

DNA shape changed by scientists to create tiny machines and computers

Structures can be employed as building blocks to create nanobots and basic computing systems



The basic double helix structure of DNA can be changed to create shapes such as 'i-motifs' and 'hairpins'. The shape of DNA can be manipulated to create tiny machines and computers, and scientists have discovered a range of new “triggers” to control this process. Adding substances like copper and oxygen to molecules of DNA can force it to change its shape. Creating a range of DNA shapes provides scientists with a toolkit they can then use to construct tiny pieces of technology from the building blocks of life. “The structure of DNA is usually assumed to be a double helix – that iconic structure that was first proposed by Watson and Crick in 1953 – but DNA is able to change structure,” Dr Zoe Waller from the University of East Anglia (UEA) told *The Independent*. Dr Waller’s team work on a particular structure called the “i-motif”, a four-stranded, knot-like structure that was identified in living cells for the first time in April. Though alternative DNA structures are thought to have a role in the onset of certain genetic diseases such as diabetes and cancer, the UEA research team was not looking for medical applications. “We know these structures do play a role in gene expression, but that was not the role of this study – DNA can be used as a material in making things,” she explained. DNA has potential as a construction material for a variety of technological applications, from nanobots to DNA-coded computers. As its structure is so different, the i-motif can be used as a switch when paired with regular DNA – with the two different shapes being recognised as either “on” or “off”. This has already been applied in basic nanomachine applications, and work by Dr Waller and her colleagues has expanded the repertoire of switches that can be used in such settings. By adding copper salts to DNA in oxygen-free conditions, they found DNA could

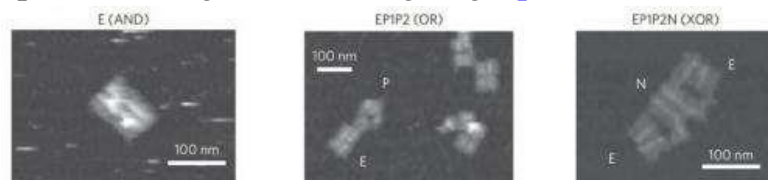
be changed into an i-motif shape. This could then be further modified into another shape called a “hairpin” by adding oxygen to the mix. These results were published in the journal *Nucleic Acids Research*. “One of the direct applications is in DNA-based computing,” explained Dr Waller.

The concept of DNA computing has floated around for years, with Microsoft investigating potential applications and using DNA for data storage. Some scientists have used the code of DNA to store information, or constructed simple logic gates and circuits. “You can use DNA to make logic gates and one of the advantages in using DNA is computing is that you can carry out calculations in parallel if your different types of logic gates are represented by different triggers or ingredients,” said Dr Waller. “So the fact we have discovered separate triggers for the same type of DNA means you could increase the output you could actually use.” Other technological applications of DNA include the creation of tiny “nanobots” that can deliver drugs to parts of the body. “DNA is biocompatible, so if you make a nanomachine out of DNA you can introduce it to a cell and it doesn’t get destroyed or recognised as quickly as some other agents we introduce,” said Dr Waller.

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## Researchers use DNA strands to create nanobot computer inside living animal

April 10, 2014 by Bob Yirka, *Phys.org* [report](#)



Atomic force microscope images of robot architectures. Credit: (c) *Nature Nanotechnology* (2014) doi:10.1038/nnano.2014.58

(Phys.org) —A team of researchers at Bar-Ilan University in Israel has successfully demonstrated an ability to use strands of DNA to create a nanobot computer inside of a living creature—a cockroach. In their paper published in *Nature Nanotechnology*, the researchers describe how they created several nanobot structures using strands of DNA, injected them into a living cockroach, then watched as they worked together as a computer to target one of the insects cells. Prior research has shown that DNA strands can be programmable, mimicking circuits and even solving simple math problems. The team in Israel has now extended that work to show that such programmability can be used inside of a living organism to perform work such as destroying cancer cells.

**DNA strands can be programmed because of their natural tendency to react to different proteins. In this new effort, the team unwound DNA strands and then tied them together in an origami type box structure.**

The box was then "filled" with a single chemical molecule. Next, other such objects were created for the purpose of interacting with both the box structure and certain proteins found inside of the cockroach. **The whole point was to create multiple scenarios in which the box would open automatically upon colliding with certain proteins.** Adding multiple nanostructures allows for increasing the number of possibilities. For example, if the box structure will only open if it encounters three kinds of proteins, **one made naturally by the cockroach, and two others carried by two different DNA origami structures.** By mixing the combinations, it's possible to cause the box to open using logic operations such as AND, OR, NOT (where the box will not open if a certain protein is present) etc., and that of course **means that computational operations can be carried out—all inside of a living organism.** In their study, the researchers filled the origami box with a chemical that binds with hemolymph molecules, which are found inside a cockroach's version of a bloodstream. **All of the injected nanobots were imbued with a fluorescent marker so that the researchers could follow their progress inside the cockroach.** They report that their experiments worked as envisioned—**they were able to get the box to open or not, depending on the programming of the entire fleet of nanobots sent into the insect on multiple occasions under a variety of scenarios.** Clearly impressed with their own results, the team suggests that **similar nanobot computers could be constructed and be ready for trial in humans in as little as five years.**

**Explore further:** [Nanomolecular origami boxes hold big promise for energy storage](#) **More information:** Universal computing by DNA origami robots in a living animal, *Nature Nanotechnology* (2014) DOI: [10.1038/nnano.2014.58](#)

#### **Abstract**

**Biological systems are collections of discrete molecular objects that move around and collide with each other. Cells carry out elaborate processes by precisely controlling these collisions,** but developing artificial machines that can interface with and control such interactions remains a significant challenge. **DNA is a natural substrate for computing and has been used to implement a diverse set of mathematical problems, logic circuits and robotics.** The molecule also interfaces naturally with living systems, and different forms of **DNA-based biocomputing have already been demonstrated.** **Here, we show that DNA origami can be used to fabricate nanoscale robots that are capable of dynamically interacting with each other in a living animal.** The interactions generate logical outputs, which are relayed to switch molecular payloads on or off. As a proof of principle, we use the system to create architectures that emulate various logic gates (AND, OR, XOR, NAND, NOT, CNOT and a half adder). Following an ex vivo prototyping phase, we successfully used the DNA origami robots in living

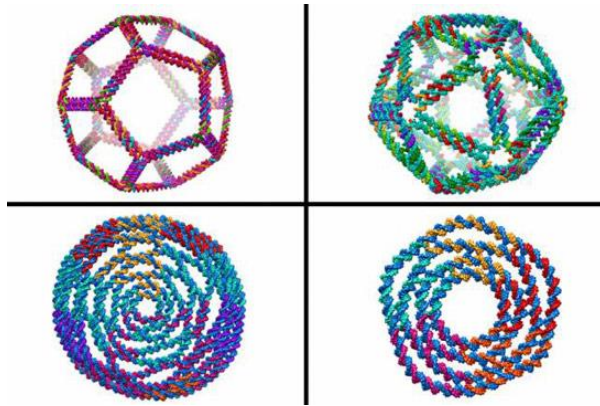
cockroaches (*Blaberus discoidalis*) **to control a molecule that targets their cells.** Read more at: <https://phys.org/news/2014-04-dna-strands-nanobot-animal.html#jCp>

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## New Computer Model Designs Complicated 3D Structures from DNA

TOPICS: [Biotechnology](#) [DNA](#) [MIT](#) [Nanoscience](#) [Nanotechnology](#)

December 4, 2014



Top row: 3-D structural predictions generated using CanDo by Stavros Gaitanaros, a researcher in MIT's Laboratory for Computational Biology and Biophysics (LCBB), based on sequence designs provided by Fei Zhang of the Hao Yan Lab at Arizona State University. Bottom row: designs by Keyao Pan (LCBB)/Nature Communications

Biological engineers from MIT have developed a new computer model that enables them to design the most complicated 3D structures ever made from DNA, including rings, bowls, and geometric structures such as icosahedrons that resemble viral particles. This design program could allow researchers to build DNA scaffolds to anchor arrays of proteins and light-sensitive molecules called chromophores that mimic the photosynthetic proteins found in plant cells, or to create new delivery vehicles for drugs or RNA therapies, says Mark Bathe, an associate professor of biological engineering. "The general idea is to spatially organize proteins, chromophores, RNAs, and nanoparticles with nanometer-scale precision using DNA. The precise nanometer-scale control that we have over 3-D architecture is what is centrally unique in this approach," says Bathe, the senior author of a [paper describing the new design approach in the December 3 issue of Nature Communications](#).

Commented [i3]: The Bull Shit never Ceases-- always about being a benefactor when in reality all they have ever done is weaponize everything

The paper's lead authors are postdoc Keyao Pan and former MIT postdoc Do-Nyun Kim, who is now on the faculty at Seoul National University. Other authors of the paper are MIT graduate student Matthew Adendorff and Professor Hao Yan and graduate student Fei Zhang, both of Arizona State University.

## DNA by design

**Because DNA is so stable and can easily be programmed by changing its sequence, many scientists see it as a desirable building material for nanoscale structures.**

Around 2005, scientists began **creating tiny two-dimensional structures from DNA using a strategy called DNA origami — the construction of shapes from a DNA “scaffold” strand and smaller “staple” strands that bind to the scaffold. This approach was later translated to three dimensions.** Designing these shapes is tedious and time-consuming, and synthesizing and validating them experimentally is expensive and slow, **so researchers including Bathe have developed computer models to aid in the design process.** In 2011, Bathe and colleagues came up with a program called CanDo that could generate 3-D DNA structures, but it was restricted to a limited class of shapes that had to be built on a rectangular or hexagonal close-packed lattice of DNA bundles. In the new paper, Bathe and colleagues report a computer algorithm that can take sequences of DNA scaffold and staple strands and predict the 3-D structure of arbitrary programmed DNA assemblies. **With this model, they can create much more complex structures than were previously possible.** The new approach relies on virtually cutting apart sequences of DNA into subcomponents called multi-way junctions, which are the fundamental building blocks of **programmed DNA nanostructures.** These junctions, which are similar to those that form naturally during DNA replication, consist of two parallel DNA helices in which the strands unwind and “cross over,” **binding to a strand of the adjacent DNA helix.** After virtually cutting DNA into these smaller sections, Bathe's program then reassembles them computationally into larger programmed assemblies, such as rings, discs, and spherical containers, all with nanometer-scale dimensions. **By programming the sequences of these DNA components, designers can also easily create arbitrarily complex architectures, including symmetric cages such as tetrahedrons, octahedrons, and dodecahedrons.** “The principal innovation was in recognizing that we can virtually cut these junctions apart only to reassemble them in silico to predict their 3-D structure,” Bathe says. “Predicting their 3-D structure in silico is central to diverse functional applications we're pursuing, since ultimately **it is 3-D structure that gives rise to function, not DNA sequence alone.**” The new program should enable researchers to design many more structures than those allowed by the CanDo program, says Paul Rothemund, a senior research associate at Caltech who was not part of the research team. “Since a large fraction of the DNA nanotech community is currently using molecules whose structures could not be treated by the original CanDo, the current work is a highly welcome advance,” Rothemund says. The researchers plan to make their algorithm publicly available within the next few months so that other DNA designers can also benefit from it. In the current version of the model, the designer has to come up with the DNA sequence, but Bathe hopes to soon create a version in which the designer can simply give the computer model a specific shape and obtain the sequence that will

produce that shape. **This would enable true nanometer-scale 3-D printing, where the “ink” is synthetic DNA.**

### **Scaffolds and molds**

Once researchers have access to printing 3-D nanoscale DNA objects of arbitrary geometries, they can use them for many different applications by combining them with other kinds of molecules. **“These DNA objects are passive structural scaffolds,” Bathe says. “Their function comes from other molecules attached to them.”**

One type of molecule that Bathe has begun working with is light-harvesting molecules called chromophores, which are a key component of photosynthesis. In living cells, these molecules are arranged on a protein scaffold, but proteins are more difficult to engineer into nanoscale assemblies, so Bathe’s team is trying to mimic the protein scaffold structure with DNA.

Another possible application is designing scaffolds that would allow researchers to mimic bacterial toxin assemblies made from multiple protein subunits. For example, the Shiga toxin consists of five protein subunits arranged in a specific pentameric structure that enables stealthy entry into cells. If researchers could reproduce this structure, they could create a version whose toxic parts are disabled, so that the remainder can be used for delivering drugs and micro- or messenger RNAs.

“This targeting subunit is very effective at getting into cells, and in a way that does not set off a lot of alarms, or result in its degradation by cellular machinery,” Bathe says. “With DNA we can build a scaffold for that entry vehicle part and then attach it to other things — cargo like microRNAs, mRNAs, cancer drugs, and other therapeutics.”

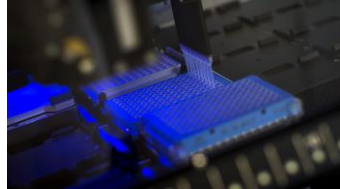
The researchers have also used DNA nanostructures as molds to form tiny particles of gold or other metals. In a recent Science paper, Bathe and colleagues at Harvard University’s Wyss Institute for Biologically Inspired Engineering demonstrated that DNA molds can shape gold and silver into cubes, spheres, and more complex structures, such as Y-shaped particles, with programmed optical properties that can be predicted by computer model. This approach offers a “made-to-order” nanoparticle design and synthesis procedure with diverse applications in nanoscale science and technology.

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**Publication:** Keyao Pan, et al., “Lattice-free prediction of three-dimensional structure of programmed DNA assemblies,” Nature Communications 5, Article number: 5578; doi:10.1038/ncomms6578

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A DNA computer has a trillion siblings and replicates itself to make a decision



Liquid machines. (Reuters/Mike Segar)

Think of a computer.

You're probably imagining a smartphone or laptop, or even one of Google or Amazon's huge server buildings if you're in the know about [the physical internet](#).

Those modern computers serve us well, but in the future, the word “computer” may conjure images of something much more...squishy. Researchers from the University of **Manchester announced last week that they've taken another step towards building computers from DNA**, a far cry from the silicon processors that underpin our digital infrastructure today. Previous research has shown [these computers are possible](#), but Manchester researchers have built early versions of a theoretical computer called a non-deterministic universal Turing machine (NUTM)—or one that could branch off to explore a series of decisions when given a problem, published in [Journal of the Royal Society Interface](#). To date these machines have only been theoretical, because an infinite and exponential expansion of code would overload even the world's highest-capacity computers. **But DNA is infinitesimal and can self-replicate: a strand of DNA can copy itself an unlimited number of times with slight variations every time it is confronted with a decision—and still fit in a few drops of liquid,** according to co-author Ross King. The underlying research out of Manchester is complicated, but here are the basics: A strand of DNA is built by arranging [the four chemical bases](#) that make up genetic code into specific sequences. **The DNA is then cycled through 14 parallel chambers containing gene-editing molecules, which prompt the DNA to shuffle itself into trillions and trillions of random combinations.** King offers an analogy: imagine a computer trying to solve a problem is actually trying to navigate a maze. Instead of tracing one path of the maze at a time, **DNA could replicate itself at every junction—and at each point in the maze incorporate new information gleaned from solving the previous step.** **This would let the DNA explore exponentially faster than modern computer processors. Each strand of DNA is a processor,** because it's executing the command of replicating itself with a slight variation, **building another processor which can take up its mantle.** Unlike our modern computers which utilize processors that are more or less permanent and can run unlimited kinds of code, these are single-use and disposable, the exact opposite.--The researchers

demonstrated the feasibility of this machine in lab conditions, but did not build a complete working NUTM. One problem is the ability to find the code that “solves” the problem (or the right instructions to complete the maze in our analogy). King says the team is working on labels, or easily-detectable markers generated when a solution is found. **This makes it easier for the computer to locate the strands of DNA that are actually useful, which would be floating amidst trillions of similar versions of itself.** Even though DNA sequencing has taken huge leaps since [the late 1970s](#), a machine still wouldn’t fit inside your MacBook and probably would take too long to get much work done. Plus, the kinds of pure math problems that NUTMs would solve aren’t of much use when browsing Facebook or making spreadsheets. But any research on this front helps us understand how we could use this technology in the far future, whether that means an Amazon server that looks like a gallon of water, liquid data pipelines, or a [computer injected into your head](#).