

Protein Error-Free Nanostructures

Using a DNA-binding protein called RecA as a kind of nanoscale rebar, or reinforcing bar, to support the floppy DNA scaffolding, researchers at the National Institute of Standards and Technology (NIST) have constructed several of the largest rectangular, linear and other shapes ever assembled from DNA. [25]

The technique, dubbed DNA origami, enabled scientists to create self-assembling DNA structures that could carry any specified pattern, such as a 100-nanometer-wide smiley face. [24]

For the past few decades, scientists have been inspired by the blueprint of life, DNA, as the shape of things to come for nanotechnology. [23]

The new study involves innovations in the field of DNA origami, which, as the name implies, uses nucleic acids like DNA and RNA to fold and self-assemble into complex forms. [22]

In a new study that supports the trend of DNA-based information carriers, scientists have engineered a DNA navigator system that can perform single-molecule, parallel, depth-first search operations on a two-dimensional origami platform. [21]

In new research, Hao Yan of Arizona State University and his colleagues describe an innovative DNA [HYPERLINK "https://phys.org/tags/walker/"](https://phys.org/tags/walker/) walker, capable of rapidly traversing a prepared track. [20]

Just like any long polymer chain, DNA tends to form knots. Using technology that allows them to stretch DNA molecules and image the behavior of these knots, MIT researchers have discovered, for the first time, the factors that determine whether a knot moves along the strand or "jams" in place. [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 ratio and the Weak and Strong Interactions by the diffraction patterns. The Weak Interaction changes the diffraction patterns by moving the electric charge from one side to the other side of the diffraction pattern, which violates the CP and Time reversal symmetry.

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

Contents

Preface	5
Protein 'rebar' could help make error-free nanostructures	6
Scientists 'paint' the world's smallest Mona Lisa on the world's largest DNA canvas	7
Spaghetti-like, DNA 'noodle origami' the new shape of things to come for nanotechnology ...	9
Size matters	10
Form and function	11
A new design school	12
Tying the knot: New DNA nanostructures	13
Bringing DNA into the fold	13
Nature's knots	14
Designer DNA (and RNA)	15
Solving mazes with single-molecule DNA navigators	16
Built for speed: DNA nanomachines take a (rapid) step forward	20
Building with DNA	20
Race walking	22
Freewheeling nanorobot	22
Future steps	22
Chemical engineers discover how to control knots that form in DNA molecules	23
Knots in motion	23
Knot removal	24
Researchers build DNA replication in a model synthetic cell	24

Closing the cycle.....	25
Composing DNA	25
Combining machinery	25
Building a synthetic cell	26
Study reveals the inner workings of a molecular motor that packs and unpacks DNA.....	26
Biomimetic chemistry—DNA mimic outwits viral enzyme	27
Simulations document self-assembly of proteins and DNA.....	28
Scientists explore the structure of a key region of longevity protein telomerase	29
Custom sequences for polymers using visible light.....	30
Artificial and biological cells work together as mini chemical factories	31
New interaction mechanism of proteins discovered	32
Particles in charged solution form clusters that reproduce.....	34
Experiment demonstrates quantum mechanical effects from biological systems.....	34
Quantum biology: Algae evolved to switch quantum coherence on and off	36
Photoactive Prebiotic Systems	37
Significance Statement.....	37
Figure legend.....	39
Quantum Biology.....	40
Quantum Consciousness.....	40
Creating quantum technology	41
Quantum Entanglement	41
The Bridge.....	42
Accelerating charges	42
Relativistic effect.....	42
Heisenberg Uncertainty Relation	42
Wave – Particle Duality	42
Atomic model	42
The Relativistic Bridge	43
The weak interaction.....	43
The General Weak Interaction.....	44
Fermions and Bosons	45
Van Der Waals force	45
Electromagnetic inertia and mass.....	45
Electromagnetic Induction	45
Relativistic change of mass	45

The frequency dependence of mass	45
Electron – Proton mass rate	46
Gravity from the point of view of quantum physics	46
The Gravitational force	46
The Higgs boson	47
Higgs mechanism and Quantum Gravity	47
What is the Spin?.....	48
The Graviton	48
Conclusions.....	48
References.....	49

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.

Protein 'rebar' could help make error-free nanostructures

DNA is the stuff of life, but it is also the stuff of nanotechnology. Because molecules of DNA with complementary chemical structures recognize and bind to one another, strands of DNA can fit together like Lego blocks to make nanoscale objects of complex shape and structure.

But researchers need to work with much larger assemblages of DNA to realize a key goal: building durable miniature devices such as biosensors and drug-delivery containers. That's been difficult because long chains of DNA are floppy and the standard method of assembling long chains is prone to error.

Using a DNA-binding protein called RecA as a kind of nanoscale rebar, or reinforcing bar, to support the floppy DNA scaffolding, researchers at the National Institute of Standards and Technology (NIST) have constructed several of the largest rectangular, linear and other shapes ever assembled from DNA. The structures can be two to three times larger than those built using standard DNA self-assembly techniques.

In addition, because the new method requires fewer chemically distinct pieces to build organized structures than the standard technique, known as DNA origami, it is likely to reduce the number of errors in constructing the shapes. That's a big plus for the effort to produce reliable DNA-based devices in large quantities, said NIST researcher Alex Liddle.

Although RecA's ability to bind to double-stranded DNA has been known for years, the NIST team is the first to integrate filaments of this protein into the assembly of DNA structures. The addition of RecA offers a particular advantage: Once one unit of the protein binds to a small segment of double-stranded DNA, it automatically attracts other units to line up alongside it, in the same way that bar magnets will join end-to-end. Like bricks filling out a foundation, RecA lines the entire length of the DNA strand, stretching, widening and strengthening it. A floppy, 2-nanometer-wide strand of DNA can transform into a rigid structure more than four times as wide.

"The RecA method greatly extends the ability of DNA self-assembly methods to build larger and more sophisticated structures," said NIST's Daniel Schiffels.

Schiffels, Liddle and their colleague Veronika Szalai describe their work in a recent article in *ACS Nano*.

The new method incorporates the DNA origami technique and goes beyond it, according to Liddle. In DNA origami, short strands of DNA that have a specific sequence of four base pairs are used as staples to tie together long sections of DNA. To make the skinny DNA skeleton stronger and thicker, the strand may loop back on itself, quickly using up the long string.

If DNA origami is all about the folding, Liddle likened his team's new method to building a room, starting with a floor plan. The location of the short, single-stranded pieces of DNA that act as staples mark the corners of the room. Between the corners lies a long, skinny piece of single-stranded DNA. The enzyme DNA polymerase transforms a section of the long piece of single-stranded DNA into the double-stranded version of the molecule, a necessary step because RecA only binds strongly to double-stranded DNA. Then RecA assembles all along the double strand, reinforcing the DNA [structure](#) and limiting the need for extra staples to maintain its shape.

With fewer staples required, the RecA method is likely able to build organized structures with fewer errors than DNA origami, Liddle said. [25]

Scientists 'paint' the world's smallest Mona Lisa on the world's largest DNA canvas

In 2006, Caltech's Paul Rothemund (BS '94)—now research professor of bioengineering, computing and mathematical sciences, and computation and neural systems—developed a method to fold a long strand of DNA into a prescribed shape. The technique, dubbed DNA origami, enabled scientists to create self-assembling DNA structures that could carry any specified pattern, such as a 100-nanometer-wide smiley face.

DNA origami revolutionized the field of nanotechnology, opening up possibilities of building tiny molecular devices or "smart" programmable materials. However, some of these applications require much larger DNA origami structures.

Now, scientists in the laboratory of Lulu Qian, assistant professor of bioengineering at Caltech, have developed an inexpensive method by which DNA origami self-assembles into large arrays with entirely customizable patterns, creating a sort of canvas that can display any image. To demonstrate this, the team created the world's smallest recreation of Leonardo da Vinci's Mona Lisa—out of DNA.

The work is described in a paper appearing in the December 7 issue of the journal *Nature*.

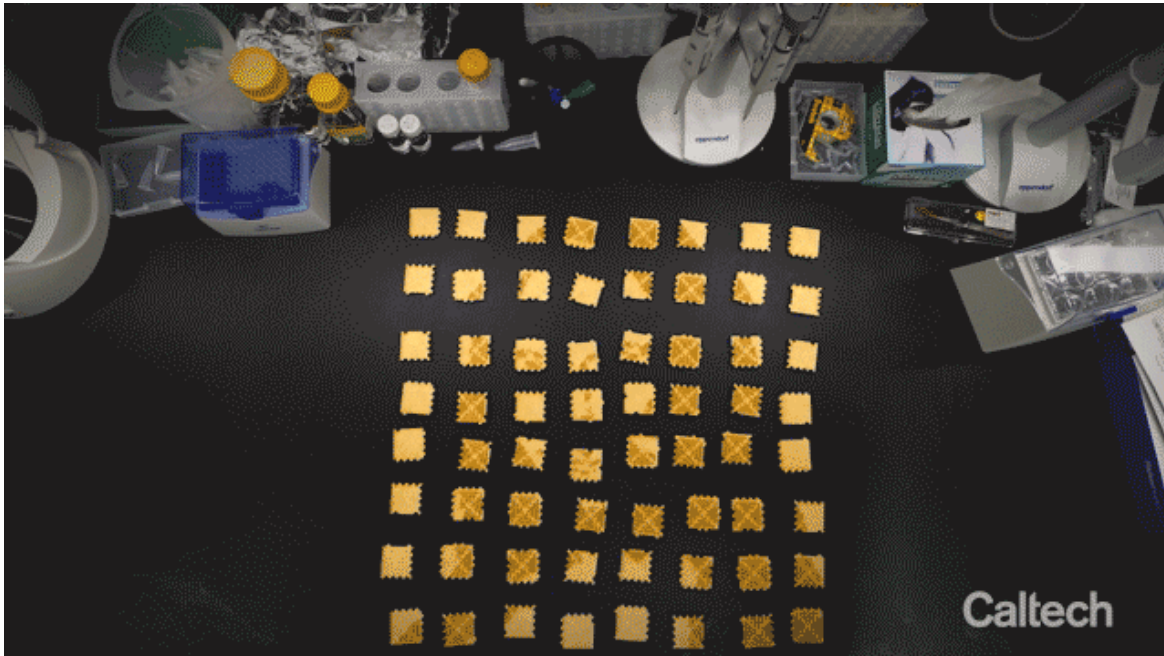
While DNA is perhaps best known for encoding the genetic information of living things, the molecule is also an excellent chemical building block. A single-stranded DNA molecule is composed of smaller molecules called nucleotides—abbreviated A, T, C, and G—arranged in a string, or sequence. The nucleotides in a single-stranded DNA molecule can bond with those of another single strand to form double-stranded DNA, but the nucleotides bind only in very specific ways: an A nucleotide with a T or a C nucleotide with a G. These strict base-pairing "rules" make it possible to design DNA origami.

To make a single square of DNA origami, one just needs a long single strand of DNA and many shorter single strands—called staples—designed to bind to multiple designated places on the long strand. When the short staples and the long strand are combined in a test tube, the staples pull regions of the long strand together, causing it to fold over itself into the desired shape. A large DNA canvas is assembled out of many smaller square origami tiles, like putting together a puzzle. Molecules can be selectively attached to the staples in order to create a raised pattern that can be seen using atomic force microscopy.

The Caltech team developed software that can take an image such as the Mona Lisa, divide it up into small square sections, and determine the DNA sequences needed to make up those squares. Next, their challenge was to get those sections to self-assemble into a superstructure that recreates the Mona Lisa.

"We could make each tile with unique edge staples so that they could only bind to certain other tiles and self-assemble into a unique position in the superstructure," explains Grigory Tikhomirov, senior postdoctoral scholar and the paper's lead author, "but then we would have to have hundreds of unique edges, which would be not only very difficult to design but also extremely expensive to

synthesize. We wanted to only use a small number of different edge staples but still get all the tiles in the right places."



The process of fractal assembly, using wooden puzzle pieces. Credit: Caltech

The key to doing this was to assemble the tiles in stages, like assembling small regions of a puzzle and then assembling those to make larger regions before finally putting the larger regions together to make the completed puzzle. Each mini puzzle utilizes the same four edges, but because these puzzles are assembled separately, there is no risk, for example, of a corner tile attaching in the wrong corner. The team has called the method "fractal assembly" because the same set of assembly rules is applied at different scales.

"Once we have synthesized each individual tile, we place each one into its own test tube for a total of 64 tubes," says Philip Petersen, a graduate student and co-first author on the paper. "We know exactly which tiles are in which tubes, so we know how to combine them to assemble the final product. First, we combine the contents of four particular tubes together until we get 16 two-by-two squares. Then those are combined in a certain way to get four tubes each with a four-by-four square. And then the final four tubes are combined to create one large, eight-by-eight square composed of 64 tiles. We design the edges of each tile so that we know exactly how they will combine."

The Qian team's final structure was 64 times larger than the original DNA origami structure designed by Rothemund in 2006. Remarkably, thanks to the recycling of the same edge interactions, the number of different DNA strands required for the assembly of this DNA superstructure was about the same as for Rothemund's original origami. This should make the new method similarly affordable, according to Qian.

"The hierarchical nature of our approach allows using only a small and constant set of unique building blocks, in this case DNA strands with unique sequences, to build structures with increasing sizes and, in principle, an unlimited number of different paintings," says Tikhomirov. "This economical approach

of building more with less is similar to how our bodies are built. All our cells have the same genome and are built using the same set of building blocks, such as amino acids, carbohydrates, and lipids. However, via varying gene expression, each cell uses the same building blocks to build different machinery, for example, muscle cells and cells in the retina."

The team also created software to enable scientists everywhere to create DNA nanostructures using fractal assembly.

"To make our technique readily accessible to other researchers who are interested in exploring applications using micrometer-scale flat DNA nanostructures, we developed an online software tool that converts the user's desired image to DNA strands and wet-lab protocols," says Qian. "The protocol can be directly read by a liquid-handling robot to automatically mix the DNA strands together. The DNA nanostructure can be assembled effortlessly."

Using this online software tool and automatic liquid-handling techniques, several other patterns were designed and assembled from DNA strands, including a life-sized portrait of a bacterium and a bacterium-sized portrait of a rooster.

"Other researchers have previously worked on attaching diverse molecules such as polymers, proteins, and nanoparticles to much smaller DNA canvases for the purpose of building electronic circuits with tiny features, fabricating advanced materials, or studying the interactions between chemicals or biomolecules," says Petersen. "Our work gives them an even larger canvas to draw upon." [24]

Spaghetti-like, DNA 'noodle origami' the new shape of things to come for nanotechnology

For the past few decades, scientists have been inspired by the blueprint of life, DNA, as the shape of things to come for nanotechnology.

This burgeoning field is called DNA origami. Scientist borrowed its moniker from the paper artists who conjure up birds, flowers and planes from imaginatively folding a single sheet of paper.

Similarly, DNA origami scientists are dreaming up a variety of shapes —at a scale one thousand times smaller than a human hair—that they hope will one day revolutionize computing, electronics and medicine.

Now, a team of Arizona State and Harvard scientists has invented a major new advance in DNA nanotechnology. Dubbed "single-stranded origami," their new strategy uses one long, thin noodle-like strand of DNA, or its chemical cousin RNA, that can self-fold —without even a single knot —into the largest, most complex structures to date.

And, the strands forming these structures can be made inside living cells or using enzymes in a test tube, allowing scientists the potential to plug-and-play with new designs and functions for nanomedicine—like tiny, nanobots playing doctor and delivering drugs within cells to the site of injury.

"I think this is an exciting breakthrough, and a great opportunity for synthetic biology as well," said Hao Yan, a co-inventor of the technology, director of the ASU Biodesign Institute's Center for Molecular Design and Biomimetics, and the Milton Glick Professor in the School of Molecular Sciences.

"We are always inspired by nature's designs to make information-carrying molecules that can self-fold into the nanoscale shapes we want to make,"

As proof of concept, they've pushed the envelope to make Emoji-like smiley faces, hearts, triangle shapes—18 shapes in total— that significantly expand the design studio space and material scalability for so-called, "bottom-up" nanotechnology.

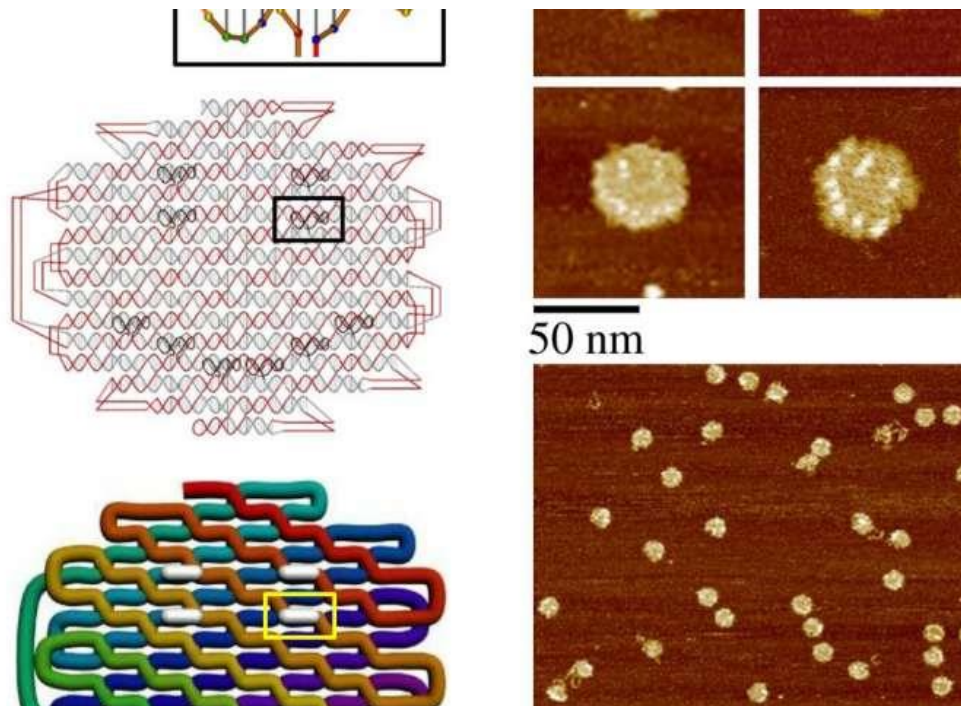
Size matters

To date, DNA nanotechnology scientists have had to rely on two main methods for making spatially addressable structures with finite dimensions.

The first was molecular bricks, small, short pieces of DNA that can fold together to make a single structure. The second method was scaffolded DNA, where a single strand is shaped into a structure by using helper strands of DNA, that staple the structure into place.

"These two methods are not very scalable in terms of synthesis," said Fei Zhang, a senior co-author on the paper. "When you have so many short pieces of DNA, you can't replicate it using biological systems. One way around this is to engineer one long strand that could fold itself into any design or architecture."

Furthermore, each method has been limited because as the size of the structure increases, the ability to fold correctly becomes more challenging.



A DNA origami with an emoji-like smiley face. Credit: Biodesign Institute, Arizona State University

Now, there is a new third way.

For Yan and his team to make their breakthrough, they had to go back to the drawing board, which meant looking at nature again for inspiration. They found what they were looking for with a chemical cousin of DNA, in the form of complex, RNA structures.

The complex RNA structures discovered to date contain single-stranded RNA molecules that self-fold into structures without any topological knots. Could this trick work again for single-stranded DNA or RNA origami?

They were able to crack the code of how RNA makes structures to develop a fully programmable single-stranded origami architecture.

"The key innovation of our study is to use DNA and RNA to construct a structurally complex yet knot-free structure that can be folded smoothly from a single strand," Yan said. "This gave us a design strategy to allow us to fold one long strand into complex architecture."

"With help from a computer scientist in the team, we could also codify the design process as a mathematically rigorous formal algorithm and automate the design by developing a user-friendly software tool," said Yan.

The algorithm and software were validated by the automated design and experimental construction of six distinct DNA ssOrigami structures (four rhombuses and two heart shapes).

Form and function

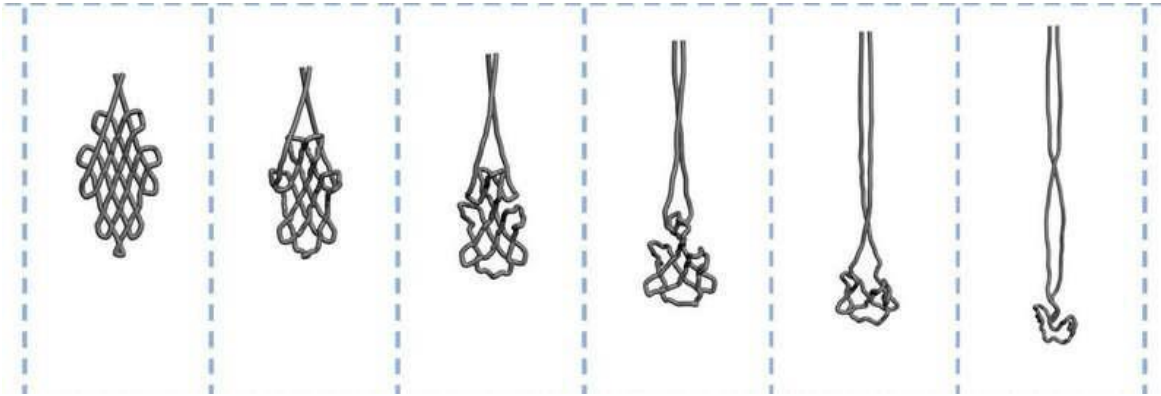
It's one thing to make crafty patterns and smiley faces with DNA, but critics of DNA origami have been wondering when the practical applications would come about.

Now, these are possible. "I think we are much closer to real practical applications of the technology," said Yan. "We are actively looking at the first nanomedicine applications with our ssOrigami technology."

They were also able to demonstrate that a folded ssOrigami structure can be melted and used as a template for amplification by DNA copying enzymes in a test tube and that the ssOrigami strand can be replicated and amplified via clonal production in living cells.

"Single-stranded DNA nanostructures formed via self-folding offer greater potential of being amplifiable, replicable, and clonable, and hence the opportunity for cost-efficient, large-scale production using enzymatic and biological replication, as well as the possibility for using in vitro evolution to produce sophisticated phenotypes and functionalities," said Yan.

These same design rules could be used for DNA's chemical cousin, RNA.



Model of unravelling ssOrigami under simulated gravity. Credit: D. Han et al., *Science* (2017)

A key design feature of single-stranded origami (ssOrigami) is that the strand can be made and copied in the lab and in living cells and subsequently folded into designer structures by heating and cooling the DNA.

To make it inside the lab, they used the photocopy of cloning sequences, called PCR, to replicate and produce ssDNA.

Inside living cells, they first placed it inside a mule of molecular cloning, called a plasmid, after it was placed into a common lab bacteria called *E. coli* cells. When they treated the bacteria with enzymes to free up the ssDNA, they could isolate it, and then fold it into its target structure.

"Because plasmid DNA can be easily replicated in *E. coli*, the production can be scaled up by growing a large volume of *E. coli* cells with low cost," said Yan. This gets around the constraint of having to synthesize all of the DNA in the lab from scratch, which is far more expensive.

It also moves them in a direction now, where they can potentially make the structures inside of cells.

"Here we show bacteria to make the strand, but still need to do thermal annealing outside the bacteria to form the structure," said Yan. "The ideal situation would be to design an RNA sequence that can get transcribed inside the bacteria, and fold inside the bacteria so we can use bacteria as a nanofactory to produce the material."

Here, they demonstrated a framework to design and synthesize a single DNA or RNA strand to efficiently self-fold into an unknotted compact ssOrigami structure that approximates any arbitrary user-prescribed target shape.

"Its single-strandedness enabled the demonstration of facile replication of the strand in vitro and in living cells, and its programmability allowed us to codify the design process and develop a simple web-based automated design tool."

A new design school

In the software (see <http://dna.kwonan.com/>), made through a collaboration with BioNano Research Group, Autodesk Research, first, the user selects a target shape, which is converted into pixelated representation. The user can upload a 2D image or draw a shape using a 2D pixel design editor.

The user can optionally add DNA hairpins or loops, which can serve as surface markers or handles for attaching external entities. The pixels are converted into DNA helical domains and locking domains to do the folding. The software will then generate ssOrigami structures and sequences, and the user can view the molecular structure via an embedded molecular viewer. Finally, the DNA sequence is assigned to the cycle strand, and the expected folded [structure](#) manufactured in the lab and visually confirmed by viewing it under a powerful microscope that are the eyes of nanotechnology, atomic force microscopy, or AFM.

"We've really scaled up the complexity while scaling down the costs," said Yan. "This study significantly expands the design space and scalability for bottom-up nanotechnology, and opens the door for health applications." [23]

Tying the knot: New DNA nanostructures

Knots are indispensable tools for such human activities as sailing, fishing and rock climbing, (not to mention, tying shoes). But tying a knot in a lacelike strand of DNA, measuring just billionths of a meter in length, requires patience and highly specialized expertise.

Hao Yan, a researcher at ASU, is a practiced hand in this delicate and exotic field, operating at the crossroads of nanotechnology and fine art.

In new research appearing in the journal *Nature Communications*, Yan and his colleagues Fei Zhang, Xiaodong Qi and others describe a method for coaxing segments of single-stranded DNA into complex 2- and 3-D knotted structures.

The results represent an important advance in the fast-paced field of DNA nanotechnology, in which the molecule of life is used as a structural building material for a vast array of tiny configurations. Among these are miniscule robotic devices, photonic applications, drug delivery systems, logic gates, as well as diagnostic and therapeutic applications.

"The knotted DNA structures demonstrated in this work exhibit unprecedented topological complexity, far beyond what has been achieved before using single stranded folding," Yan says. "Indeed, it is not only amazing but also surprising that the single-stranded DNA and RNA can thread through its own chains and find a way to form such highly knotted structures, given the fact that the single strand has to weave through so many tangles."

Yan directs the Biodesign Center for Molecular Design and Biomimetics and is the Martin D. Glick Distinguished Professor in the School of Molecular Sciences at ASU.

Bringing DNA into the fold

The new study involves innovations in the field of DNA origami, which, as the name implies, uses nucleic acids like DNA and RNA to fold and self-assemble into complex forms. This occurs when complementary nucleotide bases in DNA's 4-letter alphabet come in contact and bind, according to a strict regimen: C bases always pair with G and A bases always pair with T.

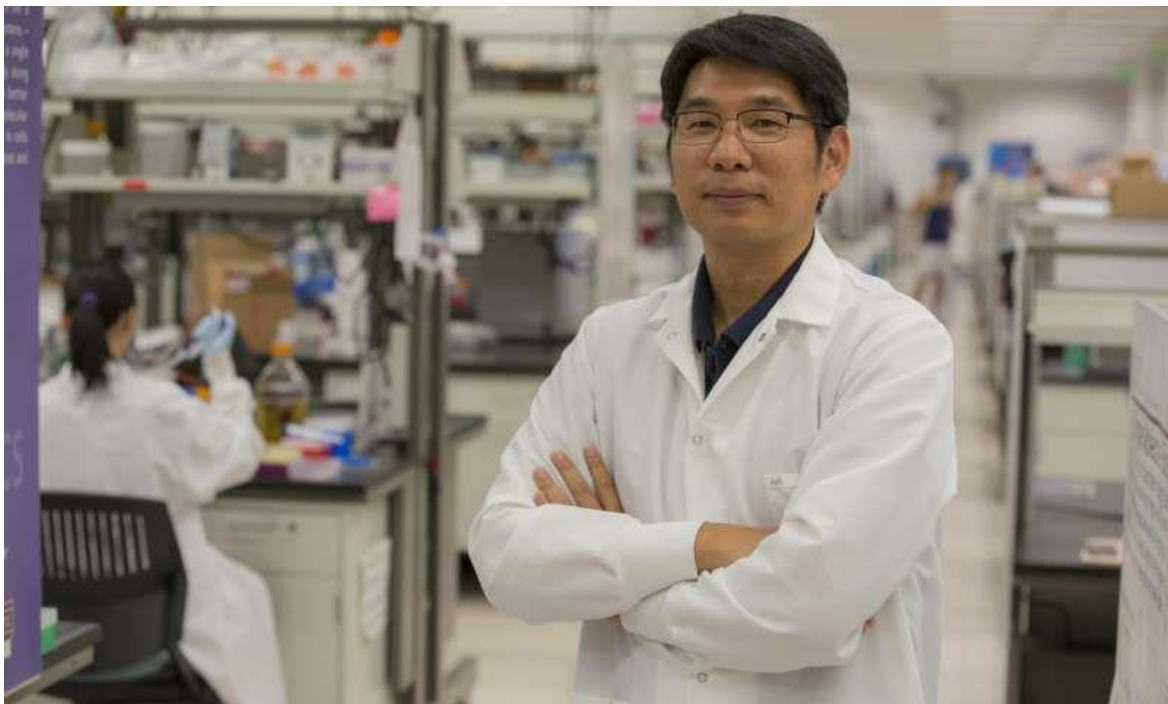
In nature, strings of nucleic acids provide the code needed to make complex proteins. This basic biology provides the underpinning for all earthly life. Taking advantage of the simple base-pairing

properties of DNA, it is possible to design structures that will self-assemble in the lab. The method has been applied to both single-stranded and double-stranded DNA forms, resulting in nanostructures of increasing complexity and sophistication.

While DNA origami has made startling advances since its inception, one technical innovation has been vexingly difficult to achieve. Until now, creating complex knotted structures in DNA in a predictable and programmable way has eluded researchers.

The new work overcomes this hurdle, establishing precise design rules that permit single-stranded segments of DNA (or RNA) ranging from 1800-7500 nucleotides to form knot-like nanostructures with crossing numbers (where the DNA strand weaves in and out of its own length) ranging from 9 to 57.

The group further demonstrated that these nucleic acid nanostructures can be replicated and amplified, both under laboratory conditions and within living systems.



Hao Yan directs the Biodesign Center for Molecular Design and Biomimetics and is the Martin D. Glick Distinguished Professor in the School of Molecular Sciences at ASU. Credit: Biodesign Institute

Nature's knots

Knotted structures, like those Yan has fabricated, (but much simpler than the synthetic ones), have correlates in the natural world. They have been observed in DNA and proteins and generally form during replication and transcription, (when a DNA sequence is copied into messenger RNA). They can also occur in the genomes of phages—viruses that infect bacterial cells.

Nevertheless, the construction of molecular knots at the nanometer scale, displaying well-defined and consistent geometries requires enormous control and precision. As it happens, nucleic acids like DNA are ideal for the design and synthesis of such molecular knots.

Previously, lengths of double-stranded DNA have been used for nanoscale constructions, with the addition of short pieces or "staple strands" to fasten resulting structures together. The new study instead uses a single length of DNA designed to wrap around itself in a precise, pre-programmed sequence of steps.

Once the knotted DNA nanostructures successfully assemble themselves, they are imaged using atomic force microscopy. Careful calculation allows the researchers to optimize the folding pathways to produce the highest yield for each synthetic structure. The use of single- rather than double-stranded DNA allows the structures to be produced in abundance at much lower cost.

A single-stranded approach opens the door for the design of nanoarchitectures with specific, well-defined functions, which can be produced through successive rounds of in vitro evolution, where desired attributes are selected for in a repetitive process of refinement. Further, the approach outlined in the new study provides a general platform for the design of molecular structures of increased size and unprecedented complexity, paving the way for advances in nanophotonics, drug delivery, cryo-EM analysis and DNA-based memory storage.

Designer DNA (and RNA)

For one of the initial knot designs the strategy Yan and his colleagues developed involved threading a single strand of DNA or RNA through itself 9 times according to a pre-programmed sequence, demonstrating that the new method is capable of producing intricate geometric shapes that are programmable, replicable and scalable.

The design strategy was subsequently expanded to include single-stranded RNA structures and 3-D DNA knots, whose forms were reconstructed using a technique known as cryogenic transmission electron microscopy, confirming their proper folding into the desired shapes.

"One of the challenges in this work is how to increase the assembly yield of highly knotted structures." Said Fei. Unlike classic DNA nanostructures, the single-stranded knots are less forgiving in terms of precise folding order due to the topological complexity. If a single crossing is misfolded during the process, the error will hardly be self-corrected and most of the misfoldings will remain in the completed structure. "We developed a hierarchical folding strategy to guide the correct formation of knots. We compared the folding efficiency of a knot with 23 crossings by using different folding pathways. The AFM images showed a dramatic increase in the folding yield of well-form structures from 0.9% to 57.9% by applying optimized hierarchical folding pathway." Fei added.

The design rules used to optimize the folding pathways are based on the number of crossing points, the length of DNA and the number of base pairs in the designed structure. Three primary rules were established. First, linear folding paths were found to be preferable to branched paths. Second, the unfolded section of a DNA strand should not thread through itself in the early stages when the strand is still long. Finally, edges of the desired form that have three crossings should fold before those with two crossings.

Following the design strategy, the team was able to create more complex DNA knots with increasing crossing numbers.

Longer chains of single-stranded DNA pose unique challenges for designing programmed nanostructures due to the increased likelihood of unintended self-complementarity of the bases making up the chain. A DNA knot [structure](#) boasting 57 crossed nodes successfully assembled, though with lower yield and less precision. When the crossing number was increased to 67, the yield significantly dropped and the resulting structures, imaged by AFM, showed more errors of assembly.

The study reports the largest DNA knots yet assembled, formed from up to 7.5k bases, featuring the most complicated topologies, with up to 57 crossing regions. The single-stranded DNA sequences can be mass produced in living cells for greater efficiency at lower cost. Ultimately, DNA nanostructures of diverse function may be formed within cells, innovations to be pursued in future work. [22]

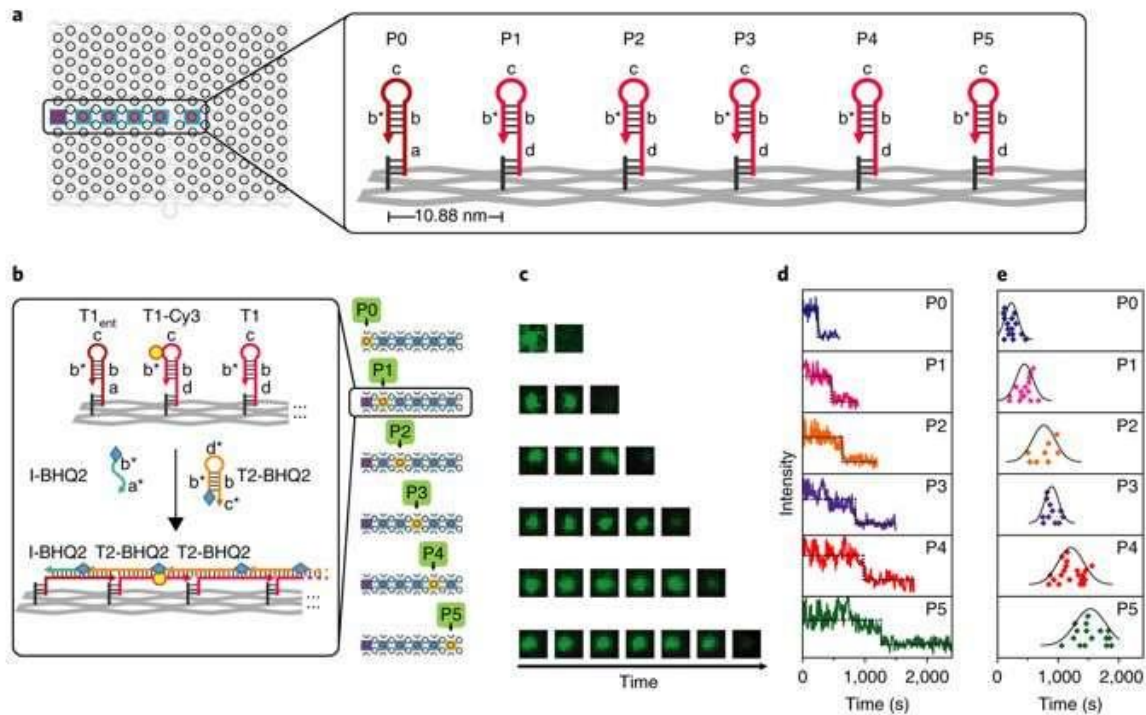
Solving mazes with single-molecule DNA navigators

The field of intelligent nanorobotics is based on the great promise of molecular devices with information processing capabilities. In a new study that supports the trend of DNA-based information carriers, scientists have engineered a DNA navigator system that can perform single-molecule, parallel, depth-first search operations on a two-dimensional origami platform.

Pathfinding operations with DNA navigators make use of a localized strand exchange cascade process initiated at a unique trigger site on the origami platform. Automatic progression along paths is enabled by DNA hairpins containing a universal traversal sequence. By design, each single-molecule navigator can autonomously explore any of the possible paths through a 10-vertex rooted tree constructed in the study. The mazes were equivalent to a tree with an entrance at the root and an exit through one of the leaves. The study conducted by Jie Chao and co-workers resulted in exploring all paths taken by the DNA navigators to extract a specific solution path that connected a given pair of start and end vertices in the maze. As a result, the solution path was laid plainly on the origami platform and illustrated using single-molecule imaging. The approach is now published in *Nature Materials*, detailing the realization of molecular materials with embedded biomolecular computational functions to operate at the level of the single-molecule with potential to engineer intelligent nanorobots for future applications in industry and medicine.

Sophisticated molecular tools were used in the past to [create molecular machines](#) that convert chemical, photonic or electric energy into rotary or linear movements at the nanoscale. For instance, Brownian motion at the nanoscale can be controllably converted into directed movements within [DNA-based nanomachines](#) using DNA hybridization reactions. Such [DNA-based machines](#) operate autonomously by following an embedded 'molecular program' pre-designed as a cascade reaction manually triggered via an external stimulus for each step of the operation.

The focus of the field has progressively shifted to actualize DNA-based logic circuits using aptamers and DNazymes to design [molecular logic gates](#). For example, in 2006, Stojanovic and co-workers integrated more than 100 DNA logic gates to engineer an automation called [MAYA-II](#) to play a game of Tic-Tac-Toe. Preceding studies demonstrated an [enzyme free computing system](#) based on hybridization chain reactions (HCR) to create logic-gates and logic circuits for more robust and efficient performance than the original systems.



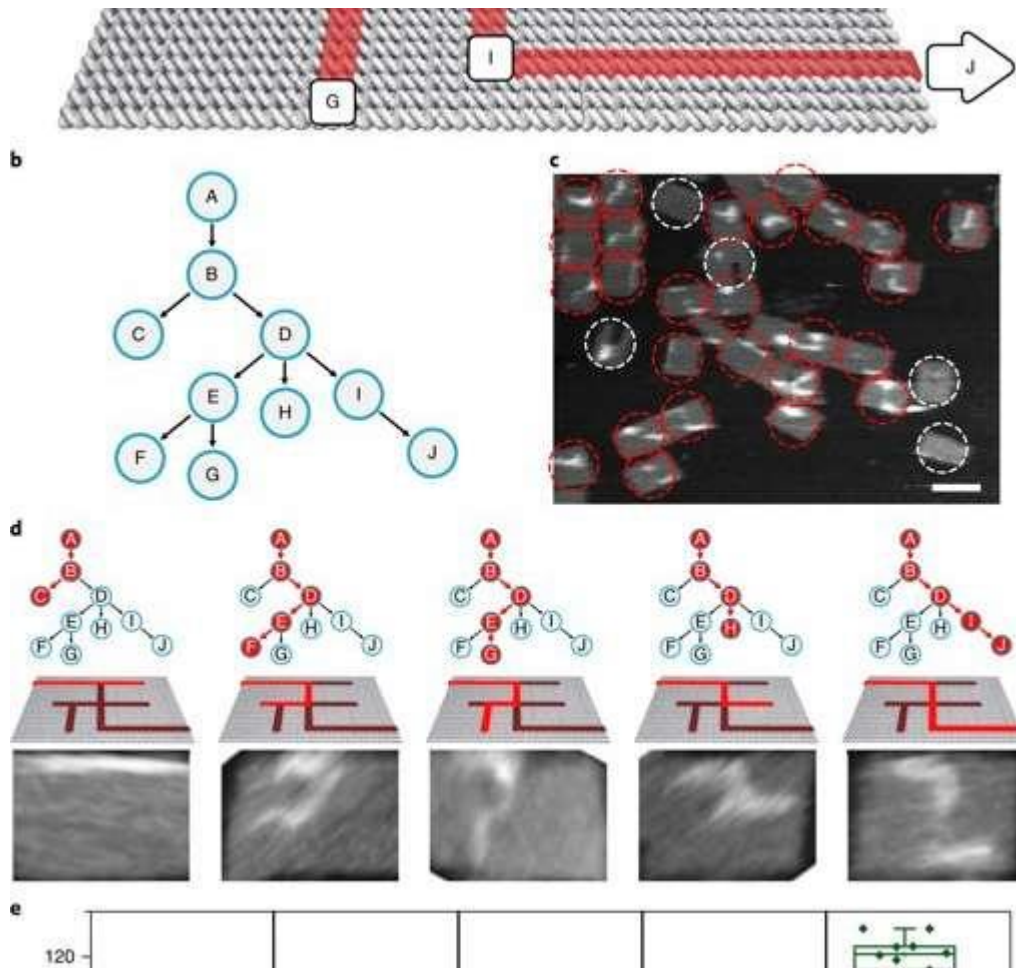
Single-molecule characterization of PSEC kinetics. a) A straight line in the middle of the DNA origami was used as the test bed. Vertex P0 is the starting point and vertices P1-P5 are intermediate points. b) Details of the design of six ...[more](#)

In the present study by Chao et al, the same basic principle of the HCR reaction scheme was used in a different computational context to develop a single-molecule DNA-navigator system. The platform explored all possible paths through a tree graph designed on an origami structure as a simply connected maze without cyclic paths. Such DNA origami structures are [information-bearing nanostructures](#) by nature with well-defined nanoscale geometry. The maze could be explored by proximal strand exchange cascade (PSEC) based on hybridization chain reactions. The researchers demonstrated that a system with a large number of single-molecule DNA navigators could collectively conduct [parallel depth-first search](#) (PDFS) on the tree to efficiently perform maze solving within 2-D origami. Initially the researchers conducted studies to test the PSEC design.

The proximal strand exchange cascade (PSEC) system (working principle of the DNA navigator) was facilitated on a rectangular origami substrate made of three components, which included the physical implementation of a tree graph, full strands and an initiator strand. Vacant areas without staple extensions corresponded to walls in the maze, preventing propagation of the strand exchange cascade. The entrance and exit were defined and denoted as ENT and EXIT respectively. In the second component, two types of DNA hairpins, T1 and T2, were used as fuels to drive the PSEC on the tree graph. The two hairpins coexisted metastably in solution to hybridize and fuel the PSEC process with [free energy](#).

By design, information only propagated through the network in the presence of an initiator (Initiator I). Upon addition of initiator I, PSEC was conducted and observed using atomic force microscopy (AFM). To visualize an established formation, the scientists enabled DNA-navigator-based formation

of the number 2017 as a proof-of-principle. Another technique known as DNA-PAINT was employed as a single-molecule, super-resolution imaging technique to reveal molecular features at the nanoscale to further substantiate the PSEC-based path paving process. The on-origami PSEC was highly specific, without intra- or inter-origami crosstalk.

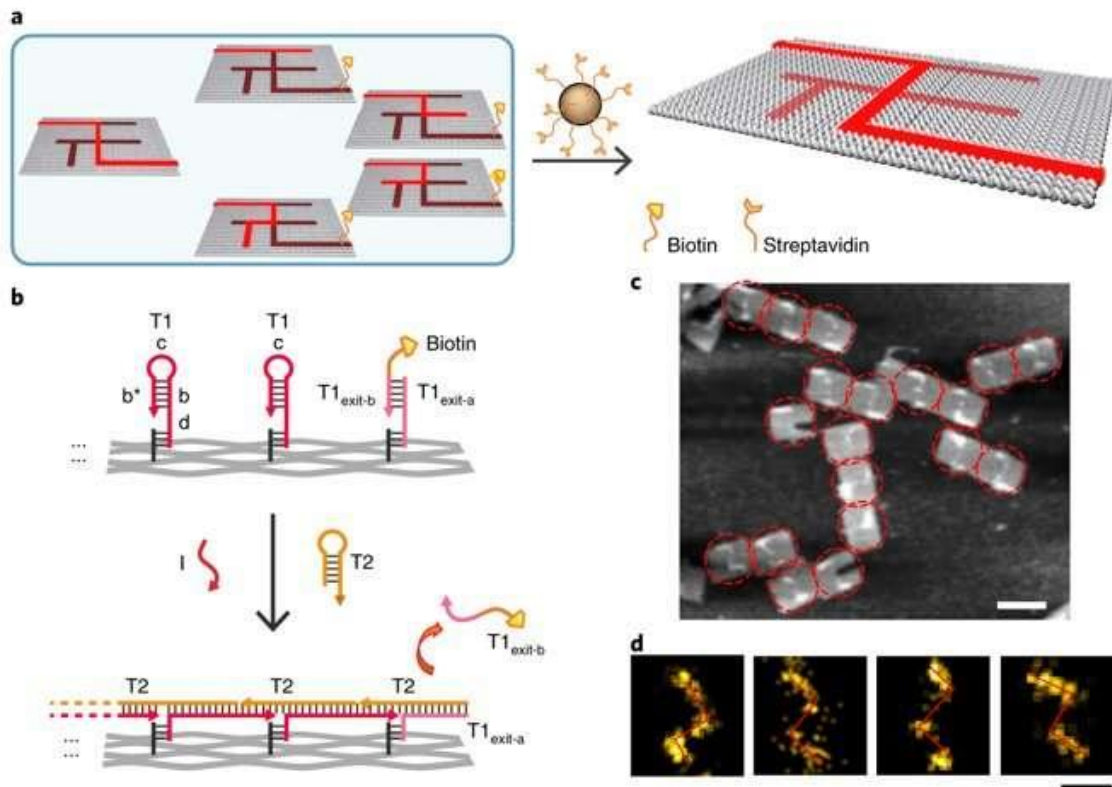


The PSEC-driven graph traversal on a maze. a) A maze design with 10 vertices. Arrows indicate the entrance vertex A and exit vertex J. b) The maze is equivalent to a rooted tree with 10 vertices. The entrance vertex A corresponds to the [...more](#)

Kinetics of the process were investigated at the single-molecule level in the study using time-resolved total internal reflection fluorescence microscopy (TIRF) in a setup with a prescribed starting point (P0) and five intermediate steps (P1-P5). Fluorescence in the setup was quenched using fluorescence resonance energy transfer (FRET), and the cascade was observed in real time by recording fluorescence signals continuously. The average speed of propagation was recorded to be 2.46 nm per minute, propagation across the straight line (54.4 nm) took approximately 22 minutes.

The scientists then constructed the main model maze with 10 vertices that included an entrance vertex A and an exit vertex J, three junctions (B, D, E) an intermediate vertex (I) and four dead ends (C, F, G, H). Each path of the maze that was equivalent to a tree with 10 vertices was investigated using DNA investigators starting at root A. The PSEC reactions produced a mixture of various paths on

the maze, confirmed with AFM. Each individual PSEC could progress on one of the five possible paths. Statistical analysis of the length distribution showed that the measured paths coincided well with the values predicted.



Single-molecule DNA navigators for maze-solving. a) Schematic illustration of magnetic bead-based selection. Exit vertex J is labelled with biotin to enable differentiation between the correct and wrong paths. Only if the PSEC reaches the ...[more](#)

To prevent the navigators from propagating through a wrong path with dead ends, the scientists designed a streptavidin-biotin tag-based method to selectively eliminate inaccurate path navigation. Only the correct path (P_{ABDU}) was followed in the maze therefore. The computational context used in the study allowed exploration of paths through tree graphs defined on the origami. The autonomous path explored by the DNA navigators proceeded unidirectionally and irreversibly, turning at junctions and corners on the origami platform as they were designed to. The design enabled parallel depth first search (PDFS) allowing each DNA navigator to individually explore any one of the paths through the given graph at a defined speed, greater than that [previously achieved](#).

The main advantage of the described biomolecular computer schemes in comparison to conventional electronic computing is they can be interfaced directly with biologically relevant processes. As a result, the [scientists](#) envision translational biomedical sensing and decision-making platforms with DNA origami and single-molecule diagnostics using [decision trees](#). Future applications will also include simple sensors or those coupled to a molecular actuator to trigger downstream molecular cascades. [21]

Built for speed: DNA nanomachines take a (rapid) step forward

When it comes to matching simplicity with staggering creative potential, DNA may hold the prize. Built from an alphabet of just four nucleic acids, DNA provides the floorplan from which all earthly life is constructed.

But DNA's remarkable versatility doesn't end there. Researchers have managed to coax segments of DNA into performing a host of useful tricks. DNA sequences can form logical circuits for nanoelectronic applications. They have been used to perform sophisticated mathematical computations, like finding the optimal path between multiple cities. And DNA is the basis for a new breed of tiny robots and nanomachines. Measuring thousands of times smaller than a bacterium, such devices can carry out a multitude of tasks.

In new research, Hao Yan of Arizona State University and his colleagues describe an innovative DNA walker, capable of rapidly traversing a prepared track. Rather than slow, tentative steps across a surface, the DNA acrobat cartwheels head over heels, covering ground 10- to 100-fold faster than previous devices.

"It is exciting to see that DNA walkers can increase their speed significantly by optimizing DNA strand length and sequences, the collaborative effort really made this happen," Yan said.

Yan is the Milton D. Glick Distinguished Professor of Chemistry and Biochemistry at ASU and director of the Biodesign Center for Molecular Design and Biomimetics.

The study was led by Nils G. Walter, Francis S. Collins Collegiate Professor of Chemistry, Biophysics & Biological Chemistry, founding director of the Single Molecule Analysis in Real-Time (SMART) Center and founding co-director of the Center for RNA Biomedicine at the University of Michigan, and his team, along with collaborators from the Wyss Institute, the Dana Farber Cancer Institute and the Department of Biological Chemistry at Harvard (all in Boston, Massachusetts).

"The trick was to make the walker go head over heels, which is so much faster than the hopping used before—just as you would see in a kung fu action movie where the hero speeds up by cartwheeling to catch the villain," says Walter.

The improvements in speed and locomotion displayed by the new walker should encourage further innovations in the field of DNA nanotechnology.

The group's findings appear in the advanced online issue of the journal *Nature Nanotechnology*.

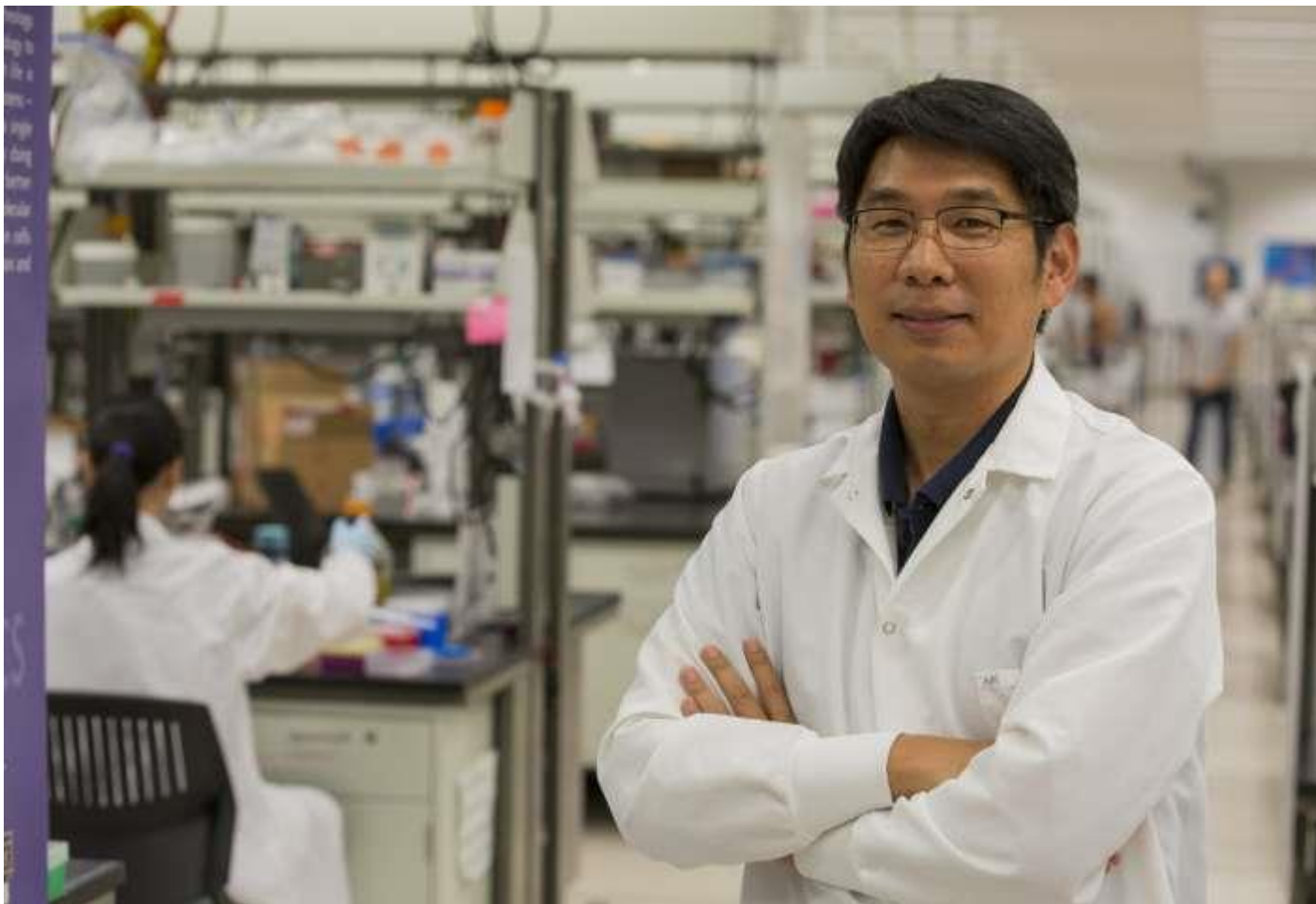
Building with DNA

Nanoarchitects build their DNA structures, motors and circuits using the same basic principle as Nature. The four nucleotides, labeled A,T,C and G, bind to each other according to a simple and predictable rule: Cs always pair with Gs and As always pair with Ts. Thus, varying lengths of DNA may be programmed to self-assemble, snapping together to form an unlimited variety of two- and 3-dimensional nanostructures. With clever refinement, researchers have been able to outfit their once-static nano-creations with dynamical properties.

One of the more innovative applications of DNA nanotechnology has been the design of robotic walking devices composed of DNA strands that successively move in a stepwise fashion across a path. The method enabling DNA segments to stroll across a defined area is known as strand displacement.

The process works like this: One leg of the robotic device is DNA strand 1, which is bound to complementary strand 2, through normal base pairing. Strand 1 contains an additional, unpaired sequence dangling from its end, which is known as the toehold.

Next, DNA strand 3 is encountered. This strand is complementary to DNA strand 1 and includes a toehold sequence complementary to DNA strand 1. Once the toehold of strand 3 binds with the toehold of strand 1, it begins sequentially displacing each strand 2 nucleotide, one by one, until strand 2 has been completely replaced by strand 3. Strand 2 then dissociates from strand 1 and the process can begin again. (See figure 1).



Hao Yan is the Milton D. Glick Distinguished Professor of Chemistry and Biochemistry at ASU and director of the Biodesign Center for Molecular Design and Biomimetics. Credit: Biodesign Institute at Arizona State University

Toehold-mediated strand displacement, which forms the basis of other DNA nanodevices, allows DNA structures to move from one complementary foothold on the walking surface to the next. As each DNA strand is displaced by a new strand, the nano-creature takes a step forward.

Race walking

Successful DNA walkers of various kinds have been designed and have demonstrated the ability to ferry nano-sized cargo from place to place. Until now, however, the strand displacement reactions they rely on have been slow, generally requiring several minutes to move a short distance. This is much slower than naturally occurring processes in living systems like protein motors, which can perform feats of dissociation similar to strand displacement in much faster time frames.

While theoretical calculations suggest that individual operations by such nanodevices should occur in seconds or less, in practice, such operations typically require minutes or even hours. (A recently designed cargo-sorting walker for example required 5 minutes for each step, with foothold spacings just 6 nm apart. This speed was on a par with similar strand-displacement walkers.)

In the new study, researchers sought to optimize this process to see how quickly a walker designed with speed in mind could move. The limiting factor in terms of speed did not appear to be the strand displacement process itself, but rather the lack of fine-tuned optimization in the overall walker design.

The team redesigned their walker for maximum speed and used a fluorescent imaging technique known as smFRET (for single-molecule fluorescence resonance imaging transfer) to chart the DNA walker's progress and evaluate its subtle kinetic properties.

By altering the lengths of toehold sequences and branching migration points, the stepping rate could be keenly optimized, making for a briskly moving nanorobot that left competitors in the dust, boasting stepping rates a full order of magnitude faster than previous DNA walkers.

Freewheeling nanorobot

Part of the robot's advantage over its competitors is due to its unusual technique of locomotion. Rather than simply stepping from one surface foothold to the next, the acrobatic walker moves head over heels in a cartwheel fashion, while remaining securely bound to at least one foothold at all times.

The stability of the double-stranded sequences anchoring the base of the robot to the track surface, while the free toehold searches out the next complementary sequence, may be one factor improving the walker's speed. The cartwheeling design also allows strand displacement to sequentially proceed in a direction away from the foothold surface, which improves efficiency.

Once the walker was optimized, super-resolved single particle tracking was used to observe the device's movement over a 2-D surface studded with footholds for the walker, covering a range of up to 2 microns. The best walker optimized in the study was able to search ~43 foothold sites per minute with a stepping distance of ~ 10nm. Strand displacement occurred at rates of about a tenth of a second. Analysis suggests the device can take hundreds of steps without dissociating.

Future steps

While still lagging behind naturally occurring protein reactions, the optimized cartwheeling walker offers a marked advancement in performance, representing an order of magnitude improvement over earlier versions, while not consuming any fuel. Borrowing further insights from natural systems

may allow dynamical DNA devices like the walker to accelerate even more in the future by converting chemical energy into directed speed.

The study underlines the opportunities for optimization of a range of DNA nanostructures, considerably enhancing their speed and versatility. [20]

Chemical engineers discover how to control knots that form in DNA molecules

Just like any long polymer chain, DNA tends to form knots. Using technology that allows them to stretch DNA molecules and image the behavior of these knots, MIT researchers have discovered, for the first time, the factors that determine whether a knot moves along the strand or "jams" in place.

"People who study polymer physics have suggested that knots might be able to jam, but there haven't been good model systems to test it," says Patrick Doyle, the Robert T. Haslam Professor of Chemical Engineering and the senior author of the study. "We showed the same knot could go from being jammed to being mobile along the same molecule. You change conditions and it suddenly stops, and then change them again and it suddenly moves."

The findings could help researchers develop ways to untie DNA knots, which would help improve the accuracy of some genome sequencing technologies, or to promote knot formation. Inducing knot formation could enhance some types of sequencing by slowing down the DNA [molecules'](#) passage through the system, the researchers say.

MIT postdoc Alexander Klotz is the first author of the paper, which appears in the May 3 issue of *Physical Review Letters*.

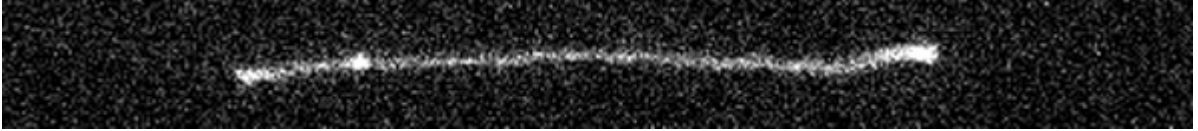
Knots in motion

Doyle and his students have been studying the physics of polymer knots such as DNA for many years. DNA is well-suited for such studies because it is a relatively large molecule, making it simple to image with a microscope, and it can be easily induced to form knots.

"We have a mechanism that causes DNA molecules to collapse into a tiny ball, which when we stretch out contains very big knots," Klotz says. "It's like sticking your headphones in your pocket and pulling them out full of knots."

Once the knots form, the researchers can study them using a special microfluidic system that they designed. The channel is shaped like a T, with an electric field that diverges at the top of the T. A DNA molecule located at the top of the T will be pulled equally toward each arm, forcing it to stay in place.

The MIT team found that they could manipulate knots in these pinned DNA molecules by varying the strength of the electric field. When the field is weak, knots tend to move along the molecule toward the closer end. When they reach the end, they unravel.



A knot near the end of a stretched DNA molecule is driven toward the end and unties, leaving an unknotted molecule. Credit: Alex Klotz

"When the tension isn't too strong, they look like they're moving around randomly. But if you watch them for long enough, they tend to move in one direction, toward the closer end of the molecule," Klotz says.

When the field is stronger, forcing the DNA to fully stretch out, the knots become jammed in place. This phenomenon is similar to what happens to a knot in a bead necklace as the necklace is pulled more tightly, the researchers say. When the necklace is slack, a knot can move along it, but when it is pulled taut, the beads of the necklace come closer together and the knot gets stuck.

"When you tighten the [knot](#) by stretching the DNA molecule more, it brings the strands closer to each other, and this ramps up the friction," Klotz says. "That can overwhelm the driving force caused by the electric field."

Knot removal

DNA knots also occur in living cells, but cells have specialized enzymes called topoisomerases that can untangle such knots. The MIT team's findings suggest a possible way to remove knots from DNA outside of cells relatively easily by applying an [electric field](#) until the knots travel all the way to the end of the molecule.

This could be useful for a type of DNA sequencing known as nanochannel mapping, which involves stretching DNA along a narrow tube and measuring the distance between two genetic sequences. This technique is used to reveal large-scale genome changes such as gene duplication or genes moving from one chromosome to another, but knots in the DNA can make it harder to get accurate data.

For another type of DNA sequencing known as nanopore sequencing, it could be beneficial to induce knots in DNA because the knots make the molecules slow down as they travel through the sequencer. This could help researchers get more accurate sequence information.

Using this approach to remove knots from other types of polymers such as those used to make plastics could also be useful, because knots can weaken materials.

The researchers are now studying other phenomena related to knots, including the process of untying more complex knots than those they studied in this paper, as well as the interactions between two knots in a molecule. [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 α , acts as a kind of shuttle that deposits and removes the histone from the DNA. This process determines whether or not genes in specific parts of the DNA can be read. Both proteins are involved in several regulatory processes in the body, such as cell division and proliferation, and therefore also play a role when it comes to a number of diseases, including cancer. Ben Schuler, professor at the Department of Biochemistry at UZH and head of the research project published in *Nature*, says, "The interesting thing about these proteins is that they're completely unstructured—like boiled noodles in water." How such disordered proteins should be able to interact according to the key/lock principle had puzzled the team of researchers.

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

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

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

Particles in charged solution form clusters that reproduce

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

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

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

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

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

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

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

Experiment demonstrates quantum mechanical effects from biological systems

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

The next step will be to compare the biology of different cryptophytes, such as whether they inhabit different environmental niches, to work out whether the quantum coherence effect is assisting their survival. [8]

Photoactive Prebiotic Systems

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

Significance Statement

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

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

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

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

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

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

Figure legend



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

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

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

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

Quantum Biology

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

Quantum Consciousness

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

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

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

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

Creating quantum technology

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

Quantum Entanglement

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

The Bridge

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

Accelerating charges

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

Relativistic effect

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

Heisenberg Uncertainty Relation

In the atomic scale the Heisenberg uncertainty relation gives the same result, since the moving electron in the atom accelerating in the electric field of the proton, causing a charge distribution on Δx position difference and with a Δp momentum difference such a way that they product is about the half Planck reduced constant. For the proton this Δx much less in the nucleon, than in the orbit of the electron in the atom, the Δp 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 Δx position with Δp 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 ν frequency. It means that the mass of the proton and electron are electromagnetic and the result of the electromagnetic induction, caused by the changing acceleration of the spinning and moving charge! It could be that the m_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.

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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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