## Footprints of Protein Synthesis

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Portland State University researchers have made a significant breakthrough by developing the 3-D structure of proteins from inside the eye lens that control how cells communicate with each other, which could open the door to treating diseases such as cataracts, stroke and cancer. [37]

A new computational model developed by researchers from The City College of New York and Yale gives a clearer picture of the structure and mechanics of soft, shape-changing cells that could provide a better understanding of cancerous tumor growth, wound healing, and embryonic development. [36]

A team of researchers at the Laboratory for fundamental BioPhotonics (LBP) within EPFL's School of Engineering (STI) has come up with a way to monitor changes in membrane potential and to observe ion fluxes by studying the behavior of the water HYPERLINK "https://phys.org/tags/molecules/" molecules surrounding the membranes of the HYPERLINK "https://phys.org/tags/neurons/" neurons. [35]

One recent measure to improve the visualization of the brain has been to create more comprehensive brain models that simulate neural activity. [34]

Brain-machine interfaces provide one way to connect with this puzzling organ system, including the brain. [33]

Measuring optical blood flow in the resting human brain to detect spontaneous activity has for the first time been demonstrated by Wright State University imaging researchers, holding out promise for a better way to study people with autism, Alzheimer's and depression. [32]

UCLA biologists report they have transferred a memory from one marine snail to another, creating an artificial memory, by injecting RNA from one to another. [31]

Scientists at the Wellcome Trust/ Cancer Research UK Gurdon Institute, University of Cambridge, have identified a new type of stem cell in the brain which they say has a high potential for repair following brain injury or disease. [30]

A team of researchers working at the Weizmann Institute of Science has found that organoids can be used to better understand how the human brain wrinkles as it develops. [29]

A team of biologists has found an unexpected source for the brain's development, a finding that offers new insights into the building of the nervous system. [28]

Researchers discover both the structure of specific brain areas and memory are linked to genetic activity that also play important roles in immune system function. [27]

The inner workings of the human brain have always been a subject of great interest. Unfortunately, it is fairly difficult to view brain structures or intricate tissues due to the fact that the skull is not transparent by design. [26]

But now there is a technology that enables us to "read the mind" with growing accuracy: functional magnetic resonance imaging (fMRI). [25]

Advances in microscopy techniques have often triggered important discoveries in the field of neuroscience, enabling vital insights in understanding the brain and promising new treatments for neurodegenerative diseases such as Alzheimer's and Parkinson's. [24]

What is the relationship of consciousness to the neurological activity of the brain? Does the brain behave differently when a person is fully conscious, when they are asleep, or when they are undergoing an epileptic seizure? [23]

Consciousness appears to arise naturally as a result of a brain maximizing its information content. So says a group of scientists in Canada and France, which has studied how the electrical activity in people's brains varies according to individuals' conscious states. The researchers find that normal waking states are associated with maximum values of what they call a brain's "entropy". [22]

New research published in the New Journal of Physics tries to decompose the structural layers of the cortical network to different hierarchies enabling to identify the network's nucleus, from which our consciousness could emerge. [21]

Where in your brain do you exist? Is your awareness of the world around you and of yourself as an individual the result of specific, focused changes in your brain, or does that awareness come from a broad network of neural activity? How does your brain produce awareness? [20]

In the future, level-tuned neurons may help enable neuromorphic computing systems to perform tasks that traditional computers cannot, such as learning from their environment, pattern recognition, and knowledge extraction from big data sources. [19]

*IBM scientists have created randomly spiking neurons using phase-change materials to store and process data. This demonstration marks a significant step forward in the* 

development of energy-efficient, ultra-dense integrated neuromorphic technologies for applications in cognitive computing. [18]

An ion trap with four segmented blade electrodes used to trap a linear chain of atomic ions for quantum information processing. Each ion is addressed optically for individual control and readout using the high optical access of the trap. [17]

To date, researchers have realised qubits in the form of individual electrons (aktuell.ruhr-uni-bochum.de/pm2012/pm00090.html.en). However, this led to interferences and rendered the information carriers difficult to programme and read. The group has solved this problem by utilising electron holes as qubits, rather than electrons. [16]

Physicists from MIPT and the Russian Quantum Center have developed an easier method to create a universal quantum computer using multilevel quantum systems (qudits), each one of which is able to work with multiple "conventional" quantum elements – qubits. [15]

*Precise atom implants in silicon provide a first step toward practical quantum computers.* [14]

A method to produce significant amounts of semiconducting nanoparticles for lightemitting displays, sensors, solar panels and biomedical applications has gained momentum with a demonstration by researchers at the Department of Energy's Oak Ridge National Laboratory. [13]

A source of single photons that meets three important criteria for use in quantuminformation systems has been unveiled in China by an international team of physicists. Based on a quantum dot, the device is an efficient source of photons that emerge as solo particles that are indistinguishable from each other. The researchers are now trying to use the source to create a quantum computer based on "boson sampling". [11]

With the help of a semiconductor quantum dot, physicists at the University of Basel have developed a new type of light source that emits single photons. For the first time, the researchers have managed to create a stream of identical photons. [10]

Optical photons would be ideal carriers to transfer quantum information over large distances. Researchers envisage a network where information is processed in certain nodes and transferred between them via photons. [9]

While physicists are continually looking for ways to unify the theory of relativity, which describes large-scale phenomena, with quantum theory, which describes small-scale phenomena, computer scientists are searching for technologies to build the quantum computer using Quantum Information.

In August 2013, the achievement of "fully deterministic" quantum teleportation, using a hybrid technique, was reported. On 29 May 2014, scientists announced a reliable way of

transferring data by quantum teleportation. Quantum teleportation of data had been done before but with highly unreliable methods.

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 and making possible to build the Quantum Computer with the help of Quantum Information.

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Author: George Rajna

## Preface

Where in your brain do you exist? Is your awareness of the world around you and of yourself as an individual the result of specific, focused changes in your brain, or does that awareness come from a broad network of neural activity? How does your brain produce awareness? [20]

While physicists are continually looking for ways to unify the theory of relativity, which describes large-scale phenomena, with quantum theory, which describes small-scale phenomena, computer scientists are searching for technologies to build the quantum computer.

Australian engineers detect in real-time the quantum spin properties of a pair of atoms inside a silicon chip, and disclose new method to perform quantum logic operations between two atoms. [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.

## Tracking the footprints of protein synthesis

To trace which proteins are produced and when, researchers say, just follow the ribosome "footprints."

Researchers are tracking these large molecular machines, following their trails of <u>protein</u> synthesis to determine how precisely cells produce their <u>protein components</u>. Building too few might upset growth, metabolism, and maintenance, while too many might be wasteful and potentially toxic. Whether <u>eukaryotic cells</u> tune their <u>gene expression</u> to produce just enough of each protein remains a longstanding question.

Bacteria appear to generate the exact levels needed to function—no more, no less. However, more <u>complex organisms</u> have different metabolic needs, means to control gene expression, and ways to eliminate unwanted proteins, perhaps engendering a different strategy to ensure correct protein levels. Using a combination of their own experiments and open access databases, a duo of scientists from the MIT Department of Biology aimed to establish how precisely cells from organisms like budding yeast, zebrafish, mice, and humans tune their <u>protein production</u>. Do these eukaryotic cells generate precise amounts of protein, or do they make roughly the correct amount and rely on processes like degradation to trim the excess?

To answer this question, the researchers refined an existing technique, known as ribosome profiling, to quantify the protein synthesis rates by tracking the ribosome footprints. They were intrigued to find that, for the proteins they studied, eukaryotes precisely tuned their protein production just like bacteria. Despite the fundamental differences between these organisms, they shared a basic strategy.

"We tend to think of gene expression as a production line, transforming genetic information into well-defined protein machines," says Gene-Wei Li, an assistant professor of biology and senior author of the study. "But in actuality, it's not yet clear whether all organisms or all cells operate under the same principles of protein production. The impetus of this study was to understand if proteins are made as precisely in eukaryotes as they are in bacteria, while also resolving ambiguities in existing methods for measuring protein synthesis rates."

Graduate student James Taggart was the first author of this study, which appears in the journal *Cell Systems* on Dec. 12.

### A clear case of proportional synthesis

In 2014, when Li was still a postdoc at the University of California at San Francisco, he and his colleagues set out to measure protein synthesis rates in bacteria. They examined the subunits of multi-protein complexes in Escherichia coli, and showed that the bacteria operated under laws of proportional synthesis—meaning they were generating proteins in the exact ratio needed for cellular function. If bacteria produce too much for some reason, a degradation pathway is activated to break down those subunits, but this process constitutes more of a failsafe than the primary means to regulate protein abundance.

In the present study, Li and Taggart aimed to make similar measurements in eukaryotes, starting with budding yeast. They used the same technique as Li in 2014—ribosome profiling—but with a few modifications.

Developed in 2009, ribosome profiling permits researchers to capture a snapshot of which mRNAs are being translated at a single moment in time. By using drugs that literally stop ribosomes in their tracks, scientists can freeze these molecular machines in place and destroy any un-protected mRNA that is not occupied (and thus shielded) by a stagnant ribosome. The fragments of mRNA—the ribosome footprints—can be sequenced to provide a barcode identifying which proteins were being made. The density of such footprints reveals the synthesis rates of each protein relative to the others.

Although ribosome profiling revolutionized our ability to gauge protein synthesis across the entire genome, it is sometimes difficult to map each mRNA fragment back to its original location within the genome and the protein product to which it corresponds. A portion of one gene may have a sequence that's identical to another gene that encodes an entirely separate protein.

Here's where Taggart tweaked the approach slightly: he excluded these ambiguous mRNA fragments in his analysis, and only counted the unique ribosome footprints that he could trace back to specific proteins. He then divided the number of ribosome footprints by the length of the gene, minus the ambiguous sequences and non-coding intron regions. While more common analytic approaches fail to accurately account for these ambiguous footprints, Taggart only considered what he calls "meaningful" footprints that he could map to specific regions on the genome. As a result, his modifications generated more precise synthesis rates.

He ultimately curated a comprehensive list of roughly 500 proteins in yeast, comprising about 100 different protein complexes. As he monitored the yeast's protein output, it appeared they produced just the right amount of subunits to complete the complex—no more, no less. It was a clear case of proportional synthesis.

#### **Protein overload**

Once they fine-tuned their method of quantifying protein production, the researchers wondered what would happen if they upset the cell's careful synthesis balance. Do eukaryotes have a widespread mechanism to regulate the amount of protein they produce?

Although yeast normally only have 16 chromosomes, with the help of Angelika Amon's lab, the researchers duplicated each of them, one at a time, so the cell would have the capacity to build twice as many proteins using the genetic information from that extra chromosome. In humans, this kind of imbalance, known as aneuploidy, can lead to disorders like Down syndrome.

Rather than sensing the excess protein and subsequently reducing production, the yeast did not initiate any internal communication to shut down operations at the level of transcription or translation. This runs counter to what is observed in some bacteria.

"It was interesting to see that bacteria and yeast both make the exact amount of protein they need," Taggart says, "although the ways they ensure precise synthesis are different. Many bacterial genes possess the negative feedback loops that yeast appear to lack."

Using data from open access databases, the researchers also identified proportional synthesis in higher eukaryotes, including zebrafish, mice, and humans for the subunits they examined from three large, highly conserved protein complexes. Despite the clear physiological and genetic difference between organisms, the complexes were produced in just the right ratios. The only exception was during zebrafish embryonic development, when the researchers concluded that protein production may not be proportional. This signified that the requirements for proportional synthesis might vary over the course of an organism's lifetime, depending on age, nutrient availability, and stress.

"Perhaps this precision is something we can learn from biology," Li says. Once researchers fully understand how cells fine-tune their protein production, he explains, they can apply that knowledge to designing their own molecules and pathways.

Eduardo Torres, an assistant professor of molecular, cell and cancer biology at the University of Massachusetts Medical School, says these requirements are conserved from bacteria to humans, "suggesting that the evolutionary pressure to produce protein amounts efficiently is a fundamental aspect of cell biology."

"The next step would be to understand the mechanisms behind the balanced synthesis of protein complexes," says Torres, who was not involved in the study. "Future studies integrating knowledge of several aspects of the regulation of gene expression will be necessary to understand how cells fine-tune the expression of each subunit of a particular complex."

Taggart also finds their findings compelling from an evolutionary perspective. "It appears eukaryotes have also evolved under pressure to achieve this proportional synthesis even though they're different from bacteria in so many other ways," he says. "In all domains of life, protein <u>synthesis</u> is both an engine for proliferation and a hub for regulation." [39]

# Newly identified enzyme could play key role in childbirth and muscle diseases

Since the 1960s, scientists have known of a modification that occurs to a particular molecule in muscles, especially after exercise. What scientists haven't known is how that modification happens, or even why.

Now, in a serendipitous finding that started with seemingly unrelated work in <u>viral infections</u>, a team of Stanford scientists discovered not only how the modification takes place – it's through an enzyme called SETD3 – but found that the enzyme likely helps coordinate muscle contractions by the uterus during childbirth. More broadly, SETD3 could also be a hitherto unrealized factor in a range of human muscle tissue diseases.

The modification to muscle cells involves the <u>protein actin</u>, which in part makes up the filaments that contract within muscles. The actin gets adorned with a molecule, called a <u>methyl group</u>, at a certain location where a molecule dubbed <u>histidine</u> is found. Because of this activity – transferring a methyl to a histidine – the newly identified SETD3 is what's known as a histidine methyltransferase.

Until now, nobody had identified a histidine methyltransferase in humans or other animals. The study revealed that the methylation accelerates the formation of new actin filaments in cells, priming them for greater strength when next flexed.

"The histidine methylation we uncovered in this study appears to be a far more common way of regulating proteins than previously appreciated," said co-lead author Alex Wilkinson, a postdoctoral scholar in the lab of Or Gozani, the Dr. Morris Herzstein Professor of Biology. The study was published Dec. 10 in the journal *Nature*.

"Overall, there are a lot of 'firsts' in the study," said Gozani, a study co-author. "We discovered a first-in-class enzyme, the first function for histidine methylation in animals or plants, solved a 50-year-old mystery by determining the function of actin histidine methylation and raised the curtain on a new field that may impact human health."

Study co-lead author Jonathan Diep, a graduate student in the lab of Stanford associate professor of microbiology and immunology Jan Carette, pointed out there could be other histidine methyltransferases hiding right under our noses. "The discovery of an entirely new class of methyltransferases could have major implications in expanding our repertoire of cellular targets for drug development," Diep said.

### A fortunate find

The truth about SETD3's function might have remained a secret for another half-century had Carette's lab not stumbled upon the enzyme while investigating viral infections. To understand the enzyme's activity in normal animal physiology, Carette reached out to Gozani, an international expert in methyltransferases, who happened to be working just a few buildings away. Despite their expertise, Gozani's group initially could not make heads or tails out of the obscure biomolecule. "All of us were struck by how little was known about this enzyme," Carette said. To characterize SETD3 and figure out its function, Wilkinson, Diep and their colleagues at Stanford and in Xiaodong Cheng's lab at the University of Texas MD Anderson Cancer Center conducted a series of experiments and measurements. These included gauging its mass, testing its biological activity on actin, as well as other molecules, and crystallizing the enzyme to observe its structure.

Wilkinson ultimately put the puzzle pieces together, deducing that SETD3 was not just any methyltransferase, but the first histidine methyltransferase to be found in animals; the only kind previously documented occurs in yeasts. "It was one of those times when everything came together and it's why we do science," said Gozani.

#### **Aiding uterine contractions**

Claude Nagamine, an associate professor of comparative medicine, led the genetic experiments that revealed SETD3's impact on childbirth. The researchers bred mice that lacked SETD3. In the absence of that enzyme, the precise smooth muscle coordination necessary for uterine contractions during labor could not take place, a condition known as dystocia.

The Stanford scientists found that SETD3 might have a similar part to play in humans. Working with cultures of human uterine smooth muscle cells, the team showed that low levels of SETD3 impaired contraction under conditions that model labor.

In mice at least, dystocia is not terribly problematic. Unborn fetuses are eventually reabsorbed by the mother without ill effect to her. For dystocia in humans, in some cases a doctor can administer a hormone (or its synthetic equivalent) called oxytocin to stimulate contractions. In women with SETD3 dysfunction, that oxytocin wouldn't work and those women would require caesarean sections. This surgery carries far more risks than a normal vaginal delivery and requires longer hospital stays. Studies have also found better health outcomes in children born naturally.

If SETD3 mutations do turn out to impair childbirth in people, women and their physicians could plan ahead for the possibility of a caesarean section. "Clinicians could possibly screen women to help identify those who might be at higher risk for C-sections," said Gozani. "Overall, given that actin is an essential protein for a diverse set of cellular functions, we think we may be only scratching the surface when it comes to this enzyme's methylation effects across the animal kingdom." [38]

## Unlocking the secrets of how cells communicate offers insights into treating diseases

Portland State University researchers have made a significant breakthrough by developing the 3-D structure of proteins from inside the eye lens that control how cells communicate with each other, which could open the door to treating diseases such as cataracts, stroke and cancer.

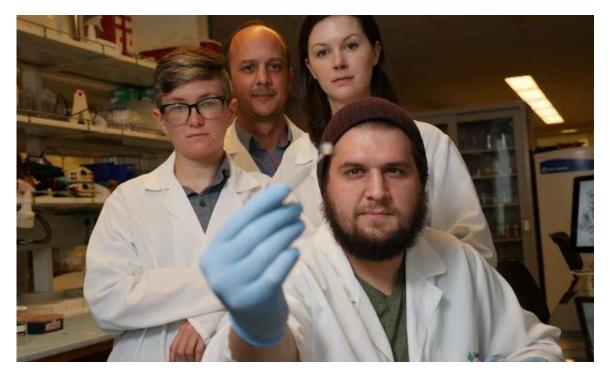
The PSU research team, led by chemistry professor Steve Reichow, used a multimillion-dollar microscope and a <u>novel technique</u> developed by three Nobel Prize-winning biophysicists called <u>cryo-electron microscopy</u> (Cryo-EM) to view membrane <u>protein</u> channels—or transportation tunnels in cell walls—at the atomic level. This allowed Reichow's team, whose research is supported by the National Institutes of Health, to create a 3-D image of the membrane <u>channel</u> to better understand the processes involved in cell-to-cell communication.

Portland State researchers used Cryo-EM—a microscope technique that freezes biomolecules in mid-movement and takes ultra-high-resolution images—and computer modeling to see the 3-D structure of gap junction proteins that had been isolated from eye lenses. Gap junctions are tiny channels that allow neighboring cells to communicate with one another and are found in many places throughout the body.

Their findings—published Dec. 12 in the scientific journal *Nature* - showed for the first time how <u>gap junctions</u> selectively pass or block chemical information. Until now, it was not known how these channels would allow certain messages to pass between cells while specifically blocking others.

Reichow said the detailed images may open the door to understanding, and potentially treating, different types of diseases that are associated with the loss of function in cellular communication involving gap junctions such as cataracts, cardiac arrhythmia, stroke and certain cancers.

"Currently there's no drug on the market today that can specifically block or activate gap junction proteins," Reichow said. "But our discovery may one day pave the way for development of pharmaceuticals that can control heart disease or other diseases that are associated with the malfunctions or mis-regulations of these protein channels."



Members of Portland State University's Reichow Lab and co-authors of the study, graduate student Bassam Haddad (center, holding an eye lens), graduate student Janette Myers, assistant chemistry professor Steve Reichow, and senior research ...<u>more</u>

Now that the Reichow Lab has established a method for characterizing the proteins, they are trying to understand the nuances of how the body uses gap junctions differently across tissues and organs. [37]

## Researchers make shape shifting cell breakthrough

A new computational model developed by researchers from The City College of New York and Yale gives a clearer picture of the structure and mechanics of soft, shape-changing cells that could provide a better understanding of cancerous tumor growth, wound healing, and embryonic development.

Mark D. Shattuck, professor of physics at City College's Benjamin Levich Institute, and researchers at Yale developed the new efficient <u>computational model</u>. It allows simulated particles to realistically change shape while conserving volume during interactions with other particles. Their results appear in the latest edition of *Physical Review Letters*.

Developing computer simulations of particles, such as sand grains and ball bearings, is straightforward because they do not readily change shape. Doing the same for cells and other deformable particles is more difficult, and the computational models researchers currently use do not accurately capture how soft particles deform.

The computational model developed by Shattuck and lead investigator from Yale, Corey O'Hern, tracks points on the surfaces of polygonal cells. Each surface point moves independently, in accordance with its surroundings and neighboring particles, allowing the shape of the particle to change. It is more computationally demanding than current simulations, but necessary to correctly model particle deformation.

"We now have an efficient accurate computational model to investigate how discrete, deformable particles pack," Shattuck said. It also allows researchers to easily adjust cell-cell interactions, consider directed motion, and can be used for both 2-D and 3-D systems.

One unexpected result from the model shows that deformable particles must deviate from a sphere by more than 15% to completely fill a space.

"In our new <u>model</u>, if no external pressure is applied to the system, the particles are spherical," O'Hern said. "As the pressure is increased, the particles deform, increasing the fraction of space that they occupy. When the <u>particles</u> completely fill the space, they will be 15% deformed. Whether it's bubbles, droplets, or cells, it's a universal result for soft, particle systems."

Among other applications, this technology may give researchers a new tool to examine how cancerous tumors metastasize. "We can now create realistic models of the packing of <u>cells</u> in tumors using computer simulations, and ask important questions such as whether a cell in a tumor needs to change its shape to become more capable of motion and eventually leave the <u>tumor</u>." [36]

## Using water molecules to unlock neurons' secrets

Neurons are brain cells that communicate with each other by sending electrochemical signals along axons. When a neuron is about to release a signal in the form of an electric charge, it allows ions to pass through its membrane via ion channels. This ion transfer creates an electrical potential difference between the inside and outside of the cell, and that difference is referred to as the membrane potential.

A team of researchers at the Laboratory for fundamental BioPhotonics (LBP) within EPFL's School of Engineering (STI) has come up with a way to monitor changes in membrane potential and to observe ion fluxes by studying the behavior of the water <u>molecules</u> surrounding the membranes of the <u>neurons</u>. The researchers, who successfully tested their method on in vitro mouse neurons, have just published their findings in *Nature Communications*.

### No more electrodes or fluorophores

A better understanding of the electrical activity of neurons could provide insight into a number of processes taking place in our brains. For example, scientists could see whether a neuron is active or resting, or if it is responding to drug treatment. Up until now, the only way to monitor neurons was by injecting fluorophores into, or attaching electrodes onto, the part of the brain being studied—but fluorophores can be toxic, and electrodes can damage the neurons.

Recently, the LBP researchers developed a way of tracking <u>electrical activity</u> in neurons simply by looking at the interactions between water molecules and the neural membranes. "Neurons are surrounded by water molecules, which change orientation in the presence of an electric charge," says Sylvie Roke, director of the LBP. "When the membrane potential changes, the water molecules will re-orient—and we can observe that."

In their study, the researchers altered the neuronal membrane potential by subjecting the neurons to a rapid influx of potassium ions. This caused the <u>ion channels</u> on the neurons' surface—which serve to regulate the membrane potential—to open and let the ions through. The researchers then turned off the flow of ions, and the neurons released the ions that they had picked up.

In order to monitor this activity, the researchers probed the hydrated neuronal lipid membranes by illuminating the cells with two <u>laser beams</u> of the same frequency. These beams consist of femtosecond laser pulses -using technology for which the 2018 Nobel prize in physics was awarded-so that the <u>water molecules</u> on the interface of the <u>membrane</u> generate photons with a different frequency, known as second-harmonic light.

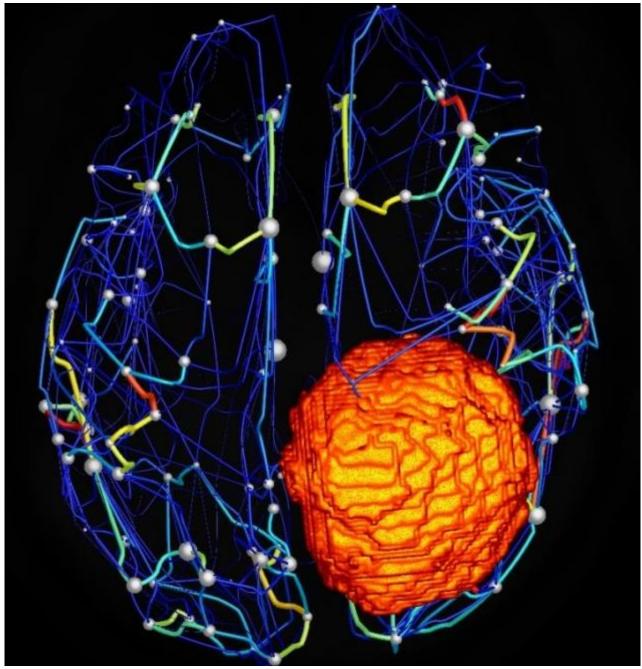
"We see both fundamental and applied implications of our research. Not only can it help us understand the mechanisms that the brain uses to send information, but it could also appeal to pharmaceutical companies interested in in vitro product testing," adds Roke. "And we have now shown that we can analyze a single neuron or any number of neurons at a time." [35]

## Software creates personalized 'virtual brain' models

Researchers from Belgium have created virtual models of the brain individually tailored to patients' functional MR images (fMRI), according to an article published online in *eNeuro*. These models can predict the effects of brain tumours and may help improve surgical planning for their removal (*eNeuro 10.1523/ENEURO.0083-18.2018*).

When planning for brain tumour resection, clinicians typically examine functional MR images to identify key areas around the tumour as they develop a surgical strategy. But the complex dynamics of the brain make it difficult to predict postsurgical outcome based on the limited information these images provide.

One recent measure to improve the visualization of the brain has been to create more comprehensive brain models that simulate neural activity. These models can integrate fMRI data with the biophysics of the brain to predict brain function and help determine the optimal surgical approach, wrote senior author Daniele Marinazzo and colleagues from Ghent University.



Structural brain network of a patient with a meningioma (orange). (Courtesy: Hannelore Aerts)

To test the viability of this technique, Marinazzo and colleagues used open-source software called the Virtual Brain to construct personalized brain models. They used neuroimaging data from 25 patients who had brain tumours and who underwent an MRI exam at Ghent University Hospital between May 2015 and October 2017. They also made similar brain models of 11 patients without brain tumours.

The investigators found that studying these models allowed the surgical team to assess brain function in all of the patients, as well as accurately predict the effect of tumours on brain function. Specifically, the models revealed that the number of connections in the tumour regions of the brain was much lower (p = 0.0007) and more variable (p = 0.01) than in non-tumour areas.

"Reliable prediction of patient-specific large-scale brain dynamics would open up the possibility ... to investigate what types or extent of damage the brain can withstand, and conversely, which kind of distortions can be expected after brain lesions, including those purposively induced by surgery," the authors wrote.

One of the main limitations of the study was its small sample size, but the authors plan to expand their research in the future and look into whether the virtual brain model can reliably predict postsurgical brain function.

"This [future research] would be a major step toward presurgical virtual exploration of different neurosurgical approaches and to identify an optimal surgical strategy," they wrote. [34]

### Interfacing with the brain

The nervous system is loaded with encoded information: thoughts, emotions, motor control. This system in our bodies is an enigma, and the more we can do to understand it, the more we can do to improve human life. Brain-machine interfaces provide one way to connect with this puzzling organ system, including the brain. But because electronic devices are stiff, planar, and rigid, they cause injury to the brain's soft tissue.

Until now, it's been extremely challenging to develop a material and fabrication method that is flexible enough to meld with the brain, but adhesive enough to stay in one place. However, Carnegie Mellon University Associate Professor of Materials Science and Engineering and Biomedical Engineering Chris Bettinger and his group have created a hydrogel material and fabrication process for electrodes that stick to the brain, matching its soft, squishy makeup.

"Imagine you have a bowl of Jell-O, and you insert a rigid plastic fork into the bowl and move it around," says Bettinger. "It's going to damage the Jell-O, producing defects and irreversible structural changes. That situation is analogous to inserting a rigid electronic probe into soft tissue such as someone's brain. It's a combination of what we call micro-motion and mechanics, which work together to not only damage the brain, but also compromise the function of the implanted sensor."

The rigid electrode detects when neurons are firing and records the voltages associated with those firing neurons. But over time, the body interprets this material as an injury and a foreign body that needs to be attacked, degraded, isolated, and removed. Inflammatory cells then surround the probe, disrupting the signal strength of the neurons in that area.

In the past twenty years, silicon-based electronics have progressed from rigid and planar in form to curved, flexible, and stretchable. The rigidity of these electronics has evolved from being stiff like wood, to thin and flexible like paper, to stretchy and pliable like rubber bands. Now, Bettinger's team is taking it one step further, making them not only flexible and stretchable, but also extremely soft and adhesive.

"If we could fabricate <u>electronic devices</u> that have mechanical properties closer to 'Jell-O' rather than wood or plastic, then we can surreptitiously interface neural probes with the brain in a more benign manner," says Bettinger.

The challenge is that the processes used to make sophisticated electronics require high temperatures (400 C or higher), a vacuum, and exotic solvents, buffers, acids, and bases to etch <u>materials</u> and patterns. None of these are compatible with soft hydrogel materials.

To combat these fundamental issues, Bettinger and his team created a new way to fabricate the electronics—decoupling the fabrication processes of the electronic part and the soft substrate it's embedded in. First, they construct the electronic part on a substrate that is compatible with <u>high temperatures</u>, extreme solvents, and a vacuum, and create the hydrogel substrate separately. Then, they remove the electronic piece from its original substrate and adhere it to the hydrogel substrate. The final device contains a thin layer of electronics on a soft, flexible, and sticky substrate that has <u>mechanical properties</u> similar to those of the nervous system.

Another challenge was creating a material that was still adhesive in fluid. If the material can't adhere when wet, it would be like trying to keep a Band-Aid on while in the pool. For the electrode to work it needs to stick in one place for a long period of time. The researchers studied the properties of animals like the blue mussel, which sticks to rocks underwater. They applied those same chemical principles when creating the hydrogel substrate.

"Instead of having to take a brain or a spinal cord and then stick something into it and then injure it," says Bettinger, "we can laminate it on top and avoid injury to the tissue."

The fact that the nodes do not injure the tissue and do not move around means that they are able to record a stronger and more accurate signal from the firing neurons. The probes could now be used not only to record signals, but also to stimulate therapies.

For example, the electrode array in the probe could block the signal that induces inflammation in people with rheumatoid arthritis. Instead of using painkillers like opiates, an electronic-based therapy that stimulates appropriate regions of the <u>spinal cord</u> could be more targeted and effective, while avoiding the risk of addiction when compared to pharmaceutical-based interventions. The electrodes can also be used for long-term recording applications, such as testing how a new drug could affect the heart. A sticky, soft electrode that can bend and flex can ensconce the heart, record its contractions, and indicate which drug might be most effective.

"We're trying to improve the temporal bandwidth of these probes, by preserving the longevity of the material. Then we can acquire more information and maintain a suitable signal-to-noise ratio," said Bettinger. "Researchers in multiple disciplines are trying to improve the way that electronic devices can interface with the nervous system. We feel that we are contributing to this broader effort by expanding the materials toolbox to improve device performance."

Bettinger and his group are collaborating with researchers in electrical and computer engineering at Carnegie Mellon and with researchers at the University of Pittsburgh. Their findings have been published in *Advanced Functional Materials*. [33]

## Researchers demonstrate a novel approach for measuring brain function connectivity

Measuring optical blood flow in the resting human brain to detect spontaneous activity has for the first time been demonstrated by Wright State University imaging researchers, holding out promise for a better way to study people with autism, Alzheimer's and depression.

Ulas Sunar, associate professor of biomedical, industrial and human factors engineering, and his team of researchers have shown that optical <u>blood</u> <u>flow</u> contrast measured by Diffuse Correlation Spectroscopy can be used to detect Resting State Functional Connectivity (RSFC) in the brain.

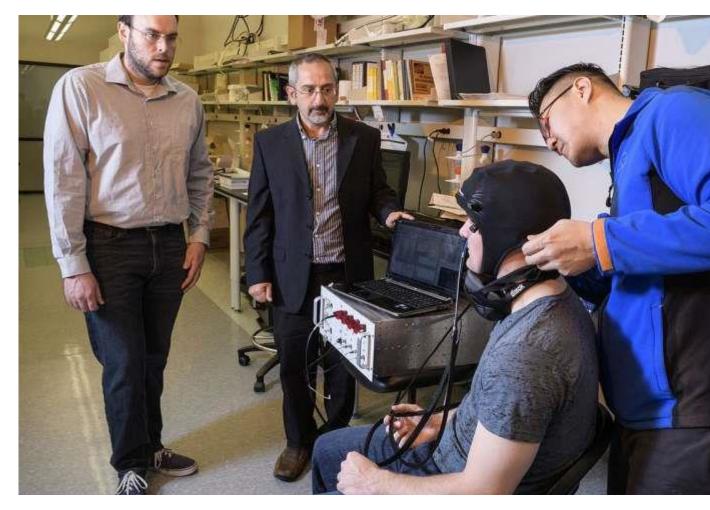
The research team includes Sunar, who holds the endowed position of the Ohio Research Scholar for Medical Imaging at Wright State, and his researchers Chien Poon, Jun Li, Jeremy Kress and Dan Rohrbach.

The team's findings were recently published in one of the top optical journals, the Journal of Biophotonics, covering research on the interactions between light and biological materials. The work has also been featured in the Biophotonics.World, which serves the worldwide biophotonics community as a central access point for the latest news and articles about recent scientific developments in academia and industry.

The team's novel optical approach is based on detecting light scattering from moving blood cells and can quantify absolute cerebral blood flow-related contrast. It is a complementary technique to widely known functional near infrared spectroscopy that measures blood oxygenation.

"We are seeing that blood flow shows higher contrast than oxygenation in our neuroimaging experiments," said Sunar. "Under neuronal firing brain may ask for more blood flow. That's why blood flow is an important parameter for assessing human brain resting state functional connectivity. And also the blood flow imaging technique is relatively new. The custom system was built here, by my Ph.D. student Chien Poon, and we demonstrated the resting state approach for the first time in our field."

The researchers used blood flow parameter to quantify RSFC in nine healthy adult males as a proofof-concept study. The technique showed high connectivity between certain areas of the brain and low connectivity between other areas. The results match similar studies performed previously with other methods such as functional magnetic resonance imaging (fMRI).



From left: Dan Rohrbach, Ulas Sunar, Ben Rinehart and Chien Poon in the Sunar Research Group lab in the Neuroscience Engineering Collaboration Building. Credit: Wright State University

"These are exciting results in our field since the study has proven the potential of optical blood flow method as a non-invasive mean to assess RSFC in humans," Sunar told Biophotonics.World. "Cerebral blood flow is a very important parameter for neuronal disease characterization due to its high contrast."

RSFC studies are a valuable tool for studying people with disorders that can make performing tasks difficult. But many people, such as young autistic children, are poor candidates for RSFC assessment by fMRI, which requires them to hold still for long intervals inside a confined imaging space with loud noise from the magnet.

Optical imaging is highly suitable for such people because it is fast and can be performed by optical probes that can be worn by the patient. The researchers expect that this will ultimately become a highly useful tool for non-invasively assessing brain function in young and disabled patients.

Sunar said the technology could also be used for assessing human performance to understand if a task increases <u>cerebral blood flow</u> and neural activity.

"When a task is performed, what happens to the blood flow in the brain?" he said. "Is there a relationship? Is the brain network more connected at the resting state and performing state? These are interesting questions to investigate."

The next step for the research team will be to modify the optical system to enable it to show both blood flow and oxygenation.

"We are working on combining multiple imaging contrasts to get a more complete picture of the <u>brain</u> function," Sunar said. "For example, we can quantify cerebral metabolic rate of oxygen consumption by combining <u>blood flow</u> and oxygenation measurements. This approach will have a high impact in many areas, from neurological disease characterization in clinical settings to assessing the human performance relevant to military research." [32]

## **Biologists 'transfer' a memory**

UCLA biologists report they have transferred a memory from one marine snail to another, creating an artificial memory, by injecting RNA from one to another. This research could lead to new ways to lessen the trauma of painful memories with RNA and to restore lost memories.

"I think in the not-too-distant future, we could potentially use RNA to ameliorate the effects of Alzheimer's disease or post-traumatic stress disorder," said David Glanzman, senior author of the study and a UCLA professor of integrative biology and physiology and of neurobiology. The team's research is published May 14 in *eNeuro*, the online journal of the Society for Neuroscience.

RNA, or ribonucleic acid, has been widely known as a cellular messenger that makes proteins and carries out DNA's instructions to other parts of the cell. It is now understood to have other important functions besides protein coding, including regulation of a variety of cellular processes involved in development and disease.

The researchers gave mild electric shocks to the tails of a species of marine snail called Aplysia. The snails received five tail shocks, one every 20 minutes, and then five more 24 hours later. The shocks enhance the snail's defensive withdrawal reflex, a response it displays for protection from potential harm. When the researchers subsequently tapped the snails, they found those that had been given the shocks displayed a defensive contraction that lasted an average of 50 seconds, a simple type of learning known as "sensitization." Those that had not been given the shocks contracted for only about one second.

The life scientists extracted RNA from the nervous systems of marine snails that received the tail shocks the day after the second series of shocks, and also from marine snails that did not receive any shocks. Then the RNA from the first (sensitized) group was injected into seven marine snails that had not received any shocks, and the RNA from the second group was injected into a control group of seven other snails that also had not received any shocks.



UCLA Professor David Glanzman holding a marine snail. Credit: Christelle Snow/UCLA

Remarkably, the scientists found that the seven that received the RNA from snails that were given the shocks behaved as if they themselves had received the tail shocks: They displayed a defensive contraction that lasted an average of about 40 seconds.

"It's as though we transferred the memory," said Glanzman, who is also a member of UCLA's Brain Research Institute.

As expected, the control group of snails did not display the lengthy contraction.

Next, the researchers added RNA to Petri dishes containing neurons extracted from different snails that did not receive shocks. Some dishes had RNA from marine snails that had been given electric tail shocks, and some dishes contained RNA from snails that had not been given shocks. Some of the dishes contained sensory neurons, and others contained motor neurons, which in the snail are responsible for the reflex.

When a marine snail is given electric tail shocks, its sensory neurons become more excitable. Interestingly, the researchers discovered, adding RNA from the snails that had been given shocks also produced increased excitability in sensory neurons in a Petri dish; it did not do so in motor neurons. Adding RNA from a marine snail that was not given the tail shocks did not produce this increased excitability in sensory neurons.



David Glanzman holding a marine snail. Credit: Christelle Snow/UCLA

In the field of neuroscience, it has long been thought that memories are stored in synapses. (Each neuron has several thousand synapses.) Glanzman holds a different view, believing that memories are stored in the nucleus of neurons.

"If memories were stored at synapses, there is no way our experiment would have worked," said Glanzman, who added that the marine snail is an excellent model for studying the brain and memory.

Scientists know more about the cell biology of this simple form of learning in this animal than any other form of learning in any other organism, Glanzman said. The cellular and molecular processes seem to be very similar between the marine snail and humans, even though the snail has about 20,000 neurons in its central nervous system and humans are thought to have about 100 billion.

In the future, Glanzman said, it is possible that RNA can be used to awaken and restore memories that have gone dormant in the early stages of Alzheimer's disease. He and his colleagues published research in the journal eLife in 2014 indicating that lost memories can be restored.

There are many kinds of RNA, and in future research, Glanzman wants to identify the types of RNA that can be used to transfer memories. [31]

### 'Sleeping' stem cells could aid brain repair

Scientists at the Wellcome Trust/ Cancer Research UK Gurdon Institute, University of Cambridge, have identified a new type of stem cell in the brain which they say has a high potential for repair following brain injury or disease.

A major goal of regenerative research is to repair the <u>brain</u> efficiently following injury, for example due to stroke, Alzheimer's disease or head trauma, disease or ageing. The brain is poor at repairing itself; however, it may become possible to improve repair without surgery by targeting stem <u>cells</u> residing in patients' brains. Stem cells have the unique capacity to produce all of the cells in the brain but are normally kept inactive in a form of cellular 'sleep' known as quiescence. Quiescent cells do not proliferate or generate new cells. Thus, any regenerative therapy targeting stem cells must first awaken them from quiescence.

In a study published today in the journal *Science*, PhD student Leo Otsuki and his supervisor Professor Andrea Brand report the discovery in the brain of a new type of quiescent stem cell (known as 'G2 quiescent stem cell') with higher regenerative potential than quiescent stem cells identified previously. Importantly, G2 quiescent stem cells awaken to make the key types of cell in the brain - neurons and glia - much faster than known quiescent stem cells, making them attractive targets for therapeutic design.



Stem cells are labelled in red, nuclear membranes in green and DNA in blue. Credit: Andrea Brand/Leo Otsuki

"The brain is not good at repairing itself, but these newly-discovered stem cells suggest there may be a way to improve its ability," says Professor Brand. "These stem cells are in a dormant state, but once awake, they have the ability to generate key brain cells."

By studying the fruit fly (Drosophila), the authors identified a gene known as tribbles that selectively regulates G2 quiescent stem cells. The DNA of fruit flies has many similarities with that of humans, making them a useful model to understand human biology, and 60% of human <u>genes</u> associated with disease are also found in Drosophila. The tribbles gene has counterparts in the mammalian genome that are expressed in stem cells in the brain. The researchers believe that drugs that target tribbles might be one route to awakening G2 quiescent stem cells.

"We've found the gene that directs these cells to become quiescent," adds Otsuki. "The next step is to identify potential drug-like molecules that block this gene and awaken a person's stem cells.

"We believe there may be similar quiescent <u>stem cells</u> in other organs, and this discovery could help improve or develop new regenerative medicines." [30]

## Using organoids to understand how the brain wrinkles

A team of researchers working at the Weizmann Institute of Science has found that organoids can be used to better understand how the human brain wrinkles as it develops. In their paper published in the journal *Nature Physics*, the team describes how they used a modified form of organoid development to study the development of brain wrinkles. Larry Taber with Washington University offers a News & Views <u>piece</u> on the work done by the team in the same journal issue.

An organoid is an artificially grown mass of <u>cells</u> meant to replicate human or other animal organs. They are typically much smaller than the organs they are meant to mimic, but allow researchers a unique means of studying how organs develop. In this new effort, the researchers sought to better understand the process by which the <u>human brain</u> develops wrinkles. Realizing that the standard approach used for creating organoids would not work in such a study, the team tried another tactic—they grew stem cells on platform that resulted in a brain organoid that was much thinner and rounder than it would naturally grow—and it was also grown on a form surrounding a narrow space. The end result, the team reports, was a brain organoid that resembled a pita. This configuration allowed the researchers to take images of folds as they developed and to supply nutrients to all the cells since blood vessels typically do not develop in organoids.

In studying the images of the developing organoid, the researchers found that the folds developed as expected—opposing forces resulting from growth differences in brain material. In this case, it was the cytoskeleton in the organoid's core and the cell nucleus expanding at the organoid's outer edges. Uneven expansion between the two causes one or the other to fold as a means of dealing with the increase in pressure.

To learn more about the development of folds, the researchers ran the same experiment again, but used <u>stem cells</u> from a patient with smooth brain syndrome, which, as it sounds, is a condition in which the brain develops without folds. As expected, the organoid developed very few folds. A closer look showed differences in elasticity between the cells in the organoid grown with <u>healthy</u> <u>cells</u> and the those with the mutated genes that are behind smooth <u>brain</u> syndrome. [29]

## Biologists find new source for brain's development

A team of biologists has found an unexpected source for the brain's development, a finding that offers new insights into the building of the nervous system.

The research, which appears in the journal Science, discovered that glia, a collection of nonneuronal cells that had long been regarded as passive support cells, in fact are vital to nerve-cell development in the brain.

"The results lead us to revise the often neuro-centric view of brain development to now appreciate the contributions for non-neuronal cells such as glia," explains Vilaiwan Fernandes, a postdoctoral fellow in New York University's Department of Biology and the study's lead author. "Indeed, our study found that fundamental questions in brain development with regard to the timing, identity,

and coordination of nerve cell birth can only be understood when the glial contribution is accounted for."

The brain is made up of two broad cell types, nerve cells or neurons and glia, which are non-nerve cells that make up more than half the volume of the brain. Neurobiologists have tended to focus on the former because these are the cells that form networks that process information.

However, given the preponderance of glia in the brain's cellular make-up, the NYU researchers hypothesized that they could play a fundamental part in brain development.

To explore this, they examined the visual system of the fruit fly. The species serves as a powerful model organism for this line of study because its visual system, like the one in humans, holds repeated mini-circuits that detect and process light over the entire visual field.

This dynamic is of particular interest to scientists because, as the brain develops, it must coordinate the increase of neurons in the retina with other neurons in distant regions of the brain.

In their study, the NYU researchers found that the coordination of nerve-cell development is achieved through a population of glia, which relay cues from the retina to the brain to make cells in the brain become nerve cells.

"By acting as a signaling intermediary, glia exert precise control over not only when and where a neuron is born, but also the type of neuron it will develop into," notes NYU Biology Professor Claude

Desplan, the paper's senior author. [28]

## Link Between Immune System, Memory and Brain Structure Discovered

The body's immune system performs essential functions, such as defending against bacteria and cancer cells. However, the human brain is separated from immune cells in the bloodstream by the so-called blood-brain barrier. This barrier protects the brain from pathogens and toxins circulating in the blood, while also dividing the immune cells of the human body into those that fulfill their function in the blood and those that work specifically in the brain. Until recently, it was thought that brain function was largely unaffected by the peripheral immune system.

However, in the past few years, evidence has accumulated to indicate that the blood's immune system could in fact have an impact on the brain. Scientists from the University of Basel's Transfaculty Research Platform Molecular and Cognitive Neurosciences (MCN) have now carried out two independent studies that demonstrate that this link between the immune system and brain is more significant than previously believed.

#### Search for regulatory patterns

In the first study, the researchers searched for epigenetic profiles, i.e. regulatory patterns, in the blood of 533 young, healthy people. In their genome-wide search, they identified an epigenetic profile that is strongly correlated with the thickness of the cerebral cortex, in particular in a region of the brain that is important for memory functions. This finding was confirmed in an independent examination of a further 596 people. It also showed that it is specifically those genes that are

responsible for the regulation of important immune functions in the blood that explain the link between the epigenetic profile and the properties of the brain.

#### Gene variant intensifies traumatic memories

In the second study, the researchers investigated the genomes of healthy participants who remembered negative images particularly well or particularly poorly. A variant of the TROVE2 gene, whose role in immunological diseases is currently being investigated, was linked to participants' ability to remember a particularly high number of negative images, while their general memory remained unaffected.

This gene variant also led to increased activity in specific regions of the brain that are important for the memory of emotional experiences. The researchers also discovered that the gene is linked to the strength of traumatic memories in people who have experienced traumatic events.

The results of the two studies show that both brain structure and memory are linked to the activity of genes that also perform important immune regulatory functions in the blood. "Although the precise mechanisms behind the links we discovered still need to be clarified, we hope that this will ultimately lead to new treatment possibilities," says Professor Andreas Papassotiropoulos, CoDirector of the University of Basel's MCN research platform. The immune system can be precisely affected by certain medications, and such medications could also have a positive effect on impaired brain functions.

### **Innovative research methods**

These groundbreaking findings were made possible thanks to cutting edge neuroscientific and genetic methods at the University of Basel's MCN research platform. Under the leadership of Professor Andreas Papassotiropoulos and Professor Dominique de Quervain, the research platform aims to help us better understand human brain functions and to develop new treatments for psychiatric disorders. [27]

## Researcher looking to shed light deeper into the human brain

The inner workings of the human brain have always been a subject of great interest. Unfortunately, it is fairly difficult to view brain structures or intricate tissues due to the fact that the skull is not transparent by design. The reality is that light scattering is the major obstacle for deep penetration into tissue.

Dr. Vladislav Yakovlev, professor in the Department of Biomedical Engineering at Texas A&M University, has been developing a more efficient way of propagating light through an opaque medium. Propagation of light refers to the way that light travels from one point to another, in this case, through a medium, such as human tissue.

The new method involves making a minimally invasive hole within the medium, which is smaller in diameter than needles that are currently being used within the medical field. The process shows a great deal of promise in many uses, including viewing brain structure through the skull and imaging blood through skin tissue.

The technology could even be extended outside the realm of biomedical engineering to develop a more efficient way of seeing through fog while driving. This can be accomplished by deploying a laser pulse that could be sent through fog and evaporate water. This would allow drivers to have a safer experience during hazardous driving conditions and would work exactly as the method used in biomedical engineering applications.

The holes used to pass the light through are a few hundred micrometers in depth and a width of 20 to 30 microns. A micron is one millionth of a meter, and by comparison a single strand of human hair is about 75 microns in diameter. The light is then coupled into the opaque material resulting in an increase of magnitude of optical transmission into the material. The material that light is passed through is also referred to as the scattering medium.

The report documenting the work of Yakovlev was recently published in Proceedings of the National Academy of Sciences of the United States of America and definitively demonstrated that light injected into the scattering medium will remain there for an extended period of time. The amount of time that the photons remained was increased by a factor of 100.

One of the challenges facing researchers is that of optical absorption within tissues. However, because the new method is wavelength independent, the wavelength can be specified to perform measurements in a specific part of the light spectrum. This approach has the potential to yield analytical information about the composition and structure of the medium or tissue. [26]

## Brain scanners allow scientists to 'read minds'—could they now enable a 'Big Brother' future?

Are you lying? Do you have a racial bias? Is your moral compass intact?To find out what you think or feel, we usually have to take your word for it. But questionnaires and other explicit measures to reveal what's on your mind are imperfect: you may choose to hide your true beliefs or you may not even be aware of them.

But now there is a technology that enables us to "read the mind" with growing accuracy: functional magnetic resonance imaging (fMRI). It measures brain activity indirectly by tracking changes in blood flow – making it possible for neuroscientists to observe the brain in action. Because the technology is safe and effective, fMRI has revolutionised our understanding of the human brain. It has shed light on areas important for speech, movement, memory and many other processes.

More recently, researchers have used fMRI for more elaborate purposes. One of the most remarkable studies comes from Jack Gallant's lab at the University of California. His team showed movie trailers to their volunteers and managed to reconstruct these video clips based on the subjects' brain activity, using a machine learning algorithm.

In this approach, the computer developed a model based on the subject's brain activity rather than being fed a pre-programmed solution by the researchers. The model improved with practice and after having access to enough data, it was able to decode brain activity. The reconstructed clips were blurry and the experiment involved extended training periods. But for the first time, brain activity was decoded well enough to reconstruct such complex stimuli with impressive detail.

#### **Enormous potential**

So what could fMRI do in the future? This is a topic we explore in our new book Sex, Lies, and Brain Scans: How fMRI Reveals What Really Goes on in our Minds. One exciting area is lie detection. While early studies were mostly interested in finding the brain areas involved in telling a lie, more recent research tried to actually use the technology as a lie detector.

As a subject in these studies, you would typically have to answer a series of questions. Some of your answers would be truthful, some would be lies. The computer model is told which ones are which in the beginning so it gets to know your "brain signature of lying" – the specific areas in your brain that light up when you lie, but not when you are telling the truth.

Afterwards, the model has to classify new answers as truth or lies. The typical accuracy reported in the literature is around 90%, meaning that nine out of ten times, the computer correctly classified answers as lies or truths. This is far better than traditional measures such as the polygraph, which is thought to be only about 70% accurate. Some companies have now licensed the lie detection algorithms. Their next big goal: getting fMRI-based lie detection admitted as evidence in court.

They have tried several times now, but the judges have ruled that the technology is not ready for the legal setting – 90% accuracy sounds impressive, but would we want to send somebody to prison if there is a chance that they are innocent? Even if we can make the technology more accurate, fMRI will never be error proof. One particularly problematic topic is the one of false memories. The scans can only reflect your beliefs, not necessarily reality. If you falsely believe that you have committed a crime, fMRI can only confirm this belief. We might be tempted to see brain scans as hard evidence, but they are only as good as your own memories: ultimately flawed.

Still, this raises some chilling questions about the possibility for a "Big Brother" future where our innermost thoughts can be routinely monitored. But for now fMRI cannot be used covertly. You cannot walk through an airport scanner and be asked to step into an interrogation room, because your thoughts were alarming to the security personnel.

Undergoing fMRI involves lying still in a big noise tube for long periods of time. The computer model needs to get to know you and your characteristic brain activity before it can make any deductions. In many studies, this means that subjects were being scanned for hours or in several sessions. There's obviously no chance of doing this without your knowledge – or even against your will. If you did not want your brain activity to be read, you could simply move in the scanner. Even the slightest movements can make fMRI scans useless.

Although there is no immediate danger of undercover scans, fMRI can still be used unethically. It could be used in commercial settings without appropriate guidelines. If academic researchers want to start an fMRI study, they need to go through a thorough process, explaining the potential risks and benefits to an ethics committee. No such guidelines exist in commercial settings. Companies are free to buy fMRI scanners and conduct experiments with any design. They could show you traumatising scenes. Or they might uncover thoughts that you wanted to keep to yourself. And if your scan shows any medical abnormalities, they are not forced to tell you about it.

Mapping the brain in great detail enables us to observe sophisticated processes. Researchers are beginning to unravel the brain circuits involved in self control and morality. Some of us may want to use this knowledge to screen for criminals or detect racial biases. But we must keep in mind that

fMRI has many limitations. It is not a crystal ball. We might be able to detect an implicit racial bias in you, but this cannot predict your behaviour in the real world.

fMRI has a long way to go before we can use it to fire or incarcerate somebody. But neuroscience is a rapidly evolving field. With advances in clever technological and analytical developments such as machine learning, fMRI might be ready for these futuristic applications sooner than we think. Therefore, we need to have a public discussion about these technologies now. Should we screen for terrorists at the airport or hire only teachers and judges who do not show evidence of a racial bias? Which applications are useful and beneficial for our society, which ones are a step too far? It is time to make up our minds. [25]

## 'Latest spoke in the wheel' drives brain-mapping advances

Advances in microscopy techniques have often triggered important discoveries in the field of neuroscience, enabling vital insights in understanding the brain and promising new treatments for neurodegenerative diseases such as Alzheimer's and Parkinson's. A special section on "Superresolution Microscopy of Neural Structure and Function" in the current issue of the journal Neurophotonics, published by SPIE, the international society for optics and photonics, details this work in reports on ground-breaking new research and reviews.

Starting with the Golgi technique at the end of the 19th century, to electron microscopy in the 1950s, to fluorescent confocal and two-photon microscopy at the close of the 20th century, microscopy techniques have driven important breakthroughs in neuroscience, note guest editors Valentin Nägerl and Jean-Baptiste Sibarita of the Université de Bordeaux and the CNRS in their editorial for the special section.

"By providing higher spatial and temporal resolutions, as well as more contrast and specificity, these ground-breaking techniques have greatly informed our view of how the brain works," the editors write.

Super-resolution fluorescence microscopy "is the latest spoke in the revolutionary wheel," the guest editors note. "Recognized with the Nobel Prize in chemistry in 2014 for overcoming the diffraction barrier of light microscopy, it unlocks a new potential to upend biological research at the molecular level. Ten years after their development in a handful of laboratories, super-resolution microscopy techniques have caught on like wildfire and are now routinely used in a large number of biology labs."

While super-resolution microscopy is a relative recent addition to the arsenal of tools available for neuroscientific research, said Neurophotonics editor-in-chief David Boas of Massachusetts General Hospital, Harvard Medical School, "the breadth of impactful applications is growing rapidly. This special section provides a snapshot of this growth with a collection of exciting papers illustrating the breadth of applications."

Articles in the section, many of them accessible via open access, help validate and assess new techniques by comparing them with more established approaches. Among them:

In "Filling the gap: adding super-resolution to array tomography for correlated ultrastructural and molecular identification of electrical synapses at the C. elegans connectome," Sebastian Matthias

Markert of the University of Würzburg and co-authors describe a new method to correlate molecular information with ultrastructural context. Their aim is to allow researchers to dissect the molecular underpinnings of the ultrastructural organization and function of electrical synapses precisely and confidently.

Producing nanoscale maps of protein organization on cell surfaces or within organelles is another exciting prospect in super-resolution microscopy. In "Counting numbers of synaptic proteins: absolute quantification and single molecule imaging techniques," Angela Patrizio and Christian Specht of École Normale Supérieure describe how single-molecule-based microscopy techniques offer unparalleled opportunities to study protein content and dynamics in key functional compartments.

An early hallmark of neurodegenerative diseases such as Alzheimer's and Parkinson's is the misfolding and self-aggregation of proteins into amyloid structures that are believed to wreak havoc on neurons and synapses. In "Probing amyloid protein aggregation with optical super-resolution methods: from the test tube to models of disease", Clemens Kaminski and Gabriele Kaminski Schierle of the University of Cambridge explain the potential of new optical super-resolution techniques to provide insight on the molecular mechanism of the pathogenic self-assembly process in vitro and inside cells. [24]

#### **Consciousness and Entropy**

What is the relationship of consciousness to the neurological activity of the brain? Does the brain behave differently when a person is fully conscious, when they are asleep, or when they are undergoing an epileptic seizure? A recent study by R. Guevara Erra, D. M. Mateos, R. Wennberg, J.L. Perez Velazquez of the University of Toronto, suggests that consciousness if correlated to a maximum number of neurological connections. In thermodynamics, this quantity, describing the complexity of a system, is entropy. In their paper, published in Physics Letters, they write:

It has been said that complexity lies between order and disorder. In the case of brain activity, and physiology in general, complexity issues are being considered with increased emphasis. We sought to identify features of brain organization that are optimal for sensory processing, and that may guide the emergence of cognition and consciousness, by analysing neurophysiological recordings in conscious and unconscious states. We find a surprisingly simple result: normal wakeful states are characterised by the greatest number of possible configurations of interactions between brain networks, representing highest entropy values. Therefore, the information content is larger in the network associated to conscious states, suggesting that consciousness could be the result of an optimization of information processing. These findings encapsulate three main current theories of cognition, as discussed in the text, and more specifically the conceptualization of consciousness in terms of brain complexity. We hope our study represents the preliminary attempt at finding organising principles of brain function that will help to guide in a more formal sense inquiry into how consciousness arises from the organization of matter.

The authors are rightly cautious about the significance of the correlation. Just because A and B are correlated, does not mean that A causes B. However the recognition that a phenomenon such as entropy may describe consciousness opens a new direction for consciousness research. [23]

## Consciousness is tied to 'entropy', say researchers

Consciousness appears to arise naturally as a result of a brain maximizing its information content. So says a group of scientists in Canada and France, which has studied how the electrical activity in people's brains varies according to individuals' conscious states. The researchers find that normal waking states are associated with maximum values of what they call a brain's "entropy".

Statistical mechanics is very good at explaining the macroscopic thermodynamic properties of physical systems in terms of the behaviour of those systems' microscopic constituent particles. Emboldened by this success, physicists have increasingly been trying to do a similar thing with the brain: namely, using statistical mechanics to model networks of neurons. Key to this has been the study of synchronization – how the electrical activity of one set of neurons can oscillate in phase with that of another set. Synchronization in turn implies that those sets of neurons are physically tied to one another, just as oscillating physical systems, such as pendulums, become synchronized when they are connected together.

The latest work stems from the observation that consciousness, or at least the proper functioning of brains, is associated not with high or even low degrees of synchronicity between neurons but by middling amounts. Jose Luis Perez Velazquez, a biochemist at the University of Toronto, and colleagues hypothesized that what is maximized during consciousness is not connectivity itself but the number of different ways that a certain degree of connectivity can be achieved.

#### Many ways of connecting

Perez Velazquez's colleague Ramon Guevarra Erra, a physicist at the Paris Descartes University, points out that there is only one way to connect each set of neurons in a network with every other set, just as there is only one way to have no connections at all. In contrast, he notes, there are many different ways that an intermediate medium-sized number of connections can be arranged.

To put their hypothesis to the test, the researchers used data previously collected by Perez Velazquez showing electric- and magnetic-field emissions from the brains of nine people, seven of whom suffered from epilepsy. With emissions recorded at dozens of places across the subjects' scalps, the researchers analysed every possible pairing of these data "channels" to establish whether the emissions in each case were in phase with one another. They added up the number of synchronized pairs and plugged that figure along with the total number of all possible pairings into a fairly straightforward statistical formula to work out how many different brain configurations that level of synchronicity yields. They then took the logarithm of that number to establish the brain's entropy.

The data were analysed in two parts. In one, they compared the emissions from four of the epileptic patients when undergoing a seizure and when in a normal "alert" state. In the second, they compared emissions from the other five individuals when sleeping and when awake. In both cases, the bottom line was the same: subjects' brains display higher entropy, or a higher value of a similar quantity known as Lempel–Ziv (LZ) complexity, when in a fully conscious state.

### **Varying results**

Guevarra Erra admits that the results are not watertight. Indeed, the LZ complexity of one of the four epileptic patients in the first analysis showed no change between seizure and alert states (although that person did remain conscious during part of the seizure). In another individual, LZ

complexity actually increased in the second analysis while that person was asleep. Guevarra Erra says that he and his colleagues didn't carry out a statistical analysis of their results in part because of the "very heterogeneous" nature of those results. But he nevertheless remains "highly confident" that the correlations they have identified are real, particularly, he argues, because they were seen in "two very different sets of data".

Peter McClintock, a physicist who works on nonlinear dynamics at Lancaster University in the UK, describes the research as "intriguing" but says that the consciousness—entropy correlation should be confirmed using a larger number of subjects. He also suggests investigating "what happens in other brain states where consciousness is altered", such as anaesthesia.

#### **Emergent property**

Perez Velazquez and colleagues argue that consciousness could simply be an "emergent property" of a system – the brain – that seeks to maximize information exchange and therefore entropy, since doing so aids the survival of the brain's bearer by allowing them to better model their environment. On the question of entropy, however, Guevarra Erra is cautious. He says that personally he would like to have a better understanding of the physical processes taking place in the brain before employing the label "entropy", explaining that Perez Velazquez was keen to use the term in their paper. One option, he says, would be to carry out fresh experiments that measure thermodynamic quantities in subjects' brains. He notes, for example, that magnetic resonance imaging can be used to measure oxygenation, which is directly related to metabolism and therefore to the generation of heat.

Guevarra Erra adds that he would like to extend their investigations beyond the hospital to cover more subtle but general cognitive behaviour. The idea would be to monitor a person's changing brain activity as they focus on carrying out a specific task, such as discriminating between musical tones or trying to find their way round a labyrinth. This, he says, should help to establish whether varying "entropy" correlates with degree of awareness as well as simply with the presence or absence of consciousness.

A paper describing the work will be published in Physical Review E and is also available on arXiv. [22]

### A new study looks for the cortical conscious network

New research published in the New Journal of Physics tries to decompose the structural layers of the cortical network to different hierarchies enabling to identify the network's nucleus, from which our consciousness could emerge.

The brain is a very complex network, with approximately 100 billion neurons and 100 trillion synapses between the neurons. In order to cope with its enormous complexity and to understand how brain function eventually creates the conscious mind, science uses advanced mathematical tools. Ultimately, scientists want to understand how a global phenomenon such as consciousness can emerge from our neuronal network.

A team of physicists from Bar Ilan University in Israel led by Professor Shlomo Havlin and Professor Reuven Cohen used network theory in order to deal with this complexity and to determine how the structure of the human cortical network can support complex data integration and conscious activity. The gray area of the human cortex, the neuron cell bodies, were scanned with MRI imaging and used to form 1000 nodes in the cortical network. The white matter of the human cortex, the neuron bundles, were scanned with DTI imaging, forming 15,000 links or edges that connected the network's nodes. In the end of this process, their network was an approximation of the structure of the human cortex.

Previous studies have shown that the human cortex is a network with small world properties, which means that it has many local structures and some shortcuts from global structures that connect faraway areas (similar to the difference between local buses and cross-country trains). The cortex also has many hubs, which are nodes that have a high number of links (like central stations), that are also strongly interconnected between themselves, making it easy to travel between the brain's information highways.

Nir Lahav, the lead author of the study, says, "In order to examine how the structure of the network can support global emerging phenomena like consciousness, we applied a network analysis called Kshell decomposition. This analysis takes into account the connectivity profile of each node, making it easy to uncover different neighborhoods of connections in the cortical network, which we called shells."

The most connected neighborhood in the network is termed the network's nucleus. Nir says, "In the process, we peel off different shells of the network to get the most connected area of the network, the nucleus. Until today, scientists were only interested in the network's nucleus, but we found that these different shells can hold important information about how the brain integrates information from the local levels of each node to the entire global network. For the first time, we could build a comprehensive topological model of the cortex."

This topological model reveals that the network's nucleus includes 20 percent of all nodes and that the remaining 80 percent are strongly connected across all of the shells. Interestingly, comparing this topology to that of other networks, such as the internet, noticeable differences are apparent. For instance, in internet network topology, almost 25 percent of the nodes are isolated, meaning they don't connect to any other shells but the nucleus. In the cortical network, however, there are hardly any isolated nodes. It seems that the cortex is much more connected and efficient than the internet.

Looking at all the shells of the cortical network, the authors were able to define the network's hierarchical structure and essentially model how information flows within the network. The structure revealed how shells of low connectivity are nodes that typically perform specific functions like face recognition. From there, the data is transferred to higher, more connected shells that enable additional data integration. This reveals regions of the executive network and working memory. With these areas, researchers can focus on task performance, for example.

The integrated information then 'travels' to the most connected neighborhood of nodes, the nucleus, which spans across several regions of the cortex. According to Nir, "It's an interconnected collective which is densely linked with itself and can perform global functions due to its great number of global structures, which are widespread across the brain."

Which global function might the nucleus serve? The authors suggest the answer is no less than consciousness itself.

"The connection between brain activity and consciousness is still a great mystery," says Nir. The main hypothesis today is that in order to create conscious activity, the brain must integrate relevant information from multiple areas of the network. According to this theory, led by Professor Giulio Tononi from the University of Wisconsin, if the level of integrated information crosses a certain limit, a new and emergent state is entered—consciousness. This model suggests that consciousness depends on both information integration and information segregation. Loosely speaking, consciousness is generated by a "central" network structure with a high capacity for information integration, with the contribution of sub-networks that contain specific and segregated information without being part of the central structure. In other words, certain parts of the brain are more involved than others in the conscious complex of the brain, yet other connected parts still contribute, working quietly outside the conscious complex.

The authors demonstrate how the nucleus and the shells satisfy all of the requirements of these recent consciousness theories. The shells calculate and contribute to data integration without actually being part of the conscious complex, while the nucleus receives relevant information from all other hierarchies and integrates it to a unified function using its global interconnected structure.

The nucleus could thus be this conscious complex, serving as a platform for consciousness to emerge from the network activity.

When the authors examined the different regions that make up the nucleus, they revealed that, indeed, these regions have been previously associated with conscious activities. For example, structures within the brain's midline, which form the majority of the network's nucleus, were found to be associated with the stream of consciousness, and some researchers, like Professor Georg Northoff from the University of Ottawa, have suggested that these regions are involved with creating our sense of self.

"Now, we need to use this analysis on the whole brain, and not only on the cortex in order to reveal a more exact model of the brain's hierarchy, and later on understand what, exactly, are the neuronal dynamics that lead to such global integration and ultimately consciousness." [21]

## Network theory sheds new light on origins of consciousness

Where in your brain do you exist? Is your awareness of the world around you and of yourself as an individual the result of specific, focused changes in your brain, or does that awareness come from a broad network of neural activity? How does your brain produce awareness?

Vanderbilt University researchers took a significant step toward answering these longstanding questions with a recent brain imaging study, in which they discovered global changes in how brain areas communicate with one another during awareness. Their findings, which were published March 9 in the Proceedings of the National Academy of Sciences, challenge previous theories that hypothesized much more restricted changes were responsible for producing awareness.

"Identifying the fingerprints of consciousness in humans would be a significant advancement for basic and medical research, let alone its philosophical implications on the underpinnings of the

human experience," said René Marois, professor and chair of psychology at Vanderbilt University and senior author of the study. "Many of the cognitive deficits observed in various neurological diseases may ultimately stem from changes in how information is communicated throughout the brain."

Using graph theory, a branch of mathematics concerned with explaining the interactive links between members of a complex network, such as social networks or flight routes, the researchers aimed to characterize how connections between the various parts of the brain were related to awareness.

"With graph theory, one can ask questions about how efficiently the transportation networks in the United States and Europe are connected via transportation hubs like LaGuardia Airport in New York," Douglass Godwin, graduate student and lead author on the research, said. "We can ask those same questions about brain networks and hubs of neural communication."

Modern theories of the neural basis of consciousness fall generally into two camps: focal and global. Focal theories contend there are specific areas of the brain that are critical for generating consciousness, while global theories argue consciousness arises from large-scale brain changes in activity. This study applied graph theory analysis to adjudicate between these theories.

The researchers recruited 24 members of the university community to participate in a functional magnetic resonance imaging (fMRI) experiment. While in the fMRI scanner, participants were asked to detect a disk that was briefly flashed on a screen. In each trial, participants responded whether they were able to detect the target disk and how much confidence they had in their answer. Experimenters then compared the results of the high-confidence trials during which the target was detected to the trials when it was missed by participants. These were treated as "aware" and "unaware" trials, respectively.

Comparison of aware and unaware trials using conventional fMRI analyses that assess the amplitude of brain activity showed a pattern of results typical of similar studies, with only a few areas of the brain showing more activity during detection of the target than when participants missed seeing it. The present study, however, was interested not simply in what regions might be more activated with awareness, but how they communicate with one another.

Unlike the focal results seen using more conventional analysis methods, the results via this network approach pointed toward a different conclusion. No one area or network of areas of the brain stood out as particularly more connected during awareness of the target; the whole brain appeared to become functionally more connected following reports of awareness.

"We know there are numerous brain networks that control distinct cognitive functions such as attention, language and control, with each node of a network densely interconnected with other nodes of the same network, but not with other networks," Marois said. "Consciousness appears to break down the modularity of these networks, as we observed a broad increase in functional connectivity between these networks with awareness."

The research suggests that consciousness is likely a product of this widespread communication, and that we can only report things that we have seen once they are being represented in the brain in this manner. Thus, no one part of the brain is truly the "seat of the soul," as René Descartes once

wrote in a hypothesis about the pineal gland, but rather, consciousness appears to be an emergent property of how information that needs to be acted upon gets propagated throughout the brain.

"We take for granted how unified our experience of the world is. We don't experience separate visual and auditory worlds, it's all integrated into a single conscious experience," Godwin said. "This widespread cross-network communication makes sense as a mechanism by which consciousness gets integrated into that singular world." [20]

## Neuromorphic computing mimics important brain feature

When you hear a sound, only some of the neurons in the auditory cortex of your brain are activated. This is because every auditory neuron is tuned to a certain range of sound, so that each neuron is more sensitive to particular types and levels of sound than others. In a new study, researchers have designed a neuromorphic ("brain-inspired") computing system that mimics this neural selectivity by using artificial level-tuned neurons that preferentially respond to specific types of stimuli.

In the future, level-tuned neurons may help enable neuromorphic computing systems to perform tasks that traditional computers cannot, such as learning from their environment, pattern recognition, and knowledge extraction from big data sources.

The researchers, Angeliki Pantazi et al., at IBM Research-Zurich and École Polytechnique Fédérale de Lausanne, both in Switzerland, have published a paper on the new neuromorphic architecture in a recent issue of Nanotechnology.

Like all neuromorphic computing architectures, the proposed system is based on neurons and their synapses, which are the junctions where neurons send signals to each other. In this study, the researchers physically implemented artificial neurons using phase-change materials. These materials have two stable states: a crystalline, low-resistivity state and an amorphous, high-resistivity state. Just as in traditional computing, the states can be switched by the application of a voltage.

When the neuron's conductance reaches a certain threshold, the neuron fires.

"We have demonstrated that phase-change-based memristive devices can be used to create artificial neurons and synapses to store and process data," coauthor Evangelos Eleftheriou at IBM ResearchZurich told Phys.org. "A phase-change neuron uses the phase configuration of the phasechange material to represent its internal state, the membrane potential. For the phase-change synapse, the synaptic weight—which is responsible for the plasticity—is encoded by the conductance of the nanodevice."

In this architecture, each neuron is tuned to a specific range, or level. Neurons receive signals from many other neurons, and a level is defined as the cumulative contribution of the sum of these incoming signals.

"We have introduced the biologically inspired architecture of level-tuned neurons that is able to distinguish different patterns in an unsupervised way," Eleftheriou said. "This is important for the development of ultra-dense, scalable and energy-efficient neuromorphic computing."

One of the main advantages of these highly selective level-tuned neurons is their improved learning ability. In neuromorphic computing, learning occurs through repeated incoming signals, which strengthens certain synaptic connections. The researchers showed that level-tuned neurons are very good at learning multiple input patterns, even in the presence of input noise.

"Even a single neuron can be used to detect patterns and to discover correlations in real-time streams of event-based data," Eleftheriou said. "Level-tuned neurons increase the capability of a single-neuron network for discriminating information when multiple patterns appear at the input. Level-tuned neurons, along with the high-speed and low-energy characteristics of their phasechange-based implementation, will be particularly useful for various emerging applications, such as Internet of Things, that collect and analyze large volumes of sensory information and applications to detect patterns in data sources, such as from social media to discover trends, or weather data for real-time forecasts, or healthcare data to detect patterns in diseases, etc."

In the future, the researchers plan to further develop the concept of artificial level-tuned neurons in order to design enhanced large-scale neural networks.

"We will be looking into more complex computational tasks based on artificial spiking neurons and their synapses," Eleftheriou said. "We are interested in studying the scaling potential and applications of such neuromorphic systems in cognitive computing systems." [19]

# IBM scientists imitate the functionality of neurons with a phasechange device

IBM scientists have created randomly spiking neurons using phase-change materials to store and process data. This demonstration marks a significant step forward in the development of energyefficient, ultra-dense integrated neuromorphic technologies for applications in cognitive computing.

Inspired by the way the biological brain functions, scientists have theorized for decades that it should be possible to imitate the versatile computational capabilities of large populations of neurons. However, doing so at densities and with a power budget that would be comparable to those seen in biology has been a significant challenge, until now.

"We have been researching phase-change materials for memory applications for over a decade, and our progress in the past 24 months has been remarkable," said IBM Fellow Evangelos Eleftheriou. "In this period, we have discovered and published new memory techniques, including projected memory, stored 3 bits per cell in phase-change memory for the first time, and now are demonstrating the powerful capabilities of phase-change-based artificial neurons, which can perform various computational primitives such as data-correlation detection and unsupervised learning at high speeds using very little energy."

The artificial neurons designed by IBM scientists in Zurich consist of phase-change materials, including germanium antimony telluride, which exhibit two stable states, an amorphous one (without a clearly defined structure) and a crystalline one (with structure). These materials are the basis of re-writable Blu-ray discs.

However, the artificial neurons do not store digital information; they are analog, just like the synapses and neurons in our biological brain.

In the published demonstration, the team applied a series of electrical pulses to the artificial neurons, which resulted in the progressive crystallization of the phase-change material, ultimately causing the neuron to fire. In neuroscience, this function is known as the integrate-and-fire property of biological neurons. This is the foundation for event-based computation and, in principle, is similar to how our brain triggers a response when we touch something hot.

Exploiting this integrate-and-fire property, even a single neuron can be used to detect patterns and discover correlations in real-time streams of event-based data.

For example, in the Internet of Things, sensors can collect and analyze volumes of weather data collected at the edge for faster forecasts. The artificial neurons could be used to detect patterns in financial transactions to find discrepancies or use data from social media to discover new cultural trends in real time. Large populations of these high-speed, low-energy nano-scale neurons could also be used in neuromorphic coprocessors with co-located memory and processing units.

IBM scientists have organized hundreds of artificial neurons into populations and used them to represent fast and complex signals. Moreover, the artificial neurons have been shown to sustain billions of switching cycles, which would correspond to multiple years of operation at an update frequency of 100 Hz. The energy required for each neuron update was less than five picojoule and the average power less than 120 microwatts—for comparison, 60 million microwatts power a 60 watt lightbulb.

"Populations of stochastic phase-change neurons, combined with other nanoscale computational elements such as artificial synapses, could be a key enabler for the creation of a new generation of extremely dense neuromorphic computing systems," said Tomas Tuma, a co-author of the paper. [18]

# Programmable ions set the stage for general-purpose quantum computers

An ion trap with four segmented blade electrodes used to trap a linear chain of atomic ions for quantum information processing. Each ion is addressed optically for individual control and readout using the high optical access of the trap.

Quantum computers promise speedy solutions to some difficult problems, but building large-scale, general-purpose quantum devices is a problem fraught with technical challenges.

To date, many research groups have created small but functional quantum computers. By combining a handful of atoms, electrons or superconducting junctions, researchers now regularly demonstrate quantum effects and run simple quantum algorithms—small programs dedicated to solving particular problems.

But these laboratory devices are often hard-wired to run one program or limited to fixed patterns of interactions between the quantum constituents. Making a quantum computer that can run arbitrary algorithms requires the right kind of physical system and a suite of programming tools. Atomic ions, confined by fields from nearby electrodes, are among the most promising platforms for meeting these needs.

In a paper published as the cover story in Nature on August 4, researchers working with Christopher

Monroe, a Fellow of the Joint Quantum Institute and the Joint Center for Quantum Information and Computer Science at the University of Maryland, introduced the first fully programmable and reconfigurable quantum computer module. The new device, dubbed a module because of its potential to connect with copies of itself, takes advantage of the unique properties offered by trapped ions to run any algorithm on five quantum bits, or qubits—the fundamental unit of information in a quantum computer.

"For any computer to be useful, the user should not be required to know what's inside," Monroe says. "Very few people care what their iPhone is actually doing at the physical level. Our experiment brings high-quality quantum bits up to a higher level of functionality by allowing them to be programmed and reconfigured in software."

The new module builds on decades of research into trapping and controlling ions. It uses standard techniques but also introduces novel methods for control and measurement. This includes manipulating many ions at once using an array of tightly-focused laser beams, as well as dedicated detection channels that watch for the glow of each ion.

"These are the kinds of discoveries that the NSF Physics Frontiers Centers program is intended to enable," says Jean Cottam Allen, a program director in the National Science Foundation's physics division. "This work is at the frontier of quantum computing, and it's helping to lay a foundation and bring practical quantum computing closer to being a reality."

The team tested their module on small instances of three problems that quantum computers are known to solve quickly. Having the flexibility to test the module on a variety of problems is a major step forward, says Shantanu Debnath, a graduate student at JQI and the paper's lead author. "By directly connecting any pair of qubits, we can reconfigure the system to implement any algorithm," Debnath says. "While it's just five qubits, we know how to apply the same technique to much larger collections."

At the module's heart, though, is something that's not even quantum: A database stores the best shapes for the laser pulses that drive quantum logic gates, the building blocks of quantum algorithms. Those shapes are calculated ahead of time using a regular computer, and the module uses software to translate an algorithm into the pulses in the database.

### Putting the pieces together

Every quantum algorithm consists of three basic ingredients. First, the qubits are prepared in a particular state; second, they undergo a sequence of quantum logic gates; and last, a quantum measurement extracts the algorithm's output.

The module performs these tasks using different colors of laser light. One color prepares the ions using a technique called optical pumping, in which each qubit is illuminated until it sits in the proper quantum energy state. The same laser helps read out the quantum state of each atomic ion at the end of the process. In between, a separate laser strikes the ions to drive quantum logic gates.

These gates are like the switches and transistors that power ordinary computers. Here, lasers push on the ions and couple their internal qubit information to their motion, allowing any two ions in the module to interact via their strong electrical repulsion. Two ions from across the chain notice each other through this electrical interaction, just as raising and releasing one ball in a Newton's cradle transfers energy to the other side.

The re-configurability of the laser beams is a key advantage, Debnath says. "By reducing an algorithm into a series of laser pulses that push on the appropriate ions, we can reconfigure the wiring between these qubits from the outside," he says. "It becomes a software problem, and no other quantum computing architecture has this flexibility."

To test the module, the team ran three different quantum algorithms, including a demonstration of a Quantum Fourier Transform (QFT), which finds how often a given mathematical function repeats. It is a key piece in Shor's quantum factoring algorithm, which would break some of the most widelyused security standards on the internet if run on a big enough quantum computer.

Two of the algorithms ran successfully more than 90% of the time, while the QFT topped out at a 70% success rate. The team says that this is due to residual errors in the pulse-shaped gates as well as systematic errors that accumulate over the course of the computation, neither of which appear fundamentally insurmountable.

They note that the QFT algorithm requires all possible two-qubit gates and should be among the most complicated quantum calculations.

The team believes that eventually more qubits—perhaps as many as 100—could be added to their quantum computer module. It is also possible to link separate modules together, either by physically moving the ions or by using photons to carry information between them.

Although the module has only five qubits, its flexibility allows for programming quantum algorithms that have never been run before, Debnath says. The researchers are now looking to run algorithms on a module with more qubits, including the demonstration of quantum error correction routines as part of a project funded by the Intelligence Advanced Research Projects Activity. [17]

# **Realizing quantum bits**

A research team from Germany, France and Switzerland has realised quantum bits, short qubits, in a new form. One day, they might become the information units of quantum computers.

To date, researchers have realised qubits in the form of individual electrons (aktuell.ruhrunibochum.de/pm2012/pm00090.html.en). However, this led to interferences and rendered the information carriers difficult to programme and read. The group has solved this problem by utilising electron holes as qubits, rather than electrons.

A report has been published in the journal Nature Materials by a team of researchers from RuhrUniversität Bochum, the University of Basel, and Lyon University; among its contributors were the two Bochum-based researchers Prof Dr Andreas Wieck and Dr Arne Ludwig from the Chair of Applied Solid State Physics. The project was headed by the Swiss researcher Prof Dr Richard Warburton.

### **Electrons as qubits**

In order to realise qubits in the form of electrons, an electron is locked in a tiny semiconductor volume, the so-called quantum dot. The spin turns the electron into a small permanent magnet. Researchers are able to manipulate the spin via an external magnetic field and initiate precession. The direction of the spin is used to code information.

The problem: the nuclear spins of the surrounding atoms also generate magnetic fields, which distort the external magnetic field in a random, unpredictable manner. This, in turn, interferes with programming and reading qubits. Consequently, the team searched for another method. The solution: rather than locking individual electrons in the quantum dot, the team removed specific electrons. Thus, positively charged vacancies were generated in the electron structure, so-called electron holes.

# **Advantages of electron holes**

Electron holes have a spin, too. Researchers can manipulate it via the magnetic field in order to code information. As the holes are positively charged, they are decoupled from the nuclei of the surrounding atoms, which are likewise positively charged. This is why they are virtually immune against the interfering forces of the nuclear spin.

"This is important if we one day want to manufacture reproducible components that are based on quantum bits," explains Andreas Wieck. However, this method is only applicable at low temperatures, as the holes are more likely to be disturbed by warmth than the electrons.

At Ruhr-Universität, researchers are able to generate quantum dots of outstanding quality. The experiment could be conducted thanks to a structural design developed by Arne Ludwig in Basel and subsequently realised at the RUB Department headed by Andreas Wieck. It enabled the researcher to apply not just individual electrons to quantum dots, but also electron holes. Sascha René Valentin, PhD student from Bochum, utilised the technique for the purpose of the current study. [16]

# Russian physicists discover a new approach for building quantum computers

Physicists from MIPT and the Russian Quantum Center have developed an easier method to create a universal quantum computer using multilevel quantum systems (qudits), each one of which is able to work with multiple "conventional" quantum elements – qubits.

Professor Vladimir Man'ko, Aleksey Fedorov and Evgeny Kiktenko have published the results of their studies of multilevel quantum systems in a series of papers in Physical Review A, Physics Letters A, and also Quantum Measurements and Quantum Metrology.

"In our studies, we demonstrated that correlations similar to those used for quantum information technologies in composite quantum systems also occur in non-composite systems – systems which we suppose may be easier to work with in certain cases. In our latest paper we proposed a method

of using entanglement between internal degrees of freedom of a single eight-level system to implement the protocol of quantum teleportation, which was previously implemented experimentally for a system of three two-level systems," says Vladimir Man'ko.

Quantum computers, which promise to bring about a revolution in computer technology, could be built from elementary processing elements called quantum bits – qubits. While elements of classical computers (bits) can only be in two states (logic zero and logic one), qubits are based on quantum objects that can be in a coherent superposition of two states, which means that they can encode the intermediate states between logic zero and one. When a qubit is measured, the outcome is either a zero or a one with a certain probability (determined by the laws of quantum mechanics).

In a quantum computer, the initial condition of a particular problem is written in the initial state of the qubit system, then the qubits enter into a special interaction (determined by the specific problem). Finally, the user reads the answer to the problem by measuring the final states of the quantum bits.

Quantum computers will be able to solve certain problems that are currently far beyond the reach of even the most powerful classical supercomputers. In cryptography, for example, the time required for a conventional computer to break the RSA algorithm, which is based on the prime factorization of large numbers, would be comparable to the age of the universe. A quantum computer, on the other hand, could solve the problem in a matter of minutes.

However, there is a significant obstacle standing in the way of a quantum revolution – the instability of quantum states. Quantum objects that are used to create qubits – ions, electrons, Josephson junctions etc. can only maintain a certain quantum state for a very short time. However, calculations not only require that qubits maintain their state, but also that they interact with one another. Physicists all over the world are trying to extend the lifespan of qubits. Superconducting qubits used to "survive" only for a few nanoseconds, but now they can be kept for milliseconds before decoherence – which is closer to the time required for calculations.

In a system with dozens or hundreds of qubits, however, the problem is fundamentally more complex.

Man'ko, Fedorov, and Kiktenko began to look at the problem from the other way around – rather than try to maintain the stability of a large qubit system, they tried to increase the dimensions of the systems required for calculations. They are investigating the possibility of using qudits rather than qubits for calculations. Qudits are quantum objects in which the number of possible states (levels) is greater than two (their number is denoted by the letter D). There are qutrits, which have three states; ququarts, which have four states, etc. Algorithms are now actively being studied in which the use of qudits could prove to be more beneficial than using qubits.

"A qudit with four or five levels is able to function as a system of two "ordinary" qubits, and eight levels is enough to imitate a three-qubit system. At first, we saw this as a mathematical equivalence allowing us to obtain new entropic correlations. For example, we obtained the value of mutual information (the measure of correlation) between virtual qubits isolated in a state space of a single four-level system," says Fedorov.

He and his colleagues demonstrated that on one qudit with five levels, created using an artificial atom, it is possible to perform full quantum computations—in particular, the realization of the Deutsch algorithm. This algorithm is designed to test the values of a large number of binary variables.

It can be called the fake coin algorithm: imagine that you have a number of coins, some of which are fake – they have the same image on the obverse and reverse sides. To find these coins using the "classical method", you have to look at both sides. With the Deutsch algorithm, you "merge" the obverse and reverse sides of the coin and you can then see a fake coin by only looking at one side.

The idea of using multilevel systems to emulate multi-qubit processors was proposed earlier in the work of Russian physicists from the Kazan Physical-Technical Institute. To run a two-qubit Deutsch algorithm, for example, they proposed using a nuclear spin of 3/2 with four different states. In recent years, however, experimental progress in creating qudits in superconducting circuits has shown that they have a number of advantages.

However, superconducting circuits require five levels: the last level performs an ancillary role to allow for a complete set of all possible quantum operations.

"We are making significant progress, because in certain physical implementations, it is easier to control multilevel qudits than a system of the corresponding number of qubits, and this means that we are one step closer to creating a full-fledged quantum computer. Multilevel elements offer advantages in other quantum technologies too, such as quantum cryptography," says Fedorov. [15]

# Precise atom implants in silicon provide a first step toward practical quantum computers

Sandia National Laboratories has taken a first step toward creating a practical quantum computer, able to handle huge numbers of computations instantaneously.

Here's the recipe:

A "donor" atom propelled by an ion beam is inserted very precisely in microseconds into an industrystandard silicon substrate.

The donor atom—in this case, antimony (Sb) —carries one more electron (five) than a silicon atom (four). Because electrons pair up, the odd Sb electron remains free.

Instruments monitor the free electron to determine if, under pressure from an electromagnetic field, it faces up or down, a property called "spin." Electrons in this role, called qubits, signal "yes" or "no" from the subatomic scale, and so act as the information bearers of a quantum computer.

The ability to precisely place a donor atom in silicon means that it should be possible to insert a second donor atom just far enough away, in the "Goldilocks" zone where communication is neither lost through distance nor muffled by too-close proximity. Sandia will try to do this later this year, said lead researcher Meenakshi Singh, a postdoctoral fellow. Qubits "talking" to each other are the basis of quantum computing circuits.

The successful Sandia first step, reported in Applied Physics Letters, makes use of electromagnetic forces provided by a neighboring quantum dot pre-embedded in the silicon. The quantum dot—itself a tiny sea of electrons—contains a variety of energy levels and operates like a transistor to block or pass the qubit.

If an available dot energy level is compatible with the electron, the transistor gate is effectively open and the electron jumps into the dot. If not, the qubit stays put. That action is reported back to the surface by a photodiode sensor sensitive to current flows rather than photon movement. Because of the multiple "gates" in the quantum dot, many qubits at different energy levels could pass through the transistor, or be denied passage, theoretically making possible an extremely wide array of information processing.

"Our method is promising because, since it reads the electron's spin rather than its electrical charge, its information is not swallowed by background static and instead remains coherent for a relatively long time," Singh said. "Also, we use silicon as our basic material, for which commercial fabrication technologies are already developed, rather than employing superconducting components that can be expensive."

A third unique quality of the Sandia method is the precise and rapid placement of donor atoms exactly where they should be, placed in microseconds within nanometers of their target, instead of a buckshot approach that places qubits only where they statistically average to Goldilocks distances.

While components of this experiment have been demonstrated before, this is the first time all have worked together on a single chip, with researchers knowing accurately the vertical and horizontal placement of each qubit, instead of mere statistical approximations.

Sandia researcher and paper author Mike Lilly expects "the Sandia technique will allow fabrication of more complicated multi-qubit structures and do so at higher yield than existing donor implant approaches."

Components of the successful silicon device were fabricated in Sandia's Microsystems and Engineering Sciences Application (MESA) facility. The donor atoms were placed at Sandia's Ion Beam Laboratory. Experiment measurements were made at the Sandia/Los Alamos Center for Integrated Nanotechnologies, a user facility supported by DOE's Office of Basic Energy Sciences.

The method in its entirety is straightforward but requires a range of technical expertise and machinery, Singh said. "We used ion beams, silicon fabrication facilities, low-temperature measurements and simulations. It's hard to find a non-commercial place outside of a national lab that can do all of this." [14]

# Team demonstrates large-scale technique to produce quantum dots

A method to produce significant amounts of semiconducting nanoparticles for light-emitting displays, sensors, solar panels and biomedical applications has gained momentum with a demonstration by researchers at the Department of Energy's Oak Ridge National Laboratory.

While zinc sulfide nanoparticles - a type of quantum dot that is a semiconductor - have many potential applications, high cost and limited availability have been obstacles to their widespread use. That could change, however, because of a scalable ORNL technique outlined in a paper published in Applied Microbiology and Biotechnology.

Unlike conventional inorganic approaches that use expensive precursors, toxic chemicals, high temperatures and high pressures, a team led by ORNL's Ji-Won Moon used bacteria fed by inexpensive sugar at a temperature of 150 degrees Fahrenheit in 25- and 250-gallon reactors. Ultimately, the team produced about three-fourths of a pound of zinc sulfide nanoparticles - without process optimization, leaving room for even higher yields.

The ORNL biomanufacturing technique is based on a platform technology that can also produce nanometer-size semiconducting materials as well as magnetic, photovoltaic, catalytic and phosphor materials. Unlike most biological synthesis technologies that occur inside the cell, ORNL's biomanufactured quantum dot synthesis occurs outside of the cells. As a result, the nanomaterials are produced as loose particles that are easy to separate through simple washing and centrifuging.

The results are encouraging, according to Moon, who also noted that the ORNL approach reduces production costs by approximately 90 percent compared to other methods.

"Since biomanufacturing can control the quantum dot diameter, it is possible to produce a wide range of specifically tuned semiconducting nanomaterials, making them attractive for a variety of applications that include electronics, displays, solar cells, computer memory, energy storage, printed electronics and bio-imaging," Moon said.

Successful biomanufacturing of light-emitting or semiconducting nanoparticles requires the ability to control material synthesis at the nanometer scale with sufficiently high reliability, reproducibility and yield to be cost effective. With the ORNL approach, Moon said that goal has been achieved.

Researchers envision their quantum dots being used initially in buffer layers of photovoltaic cells and other thin film-based devices that can benefit from their electro-optical properties as lightemitting materials. [13]

# Superfast light source made from artificial atom

All light sources work by absorbing energy – for example, from an electric current – and emit energy as light. But the energy can also be lost as heat and it is therefore important that the light sources emit the light as quickly as possible, before the energy is lost as heat. Superfast light sources can be used, for example, in laser lights, LED lights and in single-photon light sources for quantum technology. New research results from the Niels Bohr Institute show that light sources can be made much faster by using a principle that was predicted theoretically in 1954. The results are published in the scientific journal, Physical Review Letters.

Researchers at the Niels Bohr Institute are working with quantum dots, which are a kind of artificial atom that can be incorporated into optical chips. In a quantum dot, an electron can be excited (i.e. jump up), for example, by shining a light on it with a laser and the electron leaves a 'hole'. The stronger the interaction between light and matter, the faster the electron decays back into the hole and the faster the light is emitted.

But the interaction between light and matter is naturally very weak and it makes the light sources very slow to emit light and this can reduce energy efficiency.

Already in 1954, the physicist Robert Dicke predicted that the interaction between light and matter could be increased by having a number of atoms that 'share' the excited state in a quantum superposition.

### Quantum speed up

Demonstrating this effect has been challinging so far because the atoms either come so close together that they bump into each other or they are so far apart that the quantum speed up does not work. Researchers at the Niels Bohr Institute have now finally demonstrated the effect experimentally, but in an entirely different physical system than Dicke had in mind. They have shown this so-called superradiance for photons emitted from a single quantum dot.

"We have developed a quantum dot so that it behaves as if it was comprised of five quantum dots, which means that the light is five times stronger. This is due to the attraction between the electron and the hole. But what is special is that the quantum dot still only emits a single photon at a time. It is an outstanding single-photon source," says Søren Stobbe, who is an associate professor in the Quantum Photonic research group at the Niels Bohr Institute at the University of Copenhagen and led the project. The experiment was carried out in collaboration with Professor David Ritchie's research group at the University of Cambridge, who have made the quantum dots.

Petru Tighineanu, a postdoc in the Quantum Photonics research group at the Niels Bohr Institute, has carried out the experiments and he explains the effect as such, that the atoms are very small and light is very 'big' because of its long wavelength, so the light almost cannot 'see' the atoms – like a lorry that is driving on a road and does not notice a small pebble. But if many pebbles become a larger stone, the lorry will be able to register it and then the interaction becomes much more dramatic. In the same way, light interacts much more strongly with the quantum dot if the quantum dot contains the special superradiant quantum state, which makes it look much bigger.

# **Increasing the light-matter interaction**

"The increased light-matter interaction makes the quantum dots more robust in regards to the disturbances that are found in all materials, for example, acoustic oscillations. It helps to make the photons more uniform and is important for how large you can build future quantum computers," says Søren Stobbe.

He adds that it is actually the temperature, which is only a few degrees above absolute zero, that limits how fast the light emissions can remain in their current experiments. In the long term, they will study the quantum dots at even lower temperatures, where the effects could be very dramatic. [12]

# Single-photon source is efficient and indistinguishable

Devices that emit one – and only one – photon on demand play a central role in light-based quantum-information systems. Each photon must also be emitted in the same quantum state, which makes each photon indistinguishable from all the others. This is important because the quantum state of the photon is used to carry a quantum bit (qubit) of information.

Quantum dots are tiny pieces of semiconductor that show great promise as single-photon sources. When a laser pulse is fired at a quantum dot, an electron is excited between two distinct energy levels. The excited state then decays to create a single photon with a very specific energy. However, this process can involve other electron excitations that result in the emission of photons with a wide range of energies – photons that are therefore not indistinguishable.

## **Exciting dots**

This problem can be solved by exciting the quantum dot with a pulse of light at the same energy as the emitted photon. This is called resonance fluorescence, and has been used to create devices that are very good at producing indistinguishable single photons. However, this process is inefficient, and only produces a photon about 6% of the time.

Now, Chaoyang Lu, Jian-Wei Pan and colleagues at the University of Science and Technology of China have joined forces with researchers in Denmark, Germany and the UK to create a resonancefluorescence-based source that emits a photon 66% of the time when it is prompted by a laser pulse. Of these photons, 99.1% are solo and 98.5% are in indistinguishable quantum states – with both figures of merit being suitable for applications in quantum-information systems.

Lu told physicsworld.com that nearly all of the laser pulses that strike the source produce a photon, but about 34% of these photons are unable to escape the device. The device was operated at a laser-pulse frequency of 81 MHz and a pulse power of 24 nW, which is a much lower power requirement than other quantum-dot-based sources.

## **Quantum sandwich**

The factor-of-ten improvement in efficiency was achieved by sandwiching a quantum dot in the centre of a "micropillar" created by stacking 40 disc-like layers (see figure). Each layer is a "distributed Bragg reflector", which is a pair of mirrors that together have a thickness of one quarter the wavelength of the emitted photons.

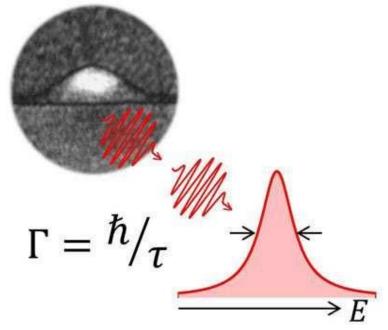
The micropillar is about 2.5  $\mu$ m in diameter and about 10  $\mu$ m tall, and it allowed the team to harness the "Purcell effect", whereby the rate of fluorescence is increased significantly when the emitter is placed in a resonant cavity.

Lu says that the team is already thinking about how the photon sources could be used to perform boson sampling (see "'Boson sampling' offers shortcut to quantum computing"). This involves a network of beam splitters that converts one set of photons arriving at a number of parallel input ports into a second set leaving via a number of parallel outputs. The "result" of the computation is the probability that a certain input configuration will lead to a certain output. This result cannot be easily calculated using a conventional computer, and this has led some physicists to suggest that boson sampling could be used to solve practical problems that would take classical computers vast amounts of time to solve.

Other possible applications for the source are the quantum teleportation of three properties of a quantum system – the current record is two properties and is held by Lu and Pan – or quantum cryptography.

The research is described in Physical Review Letters. [11]

# Semiconductor quantum dots as ideal single-photon source



A single-photon source never emits two or more photons at the same time. Single photons are important in the field of quantum information technology where, for example, they are used in quantum computers. Alongside the brightness and robustness of the light source, the indistinguishability of the photons is especially crucial. In particular, this means that all photons must be the same color. Creating such a source of identical single photons has proven very difficult in the past.

However, quantum dots made of semiconductor materials are offering new hope. A quantum dot is a collection of a few hundred thousand atoms that can form itself into a semiconductor under certain conditions. Single electrons can be captured in these quantum dots and locked into a very small area. An individual photon is emitted when an engineered quantum state collapses.

#### Noise in the semiconductor

A team of scientists led by Dr. Andreas Kuhlmann and Prof. Richard J. Warburton from the University of Basel have already shown in past publications that the indistinguishability of the photons is reduced by the fluctuating nuclear spin of the quantum dot atoms. For the first time ever, the scientists have managed to control the nuclear spin to such an extent that even photons sent out at very large intervals are the same color.

Quantum cryptography and quantum communication are two potential areas of application for single-photon sources. These technologies could make it possible to perform calculations that are far beyond the capabilities of today's computers. [10]

# How to Win at Bridge Using Quantum Physics

Contract bridge is the chess of card games. You might know it as some stuffy old game your grandparents play, but it requires major brainpower, and preferably an obsession with rules and strategy. So how to make it even geekier? Throw in some quantum mechanics to try to gain a

competitive advantage. The idea here is to use the quantum magic of entangled photons–which are essentially twins, sharing every property–to transmit two bits of information to your bridge partner for the price of one. Understanding how to do this is not an easy task, but it will help elucidate some basic building blocks of quantum information theory. It's also kind of fun to consider whether or not such tactics could ever be allowed in professional sports. [6]

# **Quantum Information**

In quantum mechanics, quantum information is physical information that is held in the "state" of a quantum system. The most popular unit of quantum information is the qubit, a two-level quantum system. However, unlike classical digital states (which are discrete), a two-state quantum system can actually be in a superposition of the two states at any given time.

Quantum information differs from classical information in several respects, among which we note the following:

However, despite this, the amount of information that can be retrieved in a single qubit is equal to one bit. It is in the processing of information (quantum computation) that a difference occurs.

The ability to manipulate quantum information enables us to perform tasks that would be unachievable in a classical context, such as unconditionally secure transmission of information. Quantum information processing is the most general field that is concerned with quantum information. There are certain tasks which classical computers cannot perform "efficiently" (that is, in polynomial time) according to any known algorithm. However, a quantum computer can compute the answer to some of these problems in polynomial time; one well-known example of this is Shor's factoring algorithm. Other algorithms can speed up a task less dramatically - for example, Grover's search algorithm which gives a quadratic speed-up over the best possible classical algorithm.

Quantum information, and changes in quantum information, can be quantitatively measured by using an analogue of Shannon entropy. Given a statistical ensemble of quantum mechanical systems with the density matrix S, it is given by.

Many of the same entropy measures in classical information theory can also be generalized to the quantum case, such as the conditional quantum entropy. [7]

# **Heralded Qubit Transfer**

Optical photons would be ideal carriers to transfer quantum information over large distances. Researchers envisage a network where information is processed in certain nodes and transferred between them via photons. However, inherent losses in long-distance networks mean that the information transfer is subject to probabilistic errors, making it hard to know whether the transfer of a qubit of information has been successful. Now Gerhard Rempe and colleagues from the Max Planck Institute for Quantum Optics in Germany have developed a new protocol that solves this problem through a strategy that "heralds" the accurate transfer of quantum information at a network node.

The method developed by the researchers involves transferring a photonic qubit to an atomic qubit trapped inside an optical cavity. The photon-atom quantum information transfer is initiated via a quantum "logic-gate" operation, performed by reflecting the photon from the atom-cavity system, which creates an entangled atom-photon state. The detection of the reflected photon then collapses the atom into a definite state. This state can be one of two possibilities, depending on the photonic state detected: Either the atom is in the initial qubit state encoded in the photon and the transfer process is complete, or the atom is in a rotated version of this state. The authors were able to show that the roles of the atom and photon could be reversed. Their method could thus be used as a quantum memory that stores (photon-to-atom state transfer) and recreates (atom-to-photon state transfer) a single-photon polarization qubit. [9]

## **Quantum Teleportation**

Quantum teleportation is a process by which quantum information (e.g. the exact state of an atom or photon) can be transmitted (exactly, in principle) from one location to another, with the help of classical communication and previously shared quantum entanglement between the sending and receiving location. Because it depends on classical communication, which can proceed no faster than the speed of light, it cannot be used for superluminal transport or communication of classical bits. It also cannot be used to make copies of a system, as this violates the no-cloning theorem. Although the name is inspired by the teleportation commonly used in fiction, current technology provides no possibility of anything resembling the fictional form of teleportation. While it is possible to teleport one or more qubits of information between two (entangled) atoms, this has not yet been achieved between molecules or anything larger. One may think of teleportation either as a kind of transportation, or as a kind of communication; it provides a way of transporting a qubit from one location to another, without having to move a physical particle along with it.

The seminal paper first expounding the idea was published by C. H. Bennett, G. Brassard, C. Crépeau, R. Jozsa, A. Peres and W. K. Wootters in 1993. Since then, quantum teleportation has been realized in various physical systems. Presently, the record distance for quantum teleportation is 143 km (89 mi) with photons, and 21 m with material systems. In August 2013, the achievement of "fully deterministic" quantum teleportation, using a hybrid technique, was reported. On 29 May 2014, scientists announced a reliable way of transferring data by quantum teleportation. Quantum teleportation of data had been done before but with highly unreliable methods. [8]

### **Quantum Computing**

A team of electrical engineers at UNSW Australia has observed the unique quantum behavior of a pair of spins in silicon and designed a new method to use them for "2-bit" quantum logic operations.

These milestones bring researchers a step closer to building a quantum computer, which promises dramatic data processing improvements.

Quantum bits, or qubits, are the building blocks of quantum computers. While many ways to create a qubits exist, the Australian team has focused on the use of single atoms of phosphorus, embedded inside a silicon chip similar to those used in normal computers.

The first author on the experimental work, PhD student Juan Pablo Dehollain, recalls the first time he realized what he was looking at.

"We clearly saw these two distinct quantum states, but they behaved very differently from what we were used to with a single atom. We had a real 'Eureka!' moment when we realized what was happening – we were seeing in real time the `entangled' quantum states of a pair of atoms." [5]

### **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 delta x position difference and with a delta p momentum difference such a way that they product is about the half Planck reduced constant. For the proton this delta x much less in the nucleon, than in the orbit of the electron in the atom, the delta p 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 delta x position with delta p 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 it's 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 it 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 1/2spin creator particle to make equal the spins of the weak interaction, for example neutron decay to 2 fermions, every particle is fermions with ½ 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 Tsymmetry 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 ½ 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 then 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 = hv and  $E = mc^2$ ,  $m = hv/c^2$  that is the m depends only on the v 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  $m_o$  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 lambda 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 Bing 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 Mp=1840 Me. 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<sup>±</sup>, 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 method developed by the researchers involves transferring a photonic qubit to an atomic qubit trapped inside an optical cavity. The photon-atom quantum information transfer is initiated via a quantum "logic-gate" operation, performed by reflecting the photon from the atom-cavity system, which creates an entangled atom-photon state. [9]

In August 2013, the achievement of "fully deterministic" quantum teleportation, using a hybrid technique, was reported. On 29 May 2014, scientists announced a reliable way of transferring data by quantum teleportation. Quantum teleportation of data had been done before but with highly unreliable methods. [8]

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

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. 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]

The key breakthrough to arrive at this new idea to build qubits was to exploit the ability to control the nuclear spin of each atom. With that insight, the team has now conceived a unique way to use the nuclei as facilitators for the quantum logic operation between the electrons. [5] 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 also.

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