Genome Sequencing

It's mind-blowing that we are able to routinely sequence patients' genomes when just a few years ago this was unthinkable. [28]

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Rutgers researchers have developed a new way to analyze hundreds of thousands of cells at once, which could lead to faster and more accurate diagnoses of illnesses, including tuberculosis and cancers. [24]

An international team including researchers from MIPT has shown that iodide phasing—a long-established technique in structural biology—is universally applicable to membrane protein structure determination. [23]

Scientists in Greece have devised a new form of biometric identification that relies on humans' ability to see flashes of light containing just a handful of photons. [22]

A research team led by Professor CheolGi Kim has developed a biosensor platform using magnetic patterns resembling a spider web with detection capability 20 times faster than existing biosensors. [21]

Researchers at Columbia University have made a significant step toward breaking the so-called "color barrier" of light microscopy for biological systems, allowing for much more comprehensive, system-wide labeling and imaging of a greater number of biomolecules in living cells and tissues than is currently attainable. [20]

Scientists around the Nobel laureate Stefan Hell at the Max Planck Institute for Biophysical Chemistry in Göttingen have now achieved what was for a long time considered impossible – they have developed a new fluorescence microscope, called MINFLUX, allowing, for the first time, to optically separate molecules, which are only nanometers (one millionth of a millimeter) apart from each other. [19]

Dipole orientation provides new dimension in super-resolution microscopy [18]

Fluorescence is an incredibly useful tool for experimental biology and it just got easier to tap into, thanks to the work of a group of University of Chicago researchers. [17]

Molecules that change colour can be used to follow in real-time how bacteria form a protective biofilm around themselves. This new method, which has been developed in collaboration between researchers at Linköping University and Karolinska Institutet in Sweden, may in the future become significant both in medical care and the food industry, where bacterial biofilms are a problem. [16]

Researchers led by Carnegie Mellon University physicist Markus Deserno and University of Konstanz (Germany) chemist Christine Peter have developed a computer simulation that crushes viral capsids. By allowing researchers to see how the tough shells break apart, the simulation provides a computational window for looking at how viruses and proteins assemble. [15]

IBM scientists have developed a new lab-on-a-chip technology that can, for the first time, separate biological particles at the nanoscale and could enable physicians to detect diseases such as cancer before symptoms appear. [14]

Scientists work toward storing digital information in DNA. [13]

Leiden theoretical physicists have proven that DNA mechanics, in addition to genetic information in DNA, determines who we are. Helmut Schiessel and his group simulated many DNA sequences and found a correlation between mechanical cues and the way DNA is folded. They have published their results in PLoS One. [12]

We model the electron clouds of nucleic acids in DNA as a chain of coupled quantum harmonic oscillators with dipole-dipole interaction between nearest neighbours resulting in a van der Waals type bonding. [11]

Scientists have discovered a secret second code hiding within DNA which instructs cells on how genes are controlled. The amazing discovery is expected to open new doors to the diagnosis and treatment of diseases, according to a new study. [10]

There is also connection between statistical physics and evolutionary biology, since the arrow of time is working in the biological evolution also.

From the standpoint of physics, there is one essential difference between living things and inanimate clumps of carbon atoms: The former tend to be much better at capturing energy from their environment and dissipating that energy as heat. [8]

This paper contains the review of quantum entanglement investigations in living systems, and in the quantum mechanically modeled photoactive prebiotic kernel systems. [7]

The human body is a constant flux of thousands of chemical/biological interactions and processes connecting molecules, cells, organs, and fluids, throughout the brain, body, and nervous system. Up until recently it was thought that all these interactions operated in a linear sequence, passing on information much like a runner passing the baton to the next runner. However, the latest findings in quantum biology and biophysics have discovered that there is in fact a tremendous degree of coherence within all living systems.

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 understand the Quantum Biology.

Contents

Author: George Rajna

Preface

Scientists have discovered a secret second code hiding within DNA which instructs cells on how genes are controlled. The amazing discovery is expected to open new doors to the diagnosis and treatment of diseases, according to a new study. Ever since the genetic code was deciphered over 40 years ago, scientists have believed that it only described how proteins are made. However, the revelation made by the research team led by John Stamatoyannopoulos of the University of Washington indicates that genomes use the genetic code to write two separate languages. [10]

Jeremy England, a 31-year-old assistant professor at the Massachusetts Institute of Technology, has derived a mathematical formula that he believes explains this capacity. The formula, based on

established physics, indicates that when a group of atoms is driven by an external source of energy (like the sun or chemical fuel) and surrounded by a heat bath (like the ocean or atmosphere), it will often gradually restructure itself in order to dissipate increasingly more energy. This could mean that under certain conditions, matter inexorably acquires the key physical attribute associated with life. [8]

We define our modeled self-assembled supramolecular photoactive centers, composed of one or more sensitizer molecules, precursors of fatty acids and a number of water molecules, as a photoactive prebiotic kernel system. [7]

The human body is a constant flux of thousands of chemical/biological interactions and processes connecting molecules, cells, organs, and fluids, throughout the brain, body, and nervous system. Up until recently it was thought that all these interactions operated in a linear sequence, passing on information much like a runner passing the baton to the next runner. However, the latest findings in quantum biology and biophysics have discovered that there is in fact a tremendous degree of coherence within all living systems. [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.

For the first time in a patient, researchers use long-read genome sequencing

When Ricky Ramon was 7, he went for a routine checkup. The pediatrician, who lingered over his heartbeat, sent him for a chest X-ray, which revealed a benign tumor in the top-left chamber of his heart. For Ramon, it was the beginning of a long series of medical appointments, procedures and surgeries that would span nearly two decades.

During this time, noncancerous tumors kept reappearing in Ramon's heart and throughout his body—in his pituitary gland, adrenal glands above his kidneys, nodules in his thyroid.

The trouble was, doctors couldn't diagnose his condition.

When Ramon was 18, doctors thought his symptoms were suggestive of Carney complex, a genetic condition caused by mutations in a gene called PRKAR1A. However, evaluation of Ramon's DNA revealed no disease-causing variations in this gene.

Now, eight years later, researchers at the Stanford University School of Medicine have used a next-generation technology—long-read sequencing—to secure a diagnosis for Ramon. It's the first time long-read, whole-genome sequencing has been used in a clinical setting, the researchers report in a paper to be published online June 22 in Genetics in Medicine.

Genome sequencing involves snipping DNA into pieces, reading the fragments, and then using a computer to patch the sequence together. DNA carries our genetic blueprint in a double-stranded string of molecular "letters" called nucleotides, or base pairs. The four types of nucleotides are each represented by a letter—C for cytosine and G for guanine, for example—and they form links across the two strands to hold DNA together.

'Illuminating a dark corner'

Current sequencing technologies cut DNA into "words" that are about 100 base-pairs, or letters, long, according to the study's senior author, Euan Ashley, DPhil, FRCP, professor of cardiovascular medicine, of genetics and of biomedical data science. Long-read sequencing, by comparison, cuts DNA into words that are thousands of letters long.

"This allows us to illuminate dark corners of the genome like never before," Ashley said.

"Technology is such a powerful force in medicine. It's mind-blowing that we are able to routinely sequence patients' genomes when just a few years ago this was unthinkable."

The study was conducted in collaboration with Pacific Biosciences, a biotechnology company in Menlo Park, California, that has pioneered a type of long-read sequencing. Lead authorship of the paper is shared by Jason Merker, MD, PhD, assistant professor of pathology and co-director of the Stanford Clinical Genomics Service, and Aaron Wenger, PhD, of Pacific Biosciences.

The type of long-read sequencing developed by the research team's collaborators at Pacific Biosciences can continuously spool long threads of DNA for letter-by-letter analysis, limiting the number of cuts needed.

"This is exciting," said Ashley, "because instead of having 100-base-pair 'words,' you now have 7,000- to 8,000-letter words."

Falling cost

Thanks to technological advances and increased efficiency, the cost of long-read sequencing has been falling dramatically. Ashley estimated the current cost of the sequencing used for this study at between $5,000 and $6,000 per genome.

Though the cost of short-read sequencing is now below $1,000, according to Ashley, parts of the genome not accessible when cutting DNA into small fragments. Throughout the genome, series of repeated letters, such as GGCGGCGGC, can stretch for hundreds of base pairs. With only 100-letter words, it is impossible to know how long these stretches are, and the length can critically determine someone's predisposition to disease.

Additionally, some portions of the human genome are redundant, meaning there are multiple places a 100-base pair segment could potentially fit in, said Ashley. This makes it impossible to know where to place those segments when reassembling the genome. With longer words, that happens much less often.

Given these issues, 5 percent of the genome cannot be uniquely mapped, the researchers wrote. And any deletions or insertions longer than about 50 letters are too long to detect.

For patients with undiagnosed conditions, short-read sequencing can help doctors provide a diagnosis in about one-third of cases, said Ashley. But Ramon's case was not one of those.

The technique initially used to analyze Ramon's genes failed to identify a mutation in the gene responsible for Carney complex, though Ashley said co-author Tam Sneddon, DPhil, a clinical data scientist at Stanford Health Care who browsed through the database of Ramon's sequenced genome by hand, did notice something looked wrong. Ultimately, the long-read sequencing of Ramon's genome identified a deletion of about 2,200 base-pairs and confirmed that a diagnosis of Carney complex was indeed correct.

This work is an example of Stanford Medicine's focus on precision health, the goal of which is to anticipate and prevent disease in the healthy and precisely diagnose and treat disease in the ill.

An 'exceedingly rare' condition

Carney complex arises from mutations in the PRKAR1A gene, and is characterized by increased risk for several tumor types, particularly in the heart and hormone-producing glands, such as ovaries, testes, adrenal glands, pituitary gland and thyroid. According to the National Institutes of Health, fewer than 750 individuals with this condition have been identified.

The most common symptom is benign heart tumors, or myxomas. Open heart surgery is required to remove cardiac myxomas; by the time Ramon was 18 years old, he'd had three such surgeries. He is under consideration for a heart transplant, and having the correct diagnosis for his condition was important for the transplant team. Beyond the typical screening for a transplant, Ashley said the team needed to ensure there weren't other health issues that could be exacerbated by immune suppressants, which heart transplant patients must take to avoid rejection of the donated organ.

Though it helps his medical team to have a confirmed diagnosis of Carney complex, Ramon has found it disheartening to face the fact that he cannot escape his condition. "I was pretty sad," he said. "It took me a while to come to terms with the fact that I'll have this until the day I die."

He tries not to dwell on it, though. "Live one day at a time," he said. "The bad days are temporary storms, and they'll pass."

"His story is quite incredible," said Ashley, who said it was a privilege to be working on Ramon's team. "To have such a burden on such young shoulders, and to decide whether or not he wants a transplant, requires incredible courage."

Because he couldn't wait any longer for a transplant, Ramon recently underwent his fourth surgery to remove three tumors in his heart. Joseph Woo, MD, professor and chair of cardiothoracic surgery at Stanford, performed the operation. "It is exceedingly rare to have tumors in the heart," said Ashley. "It was a particularly heroic operation." Though Ramon is still under consideration for a transplant, the need is less urgent now.

"I'm in good hands," Ramon said of the Stanford team. "I'm glad to be here."

A future in the clinic?

Ashley said he and many other doctors believe that long-read technology is part of the future of genomics.

"Now we get to see how to do it better," said Ashley. "If we can get the cost of long-read sequencing down to where it's accessible for everyone, I think it will be very useful." [28]

Water forms 'spine of hydration' around DNA, group finds

Water is the Earth's most abundant natural resource, but it's also something of a mystery due to its unique solvation characteristics – that is, how things dissolve in it.

"It's uniquely adapted to biology, and vice versa," said Poul Petersen, assistant professor of chemistry and chemical biology. "It's super-flexible. It dissipates energy and mediates interactions, and that's becoming more recognized in biological systems."

How water relates to and interacts with those systems – like DNA, the building block of all living things – is of critical importance, and Petersen's group has used a relatively new form of spectroscopy to observe a previously unknown characteristic of water.

"DNA's chiral spine of hydration," published May 24 in the American Chemical Society journal Central Science, reports the first observation of a chiral water superstructure surrounding a biomolecule. In this case, the water structure follows the iconic helical structure of DNA, which itself is chiral, meaning it is not superimposable on its mirror image. Chirality is a key factor in biology, because most biomolecules and pharmaceuticals are chiral.

"If you want to understand reactivity and biology, then it's not just water on its own," Petersen said. "You want to understand water around stuff, and how it interacts with the stuff. And particularly with biology, you want to understand how it behaves around biological material – like protein and DNA."

Water plays a major role in DNA's structure and function, and its hydration shell has been the subject of much study. Molecular dynamics simulations have shown a broad range of behaviors of the water structure in DNA's minor groove, the area where the backbones of the helical strand are close together.

The group's work employed chiral sum frequency generation spectroscopy (SFG), a technique Petersen detailed in a 2015 paper in the Journal of Physical Chemistry. SFG is a nonlinear optical method in which two photon beams – one infrared and one visible – interact with the sample, producing an SFG beam containing the sum of the two beams' frequencies, or energies. In this case, the sample was a strand of DNA linked to a silicon-coated prism.

More manipulation of the beams and calculation proved the existence of a chiral water superstructure surrounding DNA.

In addition to the novelty of observing a chiral water structure template by a biomolecule, chiral SFG provides a direct way to examine water in biology.

"The techniques we have developed provide a new avenue to study DNA hydration, as well as other supramolecular chiral structures," Petersen said.

The group admits that their finding's biological relevance is unclear, but Petersen thinks the ability to directly examine water and its behavior within biological systems is important.

"Certainly, chemical engineers who are designing biomimetic systems and looking at biology and trying to find applications such as water filtration would care about this," he said.

Another application, Petersen said, could be in creating better anti-biofouling materials, which are resistant to the accumulation of microorganisms, algae and the like on wetted surfaces. [27]

Scientists borrow from electronics to build circuits in living cells

Living cells must constantly process information to keep track of the changing world around them and arrive at an appropriate response.

Through billions of years of trial and error, evolution has arrived at a mode of information processing at the cellular level. In the microchips that run our computers, information processing capabilities reduce data to unambiguous zeros and ones. In cells, it's not that simple. DNA, proteins, lipids and sugars are arranged in complex and compartmentalized structures.

But scientists—who want to harness the potential of cells as living computers that can respond to disease, efficiently produce biofuels or develop plant-based chemicals—don't want to wait for evolution to craft their desired cellular system.

In a new paper published May 25 in Nature Communications, a team of UW synthetic biology researchers have demonstrated a new method for digital information processing in living cells, analogous to the logic gates used in electric circuits. They built a set of synthetic genes that function in cells like NOR gates, commonly used in electronics, which each take two inputs and only pass on a positive signal if both inputs are negative. NOR gates are functionally complete, meaning one can assemble them in different arrangements to make any kind of information processing circuit.

The UW engineers did all this using DNA instead of silicon and solder, and inside yeast cells instead of at an electronics workbench. The circuits the researchers built are the largest ever published to date in eurkaryotic cells, which, like human cells, contain a nucleus and other structures that enable complex behaviors.

"While implementing simple programs in cells will never rival the speed or accuracy of computation in silicon, genetic programs can interact with the cell's environment directly," said senior author and UW electrical engineering professor Eric Klavins. "For example, reprogrammed cells in a patient could make targeted, therapeutic decisions in the most relevant tissues, obviating the need for complex diagnostics and broad spectrum approaches to treatment."

Each cellular NOR gate consists of a gene with three programmable stretches of DNA—two to act as inputs, and one to be the output. The authors then took advantage of a relatively new technology known as CRISPR-Cas9 to target those specific DNA sequences inside a cell. The Cas9 protein acts like a molecular gatekeeper in the circuit, sitting on the DNA and determining if a particular gate will be active or not.

If a gate is active, it expresses a signal that directs the Cas9 to deactivate another gate within the circuit. In this way, the researchers can "wire" together the gates to create logical programs in the cell.

What sets the study apart from previous work, researchers said, is the scale and complexity of the circuits successfully assembled—which included up to seven NOR gates assembled in series or parallel.

At this size, circuits can begin to execute really useful behaviors by taking in information from different environmental sensors and performing calculations to decide on the correct response. Imagined applications include engineered immune cells that can sense and respond to cancer markers or cellular biosensors that can easily diagnose infectious disease in patient tissue.

These large DNA circuits inside cells are a major step toward an ability to program living cells, the researchers said. They provide a framework where logical programs can be easily implemented to control cellular function and state. [26]

Controlling 3-D behavior of biological cells using laser holographic techniques

A research team led by Professor YongKeun Park of the Physics Department at KAIST has developed an optical manipulation technique that can freely control the position, orientation, and shape of microscopic samples having complex shapes. The study has been published online in Nature Communications on May 22.

Conventional optical manipulation techniques called "optical tweezers," have been used as an invaluable tool for exerting micro-scale force on microscopic particles and manipulating three-dimensional (3-D) positions of particles. Optical tweezers employ a tightly-focused laser whose beam diameter is smaller than one micrometer (1/100 of hair thickness), which can generate attractive force on neighboring microscopic particles moving toward the beam focus. Controlling the positions of the beam focus enabled researchers to hold the particles and move them freely to other locations so they coined the name "optical tweezers," and have been widely used in various fields of physical and biological studies.

So far, most experiments using optical tweezers have been conducted for trapping spherical particles because physical principles can easily predict optical forces and the responding motion of microspheres. For trapping objects having complicated shapes, however, conventional optical tweezers induce unstable motion of such particles, and controllable orientation of such objects is limited, which hinder controlling the 3-D motion of microscopic objects having complex shapes such as living cells.

Real-time optical control of arbitrarily shaped particles by combining the wavefront shaping of atrapping beam and measurements of the 3-D refractive index distribution of samples. Credit: KAIST

The research team has developed a new optical manipulation technique that can trap complex objects of arbitrary shapes. This technique first measures 3-D structures of an object in real time using a 3-D holographic microscope, which shares the same physical principle of X-Ray CT imaging. Based on the measured 3-D shape of the object, the researchers precisely calculates the shape of light that can stably control the object. When the shape of light is the same as the shape of the object, the energy of the object is minimized, which provides the stable trapping of the object having the complicated shape.

Moreover, by controlling the shape of light to have various positions, directions, and shapes of objects, it is possible to freely control the 3-D motion of the object and make the object have a desired shape. This process resembles the generation of a mold for casting a statue having desired shape so the researchers coined the name of the present technique "tomographic mold for optical trapping (TOMOTRAP)." The team succeeded in trapping individual human red blood cells stably, rotating them with desired orientations, folding them in an L-shape, and assembling two red blood cells together to form a new structure. In addition, colon cancer cells having a complex structure could be stably trapped and rotated at desired orientations. All of which have been difficult to be realized by the conventional optical techniques.

Professor Park said, "Our technique has the advantage of controlling the 3-D motion of complex shaped objects without knowing prior information about their shape and optical characteristics, and can be applied in various fields including physics, optics, nanotechnology, and medical science."

Dr. Kyoohyun Kim, the lead author of this paper, noted that this technique can induce controlled deformation of biological cells with desired shapes. "This approach can be also applied to real-time monitoring of surgical prognosis of cellular-level surgeries for capturing and deforming cells as well as subcellular organelles," added Kim. [25]

Researchers develop protocol to analyze many cells at once

Rutgers researchers have developed a new way to analyze hundreds of thousands of cells at once, which could lead to faster and more accurate diagnoses of illnesses, including tuberculosis and cancers.

With the new FISH-Flow protocol, researchers are able to evaluate multitudes of cells at once for telltale mRNA species and proteins. The blended procedure provides a chance to see how multiple kinds of immune cells are responding to a foreign substance, making it possible to detect the presence of disease faster and earlier.

"This new process allows us to see how individual immune cells are reacting in real time without using artificial reagents that alter what the cells are doing when they respond to a foreign substance," said Maria Laura Gennaro, a professor of medicine at Rutgers' Public Health Research Institute (PHRI).

Gennaro is the lead author of a paper published in the journal Nature Protocols, which details the new method to observe how cells respond to antigens. The protocol could be used to identify telltale indicators of other illnesses. Gennaro said researchers plan to study applying it to early diagnosis and treatment of other infectious and non-infectious lung diseases and certain cancers.

"This powerful diagnostic technology exploits a person's own immune system to assess their potential for developing a wide range of acute and chronic diseases - including those caused by infectious agents and those resulting from host dysfunction like cancer, asthma or autoimmune disorders," said David Perlin, executive director of Rutgers New Jersey Medical School's Public Health Research Institute.

The procedure will be particularly useful in finding ways to help identify people who are predisposed to developing tuberculosis, making it possible to treat them and help reduce the spread of the

disease. Nearly 2 billion people worldwide are afflicted with latent TB, but many never develop full-blown TB. Currently, the only way to determine if latent TB is present is to study the immunological response to TB antigens through skin tests and blood tests. However, treatment is not widely offered to people with latent TB because of the prohibitive cost of treating them all.

"If you can have a method that helps you determine who among the people who are latently affected by TB are predisposed to illness, you can target treatment of latent TB to those people and the risk of spread is reduced," Gennaro said.

The FISH-Flow protocol combines flow-cytometry - a technology used to analyze particles in a fluid as they pass through a laser and are fluorescently labelled so they emit light at varying wavelengths - with a nucleic acid hybridization technology - originally developed for fluorescence microscopy - that marks molecules of mRNA inside cells. Gennaro developed the method with senior colleagues Yuri Bushkin, Richard Pine and Sanjay Tyagi at PHRI. [24]

Iodine ensures successful solution of biomolecule structures

An international team including researchers from MIPT has shown that iodide phasing—a long-established technique in structural biology—is universally applicable to membrane protein structure determination. Knowledge of these structures enables a molecular-level understanding of the workings of eyesight and smell, as well as the nervous and cardiovascular systems.

The authors of the study, which was published in Science Advances, applied the established method of iodide phasing to four membrane proteins representing different classes and discovered that iodide (an ion of iodine) interacts with all four in the same way. This means the method is guaranteed to be successful in uncovering new protein structures vital for pharmaceutics. Because iodide phasing is easy and fast, it can accelerate computer-aided drug development and make it cheaper.

Membrane proteins: the customs service of a cell

All living things are known to be composed of cells. The cells that make up any organism share a common structure. In particular, all cells are surrounded by a protective cell membrane that blocks the passage of the molecules of most substances. Enclosed by a membrane, a cell can maintain internal conditions necessary for complex biochemical processes to run smoothly. However, the survival of a cell also depends on its ability to monitor changes in its external environment and react to them. This is why the genome of every cell encodes several hundred special proteins that are responsible for the cell's interaction with its surroundings. Since these proteins are embedded in the cell membrane, they are referred to as membrane proteins. Another of their functions is to allow molecules into the cell that are blocked by the membrane cell but are nevertheless necessary for nutrition or biochemical reactions.

Iodine ensures successful solution of biomolecule structures

Iodide binding sites in various protein structures. Panels A, B, C, and D show different protein structures with traces of iodide ions depicted in purple (on the left). The same structures are shown embedded in the cell membrane (right). …more

The biggest breakthrough in structural biology is associated with the Nobel Prize-winning discovery of the double-stranded structure of DNA by Watson and Crick in 1953. The elegant model created by the two scientists was based on prior structural research conducted by their colleague Rosalind Franklin. The double-stranded structure of the DNA molecule (aka the double helix) successfully accounted for the transfer of genetic information between cells and laid the foundation for modern biology.

Crystallography is the chief method employed by structural biology. It enables researchers to elucidate the structure of biomolecules (these are usually proteins) with atomic resolution. Such precision means it is possible not only to look into protein operation at the basic level but also to model protein behavior using physical laws.

Crystallography relies heavily on the physical phenomenon of diffraction. To collect diffraction data, a protein crystal is exposed to an X-ray beam. Because molecules in the crystal are in a highly ordered configuration, the X-ray beam diffracts into numerous directions with its intensity amplified manyfold. These diffracted beams can then be picked up and interpreted as the signal whereby their intensity is measured. However, only averaged signal values for a given direction are available, and part of the information is lost. This is known as the phase problem: The lost phases, i.e., the delay of one signal relative to another, are required for determining the structure of a molecule using diffraction data. Picking up the signal that lacks phases is a little bit like looking at a black-and-white copy of a color image—you can perceive the intensity of every individual point, but the colors are absent, and so most of the information is lost.

Phase recovery

Because many crystal structures have already been solved, it is possible to recover the lost phases in studies of new molecules using computer-aided techniques. This involves inferring phases from a known structure and refining them by hand. However, this approach often yields no satisfactory results, particularly in the case of low-resolution data typical for membrane proteins or completely new structures that are not quite like anything that has been solved. Therefore, a different technique is often preferred to deal with these crystals. It is based on the phenomenon of anomalous diffraction, i.e., a certain asymmetry in the diffraction signals produced by heavy elements such as iodine, gadolinium, bromine, and sometimes sulfu. For this method to work, the heavy elements need to strongly bind to the protein molecules in the crystal. This ensures that their atoms are as strictly ordered as the protein molecules themselves to produce a strong diffraction signal. It often takes a long time before the right heavy element is found by trial and error, and many valuable protein crystals are used up in the process.

The researchers showed that anomalous scattering is guaranteed to work if membrane proteins are treated with iodide ions in solution. This is made possible by a common feature of every membrane protein that exists in nature: They are all structured in such a way that there is an extra positive charge on the membrane–solution interface, compensating the negative charge on the membrane surface. Iodide interacts strongly with these charges and is selectively attracted to very specific spots on the protein called binding sites, ensuring the success of experimental phase recovery.

"In our study, we demonstrated a successful solution of the structures of four proteins already known from earlier research. The proteins, which come from different organisms, are the following:

the light-driven sodium pump from the marine bacterium Krokinobacter eikastus, a fragment of histidine kinase from the Escherichia coli bacterium, a human adenosine receptor, and the proton pump from the marine Actinobacteria clade. With each of the four structures, it can be seen that iodide ions actually bind to the positively charged amino acids at the sites where a protein protrudes from the membrane. Compared to bromide, which is also sometimes used to address the phase problem, iodide is more reliable, giving more precision in the diffraction measurements," says Igor Melnikov of the European Synchrotron Radiation Facility, the first author of the study, an MIPT graduate. [23]

Quantum biometric targets the retina

Scientists in Greece have devised a new form of biometric identification that relies on humans' ability to see flashes of light containing just a handful of photons. The technique involves using very weak laser pulses to measure how a person's sensitivity to light varies across their retina. According to its inventors, such a quantum-based retinal map could provide a more powerful and secure form of identification than is possible with conventional biometrics such as fingerprints or iris scans.

It has been known since the 1940s that humans are able to detect light pulses containing very few photons. However, whether we can actually see single photons is still unclear: one group last year said it had carried out experiments showing this to be the case but others questioned the claim. In the 1940s, Selig Hecht and colleagues at Columbia University in the US showed that variations in our perception of very low light levels are in fact governed by quantum statistics. By exposing several individuals to very dim flashes of light of differing average intensity, they found that the intensity-induced variation in the probability of seeing a flash could be modelled by assuming that the actual number of photons a person sees follows a Poisson distribution.

This result held true across the different people examined, although the specific responses depended on an individual's value of alpha – a parameter describing the fraction of photons arriving at a person's eye that are then detected by their retina. Losses caused by absorption or scattering within the cornea, pupil, lens and body of the eyeball, as well as a finite probability of absorption within the retina itself, means that alpha typically varies between 0 and 0.2. This variation led to a series of curves describing seeing probability versus average intensity, whose precise shape depended on alpha.

Unique variations

In the latest work, Iannis Kominis of the University of Crete and colleagues use these variations as the basis of the new biometric scheme. They say that the value of alpha changes by up to a factor of 100 from one point to another on an individual's retina, while variations between retinas can be up to 50%. As such, they argue that people could be uniquely identified by precisely mapping the variation of alpha across their retinas.

The "alpha map" of a particular individual, who the researchers call Alice, would be created by exposing that person to large numbers of very weak laser pulses. The pulses would have a range of average intensities, and the exercise would be repeated across multiple points on Alice's retina. For each pulse, Alice would be asked whether or not she saw a flash of light. With the map stored on a secure database, Alice could then be identified by examining a subset of points on her retina. Again,

she would be exposed to a series of weak laser pulses and asked on each occasion whether or not she sees the pulse. Only if her answers closely match what would be expected from her map would she be allowed to proceed.

As Kominis and colleagues explain in a preprint uploaded to the arXiv server, Alice must be subject to a sufficient number of yes/no interrogations to limit two types of error as far as possible. One type of error is the "false negative", which means that Alice is not recognized as herself. The other type is the "false positive", in which an impostor, known as Eve, successfully fools the system into thinking that she is Alice.

Fifty interrogations

For the scheme to be implemented on a practical timescale, the number of interrogations must be limited. Simply choosing a random subset of points on Alice's retina would involve 2500 interrogations to reach certain benchmarks – generating a false negative less than once every 10,000 identifications and a false positive less than one every 10 billion. However, by refining their technique in a number of ways – choosing only very low or very high alpha regions on the retina, using Bayesian statistics and employing pattern recognition – the researchers calculated that just 50 interrogations would do the job.

In addition, they assessed how well their scheme would cope if Eve was able to measure the number of photons entering Alice's eye as well as monitoring her brain activity. Their conclusion: Eve would need to make extremely precise measurements of both the thermal energy dumped in Alice's eye and the magnetic energy emitted by her head – something that would be very difficult to achieve.

Rebecca Holmes of the University of Illinois in the US praises Kominis and colleagues for having "put a lot of thought into how to optimise" their biometric technique. But she says she is "sceptical" about the scheme's practicality, pointing out that up to half an hour would be needed just to acclimatize Alice's eyes to the very dark conditions required. Holmes also disputes the technique's "quantum" label, arguing that although it involves small numbers of photons, it does not provide a physics-based guarantee of complete security, as quantum cryptography (in principle) can do. [22]

Researchers develop faster biosensor platform using a magnetic field

A research team led by Professor CheolGi Kim has developed a biosensor platform using magnetic patterns resembling a spider web with detection capability 20 times faster than existing biosensors.

The sensing capability of a biosensor is determined by the resolution of the sensor and the movement and reaction rate of molecules. Many research groups in Korea and other countries have been improving the resolution through with nanomaterials innovations, but there improving the sensitivity is challenging due to the low diffusion transport of biomolecules toward the sensing region.

Professor Kim and his research team used a magnetic field to overcome the slow movement of biomolecules such as proteins and DNA is slow when the transport depends on diffusion. Biomolecules labeled with superparamagnetic particles could be controlled with the use of an external magnetic field and detected with an ultra-sensitive magnetic sensor. The research team's biosensor platform uses a spider web-shaped micro-magnetic pattern that improves the sensing

ability of the biosensor by attracting biomolecules labeled with the superparamagnetic particles to the sensing area.

DGIST develops 20 times faster biosensor

a. Schematic representation of the sensor-integrated magnetic spider web; b. Scanning electron microscope (SEM) image of the sensor integrated with the spider web net; c. Schematic cross-sectional view of the layered structures of the …more

The first author Byeonghwa Lim at DGIST's Ph.D program of Emerging Materials Science elaborated on the biosensor platform: "When a rotating magnetic field is applied to a spider web-shaped magnetic pattern, it can attract biomolecules labeled with superparamagnetic particles faster to the sensor. The speed is very fast and it can detect the subject 20 times faster than the diffusion method."

The research team also succeeded in monitoring the biomolecules conjugated to the superparamagnetic particles at a distance from the sensing area by utilizing the biosensor platform. In addition, the team found that the superparamagnetic particles not only play the role of biomolecular cargo for transportation, but also act as labels for the sensor to indicate the location of biomolecules.

Professor Kim said, "The existing biosensors require a long time to detect low-density biomolecules, and have poor sensing efficiency as they only depend on diffusion. The magnetic field-based biosensor platform improves the collection capability of biomolecules and increases the speed and sensitivity of the biomolecules movement. Therefore, we are planning to use this platform for early diagnosis as well as recurrence diagnosis of diseases such as cancer. " [21]

New microscopy method breaks color barrier of optical imaging

Researchers at Columbia University have made a significant step toward breaking the so-called "color barrier" of light microscopy for biological systems, allowing for much more comprehensive, system-wide labeling and imaging of a greater number of biomolecules in living cells and tissues than is currently attainable. The advancement has the potential for many future applications, including helping to guide the development of therapies to treat and cure disease.

In a study published online April 19 in Nature, the team, led by Associate Professor of Chemistry Wei Min, reports the development of a new optical microscopy platform with drastically enhanced detection sensitivity. Additionally, the study details the creation of new molecules that, when paired with the new instrumentation, allow for the simultaneous labeling and imaging of up to 24 specific biomolecules, nearly five times the number of biomolecules that can be imaged at the same time with existing technologies.

"In the era of systems biology, how to simultaneously image a large number of molecular species inside cells with high sensitivity and specificity remains a grand challenge of optical microscopy," Min said. "What makes our work new and unique is that there are two synergistic pieces - instrumentation and molecules - working together to combat this long-standing obstacle. Our platform has the capacity to transform understanding of complex biological systems: the vast human

cell map, metabolic pathways, the functions of various structures within the brain, the internal environment of tumors, and macromolecule assembly, to name just a few."

All existing methods of observing a variety of structures in living cells and tissues have their own strengths, but all are also hindered by fundamental limitations, not the least of which is the existence of a "color barrier."

Fluorescence microscopy, for example, is extremely sensitive and, as such, is the most prevalent technique used in biology labs. The microscope allows scientists to monitor cellular processes in living systems by using proteins that are broadly referred to as "fluorescent proteins" with usually up to five colors. Each of the fluorescent proteins has a target structure that it applies a "tag," or color to. The five fluorescent proteins, or colors, typically used to tag these structures are BFP (Blue Fluorescent Protein), ECFP (Cyan Fluorescent Protein), GFP (Green Fluorescent Protein), mVenus (Yellow Fluorescent Protein), and DsRed (Red Fluorescent Protein).

Despite its strengths, fluorescence microscopy is impeded by the "color barrier," which limits researchers to seeing a maximum of only five structures at a time because the fluorescent proteins used emit a range of indistinguishable shades that, as a result, fall into five broad color categories.

If a researcher is trying to observe all of the hundreds of structures and different cell types in a live brain tumor tissue sample, for example, she would be restricted to seeing only up to five structures at a time on a single tissue sample. If she wanted to see more than those five, she would have to clean the tissue of the fluorescent labels she used to identify and tag the last five structures in order to use those same fluorescent labels to identify another set of up to five structures. She would have to repeat this process for every set of up to five structures she wants to see. Not only is observing a maximum of five structures at a time labor intensive, but in cleaning the tissue, vital components of that tissue could be lost or damaged.

"We want to see them all at the same time to see how they're operating on their own and also how they're interacting with each other," said Lu Wei, lead author on the study and a postdoctoral researcher in the Min lab. "There are lots of components in a biological environment and we need to be able to see everything simultaneously to truly understand the processes."

In addition to fluorescence microscopy, there are currently a variety of Raman microscopy techniques in use for observing living cell and tissue structures that work by making visible the vibrations stemming from characteristic chemical bonds in structures. Traditional Raman microscopy produces the highly-defined colors lacking in fluorescence microscopy, but is missing the sensitivity. As such, it requires a strong, concentrated vibrational signal that can only be achieved through the presence of millions of structures with the same chemical bond. If the signal from the chemical bonds is not strong enough, visualizing the associated structure is near impossible.

To address this challenge, Min and his team, including Profs. Virginia Cornish in chemistry and Rafael Yuste in neuroscience, pursued a novel hybrid of existing microscopy techniques.

They developed a new platform called electronic pre-resonance stimulated Raman scattering (epr-SRS) microscopy that combines the best of both worlds, bringing together a high level of sensitivity and selectivity. The innovative technique identifies, with extreme specificity, structures with significantly lower concentration - instead of millions of the same structure needed to identify the

presence of that structure in traditional Raman microscopy, the new instrument requires only 30 for identification. The technique also utilizes a novel set of tagging molecules designed by the team to work synergistically with the ultramodern technology. The amplified "color palette" of molecules broadens tagging capabilities, allowing for the imaging of up to 24 structures at a time instead of being limited by only five fluorescent colors. The researchers believe there's potential for even further expansion in the future.

The team has successfully tested the epr-SRS platform in brain tissue. "We were able to see the different cells working together," Wei said. "That's the power of a larger color palette. We can now light up all these different structures in brain tissue simultaneously. In the future we hope to watch them function in real time." Brain tissue is not the only thing the researchers envision this technique being used for, she added. "Different cell types have different functions, and scientists usually study only one cell type at a time. With more colors, we can now start to study multiple cells simultaneously to observe how they interact and function both on their own and together in healthy conditions versus in disease states."

The new platform has many potential applications, Min said, adding that it is possible the technique could one day be used in the treatment of tumors that are hard to kill with available drugs. "If we can see how structures are interacting in cancer cells, we can identify ways to target specific structures more precisely," he said. "This platform could be game-changing in the pursuit of understanding anything that has a lot of components." [20]

Researchers achieve ultimate resolution limit in fluorescence microscopy

It is the holy grail of light microscopy: improving the resolving power of this method such that one can individually discern molecules that are very close to each other. Scientists around the Nobel laureate Stefan Hell at the Max Planck Institute for Biophysical Chemistry in Göttingen have now achieved what was for a long time considered impossible – they have developed a new fluorescence microscope, called MINFLUX, allowing, for the first time, to optically separate molecules, which are only nanometers (one millionth of a millimeter) apart from each other. This microscope is more than 100 times sharper than conventional light microscopy and surpasses even the best super-resolution light microscopy methods to date, namely STED developed by Hell and PALM/STORM described by Nobel laureate Eric Betzig, by up to 20 times. For MINFLUX, Hell used the advantages of STED and PALM/STORM in a completely new concept. This breakthrough opens up new opportunities for researchers to investigate how life functions at the molecular level.

"We have routinely achieved resolutions of a nanometer with MINFLUX, which is the diameter of individual molecules – the ultimate limit of what is possible in fluorescence microscopy," explains Hell, Director at the Max Planck Institute for Biophysical Chemistry. "I am convinced that MINFLUX microscopes have the potential to become one of the most fundamental tools of cell biology. With this concept it will be possible to map cells in molecular detail and to observe the rapid processes in their interior in real time. This could revolutionize our knowledge of the molecular processes occurring in living cells."

The Göttingen physicist, who also works at the Max Planck Institute for Medical Research and the German Cancer Research Center in Heidelberg, has long been convinced that fluorescence microscopy resolution can be increased down to the dimension of individual molecules – with classical use of focused light and conventional lenses.

In fact, the physicist Ernst Abbe had formulated in 1873 that the resolution of light microscopes is limited to half the wavelength of light, which is about 200 nanometers. More than 100 years later, this Abbe limit is still valid. However, Hell was the first to show that this limit can be overcome with STED microscopy, which he conceived in 1994 and established experimentally five years later.

STED as well as PALM/STORM, developed a few years later, in practice achieve a separation sharpness of about 20 to 30 nanometers – about ten times better than the Abbe limit. For the development of these ultra-high resolution light microscopy techniques, Hell and Betzig together with William E. Moerner were awarded the 2014 Nobel Prize in Chemistry.

Advantages of STED and PALM/STORM combined

Both STED and PALM/STORM separate neighboring fluorescing molecules by switching them on and off one after the other so that they emit fluorescence sequentially. However, the methods differ in one essential point: STED microscopy uses a doughnut-shaped laser beam to turn off molecular fluorescence at a fixed location in the sample, i.e. everywhere in the focal region except at the doughnut center. The advantage is that the doughnut beam defines exactly at which point in space the corresponding glowing molecule is located. The disadvantage is that in practice the laser beam is not strong enough to confine the emission to a single molecule at the doughnut center. In the case of PALM/STORM, on the other hand, the switching on and off is at random locations and at the single-molecule level. The advantage here is that one is already working at the single-molecule level, but a downside is that one does not know the exact molecule positions in space. The positions have to be found out by collecting as many fluorescence photons as possible on a camera; more than 50,000 detected photons are needed to attain a resolution of less than 10 nanometers. In practice, one therefore cannot routinely achieve molecular (one nanometer) resolution.

Hell had the idea to uniquely combine the strengths of both methods in a new concept. "This task was anything but trivial. But my co-workers Francisco Balzarotti, Yvan Eilers, and Klaus Gwosch have done a wonderful job in implementing this idea experimentally with me." Their new technique, called MINFLUX (MINimal emission FLUXes), is now introduced by Hell together with the three junior scientists as first authors in Science.

MINFLUX, like PALM/STORM, switches individual molecules randomly on and off. However, at the same time, their exact positions are determined with a doughnut-shaped laser beam as in STED. In contrast to STED, the doughnut beam here excites the fluorescence. If the molecule is on the ring, it will glow; if it is exactly at the dark center, it will not glow but one has found its exact position. Balzarotti developed a clever algorithm so that this position could be located very fast and with high precision. "With this algorithm it was possible to exploit the potential of the doughnut excitation beam," the young scientist explains. Gwosch, who obtained the molecular resolved images, adds "It was an incredible feeling as we, for the first time, were able to distinguish details with MINFLUX on the scale of a few nanometers."

100 times better resolution

In addition to the molecular resolution, the combination of STED and PALM/STORM offers an additional major advantage: "MINFLUX is much faster in comparison. Since it works with a doughnut laser beam, it requires much lower light signal, i.e. fewer fluorescence photons, per molecule as compared to PALM/STORM for attaining the ultimate resolution," Hell states. Already with STED one could record real-time videos from the inside of living cells. But now it was possible to trace the movement of molecules in a cell with a 100 times better temporal resolution, as Eilers emphasizes. He managed to film the movement of molecules in a living E. coli bacterium with MINFLUX for the first time, with an unprecedented spatio-temporal resolution. "As far as speed is concerned, we have not made the most of the possibilities with MINFLUX," Eilers says. The researchers are convinced that even extremely fast-occurring changes in living cells can be investigated in the future, like for example the movement of cellular nanomachines or the folding of proteins. [19]

Dipole orientation provides new dimension in super-resolution microscopy

Recently, a new polarization-dipole azimuth-based super-resolution technique has been proposed by a group of researchers in Peking University (China), Tsinghua University (China), and University of Technology Sydney (Australia). It not only provides a new dimension for super-resolution, but also provides a timely solution to a recent hot debate in the field.

Since fluorescence polarization was discovered on 1926, multiple fluorescence anisotropy techniques have been developed to study dipole orientation of fluorophores. However, in the case of super-resolution, while other properties of fluorescence such as intensity, spectrum, fluorescence lifetime, etc., have been well applied, little attention is paid to the direction of the fluorescence dipole (polarization). In 2014, Walla team published an article in Nature Methods to achieve sparse reconstructed super-resolution imaging by polarization-modulating excitation. In early 2016, Keller group published a comment on this article on Nature Methods, which stated that fluorescence polarization adds little additional information to (fluorescence intensity) super-resolution. This raised an interesting debate: whether the polarization modulation can provide super-resolution information or not?

However, both the Walla and Keller groups investigated this problem from a conventional fluorescence intensity point of view. Taking into account fluorescence intensity and fluorescence anisotropy, this work introduces the dipole angle to distinguish fluorescence through the fourth dimension of the fluorescence, and perfectly answers this controversy.

Traditional fluorescence anisotropy techniques are limited to samples of relative uniform polarization. Fluorescence polarization would be affected by a bulk of fluorophores due to Abbe's diffraction limit when it comes to complex samples. SDOM utilizes polarization modulation of excitation laser and demodulation of both intensity and polarization, which improves the spatial resolution as well as the detection accuracy of dipole orientation. With the additional information of fluorescence polarization imposed on the original super-resolution intensity image, Xi group has observed several interesting findings in biological samples. SDOM technology has a very fast imaging speed (up to five frames per second in super-resolution), and the excitation light power

requirements are very low (milliwatts level), which is ideal for live cell observation. The observation of living yeast cells was demonstrated in the laboratory. [18]

New tool enables viewing spectrum from specific structures within samples

Fluorescence is an incredibly useful tool for experimental biology and it just got easier to tap into, thanks to the work of a group of University of Chicago researchers.

The group created a new tool as part of a lab class within the Biophysical Sciences graduate program at The University of Chicago, enabling its users to zero in on the spectrum from specific structures within samples.

"The bulk of the work was done by graduate students during their first semester," said Adam Hammond, curriculum director and senior lecturer in the Biophysical Sciences program at the Gordon Center for Integrative Sciences. "Their enthusiasm and creativity made this project possible."

As the group reports this week in the journal Review of Scientific Instruments, from AIP Publishing, the goal of their instrumentation is to observe the spectrum of light that comes from part of a sample on a microscope—but not the entire sample.

"The value of a microscope is that it allows you to observe the variations within a sample," Hammond explained. "We wanted to be able to ask, 'what's the spectrum from that specific structure right there?' This isn't a new desire and instruments that can do it exist, but none, as far as I know, as simply as ours."

During his first year in graduate school, Peter Dahlberg, first author of the article who is now at Stanford University in California, got to build a selective excitation microscope. "Subconsciously, I think the idea started then," he said. "Why not do the same thing, but in reverse?"

How does the group's tool work? First, it splits the light that comes from a sample. Half goes to a camera for normal imaging and the other half goes to a spectrometer. But before it gets to the spectrometer, that half passes through a few optical components that allow users to choose any arbitrary portion of the image and block everything else out.

"There's nothing tricky about these optical components—a spatial light modulator (SLM) between crossed polarizers," Hammond said. "SLMs are common now, with at least three in many modern digital projectors. They have an array of pixels that can each manipulate the phase of the light that passes through them."

Although there are several tricks you can do with a SLM, the group is using the most straightforward one.

"We focus the image from the sample onto the SLM and shift the phase of only those pixels that we want to obtain a spectrum from," he continued. "The shifted light passes through a second polarizer; everything else gets blocked out. Then that light is collected and can be sent to any kind of optical instrument you choose. Right now we send it to a small UV/Vis spectrometer to get a full spectrum."

The group's instrument is, perhaps, best summed up as a "workhorse tool." Its simple concepts and components can easily be adapted for many different purposes and added to existing microscopes easily and inexpensively.

"We set out to build it for one specific use: To measure the spectral shift of fluorescent indicators," Hammond said. "We didn't really think about making it versatile or how to arrange the SLM and polarizers when we started. But we had an enjoyable series of realizations along the way."

One such realization was that their instrument could also be used for absorbance measurements.

"Often, the most important samples are tiny and hard to create or purify—like crystal forms," he said. "It's arduous work to purify the two types away from each other in sufficient quantities to fill a cuvette. When you put the mixture on a microscope slide, it gets easier. Crystals can be measured one at a time, and so can cells that express variable chromophores (molecules responsible for color). This opens up a whole new area that wasn't part of our original plan."

The group's instrument can "take the full spectrum of one or more user-defined regions of interest while simultaneously capturing standard fluorescence images of the whole field of view," Hammond said. "So what you can do with it depends on the sample. We're using it now to follow fluorescent probes for pH and calcium. But an example of a very different application is its ability to identify individual microorganisms within a mixed sample by their absorbance fingerprint."

What's next for the researchers?

"By using a pulsed excitation source, the fluorescence lifetime of a probe could be measured from a select region of interest," said Hammond. "One interesting potential application is within the field of neuroscience for resolving single action potentials with dyes that are sensitive to membrane potential. Fluorescence lifetime measurements provide an advantage over direct fluorescence measurements because they're independent of the concentration of the probe." [17]

Molecular chameleons reveal bacterial Biofilms

Molecules that change colour can be used to follow in real-time how bacteria form a protective biofilm around themselves. This new method, which has been developed in collaboration between researchers at Linköping University and Karolinska Institutet in Sweden, may in the future become significant both in medical care and the food industry, where bacterial biofilms are a problem.

Biofilms are formed when bacteria growing on a surface form three-dimensional colonies in which they survive better than when living alone.

"What characterises biofilms in particular is that the bacteria produce a special slime that binds the bacteria to each other. The biofilm helps the bacteria to withstand external stresses, such as antibiotics, the flow of fluid in a catheter and detergents in the form of dishwashing liquid and other cleaning agents," says Professor Agneta Richter-Dahlfors at Karolinska Institutet, who has led the study together with Professor Peter Nilsson at Linköping University.

The protective biofilm is a problem in, for example, medical care and the food industry. Until now, no specific method to detect biofilms has been available.

"This is the first method that specifically labels the biofilm components. This means that researchers who want to study the mechanisms behind how bacteria form biofilms now have access to a new tool in understanding the process," says Agneta Richter-Dahlfors.

In the present study, published in Nature Journal Biofilms and Microbiomes, the investigators have developed molecules that emit a sort of optical fingerprint that depends on what they bind to. One part of the molecule has the ability to emit light, while another part can bind specifically to a target molecule. In this case, this is a molecule present in the biofilm. When the tracer molecule has bound to the target molecule, the colour of the light emitted changes.

"The molecules that we have developed are unique in that they can emit different colours, depending on their conformation. We call them 'molecular chameleons', since they change colour according to the surroundings," says Peter Nilsson at Linköping University, whose research group has developed these tracer molecules.

The researchers have demonstrated in the project how the method can be used to study Salmonella bacteria, both in cell cultures and in infected tissue. The researchers hope that it will be possible eventually to use the method within medical care and the food industry, where biofilms are a problem. There are, however, also contexts in which the ability of bacteria to form biofilms is positive, for example when bacteria are used to produce biogas to be used as fuel.

"It is possible with the new method to follow in real-time how the bacteria form a biofilm. Now that we have a tool that we can use to see how biofilms are formed, we can also use it to evaluate methods that influence the process," says Peter Nilsson.

The research has been financed with support from the Swedish Research Council, the Swedish Foundation for Strategic Research, the Erling-Persson Family Foundation and Carl Bennet AB. Some of the researchers who work in the study are part-owners in a company that may commercialise the molecules for use within medical care and industry. [16]

Computer simulation breaks virus apart to learn how it comes together

Researchers led by Carnegie Mellon University physicist Markus Deserno and University of Konstanz (Germany) chemist Christine Peter have developed a computer simulation that crushes viral capsids. By allowing researchers to see how the tough shells break apart, the simulation provides a computational window for looking at how viruses and proteins assemble. The study is published in the October issue of The European Physical Journal Special Topics.

"The concept of breaking something to see how it's made isn't new. It's what's being done at particle accelerators and in materials science labs worldwide—not to mention by toddlers who break their toys to see what's inside," said Deserno, a professor in the department of physics and member of the department's Biological Physics Initiative. "With a simulation we can build the virus, crush it and see what happens at a very high level of resolution."

Viral capsids, the protein shells that encapsulate and transport the viral genome, are one of nature's strongest nanocontainers. The shells are made when copies of capsid proteins spontaneously come

together and assemble into a round, geometric shell. Understanding how these proteins come together to form capsids may help researchers to make similar nanocontainers for a variety of uses, including targeted drug delivery. Additionally, the simulation could fill a void for virologists, allowing them to study the stages of viral assembly that they aren't able to see experimentally.

Studying the self-assembly of viral capsids is difficult. Most viruses are too small—about 30 to 50 nanometers—and the capsid proteins come together too rapidly for their assembly to be seen using traditional microscopy. As an alternative, Deserno and colleagues thought that a better way to learn about capsid assembly might be to see what happens when an already formed capsid breaks apart.

To do this, Deserno and colleagues created a coarse-grained model of the Cowpea Chlorotic Mottle Virus (CCMV) capsid. In the simulation, they applied forces to the capsid and viewed how it responded to those forces. Their model is based on the MARTINI force field, a commonly used coarse-grained model, with an added stabilizing network within the individual proteins that compensated for the model's shortcomings in stabilizing a protein's folding geometry.

The CCMV capsid is made up of 180 identical proteins. In assembly, the proteins first form pairs, called dimers, and those dimers then join together at interfaces.

While the proteins are the same, the interfaces can be different. At some locations on the capsid, five proteins meet; at others, six. In the simulation, the researchers found that when force was applied to the capsid, the capsid would start to fracture at the hexametric interfaces first, indicating that those protein-protein contacts were weaker than those at the pentametric interfaces. In contrast, the pentametric contacts never broke. Since stronger connections assemble first and weaker ones assemble later, the researchers can use this information to begin to recreate how the capsid formed.

In the simulation, the researchers also found a likely explanation for a strange structural feature found in the CCMV capsid. At the center of the hexametric association site, the tail-ends of the six proteins come together and form a beta barrel. Beta barrels are coiled secondary protein structures. The researchers believe that they act to provide further late-stage stabilization to the weaker hexametric interfaces. [15]

IBM lab-on-a-chip breakthrough aims to help physicians detect cancer

IBM scientists have developed a new lab-on-a-chip technology that can, for the first time, separate biological particles at the nanoscale and could enable physicians to detect diseases such as cancer before symptoms appear.

As reported today in the journal Nature Nanotechnology, the IBM team's results show size-based separation of bioparticles down to 20 nanometers (nm) in diameter, a scale that gives access to important particles such as DNA, viruses and exosomes. Once separated, these particles can potentially be analyzed by physicians to reveal signs of disease even before patients experience any physical symptoms and when the outcome from treatment is most positive. Until now, the smallest bioparticle that could be separated by size with on-chip technologies was about 50 times or larger, for example, separation of circulating tumor cells from other biological components.

IBM is collaborating with a team from the Icahn School of Medicine at Mount Sinai to continue development of this lab-on-a-chip technology and plans to test it on prostate cancer, the most common cancer in men in the U.S.

In the era of precision medicine, exosomes are increasingly being viewed as useful biomarkers for the diagnosis and prognosis of malignant tumors. Exosomes are released in easily accessible bodily fluids such as blood, saliva or urine. They represent a precious biomedical tool as they can be used in the context of less invasive liquid biopsies to reveal the origin and nature of a cancer.

The IBM team targeted exosomes with their device as existing technologies face challenges for separating and purifying exosomes in liquid biopsies. Exosomes range in size from 20-140nm and contain information about the health of the originating cell that they are shed from. A determination of the size, surface proteins and nucleic acid cargo carried by exosomes can give essential information about the presence and state of developing cancer and other diseases.

IBM's results show they could separate and detect particles as small as 20 nm from smaller particles, that exosomes of size 100 nm and larger could be separated from smaller exosomes, and that separation can take place in spite of diffusion, a hallmark of particle dynamics at these small scales. With Mt. Sinai, the team plans to confirm their device is able to pick up exosomes with cancer-specific biomarkers from patient liquid biopsies.

"The ability to sort and enrich biomarkers at the nanoscale in chip-based technologies opens the door to understanding diseases such as cancer as well as viruses like the flu or Zika," said Gustavo Stolovitzky, Program Director of Translational Systems Biology and Nanobiotechnology at IBM Research. "Our lab-on-a-chip device could offer a simple, noninvasive and affordable option to potentially detect and monitor a disease even at its earliest stages, long before physical symptoms manifest. This extra amount of time allows physicians to make more informed decisions and when the prognosis for treatment options is most positive."

With the ability to sort bioparticles at the nanoscale, Mt. Sinai hopes that IBM's technology can provide a new method to eavesdrop on the messages carried by exosomes for cell-to-cell communications. This can elucidate important questions about the biology of diseases as well as pave the way to noninvasive and eventually affordable point-of-care diagnostic tools. Monitoring this intercellular conversation more regularly could allow medical experts to track an individual's state of health or progression of a disease.

"When we are ahead of the disease we usually can address it well; but if the disease is ahead of us, the journey is usually much more difficult. One of the important developments that we are attempting in this collaboration is to have the basic grounds to identify exosome signatures that can be there very early on before symptoms appear or before a disease becomes worse," said Dr. Carlos Cordon-Cardo, Professor and Chairman for the Mount Sinai Health System Department of Pathology. "By bringing together Mount Sinai's domain expertise in cancer and pathology with IBM's systems biology experience and its latest nanoscale separation technology, the hope is to look for specific, sensitive biomarkers in exosomes that represent a new frontier to offering clues that might hold the answer to whether a person has cancer or how to treat it."

Sorting bioparticles at the nanoscale

Lab-on-a-chip technologies have become an incredibly helpful diagnostic tool for physicians as they can be significantly faster, portable, easy to use and require less sample volume to help detect diseases. The goal is to shrink down to a single silicon chip all of the processes necessary to analyze a disease that would normally be carried out in a full-scale biochemistry lab.

Using a technology called nanoscale deterministic lateral displacement, or nano-DLD, IBM scientists Dr. Joshua Smith and Dr. Benjamin Wunsch led development of a lab-on-a-chip technology that allows a liquid sample to be passed, in continuous flow, through a silicon chip containing an asymmetric pillar array. This array allows the system to sort a microscopic waterfall of nanoparticles, separating particles by size down to tens of nanometers resolution. IBM has already scaled down the chip size to 2cm by 2cm, while continuing development to increase the device density to improve functionality and throughput.

Much like how a road through a small tunnel only allows smaller cars to pass while forcing bigger trucks to detour around, nano-DLD uses a set of pillars to deflect larger particles while allowing smaller particles to flow through the gaps of the pillar array unabated, effectively separating this particle "traffic" by size while not disrupting flow. Interestingly, IBM scientists noticed that nano-DLD arrays can also split a mixture of many different particle sizes into a spread of streams, much like a prism splits white light into different colors. The continuous flow nature of this technology circumvents stop-and-go batch processing typical of conventional separation techniques.

Leveraging IBM's vast semiconductor expertise with its growing capabilities in experimental biology, IBM scientists used manufacturable silicon processes to produce the nano-DLD arrays for their lab-on-a-chip device. As part of its on-going strategy, IBM researchers are working to increase the diversity of bioparticles that can be separated with their device, and improving the precision and specificity for real-world clinical applications. [14]

Scientists work toward storing digital information in DNA

Her computer, Karin Strauss says, contains her "digital attic"—a place where she stores that published math paper she wrote in high school, and computer science schoolwork from college.

She'd like to preserve the stuff "as long as I live, at least," says Strauss, 37. But computers must be replaced every few years, and each time she must copy the information over, "which is a little bit of a headache."

It would be much better, she says, if she could store it in DNA—the stuff our genes are made of.

Strauss, who works at Microsoft Research in Redmond, Washington, is working to make that sci-fi fantasy a reality.

She and other scientists are not focused in finding ways to stow high school projects or snapshots or other things an average person might accumulate, at least for now. Rather, they aim to help companies and institutions archive huge amounts of data for decades or centuries, at a time when the world is generating digital data faster than it can store it.

To understand her quest, it helps to know how companies, governments and other institutions store data now: For long-term storage it's typically disks or a specialized kind of tape, wound up in cartridges about three inches on a side and less than an inch thick. A single cartridge containing about half a mile of tape can hold the equivalent of about 46 million books of 200 pages apiece, and three times that much if the data lends itself to being compressed.

A tape cartridge can store data for about 30 years under ideal conditions, says Matt Starr, chief technology officer of Spectra Logic, which sells data-storage devices. But a more practical limit is 10 to 15 years, he says.

It's not that the data will disappear from the tape. A bigger problem is familiar to anybody who has come across an old eight-track tape or floppy disk and realized he no longer has a machine to play it. Technology moves on, and data can't be retrieved if the means to read it is no longer available, Starr says.

So for that and other reasons, long-term archiving requires repeatedly copying the data to new technologies.

Into this world comes the notion of DNA storage. DNA is by its essence an information-storing molecule; the genes we pass from generation to generation transmit the blueprints for creating the human body. That information is stored in strings of what's often called the four-letter DNA code. That really refers to sequences of four building blocks—abbreviated as A, C, T and G—found in the DNA molecule. Specific sequences give the body directions for creating particular proteins.

Digital devices, on the other hand, store information in a two-letter code that produces strings of ones and zeroes. A capital "A," for example, is 01000001.

Converting digital information to DNA involves translating between the two codes. In one lab, for example, a capital A can become ATATG. The idea is once that transformation is made, strings of DNA can be custom-made to carry the new code, and hence the information that code contains.

One selling point is durability. Scientists can recover and read DNA sequences from fossils of Neanderthals and even older life forms. So as a storage medium, "it could last thousands and thousands of years," says Luis Ceze of the University of Washington, who works with Microsoft on DNA data storage.

Advocates also stress that DNA crams information into very little space. Almost every cell of your body carries about six feet of it; that adds up to billions of miles in a single person. In terms of information storage, that compactness could mean storing all the publicly accessible data on the internet in a space the size of a shoebox, Ceze says.

In fact, all the digital information in the world might be stored in a load of whitish, powdery DNA that fits in space the size of a large van, says Nick Goldman of the European Bioinformatics Institute in Hinxton, England.

What's more, advocates say, DNA storage would avoid the problem of having to repeatedly copy stored information into new formats as the technology for reading it becomes outmoded.

"There's always going to be someone in the business of making a DNA reader because of the health care applications," Goldman says. "It's always something we're going to want to do quickly and inexpensively."

Getting the information into DNA takes some doing. Once scientists have converted the digital code into the 4-letter DNA code, they have to custom-make DNA.

For some recent research Strauss and Ceze worked on, that involved creating about 10 million short strings of DNA.

Twist Bioscience of San Francisco used a machine to create the strings letter by letter, like snapping together Lego pieces to build a tower. The machine can build up to 1.6 million strings at a time.

Each string carried just a fragment of information from a digital file, plus a chemical tag to indicate what file the information came from.

To read a file, scientists use the tags to assemble the relevant strings. A standard lab machine can then reveal the sequence of DNA letters in each string.

Nobody is talking about replacing hard drives in consumer computers with DNA. For one thing, it takes too long to read the stored information. That's never going to be accomplished in seconds, says Ewan Birney, who works on DNA storage with Goldman at the bioinformatics institute.

But for valuable material like corporate records in long-term storage, "if it's worth it, you'll wait," says Goldman, who with Birney is talking to investors about setting up a company to offer DNA storage.

Sri Kosuri of the University of California Los Angeles, who has worked on DNA information storage but now largely moved on to other pursuits, says one challenge for making the technology practical is making it much cheaper.

Scientists custom-build fairly short strings DNA now for research, but scaling up enough to handle information storage in bulk would require a "mind-boggling" leap in output, Kosuri says. With current technology, that would be hugely expensive, he says.

George Church, a prominent Harvard genetics expert, agrees that cost is a big issue. But "I'm pretty optimistic it can be brought down" dramatically in a decade or less, says Church, who is in the process of starting a company to offer DNA storage methods.

For all the interest in the topic, it's worth noting that so far the amount of information that researchers have stored in DNA is relatively tiny.

Earlier this month, Microsoft announced that a team including Strauss and Ceze had stored a record 200 megabytes. The information included 100 books—one, fittingly, was "Great Expectations"—along with a brief video and many documents. But it was still less than 5 percent the capacity of an ordinary DVD.

Yet it's about nine times the mark reported just last month by Church, who says the announcement shows "how fast the field is moving."

Meanwhile, people involved with archiving digital data say their field views DNA as a possibility for the future, but not a cure-all.

"It's a very interesting and promising approach to the storage problem, but the storage problem is really only a very small part of digital preservation," says Cal Lee, a professor at the University of North Carolina's School of Information and Library Science.

It's true that society will probably always have devices to read DNA, so that gets around the problem of obsolete readers, he says. But that's not enough.

"If you just read the ones and zeroes, you don't know how to interpret it," Lee says.

For example, is that string a picture, text, a sound clip or a video? Do you still have the software to make sense of it?

What's more, the people in charge of keeping digital information want to check on it periodically to make sure it's still intact, and "I don't know how viable that is with DNA," says Euan Cochrane, digital preservation manager at the Yale University Library. It may mean fewer such check-ups, he says.

Cochrane, who describes his job as keeping information accessible "10 years to forever," says DNA looks interesting if its cost can be reduced and scientists find ways to more quickly store and recover information.

Starr says his data-storage device company hasn't taken a detailed look at DNA technology because it's too far in the future.

There are "always things out on the horizon that could store data for a very long time," he says. But the challenge of turning those ideas into a practical product "really trims the field down pretty quickly." [13]

Second layer of information in DNA confirmed

Leiden theoretical physicists have proven that DNA mechanics, in addition to genetic information in DNA, determines who we are. Helmut Schiessel and his group simulated many DNA sequences and found a correlation between mechanical cues and the way DNA is folded. They have published their results in PLoS One.

When James Watson and Francis Crick identified the structure of DNA molecules in 1953, they revealed that DNA information determines who we are. The sequence of the letters G, A, T and C in the famous double helix determines what proteins are made ny our cells. If you have brown eyes, for example, this is because a series of letters in your DNA encodes for proteins that build brown eyes. Each cell contains the exact same letter sequence, and yet every organ behaves differently. How is this possible?

Mechanical cues

Since the mid 1980s, it has been hypothesized that there is a second layer of information on top of the genetic code consisting of DNA mechanical properties.

Each of our cells contains two meters of DNA molecules, and these molecules need to be wrapped up tightly to fit inside a single cell. The way in which DNA is folded determines how the letters are read out, and therefore which proteins are actually made. In each organ, only relevant parts of the genetic information are read. The theory suggests that mechanical cues within the DNA structures determine how preferentially DNA folds.

Simulation

For the first time, Leiden physicist Helmut Schiessel and his research group provide strong evidence that this second layer of information indeed exists. With their computer code, they have simulated the folding of DNA strands with randomly assigned mechanical cues. It turns out that these cues indeed determine how the DNA molecule is folded into so-called nucleosomes. Schiessel found correlations between the mechanics and the actual folding structure in the genome of two organisms—baker's yeast and fission yeast. This finding reveals evolutionary changes in DNA—mutations—that have two very different effects: The letter sequence encoding for a specific protein can change, or the mechanics of the DNA structure can change, resulting in different packaging and levels of DNA accessibility, and therefore differing frequency of production of that protein. [12]

Quantum entanglement between the electron clouds of nucleic acids in DNA

We model the electron clouds of nucleic acids in DNA as a chain of coupled quantum harmonic oscillators with dipole-dipole interaction between nearest neighbours resulting in a van der Waals type bonding. Crucial parameters in our model are the distances between the acids and the coupling between them, which we estimate from numerical simulations . We show that for realistic parameters nearest neighbour entanglement is present even at room temperature. We quantify the amount of entanglement in terms of negativity and single base von Neumann entropy. We find that the strength of the single base von Neumann entropy depends on the neighbouring sites, thus questioning the notion of treating single bases as logically independent units. We derive an analytical expression for the binding energy of the coupled chain in terms of entanglement and show the connection between entanglement and correlation energy, a quantity commonly used in quantum chemistry. [11]

Scientists discover secret code hidden within human DNA

This undated handout illustration shows the DNA double helix (AFP Photo)This undated handout illustration shows the DNA double helix (AFP Photo)

Scientists have discovered a secret second code hiding within DNA which instructs cells on how genes are controlled. The amazing discovery is expected to open new doors to the diagnosis and treatment of diseases, according to a new study.

Ever since the genetic code was deciphered over 40 years ago, scientists have believed that it only described how proteins are made. However, the revelation made by the research team led by John Stamatoyannopoulos of the University of Washington indicates that genomes use the genetic code to write two separate languages.

“For over 40 years we have assumed that DNA changes affecting the genetic code solely impact how proteins are made,” said Stamatoyannopoulos, according to the press release. “Now we know that this basic assumption about reading the human genome missed half of the picture.”

Scientists discovered that the second language instructs the cells on how genes are controlled, according to findings published in Science magazine on Friday. The study is part of the Encyclopedia of DNA Elements Project, also known as ENCODE.

DNA (Deoxyribonucleic acid) is a nucleic acid that is the main constituent of the chromosomes of all organisms, except some viruses. DNA is self-replicating, plays a central role in protein synthesis, and is responsible for the transmission of hereditary characteristics from parents to offspring.

The second language remained hidden for so long because one language is written on top of the other, scientists said.

Scientists already knew that the genetic code uses a 64-letter alphabet called codons. The research team discovered that some of the codons can have two meanings – one related to proteins, the other to gene control. Those codons were given the name 'duons.'

And it's those duons that are expected to change the way physicians interpret human genomes, and give clues for the treatments of diseases.

"The fact that the genetic code can simultaneously write two kinds of information means that many DNA changes that appear to alter protein sequences may actually cause disease by disrupting gene control programs or even both mechanisms simultaneously," said Stamatoyannopoulos.

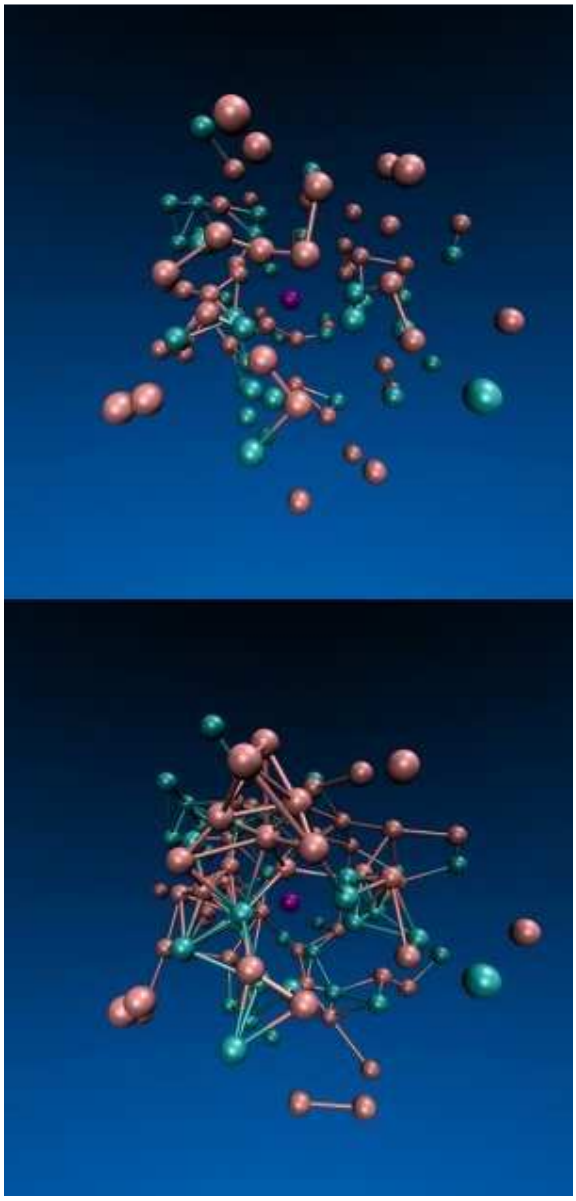
Speaking about the discovery, Stamatoyannopoulos said that the "new findings highlight that DNA is an incredibly powerful information storage device, which nature has fully exploited in unexpected ways." [10]

This Physicist Has a Groundbreaking Idea about Why Life Exists

"You start with a random clump of atoms, and if you shine light on it for long enough, it should not be so surprising that you get a plant," England said.

England's theory is meant to underlie, rather than replace, Darwin's theory of evolution by natural selection, which provides a powerful description of life at the level of genes and populations. "I am certainly not saying that Darwinian ideas are wrong," he explained. "On the contrary, I am just saying that from the perspective of the physics, you might call Darwinian evolution a special case of a more general phenomenon."

At the heart of England's idea is the second law of thermodynamics, also known as the law of increasing entropy or the "arrow of time." Hot things cool down, gas diffuses through air, eggs scramble but never spontaneously unscramble; in short, energy tends to disperse or spread out as time progresses. Entropy is a measure of this tendency, quantifying how dispersed the energy is among the particles in a system, and how diffuse those particles are throughout space. It increases as a simple matter of probability: There are more ways for energy to be spread out than for it to be concentrated.



A computer simulation by Jeremy England and colleagues shows a system of particles confined inside a viscous fluid in which the turquoise particles are driven by an oscillating force. Over time (from top to bottom), the force triggers the formation of more bonds among the particles.

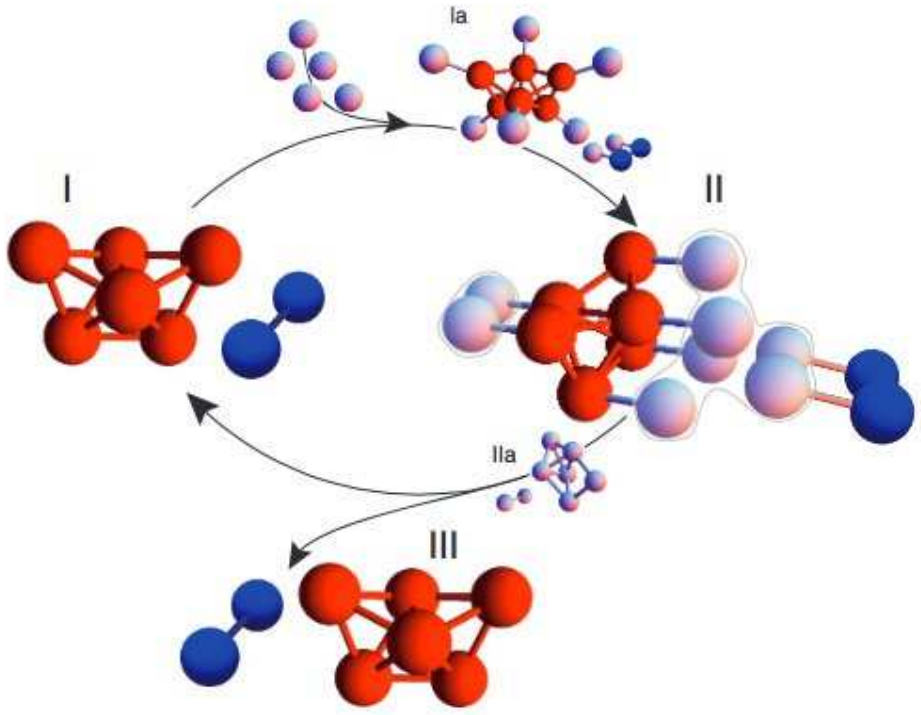
Thus, as particles in a system move around and interact, they will, through sheer chance, tend to adopt configurations in which the energy is spread out. Eventually, the system arrives at a state of maximum entropy called “thermodynamic equilibrium,” in which energy is uniformly distributed. A cup of coffee and the room it sits in become the same temperature, for example.

Although entropy must increase over time in an isolated or “closed” system, an “open” system can keep its entropy low — that is, divide energy unevenly among its atoms — by greatly increasing the entropy of its surroundings. In his influential 1944 monograph “What Is Life?” the eminent quantum physicist Erwin Schrödinger argued that this is what living things must do. A plant, for example, absorbs extremely energetic sunlight, uses it to build sugars, and ejects infrared light, a much less

concentrated form of energy. The overall entropy of the universe increases during photosynthesis as the sunlight dissipates, even as the plant prevents itself from decaying by maintaining an orderly internal structure.

Self-replication (or reproduction, in biological terms), the process that drives the evolution of life on Earth, is one such mechanism by which a system might dissipate an increasing amount of energy over time.

As England put it, “A great way of dissipating more is to make more copies of yourself.”



Self-Replicating Sphere Clusters: According to new research at Harvard, coating the surfaces of microspheres can cause them to spontaneously assemble into a chosen structure, such as a polytetrahedron (red), which then triggers nearby spheres into forming an identical structure.

Scientists have already observed self-replication in nonliving systems. According to new research led by Philip Marcus of the University of California, Berkeley, and reported in Physical Review Letters in August, vortices in turbulent fluids spontaneously replicate themselves by drawing energy from shear in the surrounding fluid. And in a paper in Proceedings of the National Academy of Sciences, Michael Brenner, a professor of applied mathematics and physics at Harvard, and his collaborators present theoretical models and simulations of microstructures that self-replicate. These clusters of specially coated microspheres dissipate energy by roping nearby spheres into forming identical clusters. “This connects very much to what Jeremy is saying,” Brenner said. [8]

Photoactive Prebiotic Systems

We propose that life first emerged in the form of such minimal photoactive prebiotic kernel systems and later in the process of evolution these photoactive prebiotic kernel systems would have produced fatty acids and covered themselves with fatty acid envelopes to become the minimal cells of the Fatty Acid World. Specifically, we model self-assembling of photoactive prebiotic systems with observed quantum entanglement phenomena. We address the idea that quantum entanglement was important in the first stages of origins of life and evolution of the biospheres because simultaneously excite two prebiotic kernels in the system by appearance of two additional quantum entangled excited states, leading to faster growth and self-replication of minimal living cells.
The quantum mechanically modeled possibility of synthesizing artificial self-reproducing quantum entangled prebiotic kernel systems and minimal cells also impacts the possibility of the most probable path of emergence of photocells on the Earth or elsewhere. We also examine the quantum entangled logic gates discovered in the modeled systems composed of two prebiotic kernels. Such logic gates may have application in the destruction of cancer cells or becoming building blocks of new forms of artificial cells including magnetically active ones.

Significance Statement

Our investigated self-assembly of molecules towards supramolecular bioorganic and minimal cellular systems depends on the quantum mechanics laws which induce hydrogen and Van der Waals bindings (Tamulis A, Grigalavicius, M, Orig Life Evol Biosph 41:51-71, 2011).

In the work presented here, quantum entanglement takes the form of a quantum superposition of the active components in synthesized self-assembling and self-replicating living systems. When a quantum calculation of an entangled system is made that causes one photoactive biomolecule of such a pair to take on a definite value (e.g., electron density transfer or electron spin density transfer), the other member of this entangled pair will be found to have taken the appropriately correlated value (e.g., electron density transfer or electron spin density transfer). In our simulations, the separation distance of supramolecular bio systems changes took place during geometry optimization procedures, which mimic real-world intermolecular interaction processes.

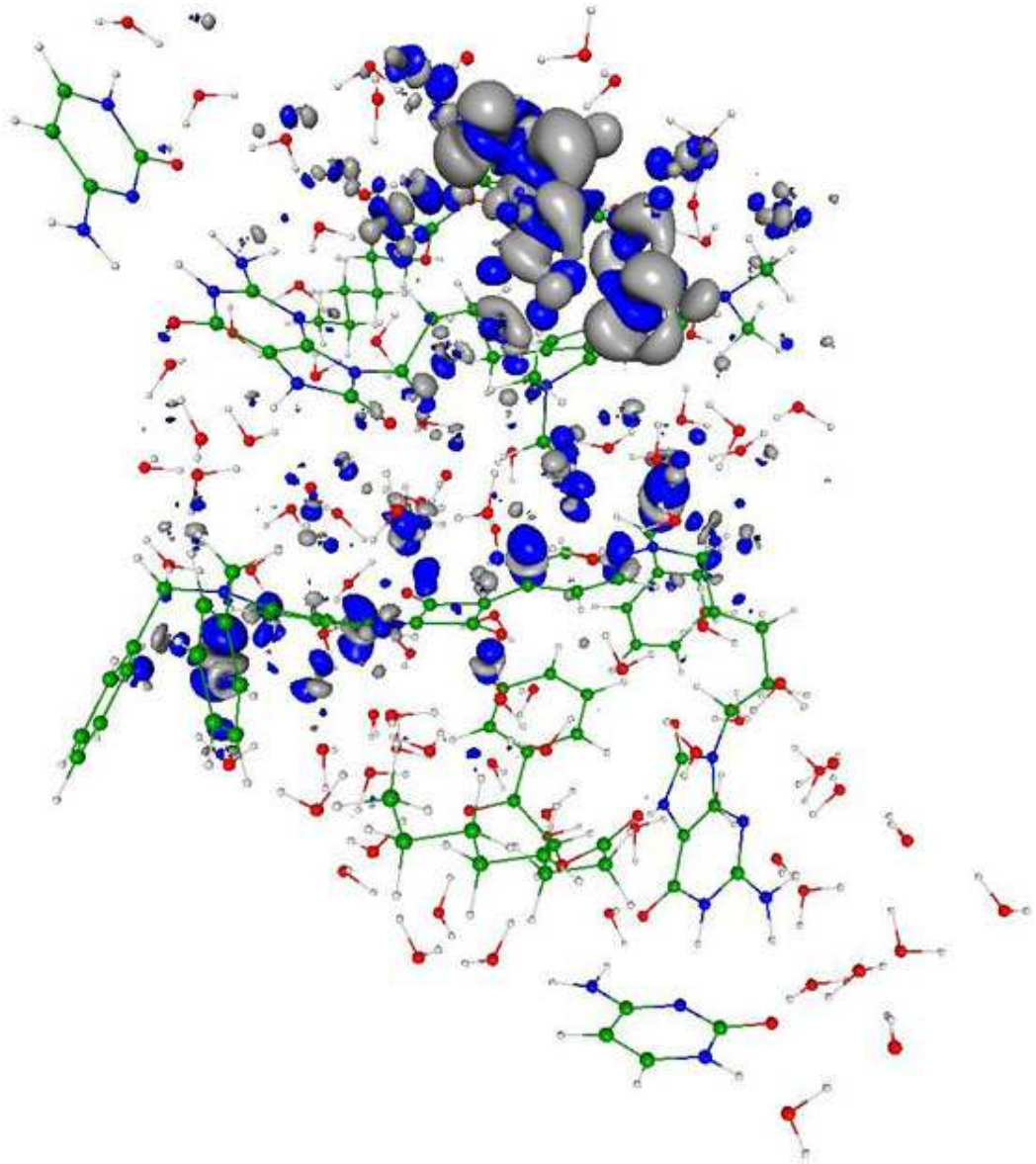
Our discovered phenomenon of the quantum entanglement in the prebiotic systems enhance the photosynthesis in the proposed systems because simultaneously excite two prebiotic kernels in the system by appearance of two additional quantum entangled excited states (Tamulis A, Grigalavicius M, Baltrusaitis J, Orig Life Evol Biosph 43:49-66, 2013; Tamulis A, Grigalavicius M, Krisciukaitis S (2014) , J Comput Theor Nanos, 11, 1597-1608, 2014; Tamulis A, Grigalavicius M, 8:117-140, 2014.). We can propose that quantum entanglement enhanced the emergence of photosynthetic prebiotic kernels and accelerated the evolution of photosynthetic life because of additional absorbed light energy, leading to faster growth and self-replication of minimal living cells.

We can state that: Livings are self-assembled and self-replicating wet and warm stochastically moving supramolecular systems where quantum entanglement can be continuously generated and destroyed by non-equilibrium effects in an environment where no static entanglement exists; quantum entanglement involve the biomolecule inside one living or between other neighboring livings.

This warm quantum coherence is basic for the explanation of DNA stability and for the understanding of brain magnetic orientation during migration in more than 50 species of birds, fishes and insects. Exists experimental evidence for quantum-coherent is used for more efficient light-harvesting in plant photosynthesis. Quantum entanglement exists in supramolecules determining the sense of smell and in the brain neurons microtubules due to quantum vibrations.

In the work presented here, we started to design and quantum mechanical investigations of the molecular logical devices which are useful for construction of nano medicine biorobots against the molecular diseases such a cancer tumors, and against the new kinds of synthesized microorganisms and nano guns.

Figure legend



You can see in the enclosed figure the quantum entanglement phenomenon in the closely self-assembled two synthesized protocell system due to the photo excited electron charge transfer from one protocell to another that leads to closer self-assembly and exchange of energy and information.

Visualization of the electron charge tunneling associated with the 6th (467.3 nm) excited state. The transition is mainly from squarine molecule of the first protocell situated in the bottom of this bi cellular system to precursor of fatty acid (pFA) molecule of the second subsystem (in the top) and little from the 1,4-bis(N,N-dimethylamino)naphthalene molecule (in the top-right) to the same pFA molecule of the second subsystem (in the top). The electron cloud hole is indicated by the dark blue color while the transferred electron cloud location is designated by the gray color.

As a result, these nonlinear quantum interactions compressed the overall molecular system resulting in a smaller gap between the HOMO and LUMO electron energy levels which allows enhanced tunneling of photo excited electrons from the sensitizer squarine and (1,4-bis(N,N-dimethylamino)naphthalene) to the pFA molecule resulting in its cleavage. The new fatty acid joins the existing minimal cell thus increasing it in size. After reaching some critical size, the minimal cell should divide (i.e. self-replicate) into two separate smaller minimal cells. [7]

Quantum Biology

Researchers have long suspected that something unusual is afoot in photosynthesis. Particles of light called photons, streaming down from the Sun; arrive randomly at the chlorophyll molecules and other light-absorbing ‘antenna’ pigments that cluster inside the cells of every leaf, and within every photosynthetic bacterium. But once the photons’ energy is deposited, it doesn’t stay random. Somehow, it gets channeled into a steady flow towards the cell’s photosynthetic reaction centre, which can then use it at maximum efficiency to convert carbon dioxide into sugars. Quantum coherence in photosynthesis seems to be beneficial to the organisms using it. But did their ability to exploit quantum effects evolve through natural selection? Or is quantum coherence just an accidental side effect of the way certain molecules are structured? [6]

Quantum Consciousness

Extensive scientific investigation has found that a form of quantum coherence operates within living biological systems through what is known as biological excitations and biophoton emission. What this means is that metabolic energy is stored as a form of electromechanical and electromagnetic excitations. These coherent excitations are considered responsible for generating and maintaining long-range order via the transformation of energy and very weak electromagnetic signals. After nearly twenty years of experimental research, Fritz-Albert Popp put forward the hypothesis that biophotons are emitted from a coherent electrodynamics field within the living system.

What this means is that each living cell is giving off, or resonating, a biophoton field of coherent energy. If each cell is emitting this field, then the whole living system is, in effect, a resonating field-a ubiquitous nonlocal field. And since biophotons are the entities through which the living system communicates, there is near-instantaneous intercommunication throughout. And this, claims Popp, is the basis for coherent biological organization -- referred to as quantum coherence. This discovery

led Popp to state that the capacity for evolution rests not on aggressive struggle and rivalry but on the capacity for communication and cooperation. In this sense the built-in capacity for species evolution is not based on the individual but rather living systems that are interlinked within a coherent whole: Living systems are thus neither the subjects alone, nor objects isolated, but both subjects and objects in a mutually communicating universe of meaning. . . . Just as the cells in an organism take on different tasks for the whole, different populations enfold information not only for themselves, but for all other organisms, expanding the consciousness of the whole, while at the same time becoming more and more aware of this collective consciousness.

Biophysicist Mae-Wan Ho describes how the living organism, including the human body, is coordinated throughout and is "coherent beyond our wildest dreams." It appears that every part of our body is "in communication with every other part through a dynamic, tunable, responsive, liquid crystalline medium that pervades the whole body, from organs and tissues to the interior of every cell."

What this tells us is that the medium of our bodies is a form of liquid crystal, an ideal transmitter of communication, resonance, and coherence. These relatively new developments in biophysics have discovered that all biological organisms are constituted of a liquid crystalline medium. Further, DNA is a liquid-crystal, lattice-type structure (which some refer to as a liquid crystal gel), whereby body cells are involved in a holographic instantaneous communication via the emitting of biophotons (a source based on light). This implies that all living biological organisms continuously emit radiations of light that form a field of coherence and communication. Moreover, biophysics has discovered that living organisms are permeated by quantum wave forms. [5]

Information – Entropy Theory of Physics

Viewing the confined gas where the statistical entropy not needs the information addition is not the only physical system. There are for example quantum mechanical systems where the information is a very important qualification. The perturbation theory needs higher order calculations in QED or QCD giving more information on the system as in the chess games happens, where the entropy is not enough to describe the state of the matter. The variation calculation of chess is the same as the perturbation calculation of physics to gain information, where the numbers of particles are small for statistical entropy to describe the system. The role of the Feynman graphs are the same as the chess variations of a given position that is the depth of the variations tree, the Information is the same as the order of the Feynman graphs giving the Information of the micro system. [9]

Information – Entropy Theory of Life

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. The living biological systems have also entropy lowering and information growing direction by building more complicated or entangled molecules, governed by the quantum mechanics and the general weak interaction. On the other hand there is the arrow of time; the entropy growing is lowering the information by dissipating these entangled or otherwise connected biomolecules, aging the living systems.

Creating quantum technology

Another area of potential application is in quantum computing. The long-standing goal of the physicists and engineers working in this area is to manipulate data encoded in quantum bits (qubits) of information, such as the spin-up and spin-down states of an electron or of an atomic nucleus. Qubits can exist in both states at once, thus permitting the simultaneous exploration of all possible answers to the computation that they encode. In principle, this would give quantum computers the power to find the best solution far more quickly than today's computers can — but only if the qubits can maintain their coherence, without the noise of the surrounding environment, such as the jostling of neighboring atoms, destroying the synchrony of the waves. [6]

Quantum Entanglement

Measurements of physical properties such as position, momentum, spin, polarization, etc. performed on entangled particles are found to be appropriately correlated. For example, if a pair of particles is generated in such a way that their total spin is known to be zero, and one particle is found to have clockwise spin on a certain axis, then the spin of the other particle, measured on the same axis, will be found to be counterclockwise. Because of the nature of quantum measurement, however, this behavior gives rise to effects that can appear paradoxical: any measurement of a property of a particle can be seen as acting on that particle (e.g. by collapsing a number of superimposed states); and in the case of entangled particles, such action must be on the entangled system as a whole. It thus appears that one particle of an entangled pair "knows" what measurement has been performed on the other, and with what outcome, even though there is no known means for such information to be communicated between the particles, which at the time of measurement may be separated by arbitrarily large distances. [4]

The Bridge

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

Accelerating charges

The moving charges are self maintain the electromagnetic field locally, causing their movement and this is the result of their acceleration under the force of this field. In the classical physics the charges will distributed along the electric current so that the electric potential lowering along the current, by

linearly increasing the way they take every next time period because this accelerated motion. The same thing happens on the atomic scale giving a dp impulse difference and a dx way difference between the different part of the not point like particles.

Relativistic effect

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

Heisenberg Uncertainty Relation

In the atomic scale the Heisenberg uncertainty relation gives the same result, since the moving electron in the atom accelerating in the electric field of the proton, causing a charge distribution on 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 T- symmetry breaking!!! This flavor changing oscillation could prove that it could be also on higher level such as atoms, molecules, probably big biological significant molecules and responsible on the aging of the life.

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

Finally since the weak interaction is an electric dipole change with 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 $E = h\nu$ and $E = mc^2$, $m = h\nu / c^2$ that is the m depends only on the ν frequency. It means that the mass of the proton and electron are electromagnetic and the result of the electromagnetic induction, caused by the changing acceleration of the spinning and moving charge! It could be that the m_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 $W^{\pm}$, and Z weak gauge bosons through electroweak symmetry breaking. The Large Hadron Collider at CERN announced results consistent with the Higgs particle on July 4, 2012 but stressed that further testing is needed to confirm the Standard Model.

What is the Spin?

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

The Graviton

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

Conclusions

"The fact that the genetic code can simultaneously write two kinds of information means that many DNA changes that appear to alter protein sequences may actually cause disease by disrupting gene control programs or even both mechanisms simultaneously," said Stamatoyannopoulos.
Speaking about the discovery, Stamatoyannopoulos said that the "new findings highlight that DNA is an incredibly powerful information storage device, which nature has fully exploited in unexpected ways." [10]
There is also connection between statistical physics and evolutionary biology, since the arrow of time is working in the biological evolution also.
Prentiss, who runs an experimental biophysics lab at Harvard, says England's theory could be tested by comparing cells with different mutations and looking for a correlation between the amount of energy the cells dissipate and their replication rates. [8]
Exists experimental evidence for quantum-coherent is used for more efficient light-harvesting in plant photosynthesis. Quantum entanglement exists in supramolecules determining the sense of smell and in the brain neurons microtubules due to quantum vibrations.
In the work presented here, we started to design and quantum mechanical investigations of the molecular logical devices which are useful for construction of nano medicine biorobots against the molecular diseases such a cancer tumors, and against the new kinds of synthesized microorganisms and nano guns. [7]
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]
These relatively new developments in biophysics have discovered that all biological organisms are constituted of a liquid crystalline medium. Further, DNA is a liquid-crystal, lattice-type structure (which some refer to as a liquid crystal gel), whereby body cells are involved in a holographic instantaneous communication via the emitting of biophotons (a source based on light). This implies that all living biological organisms continuously emit radiations of light that form a field of coherence and communication. Moreover, biophysics has discovered that living organisms are permeated by quantum wave forms. [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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