

# Better Candidate for Chemotherapy

*When the red blood cells make their tight squeeze through the lung's tiny capillaries, the nanoparticles are sheared off and taken up by lung cells with tenfold greater success than free-floating nanoparticles, and dramatically improved the survival of mice with lung cancer metastasis. [25]*

*But a new ultrasonic method proposed by biomedical engineers from Qifa Zhou's team at the University of Southern California in Los Angeles could enable acoustic control and real-time tracking of drug release within the body. [24]*

*A Rutgers-led team has created better biosensor technology that may help lead to safe stem cell therapies for treating Alzheimer's and Parkinson's diseases and other neurological disorders. [23]*

*Biology encodes information in DNA and RNA, which are complex molecules finely tuned to their functions. [22]*

*When cells suffer DNA damage, they send out an SOS signal. When the repair crew arrives, the emergency signal is cancelled as it is no longer needed. [21]*

*Now, in a new paper published in Nature Structural & Molecular Biology, Mayo researchers have determined how one DNA repair protein gets to the site of DNA damage. [20]*

*A microscopic thread of DNA evidence in a public genealogy database led California authorities to declare this spring they had caught the Golden State Killer, the rapist and murderer who had eluded authorities for decades. [19]*

*Researchers at Delft University of Technology, in collaboration with colleagues at the Autonomous University of Madrid, have created an artificial DNA blueprint for the replication of DNA in a cell-like structure. [18]*

*An LMU team now reveals the inner workings of a molecular motor made of proteins which packs and unpacks DNA. [17]*

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

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

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

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

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

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

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

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

*A UNSW Australia-led team of researchers has discovered how algae that survive in very low levels of light are able to switch on and off a weird quantum phenomenon that occurs during photosynthesis. [8]*

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

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

*The accelerating electrons explain not only the Maxwell Equations and the*

*Special Relativity, but the Heisenberg Uncertainty Relation, the Wave-Particle Duality and the electron's spin also, building the Bridge between the Classical and Quantum Theories.*

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

*The diffraction patterns and the locality of the self-maintaining electromagnetic potential explains also the Quantum Entanglement, giving it as a natural part of the Relativistic Quantum Theory and making possible to understand the Quantum Biology.*

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Author: George Rajna

## Preface

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

The human body is a constant flux of thousands of chemical/biological interactions and processes connecting molecules, cells, organs, and fluids, throughout the brain, body, and nervous system. Up until recently it was thought that all these interactions operated in a linear sequence, passing on information much like a runner passing the baton to the next runner. However, the latest findings in quantum biology and biophysics have discovered that there is in fact a tremendous degree of coherence within all living systems. [5]

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

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

## ELeCt-ing a better candidate for chemo delivery

Chemotherapy has been the backbone of cancer treatment for decades, but it is notorious for its toxicity to healthy cells, severe side effects, and poor targeting of the intended tumors. Efforts to improve chemotherapy's efficacy and tolerability include packaging drugs into nanoparticles, which can protect them from degradation in the body, control their release pattern, and shield the patient from some of the drug's side effects. However, nanoparticles have so far failed to show significant accumulation in target sites, even when they are engineered with surface proteins designed to bind to specific tissues, largely because they are quickly cleared from the blood by the liver and spleen.

Now, a new technique called ELeCt (erythrocyte-leveraged chemotherapy) developed at Harvard's Wyss Institute for Biologically Inspired Engineering and John A. Paulson School of Engineering and Applied Sciences (SEAS) aims to resolve those problems using the age-old Trojan Horse trick to smuggle [drug](#)-loaded nanoparticles into cancerous [lung](#) tissue by mounting them onto the body's own red blood cells (erythrocytes). When the red blood cells make their tight squeeze through the lung's tiny capillaries, the nanoparticles are sheared off and taken up by lung cells with tenfold

greater success than free-floating nanoparticles, and dramatically improved the survival of mice with lung cancer metastasis. The research is reported in *Science Advances*.

"30-55% of patients with advanced cancer have metastasis to the lung, due to its large number of capillaries, and there is currently no treatment for lung metastasis itself," said co-first author Zongmin Zhao, Ph.D., a Postdoctoral Fellow in the lab of Samir Mitragotri at the Wyss Institute and SEAS. "ELeCt exploits those same blood vessels to effectively deliver drugs that fight lung metastasis, and has strong potential to be developed into a clinical treatment."

To create the ELeCt system, Zhao and his collaborators loaded doxorubicin, a common cancer chemotherapy drug, into tiny nanoparticles composed of a biodegradable polymer called PLGA. They then incubated the nanoparticles with both mouse and human erythrocytes, and found that they bound to the cells' surfaces with [high efficiency](#) and without damaging them, allowing the dose of the drug carried by the erythrocytes to be tuned to fit different required dosages.

The team next subjected erythrocyte-bound nanoparticles to lung-corresponding [shear stress](#) in vitro to simulate the conditions erythrocytes encounter when squeezing through the lung's capillaries, and observed that > 75% of the nanoparticles were sheared off of both mouse and human cells. They then injected mouse erythrocytes loaded with the ELeCt construct into the veins of living mice with melanoma that had metastasized to their lungs, and found a remarkable 16-fold higher drug content in the lungs after 20 minutes compared with mice that had received free nanoparticles. A substantial portion of the deposited nanoparticles penetrated deep into the metastatic tumors, suggesting that this method of drug delivery is more precise and effective than existing methods.

"The most serious side effect of doxorubicin in humans is cardiotoxicity, and based on our experiments, ELeCt can ensure that more of the drug ends up in the lungs rather than in the heart," said co-first author Anvay Ukidve, a graduate student in Mitragotri's lab at SEAS. "This advance could significantly reduce the danger to cancer patients receiving this drug, and increase its effectiveness against lung tumors."

To confirm that suspicion, the team monitored the degree of metastasis in the lungs of mice with early-stage disease that were given ELeCt versus those that were given free nanoparticles, and saw that metastasis was almost completely inhibited in all of the mice receiving ELeCt over the course of 23 days—a 300-fold improvement over the state of the free-nanoparticle-injected mice. ELeCt also improved the survival of treated mice by 32 days, while mice treated with free nanoparticles survived a mere 3 days more. When they repeated the experiment with mice that had late-stage disease, their survival was extended by 9 days with ELeCt while free nanoparticles produced no survival benefit.

In addition, all mice treated with ELeCt maintained a healthy body weight while [mice](#) receiving a free-drug injection experienced significant weight loss, suggesting that the side effects of doxorubicin were also mitigated by ELeCt. The researchers also demonstrated that other chemotherapy drugs could be loaded into the nanoparticles and bound to erythrocytes, including paclitaxel, docetaxel, methotrexate, and a combination of 5-fluorouracil and methotrexate.

"Our ELeCt system simultaneously provides solutions to a number of problems that plague current chemotherapy treatments, including toxic side effects, high required doses, low levels of penetrance into target tissues, rapid clearance from the body, and premature release of a drug from nanoparticles," said corresponding author Mitragotri, who is a Core Faculty member at the Wyss Institute as well as the Hiller Professor of Bioengineering and Hansjörg Wyss Professor of Biologically Inspired Engineering at SEAS.

Further studies will attempt to tease out the binding mechanisms of the [nanoparticles](#) to the red blood cells, so that the amount of shear needed to remove them (and thus the dose of the drug delivered) can be adjusted. The team also plans to determine the ideal dosing schedule to maximize metastasis inhibition as well as ELeCt's ability to treat human patient-derived lung metastasis, a critical step toward translating the ELeCt platform into a clinical tool for treating cancer.

"This technology potentially represents a huge advance in terms of increasing the efficacy and decreasing the toxicity of existing cancer chemotherapies. It is also a great example of medical breakthroughs that can be made by taking advantage of biological, in this case cellular, delivery systems that Nature has already optimized over thousands of years of evolution," said Wyss Institute Founding Director Donald Ingber, M.D., Ph.D., who is also the Judah Folkman Professor of Vascular Biology at Harvard Medical School, the Vascular Biology Program at Boston Children's Hospital, and Professor of Bioengineering at SEAS. [25]

## Using sound waves to remotely target drugs to tumors

The lack of a clinically viable method to track and direct cancer drugs to tumors is a big problem for targeted therapeutics.

But a new ultrasonic method proposed by biomedical engineers from Qifa Zhou's team at the University of Southern California in Los Angeles could enable acoustic control and real-time tracking of [drug](#) release within the body. The researchers report on their manipulation of ultrasonic waves to pinpoint [drug delivery](#) in *Applied Physics Letters*.

"In conventional drug delivery, tissue is examined ex vivo under the microscope, or radioactive materials are used to trace drugs in vivo. We propose a new way to image and move the drug precisely inside the human body by combining the new plane wave imaging method with a focused [ultrasound](#) transducer," said post-doctoral researcher Xuejun Qian.

Accurate drug delivery is crucial to ensure tumor obliteration, while avoiding the toxic side effects of cancer therapeutics on healthy tissue. Ultrasound is a popular method for noninvasively imaging inside the body. But because the conventional method lacks sensitivity, it has not been used in drug delivery previously. Zhou's team adapted a new, ultrafast ultrasound method that eliminates background noise to accurately track a drug delivery vehicle within a phantom blood vessel.

Hanmin Peng, a visiting scholar from Nanjing University of Aeronautics & Astronautics, China, and co-workers pumped water through a narrow silicone tube to mimic [blood flow](#) through a blood



vessel. They placed the tube beneath real pig tissue and imaged across this to make the setup more realistic. Microbubbles, tiny pockets of air, that can be used as vehicles for drug delivery were introduced into the fake [blood vessels](#).

In recent years, there's been much excitement over the ability to focus sound waves into "acoustic tweezers," which can manipulate particles. Zhou's team applied a focused ultrasound transducer to trap the microbubbles identified by their ultrafast imaging system.

The team predicted [microbubble](#) motion and calculated the acoustic radiation forces required to trap and move the bubbles to specific areas in the phantom blood vessel.

By balancing the acoustic radiation force from the transducer, the team moved the trapped microbubbles to a specific location on the tube wall and turned up the acoustic power to burst the bubbles.

Ultrasound waves vibrate the air contained within microbubbles, which enabled Peng and co-workers to use their novel ultrafast ultrasound imaging system to precisely track the microbubbles at depths of up to 10 millimeters within the tissue. They hope this combination of ultrasound tracking and targeting can be translated to noninvasively directing drug-containing microbubbles to blood vessels adjacent to tumor locations in the body.

"We want to try in vivo studies on rat or rabbit to see whether the proposed method can monitor and release microbubble-based drug [delivery](#) in a real body," said Qian. "We hope to further improve the imaging resolution, sensitivity and speed within a real case, and if it works, the long-term goal would be to move towards a human study." [24]

## **Better biosensor technology created for stem cells**

A Rutgers-led team has created better biosensor technology that may help lead to safe stem cell therapies for treating Alzheimer's and Parkinson's diseases and other neurological disorders.

The technology, which features a unique graphene and gold-based platform and high-tech imaging, monitors the fate of [stem cells](#) by detecting genetic material (RNA) involved in turning such cells into [brain cells](#) (neurons), according to a study in the journal *Nano Letters*.

Stem cells can become many different types of cells. As a result, stem cell therapy shows promise for regenerative treatment of neurological disorders such as Alzheimer's, Parkinson's, stroke and spinal cord injury, with diseased cells needing replacement or repair. But characterizing stem cells and controlling their fate must be resolved before they could be used in treatments. The formation of tumors and uncontrolled transformation of stem cells remain key barriers.

"A critical challenge is ensuring [high sensitivity](#) and accuracy in detecting biomarkers—indicators such as modified genes or proteins—within the complex stem cell microenvironment," said senior author KiBum Lee, a professor in the Department of Chemistry and Chemical Biology in the



School of Arts and Sciences at Rutgers University-New Brunswick. "Our technology, which took four years to develop, has demonstrated great potential for analyzing a variety of interactions in stem cells."

The team's unique biosensing platform consists of an array of ultrathin graphene layers and gold nanostructures. The platform, combined with high-tech imaging (Raman spectroscopy), detects genes and characterizes different kinds of stem cells with greater reliability, selectivity and sensitivity than today's biosensors.

The team believes the technology can benefit a range of applications. By developing simple, rapid and accurate sensing platforms, Lee's group aims to facilitate treatment of neurological disorders through [stem cell therapy](#).

Stem cells may become a renewable source of replacement cells and tissues to treat diseases including macular degeneration, spinal cord injury, stroke, burns, heart disease, diabetes, osteoarthritis and rheumatoid arthritis, according to the National Institutes of Health. [23]

## **DNA is only one among millions of possible genetic molecules**

Biology encodes information in DNA and RNA, which are complex molecules finely tuned to their functions. But are they the only way to store hereditary molecular information? Some scientists believe life as we know it could not have existed before there were nucleic acids. Thus, understanding how they came to exist on primitive Earth is a fundamental goal of basic research.

The central role of nucleic acids in biological information flow also makes them key targets for [pharmaceutical research](#), and synthetic molecules mimicking nucleic acids form the basis of many treatments for viral diseases, including HIV. Other nucleic acid-like polymers are known, yet much remains unknown regarding possible alternatives for hereditary information storage. Using sophisticated [computational methods](#), scientists from the Earth-Life Science Institute (ELSI) at the Tokyo Institute of Technology, the German Aerospace Center (DLR) and Emory University explored the "chemical neighborhood" of nucleic acid analogues. Surprisingly, they found well over 1 million variants, suggesting a vast, unexplored universe of chemistry relevant to pharmacology, biochemistry and efforts to understand the origins of life. The molecules revealed by this study could be further modified to produce hundreds of millions of potential pharmaceutical drug leads.

Nucleic acids were first identified in the 19th century, but their composition, biological role and function were not understood by scientists until the 20th century. The discovery of DNA's double-helical structure by Watson and Crick in 1953 revealed a simple explanation for biological and evolutionary functions. All living things on Earth store information in DNA, which consists of two polymer strands wrapped around each other like a caduceus, with each strand complementing the other. When the strands are pulled apart, copying the complement on either template results in two copies of the original. The DNA polymer itself is composed of a sequence of "letters," the bases adenine (A), guanine (G), cytosine (C) and thymine (T), and living organisms have evolved ways to make sure that the appropriate sequence of letters is almost always reproduced during DNA copying.

The sequence of bases is copied into RNA by proteins, which is then read into a protein sequence. The proteins themselves enable a multitude of finely tuned chemical processes that make life possible.

Small errors occasionally occur during DNA copying, and others are sometimes introduced by environmental mutagens. These small errors are the fodder for [natural selection](#): Some of these errors result in sequences that produce fitter organisms, though most have little effect; however, many can prove lethal. The ability of new sequences to favor host survival is the "ratchet" that allows biology to adapt to the constantly changing challenges of the environment. This is the underlying reason for the kaleidoscope of biological forms on Earth, from humble bacteria to tigers: The information stored in nucleic acids allows for "memory" in biology. But are DNA and RNA the only way to store this information? Or are they perhaps just the best way, discovered only after millions of years of evolutionary tinkering?

"There are two kinds of nucleic acids in biology, and maybe 20 or 30 effective nucleic acid-binding nucleic acid analogues. We wanted to know if there is one more to be found or even a million more. The answer is, there seem to be many more than was expected," says professor Jim Cleaves of ELSI.

Though biologists don't consider them organisms, viruses also use nucleic acids to store their heritable information, though some viruses use RNA, a slight variant on DNA, as their molecular storage system. RNA differs from DNA by the presence of a single atom substitution, but overall, RNA plays by very similar molecular rules as DNA. The remarkable thing is that these two molecules are essentially the only ones used among the incredible variety of organisms on Earth.

Biologists and chemists have long wondered why this should be. Are these the only molecules that could perform this function? If not, are they perhaps the best? Did other molecules once play this role during evolution that were subsequently selected for extinction?

The central importance of nucleic acids in biology has also long made them drug targets for chemists. If a drug can inhibit the ability of an organism or virus to produce similarly infectious offspring, it effectively kills the organisms or virus. Mucking up the heredity of an organism or virus is a great way to knock it dead. Fortunately, the cellular machinery that manages nucleic acid copying in each organism is slightly different, and in viruses, often very different.

Organisms with large genomes, like humans, need to be very careful about copying their hereditary information, and thus are very selective about avoiding the wrong precursors when copying their nucleic acids. Conversely, viruses, which generally have much smaller genomes, are much more tolerant of using similar but slightly different molecules to copy themselves. This means chemicals that are similar to the building blocks of nucleic acids, known as nucleotides, can sometimes impair the biochemistry of one organism more than another. Most of the important antiviral drugs used today are nucleotide or nucleoside analogues, including those used to treat HIV, herpes and viral hepatitis. Many important cancer drugs are also nucleotide or nucleoside analogs, as cancer cells sometimes have mutations that make them copy [nucleic acids](#) in unusual ways.

"Trying to understand the nature of heredity, and how else it might be embodied, is just about the most basic research one can do, but it also has some really important practical applications," says co-author Chris Butch, formerly of ELSI and now a professor at Nanjing University.

Since most scientists believe the basis of biology is heritable information, without which natural selection would be impossible, evolutionary scientists studying the origins of life have also focused on ways of making DNA or RNA from simple chemicals that might have occurred spontaneously on primitive Earth. Most scientists think RNA evolved before DNA for subtle chemical reasons. DNA is thus much more stable than RNA, and DNA became life's hard disk. However, research in the 1960s soon split the theoretical origins field in two: those who saw RNA as the simple "Occam's Razor" answer to the origins-of-biology problem and those who saw the many kinks in the armor of RNA's abiological synthesis. RNA is still a complicated molecule, and it is possible that structurally simpler molecules could have served in its place before it arose.

Co-author Dr. Jay Goodwin, a chemist with Emory University says, "It is truly exciting to consider the potential for alternate genetic systems based on these analogous nucleosides—that these might possibly have emerged and evolved in different environments, perhaps even on other planets or moons within our solar system. These alternate genetic systems might expand our conception of biology's 'central dogma' into new evolutionary directions, in response and robust to increasingly challenging environments here on Earth."

Which molecule came first? What makes RNA and DNA unique? It is difficult to explore such basic questions by physically making molecules in the laboratory. On the other hand, computing molecules before making them could potentially save chemists a lot of time. "We were surprised by the outcome of this computation," says co-author Dr. Markus Meringer. "It would be very difficult to estimate a priori that there are more than a million nucleic-[acid](#) like scaffolds. Now we know, and we can start looking into testing some of these in the lab."

"It is absolutely fascinating to think that by using modern computational techniques, we might stumble upon new drugs when searching for alternative [molecules](#) to DNA and RNA that can store hereditary information. It is cross-disciplinary studies such as this that make science challenging and fun yet impactful," says co-author Dr. Pieter Burger, also of Emory University. [22]

## **DNA SOS: Understanding DNA signaling pathways**

When cells suffer DNA damage, they send out an SOS signal. When the repair crew arrives, the emergency signal is cancelled as it is no longer needed. This two-stage process is an important one in many different diseases, but the underlying mechanisms are not well understood. ADP-ribosylation is one of the DNA damage response mechanisms used by cells to send out an SOS signal; and the ARH family of enzymes is involved in canceling the signal. In work recently published in *Cell Chemical Biology*, researchers from the University of Oxford's DNA Damage Response Lab investigated the structure of two ADP-(ribose)hydrolases (ARHs). Their results provide important insights into the differences between these two proteins and offer useful tools for targeted drug design.

## **DNA repair**

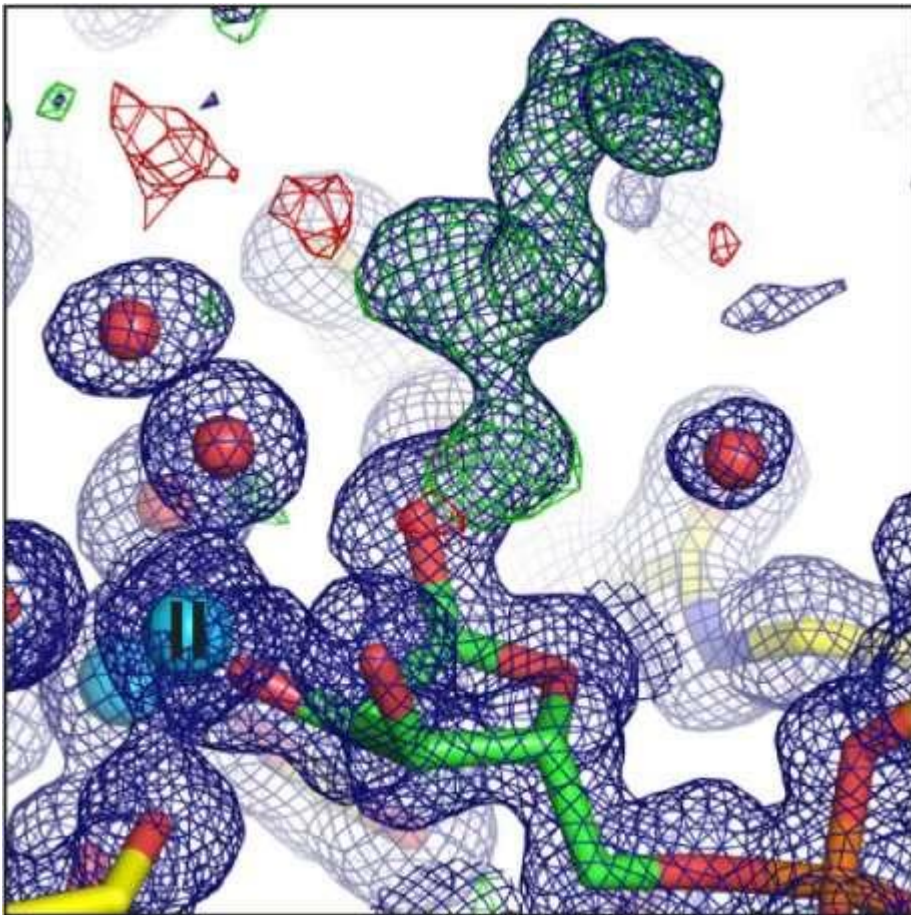
The DNA in our cells is under constant attack, and estimates suggest it is damaged thousands of times every day. Left untreated, these lesions can lead to mutations, cell death, or—in the worst case—

cancer. However, cells have a number of DNA damage response pathways by which they can counteract DNA damage, and these are generally sufficient to maintain a healthy genome.

Previous research has shown that cancer, neurodegenerative diseases, immunodeficiency or developmental abnormalities are linked to defects in DNA damage response pathways. The University of Oxford's DNA Damage Response Lab studies the protein functions and pathways underpinning genome stability, to increase our understanding and help to develop new ways to prevent and treat disease.

In this new work, researchers used Diamond's macromolecular crystallography (MX) beamlines to investigate the [structure](#) of ARH1 and ARH3. ARH1 is essential in tumor suppression and plays a role in defending against bacterial toxins. ARH3 is known to be involved in the DNA damage response.

Crystallising human ARH3 is challenging, as the protein will only crystallize in the presence of a ligand, which cannot always be detected in the corresponding structure. In order to circumvent this problem, Dr. Johannes Rack used a homologue of ARH3 from the West Indian Ocean coelacanth (*Latimeria chalumnae*), which crystallized more readily. This allowed the researchers to solve crystal structures with and without a number of ligands that they could not obtain with the human protein. These also turned out to be the first ever coelacanth protein structures published.



Close-up electron density map of the coordination of the distal ribose (green) of the hARH1:ADPr structure. Credit: Diamond Light Source

## MX at Diamond

Experiments for this research were carried out on beamlines I03, I04, I04-1, and I24. The ARH proteins are magnesium-dependent, and their structure had to be determined both with and without magnesium present. The paper, therefore, contains ten protein structures, collected at atomic resolution. This kind of intensive research was possible because the University of Oxford has BAG access to Diamond, which allows groups of users to fill a beamtime shift with a series of short experiments.

Dr. Antonio Ariza explains: "Before Diamond opened, I had to fly to Grenoble to conduct MX experiments, which was a considerable time investment. Experiments are so quick now, and Diamond makes continuous improvements. I visit Diamond several times every month now. Many of our experiments could be automated, but I like coming in person to get my hands dirty, and to keep up with the changes."

ARH1 and ARH3 are highly specialized enzymes, catalyzing different reactions. However, the results of these experiments show that they are structurally very similar, particularly in terms of their active sites. The new data on these structures will provide insights into their operation, and help us understand their differences. With no known inhibitors for this family of enzymes, the researchers hope that their work will inform future drug discovery. Their findings provide opportunities to design compounds that modulate the activities of ARH enzymes, with great promise for therapeutic potential.

Experiments for this research were carried out on beamlines I03, I04, I04-1, and I24. [21]

## Mayo researchers find off/on switch for DNA repair protein

Damage to DNA is a daily occurrence but one that human cells have evolved to manage. Now, in a new paper published in *Nature Structural & Molecular Biology*, Mayo researchers have determined how one DNA repair protein gets to the site of DNA damage. The authors say they hope this discovery research will help identify new therapies for ovarian cancer.

While the human genome is constantly damaged, cells have proteins that detect and repair the damage. One of those proteins is called 53BP1. It is involved in the repair of DNA when both strands break. In the publication, Georges Mer, Ph.D., a Mayo Clinic structural biologist, and his team report on how 53BP1 relocates to chromosomes to do its job.

Dr. Mer explains that, in the absence of DNA damage, 53BP1 is inactive—blocked by a protein called "TIRR." Using a visualization technique called X-ray crystallography, the authors show that TIRR obstructs an area on 53BP1 that 53BP1 uses to bind chromosomes. But what shifts TIRR away from 53BP1, so the repair protein can work?

The authors theorized that a type of nucleic acid called RNA was responsible for this shift. To test their theory, they engineered a protein that would bind to the 53BP1 repair protein and the RNA molecules released when DNA is damaged. This effort, plus other work detailed in the paper, provides evidence that their idea was sound. The authors report that when DNA damage occurs, RNA molecules

produced at that time can bind to TIRR, displacing it from 53BP1 and allowing 53BP1 to swing into action.

"Our study provides a proof-of-principle mechanism for how RNA molecules can trigger the localization of 53BP1 to DNA damage sites," says Dr. Mer. "The TIRR/RNA pair can be seen as an off/on switch that blocks or triggers 53BP1 relocation to DNA damage sites."

Also in the paper, the authors report that displacing TIRR increases sensitivity of cells in cell culture to olaparib, a drug used to treat patients with ovarian cancer.

"Unfortunately, over time cancer cells develop resistance to drugs in this category, called 'PARP inhibitors.' Our work provides a new target, TIRR, for developing therapeutics that would help specifically kill ovarian cancer cells," Dr. Mer says.

Collaborators on this work include the Dana-Farber Cancer Institute and the Wellcome Trust Centre for Human Genetics at the University of Oxford in the U.K. In addition to Dr. Mer, other Mayo Clinic authors are Maria Victoria Botuyan, Ph.D., Gaofeng Cui, Ph.D., James R. Thompson, Ph.D., Benoît Bragantini, Ph.D., and Debiao Zhao, Ph.D.

The authors report no conflict of interest. Funding for this research was provided by the National Institutes of Health, including the Mayo Clinic Ovarian Cancer Specialized Program of Research Excellence, and the U.S. Department of Defense. Additional funding sources are listed in the publication. [20]

## **Investigators say DNA database can be goldmine for old cases**

A microscopic thread of DNA evidence in a public genealogy database led California authorities to declare this spring they had caught the Golden State Killer, the rapist and murderer who had eluded authorities for decades.

Emboldened by that breakthrough, a number of private investigators are spearheading a call for amateur genealogists to help solve other cold cases by contributing their own genetic information to the same public database. They say a larger array of genetic information would widen the pool to find criminals who have eluded capture.

The idea is to get people to transfer profiles compiled by commercial genealogy sites such as Ancestry.com and 23andMe onto the smaller, public open-source database created in 2010, called GEDmatch. The commercial sites require authorities to obtain search warrants for the information; the public site does not.

But the push is running up against privacy concerns.

"When these things start getting used by law enforcement, it's very important that we ensure that to get all of the benefit of that technology we don't end up giving up our rights," said American Civil Liberties Union legal fellow Vera Eidelman.



She argues that when someone uploads their own DNA profile they aren't just adding themselves—they're adding everyone in their family, including dead relatives and those who haven't been born yet. She also said DNA mining could lead to someone's predisposition to mental and health issues being revealed.

"That one click between Ancestry and 23andMe and GEDmatch is actually a huge step in terms of who has access to your information," Eidelman said.

This month, DNA testing service MyHeritage announced that a security breach revealed details about over 92 million accounts. The information did not include genetic data but nonetheless reinforced anxieties.

Nevertheless, the effort is gaining steam with some genetic genealogy experts and investigators.

The shared DNA profiles "could end up being the key to solving one of these cold cases and getting the family closure and getting someone really dangerous off the streets," said CeCe Moore, the head of the genetic genealogy unit at the DNA company Parabon NanoLabs.

She's uploaded her personal [genetic information](#) to the public database and wants it to become a larger repository of information for genealogy hobbyists and investigators alike. Separately, Parabon NanoLabs has also uploaded DNA data from 100 unsolved crime scenes in hopes of finding suspects.



Private investigator Jason Jensen holds a Phenotype Report at his office Friday, June 15, 2018, in Salt Lake City. Groups of private investigators in Utah and California have been emboldened by the arrest of the suspected Golden State ...[more](#)

Genetic genealogy has traditionally been used to map family histories. Labs analyze hundreds of thousands of genetic markers in an individual's DNA, compare them with others and link up families



based on similarities. The public database was created to compare family trees and genetic profiles between the commercial sites, which don't cross-reference information.

Its potential as a police tool wasn't broadly known until the April arrest of Golden State Killer suspect Joseph DeAngelo in northern California. Prosecutors allege DeAngelo, a former police officer, is responsible for at least a dozen murders and about 50 rapes in the 1970s and '80s.

But the DNA-assisted hunt that led to his arrest wasn't flawless. It initially led authorities to the wrong man whose relative shared a rare genetic marker with crime-scene evidence. A similar thing happened when authorities used a different public DNA database to investigate a nearly two-decade-old Idaho murder in 2014.

In May, Moore used the public database to help police arrest a 55-year-old Washington man linked to the 1987 killing of a young Canadian couple. She suspects the method will lead to dozens of arrests in similar cold cases.

Courts haven't fully explored legal questions around the technique but are likely to allow it based on current law, said attorney and forensic consultant Bicka Barlow. The theory is that an individual's right to privacy does not extend to material they've abandoned, whether it's DNA or trash.

GEDmatch co-creator Curtis Rogers was initially unaware police used his site to find the suspected Golden State Killer. He's glad it's led to solving crimes but is worried about privacy issues. The site's policy was updated in May and says it can't guarantee how results will be used. Users are allowed to remove their information.

A California-based group of volunteers called the DNA Doe Project has also used the database to identify two bodies that stumped authorities for more than a decade. The group encourages its thousands of online supporters to contribute to the [public database](#).

"It's free, it's like three or four clicks and a couple minutes of your time," said co-founder Margaret Press. "It's altruistic if you have no interest in your own family history; if you did, it's a win-win."

A volunteer group of investigators and attorneys called the Utah Cold Case Coalition has made a similar appeal.

The idea may be particularly appealing in Utah, co-founder Jason Jensen suspects. An interest in genealogy is especially strong in the state, because tenets of The Church of Jesus Christ of Latter-day Saints emphasize the importance of family relationships in the afterlife.

"Arguably that one person can post up their DNA and might potentially break a case that somebody back in Nantucket (Massachusetts) is trying to solve," Jensen said. [19]

## **Researchers build DNA replication in a model synthetic cell**

Researchers at Delft University of Technology, in collaboration with colleagues at the Autonomous University of Madrid, have created an artificial DNA blueprint for the replication of DNA in a cell-like

structure. Creating such a complex biological module is an important step towards an even more ambitious goal: building a complete and functioning synthetic cell from the bottom up.

Copying DNA is an essential function of living cells. It allows for cell division and propagation of genetic information to the offspring. The mechanism underlying DNA replication consists of three important steps. First, DNA is transcribed into messenger RNA. Messenger RNA is then translated into proteins—the workhorses of the cell that carry out many of its vital functions. The job of some of these proteins, finally, is to perform the last step in the cycle: the replication (or copying) of DNA. After a cell has replicated its DNA, it can divide into two daughter cells, each containing a copy of the original genetic material.

### Closing the cycle

Researchers had already realized all of the separate steps mentioned above. Japanese scientists, for instance, created a minimal, stand-alone system for messenger RNA and protein synthesis by taking the relevant components from *E. coli* and tweaking them. But no one had yet been able to combine this system with autonomous DNA replication. "We wanted to close the cycle and be the first to reconstruct the entire flow of genetic information inside a cell-like structure called a liposome," said group leader Christophe Danelon.

Combining the Japanese system with a module for DNA replication proved difficult. "We tried a few approaches, but none seemed to work convincingly," said Danelon. Then, Ph.D. student Pauline van Nies came up with the idea to use the DNA replication machinery of a virus called  $\Phi 29$ . "Viruses are very intriguing from a molecular biology point of view," said Van Nies. "They are extremely efficient in encoding proteins in a small genome and in robustly replicating their genetic information." In human cells, DNA replication is managed by hundreds of proteins.  $\Phi 29$  only needs four.

### Composing DNA

Many years ago, researchers working at the Autonomous University of Madrid discovered the DNA replication mechanism of the  $\Phi 29$  virus and managed to isolate it. Van Nies and Danelon worked with these researchers to combine the genes that encode for the replication mechanism with the genetic code that is necessary to operate the Japanese module for transcription and translation.

Van Nies composed a unique DNA blueprint that took into account a number of different factors related to the flow of genetic information, such as a suitable binding site for the ribosome, an element that is essential for the production of proteins.

### Combining machinery

A goal that now comes into view is combining the new module that regulates the flow of genetic information with other essential cellular functions such as growth and division. Last year, the Danelon group created a way to synthesize the phospholipids that make up liposomes, such as the ones the researchers used in this project. The yield of phospholipids was still too small to sustain growth, but Danelon is confident his group can optimize this process.

Cell division may be a tougher nut to crack. In modern cells, it requires a streamlined process in which copied DNA is neatly packed and then evenly distributed towards the poles of the cell. Concurrently, specialized proteins squeeze the mother cell into two daughter cells. Danelon thinks a simple 'budding' mechanism could also do the trick. "I think we can create liposomes that grow until they

start budding. If enough DNA is being produced, hopefully enough of these primitive daughter cells will contain the new DNA to sustain a cell population." This may well be how the very first cells self-reproduced, before evolution equipped them with a more elegant and robust solution.

### **Building a synthetic cell**

The mission that ties together all of the fundamental research described above is the construction of a synthetic cell that can grow, divide and sustain itself. Scientists at Delft University of Technology play a leading role in this exciting new research direction that may ultimately lead to intimate understanding of the inner workings of a cell. Research supporting the initiative could lead to advances in biotechnology, health and energy. [18]

### **Study reveals the inner workings of a molecular motor that packs and unpacks DNA**

DNA is tightly packed into the nucleus of a cell. Nevertheless, the cellular machinery needs to constantly access the genomic information. An LMU team now reveals the inner workings of a molecular motor made of proteins which packs and unpacks DNA.

The genomic DNA of higher organisms is compacted in a highly condensed form known as chromatin. The DNA is tightly wound around a myriad of tiny histone spools called nucleosomes. A single human cell, for instance, accommodates in this manner about two meters of DNA. However, genes must be constantly transcribed into messenger RNAs to direct protein synthesis. Moreover, the entire DNA must be replicated before cell division and DNA damage needs to be repaired. Thus, there must be way to actively grant access to the genome.

This is when chromatin remodelers come into play. Chromatin remodelers have an essential role as they are molecular machines: they unpick and unpack segments of the DNA by sliding nucleosome spools back and forth, replacing individual histones, freeing up the DNA for transcription, and finally compacting it again, when the job is done. Since all of this happens in a highly dynamic fashion, chromatin remodelers enable cells to react rapidly to alterations in their environment – and this holds for brewer's yeast as well as for human cells. In mediating gene accessibility, chromatin remodelers are vital for development and cell differentiation; cell types are defined by the sets of genes they express, remodelers help to determine cell identity.

So far, however, very little is known about what remodeling proteins look like and how they go about doing what they do. In molecular terms, functional remodelers are often very large complexes comprising many different protein components, whose coordinated action makes them akin to molecular machines. These features also make it very difficult to determine their detailed structure. But a team led by Professor Karl-Peter Hopfner, who holds a Chair in Structural Molecular Biology at LMU's Gene Center, has now used cryo-electron microscopy to reconstruct the three-dimensional structure of the nucleosome-sliding remodeler INO80 (which itself consists of 15 subunits) bound to a single nucleosome. "Even with innovative approaches, the best available technology and intensive teamwork, we were always working at the cutting edge," says Dr. Sebastian Eustermann, who worked out the molecular structure of the complex on the basis of electron micrographs of thousands of individual complexes.

By analyzing images of randomly oriented views of the complex formed between INO80 and a nucleosome in the electron micrographs, Hopfner and his team have pieced together its structure at a resolution which has seldom been achieved for a chromatin complex of comparable size. This allowed the researchers to unravel the intricate interaction of the remodeler with its substrate DNA spooled around histones and dissect how the whole machinery works.

From a biochemical point of view, remodelers are responsible for heavy-duty reorganizational tasks. To perform these tasks, they must execute "large-scale conformational changes, which are carried out with astounding precision," says Eustermann. In order to alter the relative positions of nucleosomes, the INO80 complex must first weaken the contacts between the nucleosomal histones and the DNA. A molecular motor which is part of the INO80 complex segmentally detaches the double-stranded DNA from the nucleosome. In doing so, it progressively breaks the contacts that normally keep the DNA tightly wound around the histone particle.

The motor subunit feeds DNA it into the nucleosome. This results in the transient formation of a double-stranded DNA loop that is likely an important intermediate in complex remodeling reactions on the nucleosome. On one hand, the loop exposes some histone proteins that could be replaced by other histones to form a different type of nucleosome. On the other hand, the loop is eventually passed over another subunit and the machine then acts as a ratchet, allowing the nucleosome to "move" on the DNA. Throughout this unpacking process, other subunits in the complex serve to support and stabilize the partially 'denuded' nucleosome itself.

The structure of the complex revealed in the new study sheds new light on the function and mode of action of chromatin remodelers in general. These [molecular machines](#) play an essential part in the workings of the cell by maintaining the flexibility of the [chromatin](#), thus enabling the genetic apparatus to respond dynamically to changing metabolic demands. "Our results provide the first well-founded picture of how they do that," says Hopfner. "Moreover, it has recently become clear that remodelers play a central role in tumorigenesis, because they often misregulated in tumor tissue. So structural and mechanistic insights into their functions will be vital for the future development of new therapies for cancer," he adds. [17]

### **Biomimetic chemistry—DNA mimic outwits viral enzyme**

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

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

has synthesized a helical molecule that mimics surface features of the DNA double helix so closely that bona fide DNA-binding proteins interact with it.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

The activity of the enzyme may be described in a simplified way: Telomerase can be represented as a molecular machine containing an RNA molecule. This machine, with the help of a template part of RNA, binds to the end of a long chain of DNA, and synthesizes a fragment of a new DNA chain along the remaining template fragment. After that, the telomerase machine has to move to the newly synthesized end of the DNA in order to continue to build up the chain. The scientists assume that the TEN-domain allows telomerase to synthesize DNA fragments of strictly defined length, after which the RNA template should be detached from the DNA strand to move closer to its edge. Thus, the TEN domain facilitates the movement of the enzyme to building up a new region, i.e. the next telomeric fragment, and this is how the synthesis cycle is repeated.

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

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

### **Custom sequences for polymers using visible light**

Researchers from Tokyo Metropolitan University used a light-sensitive iridium-palladium catalyst to make "sequential" polymers, using visible light to change how building blocks are combined into polymer chains. By simply switching the light on or off, they were able to realize different compositions along the polymer chain, allowing precise control over physical properties and material



function. This may drastically simplify existing polymer production methods, and help overcome fundamental limits in creating new polymers.

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

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

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

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

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

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

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

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

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

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

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

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

They tested these artificial cells in a solution high in copper, which is usually highly toxic to biological cells. The team were still able to detect fluorescent chemicals in the majority of the artificial cells, meaning the biological cells were still alive and functioning inside. This ability would be useful in the human body, where the artificial cell casing would protect the foreign biological cells from attack by the body's immune system.

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

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

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

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

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

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

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

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

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

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

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

## Particles in charged solution form clusters that reproduce

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

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

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

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

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

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

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

## Experiment demonstrates quantum mechanical effects from biological systems

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

In the new study, the team used x-ray crystallography to work out the crystal structure of the 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 self-reproducing quantum entangled prebiotic kernel systems and minimal cells also impacts the possibility of the most probable path of emergence of photocells on the Earth or elsewhere. We also examine the quantum entangled logic gates discovered in the modeled systems composed of two prebiotic kernels. Such logic gates may have application in the destruction of cancer cells or becoming building blocks of new forms of artificial cells including magnetically active ones.

## Significance Statement

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

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



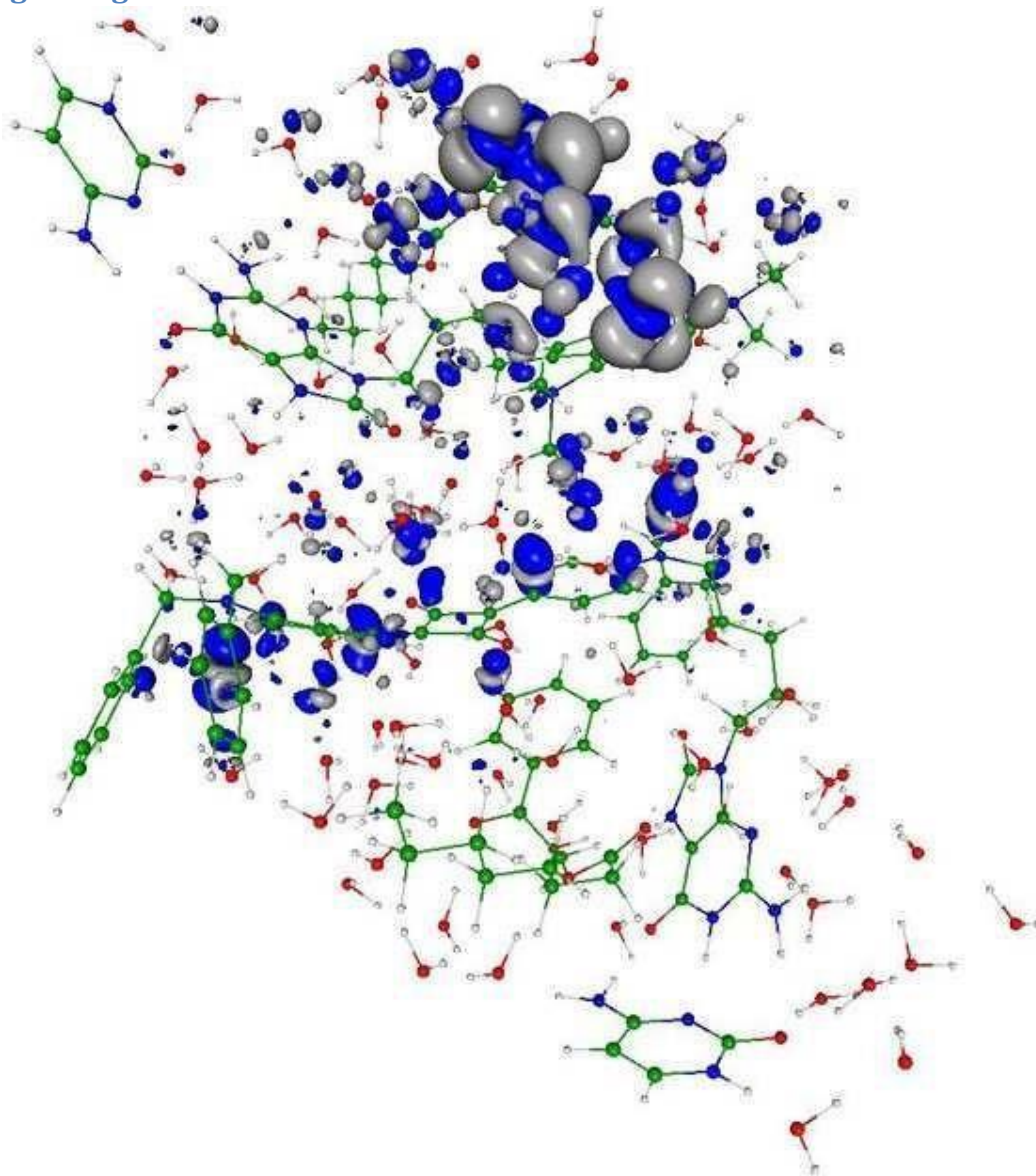
Our discovered phenomenon of the quantum entanglement in the prebiotic systems enhance the photosynthesis in the proposed systems because simultaneously excite two prebiotic kernels in the system by appearance of two additional quantum entangled excited states (Tamulis A, Grigalavicius M, Baltrusaitis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

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

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

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

## Figure legend



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

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

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

enhanced tunneling of photo excited electrons from the sensitizer squaraine and (1,4bis(N,Ndimethylamino)naphthalene) to the pFA molecule resulting in its cleavage. The new fatty acid joins the existing minimal cell thus increasing it in size. After reaching some critical size, the minimal cell should divide (i.e. self-replicate) into two separate smaller minimal cells. [7]

## Quantum Biology

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

## Quantum Consciousness

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

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

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

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

## Creating quantum technology

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

## Quantum Entanglement

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

## The Bridge

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

## Accelerating charges

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

## Relativistic effect

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

## Heisenberg Uncertainty Relation

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

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

## Wave - Particle Duality

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

## Atomic model

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

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

## The Relativistic Bridge

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

## The weak interaction

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

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

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

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

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

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

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

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

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

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

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

## The General Weak Interaction

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

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



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

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

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

## Fermions and Bosons

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

## Van Der Waals force

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

## Electromagnetic inertia and mass

### Electromagnetic Induction

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

### Relativistic change of mass

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

### The frequency dependence of mass

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

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

### **Electron – Proton mass ratio**

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

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

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

### **The Gravitational force**

The gravitational attractive force is basically a magnetic force.

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

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

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

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

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

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

There is an asymmetry between the mass of the electric charges, for example proton and electron, can be understood by the asymmetrical Planck Distribution Law. This temperature dependent energy

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

## The Higgs boson

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

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

## Higgs mechanism and Quantum Gravity

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

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

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

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

### What is the Spin?

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

### The Graviton

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

### Conclusions

Exists experimental evidence for quantum-coherent is used for more efficient light-harvesting in plant photosynthesis. Quantum entanglement exists in supramolecules determining the sense of smell and in the brain neurons microtubules due to quantum vibrations.

In the work presented here, we started to design and quantum mechanical investigations of the molecular logical devices which are useful for construction of nano medicine biorobots against the molecular diseases such a cancer tumors, and against the new kinds of synthesized microorganisms and nano guns. [7]

One of the most important conclusions is that the electric charges are moving in an accelerated way and even if their velocity is constant, they have an intrinsic acceleration anyway, the so called spin, since they need at least an intrinsic acceleration to make possible they movement . The accelerated charges self-maintaining potential shows the locality of the relativity, working on the quantum level also. [1]

The bridge between the classical and quantum theory is based on this intrinsic acceleration of the spin, explaining also the Heisenberg Uncertainty Principle. The particle – wave duality of the electric charges and the photon makes certain that they are both sides of the same thing. The

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

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

Basing the gravitational force on the accelerating Universe caused magnetic force and the Planck Distribution Law of the electromagnetic waves caused diffraction gives us the basis to build a Unified Theory of the physical interactions also.

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