

# Ordered Nanostructures in 3-D

*Scientists have developed a platform for assembling nanosized material components, or "nano-objects," of very different types—inorganic or organic—into desired 3-D structures. [26]*

*A team of physicists at Purdue University has built the most sensitive torque measuring device ever. In their paper published in the journal Nature Nanotechnology, the team describes their new device and outline how it might be used. [25]*

*Now a team of researchers at the University of Ottawa is democratizing entry into the field of nanopore research by offering up a unique tool to accelerate the development of new applications and discoveries. [24]*

*Researchers from U of T Engineering have discovered that an active, rather than passive, process dictates which nanoparticles enter solid tumors. [23]*

*Researchers at Oregon State University have developed an improved technique for using magnetic nanoclusters to kill hard-to-reach tumors. [22]*

*MIT researchers have now come up with a novel way to prevent fibrosis from occurring, by incorporating a crystallized immunosuppressant drug into devices. [21]*

*In a surprising marriage of science and art, researchers at MIT have developed a system for converting the molecular structures of proteins, the basic building blocks of all living beings, into audible sound that resembles musical passages. [20]*

*Inspired by ideas from the physics of phase transitions and polymer physics, researchers in the Divisions of Physical and Biological Sciences at UC San Diego set out specifically to determine the organization of DNA inside the nucleus of a living cell. [19]*

*Scientists from the National Institute of Standards and Technology (NIST) and the University of Maryland are using neutrons at Oak Ridge National Laboratory (ORNL) to capture new information about DNA and RNA molecules and enable more accurate computer simulations of how they interact with everything from proteins to viruses. [18]*

*The DNA molecules are chiral, which means they can exist in two forms which are mirror images, like a left and right hand. The phenomenon was dubbed "chiral induced*

*spin selectivity" (CISS), and over the last few years, several experiments were published allegedly showing this CISS effect, even in electronic devices. [17]*

*Chemist Ivan Huc finds the inspiration for his work in the molecular principles that underlie biological systems. [16]*

*What makes particles self-assemble into complex biological structures? [15]*

*Scientists from Moscow State University (MSU) working with an international team of researchers have identified the structure of one of the key regions of telomerase—a so-called "cellular immortality" ribonucleoprotein. [14]*

*Researchers from Tokyo Metropolitan University used a light-sensitive iridium-palladium catalyst to make "sequential" polymers, using visible light to change how building blocks are combined into polymer chains. [13]*

*Researchers have fused living and non-living cells for the first time in a way that allows them to work together, paving the way for new applications. [12]*

*UZH researchers have discovered a previously unknown way in which proteins interact with one another and cells organize themselves. [11]*

*Dr Martin Sweatman from the University of Edinburgh's School of Engineering has discovered a simple physical principle that might explain how life started on Earth. [10]*

*Nearly 75 years ago, Nobel Prize-winning physicist Erwin Schrödinger wondered if the mysterious world of quantum mechanics played a role in biology. A recent finding by Northwestern University's Prem Kumar adds further evidence that the answer might be yes. [9]*

*A UNSW Australia-led team of researchers has discovered how algae that survive in very low levels of light are able to switch on and off a weird quantum phenomenon that occurs during photosynthesis. [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.*

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Author: George Rajna

## Preface

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]

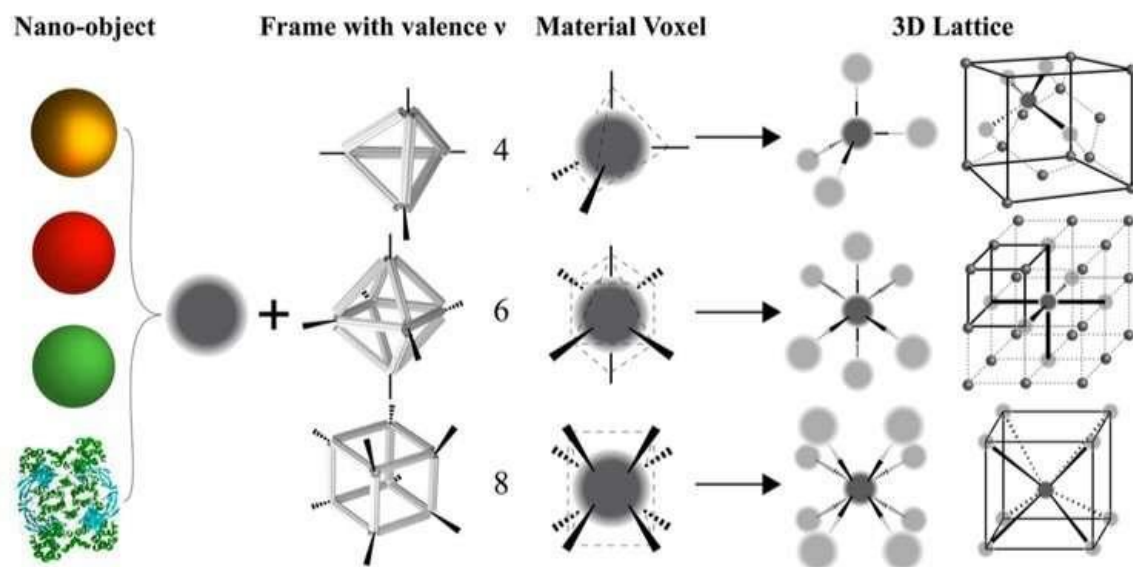
I think that we have a simple bridge between the classical and quantum mechanics by understanding the Heisenberg Uncertainty Relations. It makes clear that the particles are not point like but have a  $dx$  and  $dp$  uncertainty.

## Nano-objects of desire: Assembling ordered nanostructures in 3-D

Scientists have developed a platform for assembling nanosized material components, or "nano-objects," of very different types—inorganic or organic—into desired 3-D structures. Though self-assembly (SA) has successfully been used to organize nanomaterials of several kinds, the process has been extremely system-specific, generating different structures based on the intrinsic properties of the materials. As reported in a paper published today in *Nature Materials*, their new DNA-programmable nanofabrication platform can be applied to organize a variety of 3-D materials in the same prescribed ways at the nanoscale (billionths of a meter), where unique optical, chemical, and other properties emerge.

"One of the major reasons why SA is not a technique of choice for practical applications is that the same SA process cannot be applied across a broad range of materials to create identical 3-D ordered arrays from different nanocomponents," explained corresponding author Oleg Gang, leader of the Soft and Bio Nanomaterials Group at the Center for Functional Nanomaterials (CFN)—a U.S. Department of Energy (DOE) Office of Science User Facility at Brookhaven National Laboratory—and a professor of Chemical Engineering and of Applied Physics and Materials Science at Columbia Engineering. "Here, we decoupled the SA process from material properties by designing rigid polyhedral DNA frames that can encapsulate various inorganic or organic nano-objects, including metals, semiconductors, and even proteins and enzymes."

The scientists engineered synthetic DNA frames in the shape of a cube, octahedron, and tetrahedron. Inside the frames are DNA "arms" that only nano-objects with the complementary DNA sequence can bind to. These material voxels—the integration of the DNA frame and nano-object—are the building blocks from which macroscale 3-D structures can be made. The frames connect to each other regardless of what kind of nano-object is inside (or not) according to the complementary sequences they are encoded with at their vertices. Depending on their shape, frames have a different number of vertices and thus form entirely different structures. Any nano-objects hosted inside the frames take on that specific frame structure.



Schematic of the platform for assembling 3-D lattices from inorganic and organic nano-objects with DNA frames shaped as a tetrahedron (top row), octahedron (middle row), and cube (bottom row). The frame valence is determined by the vertices and corresponds to the number of connections (bonds) and how these connections are organized relative to one another. For example, the tetrahedral frame has a valence of four. The resulting 3-D lattices are based on the shape of the DNA frame—tetrahedral frames assemble into diamond structures, octahedral into simple cubic, and cubic into body-centered cubic—regardless of which nano-object (if any) is inside the frame. Credit: Nature Materials

To demonstrate their assembly approach, the scientists selected metallic (gold) and semiconducting (cadmium selenide) nanoparticles and a bacterial protein (streptavidin) as the inorganic and organic nano-objects to be placed inside the DNA frames. First, they confirmed the integrity of the DNA



frames and formation of material voxels by imaging with electron microscopes at the CFN Electron Microscopy Facility and the Van Andel Institute, which has a suite of instruments that operate at cryogenic temperatures for biological samples. They then probed the 3-D lattice structures at the Coherent Hard X-ray Scattering and Complex Materials Scattering beamlines of the National Synchrotron Light Source II (NSLS-II)—another DOE Office of Science User Facility at Brookhaven Lab. Columbia Engineering Bykhovsky Professor of Chemical Engineering Sanat Kumar and his group performed computational modeling revealing that the experimentally observed lattice structures (based on the X-ray scattering patterns) were the most thermodynamically stable ones that the material voxels could form.

"These material voxels allow us to begin to use ideas derived from atoms (and molecules) and the crystals that they form, and port this vast knowledge and database to systems of interest at the nanoscale," explained Kumar.

Gang's students at Columbia then demonstrated how the assembly platform could be used to drive the organization of two different kinds of materials with chemical and optical functions. In one case, they co-assembled two enzymes, creating 3-D arrays with a high packing density. Though the enzymes remained chemically unchanged, they showed about a fourfold increase in enzymatic activity. These "nanoreactors" could be used to manipulate cascade reactions and enable the fabrication of chemically active materials. For the optical material demonstration, they mixed two different colors of quantum dots—tiny nanocrystals that are being used to make television displays with high color saturation and brightness. Images captured with a fluorescence microscope showed that the formed lattice maintained color purity below the diffraction limit (wavelength) of light; this property could allow for significant resolution improvement in various display and optical communication technologies.

"We need to rethink how materials can be formed and how they function," said Gang. "Material redesign may not be necessary; simply packaging existing materials in new ways could enhance their properties. Potentially, our platform could be an enabling technology 'beyond 3-D printing manufacturing' to control materials at much smaller scales and with greater material variety and designed compositions. Using the same approach to form 3-D lattices from desired nano-objects of different material classes, integrating those that would otherwise be considered incompatible, could revolutionize nanomanufacturing." [26]

## **The most sensitive torque measuring device ever built**

A team of physicists at Purdue University has built the most sensitive torque measuring device ever. In their paper published in the journal *Nature Nanotechnology*, the team describes their new device and outline how it might be used.

Torque is a twisting force that often leads to rotation. Devices built to measure [torque](#) in a system take many forms and come in many sizes. In recent years, scientists have been working on ways to downsize torque sensors with the goal of measuring very small amounts of torque. Tiny devices that use nanofabrication and cryogenic cooling have been developed to study such things as the Casimir effect and small-scale magnetism. Prior to this new effort, the most sensitive torque sensor had

achieved a sensitivity of  $2.9 \times 10^{-24}$  N m Hz<sup>-1/2</sup> at millikelvin temperatures. The team at Purdue set themselves the goal of breaking that record.

The new [device](#) consisted of a silica nanoparticle suspended inside of a [vacuum chamber](#) by a 500-mW, 1,550-nm laser beam. The team applied torque to the nanoparticle by firing a pulsating, circularly polarized 1,020-nm laser beam at it for 100 seconds at a time. The researchers used a quarter waveplate to control polarization. The rotating waves in the electromagnet beam imparted a twisting action on the nanoparticle, making it spin at 300 billion rpm—the fastest man-made rotor ever built. The team was able to measure the amount of torque in the device by measuring how much the particle's spin speed changed during the on and off cycles using an optical sensor. The researchers point out that their system, unlike others being developed, did not require intricate nanofabrication.

Using the device, the researchers were able to measure torque to a quadrillionth of a newton-meter—making it approximately 700 times as sensitive as the previous record holder. They claim that their device will be the first to measure vacuum friction—in which [quantum mechanics](#) suggests an object spinning in a vacuum experiences drag due to electromagnetic fields that constantly appear and disappear. The team also claims that the device could be used for nanoscale magnetism research and for studying the quantum geometric phase. [25]

### **A tool to democratize nanopore research**

A nanopore is a tiny hole in a thin membrane with a diameter of around a billionth of a meter, or about the width of a single DNA molecule. The potential applications of these nanopores are so diverse—from medicine to information technology (IT)—that they could have a major impact on our daily lives. Now a team of researchers at the University of Ottawa is democratizing entry into the field of nanopore research by offering up a unique tool to accelerate the development of new applications and discoveries.

The innovative T.-Cossa Lab, which studies applied single-molecule biophysics, came up with the idea to provide the research community with the protocols, hardware designs, and software required to fabricate solid-state nanopores in a fast, low cost, and completely automated fashion. This method is now available in the online journal *Nature Protocols*.

The move is a boon for researchers developing diagnostic and sequencing applications in health, life sciences, and IT, where being able to detect and identify single biological molecules like proteins or DNA with the exacting precision of a [nanopore](#) is needed.

"For the first time, we are making our unique nanopore fabrication tool freely available," explained Vincent Tabard-Cossa, professor in the Department of Physics and Director of the Laboratory for Applied Single-Molecule Biophysics at the University of Ottawa. "We opted to offer our patented nanopore fabrication technology to the [research community](#) for free, to help disseminate it and expand the field of nanopore research."



Solid-state nanopores are now well established as single-biomolecule sensors which hold enormous promise for fast and low-cost sensing and sequencing applications, including rapid identification of pathogens, biomarker quantification for precision medicine, metagenomics, microbiome analysis, and cancer research. However, until recently, this promise had been stifled by the expensive, labor intensive, and low-yield methods by which pores were fabricated. To address this problem, Professor Tabard-Cossa and his team pioneered a cheap and scalable solid-state nanopore fabrication method in 2012 called controlled breakdown (CBD), which has since become the method of choice by which solid-state nanopores are fabricated by research groups around the world.

"To foster accessible innovation, we set out to make an instrument and workflow that could be operated successfully by someone who had never even heard of a nanopore," said Matthew Waugh, lab manager of the T.-Cossa Lab. "We've already had some amazing successes through a local scientific outreach program where [high school students](#) have been able to independently produce nanopores and detect individual DNA molecules in a single afternoon using our tools."

CBD pore fabrication replaces expensive, manually operated electron microscopes with low cost, easy-to-use, small benchtop instruments that automatically fabricate nanopores to a given size at the click of a button. According to Dr. Tabard-Cossa, researchers can now focus their attention on developing different real-world nanopore applications in various fields.

"One such application tackles the growing need to store and archive huge amounts of digital information for very long timescales," said Kyle Briggs, postdoctoral fellow in the T.-Cossa lab. "Nature solved this problem a long time ago with DNA, and a similar approach will work for us, in which the information is stored as the sequence of a synthetic polymer, reducing server farms down to the size of a fridge and saving billions of dollars in energy costs and fried hard drives. Solid-state nanopores could enable the next major breakthrough in data storage since they can be used as the element that reads the information off the polymers," he added. [24]

## **Most engineered nanoparticles enter tumours through cells, not between them**

Researchers from U of T Engineering have discovered that an active, rather than passive, process dictates which nanoparticles enter solid tumors. The finding upends previous thinking in the field of cancer nanomedicine and points toward more effective nanotherapies.

The prevailing theory in cancer nanomedicine—an approach that enables more targeted therapies than standard chemotherapy—has been that [nanoparticles](#) mainly diffuse passively into tumors through tiny gaps between [cells](#) in the endothelium, which lines the inner wall of blood vessels that support tumor growth.

The researchers previously showed that [less than one percent](#) of nanoparticle-based drugs typically reach their tumor targets. In the current study, the team found that among

nanoparticles that do penetrate tumors, more than 95 percent pass through [endothelial cells](#)—not between gaps among those cells.

"Our work challenges long-held dogma in the field and suggests a completely new theory," says Abdullah Syed, a co-lead author on the study and postdoctoral fellow in the lab of Warren Chan, a professor at the Institute of Biomaterials and Biomedical Engineering (IBBME) and the Donnelly Centre for Cellular and Biomolecular Research.

The study was published today in *Nature Materials*.

"We saw many nanoparticles enter the endothelial cells from blood vessels and exit into the tumor in various conditions. Endothelial cells appear to be crucial gatekeepers in the nanoparticle transport process."

Syed compares nanoparticles to people trying to get into popular restaurants on a busy night. "Some restaurants don't require a reservation, while others have bouncers who check if patrons made reservations," he says. "The bouncers are a lot more common than researchers thought, and most places only accept patrons with a reservation."

The researchers established that passive diffusion was not the mechanism of entry with multiple lines of evidence. They took more than 400 images of tissue samples from animal models, and saw few endothelial gaps relative to nanoparticles. They observed the same trend using 3-D fluorescent imaging and live-animal imaging.

Similarly, they found few gaps between endothelial cells in samples from human cancer patients.

The group then devised an [animal model](#) that completely stopped the transportation of nanoparticles through endothelial cells. This allowed them to isolate the contribution of passive transport via gaps between endothelial cells, which proved to be miniscule.

The researchers posit several active mechanisms by which endothelial cells might transport nanoparticles into tumors, including binding mechanisms, intra-endothelial channels and as-yet undiscovered processes, all of which they are investigating.

Meanwhile, the results have major implications for nanoparticle-based therapeutics.

"These findings will change the way we think about delivering drugs to tumors using nanoparticles," says Shrey Sindhwani, also a co-lead author on the paper and an MD/Ph.D. student in Chan's lab. "A better understanding of the nanoparticle transport phenomenon will help researchers design more effective therapies." [23]

## **Researchers reach milestone in use of nanoparticles to kill cancer with heat**

Researchers at Oregon State University have developed an improved technique for using magnetic nanoclusters to kill hard-to-reach tumors.

Magnetic nanoparticles—tiny pieces of matter as small as one-billionth of a meter—have shown anti-cancer promise for tumors easily accessible by syringe, allowing the particles to be injected directly into the cancerous growth.

Once injected into the tumor, the nanoparticles are exposed to an alternating [magnetic field](#), or AMF. This field causes the nanoparticles to reach temperatures in excess of 100 degrees Fahrenheit, which causes the cancer cells to die.

But for some [cancer types](#) such as [prostate cancer](#), or the [ovarian cancer](#) used in the Oregon State study, direct injection is difficult. In those types of cases, a "systemic" delivery method—[intravenous injection](#), or injection into the abdominal cavity—would be easier and more effective.

The challenge for researchers has been finding the right kind of nanoparticles—ones that, when administered systemically in clinically appropriate doses, accumulate in the tumor well enough to allow the AMF to heat cancer cells to death.

Olena Taratula and Oleh Taratula of the OSU College of Pharmacy tackled the problem by developing nanoclusters, multiatom collections of nanoparticles, with enhanced heating efficiency. The nanoclusters are hexagon-shaped [iron oxide nanoparticles](#) doped with cobalt and manganese and loaded into biodegradable nanocarriers.



OSU researchers Olena and Oleh Taratula's work with magnetic nanoclusters as cancer therapy was featured on the cover of *ACS Nano*. Credit: Tetiana Korzun

Findings were published in *ACS Nano*.

"There had been many attempts to develop nanoparticles that could be administered systemically in safe doses and still allow for hot enough temperatures inside the tumor," said Olena Taratula, associate professor of pharmaceutical sciences. "Our new nanoplatform is a milestone for treating difficult-to-access tumors with magnetic hyperthermia. This is a proof of concept, and the nanoclusters could potentially be optimized for even greater heating efficiency."

The nanoclusters' ability to reach therapeutically relevant temperatures in tumors following a single, low-dose IV injection opens the door to exploiting the full potential of magnetic hyperthermia in treating cancer, either by itself or with other therapies, she added.

"It's already been shown that magnetic hyperthermia at moderate temperatures increases the susceptibility of [cancer cells](#) to chemotherapy, radiation and immunotherapy," Taratula said.

The mouse model in this research involved animals receiving IV nanocluster injections after ovarian tumors had been grafted underneath their skin.

"To advance this technology, future studies need to use orthotopic animal models—models where deep-seated tumors are studied in the location they would actually occur in the body," she said. "In addition, to minimize the heating of healthy tissue, current AMF systems need to be optimized, or new ones developed." [22]

## **A better way to encapsulate islet cells for diabetes treatment**

When medical devices are implanted in the body, the immune system often attacks them, producing scar tissue around the device. This buildup of tissue, known as fibrosis, can interfere with the device's function.

MIT researchers have now come up with a novel way to prevent fibrosis from occurring, by incorporating a crystallized immunosuppressant drug into devices. After implantation, the drug is slowly secreted to dampen the immune response in the area immediately surrounding the device.

"We developed a crystallized drug formulation that can target the key players involved in the implant rejection, suppressing them locally and allowing the device to function for more than a year," says Shady Farah, an MIT and Boston Children's Hospital postdoc and co-first author of the study, who is soon starting a new position as an assistant professor of the Wolfson Faculty of Chemical Engineering and the Russell Berrie Nanotechnology Institute at Technion-Israel Institute of Technology.

The researchers showed that these crystals could dramatically improve the performance of encapsulated [islet cells](#), which they are developing as a possible treatment for patients with type 1 diabetes. Such crystals could also be applied to a variety of other implantable [medical devices](#), such as pacemakers, stents, or sensors.

Former MIT postdoc Joshua Doloff, now an assistant professor of Biomedical and Materials Science Engineering and member of the Translational Tissue Engineering Center at Johns Hopkins University School of Medicine, is also a lead author of the paper, which appears in the June 24 issue of *Nature*

*Materials.* Daniel Anderson, an associate professor in MIT's Department of Chemical Engineering and a member of MIT's Koch Institute for Integrative Cancer Research and Institute for Medical Engineering and Science (IMES), is the senior author of the paper.

### Crystalline drug

Anderson's lab is one of many research groups working on ways to encapsulate islet [cells](#) and transplant them into [diabetic patients](#), in hopes that such cells could replace the patients' nonfunctioning pancreatic cells and eliminate the need for daily insulin injections.

Fibrosis is a major obstacle to this approach, because [scar tissue](#) can block the islet cells' access to the oxygen and nutrients. In a 2017 study, Anderson and his colleagues showed that systemic administration of a drug that blocks cell receptors for a protein called CSF-1 can prevent fibrosis by suppressing the immune response to implanted devices. This drug targets immune cells called macrophages, which are the primary cells responsible for initiating the inflammation that leads to fibrosis.

"That work was focused on identifying next-generation drug targets, namely which cell and cytokine players were essential for fibrotic response," says Doloff, who was the lead author on that study, which also involved Farah. He adds, "After knowing what we had to target to block fibrosis, and screening drug candidates needed to do so, we still had to find a sophisticated way of achieving local delivery and release for as long as possible."

In the new study, the researchers set out to find a way to load the drug directly into an implantable device, to avoid giving patients drugs that would suppress their entire immune system.

"If you have a small device implanted in your body, you don't want to have your whole body exposed to drugs that are affecting the [immune system](#), and that's why we've been interested in creating ways to release drugs from the device itself," Anderson says.

To achieve that, the researchers decided to try crystallizing the drugs and then incorporating them into the device. This allows the drug molecules to be very tightly packed, allowing the drug-releasing device to be miniaturized. Another advantage is that crystals take a long time to dissolve, allowing for long-term drug delivery. Not every drug can be easily crystallized, but the researchers found that the CSF-1 receptor inhibitor they were using can form crystals and that they could control the size and shape of the crystals, which determines how long it takes for the drug to break down once in the body.

"We showed that the drugs released very slowly and in a controlled fashion," says Farah. "We took those crystals and put them in different types of devices and showed that with the help of those crystals, we can allow the medical device to be protected for a long time, allowing the device to keep functioning."

### Encapsulated islet cells

To test whether these drug crystalline formulations could boost the effectiveness of encapsulated islet cells, the researchers incorporated the drug crystals into 0.5-millimeter-diameter spheres of alginate, which they used to encapsulate the cells. When these spheres were transplanted into the abdomen or under the skin of diabetic mice, they remained fibrosis-free for more than a year. During

this time, the mice did not need any insulin injections, as the islet cells were able to control their blood sugar levels just as the pancreas normally would.

"In the past three-plus years, our team has published seven papers in *Nature* journals—this being the seventh—elucidating the mechanisms of biocompatibility," says Robert Langer, the David H. Koch Institute Professor at MIT and an author of the paper. "These include an understanding of the key cells and receptors involved, optimal implant geometries and physical locations in the body, and now, in this paper, specific molecules that can confer biocompatibility. Taken together, we hope these papers will open the door to a new generation of biomedical implants to treat diabetes and other diseases."

The researchers believe that it should be possible to create crystals that last longer than those they studied in these experiments, by altering the structure and composition of the drug crystals. Such formulations could also be used to prevent fibrosis of other types of implantable devices. In this study, the researchers showed that crystalline [drug](#) could be incorporated into PDMS, a polymer frequently used for medical devices, and could also be used to coat components of a glucose sensor and an electrical muscle stimulation device, which include materials such as plastic and metal.

"It wasn't just useful for our islet cell therapy, but could also be useful to help get a number of different devices to work long-term," Anderson says. [21]

## **By turning molecular structures into sounds, researchers gain insight into protein structures and create new variations**

Want to create a brand new type of protein that might have useful properties? No problem. Just hum a few bars.

In a surprising marriage of science and art, researchers at MIT have developed a system for converting the molecular structures of proteins, the basic building blocks of all living beings, into audible sound that resembles musical passages. Then, reversing the process, they can introduce some variations into the music and convert it back into new proteins never before seen in nature.

Although it's not quite as simple as humming a new [protein](#) into existence, the new system comes close. It provides a systematic way of translating a protein's [sequence of amino acids](#) into a musical sequence, using the physical properties of the molecules to determine the sounds. Although the sounds are transposed in order to bring them within the audible range for humans, the tones and their relationships are based on the actual vibrational frequencies of each amino acid molecule itself, computed using theories from quantum chemistry.

The system was developed by Markus Buehler, the McAfee Professor of Engineering and head of the Department of Civil and Environmental Engineering at MIT, along with postdoc Chi Hua Yu and two others. As described in the journal *ACS Nano*, the system translates the 20 types of amino acids, the building blocks that join together in chains to form all proteins, into a 20-tone scale. Any protein's long sequence of amino acids then becomes a sequence of notes.



While such a scale sounds unfamiliar to people accustomed to Western musical traditions, listeners can readily recognize the relationships and differences after familiarizing themselves with the sounds. Buehler says that after listening to the resulting melodies, he is now able to distinguish certain amino acid sequences that correspond to proteins with specific structural functions. "That's a beta sheet," he might say, or "that's an alpha helix."

### **Learning the language of proteins**

The whole concept, Buehler explains, is to get a better handle on understanding proteins and their vast array of variations. Proteins make up the structural material of skin, bone, and muscle, but are also enzymes, signaling chemicals, molecular switches, and a host of other functional materials that make up the machinery of all living things. But their structures, including the way they fold themselves into the shapes that often determine their functions, are exceedingly complicated. "They have their own language, and we don't know how it works," he says. "We don't know what makes a silk protein a silk protein or what patterns reflect the functions found in an enzyme. We don't know the code."

By translating that language into a different form that humans are particularly well-attuned to, and that allows different aspects of the information to be encoded in different dimensions—pitch, volume, and duration—Buehler and his team hope to glean new insights into the relationships and differences between different families of proteins and their variations, and use this as a way of exploring the many possible tweaks and modifications of their structure and function. As with music, the structure of proteins is hierarchical, with different levels of structure at different scales of length or time.

The team then used an artificial intelligence system to study the catalog of melodies produced by a wide variety of different proteins. They had the AI system introduce slight changes in the musical sequence or create completely new sequences, and then translated the sounds back into proteins that correspond to the modified or newly designed versions. With this process they were able to create variations of existing proteins—for example of one found in spider silk, one of nature's strongest materials—thus making new proteins unlike any produced by evolution.

Although the researchers themselves may not know the underlying rules, "the AI has learned the language of how proteins are designed," and it can encode it to create variations of existing versions, or completely new protein designs, Buehler says. Given that there are "trillions and trillions" of potential combinations, he says, when it comes to creating new proteins "you wouldn't be able to do it from scratch, but that's what the AI can do."

### **"Composing" new proteins**

By using such a system, he says training the AI system with a set of data for a particular class of proteins might take a few days, but it can then produce a design for a new variant within microseconds. "No other method comes close," he says. "The shortcoming is the model doesn't tell us what's really going on inside. We just know it works."

This way of encoding structure into music does reflect a deeper reality. "When you look at a molecule in a textbook, it's static," Buehler says. "But it's not static at all. It's moving and vibrating. Every bit of matter is a set of vibrations. And we can use this concept as a way of describing matter."

The method does not yet allow for any kind of directed modifications—any changes in properties such as mechanical strength, elasticity, or chemical reactivity will be essentially random. "You still need to do the experiment," he says. When a new protein variant is produced, "there's no way to predict what it will do."

The team also created musical compositions developed from the sounds of amino acids, which define this new 20-tone musical scale. The art pieces they constructed consist entirely of the sounds generated from amino acids. "There are no synthetic or natural instruments used, showing how this new source of sounds can be utilized as a creative platform," Buehler says. Musical motifs derived from both naturally existing proteins and AI-generated proteins are used throughout the examples, and all the sounds, including some that resemble bass or snare drums, are also generated from the sounds of amino acids.

The researchers have created a free Android smartphone app, called [Amino Acid Synthesizer](#), to play the sounds of amino acids and record protein sequences as musical compositions. [20]

### **Applying the Goldilocks principle to DNA structure**

The Goldilocks of fairy-tale fame knew something about porridge. It needed to be just right—neither too hot nor too cold. Same with furniture—neither too hard nor too soft. In a different context, scientists at UC San Diego know something about DNA. They know that the strands of our genetic code, if extended, would measure two meters, or about six feet. They also know that the strands fold into and move within the cell nucleus the size of about a hundredth of a millimeter. But they don't know how and in what state of matter this occurs, so they decided to check.

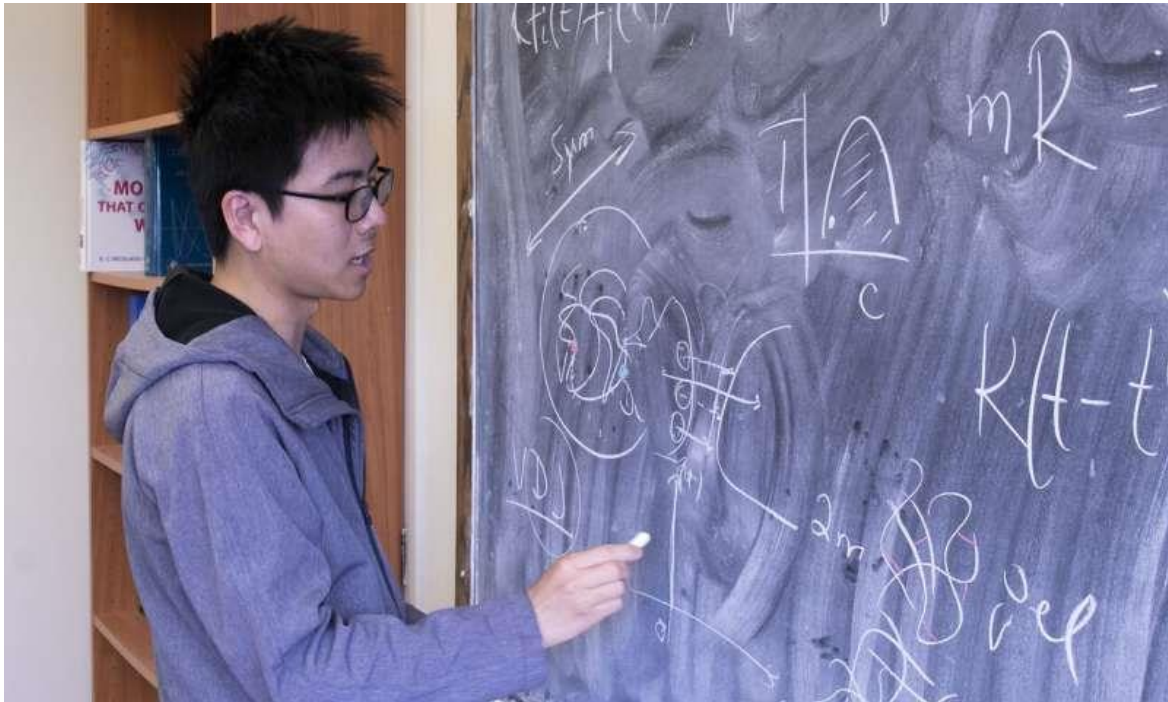
Inspired by ideas from the physics of phase transitions and polymer physics, researchers in the Divisions of Physical and Biological Sciences at UC San Diego set out specifically to determine the organization of DNA inside the nucleus of a living cell. The findings of their study, recently published in *Nature Communications*, suggest that the phase state of the genomic DNA is "just right"—a gel poised at the phase boundary between gel and sol, the solid-liquid phase transition.

Think of pudding, panna cotta—or even porridge. The consistency of these delectables must be just right to be ideally enjoyed. Just as the "sol-gel" phase transition, according to the scientists, seems just right for explaining the timing of genomic interactions that dictate gene expression and somatic recombination.

"This finding points to a general physical principle of chromosomal organization, which has important implications for many key processes in biology, from antibody production to tissue differentiation," said Olga Dudko, a theoretical biophysicist and professor in the Department of Physics at UC San Diego, who collaborated with colleague Cornelis Murre, a distinguished professor in the Section of Molecular Biology, on the study.

Along with Dudko's former graduate student Yaojun Zhang, now a postdoctoral researcher at Princeton, and Murre's postdoctoral scholar Nimish Khanna, the team collected and analyzed data on

DNA motion inside live mammalian B-cells from mice to understand how remote genomic interactions generate a diverse pool of antibodies by the adaptive immune system.



Physics graduate student Bin Wang, who works with Dudko, charts temporal and spatial aspects of the research. Credit: Michelle Fredricks, UC San Diego Physical Sciences

In mammals, such as rodents and humans, immunoglobulin gene segments are arranged in groups of variable (V), diversity (D) and joining (J) segments. These V, D and J segments randomly combine through the process of somatic recombination. This occurs before antigen contact and during B-cell development in the immune system's lymphoid tissue, or bone marrow. These random genetic interactions result in diverse protein codes that match up with antigens which activate lymphocytes.

The scientists examined the various interactions between V and DJ gene segments. While how exactly these interactions occur remains unknown, the UC San Diego researchers developed a strategy to track V and DJ motion in B-lymphocytes. They found that V and DJ segments were trapped in configurations that allowed local motion only—in other words, the segments remained spatially proximal if they were initially close or they remained separate if they were initially spatially distant. The researchers also observed, within a subset of cells, abrupt changes in V and DJ motion, plausibly caused by temporal changes in chromatin.

By comparing experimental and simulated data, the scientists concluded that constrained motion is imposed by a network of cross-linked chromatin chains, or a mesh of bridges between the DNA strands that are characteristic of a gel phase. Yet, the amount of these cross-links is "just right" to poise the DNA near the sol phase—a liquid phase describing a solution of uncross-linked chains.

This pattern suggested to the scientists that a certain organizational principle of genomic DNA exists—proximity to the sol-gel [phase](#) transition—which explains how the genome can simultaneously possess stability and responsiveness within the nucleus.

These results indicate that the packing pattern of DNA within a cell's nucleus has consequences for a cell's fate—whether it becomes a live or diseased cell.

"We have rigorous theories from physics—abstract principles and mathematical equations. We have state-of-the-art experiments on biology—innovative tracking of gene segments in live mammalian cell nuclei," noted Zhang. "It really amazes and excites me when the two aspects merge coherently into one story, where physics is not just a tool to describe the dynamics of gene segments, but helps to pinpoint the physical state of the genome, and further sheds light on the impact of the physical properties of this state on its biological function." [19]

### **Neutrons get a wider angle on DNA and RNA to advance 3-D models**

Scientists from the National Institute of Standards and Technology (NIST) and the University of Maryland are using neutrons at Oak Ridge National Laboratory (ORNL) to capture new information about DNA and RNA molecules and enable more accurate computer simulations of how they interact with everything from proteins to viruses. Resolving the 3-D structures of the body's fundamental genetic materials in solution will play a vital role in drug discovery and development for critical medical treatments.

"A better understanding of both the structure and conformational dynamics of DNA and RNA could help us answer questions about why and how medicines work and help us locate where the key interactions are taking place at the [atomic level](#)," said NIST's Alexander Grishaev, who led neutron scattering research performed at the High Flux Isotope Reactor (HFIR), a Department of Energy User Facility located at ORNL.

The team used HFIR's Bio-SANS instrument to perform small- to wide-angle neutron scattering, a technique not previously performed on DNA and RNA samples in solution because of limited experimental capabilities.

"Capturing a wider range of angles for biomolecules in solution using neutron scattering has not been possible until recently," said Grishaev, "and Oak Ridge is one of the only places you can do this kind of work."

Extending the capabilities of solution neutron scattering is part of an advancing effort toward a more integrative approach in [structural biology](#) that combines crystal studies, solution methods, and other experimental and computational techniques to enhance understanding of DNA and protein structures.

Computer simulations of biomolecules have been well informed by X-ray crystallography. The premier technique uses x-rays to determine the arrangement of atoms in a sample that has been "crystallized" for analysis. To get [high-quality data](#) with this technique, samples of biological materials that are typically dilute in solution are concentrated and solidified into crystals with a uniform structure.

X-ray crystallography works especially well for rigid biomolecules with more or less fixed structures, but flexible biomolecules like DNA and RNA that adopt multiple "conformations" or shapes are less suited to crystallization.

Inside living cells, DNA and RNA can move, change shapes, and respond differently to environmental effects such as pH or temperature, alterations that are important to represent but difficult to characterize.

"Crystallization packs the molecules in tightly, which limits their motions and masks some of the structural information we want to see," said Grishaev.

Several techniques have successfully been applied to DNA and RNA in solution, including solution X-ray scattering and nuclear magnetic resonance (NMR) spectroscopy, both of which yield important data. Yet, significant discrepancies exist between the experimental scattering data and the best available crystal structures of DNA and RNA.

The team turned to neutrons to find out why.

"Neutrons interact with biomolecules differently, so we can use them as an independent source of data for us to either validate or better define the models that we have," said Maryland's Roderico Acevedo.

Whereas x-rays work well to define heavy atoms, such as carbon, oxygen, and phosphorus, neutrons are ideal for examining lighter hydrogen atoms that connect DNA strands, for example. Additionally, neutrons offer an advantage in probing biomolecules because they are nondestructive and do not damage them.

Using the Bio-SANS instrument at HFIR, researchers were able to collect structural information in solution not readily obtainable by other experimental techniques.

The experiment required both a high neutron flux and wide-angle detectors to collect higher precision scattering patterns to reveal the atomic-level structures of DNA and RNA in solution.

Using neutrons to collect structural information on biomolecules is no ordinary feat, says Grishaev. Small biomolecular samples in dilute solutions often produce noisy scattering patterns, making the data difficult to analyze.

"HFIR's Bio-SANS is one of few neutron instruments in the world with the capability to capture small and wide scattering angles simultaneously, combining both global- and local-scale details," said Bio-SANS instrument scientist Volker Urban.

"We were able to get some of the highest-precision solution neutron scattering data ever collected at wide angles, not just on DNA and RNA, but on biomolecules in general," said Grishaev.

By adding the new information collected via solution [neutron scattering](#) to other data from [solution](#) X-ray scattering and NMR spectroscopy, the NIST-Maryland group hopes to get a more comprehensive picture of DNA and RNA structures, as well as to expand avenues for defining molecular structures with [neutron](#)-based techniques. [18]

## Theoretical model may help solve molecular mystery

Spintronics is promising for future low-power electronic devices. Spin is a quantum-mechanical property of electrons that can best be imagined as electrons spinning around their own axes, causing them to behave like small compass needles. A current of electron spins could be used in electronic devices. However, to generate a suitable spin current, you need a relatively large magnet. An alternative method that uses a special type of molecule has been proposed, but the big question is whether it works. University of Groningen Ph.D. student Xu Yang has constructed a theoretical model that describes how to test this new method.

Spin can have two directions, usually designated as "up" and "down." In a normal electron current, there are equal quantities of both spin directions, but using spin to transfer information requires a surplus of one direction. This is usually done by injecting electrons into a spintronic device through a ferromagnet, which will favor the passage of one type of spin. "But ferromagnets are bulky compared to the other components," says Yang.

### DNA

That is why a 2011 breakthrough that was published in *Science* is attracting increased attention. This paper reported that passing a current through a monolayer of DNA double helices would favor one type of spin. The DNA molecules are chiral, which means they can exist in two forms which are mirror images, like a left and right hand. The phenomenon was dubbed "chiral induced spin selectivity" (CISS), and over the last few years, several experiments were published allegedly showing this CISS effect, even in electronic devices.

"But we were not so sure," explains Yang. One type of experiment used a monolayer of DNA fragments, whereas another used an atomic force microscope to measure the current through single molecules. Different chiral helices were used in the experiments. "The models explaining why these molecules would favor one of the spins made lots of assumptions, for example, about the shape of the molecules and the path the electrons took."

### Circuits

So Yang set out to create a generic model to describe how spins would pass through different circuits under a linear regime (i.e. the regime that electronic devices operate in). "These models were based on universal rules, independent of the type of molecule," explains Yang. One such rule is charge conservation, which states that every electron that enters a circuit should eventually exit. A second rule is reciprocity, which states that if you swap the roles of the voltage and current contacts in a circuit, the signal should remain the same.

Next, Yang described how these rules would affect the transmission and reflection of spins in different components, for example, a chiral molecule and a ferromagnet between two contacts. The universal rules enabled him to calculate what happened to the spins in these components. He then used the components to model more complex circuits. This allowed him to calculate what to expect if the chiral molecules showed the CISS effect and what to expect if they did not.



## Convincing

When he modeled the CISS experiments published so far, Yang found that some are, indeed, inconclusive. "These experiments aren't convincing enough. They do not show a difference between molecules with and without CISS, at least not in the linear regime of electronic devices." Furthermore, any device using just two contacts will fail to prove the existence of CISS. The good news is that Yang has designed circuits with four contacts that will allow scientists to detect the CISS effect in electronic devices. "I am currently also working on such a circuit, but as it is made up of molecular building blocks, this is quite a challenge."

By publishing his model now, Yang hopes that more scientists will start building the circuits he has proposed, and will finally be able to prove the existence of CISS in electronic devices. "This would be a great contribution to society, as it may enable a whole new approach to the future of electronics."  
[17]

## Biomimetic chemistry—DNA mimic outwits viral enzyme

Not only can synthetic molecules mimic the structures of their biological models, they can also take on their functions and may even successfully compete with them, as an artificial DNA sequence designed by Ludwig-Maximilians-Universitaet (LMU) in Munich chemist Ivan Huc now shows.

Chemist Ivan Huc finds the inspiration for his work in the molecular principles that underlie biological systems. As the leader of a research group devoted to biomimetic supramolecular chemistry, he creates 'unnatural' molecules with defined, predetermined shapes that closely resemble the major biological polymers, proteins and DNA found in cells. The backbones of these molecules are referred to as 'foldamers' because, like origami patterns, they adopt predictable shapes and can be easily modified. Having moved to LMU from his previous position at Bordeaux University last summer, Huc has synthesized a helical molecule that mimics surface features of the DNA double helix so closely that bona fide DNA-binding proteins interact with it.

This work is described in a paper published in *Nature Chemistry*. The new study shows that the synthetic compound is capable of inhibiting the activities of several DNA-processing enzymes, including the 'integrase' used by the human immunodeficiency virus (HIV) to insert its genome into that of its host cell. The successful demonstration of the efficacy of the synthetic DNA mimic might lead to a new approach to the treatment of AIDS and other retroviral diseases.

The new paper builds on advances described in two previous publications in *Nature Chemistry* published earlier this year. In the first of these papers, Huc and his colleagues developed a pattern of binding interactions required to enable synthetic molecules to assume stable forms similar to the helical backbones of proteins. In the second, they worked out the conditions required to append their synthetic helix to natural proteins during synthesis by cellular ribosomes. "As always in biology, shape determines function," he explains. In the new study, he introduces a synthetic molecule that folds into a helical structure that mimics surface features of the DNA double helix, and whose precise shape can be altered in a modular fashion by the attachment of various substituents. This enables the experimenter to imitate in detail the shape of natural DNA double helix, in particular the position of negative charges. The imitation is so convincing that it acts as a decoy for two DNA-binding enzymes, including the HIV integrase, which readily bind to it and are essentially inactivated.

However, the crucial question is whether or not the foldamer can effectively compete for the enzymes in the presence of their normal DNA substrate. "If the enzymes still bind to the foldamer under competitive conditions, then the mimic must be a better binder than the natural DNA itself," Huc says. And indeed, the study demonstrates that the HIV integrase binds more strongly to the foldamer than to natural DNA. "Furthermore, although initially designed to resemble DNA, the foldamer owes its most useful and valuable properties to the features that differentiate it from DNA," Huc points out.

Thanks to the modular nature of foldamer design, the structures of these artificial DNA mimics can be readily altered, which enables a broad range of variants to be produced using the same basic platform. In the current study, Huc and his colleagues have focused on enzymes that are generically capable of binding to DNA, irrespective of its base sequence. However, it may also be possible to use the foldamer approach to develop DNA mimics that can block the action of the many important DNA-binding proteins whose functions depend on the recognition of specific nucleotide sequences. [16]

## **Simulations document self-assembly of proteins and DNA**

What makes particles self-assemble into complex biological structures? Often, this phenomenon is due to the competition between forces of attraction and repulsion, produced by electric charges in various sections of the particles. In nature, these phenomena often occur in particles that are suspended in a medium—referred to as colloidal particles—such as proteins, DNA and RNA. To facilitate self-assembly, it is possible to "decorate" various sites on the surface of such particles with different charges, called patches.

In a new study published in *EPJE*, physicists have developed an algorithm to simulate the molecular dynamics of these patchy [particles](#). The findings published by Silvano Ferrari and colleagues from the TU Vienna and the Centre for Computational Materials Science (CMS), Austria, will improve our understanding of what makes self-assembly in biological systems possible.

In this study, the authors model charged patchy particles, which are made up of a rigid body with only two charged patches, located at opposite poles. They then develop the equations governing the dynamics of an ensemble of such colloidal patchy particles.

Based on an existing approach originally developed for molecular particles, their simulation includes additional constraints to guarantee that the electrical charge "decorations" are preserved over time. In this regard, they develop equations for describing the particles' motion; the solutions to these equations describe the trajectories of these colloidal particles. Such [molecular dynamics](#) simulations lend themselves to being run in parallel on a huge number of particles.

With these findings, the authors complement the lessons learned from experimental observations of similar particles recently synthesised in the lab. Recent experiments have demonstrated that [colloidal particles](#) decorated at two interaction sites display a remarkable propensity for self-organising into highly unusual structures that remain stable over a broad temperature range. [15]

## Scientists explore the structure of a key region of longevity protein telomerase

Scientists from Moscow State University (MSU) working with an international team of researchers have identified the structure of one of the key regions of telomerase—a so-called "cellular immortality" ribonucleoprotein. Structural and functional studies on this protein are important for the development of potential anticancer drugs. The results of the study have been published in *Nucleic Acids Research*.

Each cell goes through a DNA replication process before division. This is a precise, fine-tuned process controlled by the coordinated work of a sophisticated enzymatic machinery. However, due to the nature of the copying process, the termini of DNA molecules are left uncopied, and DNA becomes shorter with each replication. However, no important data is lost in the process, as the termini of DNA molecules (telomeres) consist of thousands of small, repeated regions that do not carry hereditary information. When the reserve of telomere repetitions is exhausted, the cell ceases to divide, and eventually, it can die. Scientists believe that this is the mechanism of cellular aging, which is necessary for the renewal of cells and tissues of the body.

But how do "immortal" strains and stem cells that give life to a huge number of offspring cope with this? This is where the enzyme [telomerase](#) comes into play. It can restore telomeric termini of chromosomes and therefore compensate for their shortening during mitosis. The telomerase protein catalytic subunit works together with the RNA molecule, and its short fragment is used as a template to synthesize telomeric repetitions. MSU-based scientists discovered the structure of the telomerase fragment that is in charge of this process.

"Our work is aimed at the structural characterization of the telomerase complex. In a living cell, it includes a catalytic subunit, an RNA molecule, a segment of telomeric DNA, and several auxiliary components. Anomalously low activity of telomerase caused by genetics can result in serious pathogenic conditions (telomeropathy), while its anomalous activation is the reason for the cellular "immortality" of most known cancers. Information on the structure of telomerase and the relationships between its components is necessary for understanding the function and regulation of this enzyme, and in the future, for directed control of its activity," said Elena Rodina, assistant professor of the Department for the Chemistry of Natural Products, Faculty of Chemistry, MSU.

Working with thermotolerant yeast, a model eukaryotic organism, the researchers determined the structure of one of the major domains of the telomerase catalytic subunit (the so-called TEN-domain) and determined which parts of it are responsible for the interaction of the enzyme with the RNA molecule and the synthesized DNA. Based on the experimental data obtained, the scientists constructed a theoretical model of the catalytic core of telomerase.

The activity of the enzyme may be described in a simplified way: Telomerase can be represented as a molecular machine containing an RNA molecule. This machine, with the help of a template part of RNA, binds to the end of a long chain of DNA, and synthesizes a fragment of a new DNA chain along

the remaining template fragment. After that, the telomerase machine has to move to the newly synthesized end of the DNA in order to continue to build up the chain. The scientists assume that the TEN-domain allows telomerase to synthesize DNA fragments of strictly defined length, after which the RNA template should be detached from the DNA strand to move closer to its edge. Thus, the TEN domain facilitates the movement of the enzyme to building up a new region, i.e. the next telomeric fragment, and this is how the synthesis cycle is repeated.

In addition, the researchers identified the structural core of the TEN domain that remained unchanged in a variety of organisms, despite all the evolutionary vicissitudes, which indicates the important role of this core in the function of the enzyme. The team also revealed the elements specific for different groups of organisms, which interact with own proteins of individual telomerase complex.

"The data obtained bring us closer to an understanding of the structure, function and regulation of telomerase. In the future, this knowledge can be used to create drugs aimed at regulating telomerase activity—either to increase it (for example, to increase the cell life span in biomaterials for transplantology) or to reduce (for instance, for immortal cancer cells to lose their immortality)," concludes Elena Rodina. [14]

## Custom sequences for polymers using visible light

Researchers from Tokyo Metropolitan University used a light-sensitive iridium-palladium catalyst to make "sequential" polymers, using visible light to change how building blocks are combined into polymer chains. By simply switching the light on or off, they were able to realize different compositions along the polymer chain, allowing precise control over physical properties and material function. This may drastically simplify existing polymer production methods, and help overcome fundamental limits in creating new polymers.

The world is full of long, chain-like molecules known as polymers. Famous examples of "sequential" copolymers, i.e. polymers made of multiple building blocks (or "monomers") arranged in a specific order, include DNA, RNA and proteins; their specific structure imparts the vast range of molecular functionality that underpins biological activity. However, making sequential polymers from scratch is a tricky business. We can design special monomers that assemble in different ways, but the complex syntheses that are required limit their availability, scope and functionality.

To overcome these limits, a team led by Associate Professor Akiko Inagaki from the Department of Chemistry, Tokyo Metropolitan University, applied a light-sensitive catalyst containing iridium and palladium. By switching a light on and off, they were able to control the speed at which two different monomers, styrene and vinyl ether, become part of a polymer chain. When exposed to light, the styrene monomer was found to be incorporated into the copolymer structure much more rapidly than in the dark, resulting in a single copolymer chain with different compositions along its length. Parts that are rich in styrene are more rigid than those rich in vinyl ether; by using different on/off light sequences, they could create polymers with a range of physical properties e.g. different "glass transition" temperatures, above which the polymer becomes softer.

The newly developed process is significantly simpler than existing methods. The team also found that both types of monomer were built into the polymer via a mechanism known as non-radical coordination-insertion; this is a generic mechanism, meaning that this new method might be applied to make polymers using a wide range of catalysts and monomers, with the potential to overcome the limited availability of [monomer](#) candidates. [13]

## **Artificial and biological cells work together as mini chemical factories**

Researchers have fused living and non-living cells for the first time in a way that allows them to work together, paving the way for new applications.

The system, created by a team from Imperial College London, encapsulates biological cells within an [artificial cell](#). Using this, researchers can harness the natural ability of biological cells to process chemicals while protecting them from the environment.

This system could lead to applications such as cellular 'batteries' powered by photosynthesis, synthesis of drugs inside the body, and biological sensors that can withstand harsh conditions.

Previous artificial cell design has involved taking parts of biological cell 'machinery' - such as enzymes that support [chemical](#) reactions - and putting them into artificial casings. The new study, published today in *Scientific Reports*, goes one step further and encapsulates entire cells in artificial casings.

The artificial cells also contain enzymes that work in concert with the biological cell to produce new chemicals. In the proof-of-concept experiment, the artificial cell systems produced a fluorescent chemical that allowed the researchers to confirm all was working as expected.

Lead researcher Professor Oscar Ces, from the Department of Chemistry at Imperial, said: "Biological cells can perform extremely complex functions, but can be difficult to control when trying to harness one aspect. Artificial cells can be programmed more easily but we cannot yet build in much complexity.

"Our new system bridges the gap between these two approaches by fusing whole biological cells with artificial ones, so that the machinery of both works in concert to produce what we need. This is a paradigm shift in thinking about the way we design artificial cells, which will help accelerate research on applications in healthcare and beyond."

To create the system, the team used microfluidics: directing liquids through small channels. Using water and oil, which do not mix, they were able to make droplets of a defined size that contained the biological cells and enzymes. They then applied an artificial coating to the droplets to provide protection, creating an artificial cell environment.

They tested these artificial cells in a solution high in copper, which is usually highly toxic to biological cells. The team were still able to detect fluorescent chemicals in the majority of the artificial cells, meaning the biological cells were still alive and functioning inside. This ability would be useful in the

human body, where the artificial cell casing would protect the foreign biological cells from attack by the body's immune system.

First author of the study Dr Yuval Elani, an EPSRC Research Fellow also from the Department of Chemistry, said: "The system we designed is controllable and customisable. You can create different sizes of artificial cells in a reproducible manner, and there is the potential to add in all kinds of cell machinery, such as chloroplasts for performing photosynthesis or engineered microbes that act as sensors."

To improve the functionality of these artificial cell systems, the next step is to engineer the artificial coating to act more like a biological membrane, but with special functions.

For example, if the membrane could be designed to open and release the chemicals produced within only in response to certain signals, they could be used to deliver drugs to specific areas of the body. This would be useful for example in cancer treatment to release targeted drugs only at the site of a tumour, reducing side effects.

While a system like that may be a way off yet, the team say this is a promising leap in the right direction. The work is the first example of fusing living and non-living components to emerge from Imperial and King's College's new FABRICELL centre for artificial cell science. [12]

## **New interaction mechanism of proteins discovered**

UZH researchers have discovered a previously unknown way in which proteins interact with one another and cells organize themselves. This new mechanism involves two fully unstructured proteins forming an ultra-high-affinity complex due to their opposite net charge. Proteins usually bind one another as a result of perfectly matching shapes in their three-dimensional structures.

Proteins are among the most important biomolecules and are the key mediators of molecular communication between and within cells. For two proteins to bind, specific regions of their three-dimensional structures have to match one another exactly, as a key fits into a lock. The structure of proteins is extremely important for their functioning and for triggering the required responses in cells. Now, researchers at the University of Zurich, together with colleagues from Denmark and the U.S., have discovered that unstructured proteins can also have ultra-high-affinity interactions.

One of these proteins is histone H1, which, as a component of chromatin, is responsible for DNA packaging. Its binding partner, prothymosin  $\alpha$ , acts as a kind of shuttle that deposits and removes the histone from the DNA. This process determines whether or not genes in specific parts of the DNA can be read. Both proteins are involved in several regulatory processes in the body, such as cell division and proliferation, and therefore also play a role when it comes to a number of diseases, including cancer. Ben Schuler, professor at the Department of Biochemistry at UZH and head of the research project published in *Nature*, says, "The interesting thing about these proteins is that they're completely unstructured—like boiled noodles in water." How such disordered proteins should be able to interact according to the key/lock principle had puzzled the team of researchers.



Notably, the two proteins bind to one another much more strongly than the average [protein](#) partners. The research team used single-molecule fluorescence and [nuclear magnetic resonance](#) spectroscopy to determine the arrangement of the proteins. Observed in isolation, they show extended unstructured protein chains. The chains become more compact as soon as both binding partners come together and form a complex. The strong interaction is caused by the strong electrostatic attraction, since histone H1 is highly positively charged while prothymosin  $\alpha$  is highly negatively charged. Even more surprising was the discovery that the [protein complex](#) was also fully unstructured, as several analyses confirmed.

To investigate the shape of the protein complex, the researchers labeled both proteins with fluorescent probes, which they then added to selected sites on the proteins. Together with computer simulations, this molecular map yielded the following results: Histone 1 interacts with prothymosin  $\alpha$  preferably in its central region, which is the region with the highest charge density. Moreover, it emerged that the complex is highly dynamic: The proteins' position in the complex changes extremely quickly—in a matter of approx. 100 nanoseconds.

The interaction behavior is likely to be fairly common. Cells have many proteins that contain highly charged sequences and may be able to form such protein complexes. There are hundreds of such proteins in the human body alone. "It's likely that the interaction between disordered, highly charged proteins is a basic mechanism for how [cells](#) function and organize themselves," concludes Ben Schuler. According to the biophysicist, textbooks will need revision to account for this new way of binding. The discovery is also relevant for developing new therapies, since unstructured proteins are largely unresponsive to traditional drugs, which bind to specific structures on the protein surface. [11]

## Particles in charged solution form clusters that reproduce

Dr Martin Sweatman from the University of Edinburgh's School of Engineering has discovered a simple physical principle that might explain how life started on Earth.

He has shown that particles that become charged in solution, like many biological [molecules](#), can form giant clusters that can reproduce. Reproduction is shown to be driven by simple physics—a balance of forces between short-range attraction and long-range repulsion. Once cluster [reproduction](#) begins, he suggests chemical evolution of clusters could follow, leading eventually to life.

Many [biological molecules](#), like DNA and proteins, might show this behaviour. Even the building blocks of life, amino acids and nucleobases, might show this behaviour. Reproduction in modern cells might even be driven by this simple physical mechanism, i.e. chemistry is not so important.

Dr Sweatman's research uses theoretical methods and computer simulations of simple particles. They clearly show giant clusters of molecules with the right balance of forces can reproduce. No chemistry is involved. However, these theoretical predictions have yet to be confirmed by experiment.

Dr Sweatman said, "Although it will be difficult to see this behaviour for solutions of small biomolecules, it should be possible to confirm this behaviour experimentally with much larger particles that can be seen under a microscope, like charged colloids.

"If this behaviour is confirmed, then we take another step towards Darwin's idea of life beginning in a warm little pond. A simple evaporation and condensation cycle in a pond might be sufficient to drive cluster reproduction initially. Survival of the fittest clusters of chemicals might then eventually lead to life."

The research has been published in the international journal *Molecular Physics*.

## **Experiment demonstrates quantum mechanical effects from biological systems**

Nearly 75 years ago, Nobel Prize-winning physicist Erwin Schrödinger wondered if the mysterious world of quantum mechanics played a role in biology. A recent finding by Northwestern University's Prem Kumar adds further evidence that the answer might be yes.

Kumar and his team have, for the first time, created quantum entanglement from a biological system. This finding could advance scientists' fundamental understanding of biology and potentially open doors to exploit biological tools to enable new functions by harnessing quantum mechanics.

"Can we apply quantum tools to learn about biology?" said Kumar, professor of electrical engineering and computer science in Northwestern's McCormick School of Engineering and of physics and astronomy in the Weinberg College of Arts and Sciences. "People have asked this question for many, many years—dating back to the dawn of quantum mechanics. The reason we are interested in these new quantum states is because they allow applications that are otherwise impossible."

Partially supported by the Defense Advanced Research Projects Agency, the research was published Dec. 5 in *Nature Communications*.

Quantum entanglement is one of quantum mechanics' most mystifying phenomena. When two particles—such as atoms, photons, or electrons—are entangled, they experience an inexplicable link that is maintained even if the particles are on opposite sides of the universe. While entangled, the particles' behavior is tied one another. If one particle is found spinning in one direction, for example, then the other particle instantaneously changes its spin in a corresponding manner dictated by the entanglement. Researchers, including Kumar, have been interested in harnessing quantum entanglement for several applications, including quantum communications. Because the particles can communicate without wires or cables, they could be used to send secure messages or help build an extremely fast "quantum Internet."

"Researchers have been trying to entangle a larger and larger set of atoms or photons to develop substrates on which to design and build a quantum machine," Kumar said. "My laboratory is asking if we can build these machines on a biological substrate."

In the study, Kumar's team used green fluorescent proteins, which are responsible for bioluminescence and commonly used in biomedical research. The team attempted to entangle the photons generated from the fluorescing molecules within the algae's barrel-shaped protein structure by exposing them to spontaneous four-wave mixing, a process in which multiple wavelengths interact with one another to produce new wavelengths.

Through a series of these experiments, Kumar and his team successfully demonstrated a type of entanglement, called polarization entanglement, between photon pairs. The same feature used to make glasses for viewing 3D movies, polarization is the orientation of oscillations in light waves. A wave can oscillate vertically, horizontally, or at different angles. In Kumar's entangled pairs, the photons' polarizations are entangled, meaning that the oscillation directions of light waves are linked. Kumar also noticed that the barrel-shaped structure surrounding the fluorescing molecules protected the entanglement from being disrupted.

"When I measured the vertical polarization of one particle, we knew it would be the same in the other," he said. "If we measured the horizontal polarization of one particle, we could predict the horizontal polarization in the other particle. We created an entangled state that correlated in all possibilities simultaneously."

Now that they have demonstrated that it's possible to create quantum entanglement from biological particles, next Kumar and his team plan to make a biological substrate of entangled particles, which could be used to build a quantum machine. Then, they will seek to understand if a biological substrate works more efficiently than a synthetic one. [9]

## **Quantum biology: Algae evolved to switch quantum coherence on and off**

A UNSW Australia-led team of researchers has discovered how algae that survive in very low levels of light are able to switch on and off a weird quantum phenomenon that occurs during photosynthesis.

The function in the algae of this quantum effect, known as coherence, remains a mystery, but it is thought it could help them harvest energy from the sun much more efficiently. Working out its role in a living organism could lead to technological advances, such as better organic solar cells and quantum-based electronic devices.

The research is published in the journal Proceedings of the National Academy of Sciences.

It is part of an emerging field called quantum biology, in which evidence is growing that quantum phenomena are operating in nature, not just the laboratory, and may even account for how birds can navigate using the earth's magnetic field.

"We studied tiny single-celled algae called cryptophytes that thrive in the bottom of pools of water, or under thick ice, where very little light reaches them," says senior author, Professor Paul Curmi, of the UNSW School of Physics.

"Most cryptophytes have a light-harvesting system where quantum coherence is present. But we have found a class of cryptophytes where it is switched off because of a genetic mutation that alters the shape of a light-harvesting protein.

"This is a very exciting find. It means we will be able to uncover the role of quantum coherence in photosynthesis by comparing organisms with the two different types of proteins."

In the weird world of quantum physics, a system that is coherent – with all quantum waves in step with each other – can exist in many different states simultaneously, an effect known as superposition. This phenomenon is usually only observed under tightly controlled laboratory conditions.

So the team, which includes Professor Gregory Scholes from the University of Toronto in Canada, was surprised to discover in 2010 that the transfer of energy between molecules in the light harvesting systems from two different cryptophyte species was coherent.

The same effect has been found in green sulphur bacteria that also survive in very low light levels.

"The assumption is that this could increase the efficiency of photosynthesis, allowing the algae and bacteria to exist on almost no light," says Professor Curmi.

"Once a light-harvesting protein has captured sunlight, it needs to get that trapped energy to the reaction centre in the cell as quickly as possible, where the energy is converted into chemical energy for the organism.

"It was assumed the energy gets to the reaction centre in a random fashion, like a drunk staggering home. But quantum coherence would allow the energy to test every possible pathway simultaneously before travelling via the quickest route."

In the new study, the team used x-ray crystallography to work out the crystal structure of the light-harvesting complexes from three different species of cryptophytes.

They found that in two species a genetic mutation has led to the insertion of an extra amino acid that changes the structure of the protein complex, disrupting coherence.

"This shows cryptophytes have evolved an elegant but powerful genetic switch to control coherence and change the mechanisms used for light harvesting," says Professor Curmi.

The next step will be to compare the biology of different cryptophytes, such as whether they inhabit different environmental niches, to work out whether the quantum coherence effect is assisting their survival. [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 squaraine molecule of the first protocell situated in the bottom of this bicellular 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 squaraine and (1,4bis(N,Ndimethylamino)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 electrodynamic 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 unfold 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]

## 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  $1/2$  spin creator particle to make equal the spins of the weak interaction, for example neutron decay to 2 fermions, every particle is fermions with  $1/2$  spin. The weak interaction changes the entropy since more or less particles will give more or less freedom of movement. The entropy change is a result of temperature change and breaks the equality of oscillator diffraction

intensity of the Maxwell–Boltzmann statistics. This way it changes the time coordinate measure and makes possible a different time dilation as of the special relativity.

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

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

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

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

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

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

## The General Weak Interaction

The Weak Interactions T-asymmetry is in conjunction with the T-asymmetry of the Second Law of Thermodynamics, meaning that locally lowering entropy (on extremely high temperature) causes for example the Hydrogen fusion. The arrow of time by the Second Law of Thermodynamics shows the increasing entropy and decreasing information by the Weak Interaction, changing the temperature dependent diffraction patterns. A good example of this is the neutron decay, creating more particles with less known information about them.

The neutrino oscillation of the Weak Interaction shows that it is a general electric dipole change and it is possible to any other temperature dependent entropy and information changing diffraction pattern of atoms, molecules and even complicated biological living structures. We can generalize the weak interaction on all of the decaying matter constructions, even on the biological too. This gives the limited lifetime for the biological constructions also by the arrow of

time. There should be a new research space of the Quantum Information Science the 'general neutrino oscillation' for the greater than subatomic matter structures as an electric dipole change.

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

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

## Fermions and Bosons

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

## Van Der Waals force

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

## Electromagnetic inertia and mass

### Electromagnetic Induction

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

### Relativistic change of mass

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

### The frequency dependence of mass

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

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

## **Gravity from the point of view of quantum physics**

### **The Gravitational force**

The gravitational attractive force is basically a magnetic force.

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

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

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

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

The Big Bang caused acceleration created radial currents of the matter, and since the matter is composed of negative and positive charges, these currents are creating magnetic field and attracting forces between the parallel moving electric currents. This is the gravitational force experienced by the matter, and also the mass is result of the electromagnetic forces between the charged particles. The positive and negative charged currents attracts each other or by the magnetic forces or by the much stronger electrostatic forces!?

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

There is an asymmetry between the mass of the electric charges, for example proton and electron, can be 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

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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