Gene Regulates Sleep

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"Our goal is to ultimately be able to analyse all of a cell's signals," says János Vörös, Head of the Laboratory of Biosensors and Bioelectronics and last author of the publication. Nonetheless, the method can already be used to localise transport proteins in a living cell. [26]

The team created nanostructures—in the shapes of triangles and squares—using stable proteinbuilding blocks. [25]

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Researchers from Harvard University and the Broad Institute's Stanley Centre for Psychiatric Research have developed reproducible brain organoids for the first time. [23]

Researchers at the University of Twente have designed a tiny needle in which micro-channels can be used for extracting small liquid samples from a local area of the brain. [22]

The ability to grow large protein crystals is the single biggest bottleneck that limits the use of neutron protein crystallography in structural biology. [21]

The conclusion that proteins have a terrible conductance tallies well with their general physical characteristics – they lack both electronic conduction bands and high levels of structural order. [20]

In their proof-of-concept study, the protein nanowires formed an electrically conductive network when introduced into the polymer polyvinyl alcohol. [19]

Nanocages are highly interesting molecular constructs, from the point of view of both fundamental science and possible applications. [18]

DNA flows inside a cell's nucleus in a choreographed line dance, new simulations reveal. [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.

Contents

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.

Finding a gene that regulates sleep

What keeps us awake—and helps us fall asleep? The answer is complex, but involves what are called circadian rhythms, which are found in all species with sleep-wake cycles—physical, mental, and behavioral changes that follow a regular schedule.

In most animals, that cycle is twenty-four hours, and is dependent on environmental signals like light. It is regulated by a "master clock" in animals brains, comprised of a group of neurons regulating sleep and other circadian processes. Sleep is also, of course, regulated by so-called "sleep pressure," which comes into play when humans or other animals are deprived of sleep.

Rob Jackson, a professor of neuroscience at the School of Medicine, leads a lab that has been studying circadian rhythms and their genetic basis for more than thirty years. He uses fruit flies—Drosophila melanogaster is the scientific name—to study the phenomenon, since they have twenty-four-hour circadian clocks and sleep cycles similar to those of humans. "Remarkably, many of the genes underlying their rhythmic behaviors have human counterparts," he said.

Jackson's lab was the first to identify a critical role of astrocytes as important regulators of circadian rhythms. Astrocytes are glial cells of the brain that had long been thought of as support cells—brain glue, hence the name glia—but are now known to play much more important roles. Jackson and his colleagues also discovered that fly astrocytes secrete signaling factors to communicate with neurons, regulating sleep behavior.

Today the researchers report in a study published in *Current Biology* that a gene they named Noktochor (NKT) is expressed at high levels in fly astrocytes and is required for normal sleep patterns. Noktochor, which means "nocturnal" in Bengali, is not required during fly development, but is necessary in the adult brain for maintenance of healthy sleep, "suggesting a physiological function in adult flies," said Jackson.

Fruit flies that lack NKT gene expression have decreased night sleep, while their sleep during the day is normal—and yes, flies take afternoon naps. The NKT gene is expressed at high levels in fly astrocytes and at low levels in their neurons, and is required in both cell types for normal night sleep.

In addition to Jackson, the research team included Sukanya Sengupta, Lauren B. Crowe, Samantha You, and Mary A. Roberts from Tufts University School of Medicine.

Tufts Now spoke recently to Jackson about the findings, and what they might mean for people suffering from sleep issues.

Tufts Now: So, how do flies sleep exactly?

Rob Jackson: Flies sleep in bouts like us, but the sleep bouts are shorter in duration, on average about two to five hours long. Interestingly, there is also a sex difference for fly sleep, with males sleeping at night, but also taking a "siesta" during the day, while females predominantly sleep at night. In the flies generated in our lab to have little or no NKT expression, the bouts of sleep are abnormally short in duration and occur more frequently, leading to reduced consolidation—fragmented and disrupted sleep.

Why are flies a good model to study sleep?

Fly sleep has properties similar to human sleep. For example, the cell types—neurons and astrocytes—and brain neural circuits that regulate sleep are similar in humans and Drosophila. Furthermore, flies sleep more when deprived of sleep, and they do not respond to external stimuli as readily when sleeping, such as when they have increased "arousal" threshold, similar to humans.

The NKT gene is necessary in the adult brain for maintenance of healthy sleep, “suggesting a physiological function in adult flies,” said Jackson. Credit: André Karwath/Creative Commons

In addition, drug targets affecting sleep are similar in flies and humans. Finally, flies have a small, manageable genome that has been sequenced and can easily be manipulated, and the majority of fly genes have human counterparts, making them a great choice for studies of human disease.

What techniques do you and your lab use to study circadian rhythms in flies?

My lab uses genome-wide expression profiling, which is a fancy way to say we can identify all the genes expressed in a particular cell type. Using genetic techniques, we then ask which genes are important for circadian rhythms or sleep. We use automated activity-monitoring systems to trace fly circadian locomotor activity rhythms and sleep. We also use a sophisticated imaging technique—confocal microscopy—to visualize specific cell types or proteins in the brain that might be required for rhythmic behaviors. These tools allow us to better understand the role of specific genes in sleep behavior or circadian rhythms.

What is the mechanism for NKT to affect sleep?

That's a good question, and at present we don't know the full answer. We do know that NKT protein is secreted from cells to promote sleep, and we hypothesize that it acts as a communication mechanism for activation of sleep-regulating neurons. Unpublished results from our lab have identified a potential receptor for NKT on neurons and suggested that NKT may regulate mechanisms required for inhibition of specific neurons. Such an inhibition of neuronal activity is what promotes sleep.

Why doesn't the absence of NKT affect daytime sleep? Is there another set of genes dedicated to daytime sleep?

Yes, there are other fly genes that seem to be important for day sleep but not night sleep, and this suggests that there are separate mechanisms controlling the two types of sleep.

What happens when circadian rhythms or sleep are disturbed?

Disrupted circadian rhythms or sleep can lead to serious health consequences, including obesity, risk of cardiovascular events, and cognitive impairments such as mood disorders. Indeed, sleep is vital for life in most organisms, including flies and humans. Anyone who has experienced jet lag or had a bad night's sleep understands the importance of circadian and sleep mechanisms.

How do your NKT findings translate to human health?

Although there is not a human NKT gene, similar astrocyte-neuron communication mechanisms exist in flies and humans, and human astrocytes are known to regulate sleep and circadian behavior. Thus, our work has pretty direct implications for understanding mechanisms of astrocyte-to-neuron communication that are important for these rhythmic behaviors, and the health consequences of altering them.

What are your next steps studying NKT and circadian rhythms?

We know that NKT protein is secreted from astrocytes to promote sleep, and we would like to know what neurons it activates. Since the complement of sleep-regulating neurons has been identified in flies, and they are similar to their human counterparts, we know where to look in the brain, and we will employ genetic and imaging methods to ask which neurons are activated by NKT secretion from astrocytes. [29]

New protein found in strongest spider web material

A team of researchers affiliated with several institutions in the U.S. and Slovenia has found a previously unknown protein in the strongest known spider web material. In their paper published in the journal *Communications Biology*, the group describes their study of Darwin's bark spider silk and the glands that produce it.

Humans have been impressed by the silk made from spiders for thousands of years—so much so that a lot of effort has been put into harvesting it from spiders for use in making clothing—and in reproducing it in a lab to create new strong materials. In this new effort, the researchers focused their efforts on Darwin's bark spiders, their silk-producing glands and the silk that is produced.

Darwin's bark spiders are a type of orb spider, which means they make their spider webs in the shape of a spoked wheel. They make the largest known orb webs of any spider, which they spin above the surfaces of streams. Prior research has shown that the spider actually makes seven different kinds of silk for use in different parts of its web. One of those silk types, called dragline, is used to build the spokes that give the wheel its strength. Prior research has shown it to be the strongest spider silk in existence. In this new effort, the researchers took a closer look at the dragline silk and the gland that produces it.

The researchers found two familiar types of spindroins—types of repetitive proteins—called MaSp1 and MaSp2, which are found in many spider silks. But in the dragline from Darwin's bark spiders, they found another spindroin, which they named MaSp4a. Study of this proteinrevealed that contained high quanitities of an amino acid called proline, which prior research has shown is generally associated with elasticity. The protein also had less of some of the other components found in MaSp1 and MaSp2, which made it quite unique.

The researchers also found that the gland that produces the silk—the ampullae—is longer than in other spiders, perhaps providing another clue to the strength of the silk that is produced. [28]

Like film editors and archaeologists, biochemists piece together genome history

Old-school Hollywood editors cut unwanted frames of film and patched in desired frames to make a movie. The human body does something similar—trillions of times per second—through a biochemical editing process called RNA splicing. Rather than cutting film, it edits the messenger RNA that is the blueprint for producing the many proteins found in cells.

In their exploration of the evolutionary origins and history of RNA splicing and the human genome, UC San Diego biochemists Navtej Toor and Daniel Haack combined two-dimensional (2-D) images of individual molecules to reconstruct a three-dimensional (3-D) picture of a portion of RNA—what the scientists call group II introns. In so doing, they discovered a large-scale molecular movement

associated with RNA catalysis that provides evidence for the origin of RNA splicing and its role in the diversity of life on Earth. Their breakthrough research is outlined in the current edition of *Cell*.

"We are trying to understand how the human genome has evolved starting from primitive ancestors. Every human gene has unwanted frames that are non-coding and must be removed before gene expression. This is the process of RNA splicing," stated Toor, an associate professor in the Department of Chemistry and Biochemistry, adding that 15 percent of human diseases are the result of defects in this process.

Toor explained that his team works to understand the evolutionary origins of 70 percent of human DNA—a portion made up of two types of genetic elements, which are both thought to have evolved from group II introns. Specifically, spliceosomal introns, which make up about 25 percent of the human genome, are non-coding sequences that must be removed before gene expression. The other 45 percent is comprised of sequences derived from what are called retroelements. These are genetic elements that insert themselves into DNA and hop around the genome to replicate themselves via an RNA intermediate.

"Studying group II introns gives us insight into the evolution of a large portion of the human genome," noted Toor.

Working with the group II intron RNA nanomachine, Toor and Haack, a postdoctoral scholar at UC San Diego and first author of the paper, were able to isolate the group II intron complexes from a species of blue-green algae that lives at high temperature.

"Using a group II intron from a high-temperature organism facilitated structure determination due to the innate stability of the complex from this species," said Haack. "The evolution of this type of RNA splicing likely led to the diversification of life on Earth."

Haack further explained that he and Toor discovered that the group II intron and the spliceosome share a common dynamic mechanism of moving their catalytic components during RNA splicing.

"This is the strongest evidence to date that the spliceosome evolved from a bacterial group II intron," he said.

Additionally, the findings reveal how group II introns are able to insert themselves into DNA through a process called retrotransposition. This copy-and-paste process has resulted in selfish retroelements proliferating in human DNA to comprise a large portion of the genome.

"Replication of these retroelements has played a large role in shaping the architecture of the modern human genome and has even been implicated in the speciation of primates," noted Toor.

The researchers used cryo-electron microscopy (cryo-EM) to extract a molecular structure of the group II intron. They froze the RNA in a layer of thin ice and then shot electrons through this sample. According to the scientists, the electron microscope can magnify the image 39,000 times. The resulting 2-D images of individual molecules were then put together to come up with a 3-D view of the group II intron.

"This is like molecular archaeology," described Haack. "Group II introns are living fossils that give us a glimpse into how complex life first evolved on Earth." [27]

Listening to the whispers of individual cells

For the cells in our bodies to function as a unit, they must communicate with one another constantly. They secrete signalling molecules—ions, proteins and nucleic acids—that are picked up by adjacent cells, which in turn pass on the signal to other cells. Our muscles, digestive system and brain are only able to function thanks to this type of communication. And this is the only way in which our immune system can recognise pathogens or infected cells and react accordingly—again, by sending out signals to mobilise the immune defences. If something goes wrong with this signalling between cells, it can lead to diseases such as cancer or autoimmune disorders. "This is why it is important to research which signals the cells send out in which situations," says Morteza Aramesh. The biophysicist, who works in the Laboratory of Biosensors and Bioelectronics at ETH Zurich, has developed a new method that does precisely that: it listens to communication between individual cells.

An innovative nanosensor

Although it has been possible to measure these signals in the past, it could only be done for entire populations of hundreds or thousands of cells. The methods were not sensitive enough to use on individual cells, meaning that the signalling molecules from individual cells were submerged into the average of the total cell population: "It was impossible to detect differences between cells in order to identify diseased cells, for instance," says Aramesh.

The new method, which was recently published in the scientific journal *Nature Nanotechnology*, is different. Aramesh and his colleagues used what is known as a fluid force microscope, equipped with a special cantilever tip. A cantilever is a small lever arm with a fine tip that can be used with this type of microscope to scan surfaces—such as that of a cell. What is new is that a tiny sensor is placed on the tip of the cantilever. It consists of a silicon nitride pore just a few nanometres in size, which registers when a cell releases molecules.

How it works: transport proteins located in the cell membrane control how a cell releases the signalling molecules. The new nanopore sensor has such a small diameter that it can be positioned precisely over one of these transport proteins and thus intercept the molecules flowing through it. The nanopore sensor is able to measure the ionic current, which changes when ions or larger biomolecules, such as proteins or nucleic acids, flow through the pore. Different signalling molecules can then be identified depending on the nature and duration of the change in ionic current.

A close look at individual cells

The researchers have tested their method, which they call scanning nanopore microscopy, on live nerve cells from rat brain tissue. So far, they have been able to distinguish between individual signalling molecules, such as ions and certain proteins. The biophysicists now plan to develop their nanosensor further in order to identify other signalling molecules in the future. "Our goal is to ultimately be able to analyse all of a cell's signals," says János Vörös, Head of the Laboratory of

Biosensors and Bioelectronics and last author of the publication. Nonetheless, the method can already be used to localise transport proteins in a living cell.

Moreover, the newly-developed sensor has allowed the researchers to look inside cells as well, since the tip of the nanosensor is so delicate that it can puncture the cell membrane without permanent damage. Inside the cell, it is then possible to analyse what is eliminated from the cell nucleus. "RNA fragments are of particular interest here," says Vörös. They provide insight into which proteins a cell is currently producing—a key factor in the onset of many diseases.

"Our method offers biologists completely new ways of investigating the behaviour of individual cells," adds Vörös. It can not only differentiate between diseased and healthy cells, but can also be used in the development of stem cells or to determine whether cells in the lab behave in the same way as in the body. The new method is likely to help answer many other questions in the future. [26]

Engineers find new way to create single-chain protein nanostructures

The ancient art of paper folding known as origami is used to make intricate birds or other shapes. Inspired by the work of DNA origami, in which nanostructures are made from folding DNA, a team of engineers at the McKelvey School of Engineering at Washington University in St. Louis has found a new way to create single-chain protein nanostructures by using synthetic biology and protein-assembly techniques.

The team created nanostructures—in the shapes of triangles and squares—using stable protein building blocks. These protein nanostructures can endure high temperatures and harsh chemical conditions, both of which are not possible with DNA-based nanostructures. In the future, these protein nanostructures could be used to improve sensing capabilities, speeding chemical reactions, in drug delivery and other applications.

When trying to create protein nanostructures suited for particular applications, researchers typically make modifications to existing protein structures, such as virus particles. However, the shapes of nanostructures that can be made using this approach are limited to what nature provides. Now, Fuzhong Zhang, associate professor of energy, environmental & chemical engineering, and members of his lab have developed a bottom-up approach to build 2-D nanostructures, essentially starting from scratch.

"Building something that nature has not offered is more exciting," Zhang said. "We took individually folded proteins and used them as building blocks, then assembled them together piece by piece so that we can create tailored nanostructures."

The results of the work were published in *Nature Communications* July 25.

Using synthetic biology approaches, Zhang's team first biosynthesized rod-shaped protein building blocks, similar in shape to a pencil but only 12 nanometers long.

Then, they connected these building blocks together through reactive protein domains that were genetically fused to the ends of each of the rods, forming triangles with three rods and squares with four rods. These reactive protein domains are known as split inteins, which are not new to Zhang's lab—they are the same tools that his group uses to make high-strength synthetic spider silk and synthetic replicas of the adhesive mussel foot proteins.

In both cases, these split intein groups enable the production of large proteins that make the synthetic spider silk tougher and stronger and the mussel foot proteins stickier. In this case, they enable the construction of novel nanostructures.

Zhang's team worked with Rohit Pappu, the Edwin H. Murty Professor of Engineering, professor of biomedical engineering and an expert in the biophysics of intrinsically disordered proteins, phase transitions and protein folding. Both Zhang and Pappu are members of the university's Center for Science & Engineering of Living Systems (CSELS).

"Professor Pappu's lab, specifically former postdoctoral fellow Jeong-Mo Choi, helped us understand how the protein sequence at the connections determines the flexibility of these nanostructures and helped us to predict protein sequences to better control the flexibility and geometry of nanostructures," Zhang said. "The collaboration between my synthetic biology lab and Professor Pappu's biophysical modeling lab has proven very productive."

The collaboration simplified a very complex process.

"Once we understood the design strategy, the work is fairly straightforward and quite fun to do," Zhang said. "We just controlled the different functional groups, then they controlled the shapes."

Due to the versatile functionality of proteins, these nanostructures potentially could be used as scaffolds to assemble various nanomaterials. To test this idea, the team assembled 1-nanometer gold nanoparticles precisely at the vertices of the triangle. Using a state-of-the-art electron microscope in the university's Institute of Materials Science & Engineering, both the protein triangles and the gold nanoparticles assembled to the vertices of the triangles were visible.

To test the stability of these protein nanostructures, the team exposed them to high temperatures, up to 98 degrees Celsius, to chemicals such as guanidium hydrochloride, and to organic solvents such as acetone. While these conditions generally destroy protein structures, the structures from Zhang's lab stayed intact. This ultra-stability could enable more nanoscale applications that are difficult or not possible using nanostructures made from DNA or other proteins, Zhang said.

Next, the team is working with Srikanth Singamaneni, professor of mechanical engineering & materials science and a member of CSELS, to use these protein nanostructures to develop improved plasmonic sensors.

"Exploiting the interplay between highly stable structural building blocks and intrinsically disordered or flexible regions provides a novel route to designing nanostructures with customizable features for a variety of applications in synthetic biology and biomedical sciences," Pappu said. "This is one of the major thrusts of our center as reflected by the synergies among three different labs that are part of the center." [25]

New experimental insights allow researchers to probe protein-DNA interactions with greater precision

A single-molecule imaging technique, called protein-induced fluorescence enhancement (PIFE), has gained traction in recent years as a popular tool for observing DNA–protein interactions with nanometer precision. Yet, according to a new KAUST study, research laboratories have not been using the technique to its fullest potential.

The PIFE assay is predicated on the idea that DNA tagged with a fluorescent dye will glow brighter when proteins are bound in the vicinity. In many instances, this is true—which has led many scientists to adopt PIFE over other more labor-intensive techniques that rely on dual labeling of proteins and DNA.

But Samir Hamdan's graduate students Fahad Rashid, Manal Zaher and Vlad-Stefan Raducanu realized that protein binding to DNA-dye complexes could sometimes have the opposite effect as well. Instead of enhancing the fluorescent signal, protein interactions can sometimes dampen the glow, depending on certain properties of the system.

Hamdan credits the curiosity of his students for making this observation and detailing how it works. Inspiration from Rashid's previous work led the team to the phenomenon they call protein-induced fluorescence quenching (PIFQ). And as Rashid explains, "We set out to better define the conditions that lead to fluorescent booms or busts."

Through a combination of experimental and computational analyses, the KAUST team showed that the initial fluorescence state of the DNA-dye complex determines whether PIFE or PIFQ will result after protein binding. Without this knowledge, the likelihood of either event becomes equivalent to a coin toss, which can jeopardize the mechanistic interpretation of laboratory results.

"When insight into this initial state is gleaned from fluorescence and structural work, the anticipation of either effect becomes experimentally feasible," Raducanu explains.

Factors such as DNA sequence and dye position could tip the balance toward PIFE or PIFQ; the KAUST team got so good at interpreting the molecular code that they could accurately predict which would happen simply by measuring how these parameters influence the initial fluorescence state of the DNA-dye system.

"We turned every measurement into a game," Zaher says, "and we are happy to say that our hypothesis predicted the outcome more than 90 percent of the time!"

These novel insights should dramatically expand the reach and experimental promise of this powerful single-molecule imaging tool, predicts Raducanu. "By introducing PIFQ, we offer researchers in the field the possibility to address several biological questions where PIFE might not have been witnessed," he says.

Scientists may also opt to combine PIFE and PIFQ to decipher multistep and multiprotein processes with just a single DNA-dye construct.

"Taking into consideration the context-dependent nature of fluorescence modulation in the DNA-dye system opens the door to many possibilities in experimental design that could be tailored to researchers' needs," Zaher says.

"We now anticipate that interpretation of data and attribution of molecular events from single-molecule data will become easier and more precise," Rashid adds. [24]

Improvements in brain organoids open new doors in neurological research

Researchers from Harvard University and the Broad Institute's Stanley Centre for Psychiatric Research have developed reproducible brain organoids for the first time. This could potentially lead to advances in developing treatments for neurological diseases.

Modelling neurological disease is a complex task, and researchers lack appropriate models to achieve this. The goal is not to grow a synthetic brain, but to produce a simple representative model with which to understand it. In recent years, brain organoids have gained popularity as ways to model neural cells. These organoids are 3D self-assembled cultures of stem cells that are directed to develop into neurological cells. However, getting these cells to grow in the right way and in the correct order every time has so far eluded researchers.

The team has now developed a method that allows researchers to grow organoids that develop in a similar way each time (*Nature 10.1038/s41586-019-1289-x*). Additionally, under specific conditions, they managed to develop the organoids for long enough to produce the broad spectrum of cell types seen in a developing brain. This feature is crucial for developing these organoids as viable experimental tools for research.

Members of the team behind the new method (from left): Joshua Levin, Xian Adiconis, Paola Arlotta, Aviv Regev, Silvia Velasco, Amanda Kedaigle and Marina Rocha. (Courtesy: Rose Lincoln/Harvard University)

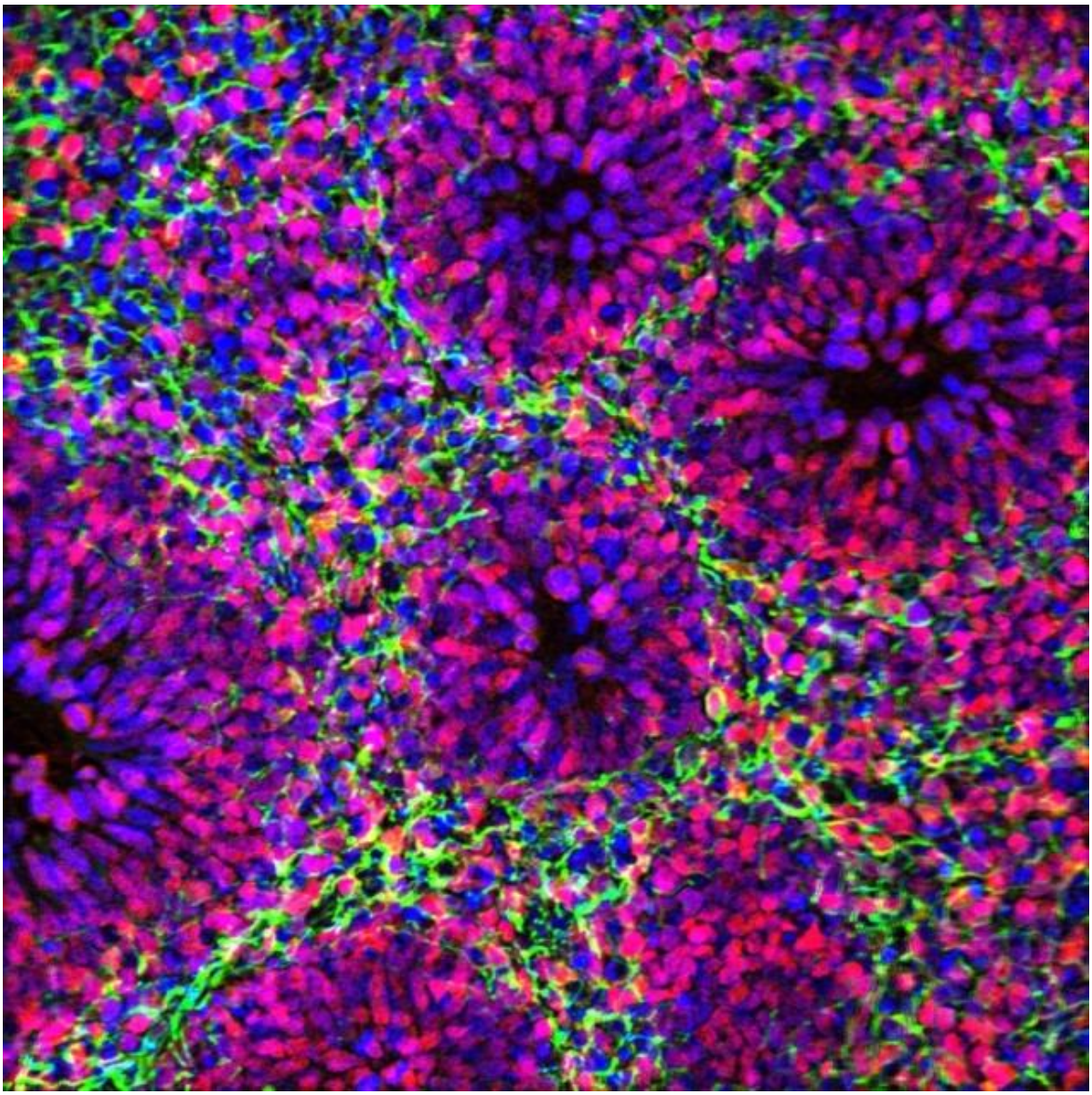
Changing things up

The group modified four well-known methods for growing organoids, enabling them to be grown in a spinning-flask bioreactor. By using this type of bioreactor, the researchers could grow the organoids for longer, as less interference was needed to provide the cells with enough oxygen.

After six months, the researchers assessed the organoids. They found that their version of the dorsally patterned organoid, an organoid directed to grow like the region of the brain at the back of the head, was the most uniformly large and regularly shaped out of the four.

However, simply looking the same as each other is not necessarily a guarantee of success; the wide distribution of cell types and their organisation is also important. The researchers used single cell RNA-sequencing to analyse hundreds of thousands of cells from 21 dorsally patterned organoids.

Comparing the cell types that developed with development in embryos revealed a remarkable degree of similarity. The organoids had similar growth trajectories and their variability was comparable to the normal diversity expected in human brains.



Organoids after one month. (Courtesy: Paola Arlotta laboratory, Harvard University)

Lead author Silvia Velasco explains: “We made organoids from multiple stem cell lines, from both male and female origins — so their genetic backgrounds were different.”

“Despite the different genetic backgrounds, we saw that the same cell types were made in the same way, in the correct order and, most importantly, in each organoid,” says Velasco. “We were really excited that this model gave us such consistency.”

The optimized method of producing organoids could change the way that researchers look at psychiatric illnesses. These organoids could be used to study genetic origins of such diseases by creating spheroids with specific mutations.

Senior author Paola Arlotta explains: “Having reproducible organoids will help us move much more swiftly towards concrete interventions, because they will direct us to the specific genetic

features that give rise to the disease. In the future, I envisage we will be able to ask far more precise questions about what goes wrong in the context of psychiatric illness." [23]

Miniaturized neuroprobe for sampling neurotransmitters in the brain

Researchers at the University of Twente have designed a tiny needle in which micro-channels can be used for extracting small liquid samples from a local area of the brain. The needle is about as thick as a human hair. Thanks to this invention, neuroscientists are now able to monitor dynamic processes more quickly (within a few seconds) and accurately (micrometre precision). The research is to be published in the renowned scientific journal *Lab on a Chip*.

The brain is a highly complex system, as a result of which neuroscientists have struggled to answer such questions as, "Why does one person get a migraine attack, and the other not?"

Doctor Mathieu Odijk of the BIOS lab-on-a-chip group explains, "To answer questions of this kind, it is important to be able to study in detail how the brain works. A key role in the working of the brain is played by the chemicals—the neurotransmitters—that carry information. However, most existing methods for monitoring neurotransmitters in the brain are not able to do so sufficiently quickly or with such localized precision."

Minute water droplets

The small needle that has been designed by Dr. Odijk and his colleagues, which is about as thick as a human hair, has micro-channels through which tiny samples of liquid from a localized part of the brain can be extracted. These samples are stored in minute water droplets of around 10 picolitre (one millionth of a raindrop) in oil. It means the information about neurotransmitters is stored in a kind of chemical memory, after which it can be processed and from which readings can be taken at a later time. This invention allows neuroscientists to monitor dynamic processes in the brain within a few seconds and to micrometre precision. [22]

Methods for large protein crystal growth for neutron protein crystallography

The ability to grow large protein crystals is the single biggest bottleneck that limits the use of neutron protein crystallography in structural biology. Protein crystals need to have volumes in the region of at least 0.1mm^3. Theoretically there is no particular reason why crystals of this size cannot be grown. If they can be, neutron protein crystallography can provide crucial information on the location of hydrogen atoms details relating to hydration hydrogen bonding and ligand interactions. This type of information is of direct relevance to academic and pharmacologically driven research in the life sciences.

The challenge is thus to achieve large crystal growth in a reproducible, time-saving, labour-saving way. It would be ideal if in the future, neutron crystallographers can, after suitable pre-characterisation work, submit their solutions to an automated or semi-automated platform that

would allow the exploration of a large range of conditions in a highly systematic way and to allow users to monitor growth from their remote computers.

Ashley Jordan at the Institut Laue-Langevin (ILL) in Grenoble, France, has been investigating two new crystal growth methods: the development of a module that could allow larger scale automated approaches in the future (task 1), and a flow crystallization system (task 2).

Task 1: A module for automated large crystal growth exploration

This SINE2020 project has focused on the development of a temperature controllable multi-well module in which crystal growth can be optimized. The idea of designing this module was to scale up the approach so that multiple crystallization wells with individual (programmable) temperature control could be used to explore a wide range of growth conditions. A prototype module was made that consisted of a custom plate design containing 6 × 4 wells where the individual crystallisation experiments can occur. Each well can be adapted to different conditions, with each having independent temperature control. The wells are heated using Peltier heating elements with a temperature feedback system that allows each well to be heated and cooled over a temperature range of 4 degrees C to 60 degrees C, with an accuracy of 0.1 degree. The set-up was designed to allow allow crystal growth to be monitored and recorded photographically.

Ashley Jordan, Ryo Mizuta and John Allibon (who developed the software) have built and tested the prototype system. Crystallization tests have been carried out using trypsin and rubredoxin.

Post-SINE2020, the idea would be to make these modules "plug and play" so that a more extended 'robotic' approach could be used. Crystallogenesis runs could be removed by the user on completion and other runs installed using another module – the module would be the working unit of a larger array – with all being camera visualisable and providing time-lapse information to a user portal.

Task 2: Flow crystallization

Another way of pursuing large crystal growth is the idea of a flow crystallization system. The idea is to maintain steady-state batch conditions around a crystal at all times during its growth, by providing a constant supply of fresh protein stock to the crystallization environment. This will maintain optimal solution conditions at all times and help minimize accumulation of impurities on crystal surfaces – such impurities may hinder crystal growth.

A Dolomite Mitos P-Pump was chosen to maintain the extremely low flow rate (between 70-1500 nl min-1) required to regulate the system. A suitable crystallization chamber that can connect to the pump was designed and made using a 3-D printer. This chamber creates a sealed environment and provides ready access to the crystals once they have grown. [21]

STM measurements redefine protein conductances

“Properly connected, proteins are the world’s best molecular wires,” says Stuart Lindsay, Director and Professor at the Biodesign Center for Single Molecule Biophysics at Arizona State University (ASU). His comments refer to recent experiments at ASU to measure the conductance of single proteins between electrodes for the first time with what he describes as “staggering” results

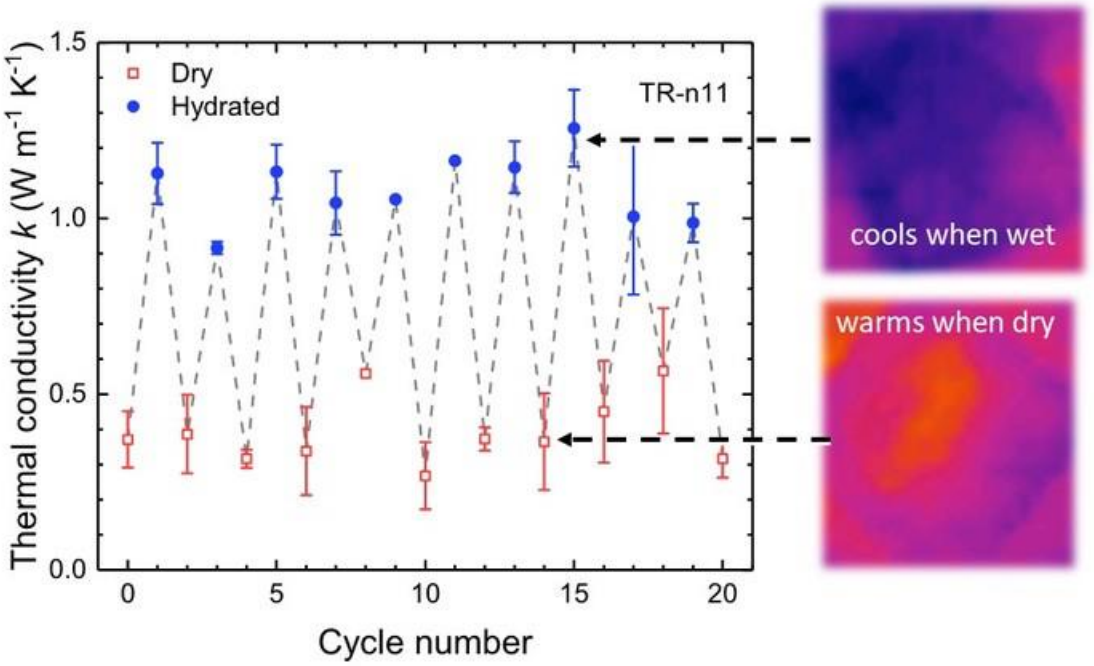
that may have uses for direct, label-free, sensitive, and very selective (background-free) single-molecule detection as well as protein motion sensing. “Measurements on peptides (small protein chains) show they are the world’s worst molecular wires,” he adds. So what changed?

Contact control

The conclusion that proteins have a terrible conductance tallies well with their general physical characteristics – they lack both electronic conduction bands and high levels of structural order. Previous experiments have attempted to investigate the conductance of proteins by injecting electrons from optically excited chromophores, but contacting the molecule to an electrode allows studies of the response to injection of electrons with much lower energies. However so far these have struggled against the uncertainty in the number of molecules contacted, the size of the gap, the nature of the contacts, and possible ionic contributions to the current measured.

Here scanning tunnelling measurements present significant advantages over macroscopic contact devices as Lindsay explains because they allow for single-molecule contacts. “In addition, we carry out the experiments under electrochemical potential control so we can be certain there are no ionic currents and we use chemically well-defined contacts, so that we know (and can control) the metal-molecule interface.”

The resulting conductances measured in the nanosiemens range over distances of several nanometres. Having ruled out ionic currents the researchers were also able to eliminate possible meaningful contributions from tunnelling, which would be five orders of magnitude weaker. Crucially, while the conductance varied little with the length of the protein, the conductance was highly dependent on the chemistry of the electrodes, which the researchers functionalized with specific ligands for different proteins.



Squid-inspired proteins make new thermal switch

Current pathways

The researchers found that the chemistry of the contacts was so significant that weaker coupling to the hydrophobic interior of the protein provided a stronger current than a stronger coupling to the hydrophilic exterior. The researchers describe the role of contact chemistry in terms of the path the current takes either across the surface or through the interior. “We hypothesize that the hydrophobic interior of proteins is a wonderful place for electrons to propagate and that electrons are injected into the interior of the protein using specific ligands,” Lindsay tells *Physics World*.

The experiments also reveal fluctuations that set in above a threshold applied bias of 100 mV in magnitude. Comparison of the lifetime of the on states with the peak current magnitude indicate a single barrier that determines both the current and bonding strength at the contact. The magnitude of this barrier within the relevant exponential expression matches that of a hydrogen bond suggesting that a hydrogen bond may be playing the role of “weak link in the circuit”. The conductance values measured are also compatible with those calculated for thermally activated hopping over a 0.22–0.47-V barrier, the size of the hydrogen bond. “We have devised and implemented a new scheme to extract the electronic decay length, and temperature dependent measurements are underway as well,” adds Lindsay.

Significant findings

Further experiments demonstrated the potential for using the strong ligand specific conductance for single-molecule, highly specific, label- and background free electronic detection of IgG antibodies to HIV and Ebola viruses, and the researchers are now working on technological applications of the results. “The wonderful thing about sorting out the connections issue is that we have a “tool kit” for bioelectronics mapped out,” says Lindsay as he lists them. “(1) For wires, use ligand connected proteins. This not only makes a fantastic contact, but it also makes a self-assembling, directed contact. (2) Multivalent proteins complete circuits and can generate branched wiring. (3) Since the conductivity “reads” the internal state of the protein, enzymes can be wired as single molecule sensors with an exquisite response. Future results from the lab will illustrate this.”

What may take a little longer to unravel is the biological role of protein conductances. Here Lindsay points towards theoretical calculations by Gabor Vattay , which show that the calculated energy level distribution in a number of proteins matches that expected for a very unusual state of matter called “quantum critical”, which also matches certain previous observations of giant protein conductance fluctuations. “If this is true, then proteins must have evolved a rather special structure. So why?” asks Lindsay. “I don’t know, but it is very interesting that ligand mediated contacts allow for sharing of electrons. Does this play a role in recognition?” he adds, highlighting the weaker contacts forged by strong, covalent modifications of residues on the outside of a protein compared with weaker contacts made by ligands that reach into the protein. In terms of biological significance, it seems these latest results raise at least as many questions as they answer.

Full details are reported in the *Proceedings of the National Association of Science*. [20]

Scientists make new 'green' electronic polymer-based films with protein nanowires

An interdisciplinary team of scientists at the University of Massachusetts Amherst has produced a new class of electronic materials that may lead to a "green," more sustainable future in biomedical and environmental sensing, say research leaders microbiologist Derek Lovley and polymer scientist Todd Emrick.

They say their new work shows it is possible to combine protein nanowires with a polymer to produce a flexible electronic composite material that retains the electrical conductivity and unique sensing capabilities of protein nanowires. Results appear in the journal *Small*.

Protein nanowires have many advantages over the silicon nanowires and carbon nanotubes in terms of their biocompatibility, stability, and potential to be modified to sense a wide range of biomolecules and chemicals of medical or environmental interest, says Lovley. However, these sensor applications require that the protein nanowires be incorporated into a flexible matrix suitable for manufacturing wearable sensing devices or other types of electronic devices.

As Lovley explains, "We have been studying the biological function of protein nanowires for over a decade, but it is only now that we can see a path forward for their use in practical fabrication of electronic devices." Postdoctoral research Yun-Lu Sun, now at the University of Texas at Austin, discovered the proper conditions for mixing protein nanowires with a non-conductive polymer to yield the electrically conductive composite material. He demonstrated that although the wires are made of protein, they are very durable and easy to process into new materials.

"An additional advantage is that protein nanowires are a truly 'green,' sustainable material," Lovley adds. "We can mass-produce protein nanowires with microbes grown with renewable feedstocks. The manufacture of more traditional nanowire materials requires high energy inputs and some really nasty chemicals." By contrast, he says, "Protein nanowires are thinner than silicon wires, and unlike silicon are stable in water, which is very important for biomedical applications, such as detecting metabolites in sweat."

Emrick adds, "These electronic protein nanowires bear surprising resemblance to polymer fibers and we're trying to figure out how to combine the two most effectively."

In their proof-of-concept study, the protein nanowires formed an electrically conductive network when introduced into the polymer polyvinyl alcohol. The material can be treated with harsh conditions, such as heat, or extreme pH such as high acidity, that might be expected to ruin a protein-based composite, but it continued to work well.

The conductivity of the protein nanowires embedded in the polymer changed dramatically in response to pH. "This is an important biomedical parameter diagnostic of some serious medical conditions," Lovley explains. "We can also genetically modify the structure of the protein nanowires in ways that we expect will enable detection of a wide range of other molecules of biomedical significance."

The electrically conductive protein nanowires are a natural product of the microorganism Geobacter discovered in Potomac River mud by Lovley more than 30 years ago. Geobacter uses the protein nanowires to make electrical connections with other microbes or minerals. He notes, "Material science experts like Todd Emrick and Thomas Russell on our team deserve the credit for bringing protein nanowires into the materials field. It's not just about mud anymore."

In this work supported by UMass Amherst campus funds for exploratory research, next steps for the collaborative materials-microbiology team include scaling up production of nanowire-polymer matrices, Lovley says.

He points out, "Materials scientists need a lot more nanowires than we're used to making. We're were making thimblefuls for our biological studies. They need buckets full, so we are now concentrating on producing larger amounts and on tailoring the nanowires so they'll respond to other molecules." The researchers have also applied for a patent on the idea of a conductive polymer made with protein nanowires. [19]

Nanocages in the lab and in the computer: how DNA-based dendrimers transport nanoparticles

How to create nanocages, i.e., robust and stable objects with regular voids and tunable properties? Short segments of DNA molecules are perfect candidates for the controllable design of novel complex structures. Physicists from the University of Vienna, the Technical University of Vienna, the Jülich Research Center in Germany and Cornell University in the U.S.A., investigated methodologies to synthesize DNA-based dendrimers in the lab and to predict their behavior using detailed computer simulations. Their results are published in *Nanoscale*.

Nanocages are highly interesting molecular constructs, from the point of view of both fundamental science and possible applications. The cavities of these nanometer-sized objects can be employed as carriers of smaller molecules, which is of critical importance in medicine for drug or gene delivery in living organisms. This idea brought together researchers from various interdisciplinary fields who have been investigating dendrimers as promising candidates for creating such nano-carriers. Their tree-like architecture and step-wise growth with repeating self-similar units results in dendrimers containing cavities, hollow objects with controllable design. Nevertheless, decades of research have showed that vast number of different dendrimer types experience back-folding of outer branches with growing dendrimer generations, giving rise to a higher density of constituents in the molecule's interior. The effect of back-folding is enhanced upon addition of salt in the solution, whereby flexible dendrimers undergo significant shrinking, becoming compact objects with no hollow spaces in their interior.

The team of collaborators consisted of Nataša Adžić and Christos Likos (University of Vienna), Clemens Jochum and Gerhard Kahl (TU Wien), Emmanuel Stiakakis (Jülich) as well as Thomas Derrien and Dan Luo (Cornell). The researchers found a way to create dendrimers rigid enough to prevent back-folding of outer arms even in the case of high branching generations, preserving regular voids in their interior. Moreover, their novel macromolecules are characterized by remarkable resistance to added salt: they showed that the morphology and conformational characteristics of these systems stay unaffected even upon of addition of salt even at high concentration. The nanocages they created, in the lab and studied computationally are DNA-based dendrimers, or so-called, dendrimer-like DNAs (DL-DNA). The building block they are composed of is a Y-shaped double-stranded DNA unit, a three-armed structure consisting of double-stranded DNA (ds-DNA), formed via hybridization of three single-stranded DNA chains (ss-DNA), each of which has partially complementary sequences to the other two. Each arm is made up of 13 base pairs and a single-stranded sticky end with four nucleobases which acts as a glue. While a single Y-DNA corresponds to the first dendrimer generation, the attachment of further Y-DNA elements yields DL-DNA of higher generations. The resulting dendrimer is a charged and hollow-containing macromolecular assembly with tree-like architecture. Due to the rigidity of dsDNA, the branches of DL-DNA are stiff so that the whole molecule is rigid. Since DNA is charged, the electrostatic repulsion enhances the rigidity of the molecule.

DL-DNA molecules have been assembled in the laboratory by the Jülich and Cornell partners with remarkable control and sub-nanometer precision through programmable sticky-end cohesions. Their step-wise growth is highly controllable, unidirectional and non-reversible. This property is of high

importance, as it has been shown that DNA-based dendrimers have been envisioned to play a promising role in developing nanoscale-barcodes, DNA-based vaccine technologies, as well as a structural probes involving multiplexed molecular sensing processes. Sizes, shapes as well as additional conformational details invisible to the experimentalists, such as the size of voids and the degree of branches back-folding, have been analyzed by computer simulations in Vienna. To describe the complex structure of DNA units, the group used a simple monomer-resolved model with interactions carefully chosen to mimic the equilibrium properties of DNA in physiological solution. The excellent agreement obtained between experiments and simulations for the dendrimer characteristics validates the theoretical models employed and paves the way for further investigation of the nanocages' properties and their applications as functional and smart nanocarriers and as building blocks for engineering biocompatible artificial materials. [18]

DNA 'dances' in first explanation of how genetic material flows through a nucleus

DNA flows inside a cell's nucleus in a choreographed line dance, new simulations reveal. The finding is the first large-scale explanation of genetic material moving within a working cell.

"Previous work mostly focused on what was going on at the microscale of DNA," says study co-author Michael Shelley, group leader for biophysical modeling at the Flatiron Institute's Center for Computational Biology in New York City and co-director of the Courant Institute's Applied Mathematics Laboratory at New York University. "People didn't really think about what was going on at the larger scale."

Shelley and colleagues simulated the motions of chromatin, the functional form of DNA inside the nucleus. Chromatin looks like beads on a string, with ball-like clusters of genetic material linked by strands of DNA. The researchers propose that molecular machines along the DNA cause segments of the chromatin to straighten and pull taut. This activity aligns neighboring strands to face the same direction. That alignment, in turn, results in a cascading waltz of genetic material shimmying across the nucleus.

The dancing DNA may play a role in gene expression, replication and remodeling, though the exact effects remain unclear, the researchers reported online October 22 in *Proceedings of the National Academy of Sciences*.

The findings help explain measurements reported in 2013 by scientists, including Alexandra Zidovska, at Harvard University. Besides previously known small-scale motions of individual genes, the scientists' experiment revealed large regions of chromatin that shifted in unison through a cell's nucleus at a rate of a fraction of a micron every few seconds. The scientists, though, couldn't identify the cause or details of the movement.

Shelley's had experience studying how microbes swim. The similar physics involved made him curious about the mechanism behind the migrating DNA. He partnered with David Saintillan of the University of California, San Diego, and Zidovska, now of New York University, to investigate.

The researchers investigated two ways a molecular machine along a DNA molecule might move nearby genetic material: pulling and pushing. A molecular machine can't exert a net force, which

means that by pulling on one piece of DNA, it must hold onto and pull something else. The two inward-pulling forces will cancel, giving zero net force and causing the DNA segment to contract. If the machine instead pushes outward, the forces will similarly cancel, and the DNA segment will extend.

These contractions and extensions take place within a gooey liquid that fills a cell's nucleus. The movement of the DNA generates a flow in the liquid that can reorient nearby lengths of molecules.

Using computer simulations, the researchers modeled how contraction and extension affected a jumble of chromatin confined within a spherical nucleus. When the lengths of DNA contracted, the resulting flow pointed nearby strands in a different direction, blocking any choreographed movements. Extension created streams of fluid that aligned nearby DNA in the same direction. That alignment resulted in a cascading effect that shifted large patches of DNA in the same direction.

"It's like part of the nucleus suddenly decides that we're all going to move over this way a little, then another bit says we're all going to move over this way," Shelley says. "The chromatin sort of wanders around."

This DNA shimmy could help distribute throughout the nucleus the molecular machinery responsible for expressing a particular gene, Shelley proposes. Finding out for sure, he says, will require more complex simulations as well as additional experiments into how chromatin cuts a rug. [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 cellsfrom 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 α, 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 α 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 α 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 lightharvesting 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 selfreproducing 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.

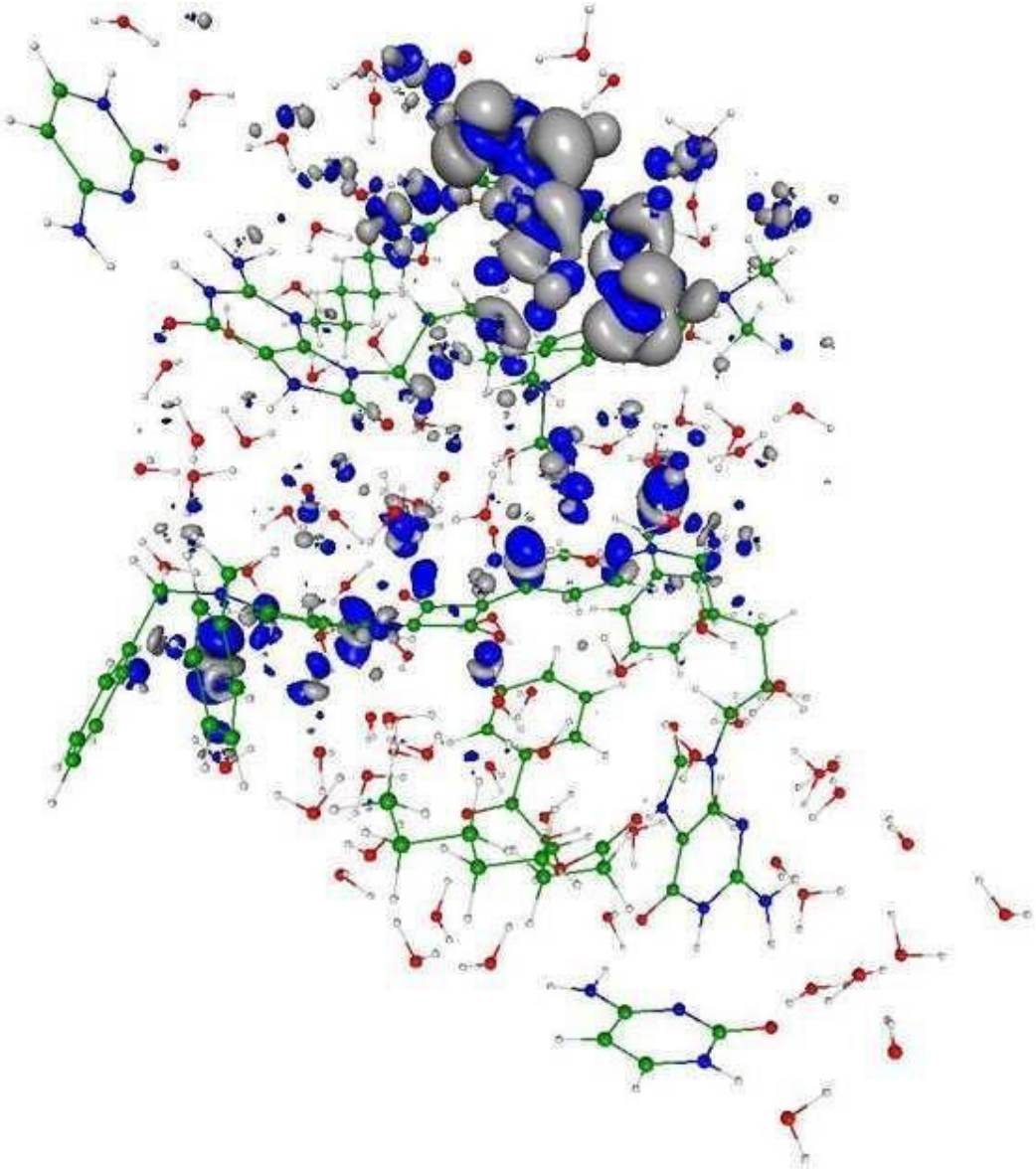
We can state that: Livings are self-assembled and self-replicating wet and warm stochastically moving supramolecular systems where quantum entanglement can be continuously generated and

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 selfassembled two synthesized protocell system due to the photo excited electron charge transfer from one protocell to another that leads to closer self-assembly and exchange of energy and information.

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

As a result, these nonlinear quantum interactions compressed the overall molecular system resulting in a smaller gap between the HOMO and LUMO electron energy levels which allows

enhanced tunneling of photo excited electrons from the sensitizer squarine and (1,4bis(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 electrodynamics field within the living system.

What this means is that each living cell is giving off, or resonating, a biophoton field of coherent energy. If each cell is emitting this field, then the whole living system is, in effect, a resonating field-a ubiquitous nonlocal field. And since biophotons are the entities through which the living system communicates, there is near-instantaneous intercommunication throughout. And this, claims Popp, is the basis for coherent biological organization -- referred to as quantum coherence. This discovery led Popp to state that the capacity for evolution rests not on aggressive struggle and rivalry but on the capacity for communication and cooperation. In this sense the built-in capacity for species evolution is not based on the individual but rather living systems that are interlinked within a coherent whole: Living systems are thus neither the subjects alone, nor objects isolated, but both subjects and objects in a mutually communicating universe of meaning. . . . Just as the cells in an organism take on different tasks for the whole, different populations enfold information not only for themselves, but for all other organisms, expanding the consciousness of the whole, while at the same time becoming more and more aware of this collective consciousness.

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

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

Creating quantum technology

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

Quantum Entanglement

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

The Bridge

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

Accelerating charges

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

Relativistic effect

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

Heisenberg Uncertainty Relation

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

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

Wave – Particle Duality

The accelerating electrons explains the wave – particle duality of the electrons and photons, since the elementary charges are distributed on delta x position with delta p impulse and creating a wave packet of the electron. The photon gives the electromagnetic particle of the mediating force of the electrons electromagnetic field with the same distribution of wavelengths.

Atomic model

The constantly accelerating electron in the Hydrogen atom is moving on the equipotential line of the proton and it's kinetic and potential energy will be constant. Its energy will change only when it

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

The Relativistic Bridge

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

The weak interaction

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

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

The right handed anti-neutrino and the left handed neutrino exist only because changing back the quark flavor could happen only in reverse, because they are different geometrical constructions, the u is 2 dimensional and positively charged and the d is 1 dimensional and negatively charged. It needs also a time reversal, because anti particle (anti neutrino) is involved.

The neutrino is a 1/2spin creator particle to make equal the spins of the weak interaction, for example neutron decay to 2 fermions, every particle is fermions with ½ spin. The weak interaction changes the entropy since more or less particles will give more or less freedom of movement. The entropy change is a result of temperature change and breaks the equality of oscillator diffraction

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

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

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

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

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

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

Finally since the weak interaction is an electric dipole change with ½ spin creating; it is limited by the velocity of the electromagnetic wave, so the neutrino's velocity cannot exceed the velocity of light.

The General Weak Interaction

The Weak Interactions T-asymmetry is in conjunction with the T-asymmetry of the Second Law of Thermodynamics, meaning that locally lowering entropy (on extremely high temperature) causes for example the Hydrogen fusion. The arrow of time by the Second Law of Thermodynamics shows the increasing entropy and decreasing information by the Weak Interaction, changing the temperature dependent diffraction patterns. A good example of this is the neutron decay, creating more particles with less known information about them.
The neutrino oscillation of the Weak Interaction shows that it is a general electric dipole change and it is possible to any other temperature dependent entropy and information changing diffraction pattern of atoms, molecules and even complicated biological living structures. We can generalize the weak interaction on all of the decaying matter constructions, even on the biological too. This gives the limited lifetime for the biological constructions also by the arrow of

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

There is also connection between statistical physics and evolutionary biology, since the arrow of time is working in the biological evolution also.
The Fluctuation Theorem says that there is a probability that entropy will flow in a direction opposite to that dictated by the Second Law of Thermodynamics. In this case the Information is growing that is the matter formulas are emerging from the chaos. So the Weak Interaction has two directions, samples for one direction is the Neutron decay, and Hydrogen fusion is the opposite direction.

Fermions and Bosons

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

Van Der Waals force

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

Electromagnetic inertia and mass

Electromagnetic Induction

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

Relativistic change of mass

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

The frequency dependence of mass

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

and the proton, they masses are different, also as the wavelengths on both sides of the diffraction pattern, giving equal intensity of radiation.

Electron – Proton mass rate

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

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

Gravity from the point of view of quantum physics

The Gravitational force

The gravitational attractive force is basically a magnetic force.

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

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

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

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

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

The gravitational force attracting the matter, causing concentration of the matter in a small space and leaving much space with low matter concentration: dark matter and energy.
There is an asymmetry between the mass of the electric charges, for example proton and electron, can understood by the asymmetrical Planck Distribution Law. This temperature dependent energy

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

The Higgs boson

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

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

Higgs mechanism and Quantum Gravity

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

In particle physics, the Higgs mechanism is a kind of mass generation mechanism, a process that gives mass to elementary particles. According to this theory, particles gain mass by interacting with the Higgs field that permeates all space. More precisely, the Higgs mechanism endows gauge bosons in a gauge theory with mass through absorption of Nambu–Goldstone bosons arising in spontaneous symmetry breaking.

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

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

What is the Spin?

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

The Graviton

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

Conclusions

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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