

3-D Images of Live Cells

The insides of living cells can be seen in their natural state in greater detail than ever before using a new technique developed by researchers in Japan. [47]

Scientists have been using fluorescence microscopy to study the inner workings of biological cells and organisms for decades. [46]

Selecting the most effective molecules for drug delivery is often a trial-and-error process, but Cornell engineers are providing some precision thanks to a technique that reveals the performance of those molecules inside living cells. [45]

Now, researchers at MIT and elsewhere have developed a system to deliver medical treatments that can be released at precise times, minimally-invasively, and that ultimately could also deliver those drugs to specifically targeted areas such as a specific group of neurons in the brain. [44]

Gene editing technology is a technology that eliminates the underlying causes of and treats diseases by removing specific genes or editing genes to restore their normal function. In particular, CRISPR gene editing technology is now commonly used for immunotherapy by correcting the genes of immune cells to induce them to attack cancer cells selectively. [43]

Bioengineers and biophysicists from the National Research Nuclear University MEPhI, the Sechenov First Moscow State Medical University, the Universite de Reims Champagne-Ardenne in France, and the University of Tübingen in Germany have discovered that the toxicity of nanoparticles depends more on their size and the extent to which their surface area is charged than on their chemical composition. [42]

That's now possible thanks to research by Rice University scientists who used the light-emitting properties of particular molecules to create a fluorescent nano-thermometer. [41]

Collaborative research at ANSTO led by Mr Shinji Kihara and A/Prof. Duncan McGillivray of The MacDiarmid Institute, New Zealand with ANSTO's Dr. Jitendra Mata, scientists from the University of Auckland and A/Prof Ingo Köper from Flinders University, SA, is contributing to a better understanding of how nanoplastics interact with blood plasma proteins and other biological molecules within the body. [40]

Our new structures show how this is achieved, providing a framework for the entire V-ATPase family". [39]

Now an ETH research group has for the first time isolated and studied all the key proteins involved in this process, laying the foundation for investigating many diseases. [38]

Cancer that has spread to the central nervous system is notoriously difficult to treat. Now, UCLA researchers have developed a drug delivery system that breaks through the blood-brain barrier in order to reach and treat cancer that has spread to the central nervous system. [37]

Nanotechnology developed at Rutgers University-New Brunswick could boost research on stem cell transplantation, which may help people with Alzheimer's disease, Parkinson's disease, other neurodegenerative diseases and central nervous system injuries. [36]

Tiny silica bottles filled with medicine and a special temperature-sensitive material could be used for drug delivery to kill malignant cells only in certain parts of the body, according to a study published recently by researchers at the Georgia Institute of Technology. [35]

The lab of Cheryl Kerfeld at Michigan State University has created a synthetic nano-sized factory, based on natural ones found in bacteria. [34]

Among these different testing systems, there is the Mimotope Variation Analysis (MVA) developed and patented by the Estonian biotechnology company Protobios which has never been used in the framework of biomaterial assessment before. [33]

Medical physicist Dr. Aswin Hoffmann and his team from the Institute of Radiooncology—OncoRay at the Helmholtz-Zentrum Dresden-Rossendorf (HZDR) have combined magnetic resonance imaging (MRI) with a proton beam, thus demonstrating for the first time that in principle, this commonly used imaging method can work with particle beam cancer treatments. [32]

Washington State University researchers for the first time have shown that they can use electrical fields to gain valuable information about the tiny, floating vesicles that move around in animals and plants and are critically important to many biological functions. [31]

Finding a fast and inexpensive way to detect specific strains of bacteria and viruses is critical to food safety, water quality, environmental protection and human health. [30]

In the perspective, Gabor and Song collect early examples in electron metamaterials and distil emerging design strategies for electronic control from them. [29]

Lawrence Livermore National Laboratory (LLNL) researchers are working to make better electronic devices by delving into the way nanocrystals are arranged inside of them. [28]

Self-assembly and crystallisation of nanoparticles (NPs) is generally a complex process, based on the evaporation or precipitation of NP-building blocks. [27]

New nanoparticle-based films that are more than 80 times thinner than a human hair may help to fill this need by providing materials that can holographically archive more than 1000 times more data than a DVD in a 10-by-10-centimeter piece of film. [26]

Researches of scientists from South Ural State University are implemented within this area. [25]

Following three years of extensive research, Hebrew University of Jerusalem (HU) physicist Dr. Uriel Levy and his team have created technology that will enable computers and all optic communication devices to run 100 times faster through terahertz microchips. [24]

When the energy efficiency of electronics poses a challenge, magnetic materials may have a solution. [23]

*An exotic state of matter that is dazzling scientists with its electrical properties, can also exhibit unusual optical properties, as shown in a theoretical study by researchers at A*STAR. [22]*

The breakthrough was made in the lab of Andrea Alù, director of the ASRC's Photonics Initiative. Alù and his colleagues from The City College of New York, University of Texas at Austin and Tel Aviv University were inspired by the seminal work of three British researchers who won the 2016 Noble Prize in Physics for their work, which teased out that particular properties of matter (such as electrical conductivity) can be preserved in certain materials despite continuous changes in the matter's form or shape. [21]

Researchers at the University of Illinois at Urbana-Champaign have developed a new technology for switching heat flows 'on' or 'off'. [20]

Thermoelectric materials can use thermal differences to generate electricity. Now there is an inexpensive and environmentally friendly way of producing them with the simplest tools: a pencil, photocopy paper, and conductive paint. [19]

A team of researchers with the University of California and SRI International has developed a new type of cooling device that is both portable and efficient. [18]

Thermal conductivity is one of the most crucial physical properties of matter when it comes to understanding heat transport, hydrodynamic evolution and energy balance in systems ranging from astrophysical objects to fusion plasmas. [17]

Researchers from the Theory Department of the MPSD have realized the control of thermal and electrical currents in nanoscale devices by means of quantum local observations. [16]

Physicists have proposed a new type of Maxwell's demon—the hypothetical agent that extracts work from a system by decreasing the system's entropy—in which the demon can extract work just by making a measurement, by taking advantage of quantum fluctuations and quantum superposition. [15]

Pioneering research offers a fascinating view into the inner workings of the mind of 'Maxwell's Demon', a famous thought experiment in physics. [14]

For more than a century and a half of physics, the Second Law of Thermodynamics, which states that entropy always increases, has been as close to inviolable as any law we know. In this universe, chaos reigns supreme. [13]

Physicists have shown that the three main types of engines (four-stroke, twostroke, and continuous) are thermodynamically equivalent in a certain quantum regime, but not at the classical level. [12]

For the first time, physicists have performed an experiment confirming that thermodynamic processes are irreversible in a quantum system—meaning that, even on the quantum level, you can't put a broken egg back into its shell. The results have implications for understanding thermodynamics in quantum systems and, in turn, designing quantum computers and other quantum information technologies. [11]

Disorder, or entropy, in a microscopic quantum system has been measured by an international group of physicists. The team hopes that the feat will shed light on the "arrow of time": the observation that time always marches towards the future. The experiment involved continually flipping the spin of carbon atoms with an oscillating magnetic field and links the emergence of the arrow of time to quantum fluctuations between one atomic spin state and another. [10]

Mark M. Wilde, Assistant Professor at Louisiana State University, has improved this theorem in a way that allows for understanding how quantum measurements can be approximately reversed under certain circumstances. The new results allow for understanding how quantum information that has been lost during a measurement can be nearly recovered, which has potential implications for a variety of quantum technologies. [9]

Today, we are capable of measuring the position of an object with unprecedented accuracy, but quantum physics and the Heisenberg uncertainty principle place

fundamental limits on our ability to measure. Noise that arises as a result of the quantum nature of the fields used to make those measurements imposes what is called the "standard quantum limit." This same limit influences both the ultrasensitive measurements in nanoscale devices and the kilometer-scale gravitational wave detector at LIGO. Because of this troublesome background noise, we can never know an object's exact location, but a recent study provides a solution for rerouting some of that noise away from the measurement. [8]

The accelerating electrons explain not only the Maxwell Equations and the Special Relativity, but the Heisenberg Uncertainty Relation, the Wave-Particle Duality and the electron's spin also, building the Bridge between the Classical and Quantum Theories.

The Planck Distribution Law of the electromagnetic oscillators explains the electron/proton mass rate and the Weak and Strong Interactions by the diffraction patterns. The Weak Interaction changes the diffraction patterns by moving the electric charge from one side to the other side of the diffraction pattern, which violates the CP and Time reversal symmetry.

The diffraction patterns and the locality of the self-maintaining electromagnetic potential explains also the Quantum Entanglement, giving it as a natural part of the relativistic quantum theory.

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Author: George Rajna

Preface

Physicists are continually looking for ways to unify the theory of relativity, which describes largescale phenomena, with quantum theory, which describes small-scale phenomena. In a new proposed experiment in this area, two toaster-sized "nanosatellites" carrying entangled condensates orbit around the Earth, until one of them moves to a different orbit with different gravitational field strength. As a result of the change in gravity, the entanglement between the condensates is predicted to degrade by up to 20%. Experimentally testing the proposal may be possible in the near future. [5]

Quantum entanglement is a physical phenomenon that occurs when pairs or groups of particles are generated or interact in ways such that the quantum state of each particle cannot be described independently – instead, a quantum state may be given for the system as a whole. [4]

I think that we have a simple bridge between the classical and quantum mechanics by understanding the Heisenberg Uncertainty Relations. It makes clear that the particles are not point like but have a dx and dp uncertainty.

Unprecedented 3-D images of live cells plus details of molecules inside

The insides of living cells can be seen in their natural state in greater detail than ever before using a new technique developed by researchers in Japan. This advance should help reveal the complex and fragile biological interactions of medical mysteries, like how stem cells develop or how to deliver drugs more effectively.

"Our system is based on a simple concept, which is one of its advantages," said Associate Professor Takuro Ideguchi from the University of Tokyo Research Institute for Photon Science and Technology. The results of Ideguchi's team were published recently in *Optica*, the Optical Society's research journal.

The new method also has the advantages of using [live cells](#) without damaging them via intense light, or artificially attaching fluorescent tags to specific molecules.

The technique combines two pre-existing microscopy tools and uses them simultaneously. The combination of these tools can be thought of simply as like a coloring book.

"We gather the black-and-white outline of the cell and we virtually color in the details about where different types of molecules are located," said Ideguchi.

Quantitative phase microscopy gathers information about the black-and-white outline of the cell using pulses of light and measuring the shift in the light waves after they pass through a sample. This information is used to reconstruct a 3-D image of the major structures inside the cell.

Molecular vibrational imaging provides the virtual color using pulses of midinfrared light to add energy to specific types of molecules. That extra energy causes the molecules to vibrate, which heats up their local surroundings. Researchers can choose to raise the temperature of specific types of chemical bonds by using different wavelengths of midinfrared light.

Researchers take a quantitative phase microscopy image of the cell with the midinfrared light turned off and an image with it turned on. The difference between those two images then reveals both the outline of major structures inside the cell and the exact locations of the type of molecule that was targeted by the infrared light.

Researchers refer to their new combined imaging method as biochemical quantitative phase imaging with midinfrared photothermal effect.

"We were impressed when we first observed the molecular vibrational signature characteristic of proteins, and we were further excited when this protein-specific signal appeared in the same location as the nucleolus, an intracellular structure where high amounts of proteins would be expected," said Ideguchi.

Ideguchi's team hopes their technique might allow researchers to determine the distribution of fundamental types of [molecules](#) inside single [cells](#). The quantitative phase microscopy outline of major structures could be virtually colored in using different wavelengths of light to specifically target proteins, lipids (fats) or nucleic acids (DNA, RNA).

Currently, capturing one complete image can take 50 seconds or longer. Researchers are confident that they can speed up the process with simple improvements to their tools, including a higher-powered [light](#) source and a more sensitive camera. [47]

Novel 3-D imaging technology makes fluorescence microscopy more efficient

Scientists have been using fluorescence microscopy to study the inner workings of biological cells and organisms for decades. However, many of these platforms are often too slow to follow the biological action in 3-D; and too damaging to the living biological specimens with strong light illumination.

To address these challenges, a research team led by Dr. Kevin Tsia, Associate Professor of the Department of Electrical and Electronic Engineering and Programme Director of Bachelor of Engineering in Biomedical Engineering of the University of Hong Kong (HKU), developed a new optical imaging technology—coded light-sheet array microscopy (CLAM) - which can perform 3-D

imaging at high speed, and is power efficient and gentle enough to preserve living specimens during scanning at a level that is not achieved by existing technologies.

This advanced imaging technology was recently published in *Light: Science & Applications*. A US patent application has been filed for the innovation.

"CLAM allows 3-D fluorescence imaging at high frame rate comparable to state-of-the-art technology (~10's volumes per second). More importantly, it is much more power efficient, being over 1,000 times gentler than the standard 3-D microscopes widely used in scientific laboratories, which greatly reduces the damage done to living specimens during scanning," explained Dr. Tsia.

Existing 3-D biological microscopy platforms are slow because the entire volume of the specimen has to be sequentially scanned and imaged point-by-point, line-by-line or plane-by-plane. In these platforms, a single 3-D snapshot requires repeated illumination on the specimen. The specimens are often illuminated with thousands to million of times more intensity than that of sunlight. This is likely to damage the specimen itself, thus is not favorable for long-term biological imaging for diverse applications like anatomical science, developmental biology and neuroscience.

Moreover, these platforms often quickly exhaust the limited fluorescence "budget"—a fundamental constraint that fluorescent light can only be generated upon illumination for a limited period before it permanently fades out in a process called "photo-bleaching," which sets a limit to how many image acquisitions can be performed on a sample.



Coded Light-sheet Array Microscopy (CLAM) Credit: @The University of Hong Kong

"Repeated illumination on the specimen not only accelerates photo-bleaching, but also generates excessive fluorescence light that does not eventually form the [final image](#). Hence, the fluorescence 'budget' is largely wasted in these imaging platforms," Dr. Tsia added.

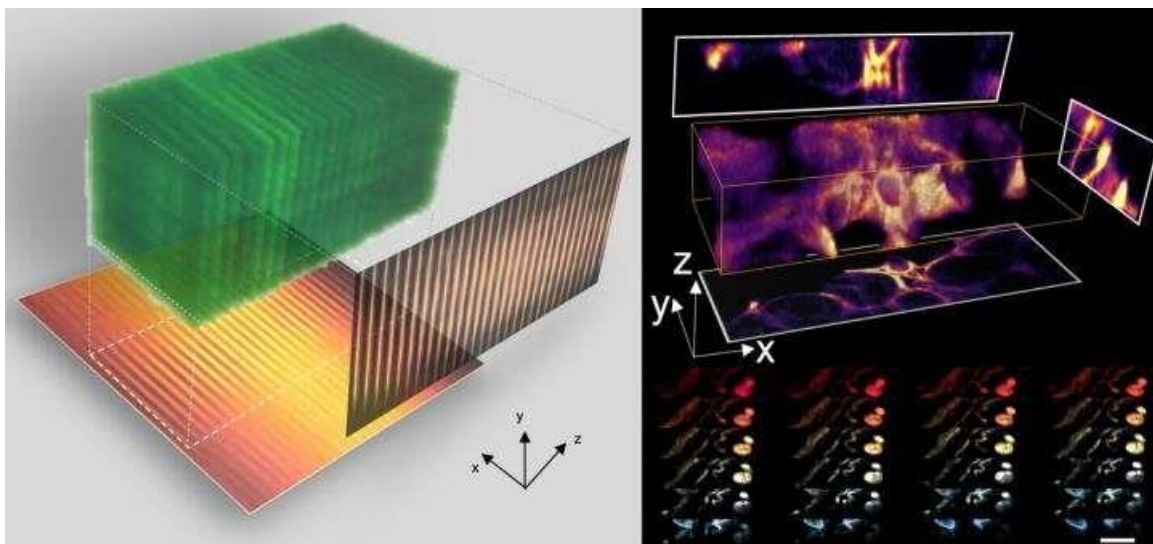
The heart of CLAM is transforming a single laser beam into a high-density array of 'light-sheets' with the use of a pair of parallel mirrors, to spread over a large area of the specimen as fluorescence excitation.

"The image within the entire 3-D volume is captured simultaneously (i.e. parallelized), without the need to scan the specimen point-by-point or line-by-line or plane-by-plane as required by other techniques. Such 3-D parallelization in CLAM leads to a very gentle and efficient 3-D fluorescence imaging without sacrificing sensitivity and speed," as pointed out by Dr. Yuxuan Ren, a postdoctoral researcher on the work. CLAM also outperforms the common 3-D fluorescence imaging methods in reducing the effect of photo-bleaching.

To preserve the image resolution and quality in CLAM, the team turned to Code Division Multiplexing (CDM), an image encoding technique which is widely used in telecommunication for sending multiple signals simultaneously.

"This encoding technique allows us to use a 2-D image sensor to capture and digitally reconstruct all image stacks in 3-D simultaneously. CDM has never been used in 3-D imaging before. We adopted the technology, which became a success," explained by Dr. Queenie Lai, another postdoctoral researcher who developed the system.

As a proof-of-concept demonstration, the team applied CLAM to capture 3-D videos of fast microparticle flow in a microfluidic chip at a volume rate of over 10 volumes per second comparable to state-of-the-art technology.



3D imaging at high speed with CLAM. Credit: The University of Hong Kong

"CLAM has no fundamental limitation in imaging speed. The only constraint is from the speed of the detector employed in the system, i.e. the camera for taking snapshots. As high-speed camera technology continually advances, CLAM can always challenge its limit to attain an even higher speed in scanning," highlighted by Dr. Jianglai Wu, the postdoctoral research who initiated the work.

The team has taken a step further to combine CLAM with HKU LKS Faculty of Medicine's newly developed tissue clearing technology to perform 3-D visualization of mouse glomeruli and intestine blood vasculature in high frame-rate.

"We anticipate that this combined technique can be extended to large-scale 3-D histopathological investigation of archival biological samples, like mapping the cellular organization in brain for neuroscience research." Dr. Tsia said.

"Since CLAM imaging is significantly gentler than all other methods, it uniquely favours long term and continuous 'surveillance' of biological specimen in their living form. This could potentially impact our fundamental understanding in many aspects of cell biology, e.g. to continuously track how an animal embryo develops into its adult form; to monitor in real-time how the cells/organisms get infected by bacteria or viruses; to see how the cancer cells are killed by drugs, and other challenging tasks unachievable by existing technologies today," Dr. Tsia added.

CLAM can be adapted to many current microscope systems with minimal hardware or software modification. Taking advantage of this, the team is planning to further upgrade the current CLAM system for research in cell biology, animal and plant developmental biology. [46]

Fluorescent probes offer fuller view of drug delivery in cells

Selecting the most effective molecules for drug delivery is often a trial-and-error process, but Cornell engineers are providing some precision thanks to a technique that reveals the performance of those molecules inside living cells.

Drug [delivery](#) systems control the time and place therapeutics are released inside the body. An essential component of many [drug delivery](#) systems is the molecule that links an antibody—which seeks out a target such as [cancer cells](#)—to a drug designed to destroy the target. The linker must not only keep the drug tethered to the antibody as it travels to a targeted cell, it must properly release the drug inside the cell, in the right place at the right time.

Biomolecular engineers gather clues about linkers' effectiveness by testing them in cell-free environments—model fluids that don't contain all the complex interactions typically found in whole, living cells. They're easier to study, but aren't always as accurate, potentially leading to linker failure in subsequent testing.

A research team led by Chris Alabi, associate professor of chemical and biomolecular engineering, has developed a method that employs [fluorescent probes](#) to see and measure the rate at which linkers successfully release drugs in living [cells](#). The research, "Responsive Antibody Conjugates Enable Quantitative Determination of Intracellular Bond Degradation Rate," published Oct. 8 in the journal *Cell Chemical Biology*.

"Right now, [pharmaceutical companies](#) make a ton of linkers and then see which functions best for a particular application by having to test each one. It's a shotgun approach," Alabi

said. "With our technique, they can now make an informed decision based on actual intracellular numbers, before they put the drug system together."

The probes consist of two [fluorescent dyes](#) that render each other invisible when they're tethered together with the antibody as part of the delivery system. When the linker breaks and untethers the dyes, they become visible using a microscope, signaling the drug has been released inside the cell.

These probes were developed in Alabi's lab and offer engineers an accurate way to measure the rate at which a linker's chemical bond breaks from the delivery system while inside the cell.

"Once we know what the timing is for different linker bonds and cell processes, then we can say, 'OK, for drug A connected to antibody B, this is how long it will take, so if we want to treat disease C, we should use this linker,'" Alabi said.

To demonstrate the probe, Alabi and his team engineered an antibody construct with a disulfide linker known to work well within the HER2 protein, a highly valued target for breast cancer treatment. Once the delivery system reached the protein, the team was able to reliably measure intracellular processes, such as the kinetics and half-life of the disulfide linker.

"For the biomolecular engineers and companies that have a target in mind, we can ... make the drug discovery process that much faster because we now know something about how long it's going to take to release the [drug](#)," said Alabi, who hopes to demonstrate the technique further through partnerships with pharmaceutical companies.

The probes can also be used by chemical biologists to learn more about intracellular processes, such as the specific agents responsible for cleaving linkers, Alabi said. [45]

A new way to deliver drugs with pinpoint targeting

Most pharmaceuticals must either be ingested or injected into the body to do their work. Either way, it takes some time for them to reach their intended targets, and they also tend to spread out to other areas of the body. Now, researchers at MIT and elsewhere have developed a system to deliver medical treatments that can be released at precise times, minimally-invasively, and that ultimately could also deliver those drugs to specifically targeted areas such as a specific group of neurons in the brain.

The new approach is based on the use of tiny magnetic particles enclosed within a tiny hollow bubble of lipids (fatty molecules) filled with water, known as a liposome. The drug of choice is encapsulated within these bubbles, and can be released by applying a magnetic field to heat up the particles, allowing the drug to escape from the liposome and into the surrounding tissue.

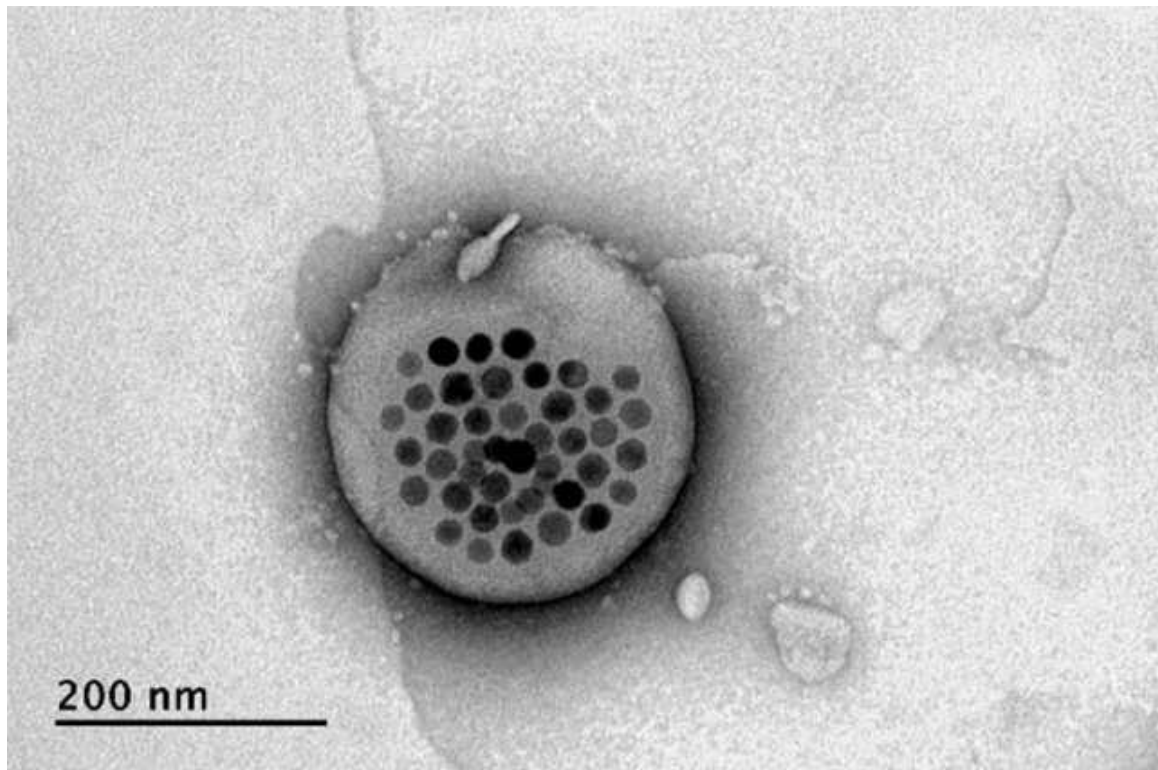
The findings are reported today in the journal *Nature Nanotechnology* in a paper by MIT postdoc Siyuan Rao, Associate Professor Polina Anikeeva, and 14 others at MIT, Stanford University, Harvard University, and the Swiss Federal Institute of Technology in Zurich.

"We wanted a system that could deliver a drug with temporal precision, and could eventually target a particular location," Anikeeva explains. "And if we don't want it to be invasive, we need to find a non-invasive way to trigger the release."

Magnetic fields, which can easily penetrate through the body—as demonstrated by detailed internal images produced by [magnetic resonance](#) imaging, or MRI—were a natural choice. The hard part was finding materials that could be triggered to heat up by using a very weak magnetic field (about one-hundredth the strength of that used for MRI), in order to prevent damage to the drug or surrounding tissues, Rao says.

Rao came up with the idea of taking magnetic nanoparticles, which had already been shown to be capable of being heated by placing them in a magnetic field, and packing them into these spheres called liposomes. These are like little bubbles of lipids, which naturally form a spherical double layer surrounding a water droplet.

When placed inside a high-frequency but low-strength magnetic field, the nanoparticles heat up, warming the lipids and making them undergo a transition from solid to liquid, which makes the layer more porous—just enough to let some of the drug molecules escape into the surrounding areas. When the [magnetic field](#) is switched off, the lipids re-solidify, preventing further releases. Over time, this process can be repeated, thus releasing doses of the enclosed drug at precisely controlled intervals.



Electron microscope image shows the actual liposome, the white blob at center, with its magnetic particles showing up in black at its center. Credit: Massachusetts Institute of Technology

The drug carriers were engineered to be stable inside the body at the normal body temperature of 37 degrees Celsius, but able to release their payload of drugs at a temperature of 42 degrees. "So we have a magnetic switch for drug delivery," and that amount of heat is small enough "so that you don't cause thermal damage to tissues," says Anikeeva, who holds appointments in the departments of Materials Science and Engineering and the Brain and Cognitive Sciences.

In principle, this technique could also be used to guide the particles to specific, pinpoint locations in the body, using gradients of magnetic fields to push them along, but that aspect of the work is an ongoing project. For now, the researchers have been injecting the particles directly into the target locations, and using the magnetic fields to control the timing of drug releases. "The technology will allow us to address the spatial aspect," Anikeeva says, but that has not yet been demonstrated.

This could enable very precise treatments for a wide variety of conditions, she says. "Many brain disorders are characterized by erroneous activity of certain cells. When neurons are too active or not active enough, that manifests as a disorder, such as Parkinson's, or depression, or epilepsy." If a medical team wanted to deliver a drug to a specific patch of neurons and at a particular time, such as when an onset of symptoms is detected, without subjecting the rest of the brain to that drug, this system "could give us a very precise way to treat those conditions," she says.

Rao says that making these nanoparticle-activated liposomes is actually quite a simple process. "We can prepare the liposomes with the particles within minutes in the lab," she says, and the process should be "very easy to scale up" for manufacturing. And the system is broadly applicable for drug delivery: "we can encapsulate any water-soluble [drug](#)," and with some adaptations, other drugs as well, she says.

One key to developing this system was perfecting and calibrating a way of making liposomes of a highly uniform size and composition. This involves mixing a water base with the fatty acid lipid molecules and magnetic nanoparticles and homogenizing them under precisely controlled conditions. Anikeeva compares it to shaking a bottle of salad dressing to get the oil and vinegar mixed, but controlling the timing, direction and strength of the shaking to ensure a precise mixing.

Anikeeva says that while her team has focused on neurological disorders, as that is their specialty, the [drug delivery](#) system is actually quite general and could be applied to almost any part of the body, for example to deliver cancer drugs, or even to deliver painkillers directly to an affected area instead of delivering them systemically and affecting the whole body. "This could deliver it to where it's needed, and not deliver it continuously," but only as needed.

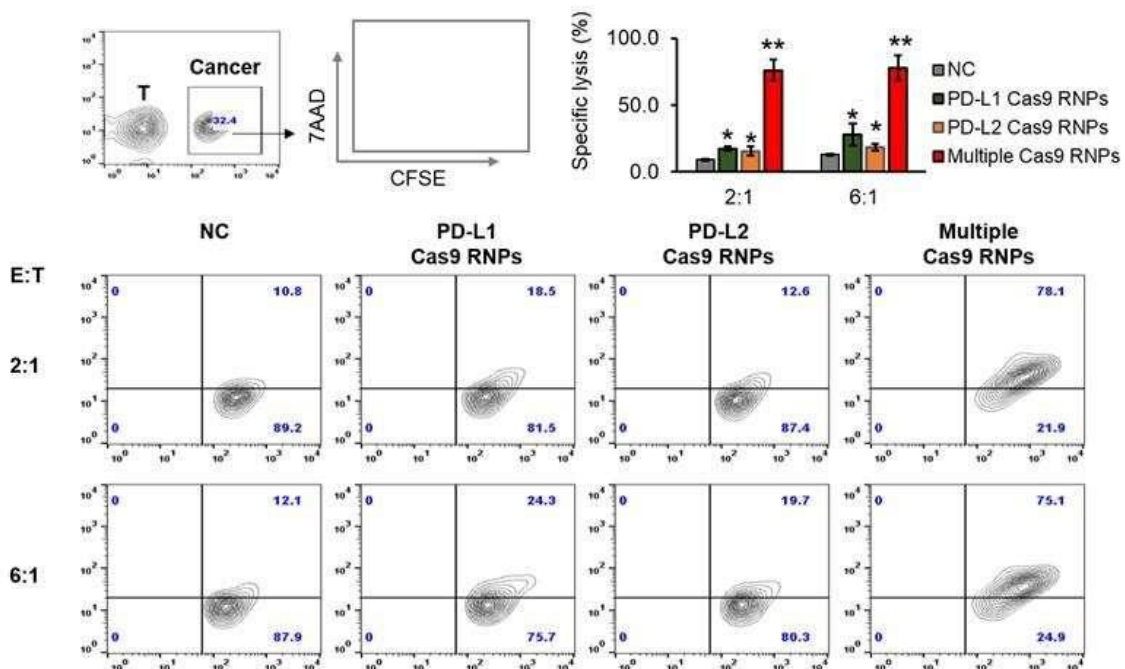
Because the magnetic particles themselves are similar to those already in widespread use as contrast agents for MRI scans, the regulatory approval process for their use may be simplified, as their biological compatibility has largely been proven. [44]

A new path to cancer therapy: Developing simultaneous multiplexed gene editing technology

Dr. Mihue Jang and her group at the Center for Theragnosis of the Korea Institute of Science and Technology (KIST, President Byung-gwon Lee) announced that they have developed a new gene editing system that could be used for anticancer immunotherapy through the simultaneous suppression of proteins that interfere with the immune system expressed on the surface of lymphoma cells and activation of cytotoxic T lymphocyte, based on the results of joint research conducted with Prof. Seokmann Hong and his group at Sejong University (President, Deg-hyo Bae).

Gene editing technology is a technology that eliminates the underlying causes of and treats diseases by removing [specific genes](#) or editing [genes](#) to restore their normal function. In particular, CRISPR gene editing technology is now commonly used for immunotherapy by correcting the genes of immune [cells](#) to induce them to attack cancer cells selectively.

Dr. Mihue Jang of KIST improved the CRISPR gene editing system to enable the penetration of the cell membrane without external carriers (*ACS Nano* 2018, 12, 8, 7750-7760). However, there are various kinds of genes that regulate immune activity, and technology for inducing safe and convenient immunotherapy is not yet sufficiently developed. The collaborative research team of Dr. Jang's group at KIST and Prof. Hong' group at Sejong University developed a technology that is applicable to immunotherapy by further improving the CRISPR gene editing system to allow for the transfer of genes to lymphoma cells without external carriers as well as the correction of several genes at the same time.



Verification of T-cell - mediated assassinations with a new gene editing system Credit: Korea Institute of Science and Technology (KIST)

Existing gene editing technology has been used to transfer genes into lymphoma cells, such as T lymphocytes, among immune cells, mainly using the viral transduction or electroporation methods. The viral transduction method often induces undesired immune responses and has a high chance of inserting genes into the wrong genome sequences. Also, the electric shock method requires separate and expensive equipment, has great difficulty correcting large numbers of cells at one time, and shows low cell viability.

This technology jointly developed by research teams of KIST and Sejong University simultaneously targets PD-L1 and PD-L2, among the inhibitory immune checkpoints known for suppressing the immune system. The treatment efficacy was confirmed, showing that targeting these immune checkpoints does not interfere with the [immune system](#) and that the cytotoxic T lymphocytes directly attack [cancer cells](#) to increase the anticancer immune response.

Dr. Mihue Jang of KIST said, "This newly developed gene editing system can be applied to various types of [immune cells](#), and is thus expected to be used in the development of treatments for various diseases, including not only cancers but also autoimmune and inflammatory diseases." [43]

Scientists find way to cut nanoparticle toxicity levels

Bioengineers and biophysicists from the National Research Nuclear University MEPhI, the Sechenov First Moscow State Medical University, the Universite de Reims Champagne-Ardenne in France, and the University of Tübingen in Germany have discovered that the toxicity of nanoparticles depends more on their size and the extent to which their surface area is charged than on their chemical composition.

"The problem of nanotoxicity became particularly relevant in connection with the prospects of using nanocrystals in medicine as an element for diagnostics and in therapeutic nanosystems," Igor Nabiev, study co-author and Professor at the University of Reims Champagne-Ardenne explained.

"We have managed to solve the problem of controlling the toxicity of nanocrystals, which allows us to either increase or practically eliminate the nanotoxicity of particles of an extremely diverse nature, regardless of their chemical [composition](#)," the scientist added.

According to Professor Nabiev, one of the major possible reasons for the molecular toxicity of nanoparticles is their interaction with proteins in the body, which in turn leads to changes in their biological composition.

These changes lead to the disruption of the [protein](#)'s function as a hormone or enzyme, sparking an autoimmune reaction, with the body fighting the altered proteins as if they were an intruding organism, and protein aggregates forming as fibrils and plaques, which are thought to cause [neurodegenerative diseases](#) such as Alzheimers and Parkinson's.

Accordingly, by altering the size and surface charge of nanoparticles, as the scientists' study suggests, their [toxicity](#) can also be altered.

Researchers say their findings help expand our understanding about the nature of nanotoxicity, and opens up the prospect of creating a new generation of pharmaceuticals capable of destroying the harmful fibrils and protein plaques. [42]

Nano-thermometer takes temperature inside cells

How do you know a cell has a fever? Take its temperature.

That's now possible thanks to research by Rice University scientists who used the light-emitting properties of particular [molecules](#) to create a fluorescent nano-thermometer.

The Rice lab of chemist Angel Martí revealed the technique in a *Journal of Physical Chemistry B* paper, describing how it modified a biocompatible molecular rotor known as boron dipyrromethene (BODIPY, for short) to reveal temperatures inside [single cells](#).

The molecule is ideally suited to the task. Its fluorescence lasts only a little while inside the cell, and the duration depends heavily on changes in both temperature and the viscosity of its environment.

But at high viscosity, the environment in typical [cells](#), its fluorescence lifetime depends on temperature alone.

It means that at a specific temperature, the light turns off at a particular rate, and that can be seen with a fluorescence-lifetime imaging microscope.

Martí said colleagues at Baylor College of Medicine challenged him to develop the technology. "Everybody knows old thermometers based on the expansion of mercury, and newer ones based on digital technology," he said. "But using those would be like trying to measure the temperature of a person with a thermometer the size of the Empire State Building."

The technique depends on the rotor. Martí and Rice graduate student and lead author Meredith Ogle constrained the rotor to go back and forth, like the flywheel in a watch, rather than letting it rotate fully.

"It pretty much wobbles," Martí said.

"What we measure is how long the molecule stays in the [excited state](#), which depends on how fast it wobbles," he said. "If you increase the temperature, it wobbles faster, and that shortens the time it stays excited."

The effect, Martí said, is conveniently independent of the concentration of BODIPY molecules in the cell and of photobleaching, the point at which the molecule's fluorescent capabilities are destroyed.

"If the environment is a bit more viscous, the molecule will rotate slower," Martí said. "That doesn't necessarily mean it's colder or hotter, just that the viscosity of the environment is different.

"We found out that if we constrain the rotation of this motor, then at high viscosities, the internal clock—the lifetime of this molecule—becomes completely independent of viscosity," he said. "This is not particularly common for these kind of probes."

Martí said the technique might be useful for quantifying the effects of tumor ablation therapy, where heat is used to destroy cancer cells, or in simply measuring for the presence of cancers. "They have a higher metabolism than other cells, which means they're likely to generate more heat," he said. "We'd like to know if we can identify [cancer cells](#) by the heat they produce and differentiate them from [normal cells](#)."

Co-authors of the paper are Rice graduate student Ashleigh Smith McWilliams; Matthew Ware, a scientist at Celgene Co., San Diego; Steven Curley, a surgeon at Christus Mother Frances Hospital, Tyler, Texas; and Stuart Corr, an assistant professor of surgical research and director of surgical innovation and technology development at Baylor College of Medicine. [41]

Exploring the interaction of polystyrene nanoplastics and blood plasma proteins

Collaborative research at ANSTO led by Mr Shinji Kihara and A/Prof. Duncan McGillivray of The MacDiarmid Institute, New Zealand with ANSTO's Dr. Jitendra Mata, scientists from the University of Auckland and A/Prof Ingo Köper from Flinders University, SA , is contributing to a better understanding of how nanoplastics interact with blood plasma proteins and other biological molecules within the body.

The motivation for this study, which was recently published in *Bioconjugate Chemistry*, arose from concerns regarding the increasing quantities of plastic waste in the environment.

In nature, these plastics undergo physical and chemical breakdown processes to form [minute particles](#) on the micro- and nanometer scale.

Studies on the toxicology of engineered [nanoparticles](#) have suggested that these particles gain easy access and mobility within the body, often side-stepping important biological barriers and defence mechanisms against foreign bodies. Unlike the engineered nanoparticles used in biomedical applications, however, the potential effects and interactions of these nanoplastics are not well-understood.

The toxicity of nanoparticles is directly linked to its physical and chemical properties. When nanoparticles enter the body, they are surrounded by layers of proteins, which is known as a "[corona](#)." Loosely-bound proteins form a "soft corona," while tightly bound proteins form a "hard corona."

With a model system of polystyrene nanoparticles and human serum albumin (HSA) protein, the investigators used a range of techniques to determine the size, composition and geometry of the polystyrene nanoparticle-protein corona complex.

HSA was selected due to its natural abundance, while positively and negatively charged nanoparticles, of two different sizes, were used to assess how [particle size](#) influenced the formation of the corona in solution under different pH conditions. The investigators used [small angle neutron scattering](#) (SANS) with contrast matching on the Bilby instrument (with Dr. Andrew Whitten) to determine the diameter of the nanoparticle and characterize its distinct structural features.

"Our facilities are quite unique in that we can explore the interaction between protein and nanoparticle at length scales from one nanometer to 10 microns, which is very difficult to do with other techniques," said Dr. Jitendra Mata, instrument scientist and co-author on the paper.

"Contrast matching allows you to see two components together, such as nanoparticles and protein corona, or we can mask out one of the components of interest. We were able to determine if there was a strong or weak interaction with the protein or if there was any shape change in the [protein](#)," he added.

The study found that both particle size and pH played a role in determining the nature of the corona. Larger particles favored the formation of a soft corona, with the hard corona being completely absent in some cases. HSA actively participated in the formation of these complexes, dotting the surface of negatively-charged nanoparticles.

Additionally, they discovered that the interaction between the soft corona and the nanoparticle surface was governed by a subtle balance of electrostatic forces.

The [ongoing research](#) seeks the usage of other neutron instruments including Kookaburra USANS and Platypus neutron reflectometry to understand how these complex corona/nanoplastic would interact with other biological entities such as cellular membranes.

The researchers anticipate that these findings will have implications on further research on nanoparticle toxicity, by providing a clearer picture of the interactions of nanoparticles with biomolecules. [40]

Structure of protein nanoturbine revealed

Cells rely on protein complexes known as ATP synthases or ATPases for their energy needs. Adenosine triphosphate (ATP) molecules power most of the processes sustaining life. Structural biologist Professor Leonid Sazanov and his research group from the Institute of Science and Technology Austria (IST Austria) in Klosterneuburg, Austria have now determined the first atomic structure of the representative of the V/A-ATPase family, filling in the gap in the evolutionary tree of these essential molecular machines. These results obtained using the latest cryo-electron

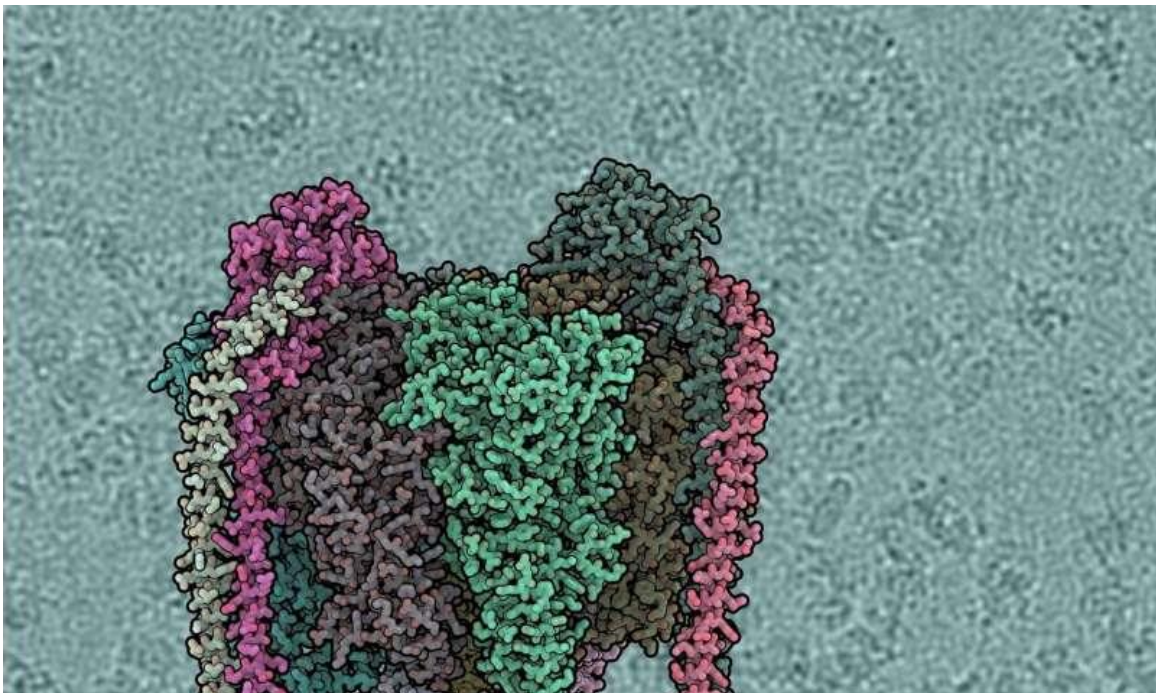
microscopy methods revealed a turbine or water mill similar structure of the enzyme and have now been published in the journal *Science*.

Rotary power

ATP synthases/ATPases are large membrane protein complexes which share overall gross building plans and rotary catalysis mechanisms. This protein family includes F-type [enzyme](#) found in mitochondria (power factories of the cell), chloroplasts (organelles that conduct photosynthesis in plants) and bacteria; V (vacuolar)-type found in intracellular compartments in eukaryotes (higher organisms with a nucleus) and A (archaeal)-type found in prokaryotes—archaea (ancient microorganisms) and some bacteria.

Different flavors of ATPases

F- and A-type enzymes usually function to produce ATP, driven by proton flow across the membrane. V-type enzymes usually work in reverse, using ATP to pump protons. V- and A-ATPases are similar structurally but they differ from the F-type by having two or three peripheral stalks and additional connecting protein subunits between V1 and Vo. V-type enzymes probably evolved from the A-type and because of these similarities A-type is also termed V/A-ATPase. Some bacteria, including *Thermus thermophilus*, acquired an A-type enzyme. Long Zhou, postdoc in the Sazanov research group of IST Austria, has purified and studied this enzyme (ThV1Vo) by cryo-EM. In contrast to F-type, for V-type ATPases only the structures of the isolated V1 and Vo domains were determined previously. How V1 is coupled to Vo was therefore not known, and the knowledge about the full catalytic cycle was lacking.



Each protein subunit is of different color. V1 domain is top, Vo bottom, peripheral stalks left and right. The background shows raw cryo-EM micrograph, with individual ATPase molecules visible. Credit: IST Austria, 2019

Plasticity and competition

The scientists determined not one, but in total five structures of the entire ThV1Vo enzyme, using cryo-electron microscopy methods developed recently in the so-called "resolution revolution" of this technique. The structures represent several conformational states of the enzyme differing by the position of the rotor inside the stator. Global conformational plasticity of ThV1Vo is revealed as substantial V1 wobbling in space in transition from one state to another. It is a result of mechanical competition between rotation of the bent central rotor and stiffness of the stator. V1-Vo coupling is achieved via close structural and electrostatic match between the shaft and V-type specific subunit linking it to the c-ring. The visualization of the proton path revealed significant differences in the distribution of charged protein residues from that in F-ATPases, with a stricter "check-point" preventing "slipping" of the enzyme.

Why additional complexity?

Instead of a single peripheral stalk of F-type enzymes, A-types such as ThV1Vo have two peripheral stalks, while eukaryotic V-types have three. But what is the advantage of the additional complexity in the already very large protein assembly, along with additional subunits linking V1 and Vo? The F1/V1 domain has a three-fold symmetry and so one ATP molecule is produced (or consumed) per each 120° rotation of the stator inside F1/V1. Professor Leonid Sazanov says: "In V/A-ATPases this step is a one-off 120° rotation, in contrast to F-ATP synthase where it is divided into several sub-steps. Thus, greater plasticity may be required in ThV1Vo in order to link these 120° steps in V1 to smaller per c subunit steps in the Vo c12-ring. This additional flexibility may be afforded in V-types by the additional peripheral stalks and connecting subunits. Our new structures show how this is achieved, providing a framework for the entire V-ATPase family". [39]

Smart interaction between proteins

Very little was known till now about DNA repair by homologous recombination, which is fundamental for human health. Now an ETH research group has for the first time isolated and studied all the key proteins involved in this process, laying the foundation for investigating many diseases.

Within our body, the process of [cell division](#) is constantly creating new cells to replace old or damaged ones. The genetic information is also duplicated and passed on to the new cells. Complex interaction of many different proteins ensures a smooth process. This is because these proteins immediately repair any errors that creep in during DNA duplication. However, the same [protein](#) machinery also performs another function: in [germ cells](#) that divide to form gametes—egg cells and sperm—it is responsible for mixing the [genetic information](#) of the original maternal and paternal side during cell division. The same mechanism therefore has to resolve two conflicting problems: in normal cell division, called mitosis, it ensures genetic preservation, while in the cell division to produce gametes, or meiosis, it ensures genetic diversity.

Both tasks are vital. If DNA repair does not work in mitosis, this can lead to cancer and other diseases. If, on the other hand, the exchange of DNA in meiosis does not function correctly, the fertility and health of the offspring may be damaged. "Although these processes are crucial for our

health, very little was known till now about how the whole system functions and is regulated," says Joao Matos, Professor for Biochemistry at ETH Zurich. His team has now studied the responsible proteins and discovered how they differentiate between the two tasks.

A complex task

The scientists began by cultivating a large number of yeast cells in the laboratory, as these cells only contain a minute quantity of the proteins involved. The production of the yeast cells was therefore extremely complex: the researchers cultivated cells in 120 6-litre containers in such a way that the division occurred simultaneously in all yeast cells. Mitosis and meiosis are highly complex processes that take place in precisely orchestrated phases. Only synchronised cell cultures can thus differentiate which proteins are important in which phase, and how they work together.

Scientists already knew that yeast, along with plants, animals and humans, have a group of seven enzymes involved in the reproduction of DNA: the recombination intermediates processing enzymes (RIPEs). For the first time, ETH scientists were able to isolate these RIPEs from the cell cultures and identify them in the mass spectrometer—from a specific phase of cell division in each instance. At the same time, they used this method to identify a series of other proteins that help regulate cell division.

The same components, but rewired

Joao Matos and his team were eventually able to identify which RIPEs are important for which phase of cell division and which helper proteins interact with the RIPEs in each case. The first unexpected result: the quantity of RIPEs remains almost constant in all phases of mitosis and meiosis. "Unlike many other processes, the cells do not regulate cell division and DNA repair through the production of the proteins involved," Matos explains. Instead, the helper proteins interact systematically with the RIPE enzymes in order to enable or disable them in a specific phase. "All the components are always there, but are rewired depending on the task," says the ETH professor.

For example, the researchers discovered that three of the RIPEs lose almost all their interaction partners precisely in the so-called metaphase of meiosis, in other words when the maternal and paternal DNA is mixed. In return, another protein complex is formed at this point. "This must be responsible for mixing up the maternal and paternal DNA," Matos concludes. In addition, ETH researchers have identified a number of new helper proteins whose role was previously unknown.

Key to understanding disease

The results from the yeast [cells](#) can be transferred to humans, as for every helper protein involved there is an equivalent in humans that functions in the same or very similar fashion. So the Matos research group and fellow scientists can build on this knowledge. They can now study specific proteins to discover whether, and how, they are involved in the development of diseases and ultimately find a remedy to combat them. [38]

Nanocapsule reaches cancer that has spread to central nervous system in mice

Cancer that has spread to the central nervous system is notoriously difficult to treat. Now, UCLA researchers have developed a drug delivery system that breaks through the blood-brain barrier in order to reach and treat cancer that has spread to the central nervous system.

In research conducted in mice, a single dose of cancer drugs in a nanoscale capsule developed by the scientists eliminated all B-cell lymphoma that had metastasized to the animals' [central nervous system](#).

About 15% to 40% of all cancers spread to the [nervous system](#), but there are few treatment options and they only work in a small number of patients. One reason treatments are ineffective is that the blood-brain barrier, a natural defense system that prevents harmful agents from entering the brain, blocks many drugs, preventing them from reaching cancer that has spread to the central nervous system.

To create a vessel that could carry cancer drugs to the central nervous system, the scientists produced a capsule measuring about one nanometer, or one billionth of a meter, across. (For reference, a sheet of paper is about 100,000 nanometers thick.) The capsule is coated with a substance called 2-methacryloyloxyethyl phosphorylcholine, which they hypothesized would be unlikely to be blocked by the [blood-brain barrier](#), which would enable the capsule to release antibodies when it came into close proximity with [cancerous cells](#).

The researchers loaded nanocapsules with the cancer-fighting drug rituximab and then administered them to mice with a human B-cell lymphoma that had metastasized to the animals' central nervous system. The scientists tracked how the tumors grew or shrank over a period of four months.

Pending additional research, including testing in human subjects, the UCLA-engineered capsule could be used to carry drugs that have already been approved by the FDA to treat cancer that has spread to the central nervous system.

The approach could be useful not only for cancers that metastasize to the central nervous system—such as breast cancer, small cell lung cancer and melanoma—but also for primary brain tumors or other brain diseases.

The study is published online in *Nature Biomedical Engineering*. [37]

New nanotechnology could aid stem cell transplantation research

Nanotechnology developed at Rutgers University-New Brunswick could boost research on stem cell transplantation, which may help people with Alzheimer's disease, Parkinson's disease, other neurodegenerative diseases and central nervous system injuries.

The nanotechnology platform, which uses special tiny rods for sensing, allows researchers to confirm the identity of human stem cell fates and their biomarkers, or biological molecules, without destroying them, according to a study in the journal *ACS Nano*. That's been a major issue during [pre-clinical research](#) on stem cells because it limits further analyses and [biomedical applications](#).

"One of the major hurdles in the current cell-based therapies is the destructive nature of the standard cell characterization step. With our technology, we can sensitively and accurately characterize the cells without compromising their viabilities," said senior author KiBum Lee, a professor in the Department of Chemistry and Chemical Biology in the School of Arts and Sciences.

Stem cells can develop into many different types of cells, including neurons that transmit information in the brain. Adult human-induced [pluripotent stem cells](#), which resemble [embryonic stem cells](#), can be used to develop drugs and model diseases, according to the National Institutes of Health. Scientists hope to use them in transplantation medicine.

While stem cells hold great potential for treating neurodegenerative diseases and central nervous system injuries, controlling and characterizing their fate are critical issues that need to be addressed before their potential use as treatments can be fully realized. Current methods for characterizing stem cell biomarkers destroy cellular activities and functions, which makes it difficult to conduct more definitive research that could lead to biomedical applications.

Using their nanotechnology platform, the scientists successfully monitored the generation of neurons from human [stem cells](#) by characterizing next generation biomarkers called exosomes—tiny particles released by cells that play a critical role in cell-to-cell communication. The scientists will further investigate their technology's versatility in other applications, such as detecting neurons in clinical settings. [36]

Nanoscale 'glass' bottles could enable targeted drug delivery

Tiny silica bottles filled with medicine and a special temperature-sensitive material could be used for drug delivery to kill malignant cells only in certain parts of the body, according to a study published recently by researchers at the Georgia Institute of Technology.

The research team devised a way to create silica-based [hollow spheres](#) around 200 nanometers in size, each with one small hole in the surface that could enable the spheres to encapsulate a wide range of payloads to be released later at certain temperatures only.

In the study, which was published on June 4 in the journal *Angewandte Chemie International Edition*, the researchers describe packing the spheres with a mixture of [fatty acids](#), a near-infrared dye, and an [anticancer drug](#). The fatty acids remain solid at human body temperature but melt a few degrees above. When an infrared laser is absorbed by the dye, the fatty acids will be quickly melted to release the therapeutic [drug](#).

"This new method could allow infusion therapies to target specific parts of the body and potentially negating certain side effects because the medicine is released only where there's an elevated temperature," said Younan Xia, professor and Brock Family Chair in the Wallace H. Coulter Department of Biomedical Engineering at Georgia Tech and Emory University. "The rest of the drug remains encapsulated by the solid fatty acids inside the bottles, which are biocompatible and biodegradable."

The researchers also showed that the size of the hole could be changed, enabling nanocapsules that release their payloads at different rates.

"This approach holds great promise for [medical applications](#) that require drugs to be released in a controlled fashion and has advantages over other methods of controlled drug release," Xia said.

An earlier method for achieving controlled [drug release](#) involves loading the temperature-sensitive material into low-density lipoproteins, which is often referred to as "bad cholesterol." Another method involves loading the mixture into gold nanocages. Both have disadvantages in how the material used to encapsulate the drugs interact with the body, according to the study.

To make the silica-based bottles, the research team started by fabricating spheres out of polystyrene with a small gold nanoparticle embedded in its surface. The spheres are then coated with a silica-based material everywhere except where the gold nanoparticle is embedded. Once the gold and polystyrene are removed, only a hollow silica [sphere](#) with a small opening remains. To adjust the size of the opening, the researchers simply changed the size of the gold nanoparticle.

The process to load the bottles with their payload involves soaking the spheres in a solution containing the mixture, removing the trapped air, then washing away the excess material and payload with water. The resulting nanocapsules contain an even mixture of the temperature-sensitive material, the therapeutic drug, and the dye.

To test the release mechanism, the researchers then put the nanocapsules in water and used a near-infrared laser to heat the dye while tracking the concentration of the released therapeutic. The test confirmed that without the use of the laser, the medicine remains encapsulated. After several minutes of heating, concentrations of the therapeutic rose in the water.

"This controlled release system enables us to deal with the adverse impacts associated with most chemotherapeutics by only releasing the drug at a dosage above the toxic level inside the diseased site," said Jichuan Qiu, a postdoctoral fellow in the Xia group. [35]

A new way to hoard resources in nano-sized factories targeted for biotech

The lab of Cheryl Kerfeld at Michigan State University has created a synthetic nano-sized factory, based on natural ones found in bacteria. This research could someday lead to new medical, industrial or bioenergy applications.

The new study is published in *Metabolic Engineering*.

Natural nanofactories are found in bacteria all over the planet. Some make nutrients. Others sequester [toxic materials](#) that would otherwise make the bacteria sick—or even die.

But all [factories](#) share a common exterior, a [shell](#) made of protein tiles. Scientists want to design new factories, based on those found in bacteria naturally, for use in biotechnology.

One way to direct useful enzymes to these factories is by physically attaching them to the tail ends of the proteins that make up the factory shells. But there is a catch.

The ends, or termini, of most shell protein tiles face the outside of a factory. So any molecules fused to the protein ends will end up on the outside surface and not the inside. This is a problem if the goal is to keep one or more enzymes inside a factory separated from the rest of the cell.

"In order to send proteins to the inside of the factory, we needed a new kind of building block that still assembled into shells," said Bryan Ferlez, a post doctorate researcher in the Kerfeld lab. "We aimed to redesign a shell protein so its termini face the inside. The end result is that cargo connected to this shell protein would also end up inside the shell."

Credit: Michigan State University

In the new study, the scientists take the most abundant shell protein, called BMC-H, and turn it 'inside-out' through a technique called circular permutation.

They shuffle segments of the [amino acid sequence](#) and glue the original ends together. They then introduce new termini on the inner face of the protein. The result is a new, synthetic shell protein that looks almost identical to its natural counterpart. Except now, both new ends face the inside of the shell.

The new structure is a usable building block to construct factory shells. The scientists have successfully produced factory shells, with the new protein. They are similar in size and appearance to the original shells.

The new structure can incorporate molecules inside the shell. The team tested the concept by fusing a fluorescent cargo protein to the new BMC-H protein. Microscopy and biochemical testing show the cargo on the inside of the shell.

Scientists can control the amount of cargo imported into the new structure.

"By making more or less of the new BMC-H protein with a fluorescent protein fused to its terminus, we were also able to control the amount of cargo that incorporates into the shell," Ferlez said.

Next, Ferlez wants to target "useful" molecules into a synthetic factory made with the new shell [protein](#).

"We can start to build [metabolic pathways](#), or assembly lines, and define the amounts and locations of enzymes within these nanofactories. Someday, we could use this system to enhance the production of rubber, biofuels, and other commodities," Ferlez explained. [34]

Risk assessment at nanoscale level: A closer look at the mimotope variation analysis

Since January 2018 the EU project PANBioRA is developing a modular system for a comprehensive risk assessment of biomaterials. The instrument will be able to compare different biomaterials and help doctors to choose the best suited material for a patient before implantation. Another function of the system is the risk assessment of new biomaterials (synthesized or obtained by modification of known biomaterials), which might have unforeseeable interactions with the immune system.

In this context, one important analysis that is part of PANBioRA's approach is the Mimotope Variation Analysis that allows the assessment of patient-specific interactions between biomaterials and the [immune system](#).

Beginning of June the 17 PANBioRA partners have met in Brussels for their first official periodic review meeting in month 18 of the project. In the presence of a representative of the European Commission each partner has presented the performed work since the beginning of the project as well as main results achieved.

The PANBioRA system is composed of four different types of analyses allowing [biomaterial](#) risk assessment at nano-, micro- and milliscale level. During the first 1½ years of the project, different project partners have worked on these analyses with significant progress.

Among these different testing systems, there is the Mimotope Variation Analysis (MVA) developed and patented by the Estonian biotechnology company Protobios which has never been used in the framework of biomaterial assessment before. Immune responses contribute to the development of many common disorders (e.g. Alzheimer's disease) but also to immunologic diseases including infectious diseases (e.g. tuberculosis, hepatitis, pneumonia). With the MVA technology, Protobios has developed a method to create a personalized outline, called immunoprofile, allowing to define an individual's humoral [immune response](#) profile. Over the past years Protobios has developed a metadata base of immunoprofiles of more than 2000 individuals. This enables them to predict an individual's susceptibility to specific diseases.

For PANBioRA, the MVA technology is being further developed and adapted to identify a patient-specific response of the immune system to biomaterials. A biomaterial specific immunoprofile database is being generated allowing to comprehensively understand the properties, interaction and fate of engineered biomaterials in relation to human health and environment. This will pave the way for the design of new generations of biomaterials with tailored functional and immunological properties. As PANBioRA is aiming to provide a faster, reliable and quantitative assessment of new biomaterials, the MVA technology plays a substantial part in the overall PANBioRA system.

One of the major challenges for the upcoming project months will be to successfully integrate the different test modules, developed within the project in one comprehensive system. Until the beginning of next year, a first prototype of the whole system will be ready in order to further test,

improve and validate. PANBioRA will provide substantial health benefits for millions of patients who are candidates for receiving medical implants by improving their function and reducing the chance of failure due to inflammation. [33]

High-contrast imaging for cancer therapy with protons

Medical physicist Dr. Aswin Hoffmann and his team from the Institute of Radiooncology—OncoRay at the Helmholtz-Zentrum Dresden-Rossendorf (HZDR) have combined magnetic resonance imaging (MRI) with a proton beam, thus demonstrating for the first time that in principle, this commonly used imaging method can work with particle beam cancer treatments. This opens up new opportunities for targeted, healthy tissue-sparing cancer therapy. The researchers have published their results in the journal *Physics in Medicine and Biology*.

Radiation therapy has long been part of the standard oncological treatment practice. A specific amount of energy is deposited into the tumor tissue, where it damages the cancer cells' genetic material, preventing them from dividing, and ideally destroying them. The most commonly used form of radiation therapy today is called photon therapy, which uses high-energy X-ray beams. Here, a substantial portion of the beam penetrates the patient's body, depositing a harmful dose in healthy tissue surrounding the tumor.

Atomic nuclei as weapons against cancer

An alternative is radiation therapy with charged atomic nuclei such as protons. The penetration depth of these particles depends on their initial energy. They release their maximum dose at the end of their trajectory. No dose will be deposited beyond this so-called "Bragg peak." The challenge for physicians administering this kind of therapy is to control the proton beam exactly to match the shape of the tumor tissue and thus spare as much of the surrounding normal tissue as possible. Before the treatment, they conduct an X-ray-based computed tomography (CT) scan to select their target volume.

"This has various disadvantages," Hoffmann says. "First of all, the soft-tissue contrast in CT scans is poor, and secondly, the dose is deposited into healthy tissue outside of the target volume." On top of this, proton therapy is more susceptible to organ motion and anatomical changes than radiation therapy with X-rays, which impairs the targeting precision when treating mobile tumors. At present, there is no direct way of visualizing tumor motion during irradiation. That is the biggest obstacle when it comes to using proton therapy. "We don't know exactly whether the proton beam will hit the tumor as planned," Hoffmann explains. Therefore, physicians today have to use large safety margins around the tumor. "But that damages more of the healthy tissue than would be necessary if radiation were more targeted. That means we are not yet exploiting the full potential of proton therapy."

First prototype for MR-guided particle therapy

Hoffmann and his team want to change that. In cooperation with the Belgian proton therapy equipment manufacturer IBA (Ion Beam Applications SA), his research group's objective is to integrate proton therapy and real-time MR imaging. Unlike X-ray or CT imaging, MRI delivers excellent soft-tissue contrast and enables continuous imaging during irradiation. "There are already

two such hybrid devices for clinical use in MR-guided photon therapy; but none exists for particle therapy."

This is mainly due to electromagnetic interactions between the MRI scanner and the proton therapy equipment. On the one hand, MRI scanners need highly homogeneous magnetic fields in order to generate geometrically accurate images. The proton beam, on the other hand, is generated in a cyclotron, a circular accelerator in which electromagnetic fields force charged particles onto a circular trajectory and accelerate them. The proton beam is also steered and shaped by magnets, whose magnetic fields can interfere with the MRI scanner's homogeneous magnetic field.

"When we launched the project three and a half years ago, many international colleagues were skeptical. They thought it was impossible to operate an MRI scanner in a proton beam because of all the electromagnetic disturbances," Hoffmann explains. "Yet we were able to show in our experiments that an MRI scanner can indeed operate in a proton beam. High-contrast real-time images and precise proton beam steering are not mutually exclusive." Many experts predicted another difficulty to occur from proton beam behavior: when electrically charged particles move in the magnetic field of an MRI scanner, Lorentz forces will deflect the beam from its straight trajectory. However, the researchers were able to demonstrate that this deflection can be anticipated and thus corrected for.

To explore these mutual interactions, Hoffmann and his team used the experimental room at the National Center for Radiation Research in Oncology—OncoRay.

"Our mission is to individualize proton therapy biologically and to optimize it technologically towards its physical limits," says Hoffmann, head of the research group on MR-guided [radiation therapy](#) at the HZDR. OncoRay has its own cyclotron to deliver the proton beam into the therapy room as well as into the experimental room. Hoffmann and his colleagues used the latter for their research activities. With the support of IBA and the Paramed MRI Unit of ASG Superconductors SpA, they installed an open MRI scanner in the path of the proton beam, realizing the world's first prototype of MR-guided particle therapy. "We are lucky to have an experimental room that is large enough to accommodate an MRI scanner. That is one of OncoRay's unique features."

Knee phantom, mixed sausage and predictable diversion

For their experiments on this first prototype, they initially used what is called a knee phantom, a small plastic cylinder filled with an aqueous contrast liquid and a variety of differently shaped plastic pieces. Hoffmann and his team used it to conduct quantitative analyses of image quality. In a second series of experiments, the researchers used a piece of Dresden mixed sausage. "When the Dutch research group studied imaging for their MR-guided photon therapy device in 2009, they used pork chop," Hoffmann says. "In 2016, Australian researchers demonstrated their MR-photon therapy device on a Kangaroo steak. Since we also wanted to go regional for our prototype in MR-guided particle therapy, we used Dresden mixed sausage." Both the series of experiments with the phantom and with the sausage showed that the magnetic fields from [proton](#) therapy did not distort the image. They merely caused minor shifts in the MR image, which can be corrected for.

The project is currently entering its next phase. The goal is to develop the world's first prototype for MR-guided particle therapy that is applicable for clinical use. [32]

Researchers develop new technique to understand biology at the nanoscale

Washington State University researchers for the first time have shown that they can use electrical fields to gain valuable information about the tiny, floating vesicles that move around in animals and plants and are critically important to many biological functions.

The new technique could make it easier and less expensive for researchers to gain important information about many biological processes—from understanding the spread of infection in people to improving drug delivery techniques. Led by graduate student Adnan Morshed and Prashanta Dutta, professor in the School of Mechanical and Materials Engineering, the work was published in *Physical Review Fluids*.

At the basis of much of biology are cells and, at even smaller scales, cell-like bubbles that float around in liquid doing critically important jobs. So, for instance, neurons communicate in our brain through vesicles that carry information and chemicals from one neuron to the next. The HIV virus is another tiny vesicle. Over time, the vesicle carrying HIV changes and becomes stiffer, which indicates that the virus is becoming more infectious.

But studying the properties of these tiny and critically important cellular sacs that travel through organisms in fluids has been difficult, especially when researchers get to the smallest floaters that are 40-100 nanometers in size. To study biological processes at tiny scales, the researchers use atomic force microscopes, which require removing the vesicles from their natural floating homes. The process is expensive, cumbersome, and slow. Furthermore, by taking them out of their natural settings, the [biological materials](#) also don't necessarily exhibit their natural behavior, said Dutta.

The WSU research team has developed a system that uses a microfluidic-based system and electric fields to better understand vesicles. Similar to a grocery store checker who identifies products as they are passed over a scanner, the researchers apply [electrical fields](#) in a liquid as the vesicle passes through a narrow pore. Because of the electric [field](#), the vesicle moves, deforms, or reacts differently depending on its chemical make-up. In the case of the HIV vesicles, for instance, the researchers should be able to see the [electric field](#) affect the stiffer, more infectious vesicle in a different way than a more flexible, less infectious vesicle. For drug delivery, the system could differentiate a [vesicle](#) that contains more or less of a drug—even if the two cells might look identical under a microscope.

"Our system is low-cost and high throughput," said Dutta. "We can really scan hundreds of samples at a time."

He added that they can change the speed of the process to allow researchers to more carefully observe property changes.

The researchers developed a model and tested it with synthetic liposomes, tiny sacs that are used for targeted [drug delivery](#). They hope to begin testing the process soon with more realistic biological materials. [31]

Detecting *E. coli* strains using molecular electronics

Finding a fast and inexpensive way to detect specific strains of bacteria and viruses is critical to food safety, water quality, environmental protection and human health. However, current methods for detecting illness-causing strains of bacteria such as *E. coli* require either time-intensive biological cell cultures or DNA amplification approaches that rely on expensive laboratory equipment.

Now, Josh Hihath, an associate professor of electrical and computer engineering at the University of California, Davis, and colleagues at the University of Washington and TOBB University of Economics and Technology in Ankara, Turkey have adapted a molecular electronic device called a single-molecule break junction to detect RNA from strains of *E. coli* known for causing illness. The findings were published online today (Nov. 5) in the journal *Nature Nanotechnology*.

"The reliable, efficient and inexpensive detection and identification of specific strains of microorganisms such as *E. coli* is a grand challenge in biology and the health sciences," said Hihath. "Our technique could pave the way for rapid, straightforward detection of pathogens, antimicrobial resistant bacterial strains and biomarkers for cancer."

Hihath and his team focused on *E. coli* since it is a common pathogen that could easily be found in the food supply, but might not cause illness in a benign form. The worst strain of *E. coli*, called *E. coli* O157:H7, produces a toxic substance called Shiga toxin that causes bloody diarrhea, kidney failure and even death.

Single-molecule break junction devices consist of two metal electrodes with atomically sharp interfaces that are brought into contact in a liquid solution of interest, such as a solution containing RNA sequences from *E. coli*. As the electrodes are brought into contact and pulled apart, an electrical bias is applied and the current is measured. This process is repeated hundreds or thousands of times to determine the conductance of a single molecule.

"One of the questions we asked is how small of a change in the sequence is needed to cause a meaningful change in the electrical conductance?" said Hihath. "The smallest thing we can change is a single-base, so we decided to see if a single-base change can be measured."

By testing short sequences of RNA bound to DNA with chemical linkers, the team examined an *E. coli* sequence that would produce Shiga toxin. Their findings showed that changes in the electrical resistance of RNA due to a single-base change could be measured, which would allow them to see not only if a sequence was *E. coli*, but the specific strain of *E. coli* that produces Shiga toxin.

"A system that could selectively identify short sequences of DNA or RNA opens up new avenues for developing an electronic sensor platform for a wide range of applications," he adds. "Eventually, we want to get to the point where we can extract RNA samples from real organisms and measure their conductance on a sensing platform." [30]

Physicists name and codify new field in nanotechnology: 'electron quantum metamaterials'

When two atomically thin two-dimensional layers are stacked on top of each other and one layer is made to rotate against the second layer, they begin to produce patterns—the familiar moiré patterns—that neither layer can generate on its own and that facilitate the passage of light and electrons, allowing for materials that exhibit unusual phenomena. For example, when two graphene layers are overlaid and the angle between them is 1.1 degrees, the material becomes a superconductor.

"It's a bit like driving past a vineyard and looking out the window at the vineyard rows. Every now and then, you see no rows because you're looking directly along a row," said Nathaniel Gabor, an associate professor in the Department of Physics and Astronomy at the University of California, Riverside. "This is akin to what happens when two atomic layers are stacked on top of each other. At certain angles of twist, everything is energetically allowed. It adds up just right to allow for interesting possibilities of energy transfer."

This is the future of new materials being synthesized by twisting and stacking atomically thin layers, and is still in the "alchemy" stage, Gabor added. To bring it all under one roof, he and physicist Justin C. W. Song of Nanyang Technological University, Singapore, have proposed this field of research be called "electron [quantum](#) metamaterials" and have just published a perspective article in *Nature Nanotechnology*.

"We highlight the potential of engineering synthetic periodic arrays with feature sizes below the wavelength of an electron. Such engineering allows the electrons to be manipulated in unusual ways, resulting in a new range of synthetic quantum metamaterials with unconventional responses," Gabor said.

Metamaterials are a class of material engineered to produce properties that do not occur naturally. Examples include optical cloaking devices and super-lenses akin to the Fresnel lens that lighthouses use. Nature, too, has adopted such techniques—for example, in the unique coloring of butterfly wings—to manipulate photons as they move through nanoscale structures.

"Unlike photons that scarcely interact with each other, however, electrons in subwavelength structured metamaterials are charged, and they strongly interact," Gabor said. "The result is an enormous variety of emergent phenomena and radically new classes of interacting quantum metamaterials."

Gabor and Song were invited by *Nature Nanotechnology* to write a review paper. But the pair chose to delve deeper and lay out the fundamental physics that may explain much of the research in electron quantum metamaterials. They wrote a [perspective paper](#) instead that envisions the current status of the field and discusses its future.

"Researchers, including in our own labs, were exploring a variety of metamaterials but no one had given the field even a name," said Gabor, who directs the Quantum Materials Optoelectronics lab at UCR. "That was our intent in writing the perspective. We are the first to codify the underlying physics. In a way, we are expressing the periodic table of this new and exciting field. It has been a

herculean task to codify all the work that has been done so far and to present a unifying picture. The ideas and experiments have matured, and the literature shows there has been rapid progress in creating quantum materials for electrons. It was time to rein it all in under one umbrella and offer a roadmap to researchers for categorizing future work."

In the perspective, Gabor and Song collect early examples in electron metamaterials and distill emerging design strategies for electronic control from them. They write that one of the most promising aspects of the new field occurs when electrons in subwavelength-structure samples interact to exhibit unexpected emergent behavior.

"The behavior of superconductivity in twisted bilayer graphene that emerged was a surprise," Gabor said. "It shows, remarkably, how electron interactions and subwavelength features could be made to work together in quantum metamaterials to produce radically new phenomena. It is examples like this that paint an exciting future for electronic [metamaterials](#). Thus far, we have only set the stage for a lot of new work to come." [29]

Nanocrystals arrange to improve electronics

Lawrence Livermore National Laboratory (LLNL) researchers are working to make better electronic devices by delving into the way nanocrystals are arranged inside of them.

Nanocrystals are promising building blocks for new and improved electronic devices, due to their size-tunable properties and ability to integrate into devices at low-cost.

While the structure of nanocrystals has been extensively studied, no one has been able to watch the full assembly process.

That's where LLNL scientists Christine Orme, Yixuan Yu, Babak Sadigh and a colleague from the University of California, Los Angeles come in.

"We think the situation can be improved if detailed quantitative information on the nanocrystal assembly process could be identified and if the crystallization process were better controlled," said Orme, an LLNL material scientist and corresponding author of a paper appearing in the journal *Nature Communications*.

Nanocrystals inside devices form ensembles, whose collective physical properties, such as charge carrier mobility, depend on both the properties of individual nanocrystals and the way they are arranged. In principle, ordered nanocrystal ensembles, or superlattices, allow for more control in charge transport by facilitating the formation of minibands. However, in practice, few devices built from ordered nanocrystal superlattices are on the market.

Most previous studies use solution evaporation methods to generate nanocrystal superlattices and probe the assembly process as the solvent is being gradually removed. It is difficult to obtain quantitative information on the assembly process, however, because the volume and shape of the nanocrystal solution is continually changing in an uncontrollable manner and the capillary forces can drive nanocrystal motion during drying.

Electric field-driven growth offers a solution to this problem. "We have recently demonstrated that an electric field can be used to drive the assembly of well-ordered, 3-D nanocrystal superlattices," Orme said.

Because the electric field increases the local concentration without changing the volume, shape or composition of nanocrystal solution, the crystallizing system can be probed quantitatively without complications associated with capillary forces or scattering from drying interfaces.

As anticipated, the team found that the electric field drives nanocrystals toward the surface, creating a concentration gradient that leads to nucleation and growth of superlattices. Surprisingly, the field also sorts the particles according to size. In essence, the electric field both concentrates and purifies the nanocrystal solution during growth.

"Because of this size sorting effect, the superlattice crystals are better ordered and the size of the nanocrystals in the lattice can be tuned during growth," Orme said. "This might be a useful tool for optoelectronic devices. We're working on infrared detectors now and think it might be an interesting strategy for improving color in monitors." [28]

Nanoparticles form supercrystals under pressure

Self-assembly and crystallisation of nanoparticles (NPs) is generally a complex process, based on the evaporation or precipitation of NP-building blocks. Obtaining high-quality supercrystals is slow, dependent on forming and maintaining homogenous crystallisation conditions. Recent studies have used applied pressure as a homogenous method to induce various structural transformations and phase transitions in pre-ordered nanoparticle assemblies. Now, in work recently published in the *Journal of Physical Chemistry Letters*, a team of German researchers studying solutions of gold nanoparticles coated with poly(ethylene glycol)- (PEG-) based ligands has discovered that supercrystals can be induced to form rapidly within the whole suspension.

Over the last few decades, there has been considerable interest in the formation of nanoparticle (NP) supercrystals, which can exhibit tunable and collective properties that are different from that of their component parts, and which have potential applications in areas such as optics, electronics, and sensor platforms. Whilst the formation of high-quality supercrystals is normally a slow and complex process, recent research has shown that applying pressure can induce gold nanoparticles to form supercrystals. Building on this and the established effect of salts on the solubility of gold nanoparticles (AuNP) coated with PEG-based ligands, Dr. Martin Schroer and his team carried out a series of experiments investigating the effect of varying pressure on gold nanoparticles in aqueous solutions. They made an unexpected observation – when a salt is added to the solution, the nanoparticles crystallise at a certain pressure. The phase diagram is very sensitive, and the crystallisation can be tuned by varying the type of salt added, and its concentration.

The team used small angle x-ray scattering (SAXS) on beamline I22 to study the crystallisation in situ with different chloride salts (NaCl, KCl, RbCl, CsCl). As Dr. Schroer explains,

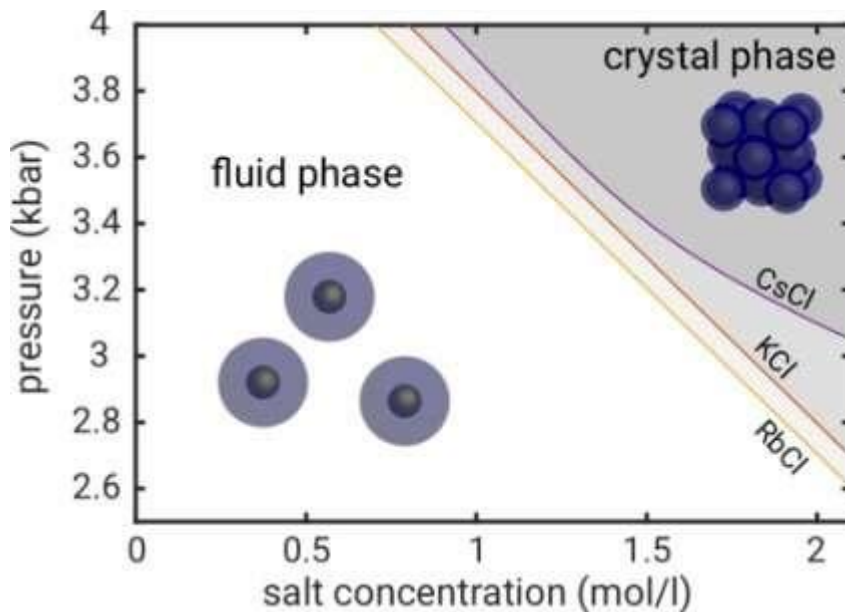


Fig. 2: Pressure – salt concentration phase diagram of AuNP@PEG. For low pressures, the particles are in the liquid state, beyond a critical pressure, face-centred cubic (fcc) superlattices are formed within solution. The crystallisation ...[more](#)

122 is one of the few beamlines to offer a high-pressure environment, and it is unusual because the experimental setup is easily managed by the users themselves. The beamline staff are excellent, and we are particularly grateful for their expertise in data processing, which was invaluable."

The resulting pressure-salt concentration phase diagram shows that the crystallisation is a result of the combined effect of salt and pressure on the PEG coatings. Supercrystal formation occurs only at high salt concentrations, and is reversible. Increasing the salt concentration leads to a continuous decrease of the crystallisation pressure, whereas the lattice structure and degree of crystallinity is independent of the [salt](#) type and concentration.

When reaching the crystallisation pressure, supercrystals form within the whole suspension; compressing the liquid further results in changes of the lattice constant, but no further crystallisation or structural transitions. This technique should be applicable to a variety of nanomaterials, and future studies may reveal insights into supercrystal formation that will help to understand crystallisation processes and enable the development of new and quicker methods for the synthesis of NP supercrystals.

The NP [crystallisation](#) appears to be instantaneous, but in this set of experiments there was a delay of around 30 seconds between applying the pressure and taking the SAXS measurements. Dr. Schroer and his team are returning to Diamond later this year to carry out time-resolved studies to further investigate this phenomenon. [27]

Researchers develop nanoparticle films for high-density data storage

As we generate more and more data, the need for high-density data storage that remains stable over time is becoming critical. New nanoparticle-based films that are more than 80 times thinner than a human hair may help to fill this need by providing materials that can holographically archive more than 1000 times more data than a DVD in a 10-by-10-centimeter piece of film. The new technology could one day enable tiny wearable devices that capture and store 3-D images of objects or people.

"In the future, these new films could be incorporated into a tiny [storage](#) chip that records 3-D color information that could later be viewed as a 3-D hologram with realistic detail," said Shencheng Fu, who led researchers from Northeast Normal University in China who developed the new films.

"Because the storage medium is environmentally stable, the device could be used outside or even brought into the harsh radiation conditions of outer space."

In the journal *Optical Materials Express*, the researchers detail their fabrication of the new films and demonstrate the technology's ability to be used for an environmentally-stable holographic storage system. The films not only hold large amounts of data, but that data can also be retrieved at speeds up to 1 GB per second, which is about twenty times the reading speed of today's flash memory.

Storing more data in less space

The new films are designed for holographic data storage, a technique that uses lasers to create and read a 3-D holographic recreation of data in a material. Because it can record and read millions of bits at once, holographic data storage is much faster than optical and magnetic approaches typically used for data storage today, which record and read individual bits one at a time. Holographic approaches are also inherently high-density because they record information throughout the 3-D volume of the material, not just on the surface, and can record multiple images in the same area using light at different angles or consisting of different colors.

Recently, researchers have been experimenting with using metal-semiconductor nanocomposites as a medium for storing nanoscale holograms with high spatial resolution. Porous films made of the semiconductor titania and silver nanoparticles are promising for this application because they change color when exposed to various wavelengths, or colors, of laser light and because a set of 3-D images can be recorded at the focus area of laser beam using a single step. Although the films could be used for multiwavelength holographic data storage, exposure to UV light has been shown to erase the data, making the films unstable for long-term information storage.



Shuangyan Liu is holding the new UV-resistant holographic storage film. The new technology could one day be used to make tiny wearable devices that capture and store 3-D images of objects or people. Credit: Northeast Normal University

Recording a holographic image into titania-silver films involves using a laser to convert the silver particles into silver cations, which have a positive charge due to extra electrons. "We noticed that UV light could erase the data because it caused electrons to transfer from the semiconductor film to the metal nanoparticles, inducing the same photo transformation as the laser," said Fu. "Introducing electron-accepting molecules into the system causes some of the electrons to flow from the semiconductor to these molecules, weakening the ability of UV light to erase the data and creating an environmentally stable high-density data storage medium."

Changing the electron flow

For the new films, the researchers used electron-accepting molecules that measured only 1 to 2 nanometers to disrupt the electron flow from the semiconductor to the metal nanoparticles. They fabricated semiconductor films with a honeycomb nanopore structure that allowed the nanoparticles, electron-accepting molecules and the semiconductor to all interface with each other. The ultrasmall size of the electron-accepting molecules allowed them to attach inside the pores without affecting the pore structure. The final films were just 620 nanometers thick.

The researchers tested their new films and found that holograms can be written into them efficiently and with high stability even in the presence of UV light. The researchers also demonstrated that using the electron-acceptors to change the [electron flow](#) formed multiple electron transferring paths, making the material respond faster to the laser light and greatly accelerating the speed of data writing.

"Particles made from noble metals such as silver are typically viewed as a slow-response media for optical storage," said Fu. "We show that using a new electron transport flow improves the optical response speed of the particles while still maintaining the particle's other advantages for information storage."

The researchers plan to test the environmental stability of the new films by performing outdoor tests. They also point out that real-life application of the [films](#) would require the development of high efficiency 3-D image reconstruction techniques and methods for color presentation for displaying or reading the stored data. [26]

Researchers developing materials for quantum computing

Creation of innovative materials is one of the most important areas of modern science. Active development of Industry 4.0 requires new properties from composite elements of electronics. Researches of scientists from South Ural State University are implemented within this area. SUSU's Crystal Growth Laboratory performs modification of properties and structure of ferrites, which are oxides of iron with other metals' oxides. This task is performed by introducing other chemical elements into the structure of barium hexaferrite in order to obtain new working characteristics of the material.

One of the latest research articles dedicated to this topic was published at the end of 2017 in *Ceramics International*.

"The specificity of ferrite crystal structure is in the fact that it has five different positions of iron in the crystal lattice. This is exactly what allows modifying the structure and properties of the material in a sufficiently wide range. Structure of the initial material changes its properties after introduction of other elements, which expands the possibilities for its use. Therefore, by changing material's chemical composition, we can modify its working characteristics. We researched distribution of indium on positions of the substitute element," says Denis Vinnik, Head of the Crystal Growth Laboratory.

The scientists have a special interest in determining which of iron's positions in the lattice of barium hexaferrite is the most preferential for the new [element](#): properties of the modified material depend on its structure. At the present time, the crystallographic positions that indium will place have been determined. Research is being carried out in the area of studying super-high frequency characteristics and the nature of other various properties of ferrites.



Viktoria Matveychuk. Credit: A. Trukhanov

"Our interest to barium ferrites is conditioned by their high functional properties," explains Aleksey Valentinovich. "Chemical stability and corrosion resistance makes these materials environmentally safe and usable for practically unlimited time. Hexaferrites possess excellent magnetic parameters. Low specific electrical conductivity allows applying hexaferrite magnets at the presence of high-frequency magnet fields, which is prospective for microelectronics. Nowadays this material has a great potential in absorbing electromagnetic interference (EMI) in the microwave range. Therefore, hexaferrites are applicable for microwave technologies and for data transmission and protection from wave exposure at high frequencies."

"We are working with a 'palette' of various chemical elements, including wolframium, aluminum, titanium, manganese and silicon. We would like to find out how such substitutions affect the material's properties," says Svetlana Aleksandrovna. "Now, we are working with lead germanate. Additionally, we are studying physical characteristics of barium hexaferrite with placeable lead and its behavior at high temperatures. At some point of heating till a specific temperature, the sample starts shrinking; this is a quite extraordinary phenomenon. Within this experiment, we calculated the linear expansion coefficient and obtained interesting dependences. There are materials with negative or zero expansion coefficient; they don't change their size during heating. This is

important at extreme temperatures, because some electronic details get overheated even under normal conditions."

Barium hexaferrite with placeable lead is one of study fields of the Crystal Growth Laboratory. The scientists have now grown monocrystals with low defect density that can be applied as working elements of electronic devices. Potentially, the material can be used for creation of a quantum computer which would have the highest performance capacity among the existing computational devices.

Development of new magnetic materials in the 21st century will allow creating memory elements with high-speed response, significant volume, and reliability. This class of materials has many applications. [25]

Terahertz computer chip now within reach

Following three years of extensive research, Hebrew University of Jerusalem (HU) physicist Dr. Uriel Levy and his team have created technology that will enable computers and all optic communication devices to run 100 times faster through terahertz microchips.

Until now, two major challenges stood in the way of creating the terahertz [microchip](#): overheating and scalability.

However, in a paper published this week in *Laser & Photonics Reviews*, Dr. Levy, head of HU's Nano-Opto Group and HU emeritus professor Joseph Shappir have shown proof of concept for an optic [technology](#) that integrates the speed of optic (light) communications with the reliability—and manufacturing scalability—of electronics.

Optic communications encompass all technologies that use light and transmit through [fiber optic cables](#), such as the internet, email, text messages, phone calls, the cloud and data centers, among others. Optic communications are super fast but in microchips they become unreliable and difficult to replicate in large quantities.

Now, by using a Metal-Oxide-Nitride-Oxide-Silicon (MONOS) structure, Levy and his team have come up with a new integrated circuit that uses flash memory technology—the kind used in flash drives and discs-on-key—in microchips. If successful, this technology will enable standard 8-16 gigahertz computers to run 100 times faster and will bring all optic devices closer to the holy grail of communications: the terahertz chip.

As Dr. Uriel Levy shared, "this discovery could help fill the 'THz gap' and create new and more powerful wireless devices that could transmit data at significantly higher speeds than currently possible. In the world of hi-tech advances, this is game-changing technology,"

Meir Grajower, the leading HU Ph.D. student on the project, added, "It will now be possible to manufacture any optical [device](#) with the precision and cost-effectiveness of flash technology." [24]

Revolutionizing computer memory—with magnets

When the energy efficiency of electronics poses a challenge, magnetic materials may have a solution.

Energy efficiency will make or break the future. As the demand for energy from electronics continues growing, the Semiconductor Research Corporation warns that within two decades, the global computational demand for energy will be greater than the total amount produced. Vincent Sokalski, an assistant professor of [materials](#) science and engineering at Carnegie Mellon University, is working on a solution to this problem—using [magnetic materials](#) for energy-efficient memory and computing.

Sokalski recently received a \$1.8 million grant from the Defense Advanced Research Projects Agency (DARPA) for his project, "Domain wall skyrmions: Topological excitations confined to 1-D channels." Along with CMU Professors Marc De Graef (MSE) and Di Xiao (Physics), Sokalski will explore new ways to efficiently process and store information with magnetic materials.

Although magnetic materials are already used in today's hard disk drives for long-term storage, semiconductors are currently used for short-term memory and processing, which is where most of the energy is consumed. However, as semiconductors shrink to meet consumer expectations for speed and density, there comes a limit to how small they can be made without risking the loss of information. DARPA recognizes this challenge, and [research projects](#) funded by DARPA's "Topological Excitations in Electronics" program center on finding ways to use "topological protection" to improve magnetic materials that can be used for computer memory storage or processors.

Imagine a bowl with a small ball rolling inside. As you shake it, the ball moves up and down the walls of the bowl, staying inside. However, if you did this with a smaller bowl, the ball might eventually fall out. Similarly, when a semiconductor is exposed to heat, it is at risk of losing information. The smaller you manufacture semiconductors, the more risk there is of data loss.

Credit: Carnegie Mellon University College of Engineering

"The fundamental physics behind that isn't something we can readily change," explains Sokalski, "but we can look at entirely different material systems and mechanisms where we're moving around magnetic features, and using those magnetic features to change the resistance of a computing device. But in order to do that, we really need to explore and discover new materials that can serve that purpose."

Enter magnetic materials. By improving magnetic materials, Sokalski hopes to one day find [new materials](#) that could augment, or even replace, semiconductors in computing.

Sokalski's project begins with magnetic skyrmions, or 2-D magnetic bubbles. If used in computer memory, each bubble would store a single bit of data.

"Skyrmions are a rebirth of the idea of bubble memory" that was widely studied in the 1970s and 80s, says Sokalski. "Except now the bubbles are much smaller, more stable, and have topological

protection, so we can move them around with greater energy efficiency than we ever could have moved them around 40 or 50 years ago."

In magnetic materials, think of each electron as a tiny bar magnet with a north and south pole that are all pointing in the same direction. These are called spins. Sokalski is interested in how to create topological defects in lines of these spins.

To understand the importance of topological protection, you first have to understand topological defects. Imagine stacking a cheese tray with a friend. One of you starts on the right side of the tray, stacking up each piece of cheese on top of the next, and the other starts on the left side. Eventually, you'll meet in the middle, and your slices of cheese will collide, rather than aligning at the same angle. That point where they collide is the essence of a topological defect.

To erase a topological defect, you'd have to flip every "slice of cheese" on one side of the defect. In magnetism, if half of your spins in a chain point inward to the left, and all the others point the opposite direction, you'd get a defect in the middle. In order to make the defect disappear, you'd have to reverse every spin on one side, moving it away to the edge of the chain.

In magnetism, these topological defects are very valuable. If you have a topological defect, that means your data are topologically protected, because if just one spin spontaneously flips to point in the opposite direction, the defect just shifts, rather than goes away.

Why is this topic suddenly emerging in magnetic materials research? All magnetism is based on something called the Heisenberg Exchange, a quantum mechanical effect that causes electron spins to align in a parallel orientation. However, the discovery of a new phenomenon called the Dzyaloshinskii-Moriya Interaction (DMI) leads to a perpendicular alignment of neighboring spins. The combination of Heisenberg Exchange and DMI, which is what Sokalski studies, gives rise to a new kind of magnetism that causes electron spins to have a continuously spiraling configuration.

"It turns out that features in magnetic materials that are stabilized by this new interaction can actually be manipulated with better efficiency than in cases where it's only the Heisenberg Exchange," says Sokalski.

Having greater control over skyrmions and topological defects would mean more reliable data storage and energy efficiency in computing.

"DARPA is looking to circumvent the pending challenge of energy-efficient electronics," says Sokalski, "and that scales from the most fundamental physical concepts of spin to the design of computers that have an entirely different circuit architecture. Our research will lead to energy-efficient computing that meets the needs of artificial intelligence and small-scale computers, while mitigating their global energy footprint."

MSE Ph.D. students Maxwell Li and Derek Lau and Physics postdoctoral researcher Ran Cheng are collaborators on this project, in addition to Co-PIs Tim Mewes and Claudia Mewes at the University of Alabama. [23]

The quantum states on the surface of conducting materials can strongly interact with light

An exotic state of matter that is dazzling scientists with its electrical properties, can also exhibit unusual optical properties, as shown in a theoretical study by researchers at A*STAR.

Atomically thin materials, such as graphene, derive some of their properties from the fact that electrons are confined to traveling in just two-dimensions. Similar phenomena are also seen in some three-dimensional materials, in which electrons confined to the [surface](#) behave very differently from those within the bulk—for example, [topological insulators](#), whose surface electrons conduct electricity even though their bulk electrons do not. Recently, another exciting class of materials has been identified: the topological semimetal.

The difference in insulator and conductor [electrical properties](#) is down to the bandgap: a gap between the ranges, or bands, of energy that an electron traveling through the material can assume. In an insulator, the lower band is full of electrons and the bandgap is too large to enable a current to flow. In a semimetal, the lower band is also full but the lower and upper bands touch at some points, enabling the flow of a small current.

This lack of a full bandgap means that topological semimetals should theoretically exhibit very different properties from those of the more conventional topological insulators.

To prove this, Li-kun Shi and Justin Song from the A*STAR Institute of High Performance Computing used an 'effective Hamiltonian' approximation to show that the two-dimensional surface states in semimetals, known as Fermi arcs, possess a light–matter interaction much stronger than that found in other gapless two-dimensional systems, such as graphene.

"Typically, the bulk dominates material absorption," explains Song. "But we show that Dirac semimetals are unusual in that they possess a very optically active surface due to these peculiar Fermi arc states."

Shi and Song analyzed a proto-typical semimetal with a symmetric band structure where the electronic bands touch at two places, known as Dirac points, and predicted the strength with which incident radiation induces electron transitions from the lower band to the upper one. They found that surface absorption depends heavily on the polarization of light, being 100 to 1,000 times stronger when light is polarized perpendicular—rather than parallel—to the crystal's rotational axis. This strong anisotropy offers a way of optically investigating and probing the topological surface states of Dirac semimetals.

"Our goal is to identify more unconventional optics that arise due to Fermi arcs," says Song.

"Topological semimetals could host unusual opto-electronic behavior that goes beyond conventional materials." [22]

Breakthrough in circuit design makes electronics more resistant to damage and defects

People are growing increasingly dependent on their mobile phones, tablets and other portable devices that help them navigate daily life. But these gadgets are prone to failure, often caused by small defects in their complex electronics, which can result from regular use. Now, a paper in today's *Nature Electronics* details an innovation from researchers at the Advanced Science Research Center (ASRC) at The Graduate Center of The City University of New York that provides robust protection against circuitry damage that affects signal transmission.

The breakthrough was made in the lab of Andrea Alù, director of the ASRC's Photonics Initiative. Alù and his colleagues from The City College of New York, University of Texas at Austin and Tel Aviv University were inspired by the seminal work of three British researchers who won the 2016 Noble Prize in Physics for their work, which teased out that particular properties of matter (such as electrical conductivity) can be preserved in certain materials despite continuous changes in the matter's form or shape. This concept is associated with topology—a branch of mathematics that studies the properties of space that are preserved under continuous deformations.

"In the past few years there has been a strong interest in translating this concept of matter topology from material science to light propagation," said Alù. "We achieved two goals with this project: First, we showed that we can use the science of topology to facilitate robust electromagnetic-wave propagation in electronics and circuit components. Second, we showed that the inherent robustness associated with these topological phenomena can be self-induced by the signal traveling in the circuit, and that we can achieve this robustness using suitably tailored nonlinearities in circuit arrays."

To achieve their goals, the team used nonlinear resonators to mold a band-diagram of the circuit array. The array was designed so that a change in signal intensity could induce a change in the band diagram's topology. For low signal intensities, the electronic circuit was designed to support a trivial topology, and therefore provide no protection from defects. In this case, as defects were introduced into the array, the signal transmission and the functionality of the circuit were negatively affected.

As the voltage was increased beyond a specific threshold, however, the band-diagram's topology was automatically modified, and the signal transmission was not impeded by arbitrary defects introduced across the circuit array. This provided direct evidence of a topological transition in the circuitry that translated into a self-induced robustness against defects and disorder.

"As soon as we applied the higher-voltage signal, the system reconfigured itself, inducing a topology that propagated across the entire chain of resonators allowing the signal to transmit without any problem," said A. Khanikaev, professor at The City College of New York and co-author in the study. "Because the system is nonlinear, it's able to undergo an unusual transition that makes signal transmission robust even when there are defects or damage to the circuitry."

"These ideas open up exciting opportunities for inherently robust electronics and show how complex concepts in mathematics, like the one of topology, can have real-life impact on common electronic devices," said Yakir Hadad, lead author and former postdoc in Alù's group, currently a professor at Tel-Aviv University, Israel. "Similar ideas can be applied to nonlinear optical [circuits](#) and extended to two and three-dimensional nonlinear metamaterials." [21]

Researchers develop heat switch for electronics

Researchers at the University of Illinois at Urbana-Champaign have developed a new technology for switching heat flows 'on' or 'off'. The findings were published in the article "Millimeter-scale liquid metal droplet thermal switch," which appeared in *Applied Physics Letters*.

Switches are used to control many technical products and engineered systems. Mechanical switches are used to lock or unlock doors, or to select gears in a car's transmission system. Electrical switches are used to turn on and off the lights in a room. At a smaller scale, [electrical switches](#) in the form of transistors are used to turn electronic devices on and off, or to route logic signals within a circuit.

Engineers have long desired a switch for heat flows, especially in electronics systems where controlling heat flows can significantly improve system performance and reliability. There are however significant challenges in creating such a heat switch.

"Heat [flow](#) occurs whenever you have a region of higher temperature near a region of lower temperature," said William King, the Andersen Chair Professor in the Department of Mechanical Science and Engineering and the project co-leader. "In order to control the [heat flow](#), we engineered a specific heat flow path between the hot region and cold region, and then created a way to break the heat flow path when desired."

"The technology is based on the motion of a liquid metal droplet," said Nenad Miljkovic, Assistant Professor in the Department of Mechanical Science and Engineering and the project co-leader. "The metal droplet can be positioned to connect a heat flow path, or moved away from the heat flow path in order to limit the heat flow."

The researchers demonstrated the technology in a system modeled after modern electronics systems. On one side of the switch there was a heat source representing the power electronics component, and on the other side of the switch, there was liquid cooling for heat removal. When the switch was on, they were able to extract heat at more than 10 W/cm². When the switch was off, the [heatflow](#) dropped by nearly 100X.

Besides King and Miljkovic, other authors of the paper include Paul Braun, Racheff Professor of Materials Science and Engineering and the Director of Materials Research Laboratory; and graduate students Tianyu Yang, Beomjin Kwon and Patricia B. Weisensee (now an assistant professor at Washington University in St. Louis) from mechanical science and engineering and Jin Gu Kang and Xuejiao Li from materials science and engineering.

King says that the next step for the research is to integrate the [switch](#) with power electronics on a circuit board. The researchers will have a working prototype later this year. [20]

Converting heat into electricity with pencil and paper

Thermoelectric materials can use thermal differences to generate electricity. Now there is an inexpensive and environmentally friendly way of producing them with the simplest tools: a pencil, photocopy paper, and conductive paint. These are sufficient to convert a temperature difference into electricity via the thermoelectric effect, which has now been demonstrated by a team at the Helmholtz-Zentrum Berlin.

The [thermoelectric effect](#) was discovered almost 200 years ago by Thomas J. Seebeck. If two metals of different temperatures are brought together, they can develop an electrical voltage. This effect allows residual heat to be converted partially into electrical energy. Residual heat is a by-product of almost all technological and natural processes, such as in power plants and household appliances, not to mention the human body. It is also one of the most under-utilised energy sources in the world.

Tiny effect

However, as useful an effect as it is, it is extremely small in ordinary metals. This is because metals not only have high electrical conductivity, but [high thermal conductivity](#) as well, so that differences in temperature disappear immediately. Thermoelectric [materials](#) need to have [low thermal conductivity](#) despite their [high electrical conductivity](#). Thermoelectric devices made of inorganic semiconductor materials such as bismuth telluride are already being used today in certain technological applications. However, such material systems are expensive and their use only pays off in certain situations. Researchers are exploring whether flexible, nontoxic organic materials based on carbon nanostructures, for example, might also be used in the human body.

The team led by Prof. Norbert Nickel at the HZB has now shown that the effect can be obtained much more simply—using a normal HB-grade [pencil](#), they covered a small area with pencil on ordinary photocopy paper. As a second material, they applied a transparent, conductive co-polymer paint (PEDOT: PSS) to the surface.

The pencil traces on the paper delivered a voltage comparable to other far more expensive nanocomposites that are currently used for flexible thermoelectric elements. And this voltage could be increased tenfold by adding indium selenide to the graphite from the pencil.

The researchers investigated graphite and co-polymer coating films using a scanning electron microscope and Raman scattering at HZB. "The results were very surprising for us as well," says Nickel. "But we have now found an explanation of why this works so well—the pencil deposit left on the paper forms a surface characterised by unordered graphite flakes, some graphene, and clay. While this only slightly reduces the electrical conductivity, heat is transported much less effectively."

These simple constituents might be usable in the future to print extremely inexpensive, environmentally friendly, and non-toxic thermoelectric components onto paper. Such tiny and flexible components could also be used directly on the body and could use body heat to operate small devices or sensors. [19]

A new efficient and portable electrocaloric cooling device

A team of researchers with the University of California and SRI International has developed a new type of cooling device that is both portable and efficient. In their paper published in the journal *Science*, the team describes their new device and possible applications for its use. Q.M. Zhang and Tian Zhang with the Pennsylvania State University offer some background on electrocaloric theory and outline the work done by the team in California in a Perspectives piece in the same journal issue.

As most everyone knows, conventional air conditioners are bulky, heavy, use a lot of electricity and often leak greenhouse gases into the atmosphere. Thus, conditions are ripe for something new. Some new devices have been developed such as thermoelectric coolers, which make use of ceramics, but they are not efficient enough to play a major role in cooling. A more recent development is the use of devices exploiting the electrocaloric effect, which is where heat moves through certain materials when an electric current is applied. In this new effort, the researchers used a polymer as the material.

The new cooling device was made by layering a polymer between a heat sink and a heat source. Applying electric current to the polymer when it was touching the heat sink caused its molecules to line up, which reduced entropy, forcing heat into the sink. The polymer was then moved into contact with the heat source while the current was turned off. The molecules relaxed, which caused the temperature to drop. Repeating this process resulted in cooling.

The researchers report that the device is extremely efficient, portable and configurable. They suggest the same technology could be used to create coolers for a chair or hat, for example, or perhaps to chill smartphone batteries. They proved this last claim by actually building such a device and using it to cool down a battery heated by ordinary use—after only five seconds, the temperature of the battery had lessened by 8° C. Comparatively, air cooling the battery reduced its temperature just 3° C in 50 seconds. [18]

Fast heat flows in warm, dense aluminum

Thermal conductivity is one of the most crucial physical properties of matter when it comes to understanding heat transport, hydrodynamic evolution and energy balance in systems ranging from astrophysical objects to fusion plasmas.

In the warm dense matter (WDM) regime, experimental data are very rare, so many theoretical models remain untested.

But LLNL researchers have tested theory by developing a platform called "differential heating" to conduct thermal conductivity measurements. Just as land and water on Earth heat up differently in sunlight, a temperature gradient can be induced between two different materials. The subsequent heat flow from the hotter material to the cooler material is detected by time-resolved diagnostics to determine thermal conductivity.

In an experiment using the Titan laser at the Lab's Jupiter Laser Facility, LLNL researchers and collaborators achieved the first measurements of thermal conductivity of warm dense aluminum—a prototype material commonly used in model development—by heating a dual-layer target of gold and aluminum with laser-generated protons.

"Two simultaneous time-resolved diagnostics provided excellent data for gold, the hotter material, and aluminum, the colder material," said Andrew Mckelvey, a graduate student from the University of Michigan and the first author of a paper appearing in Scientific Reports . "The systematic data sets can constrain both the release equation of state (EOS) and thermal conductivity."

By comparing the data with simulations using five existing thermal conductivity models, the team found that only two agree with the data. The most commonly used model in WDM, called the LeeMore model, did not agree with data. "I am glad to see that Purgatorio, an LLNL-based model, agrees with the data," said Phil Sterne, LLNL co-author and the group leader of EOS development and application group in the Physics Division. "This is the first time these thermal conductivity models of aluminum have been tested in the WDM regime."

"Discrepancy still exists at early time up to 15 picoseconds," said Elijah Kemp, who is responsible for the simulation efforts. "This is likely due to non-equilibrium conditions, another active research area in WDM."

The team is led by Yuan Ping through her early career project funded by the Department of Energy Office of Fusion Energy Science Early Career Program. "This platform can be applied to many pairs of materials and by various heating methods including particle and X-ray heating," Ping said. [17]

Controlling heat and particle currents in nanodevices by quantum observation

Researchers from the Theory Department of the MPSD have realized the control of thermal and electrical currents in nanoscale devices by means of quantum local observations.

Measurement plays a fundamental role in quantum mechanics. The best-known illustration of the principles of superposition and entanglement is Schrödinger's cat. Invisible from the outside, the cat resides in a coherent superposition of two states, alive and dead at the same time.

By means of a measurement, this superposition collapses to a concrete state. The cat is now either dead or alive. In this famous thought experiment, a measurement of the "quantum cat" can be seen as an interaction with a macroscopic object collapsing the superposition onto a concrete state by destroying its coherence.

In their new article published in npj Quantum Materials, researchers from the Max Planck Institute for the Structure and Dynamics of Matter and collaborators from the University of the Basque Country (UPV/EHU) and the Bremen Center for Computational Materials Science discovered how a microscopic quantum observer is able to control thermal and electrical currents in nanoscale devices. Local quantum observation of a system can induce continuous and dynamic changes in its

quantum coherence, which allows better control of particle and energy currents in nanoscale systems.

Classical non-equilibrium thermodynamics was developed to understand the flow of particles and energy between multiple heat and particle reservoirs. The best-known example is Clausius' formulation of the second law of thermodynamics, stating that when two objects with different temperatures are brought in contact, heat will exclusively flow from the hotter to the colder one.

In macroscopic objects, the observation of this process does not influence the flow of energy and particles between them. However, in quantum devices, thermodynamical concepts need to be revisited. When a classical observer measures a quantum system, this interaction destroys most of the coherence inside the system and alters its dynamical response.

Instead, if a quantum observer acts only locally, the system quantum coherence changes continuously and dynamically, thus providing another level of control of its properties. Depending on how strong and where these local quantum observations are performed, novel and surprising quantum transport phenomena arise.

The group of Prof. Dr. Angel Rubio at the Theory Department of the MPSD, along with their colleagues, have demonstrated how the concept of quantum measurements can offer novel possibilities for a thermodynamical control of quantum transport (heat and particle). This concept offers possibilities far beyond those obtained using standard classical thermal reservoirs.

The scientists studied this idea in a theoretical quantum ratchet. Within this system, the left and right side are connected to hot and cold thermal baths, respectively. This configuration forces the energy to flow from hot to cold and the particles to flow clockwise inside the ratchet. The introduction of a quantum observer, however, inverts the particle ring-current against the natural direction of the ratchet—a phenomenon caused by the localized electronic state and the disruption of the system's symmetry.

Furthermore, the quantum observation is also able to invert the direction of the heat flow, contradicting the second law of thermodynamics. "Such heat and particle current control might open the door for different strategies to design quantum transport devices with directionality control of the injection of currents. There could be applications in thermoelectricity, spintronics, photonics, and sensing, among others. These results have been an important contribution to my PhD thesis," says Robert Biele, first author of the paper.

From a more fundamental point of view, this work highlights the role of a quantum observer. In contrast to Schrödinger's cat, where the coherent state is destroyed via the interaction with a macroscopic "observer," here, by introducing a local quantum observer, the coherence is changed locally and dynamically, allowing researchers to tune between the coherent states of the system. "This shows how thermodynamics is very different in the quantum regime. Schrödinger's cat paradox leads to new thermodynamic forces never seen before," says César A. Rodríguez Rosario.

In the near future, the researchers will apply this concept to control spins for applications in spin injection and novel magnetic memories. Angel Rubio suggests that "The quantum observer—besides controlling the particle and energy transfer at the nanoscale—could also observe spins,

select individual components, and give rise to spin-polarized currents without spin-orbit coupling. Observation could be used to write a magnetic memory." [16]

Maxwell's demon extracts work from quantum measurement

Physicists have proposed a new type of Maxwell's demon—the hypothetical agent that extracts work from a system by decreasing the system's entropy—in which the demon can extract work just by making a measurement, by taking advantage of quantum fluctuations and quantum superposition.

The team of Alexia Auffèves at CNRS and Université Grenoble Alpes have published a paper on the new Maxwell's demon in a recent issue of Physical Review Letters.

"In the classical world, thermodynamics teaches us how to extract energy from thermal fluctuations induced on a large system (such as a gas or water) by coupling it to a hot source," Auffèves told Phys.org. "In the quantum world, the systems are small, and they can fluctuate—even if they are not hot, but simply because they are measured. In our paper, we show that it is possible to extract energy from these genuinely quantum fluctuations, induced by quantum measurement."

In the years since James Clerk Maxwell proposed the first demon around 1870, many other versions have been theoretically and experimentally investigated. Most recently, physicists have begun investigating Maxwell's demons that operate in the quantum regime, which could one day have implications for quantum information technologies.

Most quantum versions of the demon have a couple things in common: They are thermally driven by a heat bath, and the demon makes measurements to extract information only. The measurements do not actually extract any work, but rather the information gained by the measurements allows the demon to act on the system so that energy is always extracted from the cycle.

The new Maxwell's demon differs from previous versions in that there is no heat bath—the demon is not thermally driven, but measurement-driven. Also, the measurements have multiple purposes: They not only extract information about the state of the system, but they are also the "fuel" for extracting work from the system. This is because, when the demon performs a measurement on a qubit in the proposed system, the measurement projects the qubit from one state into a superposition of states, which provides energy to the qubit simply due to the measurement process. In their paper, the physicists proposed an experiment in which projective quantum non-demolition measurements can be performed with light pulses repeated every 70 nanoseconds or so.

Since recent experiments have already demonstrated the possibility of performing measurements at such high frequencies, the physicists expect that the new Maxwell's demon could be readily implemented using existing technology. In the future, they also plan to investigate potential applications for quantum computing.

"This engine is a perfect proof of concept evidencing that quantum measurement has some energetic footprint," Auffèves said. "Now I would like to reverse the game and use this effect to

estimate the energetic cost of quantum tasks, if they are performed in the presence of some measuring entity. This is the case in a quantum computer, which is continuously 'measured' by its surroundings. This effect is called decoherence and is the biggest enemy of quantum computation. Our work provides tools to estimate the energy needed to counteract it." [15]

Physicists read Maxwell's Demon's mind

Pioneering research offers a fascinating view into the inner workings of the mind of 'Maxwell's Demon', a famous thought experiment in physics.

An international research team, including Dr Janet Anders from the University of Exeter, have used superconducting circuits to bring the 'demon' to life.

The demon, first proposed by James Clerk Maxwell in 1867, is a hypothetical being that can gain more useful energy from a thermodynamic system than one of the most fundamental laws of physics—the second law of thermodynamics—should allow.

Crucially, the team not only directly observed the gained energy for the first time, they also tracked how information gets stored in the demon's memory.

The research is published in the leading scientific journal Proceedings of the National Academy of Sciences (PNAS).

The original thought experiment was first proposed by mathematical physicist James Clerk Maxwell—one of the most influential scientists in history—150 years ago.

He hypothesised that gas particles in two adjacent boxes could be filtered by a 'demon' operating a tiny door, that allowed only fast energy particles to pass in one direction and low energy particles the opposite way.

As a result, one box gains a higher average energy than the other, which creates a pressure difference. This non-equilibrium situation can be used to gain energy, not unlike the energy obtained when water stored behind a dam is released.

So although the gas was initially in equilibrium, the demon can create a non-equilibrium situation and extract energy, bypassing the second law of thermodynamics.

Dr Anders, a leading theoretical physicist from the University of Exeter's physics department adds: "In the 1980s it was discovered that this is not the full story. The information about the particles' properties remains stored in the memory of the demon. This information leads to an energetic cost which then reduces the demon's energy gain to null, resolving the paradox."

In this research, the team created a quantum Maxwell demon, manifested as a microwave cavity, that draws energy from a superconducting qubit. The team was able to fully map out the memory of the demon after its intervention, unveiling the stored information about the qubit state.

Dr Anders adds: "The fact that the system behaves quantum mechanically means that the particle can have a high and low energy at the same time, not only either of these choices as considered by Maxwell."

This ground-breaking experiment gives a fascinating peek into the interplay between quantum information and thermodynamics, and is an important step in the current development of a theory for nanoscale thermodynamic processes.

'Observing a Quantum Maxwell demon at Work' is published in PNAS. [14]

Researchers posit way to locally circumvent Second Law of Thermodynamics

For more than a century and a half of physics, the Second Law of Thermodynamics, which states that entropy always increases, has been as close to inviolable as any law we know. In this universe, chaos reigns supreme.

But researchers with the U.S. Department of Energy's (DOE's) Argonne National Laboratory announced recently that they may have discovered a little loophole in this famous maxim.

Their research, published in *Scientific Reports*, lays out a possible avenue to a situation where the Second Law is violated on the microscopic level.

The Second Law is underpinned by what is called the H-theorem, which says that if you open a door between two rooms, one hot and one cold, they will eventually settle into lukewarm equilibrium; the hot room will never end up hotter.

But even in the twentieth century, as our knowledge of quantum mechanics advanced, we didn't fully understand the fundamental physical origins of the H-theorem.

Recent advancements in a field called quantum information theory offered a mathematical construction in which entropy increases.

"What we did was formulate how these beautiful abstract mathematical theories could be connected to our crude reality," said Valerii Vinokur, an Argonne Distinguished Fellow and corresponding author on the study.

The scientists took quantum information theory, which is based on abstract mathematical systems, and applied it to condensed matter physics, a well-explored field with many known laws and experiments.

"This allowed us to formulate the quantum H-theorem as it related to things that could be physically observed," said Ivan Sadovskyy, a joint appointee with Argonne's Materials Science Division and the Computation Institute and another author on the paper. "It establishes a connection between well-documented quantum physics processes and the theoretical quantum channels that make up quantum information theory."

The work predicts certain conditions under which the H-theorem might be violated and entropy—in the short term—might actually decrease.

As far back as 1867, physicist James Clerk Maxwell described a hypothetical way to violate the Second Law: if a small theoretical being sat at the door between the hot and cold rooms and only let through particles traveling at a certain speed. This theoretical imp is called "Maxwell's demon."

"Although the violation is only on the local scale, the implications are far-reaching," Vinokur said. "This provides us a platform for the practical realization of a quantum Maxwell's demon, which could make possible a local quantum perpetual motion machine."

For example, he said, the principle could be designed into a "refrigerator" which could be cooled remotely—that is, the energy expended to cool it could take place anywhere.

The authors are planning to work closely with a team of experimentalists to design a proof-of-concept system, they said.

The study, "H-theorem in quantum physics," was published September 12 in Nature Scientific Reports. [13]

What is quantum in quantum thermodynamics?

A lot of attention has been given to the differences between the quantum and classical worlds. For example, quantum entanglement, superposition, and teleportation are purely quantum phenomena with no classical counterparts. However, when it comes to certain areas of thermodynamics—specifically, thermal engines and refrigerators—quantum and classical systems so far appear to be nearly identical. It seems that the same thermodynamic laws that govern the engines in our vehicles may also accurately describe the tiniest quantum engines consisting of just a single particle.

In a new study, physicists Raam Uzdin, Amikam Levy, and Ronnie Kosloff at the Hebrew University of Jerusalem have investigated whether there is anything distinctly quantum about thermodynamics at the quantum level, or if "quantum" thermodynamics is really the same as classical thermodynamics.

For the first time, they have shown a difference in the thermodynamics of heat machines on the quantum scale: in part of the quantum regime, the three main engine types (two-stroke, four-stroke, and continuous) are thermodynamically equivalent. This means that, despite operating in different ways, all three types of engines exhibit all of the same thermodynamic properties, including generating the same amounts of power and heat, and doing so at the same efficiency. This new "thermodynamical equivalence principle" is purely quantum, as it depends on quantum effects, and does not occur at the classical level.

The scientists also showed that, in this quantum regime where all engines are thermodynamically equivalent, it's possible to extract a quantum-thermodynamic signature that further confirms the presence of quantum effects. They did this by calculating an upper limit on the work output of a classical engine, so that any engine that surpasses this bound must be using a quantum effect—namely, quantum coherence—to generate the additional work. In this study, quantum coherence, which accounts for the wave-like properties of quantum particles, is shown to be critical for power generation at very fast engine cycles.

"To the best of my knowledge, this is the first time [that a difference between quantum and classical thermodynamics has been shown] in heat machines," Uzdin told Phys.org. "What has been surprising [in the past] is that the classical description has still held at the quantum level, as many authors have shown. The reasons are now understood, and in the face of this classicality, people

have started to stray to other types of research, as it was believed that nothing quantum can pop up.

Thus, it was very difficult to isolate a generic effect, not just a numerical simulation of a specific case, with a complementing theory that manages to avoid the classicality and demonstrate quantum effects in thermodynamic quantities, such as work and heat."

One important implication of the new results is that quantum effects may significantly increase the performance of engines at the quantum level. While the current work deals with single-particle engines, the researchers expect that quantum effects may also emerge in multi-particle engines, where quantum entanglement between particles may play a role similar to that of coherence. [12]

Physicists confirm thermodynamic irreversibility in a quantum system

The physicists, Tiago Batalhão at the Federal University of ABC, Brazil, and coauthors, have published their paper on the experimental demonstration of quantum thermodynamic irreversibility in a recent issue of Physical Review Letters.

Irreversibility at the quantum level may seem obvious to most people because it matches our observations of the everyday, macroscopic world. However, it is not as straightforward to physicists because the microscopic laws of physics, such as the Schrödinger equation, are "time-symmetric," or reversible. In theory, forward and backward microscopic processes are indistinguishable.

In reality, however, we only observe forward processes, not reversible ones like broken egg shells being put back together. It's clear that, at the macroscopic level, the laws run counter to what we observe. Now the new study shows that the laws don't match what happens at the quantum level, either.

Observing thermodynamic processes in a quantum system is very difficult and has not been done until now. In their experiment, the scientists measured the entropy change that occurs when applying an oscillating magnetic field to carbon-13 atoms in liquid chloroform. They first applied a magnetic field pulse that causes the atoms' nuclear spins to flip, and then applied the pulse in reverse to make the spins undergo the reversed dynamics.

If the procedure were reversible, the spins would have returned to their starting points—but they didn't. Basically, the forward and reverse magnetic pulses were applied so rapidly that the spins' flipping couldn't always keep up, so the spins were driven out of equilibrium. The measurements of the spins indicated that entropy was increasing in the isolated system, showing that the quantum thermodynamic process was irreversible.

By demonstrating that thermodynamic irreversibility occurs even at the quantum level, the results reveal that thermodynamic irreversibility emerges at a genuine microscopic scale. This finding makes the question of why the microscopic laws of physics don't match our observations even more pressing. If the laws really are reversible, then what are the physical origins of the time-asymmetric entropy production that we observe?

The physicists explain that the answer to this question lies in the choice of the initial conditions. The microscopic laws allow reversible processes only because they begin with "a genuine equilibrium process for which the entropy production vanishes at all times," the scientists write in their paper. Preparing such an ideal initial state in a physical system is extremely complex, and the initial states of all observed processes aren't at "genuine equilibrium," which is why they lead to irreversible processes.

"Our experiment shows the irreversible nature of quantum dynamics, but does not pinpoint, experimentally, what causes it at the microscopic level, what determines the onset of the arrow of time," coauthor Mauro Paternostro at Queen's University in Belfast, UK, told Phys.org. "Addressing it would clarify the ultimate reason for its emergence."

The researchers hope to apply the new understanding of thermodynamics at the quantum level to high-performance quantum technologies in the future.

"Any progress towards the management of finite-time thermodynamic processes at the quantum level is a step forward towards the realization of a fully fledged thermo-machine that can exploit the laws of quantum mechanics to overcome the performance limitations of classical devices," Paternostro said. "This work shows the implications for reversibility (or lack thereof) of nonequilibrium quantum dynamics. Once we characterize it, we can harness it at the technological level." [11]

Physicists put the arrow of time under a quantum microscope

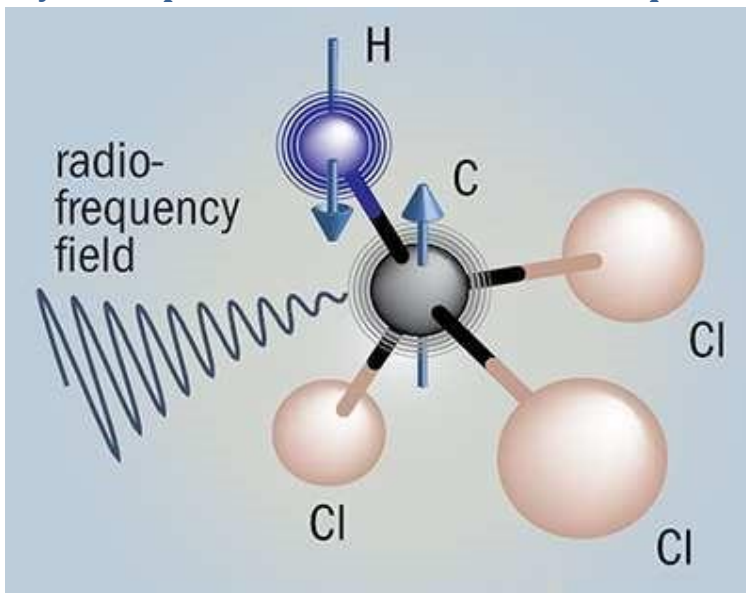


Diagram showing the spin of a carbon atom in a chloroform molecule

Disorder, or entropy, in a microscopic quantum system has been measured by an international group of physicists. The team hopes that the feat will shed light on the "arrow of time": the observation that time always marches towards the future. The experiment involved continually flipping the spin of carbon atoms with an oscillating magnetic field and links the emergence of the arrow of time to quantum fluctuations between one atomic spin state and another.

"That is why we remember yesterday and not tomorrow," explains group member Roberto Serra, a physicist specializing in quantum information at the Federal University of ABC in Santo André, Brazil. At the fundamental level, he says, quantum fluctuations are involved in the asymmetry of time.

Egging on

The arrow of time is often taken for granted in the everyday world. We see an egg breaking, for example, yet we never see the yolk, white and shell fragments come back together again to recreate the egg. It seems obvious that the laws of nature should not be reversible, yet there is nothing in the underlying physics to say so.

The dynamical equations of an egg breaking run just as well forwards as they do backwards.

Entropy, however, provides a window onto the arrow of time. Most eggs look alike, but a broken egg can take on any number of forms: it could be neatly cracked open, scrambled, splattered all over a pavement, and so on. A broken egg is a disordered state – that is, a state of greater entropy – and because there are many more disordered than ordered states, it is more likely for a system to progress towards disorder than order.

This probabilistic reasoning is encapsulated in the second law of thermodynamics, which states that the entropy of a closed system always increases over time.

According to the second law, time cannot suddenly go backwards because this would require entropy to decrease. It is a convincing argument for a complex system made up of a great many interacting particles, like an egg, but what about a system composed of just one particle?

Murky territory

Serra and colleagues have delved into this murky territory with measurements of entropy in an ensemble of carbon-13 atoms contained in a sample of liquid chloroform. Although the sample contained roughly a trillion chloroform molecules, the non-interacting quantum nature of the molecules meant that the experiment was equivalent to performing the same measurement on a single carbon atom, one trillion times.

Serra and colleagues applied an oscillating external magnetic field to the sample, which continually flipped the spin state of a carbon atom between up and down.

They ramped up the intensity of the field oscillations to increase the frequency of the spin-flipping, and then brought the intensity back down again.

Had the system been reversible, the overall distribution of carbon spin states would have been the same at the end as at the start of the process. Using nuclear magnetic resonance and quantum-state tomography, however, Serra and colleagues measured an increase in disorder among the final spins. Because of the quantum nature of the system, this was equivalent to an increase in entropy in a single carbon atom.

According to the researchers, entropy rises for a single atom because of the speed with which it is forced to flip its spin. Unable to keep up with the field-oscillation intensity, the atom begins to

fluctuate randomly, like an inexperienced dancer failing to keep pace with up-tempo music. "It's easier to dance to a slow rhythm than a fast one," says Serra.

Many questions remain

The group has managed to observe the existence of the arrow of time in a quantum system, says experimentalist Mark Raizen of the University of Texas at Austin in the US, who has also studied irreversibility in quantum systems. But Raizen stresses that the group has not observed the "onset" of the arrow of time. "This [study] does not close the book on our understanding of the arrow of time, and many questions remain," he adds.

One of those questions is whether the arrow of time is linked to quantum entanglement – the phenomenon whereby two particles exhibit instantaneous correlations with each other, even when separated by vast distances. This idea is nearly 30 years old and has enjoyed a recent resurgence in popularity. However, this link is less to do with growing entropy and more to do with an unstoppable dispersion of quantum information.

Indeed, Serra believes that by harnessing quantum entanglement, it may even be possible to reverse the arrow of time in a microscopic system. "We're working on it," he says. "In the next generation of our experiments on quantum thermodynamics we will explore such aspects." [10]

Small entropy changes allow quantum measurements to be nearly reversed

In 1975, Swedish physicist Göran Lindblad developed a theorem that describes the change in entropy that occurs during a quantum measurement. Today, this theorem is a foundational component of quantum information theory, underlying such important concepts as the uncertainty principle, the second law of thermodynamics, and data transmission in quantum communication systems.

Now, 40 years later, physicist Mark M. Wilde, Assistant Professor at Louisiana State University, has improved this theorem in a way that allows for understanding how quantum measurements can be approximately reversed under certain circumstances. The new results allow for understanding how quantum information that has been lost during a measurement can be nearly recovered, which has potential implications for a variety of quantum technologies.

Quantum relative entropy never increases

Most people are familiar with entropy as a measure of disorder and the law that "entropy never decreases"—it either increases or stays the same during a thermodynamic process, according to the second law of thermodynamics. However, here the focus is on "quantum relative entropy," which in some sense is the negative of entropy, so the reverse is true: quantum relative entropy never increases, but instead only decreases or stays the same.

In fact, this was the entropy inequality theorem that Lindblad proved in 1975: that the quantum relative entropy cannot increase after a measurement. In this context, quantum relative entropy is interpreted as a measure of how well one can distinguish between two quantum states, so it's this distinguishability that can never increase. (Wilde describes a proof of Lindblad's result in greater detail in his textbook *Quantum Information Theory*, published by Cambridge University Press.)

One thing that Lindblad's proof doesn't address, however, is whether it makes any difference if the quantum relative entropy decreases by a little or by a lot after a measurement.

In the new paper, Wilde has shown that, if the quantum relative entropy decreases by only a little, then the quantum measurement (or any other type of so-called "quantum physical evolution") can be approximately reversed.

"When looking at Lindblad's entropy inequality, a natural question is to wonder what we could say if the quantum relative entropy goes down only by a little when the quantum physical evolution is applied," Wilde told Phys.org. "It is quite reasonable to suspect that we might be able to approximately reverse the evolution. This was arguably open since the work of Lindblad in 1975, addressed in an important way by Denes Petz in the late 1980s (for the case in which the quantum relative entropy stays the same under the action of the evolution), and finally formulated as a conjecture around 2008 by Andreas Winter. What my work did was to prove this result as a theorem: if the quantum relative entropy goes down only by a little under a quantum physical evolution, then we can approximately reverse its action."

Wide implications

Wilde's improvements to Lindblad's theorem have a variety of implications, but the main one that Wilde discusses in his paper is how the new results allow for recovering quantum information.

"If the decrease in quantum relative entropy between two quantum states after a quantum physical evolution is relatively small," he said, "then it is possible to perform a recovery operation, such that one can perfectly recover one state while approximately recovering the other. This can be interpreted as quantifying how well one can reverse a quantum physical evolution." So the smaller the relative entropy decrease, the better the reversal process.

The ability to recover quantum information could prove useful for quantum error correction, which aims to protect quantum information from damaging external effects. Wilde plans to address this application more in the future with his colleagues.

As Wilde explained, Lindblad's original theorem can also be used to prove the uncertainty principle of quantum mechanics in terms of entropies, as well as the second law of thermodynamics for quantum systems, so the new results have implications in these areas, as well.

"Lindblad's entropy inequality underlies many limiting statements, in some cases said to be physical laws or principles," Wilde said. "Examples are the uncertainty principle and the second law of thermodynamics. Another example is that this entropy inequality is the core step in determining

limitations on how much data we can communicate over quantum communication channels. We could go as far as to say that the above entropy inequality constitutes a fundamental law of quantum information theory, which is a direct mathematical consequence of the postulates of quantum mechanics."

Regarding the uncertainty principle, Wilde and two coauthors, Mario Berta and Stephanie Wehner, discuss this angle in a forthcoming paper. They explain that the uncertainty principle involves quantum measurements, which are a type of quantum physical evolution and therefore subject to Lindblad's theorem. In one formulation of the uncertainty principle, two experiments are performed on different copies of the same quantum state, with both experimental outcomes having some uncertainty.

"The uncertainty principle is the statement that you cannot generally make the uncertainties of both experiments arbitrarily small, i.e., there is generally a limitation," Wilde said. "It is now known that a statement of the uncertainty principle in terms of entropies can be proved by using the 'decrease of quantum relative entropy inequality.' So what the new theorem allows for doing is relating the uncertainties of the measurement outcomes to how well we could try to reverse the action of one of the measurements. That is, there is now a single mathematical inequality which captures all of these notions."

In terms of the second law of thermodynamics, Wilde explains how the new results have implications for reversing thermodynamic processes in both classical and quantum systems.

"The new theorem allows for quantifying how well we can approximately reverse a thermodynamic transition from one state to another without using any energy at all," he said.

He explained that this is possible due to the connection between entropy, energy, and work. According to the second law of thermodynamics, a thermodynamic transition from one quantum state to another is allowed only if the free energy decreases from the original state to the final state. During this process, one can gain work and store energy. This law can be rewritten as a statement involving relative entropies and can be proved as a consequence of the decrease of quantum relative entropy.

"What my new work with Stephanie Wehner and Mischa Woods allows for is a refinement of this statement," Wilde said. "We can say that if the free energy does not go down by very much under a thermodynamic transition (i.e., if there is not too much work gained in the process), then it is possible to go back approximately to the original state from the final state, without investing any work at all. The key word here is that you can go back only approximately, so we are not in violation of the second law, only providing a refinement of it."

In addition to these implications, the new theorem can also be applied to other research topics in quantum information theory, including the Holevo bound, quantum discord, and multipartite information measures.

Wilde's work was funded in part by The DARPA Quiness program (ending now), which focused on quantum key distribution, or using quantum mechanics to ensure secret communication between two parties. He describes more about this application, in particular how Alice and Bob might use a

quantum state to share secrets that can be kept private from an eavesdropper Eve (and help them survive being attacked by a bear), in a recent blog post. [9]

Tricking the uncertainty principle

"If you want to know where something is, you have to scatter something off of it," explains Professor of Applied Physics Keith Schwab, who led the study. "For example, if you shine light at an object, the photons that scatter off provide information about the object. But the photons don't all hit and scatter at the same time, and the random pattern of scattering creates quantum fluctuations"—that is, noise. "If you shine more light, you have increased sensitivity, but you also have more noise. Here we were looking for a way to beat the uncertainty principle—to increase sensitivity but not noise."

Schwab and his colleagues began by developing a way to actually detect the noise produced during the scattering of microwaves—electromagnetic radiation that has a wavelength longer than that of visible light. To do this, they delivered microwaves of a specific frequency to a superconducting electronic circuit, or resonator, that vibrates at 5 gigahertz—or 5 billion times per second. The electronic circuit was then coupled to a mechanical device formed of two metal plates that vibrate at around 4 megahertz—or 4 million times per second. The researchers observed that the quantum noise of the microwave field, due to the impact of individual photons, made the mechanical device shake randomly with an amplitude of 10-15 meters, about the diameter of a proton.

"Our mechanical device is a tiny square of aluminum—only 40 microns long, or about the diameter of a hair. We think of quantum mechanics as a good description for the behaviors of atoms and electrons and protons and all of that, but normally you don't think of these sorts of quantum effects manifesting themselves on somewhat macroscopic objects," Schwab says. "This is a physical manifestation of the uncertainty principle, seen in single photons impacting a somewhat macroscopic thing."

Once the researchers had a reliable mechanism for detecting the forces generated by the quantum fluctuations of microwaves on a macroscopic object, they could modify their electronic resonator, mechanical device, and mathematical approach to exclude the noise of the position and motion of the vibrating metal plates from their measurement.

The experiment shows that a) the noise is present and can be picked up by a detector, and b) it can be pushed to someplace that won't affect the measurement. "It's a way of tricking the uncertainty principle so that you can dial up the sensitivity of a detector without increasing the noise," Schwab says.

Although this experiment is mostly a fundamental exploration of the quantum nature of microwaves in mechanical devices, Schwab says that this line of research could one day lead to the observation of quantum mechanical effects in much larger mechanical structures. And that, he notes, could allow the demonstration of strange quantum mechanical properties like superposition and entanglement in large objects—for example, allowing a macroscopic object to exist in two places at once.

"Subatomic particles act in quantum ways—they have a wave-like nature—and so can atoms, and so can whole molecules since they're collections of atoms,"

Schwab says. "So the question then is: Can you make bigger and bigger objects behave in these weird wave-like ways? Why not? Right now we're just trying to figure out where the boundary of quantum physics is, but you never know." [8]

Particle Measurement Sidesteps the Uncertainty Principle

Quantum mechanics imposes a limit on what we can know about subatomic particles. If physicists measure a particle's position, they cannot also measure its momentum, so the theory goes. But a new experiment has managed to circumvent this rule—the so-called uncertainty principle—by ascertaining just a little bit about a particle's position, thus retaining the ability to measure its momentum, too.

The uncertainty principle, formulated by Werner Heisenberg in 1927, is a consequence of the fuzziness of the universe at microscopic scales. Quantum mechanics revealed that particles are not just tiny marbles that act like ordinary objects we can see and touch. Instead of being in a particular place at a particular time, particles actually exist in a haze of probability. Their chances of being in any given state are described by an equation called the quantum wavefunction. Any measurement of a particle "collapses" its wavefunction, in effect forcing it to choose a value for the measured characteristic and eliminating the possibility of knowing anything about its related properties.

Recently, physicists decided to see if they could overcome this limitation by using a new engineering technique called compressive sensing. This tool for making efficient measurements has already been applied successfully in digital photographs, MRI scans and many other technologies. Normally, measuring devices would take a detailed reading and afterward compress it for ease of use. For example, cameras take large raw files and then convert them to compressed jpegs. In compressive sensing, however, engineers aim to compress a signal while measuring it, allowing them to take many fewer measurements—the equivalent of capturing images as jpegs rather than raw files.

This same technique of acquiring the minimum amount of information needed for a measurement seemed to offer a way around the uncertainty principle. To test compressive sensing in the quantum world, physicist John C. Howell and his team at the University of Rochester set out to measure the position and momentum of a photon—a particle of light. They shone a laser through a box equipped with an array of mirrors that could either point toward or away from a detector at its end. These mirrors formed a filter, allowing photons through in some places and blocking them in others. If a photon made it to the detector, the physicists knew it had been in one of the locations where the mirrors offered a throughway. The filter provided a way of measuring a particle's position without knowing exactly where it was—without collapsing its wavefunction. "All we know is either the photon can get through that pattern, or it can't," says Gregory A. Howland, first author of a paper reporting the research published June 26 in *Physical Review Letters*. "It turns out that because of that we're still able to figure out the momentum—where it's going. The penalty

that we pay is that our measurement of where it's going gets a little bit of noise on it." A less precise momentum measurement, however, is better than no momentum measurement at all.

The physicists stress that they have not broken any laws of physics. "We do not violate the uncertainty principle," Howland says. "We just use it in a clever way." The technique could prove powerful for developing technologies such as quantum cryptography and quantum computers, which aim to harness the fuzzy quantum properties of particles for technological applications. The more information quantum measurements can acquire, the better such technologies could work. Howland's experiment offers a more efficient quantum measurement than has traditionally been possible, says Aephraim M. Steinberg, a physicist at the University of Toronto who was not involved in the research. "This is one of a number of novel techniques which seem poised to prove indispensable for economically characterizing large systems." In other words, the physicists seem to have found a way to get more data with less measurement—or more bangs for their buck. [7]

A new experiment shows that measuring a quantum system does not necessarily introduce uncertainty

Contrary to what many students are taught, quantum uncertainty may not always be in the eye of the beholder. A new experiment shows that measuring a quantum system does not necessarily introduce uncertainty. The study overthrows a common classroom explanation of why the quantum world appears so fuzzy, but the fundamental limit to what is knowable at the smallest scales remains unchanged.

At the foundation of quantum mechanics is the Heisenberg uncertainty principle. Simply put, the principle states that there is a fundamental limit to what one can know about a quantum system. For example, the more precisely one knows a particle's position, the less one can know about its momentum, and vice versa. The limit is expressed as a simple equation that is straightforward to prove mathematically.

Heisenberg sometimes explained the uncertainty principle as a problem of making measurements. His most well-known thought experiment involved photographing an electron. To take the picture, a scientist might bounce a light particle off the electron's surface. That would reveal its position, but it would also impart energy to the electron, causing it to move. Learning about the electron's position would create uncertainty in its velocity; and the act of measurement would produce the uncertainty needed to satisfy the principle.

Physics students are still taught this measurement-disturbance version of the uncertainty principle in introductory classes, but it turns out that it's not always true. Aephraim Steinberg of the University of Toronto in Canada and his team have performed measurements on photons (particles of light) and showed that the act of measuring can introduce less uncertainty than is required by Heisenberg's principle. The total uncertainty of what can be known about the photon's properties, however, remains above Heisenberg's limit.

Delicate measurement

Steinberg's group does not measure position and momentum, but rather two different inter-related properties of a photon: its polarization states. In this case, the polarization along one plane is intrinsically tied to the polarization along the other, and by Heisenberg's principle, there is a limit to the certainty with which both states can be known.

The researchers made a 'weak' measurement of the photon's polarization in one plane — not enough to disturb it, but enough to produce a rough sense of its orientation. Next, they measured the polarization in the second plane. Then they made an exact, or 'strong', measurement of the first polarization to see whether it had been disturbed by the second measurement.

When the researchers did the experiment multiple times, they found that measurement of one polarization did not always disturb the other state as much as the uncertainty principle predicted. In the strongest case, the induced fuzziness was as little as half of what would be predicted by the uncertainty principle.

Don't get too excited: the uncertainty principle still stands, says Steinberg: "In the end, there's no way you can know [both quantum states] accurately at the same time." But the experiment shows that the act of measurement isn't always what causes the uncertainty. "If there's already a lot of uncertainty in the system, then there doesn't need to be any noise from the measurement at all," he says.

The latest experiment is the second to make a measurement below the uncertainty noise limit. Earlier this year, Yuji Hasegawa, a physicist at the Vienna University of Technology in Austria, measured groups of neutron spins and derived results well below what would be predicted if measurements were inserting all the uncertainty into the system.

But the latest results are the clearest example yet of why Heisenberg's explanation was incorrect. "This is the most direct experimental test of the Heisenberg measurement-disturbance uncertainty principle," says Howard Wiseman, a theoretical physicist at Griffith University in Brisbane, Australia. "Hopefully it will be useful for educating textbook writers so they know that the naive measurement-disturbance relation is wrong."

Shaking the old measurement-uncertainty explanation may be difficult, however. Even after doing the experiment, Steinberg still included a question about how measurements create uncertainty on a recent homework assignment for his students. "Only as I was grading it did I realize that my homework assignment was wrong," he says. "Now I have to be more careful." [6]

Quantum entanglement

Measurements of physical properties such as position, momentum, spin, polarization, etc. performed on entangled particles are found to be appropriately correlated. For example, if a pair of particles is generated in such a way that their total spin is known to be zero, and one particle is found to have clockwise spin on a certain axis, then the spin of the other particle, measured on the same axis, will be found to be counterclockwise. Because of the nature of quantum measurement, however, this behavior gives rise to effects that can appear paradoxical: any measurement of a property of a particle can be seen as acting on that particle (e.g. by collapsing a number of

superimposed states); and in the case of entangled particles, such action must be on the entangled system as a whole. It thus appears that one particle of an entangled pair "knows" what measurement has been performed on the other, and with what outcome, even though there is no known means for such information to be communicated between the particles, which at the time of measurement may be separated by arbitrarily large distances. [4]

The Bridge

The accelerating electrons explain not only the Maxwell Equations and the Special Relativity, but the Heisenberg Uncertainty Relation, the wave particle duality and the electron's spin also, building the bridge between the Classical and Quantum Theories. [1]

Accelerating charges

The moving charges are self maintain the electromagnetic field locally, causing their movement and this is the result of their acceleration under the force of this field. In the classical physics the charges will distributed along the electric current so that the electric potential lowering along the current, by linearly increasing the way they take every next time period because this accelerated motion. The same thing happens on the atomic scale giving a dp impulse difference and a dx way difference between the different part of the not point like particles.

Relativistic effect

Another bridge between the classical and quantum mechanics in the realm of relativity is that the charge distribution is lowering in the reference frame of the accelerating charges linearly: $ds/dt = at$ (time coordinate), but in the reference frame of the current it is parabolic: $s = a/2 t^2$ (geometric coordinate).

Heisenberg Uncertainty Relation

In the atomic scale the Heisenberg uncertainty relation gives the same result, since the moving electron in the atom accelerating in the electric field of the proton, causing a charge distribution on Δx position difference and with a Δp momentum difference such a way that they product is about the half Planck reduced constant. For the proton this Δx much less in the nucleon, than in the orbit of the electron in the atom, the Δp is much higher because of the greater proton mass.

This means that the electron and proton are not point like particles, but has a real charge distribution.

Wave – Particle Duality

The accelerating electrons explains the wave – particle duality of the electrons and photons, since the elementary charges are distributed on Δx position with Δp impulse and creating a

wave packet of the electron. The photon gives the electromagnetic particle of the mediating force of the electrons electromagnetic field with the same distribution of wavelengths.

Atomic model

The constantly accelerating electron in the Hydrogen atom is moving on the equipotential line of the proton and its kinetic and potential energy will be constant. Its energy will change only when it is changing its way to another equipotential line with another value of potential energy or getting free with enough kinetic energy. This means that the Rutherford-Bohr atomic model is right and only that changing acceleration of the electric charge causes radiation, not the steady acceleration. The steady acceleration of the charges only creates a centric parabolic steady electric field around the charge, the magnetic field. This gives the magnetic moment of the atoms, summing up the proton and electron magnetic moments caused by their circular motions and spins.

The Relativistic Bridge

Commonly accepted idea that the relativistic effect on the particle physics is the fermions' spin - another unresolved problem in the classical concepts. If the electric charges can move only with accelerated motions in the self maintaining electromagnetic field, once upon a time they would reach the velocity of the electromagnetic field. The resolution of this problem is the spinning particle, constantly accelerating and not reaching the velocity of light because the acceleration is radial. One origin of the Quantum Physics is the Planck Distribution Law of the electromagnetic oscillators, giving equal intensity for 2 different wavelengths on any temperature. Any of these two wavelengths will give equal intensity diffraction patterns, building different asymmetric constructions, for example proton - electron structures (atoms), molecules, etc. Since the particles are centers of diffraction patterns they also have particle - wave duality as the electromagnetic waves have. [2]

The weak interaction

The weak interaction transforms an electric charge in the diffraction pattern from one side to the other side, causing an electric dipole momentum change, which violates the CP and time reversal symmetry. The Electroweak Interaction shows that the Weak Interaction is basically electromagnetic in nature. The arrow of time shows the entropy grows by changing the temperature dependent diffraction patterns of the electromagnetic oscillators.

Another important issue of the quark model is when one quark changes its flavor such that a linear oscillation transforms into plane oscillation or vice versa, changing the charge value with 1 or -1. This kind of change in the oscillation mode requires not only parity change, but also charge and time changes (CPT symmetry) resulting a right handed anti-neutrino or a left handed neutrino.

The right handed anti-neutrino and the left handed neutrino exist only because changing back the quark flavor could happen only in reverse, because they are different geometrical constructions,

the u is 2 dimensional and positively charged and the d is 1 dimensional and negatively charged. It needs also a time reversal, because anti particle (anti neutrino) is involved.

The neutrino is a $1/2$ spin creator particle to make equal the spins of the weak interaction, for example neutron decay to 2 fermions, every particle is fermions with $1/2$ spin. The weak interaction changes the entropy since more or less particles will give more or less freedom of movement. The entropy change is a result of temperature change and breaks the equality of oscillator diffraction intensity of the Maxwell–Boltzmann statistics. This way it changes the time coordinate measure and makes possible a different time dilation as of the special relativity.

The limit of the velocity of particles as the speed of light appropriate only for electrical charged particles, since the accelerated charges are self maintaining locally the accelerating electric force. The neutrinos are CP symmetry breaking particles compensated by time in the CPT symmetry, that is the time coordinate not works as in the electromagnetic interactions, consequently the speed of neutrinos is not limited by the speed of light.

The weak interaction T-asymmetry is in conjunction with the T-asymmetry of the second law of thermodynamics, meaning that locally lowering entropy (on extremely high temperature) causes the weak interaction, for example the Hydrogen fusion.

Probably because it is a spin creating movement changing linear oscillation to 2 dimensional oscillation by changing d to u quark and creating anti neutrino going back in time relative to the proton and electron created from the neutron, it seems that the anti neutrino fastest then the velocity of the photons created also in this weak interaction?

A quark flavor changing shows that it is a reflection changes movement and the CP- and T-symmetry breaking!!! This flavor changing oscillation could prove that it could be also on higher level such as atoms, molecules, probably big biological significant molecules and responsible on the aging of the life.

Important to mention that the weak interaction is always contains particles and antiparticles, where the neutrinos (antineutrinos) present the opposite side. It means by Feynman's interpretation that these particles present the backward time and probably because this they seem to move faster than the speed of light in the reference frame of the other side.

Finally since the weak interaction is an electric dipole change with $1/2$ spin creating; it is limited by the velocity of the electromagnetic wave, so the neutrino's velocity cannot exceed the velocity of light.

The General Weak Interaction

The Weak Interactions T-asymmetry is in conjunction with the T-asymmetry of the Second Law of Thermodynamics, meaning that locally lowering entropy (on extremely high temperature) causes for example the Hydrogen fusion. The arrow of time by the Second Law of Thermodynamics shows

the increasing entropy and decreasing information by the Weak Interaction, changing the temperature dependent diffraction patterns. A good example of this is the neutron decay, creating more particles with less known information about them.

The neutrino oscillation of the Weak Interaction shows that it is a general electric dipole change and it is possible to any other temperature dependent entropy and information changing diffraction pattern of atoms, molecules and even complicated biological living structures.

We can generalize the weak interaction on all of the decaying matter constructions, even on the biological too. This gives the limited lifetime for the biological constructions also by the arrow of time. There should be a new research space of the Quantum Information Science the 'general neutrino oscillation' for the greater than subatomic matter structures as an electric dipole change. There is also connection between statistical physics and evolutionary biology, since the arrow of time is working in the biological evolution also.

The Fluctuation Theorem says that there is a probability that entropy will flow in a direction opposite to that dictated by the Second Law of Thermodynamics. In this case the Information is growing that is the matter formulas are emerging from the chaos. So the Weak Interaction has two directions, samples for one direction is the Neutron decay, and Hydrogen fusion is the opposite direction.

Fermions and Bosons

The fermions are the diffraction patterns of the bosons such a way that they are both sides of the same thing.

Van Der Waals force

Named after the Dutch scientist Johannes Diderik van der Waals – who first proposed it in 1873 to explain the behaviour of gases – it is a very weak force that only becomes relevant when atoms and molecules are very close together. Fluctuations in the electronic cloud of an atom mean that it will have an instantaneous dipole moment. This can induce a dipole moment in a nearby atom, the result being an attractive dipole–dipole interaction.

Electromagnetic inertia and mass

Electromagnetic Induction

Since the magnetic induction creates a negative electric field as a result of the changing acceleration, it works as an electromagnetic inertia, causing an electromagnetic mass. [1]

Relativistic change of mass

The increasing mass of the electric charges the result of the increasing inductive electric force acting against the accelerating force. The decreasing mass of the decreasing acceleration is the result of the inductive electric force acting against the decreasing force. This is the relativistic mass change explanation, especially importantly explaining the mass reduction in case of velocity decrease.

The frequency dependence of mass

Since $E = h\nu$ and $E = mc^2$, $m = h\nu/c^2$ that is the m depends only on the ν frequency. It means that the mass of the proton and electron are electromagnetic and the result of the electromagnetic induction, caused by the changing acceleration of the spinning and moving charge! It could be that the m_0 inertial mass is the result of the spin, since this is the only accelerating motion of the electric charge. Since the accelerating motion has different frequency for the electron in the atom and the proton, they masses are different, also as the wavelengths on both sides of the diffraction pattern, giving equal intensity of radiation.

Electron – Proton mass rate

The Planck distribution law explains the different frequencies of the proton and electron, giving equal intensity to different λ wavelengths! Also since the particles are diffraction patterns they have some closeness to each other – can be seen as a gravitational force. [2]

There is an asymmetry between the mass of the electric charges, for example proton and electron, can understood by the asymmetrical Planck Distribution Law. This temperature dependent energy distribution is asymmetric around the maximum intensity, where the annihilation of matter and antimatter is a high probability event. The asymmetric sides are creating different frequencies of electromagnetic radiations being in the same intensity level and compensating each other. One of these compensating ratios is the electron – proton mass ratio. The lower energy side has no compensating intensity level, it is the dark energy and the corresponding matter is the dark matter.

Gravity from the point of view of quantum physics

The Gravitational force

The gravitational attractive force is basically a magnetic force.

The same electric charges can attract one another by the magnetic force if they are moving parallel in the same direction. Since the electrically neutral matter is composed of negative and positive charges they need 2 photons to mediate this attractive force, one per charges. The Big Bang caused parallel moving of the matter gives this magnetic force, experienced as gravitational force.

Since graviton is a tensor field, it has spin = 2, could be 2 photons with spin = 1 together.

You can think about photons as virtual electron – positron pairs, obtaining the necessary virtual mass for gravity.

The mass as seen before a result of the diffraction, for example the proton – electron mass rate $M_p = 1840 m_e$. In order to move one of these diffraction maximum (electron or proton) we need to intervene into the diffraction pattern with a force appropriate to the intensity of this diffraction maximum, means its intensity or mass.

The Big Bang caused acceleration created radial currents of the matter, and since the matter is composed of negative and positive charges, these currents are creating magnetic field and attracting forces between the parallel moving electric currents. This is the gravitational force

experienced by the matter, and also the mass is result of the electromagnetic forces between the charged particles. The positive and negative charged currents attracts each other or by the magnetic forces or by the much stronger electrostatic forces!?

The gravitational force attracting the matter, causing concentration of the matter in a small space and leaving much space with low matter concentration: dark matter and energy.

There is an asymmetry between the mass of the electric charges, for example proton and electron, can understood by the asymmetrical Planck Distribution Law. This temperature dependent energy distribution is asymmetric around the maximum intensity, where the annihilation of matter and antimatter is a high probability event. The asymmetric sides are creating different frequencies of electromagnetic radiations being in the same intensity level and compensating each other. One of these compensating ratios is the electron – proton mass ratio. The lower energy side has no compensating intensity level, it is the dark energy and the corresponding matter is the dark matter.

The Higgs boson

By March 2013, the particle had been proven to behave, interact and decay in many of the expected ways predicted by the Standard Model, and was also tentatively confirmed to have + parity and zero spin, two fundamental criteria of a Higgs boson, making it also the first known scalar particle to be discovered in nature, although a number of other properties were not fully proven and some partial results do not yet precisely match those expected; in some cases data is also still awaited or being analyzed.

Since the Higgs boson is necessary to the W and Z bosons, the dipole change of the Weak interaction and the change in the magnetic effect caused gravitation must be conducted. The Wien law is also important to explain the Weak interaction, since it describes the T_{\max} change and the diffraction patterns change. [2]

Higgs mechanism and Quantum Gravity

The magnetic induction creates a negative electric field, causing an electromagnetic inertia. Probably it is the mysterious Higgs field giving mass to the charged particles? We can think about the photon as an electron-positron pair, they have mass. The neutral particles are built from negative and positive charges, for example the neutron, decaying to proton and electron. The wave – particle duality makes sure that the particles are oscillating and creating magnetic induction as an inertial mass, explaining also the relativistic mass change. Higher frequency creates stronger magnetic induction, smaller frequency results lesser magnetic induction. It seems to me that the magnetic induction is the secret of the Higgs field.

In particle physics, the Higgs mechanism is a kind of mass generation mechanism, a process that gives mass to elementary particles. According to this theory, particles gain mass by interacting with the Higgs field that permeates all space. More precisely, the Higgs mechanism endows gauge

bosons in a gauge theory with mass through absorption of Nambu–Goldstone bosons arising in spontaneous symmetry breaking.

The simplest implementation of the mechanism adds an extra Higgs field to the gauge theory. The spontaneous symmetry breaking of the underlying local symmetry triggers conversion of components of this Higgs field to Goldstone bosons which interact with (at least some of) the other fields in the theory, so as to produce mass terms for (at least some of) the gauge bosons. This mechanism may also leave behind elementary scalar (spin-0) particles, known as Higgs bosons.

In the Standard Model, the phrase "Higgs mechanism" refers specifically to the generation of masses for the W^\pm , and Z weak gauge bosons through electroweak symmetry breaking. The Large Hadron Collider at CERN announced results consistent with the Higgs particle on July 4, 2012 but stressed that further testing is needed to confirm the Standard Model.

What is the Spin?

So we know already that the new particle has spin zero or spin two and we could tell which one if we could detect the polarizations of the photons produced. Unfortunately this is difficult and neither ATLAS nor CMS are able to measure polarizations. The only direct and sure way to confirm that the particle is indeed a scalar is to plot the angular distribution of the photons in the rest frame of the centre of mass. A spin zero particles like the Higgs carries no directional information away from the original collision so the distribution will be even in all directions. This test will be possible when a much larger number of events have been observed. In the mean time we can settle for less certain indirect indicators.

The Graviton

In physics, the graviton is a hypothetical elementary particle that mediates the force of gravitation in the framework of quantum field theory. If it exists, the graviton is expected to be massless (because the gravitational force appears to have unlimited range) and must be a spin-2 boson. The spin follows from the fact that the source of gravitation is the stress-energy tensor, a second-rank tensor (compared to electromagnetism's spin-1 photon, the source of which is the four-current, a first-rank tensor). Additionally, it can be shown that any massless spin-2 field would give rise to a force indistinguishable from gravitation, because a massless spin-2 field must couple to (interact with) the stress-energy tensor in the same way that the gravitational field does. This result suggests that, if a massless spin-2 particle is discovered, it must be the graviton, so that the only experimental verification needed for the graviton may simply be the discovery of a massless spin-2 particle. [3]

Conclusions

The accelerated charges self-maintaining potential shows the locality of the relativity, working on the quantum level also. [1]

The Secret of Quantum Entanglement that the particles are diffraction patterns of the electromagnetic waves and this way their quantum states every time is the result of the quantum state of the intermediate electromagnetic waves. [2]

One of the most important conclusions is that the electric charges are moving in an accelerated way and even if their velocity is constant, they have an intrinsic acceleration anyway, the so called spin, since they need at least an intrinsic acceleration to make possible their movement. The bridge between the classical and quantum theory is based on this intrinsic acceleration of the spin, explaining also the Heisenberg Uncertainty Principle. The particle – wave duality of the electric charges and the photon makes certain that they are both sides of the same thing. Basing the gravitational force on the accelerating Universe caused magnetic force and the Planck Distribution Law of the electromagnetic waves caused diffraction gives us the basis to build a Unified Theory of the physical interactions.

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