionts do have a way to respond to environmental challenges that is not available to individual organisms: They can alter the

composition of their bacterial communities. For example, if a holobiont is attacked by a pathogen that the host cannot defend against, another symbiont may fulfill the job by manufacturing a toxin that can kill the invader. In this light, the microbes are as much part of the holobiont immune system as the host immune genes themselves.

According to Bordenstein, these ideas are gaining acceptance in the microbiology community. At the American Society of Microbiology General Meeting, he convened the inaugural session on 'Holobionts and their Hologenomes' and ASM's flagship journal *mBio* plans to publish a special issue on the topic.

However, adoption of these ideas has been slower in other fields.

"Currently, the field of biology has reached an inflection point. The silos of microbiology, zoology and botany are breaking down and we hope that this framework will help further unify these fields," said Bordenstein.

Not only will this powerful holistic approach affect the basic biological sciences but it also is likely to impact the practice of personalised medicine as well, Bordenstein said.

Take the missing heritability problem, for example. Although genome-wide studies have provided valuable insights into the genetic basis of a number of simple diseases, they have only found a small portion of the genetic causes of a number of more complex conditions, such as auto-immune and metabolic diseases.

These may in part be 'missing' because the genetic factors that cause them are in the microbiome, he pointed out.

"Instead of being so 'germophobic,' we need to accept the fact that we live in and benefit

from a microbial world. We are as much an environment for microbes as microbes are for us," said Bordenstein.

Obesity Breakthrough: Metabolic Master Switch Prompts Fat Cells to Store or Burn Fat

Obesity is one of the biggest public health challenges of the 21st century. Affecting more than 500 million people worldwide, obesity costs at least \$200 billion each year in the United States alone, and contributes to potentially fatal disorders, such as cardiovascular disease, Type 2 diabetes and cancer.

But there may now be a new approach to prevent and even cure obesity, thanks to a study led by researchers at MIT and Harvard Medical School and published in the *New England Journal of Medicine*. By analysing the cellular circuitry underlying the strongest genetic association with obesity, the researchers have unveiled a new pathway that controls human metabolism by prompting our adipocytes, or fat cells, to store fat or burn it away.

"Obesity has traditionally been seen as the result of an imbalance between the amount of food we eat and how much we exercise, but this view ignores the contribution of genetics to each individual's metabolism," says senior author Manolis Kellis, a professor of computer science and a member of MIT's Computer Science and Artificial Intelligence Laboratory (CSAIL) and of the Broad Institute.

New mechanism found

The strongest association with obesity resides in a gene region known as 'FTO,' which has been the focus of intense scrutiny since its discovery in 2007. However, previous studies have failed

to find a mechanism to explain how genetic differences in the region lead to obesity.

"Many studies attempted to link the FTO region with brain circuits that control appetite or propensity to exercise," says first author Melina Claussnitzer, a visiting professor at CSAIL and instructor in medicine at Beth Israel Deaconess Medical Center and Harvard Medical School. "Our results indicate that the obesity-associated region acts primarily in adipocyte progenitor cells in a brain-independent way."

To recognise the cell types where the obesity-associated region may act, the researchers used annotations of genomic control switches across more than 100 tissues and cell types. They found evidence of a major control switchboard in human adipocyte progenitor cells, suggesting that genetic differences may affect the functioning of human fat stores.

To study the effects of genetic differences in adipocytes, the researchers gathered adipose samples from healthy Europeans carrying either the risk or the non-risk version of the region. They found that the risk version activated a major control region in adipocyte progenitor cells, which turned on two distant genes, IRX3 and IRX5.

Control of thermogenesis

Follow-up experiments showed that IRX3 and IRX5 act as master controllers of a process known as thermogenesis, whereby adipocytes dissipate energy as heat, instead of storing it as fat. Thermogenesis can be triggered by exercise, diet, or exposure to cold, and occurs both in mitochondria-rich brown adipocytes that are developmentally related to muscle, and in beige adipocytes that are instead related to energy-storing white adipocytes.

"Early studies of thermogenesis focussed primarily on brown fat, which plays a major role in mice, but is virtually nonexistent in human adults," Claussnitzer says. "This new pathway controls thermogenesis in the more abundant white fat stores instead, and its genetic association with obesity indicates that it affects global energy balance in humans."

The researchers predicted that a genetic difference of only one nucleotide is responsible for the obesity association. In risk individuals, a thymine (T) is replaced by a cytosine (C) nucleobase, which disrupts repression of the control region and turns on IRX3 and IRX5. This then turns off thermogenesis, leading to lipid accumulation and ultimately obesity.

By editing a single nucleotide position using the CRISPR/Cas9 system — a technology that allows researchers to make precise changes to a DNA sequence — the researchers could switch between lean and obese signatures in human pre-adipocytes. Switching the C to a T in risk individuals turned off IRX3 and IRX5, restored thermogenesis to non-risk levels, and switched off lipid storage genes.

"Knowing the causal variant underlying the obesity association may allow somatic genome editing as a therapeutic avenue for individuals carrying the risk allele," says Kellis. "But more importantly, the uncovered cellular circuits may allow us to dial a metabolic master switch for both risk and non-risk individuals, as a means to counter environmental, lifestyle, or genetic contributors to obesity."

Success in human and mouse cells

The researchers showed that they could indeed manipulate this new pathway to reverse the signatures of obesity in both human cells and mice.

In primary adipose cells from either risk or non-

risk individuals, altering the expression of either IRX3 or IRX5 switched between energy-storing white adipocyte functions and energy-burning beige adipocyte functions.

Similarly, repression of IRX3 in mouse adipocytes led to dramatic changes in whole-body energy balance, resulting in a reduction of body weight and all major fat stores, and complete resistance to a high-fat diet.

"By manipulating this new pathway, we could switch between energy storage and energy dissipation programs at both the cellular and the organismal level, providing new hope for a cure against obesity," says Kellis.

The researchers are currently establishing collaborations in academia and industry to translate their findings into obesity therapeutics. They are also using their approach as a model to understand the circuitry of other disease-associated regions in the human genome.

Glitter from Silver Lights Up Alzheimer's Dark Secrets

Scientists have caught a glimpse of the elusive toxic form of the Alzheimer's molecule, during its attempt to bore into the outer covering of a cell decoy, using a new method involving laser light and fat-coated silver nano-particles.

While the origin of Alzheimer's Disease, one that robs the old of their memory, is still hotly debated, it is likely that a specific form of the Amyloid beta molecule, which is able to attack cell membranes, is a major player. Defeating this molecule would be easier if its shape and form were known better, but that has proven to be a difficult task until now.

"Everybody wants to make the key to solve Alzheimer's Disease, but we don't know what

the lock looks like. We now have a glimpse of something which could be the lock. May be it's still not the real thing, but as of now, this is our best bet," says Sudipta Maiti, who co-directed the efforts with P. K. Madhu (both from TIFR). If they are right, then designing the key, i.e., making a drug molecule which can attack the lock, may be more achievable now.

The lock looks like a bunch of amyloid beta molecules in the shape of a hairpin, but with a twist. Debanjan Bhowmik, the lead contributor of the study says, "This has been suspected earlier, but what we found was an unexpected twist in the structure, now becoming a beta-hairpin — very different from the typical hairpin structure people imagined. This may allow these bunch of amyloid beta molecules to form toxic pores in the cell membranes."

The findings published in the journal *ACS Nano* by a joint team of researchers from the Tata Institute of Fundamental Research, Indian Institute of Science and the University of Toronto, have cracked the problem that has eluded scientists for years, by using a modified version of Raman Spectroscopy.

They studied a tiny laser-induced signal from the amyloid beta which reported their shape. A critical modification in the original Raman Spectroscopy technique allowed the measurement of tiny signals that would otherwise have gone unnoticed. They encased silver nanoparticles in a fat layer ('membrane') that mimicked the outer membranes of living cells. According to co-author Gilbert Walker, "While the amyloid beta got fooled by it and stuck to the membrane, the silver inside enhanced the signal to a measurable level and acted as a light beacon to reveal the peptide signature." The technique offers promise for deciphering the shape of many such membrane molecules, some of which may be related to other types of diseases.

Each research team brought something different to the table. As Jaydeep Basu, who led the IISc team, says, "It's a great example of how contemporary science breaks all barriers to bring people together for the pure love of science and the quest for the unknown!" One hopes that the search for the key to solve Alzheimer's has taken a step forward with this finding.

Human Body has gone through Four Stages of Evolution

Research into 4,30,000-year-old fossils collected in northern Spain found that the evolution of the human body's size and shape has gone through four main stages.

A large international research team including Binghamton University anthropologist Rolf Quam studied the body size and shape in the human fossil collection from the site of the Sima de los Huesos in the Sierra de Atapuerca in northern Spain. Dated to around 4,30,000 years ago, this site preserves the largest collection of human fossils found to date anywhere in the world. The researchers found that the Atapuerca individuals were relatively tall, with wide, muscular bodies and less brain mass relative to body mass compared to Neanderthals. The Atapuerca humans shared many anatomical features with the later Neanderthals not present in modern humans, and analysis of their postcranial skeletons (the bones of the body other than the skull) indicated that they are closely related evolutionarily to Neanderthals.

"This is really interesting since it suggests that the evolutionary process in our genus is largely characterised by stasis (i.e. little to no evolutionary change) in body form for most of our evolutionary history," wrote Quam.

Comparison of the Atapuerca fossils with the rest of the human fossil record suggests

that the evolution of the human body has gone through four main stages, depending on the degree of arboreality (living in the trees) and bipedalism (walking on two legs). The Atapuerca fossils represent the third stage, with tall, wide and robust bodies and an exclusively terrestrial bipedalism, with no evidence of arboreal behaviours. This same body form was likely shared with earlier members of our genus, such as *Homo erectus*, as well as some later members, including the Neanderthals. Thus, this body form seems to have been present in the genus *Homo* for over a million years.

It was not until the appearance of our own species, *Homo sapiens*, when a new taller, lighter and narrower body form emerged. Thus, the authors suggest that the Atapuerca humans offer the best look at the general human body shape and size during the last million years before the advent of modern humans.

Seeing Quantum Motion; Even One Day Ripples in the Fabric of Space-time?

Consider the pendulum of a grandfather clock. If you forget to wind it, you will eventually find the pendulum at rest, unmoving. However, this simple observation is only valid at the level of classical physics—the laws and principles that appear to explain the physics of relatively large objects at human scale. However, quantum mechanics, the underlying physical rules that govern the fundamental behaviour of matter and light at the atomic scale, state that nothing can quite be completely at rest.

For the first time, a team of Caltech researchers and collaborators has found a way to observe—and control—this quantum motion of an object that is large enough to see. Their results are published in the 27 August online issue of the journal *Science*.

Researchers have known for years that in classical physics, physical objects indeed can be motionless. Drop a ball into a bowl, and it will roll back and forth a few times. Eventually, however, this motion will be overcome by other forces (such as gravity and friction), and the ball will come to a stop at the bottom of the bowl.

"In the past couple of years, my group and a couple of other groups around the world have learned how to cool the motion of a small micrometer-scale object to produce this state at the bottom, or the quantum ground state," says Keith Schwab, a Caltech professor of physics and applied physics, who led the study. "But we know that even at the quantum ground state, at zero-temperature, very small amplitude fluctuations—or noise—remain."

Because this quantum motion, or noise, is theoretically an intrinsic part of the motion of all objects, Schwab and his colleagues designed a device that would allow them to observe this noise and then manipulate it.

The micrometer-scale device consists of a flexible aluminum plate that sits atop a silicon substrate. The plate is coupled to a superconducting electrical circuit as the plate vibrates at a rate of 3.5 million times per second. According to the laws of classical mechanics, the vibrating structures eventually will come to a complete rest if cooled to the ground state.

But that is not what Schwab and his colleagues observed when they actually cooled the spring to the ground state in their experiments. Instead, the residual energy — quantum noise — remained.

"This energy is part of the quantum description of nature — you just can't get it out," says Schwab. "We all know quantum mechanics

explains precisely why electrons behave weirdly. Here, we're applying quantum physics to something that is relatively big, a device that you can see under an optical microscope, and we're seeing the quantum effects in a trillion atoms instead of just one."

Because this noisy quantum motion is always present and cannot be removed, it places a fundamental limit on how precisely one can measure the position of an object.

But that limit, Schwab and his colleagues discovered, is not insurmountable. The researchers and collaborators developed a technique to manipulate the inherent quantum noise and found that it is possible to reduce it periodically. Co-authors Aashish Clerk from McGill University and Florian Marquardt from the Max Planck Institute for the Science of Light proposed a novel method to control the quantum noise, which was expected to reduce it periodically. This technique was then implemented on a micron-scale mechanical device in Schwab's low-temperature laboratory at Caltech.

"There are two main variables that describe the noise or movement," Schwab explains. "We showed that we can actually make the fluctuations of one of the variables smaller—at the expense of making the quantum fluctuations of the other variable larger. That is what's called a quantum squeezed state; we squeezed the noise down in one place, but because of the squeezing, the noise has to squirt out in other places. But as long as those more noisy places aren't where you're obtaining a measurement, it doesn't matter."

The ability to control quantum noise could one day be used to improve the precision of very sensitive measurements, such as those obtained

by LIGO, the Laser Interferometry Gravitational-wave Observatory, a Caltech-and-MIT-led project searching for signs of gravitational waves, ripples in the fabric of space-time.

"We've been thinking a lot about using these methods to detect gravitational waves from pulsars—incredibly dense stars that are the mass of our sun compressed into a 10 km radius and spin at 10 to 100 times a second," Schwab says. "In the 1970s, Kip Thorne [Caltech's Richard P. Feynman Professor of Theoretical Physics, Emeritus] and others wrote papers saying that these pulsars should be emitting gravity waves that are nearly perfectly periodic, so we're thinking hard about how to use these techniques on a gram-scale object to reduce quantum noise in detectors, thus increasing the sensitivity to pick up on those gravity waves," Schwab says.

In order to do that, the current device would have to be scaled up. "Our work aims to detect quantum mechanics at bigger and bigger scales, and one day, our hope is that this will eventually start touching on something as big as gravitational waves," he says.

Urine Test for Early Stage Pancreatic Cancer Possible after Biomarker Discovery

A combination of three proteins found at high levels in urine can accurately detect early-stage pancreatic cancer, UK researchers have found. The discovery could lead to a non-invasive, inexpensive test to screen people at high risk of developing the disease.

A team at Barts Cancer Institute, Queen Mary University of London, has shown that the three-protein 'signature' can both identify the most common form of pancreatic cancer when still in

its early stages — and distinguish between this cancer and the inflammatory condition chronic pancreatitis, which can be hard to tell apart.

The study, published in the journal *Clinical Cancer Research*, was funded by the UK charity, the Pancreatic Cancer Research Fund. It looked at 488 urine samples: 192 from patients known to have pancreatic cancer, 92 from patients with chronic pancreatitis and 87 from healthy volunteers. A further 117 samples from patients with other benign and malignant liver and gall bladder conditions were used for further validation.

Around 1,500 proteins were found in the urine samples, with approximately half being common to both male and female volunteers. Of these, three proteins — LYVE1, REG1A and TFF1 — were selected for closer examination, based on biological information and performance in statistical analysis.

Patients with pancreatic cancer were found to have increased levels of each of the three proteins when compared to urine samples from healthy patients, while patients suffering from chronic pancreatitis had significantly lower levels than cancer patients. When combined, the three proteins formed a robust panel that can detect patients with stages I–II pancreatic cancer with over 90 per cent accuracy.

With few specific symptoms even at a later stage of the disease, more than 80 per cent of people with pancreatic cancer are diagnosed when the cancer has already spread. This means they are not eligible for surgery to remove the tumour — currently the only potentially curative treatment.

The five-year survival rate for pancreatic cancer in the UK is the lowest of any common cancer, standing at 3 per cent. This figure has barely improved in 40 years. There is no early diagnostic test available.

Lead researcher, Dr Tatjana Crnogorac-Jurcevic, said: "We've always been keen to develop a diagnostic test in urine as it has several advantages over using blood. It's an inert and far less complex fluid than blood and can be repeatedly and non-invasively tested. It took a while to secure proof of principle funding in 2008 to look at biomarkers in urine, but it's been worth the wait for these results. This is a biomarker panel with good specificity and sensitivity and we're hopeful that a simple, inexpensive test can be developed and be in clinical use within the next few years."

Although there is no universal cause of pancreatic cancer, people at higher risk of developing the disease include those with a family history of pancreatic cancer, heavy smokers, the obese and people over 50 years with new-onset diabetes.

The team is hoping to conduct further tests on urine samples from people in high risk groups, to further validate the study findings. Dr Crnogorac-Jurcevic is also keen to access samples of urine collected from volunteers over a period of 5–10 years. By examining samples from donors who went on to develop pancreatic cancer, this 'longitudinal' information will allow the researchers to see if the 3-biomarker signature is present during the latency period— the time between the genetic changes that will cause the cancer to develop and the clinical presentation.

"For a cancer with no early stage symptoms, it's a huge challenge to diagnose pancreatic cancer

sooner, but if we can, then we can make a big difference to survival rates," says co-author and Director of Barts Cancer Institute, Professor Nick Lemoine. "With pancreatic cancer, patients are usually diagnosed when the cancer is already at a terminal stage, but if diagnosed at stage 2, the survival rate is 20 per cent, and at stage 1, the survival rate for patients with very small tumours can increase up to 60 per cent."

Pancreatic Cancer Research Fund CEO, Maggie Blanks, said: "This is an exciting finding and we hope to see this research taken forward into a much needed early diagnostic test. Early diagnosis is an important part of our overall efforts against this aggressive cancer, alongside developing new treatments to tackle the disease once diagnosis is made. It underlines the importance of increased research efforts to help improve survival rates."

"Many of the urine samples from healthy individuals tested by Tanja's team were donated from the charity's own supporter community, and I know they will be extremely proud that they have directly contributed to research progress in ways that go beyond traditional financial support."

Source: *Science Daily Online*

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