TRN's Making the Future report

The State of an Emerging Technology and a Look at What Lies Ahead

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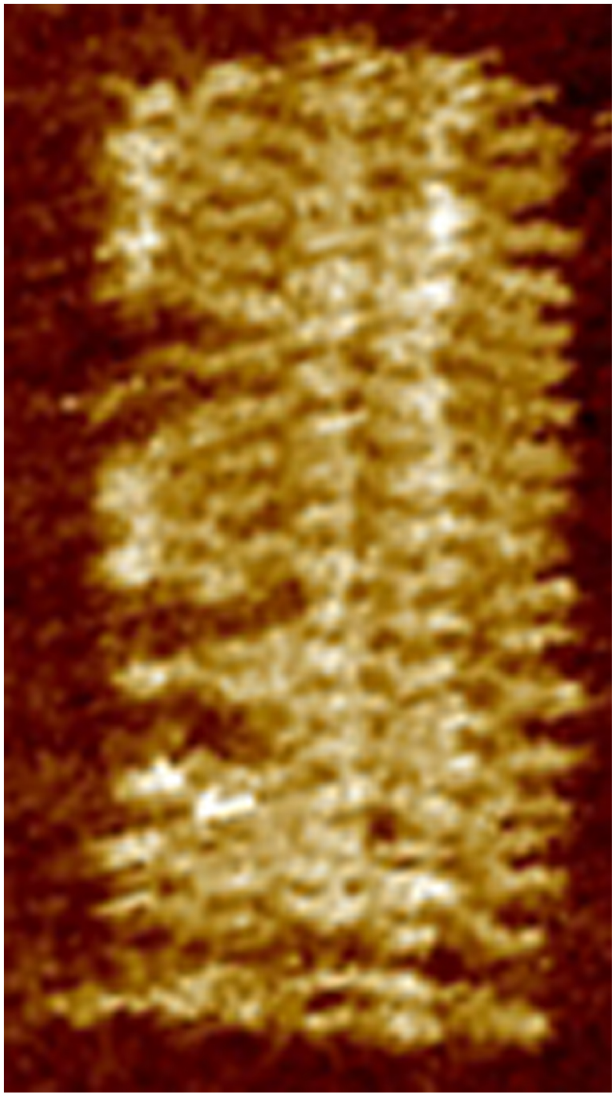
DNA Technology: Harnessing Life's Molecular Machinery



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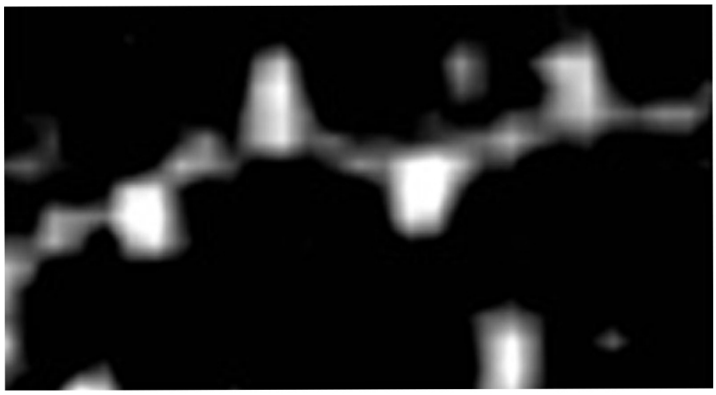

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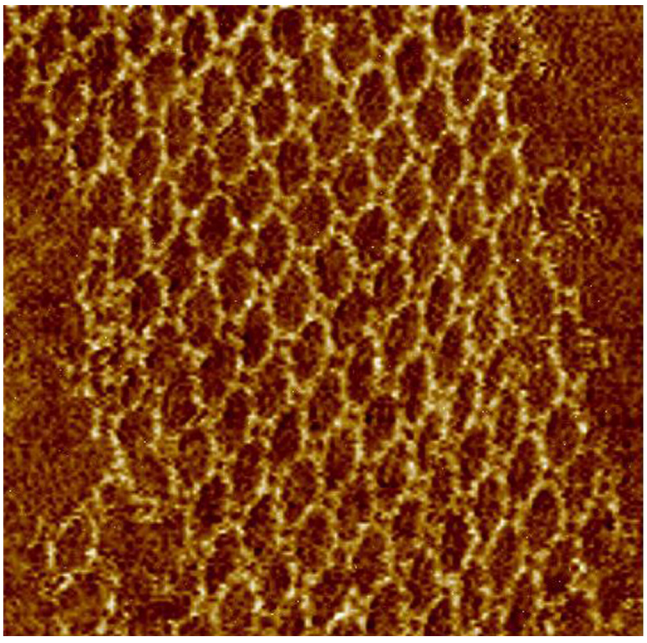

Assembly

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Executive Summary

Researchers recognized more than a decade ago that DNA's flexible format — four bases that can be sequenced to form many different combinations — makes it an extremely versatile molecule that could be bent to various technical ends.

In recent years scientists have advanced the prospects of tapping DNA to carry out massively parallel computing and mechanical assembly.

Researchers are able to make short strands of artificial DNA that contain stretches of bases that match up. When the strands join at those stretches, the DNA automatically assembles into various shapes. This includes joining multiple strands, causing strands to fold in on themselves, and carrying out sequences of changes, including cycles.

Taking stretches of DNA through various connections and disconnections makes it possible to carry out computations, including the boolean logic of silicon computers.

Connecting stretches of DNA also makes it possible to build structures from the molecules. Specific stretches of DNA can be engineered to bind to various materials, including tiny metal spheres, before self-assembling. This allows DNA to be used to assemble nanoscale machines and materials atom by atom.

(DNA can also be used to sense many types of substances, including pathogens and toxins. These sensing abilities will be the subject of a future report.)

Rather than competing with silicon, the big promise of DNA computers is as the brains for various biotechnology and nanotechnology devices, including devices that could eventually operate inside the human body.

DNA's self-assembly abilities are key to building molecular machines designed to reproduce traditional machinery like levers, valves, manipulators and motors at the nanoscale.

Making electronics molecule-by-molecule promises smaller, faster devices that use very little power.

The first computing and nanotechnology uses of DNA could become practical in five to ten years.

What to Look For

Computing:

DNA boolean logic circuits
DNA computer that cracks a practical encryption code
DNA computer that solves a 50-variable NP-complete problem
General-purpose DNA processor

Machines:

DNA manipulator used in sensor or diagnostic device
DNA motor controlling a nanodevice
Drug-dispensing molecular robot
Multi-function medical molecular robot
Intracellular molecular robot
Molecular assembler robot

Structures:

Three-dimensional DNA tiles
Three-dimensional DNA array
DNA nano containers
Computer circuit template

Assembly:

DNA-assembled smart materials
DNA-assembled electronic devices
DNA-assembled logic circuits
DNA-based molecular factory

Biology becomes technology

Researchers recognized more than a decade ago that the way deoxyribonucleic acid, or DNA, encodes instructions for life's processes could be bent to various technological ends. In recent years scientists have advanced the prospects of tapping DNA to carry out tasks as diverse as massively parallel computing and mechanical assembly.

Biological DNA is made up of four types of bases — adenine, cytosine, guanine and thymine — attached to a long sugar-phosphate chain. The order of the four bases along a strand forms a code that in nature determines the types of proteins produced by a cell's biochemical machinery. DNA directs the production of the body's proteins, and the proteins regulate the processes that maintain life.

Cells store DNA as long double helices, with two strands of DNA that contain matched bases paired like the teeth of a zipper. The DNA strands used for computing and nanotechnology applications are much shorter molecules constructed in the lab, usually using the same bases that make up biological DNA.

Researchers are able to make short strands of artificial DNA that contain stretches of bases that match up. When the strands join at those stretches, the DNA automatically assembles into various shapes. Researchers are also using enzymes similar to those that biological processes employ to cause specific DNA sequences to separate. This makes it possible to join multiple strands, cause strands to fold in on themselves, and carry out sequences of changes, including cycles.

Researchers are tapping the mechanical abilities of this artificially-constructed DNA for three broad technological uses:

- Computing
- Assembly
- Sensing

Taking stretches of DNA through various connections and disconnections makes it possible to carry out computations. This promises to enable DNA-based computers.

Connecting stretches of DNA also makes it possible to build structures from the molecules. As a nanoscale building material, DNA has useful properties: it is water-soluble and biodegradable.

In addition, certain stretches of DNA can be engineered to bind to various materials, including tiny metal spheres, before self-assembling. This allows DNA to be used to assemble nanoscale machines can materials atom by atom.

DNA can also be used to sense many types of substances. Certain stretches of DNA can be engineered to connect with specific stretches of biological DNA to identify DNA and chemicals, including pathogens and toxins. This enables DNA-based sensors that have the potential to be quick and portable.

These sensing abilities will be covered in more detail in TRN's March 2005 Making the Future report titled Sensors: Artificial Eyes, Ears and Noses. This DNA Technology report covers DNA's use in computing and nanotechnology.

Sticky ends and DNA tiles

Researchers using DNA for computation and assembly have mapped out two important concepts: sticky ends and DNA tiles.

Sticky ends are portions of single-stranded DNA that stick out from a double-stranded molecule. DNA strands join when sticky ends containing opposite bases come into contact and zip together.

DNA tiles are made from four or six strands of DNA that repeatedly cross over each other to make two or three intertwined double helices. DNA tiles are stiffer than the more familiar double helix form, and this is an advantage when putting the molecules through complicated computations and when using DNA as scaffolding for nanoscale building.

Computer in a test tube

DNA's main advantage for computing is its extremely small size: a single drop of DNA contains billions of molecules. A computer based on DNA would theoretically be able to sort through billions of possible answers to a problem at once. (See How It Works sidebar.)

Despite its advantages, though, it's unlikely that you will ever own a computer powered by DNA. DNA computers would be exceedingly slow for all but a few types of problems, notably those that lack a mathematical solution, like the traveling salesman problem.

Because such NP-complete problems cannot be solved exactly by a formula, finding a solution means checking each possible answer. In the case of the traveling salesman, as he adds destinations, the possible paths he can take to hit all the destinations in one trip increases exponentially: there are 24 possible routes through five cities, 362,880 possible routes that include 10 cities, and 87,178,291,200 possible routes through 15 cities.

However, even for these types of problems, DNA computing has its limitations. The process is prone to errors from mismatched

How It Works

Base-ics

Biological DNA is made up of strings of four types of bases — adenine, cytosine, guanine and thymine — attached to a sugar-phosphate backbone. Adenine pairs up with thymine and cytosine with guanine when two single strands of DNA combine to form DNA's familiar double helix shape.

Biological DNA acts as a code for producing the proteins that carry out life's processes. In a cell's nucleus, a DNA double helix opens to expose sections of single strands. Ribonucleic acid (RNA) makes a mirror copy of an exposed DNA strand, and the sequenced RNA serves as a template for producing proteins elsewhere in the cell.

Researchers can make artificial DNA that contains specific sequences of bases. These strands can interact to compute, and can assemble into specific shapes for nanomachines and templates for assembling other substances into devices or materials.

Operations

The basic biochemical operations used to manipulate DNA are restriction, hybridization, ligation and amplification. These operations are carried out by various enzymes. Restriction is the process of cutting strands after specific sequences of bases. Hybridization is the joining of two complementary single strands to form a double strand. Ligation is the joining of two strands at their ends. Amplification is the process of duplicating a strand many times.

Sticky ends, branches and tiles

The artificial DNA used in DNA computing and nanotechnology has a fundamental characteristic: sticky ends. Sticky ends are short sections of single-stranded DNA that extend beyond an end of a double-stranded DNA molecule. Matching sticky ends serve to join two pieces of double-stranded DNA.

Artificial DNA is usually configured in one of two basic building blocks: DNA tiles and four-armed branches. DNA tiles are made from four or six strands of DNA that repeatedly cross over each other to make two or three intertwined double helices. DNA tiles can be joined to form sheets. Branched DNA molecules consist of four single strands configured in a cross shape so that each branch is a double strand. Joining multiple branched molecules forms a two-dimensional lattice.

base pairs and inaccurate enzyme operations, and these errors increase as the size of the problem increases.

Rather than competing with silicon, the big promise of DNA computers is as the brains for various biotechnology and nanotechnology devices, including devices that could eventually operate inside the human body.

Key to making DNA computers useful is finding ways to make test-tube mixes of various types of DNA strands go through many computational steps at once without requiring a pause to add a new enzyme or stretch of DNA. This requires tricky planning to cause each step of a computation to happen in the right order without interference from the strands of DNA required for subsequent steps.

Researchers from the Weizmann Institute in Israel are using DNA to carry out several computational steps at once in a test tube. The method uses two types of sticky-ended DNA molecules: software molecules that contain instructions for the computation and input molecules that contain a problem to be solved. When software and input molecules that contain sticky ends designed to combine meet up, an enzyme seals them together. The molecule is then cut in a different place by a second enzyme, exposing another sticky end so that a second step can take place. The number of steps depends on the number of computations coded into the software DNA strand. (See "Programmable DNA Debuts", page 11.)

Researchers from the University of Southern California and the California Institute of technology have used a DNA computer to solve a problem containing 20 variables that required a search of 1,048,576 possibilities. (See "DNA Solves Big Problem", page 12.)

Researchers from Ruhr University in Germany and Accenture Technology Labs in France have designed DNA tiles that can handle two inputs and two outputs. The tiles can self-assemble into a layout that resembles an electric circuit. Using different types of tiles, it is possible to cut down on the range of possible answers to a problem in order to reduce the number that must be checked by brute force. (See "DNA Could Crack Code", page 14.)

Researchers from New York University and Duke University have coaxed DNA tiles to self-assemble into an XOR gate, which is a basic binary logic circuit. (See "DNA Does Logic", page 15.)

These DNA computing technologies could be used practically in 5 to 10 years.

Readout

Another important step in using DNA to carry out computations is finding practical ways to read results that take place at the molecular level.

A research team from Duke University has made artificial strands of DNA that self-assemble into a structure that reveals the pattern encoded in one of the DNA strands, making the order of bases on that strand readable by microscope. (See "DNA Makes Nano Barcode", page 16.)

Researchers from the University of Wisconsin-Madison and Third Wave Technologies, Inc. have adapted a method of using fluorescence to indicate a given DNA computation answer. (See "DNA Computer Readout Glows", page 17.)

Computing

There are several ways of using DNA molecules to represent information and several ways to use the molecules to carry out computations. DNA sequences can be used to represent paths in route-optimization problems, DNA sequences can be mapped to strings of binary numbers and software strands can be programmed to carry out calculations on input strands, or DNA tiles can be constructed into Boolean logic circuits.

Traveling salesman

The first DNA computing problem, solved in 1994, used DNA sequences to represent cities in the traveling salesman problem, which is the challenge of plotting the best route through a number of cities. The problem cannot be solved by a mathematical formula, meaning that all possible routes must be examined one by one. At the same time, the number of routes grows exponentially with the number of cities. While there are only 4 times 3 times 2 times 1, or 24, possible routes through five cities, the number grows to 362,880 with 10 cities, and 87,178,291,200 with 20 cities.

The 1994 DNA demo showed that it is possible to use DNA to find all of the routes through a set of five cities beginning and ending with a specific pair of cities and visiting each city only once. Each path between two cities was assigned a unique 20-base DNA strand, and many copies of these strands were mixed and allowed to combine end to end. This generated strands of various lengths representing random routes. The next step was to weed out all strands except those that began and ended with the segments representing the designated start and end points. Next, all strands except those of the minimum length, meaning one segment per city pair, were removed. The last step was removing all strands that contained repeated segments, leaving only the DNA combinations that represented routes from the origin to the destination that passed through every city only once.

Software

A system of programmable DNA maps DNA sequences to symbols like binary numbers, uses software strands to carry out calculations and uses input strands that represent possible answers to a problem. The software DNA strand is programmed to combine with certain input strands and to direct enzymes to cut the attached input strands. The system goes through a cycle of joins and cuts ending with joining an input strand to one of two marker strands that indicate whether the input was correct.

These DNA computing readout schemes could be used practically in 5 to 10 years.

Storage

Researchers are also working on using DNA to store data.

Researchers from the Pacific Northwest National Laboratory have used artificial DNA sequences to encode portions of the text of the children's song "It's a Small World" into sequences of bacterial DNA, allowed the bacteria to multiply, then extracted the message portion of the progeny's DNA strand and retrieved the input information. (See "Data Stored in Live Cells", page 18.)

Automatons

Researchers have also used DNA to make automatons, or machines that operate without human control. Automatons react spontaneously to events and changing conditions, a prerequisite for any DNA device designed to operate in the human body.

Researchers from the University of Munich in Germany have taken a step toward automating nanomachines with a method that allows instructions for a DNA-based machines to be contained in another stretch of DNA. (See "Genes Automate DNA Machines", page 19)

Researchers from the Weizmann Institute have constructed a DNA automaton that is programmed to find signs of cancer cells and, when the signs are present, dispense DNA molecules designed to eradicate the cancer cells. The researchers' prototype is a test-tube proof-of-concept. (See "DNA Bot Targets Cancer", page 20.)

Researchers from Columbia University and the University of New Mexico have fashioned a device that uses DNA to automatically play a game of tic-tac-toe. (See "DNA Plays Tic-Tac-Toe ", page 20)

DNA automatons are likely to take at least a decade to become practical.

Champion of self-assembly

Researchers working to make molecular-scale machines and structures are turning to another of DNA's abilities: self-assembly.

Self-assembly is a requirement for any practical nanotechnology because, though some microscopes are capable of traditional assembly techniques like picking and placing, natural forces like chemical bonds and electrostatic interactions between molecules are more flexible and faster because they can be applied to billions of molecules at once. The same forces also make it very difficult to use traditional assembly techniques because nanoscale parts readily stick to nanoscale manipulators. (For a more detailed look at self-assembly see TRN's Making the Future report titled Self-Assembly: The Natural Way to Make Things)

DNA tiles can be programmed to assemble in various ways by giving them different types of sticky ends, which makes them promising building blocks for assembling nanoscale devices.

Researchers from Yale and Northwestern Universities have come up with a scheme for making DNA tiles self-assemble into three-

Logic circuits

An approach that more closely mimics digital computers uses DNA tiles to configure basic logic circuits whose inputs and outputs represent the 1s and 0s of binary computing. Tiles representing input and output are designed to combine so that the output tiles represent the appropriate output of a logic gate for the given input.

Readout

DNA readout is typically carried out by the process of gel electrophoresis, which is often used to analyze biological DNA. DNA molecules naturally carry an electric charge, and placing DNA in a gel with electrodes at either end causes the DNA to move from the negative side of the gel toward the positive side. The speed of the movement is determined by the length of the molecule; the shortest molecules travel the furthest.

In computations like the traveling salesman problem, the lengths of the molecules correspond directly to the answers. In binary DNA computing, marker molecules of different lengths differentiate the answers. Scientists can then use DNA sequencing techniques on copies of the molecules to determine their compositions and see the answers. In logic circuits, recorder strands are imprinted with the coding for ones and zeros and strung together. The gel electrophoresis results directly correspond to the 1s and 0s of the answer.

Mechanics

It is possible to make machines from DNA molecules because the molecules can be made to change shape reversibly. Researchers have made tweezers that open and close and have fashioned several forms of rotary motors.

These machines usually consist of a configuration of DNA molecules in a particular shape, such as an open pair of tweezers. A single strand of a particular sequence of DNA combines with sticky ends on the DNA machine, causing the machine to change shape. In the case of DNA tweezers, the shape change puts a hairpin bend in the middle of the DNA molecule to draw the two halves of the molecule — the tweezer arms — closed.

A second strand that more readily combines with the first strand than the machine does usurps the first strand, removing it from the machine and returning the machine to its original configuration to complete the mechanical cycle.

Assembly

Tapping DNA's self-assembly abilities to build structures and devices from materials like carbon

dimensional shapes. (See "Nanotech Scheme Envisions DNA Origami", page 22.)

Molecular machinery

A key aspect of DNA is that it changes shape. In nature, double-stranded DNA zips and unzips to carry out its function. The wide range of controllable shape-changes available to researchers is a palette for designing molecular machines.

Nature is full of examples of molecular machines, and using DNA and other biological molecules as artificial molecular machines is an alternative and complementary strategy to using nonbiological materials to reproduce traditional machinery like levers, valves, manipulators and motors at the nanoscale.

In the grasp

DNA's ability to change shape can be used to bind to and release molecules in order to deposit specific molecules in specific places. This promises to be useful in building machines and materials molecule-by-molecule. It could also make it possible to deposit drugs in specific places in the body.

Researchers from Ludwig Maximlians University in Germany have built a simple molecular machine from DNA that can bind and release single molecules of a specific type of human blood-clotting protein. The device can be made to select any of many types of proteins. (See "DNA Has Nano Building in Hand", page 22.)

Molecular motors

Not only does DNA change shape, but it can do so reversibly. Cycling between shapes is the essence of a motor. DNA motors typically consist of one or more motor strands of DNA that undergo shape changes, fuel strands that the induce the shape change, and control or removal strands that reverse the work of the fuel strands.

DNA motors could be useful not only for nanotechnology applications, but also for biotechnology. Molecular motors are common in biology and a carry out a range of functions from cell movement to chemical synthesis.

Several research teams have constructed motors using DNA and RNA. The more advanced versions run continuously. The motors exert between 15 and 60 trillionths of a Newton of force. (See "DNA Motor Keeps Cranking", page 23; "RNA Forms Nanomotor", page 24; "Morphing DNA Makes Motor", page 24; "DNA Strands Form Nano-Machine" page 25.) One Newton accelerates a one-kilogram mass at a rate of one meter per second per second.

Researchers from the French National Museum of Natural History have constructed a DNA molecule that stretches and shrinks to cycle from an elongated double-strand to a more tightly coiled four-stranded form. (See "DNA Forms Nano Piston", page 26.)

DNA motors could be used practically in 2 to 10 years.

nanotubes and metal nanoparticles requires a way to attach the materials to specific DNA sequences. A common approach is to coat the materials with a particular protein, typically an antibody, that readily binds with another protein that in turn connects to a specific DNA sequence. This way, when DNA molecules combine to form programmed patterns, they also arrange the nanotubes or nanoparticles.

Who to Watch

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Assembly

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Nanotubes and nanoparticles

Many research teams are using DNA to assemble structures from atoms or other molecules. To do this they synthesize artificial DNA strands that contain bases that connect to those atoms or molecules, then take DNA through its self-assembly paces.

DNA can be made to connect to atoms and nanoparticles of various materials, and to carbon nanotubes. Carbon nanotubes are rolled-up sheets of carbon atoms that have useful electrical and optical properties, are stronger than steel by weight, and can be smaller than a nanometer in diameter.

Researchers from the Technion-Israel Institute of Technology have devised a DNA template self-assembly process that makes transistors in a test tube from a mix of DNA, carbon nanotubes, silver, gold and four types of protein molecules. (See "DNA Assembles Nanotube Transistor", page 27)

Researchers from Kyushu University in Japan have used bacterial DNA as a matrix for making structures from silicates, which are materials like glass and concrete that contain silicon. The method is akin to the reaction that takes place when fossils form. (See "Chemistry Yields DNA Fossils", page 28.)

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Researchers from DuPont Central Research and Development, the University of Illinois at Urbana-Champaign and the Massachusetts Institute of Technology have come up with a way to use DNA to separate semiconducting carbon nanotubes from metallic ones and to separate semiconducting nanotubes by diameter. (See "DNA Sorts Nanotubes", page 28.)

Researchers from the University of Tokyo in Japan have made artificial DNA whose bases attach to metal ions, and have programmed the DNA to organize the ions into atomic wires. (See "Artificial DNA Stacks Metal Atoms", page 28.)

In order to construct devices and structures from DNA, researchers must be able to choreograph the self-assembly process.

Researchers from Duke University have come up with a suite of computer-aided design (CAD) tools for designing computer circuits made from carbon nanotubes assembled by DNA. The tools are designed to build computer circuits at a density of 2,500 transistors per square micron, which is about 30 times more closely packed than today's state-of-the-art chips. (See "Tools Design DNA-NanoTube Logic", page 29.)

DNA's self-assembly abilities could be tapped for practical uses in as soon as five years.

Waffles, tubes, trees and pyramids

Researchers are proving adept at forming DNA into various shapes that are useful for creating scaffolds and templates for assembling nanoscale devices and for creating materials with specific electrical, optical and biological properties.

Researchers from Duke University have made DNA tiles whose sticky ends match up so that the connected tiles curve slightly to form a waffle-like sheet that can be used to sort proteins. They also used the method to make a waffled ribbon that served as a template for a silver nanowire built atom by atom. (See "DNA Forms Nano Waffles", page 30.)

Purdue University researchers are using two of the bases that make up DNA to make organic nanotubes that self-assemble. (See "DNA Parts Made Versatile Nanotubes", page 31.)

Cornell University researchers have found a way to make branched, or Y-shaped DNA, and have constructed tree-shaped DNA by connecting the branches. (See "Scientists Brew Tree-Shaped DNA", page 32.)

And researchers from the Scripps Research Institute have formed strings of DNA that spontaneously fold into a wireframe octahedron. (See "DNA Fold into Paired Pyramids, page 33.)

These DNA structures could be ready for practical applications within five years.

Nanowire maker

Making electronics molecule-by-molecule promises smaller, faster devices that use very little power. The smaller the electronic device, the shorter the distance signals must travel, making the devices faster. In addition, electrons travel through molecular-scale wires without scattering, which increases the speed of electrical signals and reduces their power needs.

Among the most intriguing possibilities for mass production of nanoscale electronics is DNA's assembly abilities. The challenge is finding ways to improve DNA's weak electronic properties.

Researchers typically approach the problem by causing DNA to assemble into a template that can be coated with another material, or by combining DNA with nanomaterials like carbon nanotubes or metal atoms before causing DNA to assemble into a nanostructure.

Researchers from the Max Planck Institute in Germany have shown by computer simulation that it is possible to insert DNA into a carbon nanotube. This is potentially useful for making DNA-modulated electronics. (See "Study Shows DNA Will Fill Tubes", page 33.)

DNA electronics are likely to take at least five years to become practical.

Scientists have also been exploring the possibility of DNA molecules conducting electricity. Conductive DNA could self-assemble into nanoscale circuitry, but recent developments indicate that this may be difficult.

Researchers from Osaka University have showed that guanine-cytosine-based DNA shows some electrical activity. (See "DNA Conducts", page 33.)

Researchers from the French National Center for Scientific Research, Tel Aviv University and the Russian Academy of Sciences carried out experiments that showed that DNA can conduct electricity and that it becomes a proximity-induced superconductor when its metal contacts become superconducting at very low temperatures. (See "DNA Induced to Superconductivity", page 35.)

In September 2003, however, researchers from the University of California at Los Angeles released a study that showed that DNA conductance varies with humidity levels. This indicates that the conductance is due a sheath of water molecules found around DNA molecules rather than the DNA molecules themselves.

Researchers from Brown University have engineered artificial DNA that contains zinc ions in order to make DNA behave like a semiconductor. (See "Metal Makes DNA More Conductive ", page 36.)

DNA in bulk

Researchers are also tapping DNA to form bulk materials, typically in the form of a thin film.

Researchers from the University of Lecce and the University of Bologna in Italy have coaxed a transistor semiconductor channel to self-assemble from guanosine, a derivative of the DNA base guanine. (See "DNA Part Makes Transistor", page 37) They also coaxed guanosine to form a thin film that produces an electric current when light shines on it. (See "DNA Device Detects Light Signals", page 37.)

The biochemical future

DNA is the world champion of molecular recognition — the ability to interact in specific ways with specific molecules. DNA's flexible format — four bases that can be sequenced to form many different combinations — makes it an extremely versatile molecule capable of a huge number of specific interactions.

Recent advances in the scientific understanding of DNA means that applying the molecule's extensive molecular recognition capabilities to technological ends is rapidly becoming an engineering challenge. In other words, DNA is becoming a tool.

There are many challenges remaining to make DNA computing and DNA nanotechnology applications practical:

- developing error correction techniques for DNA computers
- finding more reliable methods for configuring and reading out computations
- finding ways to produce more complicated, three-dimensional and stronger DNA structures
- integrating DNA motors into nanoscale devices
- minimizing the number of unique sequences required for large-scale assemblies

The near-term DNA-related research is likely to yield sensors. Computing and nanotechnology uses of DNA are likely to at least five years and as much as a decade away. Practical DNA supercomputers and DNA-based nano robots remain in the hazy future.

The intersection of DNA computing, nanotechnology and biotechnology is likely to produce the first practical DNA technology applications beyond sensors. These include highly selective drug delivery, and could become practical within the next decade.

Recent Key Developments

Advances in computing:

- A DNA computer that carries out multiple steps automatically (Programmable DNA Debuts, page 11)
- A DNA computer that solved a problem with more than one million possible answers (DNA Solves Big Problem, page 12)
- A design for a DNA computer that could crack encryption codes (DNA Could Crack Code, page 14)
- A basic logic function carried out by DNA (DNA Does Logic, page 15)
- A method for making DNA form barcode-like patterns that can be used to present computation output (DNA Makes Nano Barcode, page 16)
- A method for making the output of DNA computations easier to read (DNA Computer Readout Glows, page 17)
- A method of encoding data in the DNA of live bacteria (Data Stored in Live Cells, page 18)
- A fast DNA computer that requires no external heat source, Weizmann Institute, February 2003

Advances in machines:

- A method of programming genes to form DNA strands that automatically control DNA machines (Genes Automate DNA Machines, page 19)
- A DNA machine programmed to find and destroy cancer cells (DNA Bot Targets Cancer, page 20)
- A DNA-based machine that plays tic-tac-toe (DNA Plays Tic-tac-toe, page 20)
- A scheme for designing three-dimensional DNA structures (Nanotech Scheme Envisions DNA Origami, page 22)
- A DNA manipulator that can repeatedly bind and release a specific protein (DNA Has Nano Building in Hand, page 22)
- A DNA motor that cycles through its steps automatically (DNA Motor Keeps Cranking, page 23)
- A rotary motor consisting of an RNA ring and a DNA axle (RNA Forms Nanomotor, page 24)
- A four-cycle rotary motor made from DNA (Morphing DNA Makes Motor, page 24)
- A tweezer made from DNA strands (DNA Strands Form Nano-Machine, page 25)
- A DNA motor that expands and contracts (DNA Forms Nano Piston, page 26)

Advances in self-assembly:

- A self-assembly process for building carbon nanotube transistors using DNA and silver and gold particles (DNA Assembles Nanotube Transistor, page 27)
- A process for encapsulating DNA strands in silica-based materials (Chemistry Yields DNA Fossils, page 28)
- A process for using DNA to sort carbon nanotubes by diameter and electrical properties (DNA Sorts Nanotubes, page 28)
- A process for forming an artificial DNA double helix encapsulating a row of copper ions (Artificial DNA Stacks Metal Atoms, page 28)
- A set of software tools for designing integrated circuits composed of carbon nanotubes assembled by DNA (Tools Design DNA-Nanotube Logic, page 29)
- DNA-based programmed assembly of gold nanoparticles on lithographically patterned surfaces, University of California at Berkeley, August 2004
- A method of precisely positioning individual DNA strands between electrodes, Institute for Physical High Technology in Germany, April 2004
- A method of attaching DNA strands to the ends of single-walled carbon nanotubes, University of North Carolina, October 2002
- An observation that mica crystal preferentially binds to specific DNA sequences, Italian National Research Council (CNR), University of Bologna, University of Rome “La Sapienza”, September 2002

Advances in structures:

- A method for producing sequences of DNA that form a waffle-like grid (DNA Forms Nano Waffles, page 30)
- A method for making nanotubes from two of the four DNA bases (DNA Parts Make Versatile Nanotubes, page 31)
- A method for producing sequences of DNA that form branched structures (Scientists Brew Tree-Shaped DNA, page 32)
- A method for producing sequences of DNA that fold into nanoscale octahedrons (DNA Folds into Paired Pyramids, page 33)

Advances in electronics:

- A simulation that shows that single strands of DNA can be drawn inside carbon nanotubes by natural forces (Study Shows DNA Will Fill Tubes, page 33)
- A study that shows that DNA conductance is due to a water sheath found around the molecules rather than the molecules themselves, University of California at Los Angeles, September 2003
- A method for forming random, electrically-conductive networks of DNA strands on surfaces (DNA Conducts, page 33)
- A method of attaching multiple DNA strands between electrodes to produce conductive DNA wires (DNA Induced to Superconductivity, page 35)
- A method for forming DNA that contains zinc ions (Metal Makes DNA More Conductive, page 36)

Advances in materials:

- A transistor that contains a semiconductor channel made from a DNA base (DNA Part Makes Transistor, page 37)
- A photodetector made from a DNA base (DNA Device Detects Light Signals, page 37)

A prototype laser made from a DNA-based thin film, Chitose Institute of Science and Technology in Japan, August 2002

Computing

Programmable DNA Debuts

By Kimberly Patch, Technology Research News
November 28, 2001

The DNA molecule is the mechanism nature uses to construct every living being. Scientists are beginning to use the same mechanism to compute, but most of the rudimentary DNA computers built so far require researchers to manually trigger each step of a molecular calculation.

Researchers from the Weizmann Institute in Israel have found a way to automatically carry out several computational steps at once in a test tube of short, artificially-constructed DNA molecules. They put the DNA through a series of steps that, once begun, carried through to the end of a computation.

Although it takes minutes for DNA to do a single computation, many molecules can compute at once in a very small amount of space. "We get a trillion computers doing a billion operations per second in [a drop] of solution," said Ehud Shapiro, an associate professor in the departments of computer science and biological chemistry at the Weizmann Institute of Science in Israel.

This computation DNA, like biological DNA, is made up of four types of bases attached to long sugar-phosphate chains. Two of these chains, with bases attached, zip together, pairing up the bases on each chain to form DNA's classic double-helix shape.

Biological DNA uses specific sequences of the bases as blueprints to build the many proteins involved in the chemical reactions of life. The same sequences can represent numbers and be manipulated mathematically to compute.

The computation method uses two types of DNA molecules: software, or computation molecules, which are about 40 base pairs long and contain the instructions for the computation, and input molecules, which contain strings of six bases that represent the problem to be solved. A computation happens when these two types of molecules interact. Each has a sticky end, meaning one strand of the double helix is longer than the other, exposing a sequence of bases that are not paired.

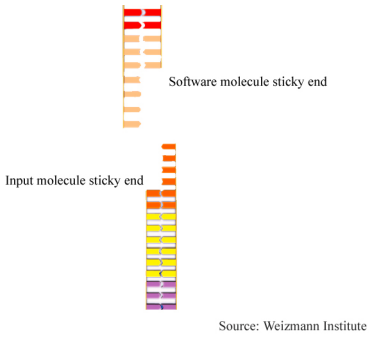
When the sticky end of an input molecule bumps into a software molecule that has a sticky end that fits, the bases of the two sticky ends join together, and an enzyme present in the solution seals them together. The molecule is then cut in

a different place by a second enzyme, exposing another sticky end so that a second step can take place. The number of steps depends on the number of computations coded into the software DNA strand.

For example, to answer the question 'does the sequence of letters "bab" contain an even number of b's?' the input DNA molecules would represent each of the three letters using a segment of DNA six bases long. The software molecules would contain a logical series of steps for determining whether the input has an even number of b's.

When the computation ends, the remaining sticky ends connect to one of two marker molecules of different lengths. One of the marker molecules contains a sequence of bases that will stick to the computation molecules' sticky end if the answer turned out to be even, and the other contains the correct sequences if the answer turned out to be odd.

Once the microscopic reshuffling of DNA bases is done, the researchers read the answer using gel electrophoresis, a process that involves putting DNA on a gel, and passing electrical current through electrodes attached to the gel. "[You] place the DNA near the minus electrode. The DNA travel slowly inside the gel towards the plus electrode at a speed that is a function of the molecule size. If you stop the process at the right time, you have a spread of the molecules according to... length," which makes it apparent which marker molecule has connected to the computation molecule, Shapiro said.



Source: Weizmann Institute

The short, artificially-constructed DNA molecules depicted here can carry out computational steps by matching and joining the exposed bases, or sticky ends.

The researchers' DNA computer can run 735 sample programs made up of sequences of the eight basic operations that are possible using six-base input strings.

Previous experiments that used DNA to compute had to be designed to solve a single problem, although some could handle varied inputs, said Nadrian Seeman, a chemistry professor at New York University. "Here, several different questions can be asked of the same system," he said. The work could lead to more generally programmable approaches to DNA-based computation, he added.

In the researchers' experiments, the DNA took nearly 17 minutes to carry out each operation; eventually DNA will probably be able to carry out an operation in a few seconds, said Shapiro.

Compared to silicon computer chips, which compute in millionths or billionths of a second, this would still be very slow, but because millions or trillions of DNA molecules could compute in parallel, this type of DNA computer could handle very large problems; more important, it works in a test tube.

The work is "different from most experimental work on DNA computers in that we do not attempt to compete with silicon computers by solving difficult problems faster. The potential is... operation in a biochemical environment," said Shapiro.

The method is "an ingenious construction that provides the capability of a basic sort of computation at the molecular scale," said John Reif, a computer science professor at Duke University. It is not new to use the molecular configuration of DNA to store the result of a computation, but this work provides a very general mechanism for using that result to then compute a further result, he said.

This type of work could eventually lead to molecular computers that could be used to control molecular processes like complex assemblies and molecular robotic devices, Reif said.

The method could be used to screen libraries of DNA in five to ten years, and could eventually be used to carry out more complicated tasks like detecting DNA anomalies and synthesizing drugs to fix them, Shapiro said, adding that this use is decades away.

Shapiro's research colleagues were Yaakov Benenson, Tamar Paz-Elizur, Rivka Adar and Zvi Livneh from the Weizmann Institute, and Ehud Keinan from the Weizmann Institute and the Scripps Research Institute. They published the research in the November 22, 2001 issue of *Nature*. The research was funded by the Weizmann Institute.

Timeline: 5-10 years, several decades
Funding: University
TRN Categories: Biological, Chemical, DNA and Molecular Computing
Story Type: News
Related Elements: Technical paper, "Programmable and Autonomous Computing Machine Made of Biomolecules," *Nature*, November 22, 2001

TRN

DNA Solves Big Problem

By Kimberly Patch, Technology Research News
March 20/27, 2002

DNA computers can theoretically solve problems that have a lot of variables because many DNA molecules can work on different parts of a problem at once. There is still a long way to go, however, before this ability can be leveraged to actually solve very large problems.

Researchers from the University of Southern California and the California Institute of Technology have taken a substantial step toward that end by solving a 20-variable problem using a DNA computer.

The problem was NP-complete, meaning solving it required an exhaustive search of its 1,048,576 possibilities. To date, it is the largest problem solved without electronic computers, according to Nickolas Chelyapov, a research scientist at the University of Southern California. "We did something that would require a human several years to do with pen and paper," he said. Previously researchers used RNA, which is chemically similar to DNA, to solve a nine-variable problem, which has 512 possibilities.

Chelyapov likened the 20-variable problem to that of a car dealer with a one million-car auto lot trying to satisfy a customer who has a complicated list of 24 intertwining criteria for the car he wants. Two of the criteria could be, for instance, that the car must be either a Cadillac or red, and if it is a Cadillac it must have four seats or a gas cap that locks.

To solve the 20-variable problem, the researchers carried out logical computations using short, artificial strands of DNA that had information embedded in the order of their bases. DNA is made up of adenine, cytosine, guanine and thymine bases strung together on a sugar-phosphate backbone. Single strands of DNA zip together to form a double helix when the bases on the two strands match in a way that allows adenine to pair with thymine, and cytosine to pair with guanine.

The variables were represented by 15-base DNA sequences. The problem involved finding a unique answer to a mathematical formula that used 20 of the sequences, or variables. The variables were strung together in sets of three, or triads. The answer contained 24 combinations of triads. The researchers made "library" strands of DNA that could combine with all the variables.

Once the pieces were in place, the "DNA computer had to take a look at all the answers and find one satisfying the formula," said Chelyapov. To do this, the researchers immobilized DNA strands representing the formula in gel-filled glass modules. They then coaxed the complementary library strands to move through the modules by electrophoresis, which uses electricity to move charged particles across a field. DNA molecules naturally carry a charge.

The library strands that had sequences complementary to the immobile ones joined with the residents and stayed in the module. Library strands without complementary sequences passed through. The researchers released the captured strands — preliminary answers — using a higher temperature electrophoresis.

The researchers were able to exhaust the possibilities and find an answer using 24 of these capture-release steps. "At each of the 24 steps [the] library was depleted of wrong answers, leaving only those involved in the formula. [The] final module contains just one answer... the correct unique assignment satisfying the formula," said Chelyapov.

One of the challenges in using DNA to solve a 20-variable problem was synthesizing the relatively long artificial DNA strands it required, said Chelyapov. Although biological DNA can be very long — our 23 pairs of chromosomes together contain about 3.3 billion base pairs — it is difficult to artificially produce even much shorter strands. The strands the researchers used were about 150 bases long.

The gel-filled modules made for a computer design that is dry and could be automated, and because the method does not damage the DNA, the strands can be reused, according to Chelyapov.

Although DNA computers are not likely to to compete with electronic computers for most uses, their ability to check many possible solutions at once could eventually allow them to solve NP-complete problems faster than for electronic computers, according to Chelyapov. A DNA computer that could solve a 50- to 60-variable problem would in theory solve it faster than today's electronic computers, he said.

In addition, because DNA computers are very energy-efficient and take up very little room, they may someday find use in environments where extreme energy-efficiency or small size are required, Chelyapov said. "Molecular computers can be considered in a broader context. They may provide a much-needed means for controlling chemical/biological systems in the same way that electronic computers have provided a means for controlling electrical/mechanical systems," he said.

It will be 10 years before DNA computers find practical uses, however, said Chelyapov.

The work is outstanding, according to Nadrian Seeman, a chemistry professor at New York University. "They have used a relatively quick electrophoretic method to go through a huge problem," he said.

The research shows that a DNA computer can solve a large problem "through a clever version of a sticker method. It works in part because the [formula DNA strand] is attached to a solid support, so that there is no competition from other molecules in solution," Seeman said.

Chelyapov's research colleagues were Ravinderjit S. Braich, Cliff Johnson and Leonard Adleman of the University of Southern California, and Paul W. K. Rothemund of the California Institute of Technology. They published the research in the March 14, 2002 issue of the journal *Science*.

The research was funded by the National Aeronautics and Space Administration (NASA), Defense Advanced Research Projects Agency (DARPA), the Office of Naval Research (ONR) and the National Science Foundation (NSF).

Timeline: 10 years
Funding: Government
TRN Categories: Biology; Biological, Chemical, DNA and Molecular Computing
Story Type: News
Related Elements: Technical paper, "Solution of a 20-Variable 3-SAT Problem on a DNA Computer," *Science*, March 14, 2002

TRN

DNA Could Crack Code

By Kimberly Patch, Technology Research News
October 24, 2001

Knowledge that electrical engineers have gained from laying out components on circuit boards could make it easier to coax DNA molecules to do computations. The result may make it possible to crack a code that requires 3,000 years to solve on today's computers.

DNA computers use the same type of molecules that make up the genetic code for all life on earth and are potentially very powerful because they can perform computations on many molecules at once.

A strand of DNA is a long string of phosphates, each attached to one of four bases: adenine, cytosine, guanine and thymine. Various types of enzymes can cut the long molecules in places where the bases appear in a certain order, causing the strands to reassemble. This setup can be co-opted to perform the logic of computing.

Researchers have already plotted the minimum requirements needed to build a DNA computer. This involves a set of standard DNA molecules, or tiles, that each handle two inputs and two outputs. The tiles compute by interacting with each other, and the answer is extracted from the resulting structural changes.

Researchers from Ruhr University in Germany and Accenture Technology Labs in France are proposing to redesign the DNA tiles that make up a DNA computer to look more like the layout of an electronic circuit.

"Because the computation is done through the spatial arrangement of DNA tiles, you have to be really careful in the way you design your tiles," said Andre Weimerskirch, a graduate student at Ruhr University. "It turns out that the schoolbook layout of an electronic circuit designed to perform multiplication can be easily translated into a design for DNA tiles," he said.

These more complicated tile designs, which the researchers equate to DNA programming, would make DNA computers easier to use, Weimerskirch said. "To make it simple, imagine a jigsaw puzzle. There's only one way [the pieces] all fit together, because there are rules governing their matching," he said. The DNA tiles are similar to the pieces of a jigsaw puzzle. "Your knowledge of the problem is encoded in the pieces, and the results of the computation is the whole jigsaw puzzle. The beauty is that you don't need to assemble the jigsaw puzzle yourself, it self-assembles," he said.

The researchers designed a multiplication tile, then went on to design even more complicated tiles. "We realized that we could do even more complicated operations... with few modifications," Weimerskirch said.

In theory, the design could be used to break a strong public key encryption system in a couple of days rather than the 3,000 years it would take an electronic computer, said Weimerskirch. The key needed to decrypt the NTRU Cryptosystems, Inc. encryption scheme is one in a very large number of possibilities: around 1,460 billion billion billion billion billion, which can also be represented as 2 to the 160th power.

The DNA computing scheme is fast; in addition, it can find an answer without having to try every number until one fits, according to Weimerskirch. Using the different types of tiles, the researchers can logically cut down on the possibilities in order to reduce the number that must be weeded out using brute force. This is essentially a type of programming. "The design of our tiles gives us the flexibility to... program the attack. The type of programming we can do is still rather crude, but we think this is... an important step in the right direction," said Weimerskirch.

There are several hurdles to carrying out the scheme on real DNA, according to the researchers.The first step is to make DNA tiles that conform to the designs. "This should not be too difficult and is within the reach of current technology," said Weimerskirch. The second challenge has to do with the error rate, he said. "We're currently performing simulations that will hopefully help us understand the problem better and hopefully allow us to give advice to the experimentalists" who may want to carry out the scheme, he said.

The researchers are also looking to find new tile designs that will solve even more complex problems, Weimerskirch said.

Doing computations using self-assembly is a very powerful method, said Nadrian Seeman, a chemistry professor at New York University. "The work... takes advantage of the notion of computation by self-assembly. However, the work remains a theoretical suggestion and its ultimate value will depend on its experimental implementation," he said.

It looks feasible to build tiles like the researchers have suggested, however, said Seeman. "We're not at this time building tiles exactly like those suggested by the authors, but we may well be able to do so in the foreseeable future," he said.

Because DNA computing is inherently more powerful than electronic computing, it could eventually be applied to many difficult problems like scheduling and cryptanalysis, said Weimerskirch. It is likely to take at least five years to overcome the experimental hurdles, he said.

Weimerskirch's research colleague was Oliver Pelletier of Accenture Technology Labs. The research was funded by Accenture Technology Labs.

Timeline: 5 years
Funding: Corporate
TRN Categories: Biological, Chemical, DNA and Molecular Computing;Cryptography and Security
Story Type: News
Related Elements: Technical paper, "Algorithmic Self-assembly of DNA Tiles and Its Application to Cryptanalysis,"

posted on the arXiv physics archive at archive at xxx.lanl.gov/abs/cs.CR/0110009

TRN

DNA Does Logic

By Kimberly Patch, Technology Research News
October 4, 2000

A group of researchers have coaxed bits of DNA to assemble themselves in a way that resulted in a logic operation.

The feat is useful for two different types of research. First, it is an important step toward using DNA to perform a vast number of computations at once. Second, this type of self-assembly could be used to build nanoscale devices.

The researchers used tiles, or short pieces of DNA, that had several distinct traits. They all had "sticky ends," meaning their ends would attach only to a corresponding end on another piece of DNA, like a lock and key. (See Figure 1) Two types of tiles represented the ones and zeros of binary logic. Each 0 tile had a site that fit with a particular restriction enzyme, while the 1 tiles did not have that site. The tiles were also divided into input, or X tiles and output, or Y tiles.

The researchers mixed the tiles in a test tube and they assembled themselves into a string of DNA in a certain order because each piece only fit with two other distinct pieces, like a puzzle. Four X tiles formed a four-digit binary number and four Y tiles formed a corresponding number. The assembly represented an XOR logic calculation. In an XOR calculation, the result is true, or 1, if the values compared are the same, and false, or 0, if they differ.

In essence, the researchers made an XOR circuit out of DNA. "We've proven we can do logic by self-assembly of DNA," said Nadrian Seeman, a chemistry professor at New York University.

This result was also a multistep logical process in a single step. "The tiles self-associated themselves to form this arrangement," said Seeman. Usually when researchers manipulate DNA, reactions are done in single step processes with researchers doing something like adding a new enzyme for each step.

To see the order of the tiles in the DNA, the researchers had to isolate the single strand that contained the 1 and 0 tiles. This recorder string wandered through the triple helixes of the DNA molecule. (See Figure 2)

The researchers extracted that strand by breaking down the weak hydrogen bonds that held the bulk of the DNA together, leaving the stronger covalent bonds that held together the tiles with the sticky ends. The researchers then determined the order of the ones and zeros by mixing the strand with the enzyme that reacts with the zero tiles.

The work goes beyond a simple molecular reaction to produce a true algorithm because it allows for "conditional information flow in a sequence of molecular interactions" said Erik Winfree, an assistant professor of computer science and computation and neural systems at Caltech. "By studying algorithmic self-assembly, [the researchers] are exploring our ability to program molecular interactions, in the true sense of the word," said Winfree.

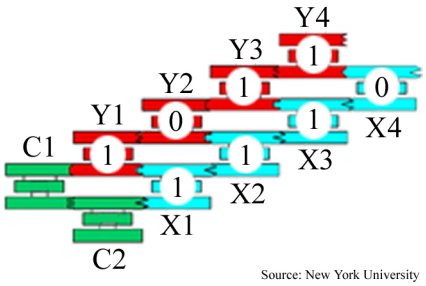
In the end, this type of algorithmic self-assembly "is computation, whether the output is numerical or a nano-fabricated device," said Winfree.

The researchers used a type of DNA that, in contrast to the double helix of biological DNA that is made up of two single strands, uses four single strands that repeatedly cross over each other to make up three double helixes. This makes for a less floppy molecule.

Using stiff DNA is important both for doing increasingly complicated calculations and for using DNA as scaffolding for nanoscale building, said Seeman. "You need stiff components not so much to get them to stay together... but to maintain their structural integrity. If you glue [marshmallows] with epoxy they'll be tough as hell in terms of the bond, but how big a house can you build out of marshmallows?"

The researchers are planning to build more complicated DNA molecules for two distinct uses, said Seeman. The XOR calculation was a very simple molecule, he said.

Enabled by the stiff DNA technology, self-assembled molecules of DNA can be expanded beyond a simple line of molecules into two or three dimensions, both to enable more complicated calculations and to form far more complex patterns, said Seeman."When I talk about patterns I'm talking about building circuits... using DNA molecules as scaffolding to direct other materials [like] nano electronic components, quantum dots, wires, switches," said Seeman. "We expect to make fairly complex patterns with relatively simple sets of input," he added.



Source: New York University

In this schematic of a DNA-based XOR calculation, geometric shapes show the different "sticky ends" of small pieces, or tiles, of DNA. The X tiles are input, and the Y tiles output. The C tiles simply provide a place to begin the reaction. The 0's and 1's are the binary numbers used in the computation. Each 0 tile fits with a particular restriction enzyme, while the 1 tiles do not.

Because many DNA strands can be created in parallel, all the possible answers to a certain arrangement can be found at once and many patterns can be created at once. For instance, the inputs and outputs of the researcher's XOR calculation were four-digit binary numbers, which yield 16 possible combinations that can be found all at once in a test tube. As calculations get vastly more complicated, massively

parallel computations that easily outstrip today's conventional computers are possible. "We don't have one molecule in our pot here, we have 10 to the 12th," said Seeman. The massively parallel nature of DNA makes it potentially cheap for both calculation and building, Seeman said.

Both practical DNA computers and processes that use DNA to assemble nanoscale devices are a decade away, he said.

Seeman's colleagues were Chengde Mao of New York University and Thomas H. Lebean and John H. Reif of Duke University. The research was funded by the National Institute of Health (NIH) the Office of Naval Research (ONR) the National Science Foundation (NSF), the U.S. Air Force and DARPA.

Timeline: 10 years
Funding: Government
TRN Categories: Biological, Chemical, DNA and Molecular Computing
Story Type: News
Related Elements: Technical paper, "Logical Computation Using Algorithmic Self-assembly of DNA Triple Crossover Molecules," Nature, September 28, 2000

TRN

DNA Makes Nano Barcode

By Kimberly Patch, Technology Research News
July 2/9, 2003

To keep Moore's Law going — the tenet that computer speed will roughly double every 18 months — manufacturers must make faster circuits, and that usually means making them smaller. If an electronic signal has less distance to travel, it will make the trip more quickly.

But as the components that make up electronic devices grow smaller it is becoming increasingly difficult for manufacturers to assemble them using traditional lithography methods, which employ light and chemicals to etch materials into shape. The transistors that form the bulk of the Pentium 4 computer chip, for instance, are already about 130 nanometers across, which is one-tenth the girth of an E. coli bacterium, or about the size of a row of 1,300 hydrogen atoms.

Lithography is ultimately limited in scale to the wavelength of light, said John Reif, a professor of computer science at Duke University. "Within one or two decades, the ultimate limitations of these top-down patterning methods will be reached," he said.

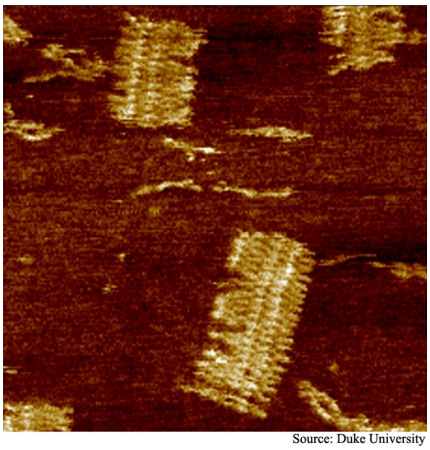
Another tack is assembling materials from the bottom up — molecule-by-molecule.

Reif and several colleagues at Duke University have moved the bottom-up method a step forward by programming strands of synthetic DNA to self-assemble into a structure that makes the pattern encoded in a DNA strand readable by microscope.

Key to the method is coaxing columns of looped and non-looped strands of DNA stack into a barcode-like lattice.

DNA is made up of sequences of four bases - adenine, cytosine, guanine and thymine — attached to a sugar-phosphate backbone. Complementary bases combine — thiamine with adenine, and cytosine with guanine — to form the familiar double-stranded helix of biological DNA.

The researchers used a single DNA "scaffolding" strand that contained sections of base sequences that were complementary to portions of DNA barcoding strands. They used two types of DNA barcoding strands — strands that contained hairpin loops, and strands that did not. The barcoding strands also contained sections of base sequences that caused barcoding strands to combine with like barcoding strands.



Source: Duke University

Stacks of DNA strands form microscopic sheets to produce bar code-like patterns that reveal data encoded in an initial strand of DNA.

The researchers mixed the scaffolding strand with barcoding strands to form a two-dimensional lattice, with an initial row of barcoding strands ordered by the scaffolding strand and additional barcoding strands stacked up on the originals, forming columns with loops and columns without loops. The columns were large enough that they could be sensed with an atomic force microscope and read like a barcode. "The barcode patterns... are determined by a scaffold strand of synthetic DNA. The other strands of DNA assemble around the scaffold strand to form the 2D barcode patterned lattice," said Reif.

The researchers programmed the process to produce two different barcodes — 01101 and 10010. The prototype DNA barcodes stored the five bits of information in a 75-nanometer long lattice of DNA.

The method is "a nice advance in assembling nano-objects," said David Harlan Wood, a professor of computer science at the University of Delaware. The ability to directly observe the assembly by looking through a microscope at the loops makes nano construction more practical, he said. "Readout techniques are sorely needed for DNA computing," he added.

This type of readout, however, is limited by the number of distinct objects. "When many multiple molecules are important, other methods, such as biochips, may be more appropriate," said Wood.

The method could eventually be used to make templates that will enable molecule-by-molecule construction of electronic circuits, said Reif. The process should yield more complicated patterns than columns if the scaffolding strand is wound back and forth, according to Reif. "Using these patterned DNA lattices as scaffolds, we intend... to self-assemble molecular electronic circuit components... with the goal of forming molecular-scale electronic circuitry," said Reif.

Molecular electronics and robotics components can be precisely positioned at specific locations on such a scaffolding, according to Reif.

There have been notable successes in constructing individual molecular components like carbon nanotubes, said Reif. The DNA scaffolding is one way to hold, shape and assemble these molecular components into complex machines and systems, he said.

The method could be ready for practical use in five to eight years, according to Reif

Reif's research colleagues were Hao Yan, Thomas H. LaBean and Liping Feng. The work appeared in the June 23, 2003 *Proceedings of the National Academy of Sciences*. The research was funded by the Defense Advanced Research Projects Agency (DARPA), the Air Force Office of Scientific Research (AFOSR), and the National Science Foundation (NSF).

Timeline: 5-8 years
Funding: Government
TRN Categories: Biological, Chemical, DNA and Molecular Computing; Nanotechnology
Story Type: News
Related Elements: Technical paper, "Directed Nucleation Assembly of DNA Tile Complexes for Barcode-Patterned Lattices," *Proceedings of the National Academy Of Sciences*, June 23, 2003

TRN

DNA Computer Readout Glows

By Kimberly Patch, Technology Research News
January 30, 2002

DNA is the ultimate biological code, packing all the information needed to make life forms as diverse as viruses, turnips and human beings into a microscopic package that can copy itself and automatically carry its own instructions.

It's no wonder that biologists and computer scientists are working toward using DNA for computing. Computers that use the microscopic molecules have the potential to solve certain types of very large problems, like finding the most efficient traveling salesman route or circuit board layout, much faster than conventional computers. This is because many DNA molecules can be used to work on all possible solutions to a problem at once.

Researchers from the University of Wisconsin-Madison have come up with a better way to read the results of a microscopic DNA computation once it is completed.

The challenge to reading DNA computing results is the molecules that represent the answer to a problem are mixed in with other DNA molecules, and it is difficult to pick out the right ones. The researchers' method makes the right molecules stand out by giving them the microscopic equivalent of the glow sticks people wave around at large outdoor events.

The approach "is a different way of finding out what is there," said Lloyd Smith, a chemistry professor at the University of Wisconsin-Madison and a director of Third Wave Technologies, Inc.

DNA molecules are made up of long strings of four types of bases connected to phosphate backbones. The order of the bases makes up a type of code.

DNA computers consist of large sets of DNA molecules that include all possible answers to a computational problem. During the DNA computing process a series of enzymes takes the DNA molecules through the logical steps needed to compute the correct answer by combining them and breaking them in different places to form new sequences. At the end of the computation there is a small subset of DNA molecules that represent the correct solutions to the problem.

The researchers' readout method involves putting the DNA into a series of wells that contain an enzyme and other DNA strands that contain inactivated fluorescent molecules. The combination lights up the correct answers by a method known as invasive cleavage. The DNA molecule representing the answer causes the enzyme to cleave, or cut, the fluorescent molecule free from its DNA strand, causing it to glow. "If a certain DNA molecule is present... the cleavage makes fluorescence appear," said Smith.

The cleavage method already existed, but it took some work to adapt it for reading DNA computing answers, said Liman Wang, part of the University of Wisconsin-Madison team, and now a senior research chemist at Merck Co. Inc. The researchers had to delete certain portions of the DNA in order to produce the specific sequence needed for the invasive cleavage method, said Wang.

The method is simpler and more accurate than previous readout methods, said Wang. "The signal uniformity has been significantly improved, and false positive signals are much less — in other words, the signal-to-noise ratio is higher."

The method is "an experimental improvement on the way Smith and his colleagues have been performing DNA-based computation for a number of years," said Nadrian Seeman, a chemistry professor at New York University. "They have increased the fidelity of their readout method," he said.

The key issue is whether the general method will work with very large problems, said Seeman. "The issues involve both the difficulty of setting up the problem and the accuracy

of the results. These authors have improved the accuracy of the results," he said.

The researchers are working to make fluorescence reaction uniform among all the different DNA answers, said Wang.

DNA computing is at least 10 years away from being used in practical applications, said Smith.

Smith and Wang's research colleagues were Jeff Hall of Third Wave Technologies, and Manchun Lu and Qinghua Lu of the University of Wisconsin-Madison. They published the research in the November, 2001 issue of *Nature Biotechnology*. The research was funded by the National Science Foundation (NSF) and the Defense Advanced Research Projects Agency (DARPA).

Timeline: Now, > 10 years
Funding: Government
TRN Categories: Biological, Chemical, DNA and Molecular Computing
Story Type: News
Related elements: Technical paper, "A DNA Computing Readout Operation Based on Structure-Specific Cleavage," *Nature Biotechnology*, November, 2001

TRN

Data Stored in Live Cells

By Kimberly Patch, Technology Research News
January 29/February 5, 2003

Every type of storage media — from stone to paper to magnetic disks — is subject to destruction. From the great fire that destroyed Alexandria's world-class library in 48 B.C. to that unfortunate hard drive crash last week, information has had a habit of suddenly disappearing because the media that contains it succumbs to the forces of nature.

Researchers from Pacific Northwest National Laboratory are tapping forces of nature to store information more permanently.

The researchers used artificial DNA sequences to encode portions of the text of the children's song It's a Small World, added the sequences to bacteria DNA, allowed the bacteria to multiply, then extracted the message part of a DNA strand and retrieved the encoded information.

Because DNA is passed down through generations of living organisms, information stored this way should survive for as long as the line of organisms survives, said Pak Wong, a chief scientist at the Pacific Northwest National Laboratory. DNA is made up of four bases attached to a sugar-phosphate backbone. Different sequences of the four bases can represent digital information.

Storing information is DNA's natural function, said Wong. "We [are] taking advantage of a time-tested, natural, nanoscale data storage technology perfected over the last 3 billion years." The encoding method could be used to store any digital information, he said. "Text, pictures, music — anything you can send or receive over the Web could be saved in this form."

DNA stores a large amount of information in a very small space. Considering that a milliliter of liquid can contain up to 10 billion bacteria, the potential capacity of bacterial-based DNA memory is enormous, assuming that the data can be retrieved in an organized way, according to Wong.

One challenge to storing information in living DNA is is that it naturally mutates, changing the information. Information stored using the researchers' method is subject to mutation, but embedding the information in the DNA of an organism that can survive harsh environments cuts down on potential errors, said Wong.

Wong's lab is also carrying out projects that involve genetically engineering hearty Deinococcus radiodurans bacteria "for bioremediation in a radioactive environment," said Wong. "The bacterium's extreme resistance to environmental insults gave us the idea of selecting it as data storage," he said.

This radiation-resistant bacteria could be used to preserve data in the event of nuclear attack or accident, according to Wong.

Organisms succumb to radiation because the radiation causes so many mutations that the organisms life processes do not work correctly. And organism that is resistant to radiation damage would by definition be resistant to mutation. "By carefully choosing the host organism and the data encoding method, the error rate caused by mutation is very low," Wong said.

In a related development, scientists from the Weizmann Institute of Science in Israel, the National Institutes of Health, and the Uniformed Services University of the Health Sciences have found a clue to the mystery of how this particular bacteria can survive high doses of radiation. The bacteria's DNA forms tightly packed rings so that when radiation slices the DNA, the pieces stay in place and the DNA mends in the correct order.

The data storage method could also produce many copies of the data, and these could be compared in order to correct the errors that do occur, said Wong. "There is very high redundancy in the message since there is a copy in each bacterial cell and there may be millions of cells in a needle-size bacterial colony," he said.

The researchers embedded DNA containing information into a circular DNA molecule capable of self-replicating within a bacterial host. They introduced the circular DNA molecules into the bacteria using high-voltage shocks. The DNA was then incorporated into the genome of the bacteria for long-term information storage.

The researchers let the bacteria propagate for 100 generations, then retrieved the encoded information by extracting the message part of the DNA strand from the youngest generation and reading it via polymerase chain

reaction, a laboratory procedure that took about two hours and involved a series of heating and cooling cycles.

The researchers used seven different bacteria to store and retrieve seven DNA fragments that ranged from 57 to 99 base pairs long and encoded text from the children's song, according to Wong. One of the segments was the text "and the oceans are wide."

Showing that it's possible to store and retrieve information using the DNA of a living organism is a step toward a new data storage medium, according to Wong.

The next step is devising a way to retrieve the information quickly enough to make the method useful. "The technical challenge will be to develop high throughput of retrieving the information already stored in the bacteria," said Wong. The researchers are currently working on an idea toward that end, he said.

Although the idea of storing information in DNA is not new, the research has merit, said Lila Kari, an associate professor of computer science at the University of Western Ontario in Canada. "DNA can accomplish astounding information density... in principle it is a worthwhile endeavor," she said.

In an experiment published in 1999, researchers from Mount Sinai School of Medicine encoded information in a strand of DNA, included the DNA in a printed period in a document, then recovered the embedded message after sending the document through the U.S. mail.

The Pacific Northwest National Laboratory researchers' experiments have moved the concept of DNA as a storage medium in a different direction by storing information-containing DNA in a living organism.

There are some potential problems with some of the researchers' projections, however, Kari said. "They say that the memory capacity would be huge because each bacteria in a colony could encode different information; it is very difficult to select a single bacteria from a colony," she said.

It's too early to tell when the method could be used to store data in a practical way, said Wong. "Being able to apply the technology practically involves not only technological advancements but also... social and environmental issues, which have not been addressed," he said.

The ultimate goal of the research "is to use living organisms to store and retrieve significant amounts of data quickly," said Wong. Living organisms, including weeds and cockroaches, that have survived on Earth now are for hundreds of millions of years are good candidates for protecting critical information for future generations, according to Wong.

Other potential applications include DNA watermarking to protect intellectual property rights to organisms like crop seeds, and even allowing people to store personal information within their own DNA, according to Wong.

Wong's research colleagues were Kwong-kwok Wong and Harlan Foote. They published the research in the January, 2003 issue of *Communications of the ACM*. The research was funded by the Pacific Northwest National Laboratory.

Timeline: Unknown
Funding: Government
TRN Categories: Biotechnology; Biological, Chemical, DNA and Molecular Computing; Data Storage Technology
Story Type: News
Related Elements: Technical paper, "Organic Data Memory Using the DNA Approach," *Communications of the ACM*, January, 2003; technical paper "Ringlike Structure of the nococcus radiodurans Genome: A Key to Radioresistance?", *Science*, January 10, 2003

TRN

Machines

Genes Automate DNA Machines

Technology Research News, June 16/23, 2004

Scientists have been working with DNA with an eye toward using it to make nanoscale machines that could eventually work autonomously in environments like the human body.

Researchers from the University of Munich in Germany have taken a step toward automating nanomachines with a method that allows instructions for a DNA-based machine to be contained in a gene, or another stretch of DNA.

The method could be used to automate any nanomachine that requires fuel DNA to be added manually to start a reaction, according to the researchers. The researchers built a DNA tweezer and a gene that closed the tweezer.

Genes work by transcribing instructions to a strand of messenger RNA, which then translates the instructions into proteins that carry out a function. The researchers' gene encoded an RNA fuel strand.

The method could be used to activate or block biological reactions or produce reactions not found in nature, according to the researchers.

The method is a step toward DNA nanomachines that can operate in living cells, but there's a lot of work to be done before this can be realized, according to the researchers. The DNA machine and the gene with the instructions for the machine would have to be delivered into a cell simultaneously in a way that cells would not treat them as foreign objects and destroy them.

The method could be used for practical applications in five to ten years, according to the researchers. The work appeared in the April 14, 2004 issue of *Nano Letters*.

TRN

DNA Bot Targets Cancer

By Kimberly Patch, Technology Research News
May 5/12, 2004

Researchers from the Weizmann Institute in Israel have constructed a molecular-size computer that is programmed to find signs of cancer cells, and when they are present, dispense DNA molecules designed to eradicate those cells.

The researchers' computer is a proof-of-concept that works only in a test tube, but the device is meant to eventually work in the human body. The prototype shows that "autonomous, molecular-scale systems are able to perform such complex tasks as disease diagnosis and treatment," said Yaakov Benenson, a researcher at the Weizmann Institute.

The computer is small enough that one trillion of them fit in a drop of water. It is made from strands of DNA and operates in liquid. It analyzes the messenger RNA molecules in its environment, and when it finds a balance of RNA levels that indicate a type of cancer it is programmed to recognize, it releases DNA molecules designed to cause cancer cells to self-destruct.

DNA consists of four types of bases — adenine, cytosine, guanine and thymine — connected to a sugar-phosphate backbone. The familiar double helix of biological DNA consists of a double strand with connected base pairs. Messenger RNA is a carbon copy of portions of the DNA stored in the nucleus of the cell, and indicates that those portions of the DNA are active.

The molecular computer consists of three modules: input, computation and output.

The input module consists of single strands of DNA that contain stretches of bases that pair up with and so identify certain stretches of messenger RNA. The computation module processes a series of input modules to determine whether the balance of certain types of messenger RNA indicates the presence of cancer cells. The output module administers a drug in the form of another DNA strand when cancer cells are indicated.

The researchers' prototype includes a second type of DNA computer that is programmed to release a DNA strand that inhibits the first computer's drug molecule if cancer cells are not present. Both DNA computers must register the presence of cancer cells for the cancer-fighting DNA strand to be administered.

The researchers' previous work and that of other researchers showed that DNA can be made to perform computations using DNA's ability to match up sequences of base pairs, and enzymes, which can be used to snip strands.

The researchers recently developed a DNA computer that operates without human intervention. They modified the autonomous computer to make the cancer-detecting computer. "We took our existing molecular computer and [changed] its program [to respond] to abnormal messenger RNA labels and/or mutations," he said. "Our computation result depends on these levels, which may indicate a disease."

In their proof-of-concept experiments, the researchers mixed DNA computers programmed to identify prostate cancer in a test tube with prostate cancer cells. The computers were able to identify the cells and release DNA strands designed to eradicate the cells. The researchers programmed a second set of DNA computers to identify a certain form of lung cancer cells, and the computers successfully identified those as well.

The method has the potential to detect multiple disease conditions at once, said Benenson. This "makes the diagnosis very selective," he said.

The key to the method is that the tiny computer is made from a material that is intrinsically compatible with living beings, said Benenson. "In situ detection and analysis of molecular signals in living organisms is impossible with electronic computers due to the insurmountable incompatibility of the materials involved," he said.

The next step is to see if practical applications like real diagnosis and cure are possible using the DNA computers, said Benenson. Even though the materials are biologically compatible, the device itself "will require major modifications to be made compatible with living systems," he said.

The first working smart drugs are likely to sense just a single disease indicator and may become available within the next three to four years. More elaborate smart drugs like the researchers' molecular-scale computer could take 10 years to reach clinical trials, said Benenson.

Benenson's research colleagues were Binyamin Gil, Uri Ben-Dor, Rivka Adar and Ehud Shapiro. The work appeared in the April 29, 2004 issue of *Nature*. The research was funded by the Israeli Science Foundation, the Moross Cancer Institute and the Minerva Foundation.

Timeline: 3-4 years, 10 years
Funding: Government; Private
TRN Categories: Biological, Chemical, DNA and Molecular Computing;Biotechnology
Story Type: News
Related Elements: Technical paper, "An Autonomous Molecular Computer for Logical Control of Gene Expression," *Nature*, April 29, 2004

TRN

DNA Plays Tic-tac-toe

By Kimberly Patch, Technology Research News
August 27/September 3, 2003

During the time they knew each other as kids in Belgrade, Serbia, Milan Stojanovic and Darko Stefanovic didn't play tic-tac-toe, according to Stojanovic. Things are different now

that they are scientists at Columbia University and the University of New Mexico.

The researchers have fashioned a device that uses pieces of artificial DNA to automatically play tic-tac-toe. And as long as it makes the first move, the device cannot be beat.

The device is made of nine wells containing solutions where DNA can react. DNA in the wells acts like logic gates. "The distribution of logic gates in wells is such that it implements a perfect [tic-tac-toe] strategy," said Stojanovic. "Tic-tac-toe is a game of perfect information and guarantees a victory or draw for the first player," he said.

This makes it a good test for an automaton — a machine that operates on its own, without human control. The device, dubbed Molecular Array of YES and ANDANDNOT gates (MAYA), is simpler than a computer, which is generally capable of storing, organizing and processing data, or controling other machines, said Stojanovic.

The researchers' method could eventually be used to control nano devices and in automata that educate people about science, said Stojanovic.

MAYA contains 24 logic gates distributed in the nine wells of solution. Some of the logic gates in each well perform Boolean calculations when short single-stranded DNA sequences, or oligonucleotides, are added. The addition triggers an enzyme to react with DNA. Depending on the result, the reaction may expose a fluorescent molecule.

DNA is formed from four types of bases - adenine, cytosine, guanine and thymine — connected to a sugar-phosphate backbone. Strands of DNA can combine to form double-stranded DNA when their base sequences match up: adenine across from thymine, and cytosine across from guanine.

The researchers' device contains two types of gates that perform two types of Boolean calculations. The DNA molecule that makes up a YES logic gate has two states, one of which is fluorescent, or active. The more complicated DNA molecule that makes up a combination ANDANDNOT gate contains eight physical states, one of which is active.

YES gates change from nonactive to active when a complementary DNA sequence combines with the DNA in the well to release a loop in the DNA, which triggers a second reaction that exposes a fluorescent molecule. The ANDANDNOT gate contains three groups and is activated only if two of three possible inputs are provided.

MAYA always goes first and always starts in the center. Then the human challenger adds a DNA sequence to all the wells to represent the second move. The DNA sequence triggers a positive reaction with the DNA contained in only one of the wells — the reaction exposes a fluorescent molecule, which makes the well glow to indicate the move.

"The game is played like this," said Stojanovic. "[The] human moves by adding oligonucleotide, takes a fluorescence reading, and adds [the] next oligonucleotide," he said. The game continues until the automaton wins, or there are no more spaces on the board, resulting in a draw.

The researchers' method differs from standard DNA computing, which is aimed at tapping DNA's massively parallel nature. In theory DNA could be used to test all possible answers to a problem at once in order to identify those that fit certain criteria. The goal of this type of DNA computing is to compete with silicon in certain applications that have large numbers of possibilities, like code-cracking.

In contrast, the researchers' method is aimed at adding relatively simple logic to nano devices. "We're not taking advantage of massively parallel processing capabilities," said Stojanovic. "Our approach is silicomimetic," he said. The researchers use molecules that behave as logic gates, and arrange these logic gates into more complicated circuits by mixing them in solution.

The researchers are aiming to eventually use the method to control nano devices in the human body, said Stojanovic. "We hope... in some distant... future, to use similar [devices] to make decisions in vivo [about] whether to release a toxic compound or not, [or] to kill a cell not," he said. Such devices could also be used to monitor in vivo disease signatures of astronauts on long space flights, he said.

Such uses are probably several decades away, Stojanovic added.

The research is also aimed at constructing automata that could help popularize science and familiarize young people with advanced concepts in nanotechnology, said Stojanovic.

The researchers are currently working on improving the tic-tac-toe device and on connecting DNA networks to sensors, said Stojanovic.

The work appeared in the August 17, 2003 issue of *Nature Biotechnology*. The research was funded by the National Aeronautics and Space Administration (NASA), and the National Science Foundation (NSF).

Timeline: Several decades
Funding: Government
TRN Categories: Biological, Chemical, DNA and Molecular Computing
Story Type: News
Related Elements: Technical paper, "A deoxyribosome-Based Molecular Automation," *Nature Biotechnology,* August 17, 2003

TRN

Nanotech Scheme Envisions DNA Origami

By Kimberly Patch, Technology Research News
February 13, 2002

The key to coaxing DNA, which provides the biological instructions for all life on earth, to construct microscopic machines is getting it to follow new instructions.

Biological DNA uses four molecular bases as a kind of code, and unfolds itself to replicate portions of the code when a cell needs to carry out particular instructions.

Researchers at Yale University and Northwestern University have come up with a scheme to combine DNA tiles to form three-dimensional structures. DNA tiles are squares of artificial DNA that can be used to compute.

The method points to a precise way to build molecular-size, three-dimensional objects. The scheme could also eventually carry out certain types of computations more quickly than is possible using today's methods.

The key to the three-dimensional self-assembly theory was coming up with a way to make every DNA tile used in a shape unique, said Vijay Ramachandran, a graduate student at Yale University. "DNA tiles can be thought of as puzzle pieces. Each of the four sides of the square has an exposed DNA sequence... the unique pattern that joins with some other puzzle piece, or maybe a border that joins with nothing at all," he said.

DNA tiles can be produced in the laboratory from made-to-order DNA sequences. "The key is designing the tiles so that they form the correct shape. Once a flat shape is formed, parts of the shape [connect to] each other, and the shape folds into a box," he said.

"We needed a way to make every shape... unique, but still make the edges within the shape... correspond so the shape could fold," said Ramachandran. The researchers came up with an algorithm that uses randomness to build a hollow cube, he said.

Different copies of the tiles have unique sticky ends, or portions of single strands of DNA that can connect to other single strands, according to Ramachandran. The algorithm generates the random sequences of DNA that make up these complementary sticky ends. The algorithm also ensures that the DNA will not stick in the wrong places, he said. "We identified the steps needed to produce shapes in solution, using a reasonable number of tiles that will not stick to each other," he said.

The researchers also looked into the way temperature can be used cut down on the number of steps needed to construct the DNA boxes. "We also tried to introduce the use of other laboratory procedures, such as using temperature to prevent or induce the binding of tiles in solution," said Ramachandran.

The method could be used as a framework for building other precise three-dimensional shapes using DNA tiles, he said.

The researchers also worked out a set of guidelines that analyze this type of algorithm, according to Ramachandran. Those measures are designed to make it easier to come up with further algorithms for three-dimensional DNA self-assembly.

"I like the idea that the authors are approaching 3D systems," said Nadrian Seeman a chemistry professor at New York University. It is difficult to judge how useful it is because the theory lacks experimental backing, however. "It would be a stronger contribution if 3-D systems had been achieved first... so that we would know more about potentially viable and inviable structural alternatives," he said.

It is difficult to know when the method could be tested in the laboratory, said Ramachandran. "Our method requires... procedures that are more complex than those currently used for computation in the lab. It is hard to tell when... implementing this idea will be possible," he said.

In addition, in order to actually carry out the three-dimensional self-assembly, a stronger type of DNA tile may be needed, according to Ramachandran.

Ramachandran's research colleague was Ming-Yang Kao of Northwestern University. The research was funded by the National Science Foundation (NSF) and the Department of Defense (DoD).

Timeline: Unknown
Funding: Government
TRN Categories: Biological, Chemical, DNA and Molecular Computing
Story Type: News
Related Elements: Technical paper, "DNA Self-assembly for Constructing 3-D Boxes," posted in the arXiv physics archive at xxx.lanl.gov/abs/cs.CC/0112009.

TRN

DNA Has Nano Building in Hand

Technology Research News, March 24/31, 2004

Researchers from Ludwig Maximilians University in Germany have built a simple molecular machine from DNA that can bind to and release single molecules of a specific type of protein.

The DNA hand can be made to select any of many types of proteins, and could eventually be used to construct materials or machines molecule-by-molecule.

The researchers used DNA branch migration, a method that allows a DNA nanostructure to switch between several arrangements of its parts, to construct the DNA hand. In one configuration, the structure contains an open sequence of bases that binds to a specific protein, and so can grab that

type of protein. A second configuration does not contain the open sequence, and so drops the protein.

The rearrangements are reversible, allowing the tiny machine to repeatedly grab and drop a molecule of a specific type of protein. DNA aptamers, or strands that bind to specific molecules, can be selected from a pool of DNA sequences, making it possible to construct a DNA hand that binds to any type of protein, according to the researchers.

The researchers demonstrated the DNA hand by having it repeatedly grab and drop molecules of the protein Thrombin.

The DNA hand could be used in simple nano construction applications in two to five years, and in more advanced applications in five to ten years, according to the researchers. The work is scheduled to appear in an upcoming issue of *Angewandte Chemie International Edition*.

TRN

DNA Motor Keeps Cranking

By Kimberly Patch, Technology Research News
April 23/30, 2003

Scientists working to harness DNA to construct and power microscopic devices have gained an important tool.

Researchers at Lucent Technologies' Bell Labs and the University of Oxford in England have found a way to keep their DNA motor running continuously. Previously, the researchers had to add particular strands of DNA at different steps in the motor's cycle to keep it going.

The free-running DNA motor could eventually power microscopic machines capable of constructing and transporting chemicals and materials molecule by molecule.

Each strand of DNA contains four types of bases — adenine, cytosine, guanine and thymine — attached to a sugar-phosphate backbone. Complementary bases — adenine with thymine, and cytosine with guanine — combine to zip a pair of single DNA strands into a double helix.

A motor works by changing shape, then changing back again. In previous work, the researchers realized that a strand of DNA could be coaxed into a hairpin-like shape by causing complementary base sequences near the middle of the strand to combine with each other. This was the first step in constructing a motor from the molecule. "We realized that the nanostructure could be restored to its initial configuration by the complement, or opposite base sequence, of the strand of DNA that was used to induce the shape change," said Bernard Yurke, a distinguished member of technical staff at Bell Labs.

The key to making a free-running motor rather than a device that required the addition of new base sequences between movements, however, was finding a way to prevent the portion of the strand that formed a hairpin — the fuel strand — and the complement that removed the hairpin shape from simply combining with each other.

The researchers accomplished this by forcing the fuel strand of DNA into a tiny loop to make it physically impossible for the removal strand to combine directly with the fuel strand. "The removal strand, because it is long and only its middle portion can [combine] with the unpaired bases of the loop, has difficulty threading its way through the loop to form a double helix," he said.

The researchers added a shorter strand of DNA, dubbed the motor strand, that was able to combine with some of the unpaired bases of the loop to open it. "Once a loop is opened, the removal strand can [combine] with unpaired bases on the fuel strand and displace the [motor] strand from the loop," said Yurke. The displaced motor strand is then free to attach itself to a new loop to start the process over again.

If the motor strand were part of a nanostructure, the structure could be repetitively switched between two states as long as a few fuel loops and removal strands were present, Yurke said.

DNA can be used to impart force due to a pair of useful properties, said Yurke. First, when double-stranded DNA is less than 50 nanometers long, it behaves like a rigid rod, while a single strand of DNA behaves more like a floppy string, he said. Second, when strands of DNA are zipping up to form double-strand DNA, they can impart a force of up to 15 piconewtons.

A nanometer is one millionth of a millimeter, and 50 nanometers is about one 20th the diameter of E. coli bacteria. A piconewton is one trillionth of a Newton, which is about the force of a falling apple.

"The change in stiffness as a single-strand of DNA is transformed into double-strand DNA and the force that can be developed during the transformation can be used to drive shape changes in nanostructures," said Yurke.

The method is the first that uses DNA to power a free running system, according to Nadrian Seeman, a professor of chemistry at New York University. "To date, all DNA-based nanomechanical devices have required [input] to change state," he said. "These [researchers] have put together a system that will, in principle, allow for a free-running machine."

Such a machine could provide power for devices like nanorobots and nanomechanical computers, Seeman said.

"This is cutting-edge work that advances DNA nanotechnology," he added.

The DNA motor could eventually power nanomachines for use in medicine, chemistry and materials science, said Yurke. "Molecular motors ought to be extremely useful. Living cells are loaded with molecular motors and these serve crucial roles in turning out a wide range of life's functions, including cell movement, molecular transport, replication and even chemical synthesis," he said.

Devising DNA-based molecular motors was an exercise in getting DNA to assemble itself into a useful device, said Yurke. Eventually it may be possible to coax DNA to assemble into much more complicated structures, including molecular-scale electronic circuits, he said.

It is too early to tell when synthetic molecular motors will be used practically, said Yurke.

Yurke's research colleagues were Andrew J. Turberfield and J. C. Mitchell at the University of Oxford, A. P. Mills, Jr., formerly at Bell Labs and now the University of California at Riverside, F. C. Simmel, formerly at Bell Labs and now at Ludwig Maximilians University in Germany, and M. I. Blakey at Bell Labs. The work appeared in the March 18, 2003 issue of Physical Review Letters. The research was funded by Lucent Technologies.

Timeline: Unknown
Funding: Corporate
TRN Categories: Nanotechnology; Biotechnology
Story Type: News
Related Elements: Technical paper, "DNA fuel for Free-Running Nanomachines," Physical Review Letters, March 21, 2003

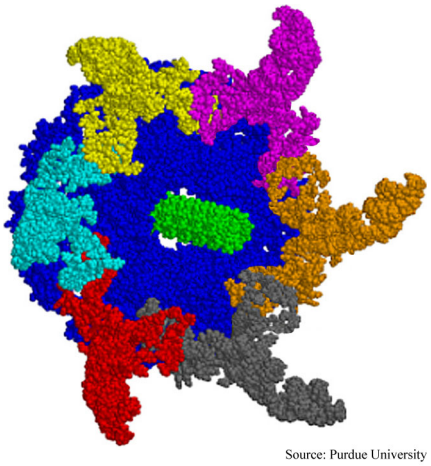
TRN

RNA Forms Nanomotor

Technology Research News, March 12/19, 2003

Researchers from Purdue University have constructed a tiny motor from DNA and RNA molecules. The device, fueled by ATP, which powers our own movements, could eventually power nanomachines.

The motor measures about 30 nanometers long, which is less than one hundredth the size of a red blood cell.



Source: Purdue University

This diagram shows a motor that is 100 times smaller than a red blood cell. The green rod is DNA and the multicolor outer ring RNA. In the presence of ATP, the substance sthat powers biological processes, the RNA spins the DNA.

It is made from six strands of RNA surrounding a center strand of DNA. In the presence of ATP, the RNA strands push the DNA axle in succession, spinning it around. This produces 50 to 60 piconewtons, or trillionths of a newton of force. A falling apple exerts about one newton of force.

The motor has potential in biological applications as well. The researchers have driven the tiny motor axle through the protective protein coat of a virus. The motor could eventually be used to deliver genes or therapeutic molecules into live cells, according to the researchers.

The motor could be used in practical applications in two to five years, according to the researchers. The work appeared in the February issue of the *Journal of Biological Chemistry*.

TRN

Morphing DNA Makes Motor

By Kimberly Patch, Technology Research News
January 16, 2002

DNA molecules are prime candidates for helping humans make microscopic machines because they have a long history of assembling things on the molecular scale. Every one of a human's 75 to100 trillion cells exists because a DNA molecule automatically unzipped, created the duplicate a cell needs to divide, then folded itself neatly back up again.

Researchers at New York University have taken a significant step forward in being able to instruct artificial DNA molecules to move in specific ways with a method that allows certain portions of DNA to bind to each other, and then release. This reversible binding method allows for control of the shape of a DNA molecule, or machine.

The researchers demonstrated the mechanism by making a four-step rotary motor out of DNA.

The motor is a four-stranded DNA molecule that, prompted by separate strands of DNA, will go through a mechanical cycle over and over again. Because the process is a reversible cycle, there are no waste products.

The four-stranded DNA molecule is essentially a pair of double helixes of DNA connected at several points along their lengths.

When the researchers add molecules of control DNA to a solution full of the motor molecules, the short, single-stranded control molecules join with the larger molecules and rearrange them by connecting two of the double strands in one place and cutting them in another. The researchers then remove the control strands using fuel strands of DNA, which are also short single-stranded lengths of DNA. This leaves the motor molecule in a different physical shape than when it started — the end of one double strand of the DNA is rotated 180 degrees relative to the strands next to it.

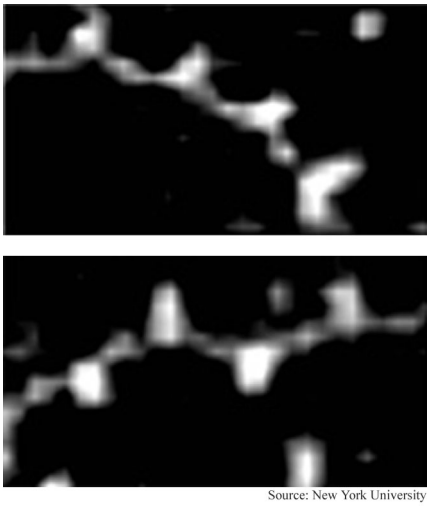
The process can be reversed by adding a different type of control strand to the solution, and that control strand can also be removed by a different type of fuel strand after it changes the molecule back. "The system can be cycled numerous times... and there are no breakdown products," said Nadrian Seeman, a chemistry professor at New York University.

The process can be adapted to many different sequences of DNA, said Seeman. "Many different species of this device can be made by changing the sequences in the region where the... strands bind," he said.

This means a wide range of similar rotary devices can be created by changing the fuel strands and the places where they bind, he said. Ten different molecules can result in 1,024 different structures, for instance.

The researchers are currently working on a method to insert the DNA devices into molecular lattices, said Seeman. This would enable still more structures. An array of four by four molecules, for instance, could produce 65,536 different shapes. "This may enable us to build nanofabrication facilities to produce new molecular species," he said.

The range of motion the molecular motors can produce ranges from .04 to 4 nanometers, but the researchers have produced motions as large as 35 nanometers using arrays, according to Seeman. A nanometer is one millionth of a millimeter. On this scale, an E. coli bacterium is a relative giant, with a girth of 1 micron, or 1,000 nanometers. A line of ten carbon atoms measures about one nanometer.



Source: New York University

The bumps on this DNA motor each consist of three joined DNA tiles. The top image shows the bumps aligned with each other. The bottom image shows the bumps alternating directions after one cycle of the motor.

The research is "great stuff," said Erik Winfree, an assistant professor of computer science and computation and neural systems at the California Institute of Technology. The method is a step forward in terms of DNA mechanics, he said. "It expands our toolbox for designing molecular machines."

The research is ultimately aimed at making nanorobotics practical, according to Seeman. "It could be used to configure a molecular pegboard or control molecular assemblers. The ability to achieve many different shapes means that you can create many different patterns; different patterns in a timed sequence are the essence of a machine or robot," he said.

Molecular machines could be used to assemble drugs molecule-by-molecule, and molecular robots may eventually work inside the human body.

It will be about a decade before the method can be used to make practical devices, said Seeman.

Seeman's research colleagues were Hao Yan, Xiaoping Zhang and Zhiyong Shen. They published the research in the January 3, 2002 issue of *Nature*. The research was funded by the National Science Foundation (NSF), Office of Naval Research (ONR), the National Institutes of Health (NIH) and the Defense Advanced Research Projects Agency (DARPA).

Timeline: 10 years
Funding: Government
TRN Categories: Biological, Chemical, DNA and Molecular Computing;Nanotechnology
Story Type: News
Related Elements: Technical paper, " A robust DNA mechanical device controlled by hybridization topology," *Nature*, January 3, 2002

TRN

DNA Strands Form Nano-Machine

By Kimberly Patch, Technology Research News
September 6, 2000

Researchers at Bell Laboratories have adopted the mechanics of DNA's replication process to make a tiny step motor entirely out of DNA. The motor could one day be used to manipulate other molecules.

The key realization that led to the motor design was that one strand of DNA can physically change another, said Bernard Yurke, a distinguished researcher at Lucent's Bell Labs.

Living things use long strands of DNA, which is made up of four types of bases, to store information. When cell DNA replicates, it unzips into two single strands and each single strand attracts complementary bases, which, in turn, form another single strand of DNA paired with the original strand. Similarly, when strands of DNA have complementary sections of bases, the sections attract each other like magnets.

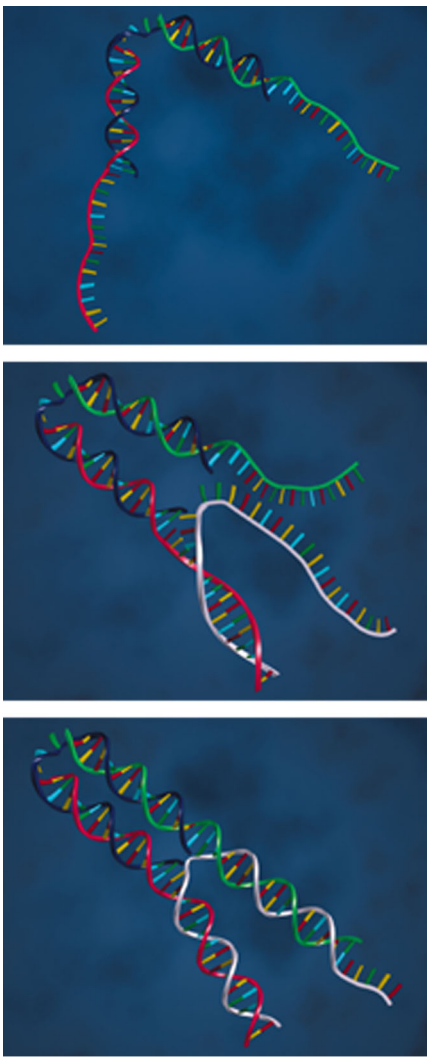
When working with DNA, Yurke noticed that a certain single strand that was manufactured with random sequences folded in on itself like a hairpin when complementary sequences on the single strand paired. What surprised him, however, was that this hairpin DNA was able to unfold and assemble into the structure he intended when complementary strands of DNA were added to the solution. The hairpin strand unfolded because the new strand had more base pairs in common with the hairpin strand as a whole, and that allowed it to also usurp the portions that had doubled up.

"We realized that one strand of DNA could induce changes in the configuration of another strand, and that led us to think about how one could actually build molecular motors out of DNA," said Yurke.

Yurke's DNA motor resembles a pair of tweezers. The tweezer's arms are made of double-stranded DNA and are

bound together on one end by a more flexible single strand. The double strands of the arms are not even, leaving single-strand overhangs on the pincer ends of the arms.

The motor works when two single strands of DNA bind with the overhangs to alternately open and shut the tweezers.



Source: Bell Labs

Bell Labs' DNA motor has two double-stranded arms connected by a single-strand hinge, and two single-stranded handles at the pincer ends of the arms (top figure).To close the tweezers, they add a "fuel" strand of DNA (middle figure), which attaches to the handles and draws the two arms of the tweezers together (bottom figure).

The tweezers shut when a "fuel" strand pairs with the overhangs on the tweezer ends. They open when a "removal" strand pairs with a longer portion of the fuel strand then the overhangs are attached to, then takes over the portion paired with the overhangs, pulling the fuel strand off the tweezers.

"When you go from open tweezer to close tweezer and then back to open tweezer you end up with a fuel strand and removal strand hybridized together and that's the waste product." said Yurke.

The DNA motor works in a step process, meaning the researchers must add the fuel strand first, which closes the tweezer, then add the removal strand. Otherwise, the two would simply pair together.

This method can be used to make DNA motors that respond to different fuel and removal strands, Yurke said. "The sequences of the overhangs on the tweezers can be changed so we can close any particular motor simply by adding the strand that closes that particular motor," he said.

This flexibility makes it a clear advance in molecular devices, said Nadrian Seeman, a chemistry professor at New York University. "We produced a device about a year and a half ago that was triggered by a small chemical [but] this one is triggered by a particular sequence. That means that they'll be able to have a bunch of them and control them all individually and that will be of great utility."

"I think of the [DNA] motors as little fingers that we now have to manipulate things on a nanoscale," said Yurke.

"And they will probably first be used to move molecules — nanoscale objects — in relation to each other for scientific purposes, simply to see how things interact as you move them in relationship to each other on that kind of length scale."

The technology could be used for this type of scientific investigation within five years, said Yurke. In a decade or more, it may enable more practical applications like medical diagnostics, medical therapeutics and synthetic substance manufacturing, he said.

Yurke's colleagues in the research were Andrew J. Turberfield of Oxford University, England and Bell Labs, and Alan P. Mills Jr., Friedrich C. Simmel, and Jennifer L. Newman, all of Bell Labs. The researchers published a technical paper on their findings in the August 10, 2000 issue of *Nature*.

Timeline: < 5 years; > 10 years
Funding: Corporate
TRN Categories: Nanotechnology:Biological, Chemical, DNA and Molecular Computing
Story Type: News
Related Elements: Diagram 1, Diagram 2, Diagram 3; Technical paper "A DNA-Fueled Molecular Machines Made of DNA" in *Nature*, August 10, 2000

TRN

DNA Forms Nano Piston

Technology Research News, February 26/March 5, 2003

DNA is a molecule of many talents. In addition to its biological role of carrying the blueprint to life, it has performed computations and self-assembled into various shapes in the laboratory. Some of those shapes are movable, which paves the way for molecular machines.

Researchers from the French National Museum Of Natural History have constructed a DNA molecule that stretches and shrinks, cycling from an elongated double strand to a more tightly coiled four-strand form. The researchers used a 21-base strand of DNA that measured 7 nanometers elongated and 1.5 in the tightly coiled position.

The researchers calculated that the force exerted by the change was about 8 piconewtons. That's about 100 billionths of the force of a falling apple. Previous research has yielded DNA machines that rotate and that open and close like scissors.

The DNA piston could eventually be used to control nanorobotic systems and to perform calculations in DNA

computers. The work appeared in the January 27, 2003 issue of the *Proceedings of the National Academy of Sciences*.

TRN

Assembly

DNA Assembles Nanotube Transistor

By Kimberly Patch, Technology Research News
November 20, 2003

Nanotechnology is all about making machines and materials molecule-by-molecule. Such precision promises to enable microscopic machines, faster electronics, and materials that harbor new properties.

Because it is difficult and tedious to manually put atoms and molecules in place, researchers are looking for ways to cause materials to self-assemble. Self-assembly is an especially attractive concept because it has the potential to be quick, relatively easy, and very inexpensive.

One way to make things assemble automatically is to coax nature's self-assembly molecule — DNA — to assemble into templates that can in turn cause other molecules to line up in all the right places.

Researchers from the Technion-Israel Institute of Technology have brought the idea a large step forward by demonstrating a DNA-template self-assembly process that makes transistors in a test tube using an assortment of raw ingredients: carbon nanotubes, silver, gold, and four types of protein molecules.

The process could eventually be used to make many types of materials, molecular machines and electronics, and even entire computers.

DNA is made up of four bases — adenine, cytosine, guanine and thymine — attached to a sugar-phosphate backbone. In cells, two strands of DNA zip together into the familiar double helix when their bases line up — adenine connects to thymine and cytosine to guanine — and sequences of bases act as templates to build proteins. Nanotubes are rolled-up sheets of carbon atoms that form naturally in soot and can be smaller than one nanometer in diameter, or 75,000 times narrower than a human hair.

Researchers have been able to make artificial DNA molecules that have tailor-made sequences of bases for some time. The key to using this type of DNA as a template for tiny components and new materials is finding ways to connect nonbiological materials like metal and carbon nanotubes to specific sequences of DNA bases. "Combining DNA, proteins, metal particles and carbon nanotubes in a test tube is not easy since these materials are alien to each other," said Erez Braun, a professor of physics at the Technicon-Israel Institute of Technology.

The researchers accomplished this by co-opting the natural antibody process. Antibodies connect to specific proteins that make up the outside cell walls of pathogens like bacteria in order to capture and dispose of the bacteria.

The researchers' process self-assembles a transistor in several steps. First, the researchers coax a long double strand of DNA and a short single strand to position the nanotube.

The short single strand is coated with a protein from an E. coli bacteria that connects to a target span of 500 bases on the double strand. The span measures about 250 nanometers, or 250 millionths of a millimeter. An antibody to the bacteria protein then binds to the protein, followed by a second antibody that binds to the first one. Finally, a carbon nanotube that has been coated with a second type of protein binds to the second antibody, connecting the nanotube along the target sequence of the double strand of DNA.

The DNA-nanotube assembly is then stretched out on a silicon wafer, where the E. coli protein carries out a second job as a resist, or shield.

When a solution of silver is mixed with the DNA, silver molecules attach only to those segments of DNA that are unprotected by the protein. This sets up the second step of the wire-building process. When the researchers add suspended gold particles and electrify the solution, gold deposits around the silver clusters to form gold wires on both sides of the nanotube.

These gold wires are the source and drain electrodes of a transistor. The nanotube forms the transistor's semiconducting channel, and the silicon surface acts as a gate electrode, which controls the flow of current running through the device to turn it on or off.

"We harnessed a basic biological process... responsible for mixing genes in cells... to create sequence-specific DNA junctions and networks, to coat DNA with metal in a sequence-specific manner and to [position] molecular objects on [a specific] address in a DNA molecule," said Braun.

The demonstration "is a very significant [advance] in developing the technology for assembling carbon nanotube-based devices," said Deepak Srivastava, a senior scientist and technical lead in computational nanotechnology at the NASA Ames Research Center. "People have always talked about using wet chemistry for assembling molecular electronic components into precise locations," he said. "This is a first proof of the principal."

The research is novel because it uses biological molecular recognition techniques to assemble synthetic building blocks, said Srivastava. The technique could eventually be used in a next generation of electronics and in other applications that require nanoscale molecular components to assemble into complex system-level architectures — like embedded sensors, molecular machines and nano-manufacturing applications, he said.

The researchers' next step is to construct a device on a DNA junction, said Braun. This would involve getting rid of the silicon substrate that acts as a gate for the current

prototype transistor. Once this is possible, "the road is open for self-assembling more complex logic circuits," he said.

Today's computer chips are largely made up of transistors arranged into circuits that carry out the basic logic of computing. Researchers are working to make transistors smaller in order to speed computing; smaller components are faster because electrical signals have less distance to travel. Self-assembly processes could eventually prove less expensive than today's silicon manufacturing techniques.

It is not clear how long it will take before the self-assembly process can be used to manufacture components, said Braun. "It's hard to predict applications," he said. "A lot needs to be done before it becomes technology, but it's a good step forward since self-assembly of carbon nanotube devices opens many possibilities for electronics and diagnostics."

Braun's research colleagues were Kinneret Keren, Rotem S. Berman, Evgeny Buchstab, and Uri Savon. The work appeared in the November 21, 2003 issue of *Science*. The research was funded by the Israeli Science Foundation, the Techinion-Israel Institute of Technology, and the Clore Foundation.

Timeline: Unknown
Funding: Government; Private; University
TRN Categories: Nanotechnology; Integrated Circuits
Story Type: News
Related Elements: Technical paper, "DNA-Templated Carbon Nanotube Field-Effect Transistor," *Science*, November 21, 2003

TRN

Chemistry Yields DNA Fossils

Technology Research News, July 28/August 4, 2004

One way to make things at the molecular scale is to use DNA, which can be coaxed to self-assemble into various structures. The trick is getting other useful materials like inorganics into the mix.

Researchers from Kyushu University in Japan have used bacterial DNA as a matrix for making structures from silicates, which are materials like glass and concrete that contain silicon.

The technique could be used to make nanoscale containers, wires, patterns, and chemical catalysts.

DNA and silicate materials are both negatively charged, meaning the two ordinarily repel each other rather than stick together. At the same time, DNA is only soluble in water, but silicates are soluble in organic solvent.

The researchers made the two compatible by adding a hydrocarbon chain to the DNA that had positively charged groups of molecules at its head and tail. The stronger positive charge at the head caused the hydrocarbon chains to attach to pairs oxygen atoms on the DNA backbone, leaving the weaker tail charge free to connect silicate particles, which then fused together. At the same time, the combination DNA-hydrocarbon chains was soluble in the organic solvent required for silicate.

Once the silicate is in place, the DNA is removed by heating. What is left can be thought of as an artificial fossil in the shape of the DNA.

The work appeared in the June 16, 2004 issue of *Angewandte Chemie International Edition*.

TRN

DNA Sorts Nanotubes

Technology Research News, February 11/18, 2004

Carbon nanotubes — rolled-up sheets of carbon atoms that have a variety of useful mechanical and electrical properties — promise to be an important ingredient in nanotechnology. One challenge, however, is separating different types of nanotubes.

Researchers from DuPont Central Research and Development, the University of Illinois at Urbana-Champaign and the Massachusetts Institute of Technology have come up with a way to use DNA to separate carbon nanotubes by electrical type — metallic or semi conducting — and by diameter. A carbon nanotubes's electrical properties and diameter are related.

Nanotubes could eventually enable super-sensitive sensors, tiny electronics, and ultra-dense computer memory.

DNA is made up of four bases — adenine, cytosine, guanine and thymine — strung along a sugar-phosphate backbone. Adenine and thymine, and cytosine and guanine connect together, and given the right sequences, DNA can be made to assemble into various structures.

The researchers discovered that a certain sequence of single-stranded DNA self-assembles into an ordered structure around individual carbon nanotubes. The electrostatic profiles of the combined DNA and nanotube structure depends on the type of tube, and, for semiconducting tubes, on the tube's diameter. The work appeared in the November 28, 2003 issue of *Science*.

TRN

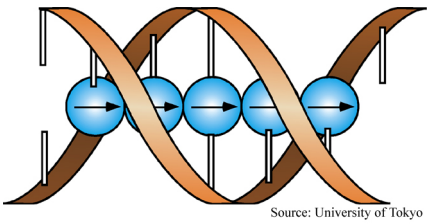
Artificial DNA Stacks Metal Atoms

Technology Research News, September 24/October 1, 2003

In recent years, researchers have replaced some of DNA's natural bases with those that attach to metal atoms in order to coax DNA to organize metal ions into tiny structures.

Researchers from the University of Tokyo in Japan have tapped the method to form stacks of single metal ions.

The work shows that DNA can be used to precisely position and control arrays of metal. The relatively simple method is a step toward building and controlling tiny metal devices and nanomachines atom by atom.



Source: University of Tokyo

This depicts a DNA double helix with five copper ions stacked inside

DNA forms from four types of bases that pair up along a pair of sugar-phosphate backbones to form the familiar double helix. Previously, the Tokyo researchers had developed an artificial base close to the size and shape of natural DNA bases that attached to a copper ion. Ions are atoms that have more or fewer electrons than normal.

When the researchers mixed DNA containing the artificial bases into a room-temperature solution of copper ions, the new bases bound to the copper; when the DNA curled into a double helix, the copper ions ended up stacked neatly inside. The researchers used the method to make a stack of five ions.

The researchers are working on adding different metals to DNA molecules, and on forming tiny junctions; the ultimate goal is to construct metal molecular devices like wires and magnets, according to the researchers.

The work appeared in the February 21, 2003 issue of *Science*.

TRN

Tools Design DNA-Nanotube Logic

By Eric Smalley, Technology Research News
August 25/September 1, 2004

Researchers have recently begun to use DNA to assemble carbon nanotubes into transistors, the building blocks of computer circuits.

Biological DNA molecules, made from long strings of four types of bases attached to a sugar-phosphate backbone, hold instructions for making the proteins that enable life's processes. Artificial DNA molecules can be caused to self-assemble into various patterns, and can also be coaxed to attach to objects like carbon nanotubes. Given the right design, DNA molecules can assemble objects.

Carbon nanotubes are rolled-up sheets of carbon atoms that have useful electrical properties and can be 1,000 times smaller than an E. Coli bacterium. A nanometer is one millionth of a millimeter.

Researchers from Duke University are aiming to make the process of assembling molecular-scale components easier with a suite of computer-aided design (CAD) tools for designing computer circuits made from carbon nanotubes assembled by DNA.

Such self-assembled, molecular-scale circuitry could be used to make cheaper, higher-performance computers than are possible using today's silicon-based chipmaking technologies.

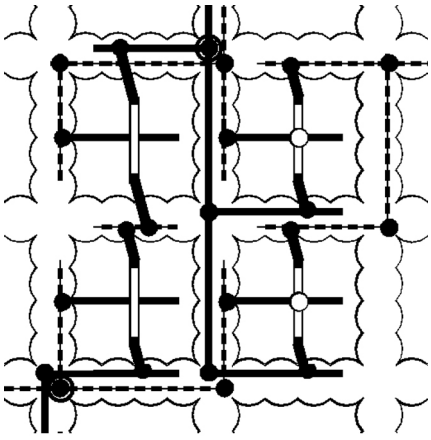
The researchers' tools make it possible to design computer circuits that could be assembled automatically by DNA, said Dwyer. "Our tools enable the design and evaluation of the circuitry... based on a DNA self-assembly process and carbon nanotubes."

The tools are designed to build computer circuits at a density of 2,500 transistors per square micron, which is about 30 times more closely packed than devices made using current chipmaking technologies, according to Chris Dwyer, an assistant professor of electrical and computer engineering at Duke University. A micron is one thousandth of a millimeter.

Transistors are arranged into logic gates, which in turn are combined by the millions into the complicated circuits that process and store data. Being able to assemble individual nanotube transistors is the prerequisite for developing a nanotube-based chipmaking technology. The key is finding ways to combine them into logic circuits.

The tools use a DNA scaffold recently created by another Duke University research team as the foundation for nanotube circuits. The scaffold is a self-assembled, grid-like fabric of DNA molecules. The grid's cavities measure 20 nanometers across.

The DNA scaffold technology is still being developed, said Dwyer. The scaffolding and tools are being developed in parallel; once the DNA scaffold technology is ready "we need the ability to reason about the performance of these devices, and the computer architectures they can lead to, [in order] to make high-level strategic decisions such as how to restructure the flow of information and how to execute computations," he said.



Source: Duke University

This diagram depicts a design for a NAND logic gate that can be made from carbon nanotubes assembled by DNA molecules. The curved lines that form a grid represent DNA. The crosses in the gaps in the grid are nanotube transistors.

The researchers' DNA-nanotube circuit architecture uses pairs of complementary sequences of DNA to connect the ends of the carbon nanotubes to points on the DNA scaffold.

Connecting a semiconducting nanotube across the middle of a cavity and a metallic nanotube across the cavity perpendicular to the first nanotube makes a field-effect nanotube transistor. The gate electrodes in field-effect transistors produce an electric field that changes the conductivity of the device's semiconductor channel.

The architecture also calls for attaching metallic nanowires along the DNA segments that make up the scaffold on both the top and bottom sides. To fill the gaps between the nanotubes at the intersections of the grid and the points where the transistor nanotubes connect to the grid, the architecture includes DNA sequences that attract metallic nanoparticles. Later in the process, the nanoparticles attract metal atoms to form a chemically-assembled solder.

Like traditional computer-aided design tools, the researchers' tools allow users to design individual devices like logic gates, connect the devices to form whole systems, generate a circuit layout, and produce a sequence of assembly steps. The assembly plan includes specific DNA sequences as well as the nanotube or nanoparticle component for each step.

The tools use specialized models that roughly gauge the performance of circuits based on the low-level behavior of nanotube transistors, said Dwyer. "With this evaluation we can estimate the speed and energy consumption of our designs; we use this to inform our decision-making process and high-level architectural simulators," he said.

In providing a framework for evaluating potential systems, they are similar to the first generation of design tools geared toward microelectronics that eventually lead to very large-scale integration (VLSI) computer-aided design tools, he said.

Nanoelectronics, and particularly the self-assembly process, require different ways of thinking about circuitry and how computations occur to make the best of the technology, said Dwyer. "Our tools provide a foundation for those future designs," he said. "Further down the road, we hope these tools will mature to the level that present-day very large-scale integration computer-aided design tools have — this will make wider access to the new technology possible."

The researchers' next step is to use the tools in simple designs, said Dwyer. "We are currently assembling a simple DNA lattice that will eventually be suitable for a NAND gate," he said.

A NAND, or Not AND, gate is one of the basic building blocks of computer circuits. It contains two input signals and one output signal. If either of the input signals is a 1, the output is 0.

One challenge is that the larger the DNA scaffold, the greater the number of unique DNA sequences required to create circuits. The researchers are working on minimizing the overall number of required sequences, according to Dwyer.

The researchers' nanotech fabrication computer-aided design tools could be used to carry out nanotube construction in five to ten years, said Dwyer. Dwyer's research colleagues were Vijeta Johri, Moky Cheung, Jaidev Patwardhan, Alvin Lebeck and Daniel Sorin. The work is slated to appear in the September issue of *Nanotechnology*. The research was funded by the National Science Foundation (NSF) and Duke University.

Timeline: 5-10 years
Funding: Government; University
TRN Categories: Nanotechnology; DNA Technology; Integrated Circuits
Story Type: News
Related Elements: Technical paper, "Design Tools for a DNA-GuidedSelf-Assembling Carbon Nanotube Technology," Nanotechnology, September 2004

TRN

Structures

DNA Forms Nano Waffles

By Kimberly Patch, Technology Research News
October 22/29, 2003

Researchers are working to control the way DNA strands interact with each other in order to coax the molecules to form tiny structures. Such structures could eventually serve as microscopic machines and as templates capable of causing other materials and devices to automatically assemble molecule-by-molecule.

Researchers from Duke University have moved DNA construction methods a step forward by coaxing DNA strands to lock together into tiles made up of nine single strands of DNA that can further self-assemble into lattices. The ribbon- and sheet-shaped lattices can be used as devices or as templates to construct devices from other materials.

The researchers demonstrated one set of tiles that self-assembled into a tiny protein detector, and another set that assembled into ribbons that served as templates for precisely formed silver nanowires.

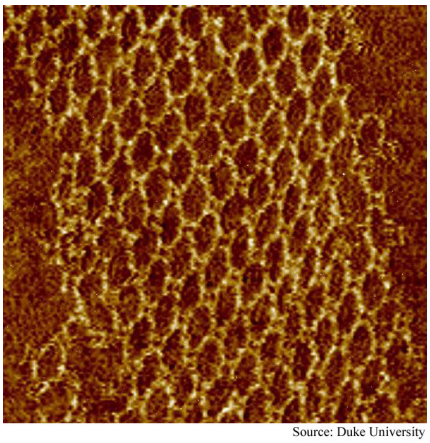
DNA is made up of four bases — adenine, cytosine, guanine and thymine — attached to a sugar-phosphate backbone. Strands of DNA connect to each other when strings of bases pair up — adenine with thymine, and cytosine with guanine.

The tiles form when single-stranded DNA molecules self-assemble into a branched structure, said Hao Yan, an assistant research professor of computer science at Duke University. "We make the DNA strands arrange themselves into cross-shaped tiles capable of forming molecular bonds on all four ends of the cross arms," said Yan.

The researchers were able to make the tiles connect to each other to form a square, waffle-patterned grid or a waffle-patterned long ribbon by making tiles with different "sticky end" configurations. Sticky ends are portions of DNA strands that remain unconnected when the nine DNA strands connect

together to form the tile and can later connect to matching DNA segments. "DNA tiles can carry sticky ends that preferentially match the sticky ends of another particular DNA tile," said Yan.

The tiles were originally designed to form perfectly flat lattices, but when the researchers reprogrammed the tiles by changing the sticky ends so that the tile faces would all orient in the same direction up or down, the tiles curved slightly in opposite directions to form a long, narrow ribbon whose surfaces were waffled, said Yan. A second modification that caused each tile face to point in the opposite direction from its neighbor resulted in the wider grid structure.



Source: Duke University

This microscopic, waffled sheet is composed of cross-shaped tiles that in turn are made of DNA strands.

The method is particularly useful because "we can easily achieve two types of lattice by slightly changing the sticky-ends without changing the tile structure itself," said Yan.

DNA makes a useful template because many other materials can chemically attach to DNA. "Self-assembled DNA arrays provide excellent templates for spatially positioning other molecules with... precision," said Yan.

The researchers formed a device that detects the protein streptavidin by adding the molecule biotin to one of the DNA strands in each grid tile. Streptavidin connects to biotin.

The researchers made precisely-formed silver nanowire using the ribbon structure, said Yan. "We used a two-step chemical procedure to coat silver onto the DNA nanoribbons to produce electricity-conducting nanowires," he said.

Such wire can eventually be used to interconnect nanoscale devices with micron-scale devices, said Yan. Connecting relatively large microscopic objects, like those around the size of a cell, to relatively small ones, like those around the size of a molecule, is a major challenge simply because the size difference is so vast. A red blood cell, for instance, is, at 5 microns across, about 15 times narrower than a human hair, but 50,000 times larger than a hydrogen atom.

The method could eventually be used to construct many types of materials and devices, including electronics, molecule-by-molecule. Such precise control over construction promises to enable materials that have new properties, and electronics that are very efficient.

The researchers are working on designing more complicated DNA nanostructures and working out chemical methods to attach nanoelectronic components like carbon nanotubes to DNA, he said.

The ultimate goal is to use DNA as a scaffold to organize any useful material into nano-size devices, sensors and even factories, said Yan.

The technology could be ready for practical applications within five years, said Yan.

Yan's research colleagues were Sung Ha Park, Gleb Finkelstein, John H. Reif and Thomas H. LaBean. The work appeared in the September 26, 2003 issue of *Science*. The research was funded by the National Science Foundation (NSF) and the Defense Advanced Research Projects Agency (DARPA).

Timeline: 5 years
Funding: Government
TRN Categories: Nanotechnology; Biotechnology; Materials Science and Engineering
Story Type: News
Related Elements: Technical paper, "DNA-Templated Self-Assembly of Protein Arrays and Highly Conductive Nanowires," *Science*, September 26, 2003

TRN

DNA Parts Make Versatile Nanotubes

By Chhavi Sachdev, Technology Research News
June 6, 2001

The perfect material for a nanoscale circuit would not only readily assemble itself, but would also have adjustable physical and chemical properties. Researchers at Purdue University have come close to that ideal with organic nanotubes that can be mass-produced and whose properties can be predetermined.

The key to these prodigious nanotubes is that they are not made of carbon. Instead, the researchers' rosette nanotubes are built from two of the bases that make up DNA.

Regular carbon nanotubes self-assemble when graphite sheets roll up. The organic rosette nanotubes, which, like DNA, form in water, self-assemble when rings of atoms stack up, forming a hollow channel in the middle.

Each stacked ring of the rosette nanotube is a supermacrocycle — a ring of atoms held by non-covalent hydrogen bonds. Each supermacrocycle has six segments. Each segment, or module, is made of guanine and cytosine bases and amino acids. The rings are rosette-shaped, like a flower with six petals.

The rosette nanotubes assemble spontaneously because parts of the module are water-repellent and parts are attracted to water. In trying to keep their water-repellent ends away from the water, the modules align themselves so that their

water-loving ends face outside, and the water-repellent ends inside, forming a ring. The rings then stack together to form a tube.

"The reason they stack up is because they don't like to get wet," said researcher Hicham Fenniri, an assistant professor of chemistry at Purdue University. "They repel water and prefer to interact with themselves. The hydrophobic and electrostatic interactions help keep the nanotube stable."

Self-assembly is a key goal in making machines at the molecular scale because it allows fairly large and complex structures to come together in a single, largely error-free step. "It is almost a Darwinian chemistry," said Fenniri. "If a module is not chemically fit, it will not be incorporated in the nanotube structure," he said.

Another benefit of self-assembly is high yield. "The chemistry used to make these tubes is scalable using standard industrial processes," said Fenniri. A small-scale industrial plant could produce up to 500 kilograms of the rosette nanotubes in a month, according to the researchers.

Rosette nanotubes are also chemically versatile.

Researchers can specify the chemical properties of the nanotubes before production because "the properties of the modules they are made of can be altered at will," said Fenniri. The modules can be tuned to transmit light or electricity, for instance, he said.

The researchers can also specify the dimensions of the tubes. "Our tubes vary in length from one nanometer to several microns," he said.

Although rosette nanotubes are relatively strong, they are not as strong as carbon nanotubes. Where there is high mechanical stress, "carbon nanotubes may be more advantageous," said Fenniri. "However, the rosette nanotubes can be modified to become mechanically very strong — several orders of magnitude stronger than nylon, for instance," he added.

Rosette nanotubes could eventually be used as fibers in new plastic-like materials or as electronic wires in computing devices, according to the researchers.

Rosette nanotubes with light-transmitting properties could be used in light-emitting devices or in solar energy transport and conversion. Since the tubes assemble in water, they could also have biological applications such as internal drug delivery, according to the researchers.

Another important use for the rosette nanotubes could be as a template for tiny nanowires, said Deepak Srivastava, a senior scientist at NASA's Ames Research Center. "If you can fill up the cavity with metal, then the metal will harden, and at that point you can wash away or dissolve the tube part [to leave behind] metal nanowires or semiconductor nanowires," he said.

"This is a major advance in the preparation of nanotubes in aqueous environments," said Steven Kornguth, a professor of neurobiology at The University of Texas, Austin. The tubes' adaptability is important, according to Kornguth. "The internal cavity of the rosette may serve as a locus for insertion of metals that will alter [their] conducting properties," he said. Their ability to anchor on to surfaces for use in photonic or electronic conduction applications may also prove useful, he said.

The researchers are currently working on making the nanotubes as long as a millimeter. The research could be applied practically within the next two years, according to Fenniri.

Fenniri's colleagues were Packiarajan Mathivanan, Kenrick L. Vidale, Debra M. Sherman, Klaas Hallenga, Karl V. Wood, and Joseph G. Stowell of Purdue University. The paper was published in the Journal of the American Chemical Society, April 25, 2001. The research was funded by the National Science Foundation (NSF), the American Chemical Society, the Showalter Foundation, Research Corporation, the American Cancer Society, 3M, and Purdue University.

Timeline: < 2 years
Funding: Institute; Corporate; University
TRN Categories: Biological, Chemical, DNA and Molecular Computing
Story Type: News
Related Elements: Technical paper, " Helical Rosette Nanotubes: Design, Self-Assembly, and racterization," the Journal of the American Chemical Society, April 25, 2001: www.chem.purdue.edu/hf/NANOTUBEpaper.pdf

TRN

Scientists Brew Tree-Shaped DNA

Technology Research News, February 11/18, 2004

Researchers from Cornell University have synthesized a new type of DNA that can be used as a nanotechnology building block.

DNA, whether biological or artificial, consists of a series of nucleotide bases attached to a sugar-phosphate backbone. DNA usually comes in straight strands; these pair up and twist to form the familiar biological double helix.

The Cornell researchers have found a way to make branched, or Y-shaped DNA, and have constructed dendrimer, or tree-shaped, DNA by connecting branched DNA.

DNA shows great promise as a nanotechnology construction tool. It is water-soluble, non-toxic and biodegradable, can be manipulated using enzymes, and segments of DNA can be programmed to connect to other segments to self-assemble structures at the scale of molecules. The Y-shaped DNA is an additional tool for this effort, according to the researchers.

The DNA could eventually be used for nanoscale construction, drug delivery and molecular sensing, according to the researchers.

Practical applications will be possible in 5 to 10 years, according to the researchers. The work appeared in the December 21, 2003 issue of *Nature Materials*.

TRN

DNA Folds into Paired Pyramids

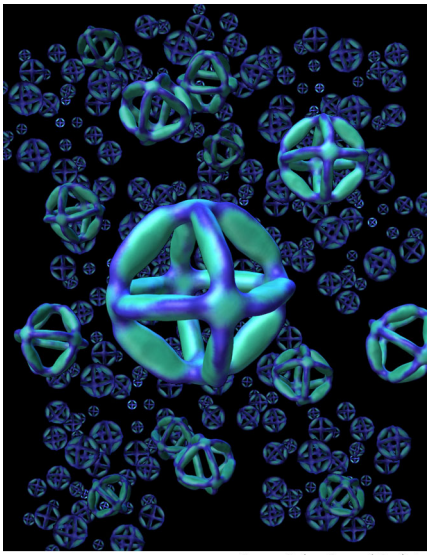
Technology Research News, April 7/14, 2004

Researchers from the Scripps Research Institute have formed strings of DNA that spontaneously fold into a wireframe octahedron, a shape that has eight triangular faces.

The shape is a step forward in the quest to use DNA to make nanoscale templates that can be used to make materials molecule-by-molecule and structures that form microscopic machines.

The octahedron has two advantages over other artificially-formed three-dimensional DNA shapes, according to the researchers. First, because the structures are triangular, they're relatively strong. Second, like a three-dimensional paper airplane made from a flat piece of paper, the octahedron is made from straight DNA strands. The three-dimensional shape forms when one long DNA strand and five shorter strands are mixed and heated.

The straight strands can be coaxed to self-replicate, making it possible to quickly produce large numbers of the octahedrons, according to the researchers. Other three-dimensional DNA shapes must be synthesized chemically rather than biologically. DNA is made up of strings of four bases attached to a sugar-phosphate backbone. DNA strands that contain complementary sequences of bases can attach to each other.



Source: Scripps Research Institute

This graphic shows the octahedral shape of a type of DNA designed for nanotechnology applications.

The DNA octahedron measures 22 nanometers across, or about one fiftieth the width of an E. coli bacterium.

The DNA octahedron could be used in practical applications in five to ten years, according to the researchers. The work appeared in the February 12, 2004 issue of *Nature*.

TRN

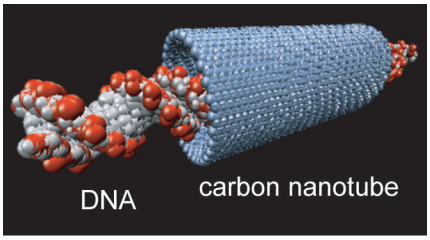
Electronics

Study Shows DNA Will Fill Tubes

Technology Research News, June 4/11, 2003

Researchers from the Max Planck Institute in Germany have shown by computer simulation that it is possible to insert DNA into a carbon nanotube.

Carbon nanotubes are rolled-up sheets of carbon atoms; they have useful electronic properties and can be smaller than one nanometer in diameter, which is the length of a row of 10 hydrogen atoms. Previous research has shown that it is possible to use DNA, the molecule that holds and replicates the code that makes up life's processes, for microelectronics.



Source: Max Planck Institute

This diagram represents a segment of DNA inside a carbon nanotube. Each sphere represents an atom.

Devices based on the DNA-nanotube combination could eventually be used to make electronics, molecular sensors, devices that sequence DNA electronically, and even gene delivery systems, according to the researchers.

The researchers' simulation showed that in a liquid environment, a combination of the van der Waals force and hydrophobic interaction forces would pull a strand of DNA into a nanotube. The van der Waals force is a weak force of attraction between atoms and molecules.

It could be possible to use the method to make DNA-modulated electronics in five to ten years, according to the researchers. The work appeared in the April 9, 2003 issue of *Nano letters*.

TRN

DNA Conducts

By Ted Smalley Bowen, Technology Research News
February 7, 2001

While popular and scientific attention has gravitated to efforts at mapping DNA and feats of DNA-scale micro-engineering, the comparatively simple act of coating a mica slab with the most famous of complex molecules could prove an effective way of creating a network that has useful electrical properties.

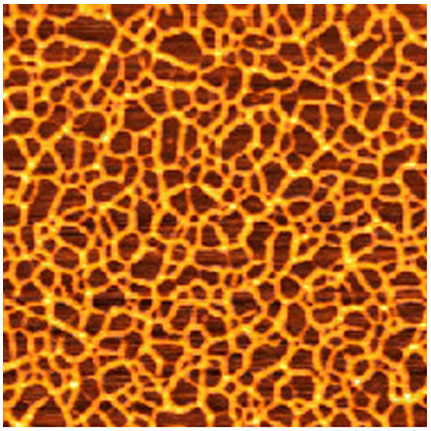
Using a method that might strike grade-school art students as familiar, researchers at Osaka University have found that

putting a drop of highly concentrated DNA on mica and blowing it off can leave a residue that amounts to a networked layer of DNA molecules.

The method is a step toward creating high-density electronic devices, and ultimately integrated circuits made of DNA, said Tomoji Kawai, a professor of physics at Osaka University.

In exploring these networks of DNA the researchers found that guanine-cytosine-based DNA shows p-type, or positive electrical properties, according to Kawai. DNA molecules can contain any mix of two types of base pairs: thymine-adenine and guanine-cytosine.

An n-type object uses negatively charged electrons to carry current. A p-type object carries current using positively charged holes, or gaps where an electron could fit. Connections between the two types allow current to flow in a single direction, giving rise to components like transistors and diodes. "[This] means that these networks can be used as p-n junctions and p-n diode[s]," Kawai said.



Source: Osaka University

DNA strands form a mesh network when a drop of solution containing DNA is applied to a mica surface and then blown off, leaving a residue to dry. The DNA in thesenetworks conducts electricity.

With these electrical traits, DNA could be used to build transistors, which are the basic building blocks of integrated circuits. "The junctions of DNA can be used as three terminal devices," Kawai said.

The way DNA conducts electricity is complex, according to Kawai. It depends on the different reduction-oxidation potentials of the bases, and the distance between bases. A molecule in reduction attracts electrons and in oxidation it sheds electrons. The DNA base guanine is the most easily oxidized of the bases, meaning it can become positively charged, or gain holes. Once this happens, the charge can be passed along a chain of bases, according to Kawai.

The group made their conduction observations by attaching five-nanometer gold particles to specific complementary base pairs within the DNA networks. These gold particles served as one electrode, while the probe tip of an atomic force microscope provided the second contact.

The question of whether DNA conducts electricity is controversial. According to Cees Dekker, a professor of applied physics at the Delft University of Technology in the Netherlands, the results are puzzling. "After two to three years of research on the intrinsic resistance of DNA I've become rather pessimistic that one can use bare DNA as molecular wires," he said.

Others, however, are cautiously optimistic. "The results fit my intuition of the base composition affect on resistivity," said Danny Porath, a physicist at the Center for Nanoscience and Nanotechnology at Tel Aviv University. He added, however, that more experiments are needed to confirm the results.

The researchers have also changed the thickness of the DNA network using electrical current or irradiation, Kawai said.

To create the networks, the researchers applied a solution of synthetic linear DNA in de-ionized water to freshly-cut muscovite green mica and blew it off after about a minute. "The droplet is blown out from the surface," said Kawai.

The result is a network of DNA molecules that is mainly a single layer, and at the edges of the network the DNA molecules are linked together, according to Kawai.

The researchers controlled the size of of a network by changing the concentration of the DNA solution and the time it remained on the substrate, according to Kawai. The resolution, or mesh size, of a network depends on the length of its DNA, he said. The researchers have made networks as large as 2 centimeters square with 10- to 100-nanometer mesh.

The droplet method should scale reliably, said Kawai. "It is easy to make larger area networks. Just increase the substrate area."

The network structure could be used in combination with a bio-chip, such as a DNA chip or a protein chip, within a few years, said Kawai. A DNA memory device could be made within five to ten years, Kawai said.

Kawai's research colleagues were Takahashi Kanno, Hiroyuki Tanaka, Norio Miyoshi. They described their work in the April 2000 Japan Journal of Applied Physics, the research was funded by the Japanese Ministry of Education, Sports and Culture.

Kimberly Patch contributed to the reporting of this story.

Timeline: 5-10 years
Funding: Government
TRN Categories: Semiconductors and Materials; Biological, Chemical, DNA and Molecular Computing
Story Type: News
Related Elements: Technical paper "A New Self-Fabrication of Large-Scale Deoxyribonucleic Acid Network on Mica Surfaces," Japan Journal of Applied Physics, April, 2000

TRN

DNA Induced to Superconductivity

By Kimberly Patch, Technology Research News
February 7, 2001

DNA has already proved itself most useful as the basis of life on earth and is showing promise for massively parallel computing in a test tube. More controversial is its potential role as a material that conducts electricity.

There have been several attempts to test the electrical conductivity of DNA molecules, and the results are mixed. In one of the latest efforts, a research group from France and Russia has shown that DNA can conduct electricity and even becomes a proximity-induced superconductor when its metal contacts become superconducting at very low temperatures.

The measurements, though preliminary, show promise for using DNA in sensing applications and eventually in building nanoscale electrical circuits.

The researchers used double-stranded, six-micron-long DNA molecules as connectors between rhenium and carbon electrodes.

The tricky part in getting the DNA to conduct was finding contacts that effectively funnel the electricity through the DNA, said Helene Bouchiat, director of research at the in the French National Center for Scientific Research. "We had made some tries with pure gold contacts with no success. We used carbon as a top layer hoping that it [would] promote chemical bonding between the molecule in the contact," she said.

If the researchers results are correct, DNA could easily be used to conduct electricity, said Danny Porath, a physicist at the Center for Nanoscience and Nanotechnology at Tel Aviv University. "The conduction properties described here are by far better than those found in previous experiments and beyond expectations of many people in the field. If this is correct that means that DNA is indeed an incredible candidate for molecular electronics," he said.

The researchers built the structures on stable, freshly cleaved mica substrates. The first layer was a two-nanometer-thick layer of rhenium. Then came a two-nanometer-thick layer of DNA molecules, which was combed into one direction using the flow of the solution. The top layer was a forest of individual carbon fibers up to 40 nanometers tall, according to Bouchiat.

The thickness of the rhenium layer was carefully controlled in order to minimize kinks in the DNA molecules at the edges of the metallic pads. Keeping kinks out of the DNA is a key to providing good conduction from the contacts through the DNA molecules, according to Bouchait.

The researchers calculations showed that 100 to 200 DNA molecules bridged the two electrodes in their samples. In several samples they destroyed some of the DNA in order to get structures that contained from 3 to 40 combed DNA molecules.

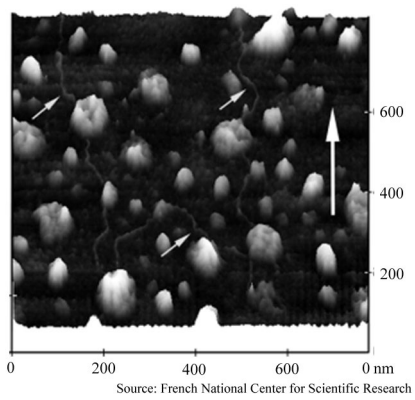
The researchers flowed electricity between the electrodes through the DNA in order to measure the resistance of the DNA.

The DNA provided an average resistance of about 300 kilohm per DNA molecule, although the actual number is likely lower because all the combed molecules were not necessarily in contact with the electrodes, according to Bouchait. For comparison, the resistance of metallic, single-walled nanotubes is typically 100 kilohm and the resistance of semiconducting nanotubes is one megaohm or higher.

The experiments showed that the molecules can conduct electricity over distances of a few hundred nanometers even at very low temperatures. The researchers also found that the resistance of DNA dropped considerably when the electrodes became superconducting at one degree Kelvin. Zero Kelvin is absolute zero, or -273 degrees Celsius.

Superconductivity occurs when electrons moving through a material face no resistance. The electrons become coherent in the quantum mechanical sense, meaning they behave as though they are a single wave.

The resistance of the DNA samples increased steadily as the temperature decreased until the temperature fell below the superconducting temperature of the contacts. At this point the resistance of the samples that had 30 and 40 combed DNA molecules decreased substantially. These transition changes showed that there was proximity-induced superconductivity in the DNA molecules themselves, according to Bouchait.



Source: French National Center for Scientific Research

The smaller arrows point to string-like DNA molecules. The clumps are carbon fibers. When metal electrodes on both ends of the DNA strands are cooled to the point of superconductivity, the electrical resistance in the strands decreases dramatically.

It has historically proven difficult to make DNA conduct electricity, which makes many researchers cautious about these results. The results are "very surprising, but very important if correct," said Porath.

According to researchers who have found conductivity in DNA, the important parameters are the contacts and the structure of the DNA. "There's no question that the connections are critical. I really think much of the variability of results [in] looking at DNA conductivity depends upon the variability in making connections," said Jacqueline Barton, a chemistry professor at the California Institute of Technology.

The exact order of the four types of base pairs that make up the DNA molecule also factor into the way DNA conducts electricity, said Barton. "We found from our solution studies the charge transport through DNA is very sensitive to base pair stacking and structure. It depends upon the overlap of the DNA base pairs."

If DNA were successfully harnessed as a conductor, self assembling networks of DNA could potentially be used eventually to build nanoscale electronic circuits. "This is one of the solutions for the prediction of Moore's Law that claims that we're heading towards the end of the conventional microelectronics," said Porath. "Possible replacements are systems that are made of building blocks and use self-assembly. The DNA, if conducting, would be a very good candidate for this purpose due to its... self-assembly properties... and large toolbox provided by enzymes," he said.

Using DNA for electronic circuits is a far-off goal, however. It is too early in the research to say whether this would even be possible, said Bouchiat.

Research applications like using conductivity to sense different types of DNA, however, could become practical within a few years, according to Bouchait.

Because the conduction in DNA is so sensitive to the order of its bases, it could be used as a way to sense various sequences, said Barton. "It provides a fundamentally new way to achieve sensitive... mutation analysis," said Barton.

Bouchiat's research colleagues were A. Yu Kasumov, M. Kociak, S. Gueron and B. Reulet from the CNRS, and V. T. Volkov and D.V. Klinov of the Russian Academy of Sciences. They published the research in the January 12, 2001 issue of *Science*. The research was funded by the CNRS and The Russian Academy of Sciences.

Timeline: < 3 years; many years
Funding: University
TRN Categories: MicroElectroMechanical Systems (MEMS)
Story Type: News
Related Elements: Technical paper, "Proximity Induced Superconductivity in DNA," *Science*, January 12, 2001

TRN

Metal Makes DNA More Conductive

By Chhavi Sachdev, Technology Research News
May 2/9, 2001

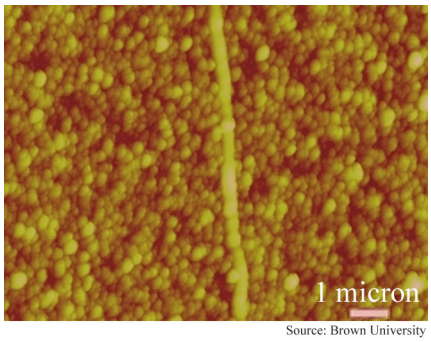
For several years, scientists have explored ways to make DNA conduct electricity. DNA's size and ability to arrange itself, or self-assemble, would make conductive DNA a valuable material for nanoscale circuitry.

One group of researchers has replaced parts of DNA's base pairs with metal ions in order to allow electrons to flow through the molecule.

Biological DNA, found in the nucleus of every cell, is essentially composed of long strands of four bases — adenine, guanine, cytosine, and thymine. The researchers engineered the conductive DNA by coaxing the base pairs to exchange a proton for a zinc ion. The addition of metal made DNA behave like a semiconductor.

"The substitution of the imino proton with a zinc ion makes the DNA hundreds of times more conductive," said researcher Jimmy Xu, an engineering and physics professor at Brown University.

The engineered DNA could eventually be used in microelectronics where there is a need for tiny, self-assembling conductors. The DNA could be the basis for "a new material system that can be controllably produced, whose properties can be…engineered, and whose ensemble can self-organize into functional structures and can collectively process massive amount of information," said Xu.



Source: Brown University

This microscope image shows a bundle of metallic DNA, composed of about 300 individual DNA strands, on a gold electrode. The bundle is about 100 nanometers wide and ranges from 20 to 30 nanometers high.

"DNA is the basic and best understood building block — a perfect place to start engineering," he said.

Engineering DNA molecules to accept the zinc was relatively simple, according to Xu. Previous research by team member Jeremy Lee, a biochemistry professor at the University of Saskatchewan, had already established that DNA readily absorbs ions of zinc, nickel and cobalt at high pH levels.

Xu's team raised the DNA's pH level to 9.0 by adding zinc ions containing acids to a test tube of DNA. The DNA molecules released the imino protons in their base pairs and took up zinc ions instead, resulting in a modified, metallic compound DNA , or M-DNA.

The conductivity of any substance depends on the placement and number of electrons in its energy bands. The wider the energy bands of a molecule, the faster the electrons move; the faster the movement of electrons, the better the conductivity. Metals generally have wider bands than semiconductors, which have wider bands than insulators.

Biological DNA shows a band-gap of a few hundred millielectron volts at room temperature, according to the researchers. This gap is an energy barrier that any electron coming from the electrode would have to overcome before it could be conducted up the molecule, said Xu.

In contrast, M-DNA's "conduction band is wide and low enough in energy that the electrons from the electrode can move into [it] without difficulty," said Xu.

This difference makes metallic DNA an ideal nanoscale semiconductor, according to Xu.

"With semiconductors you have a set of base materials - building blocks - which can be turned into a vast array of useful devices and sensors, which, in turn, can be connected up to form circuits, processors, and computers," Xu said. The engineered DNA is a new material, "and new materials are technology enablers," he said.

Metallic DNA could also be used as a biosensor to screen, among other things, genetic aberrations and environmental toxins. Metallic DNA could be used in sensors in 3 to 5 years, Xu said.

"It is interesting work, but I think there still needs to be a lot done to structurally characterize this system," said Jacqueline K. Barton, a professor of chemistry at the California Institute of Technology.

It's the first time zinc has been studied in this way, said Mark Ratner, a professor of chemistry at Northwestern University. The work is "an intriguing and important contribution," but the other research in the field of conductive DNA has produced different results. "There is lots yet to be done," he said.

Other researchers are more skeptical about the findings. "[Xu and his colleagues] find a very low gap even for simple [biological] DNA, which contrasts [with] similar measurements by us and others where we find true insulating behavior at these length scales," said Cees Dekker, a professor of physics at the Delft University of Technology in the Netherlands.

Xu's research colleagues were Andrei Rakitin, Chris Papadopoulos, and Yuri Kobzar of Brown University; Palok Aich and Jeremy S. Lee of the University of Saskatchewan; and Alex S.Vedeneev of the Russian Academy of Sciences. Their paper appeared in the journal *Physical Review Letters*, April 16, 2001.

The research was funded in part by the Canadian Institute for Advanced Research, the National Sciences and Engineering Council of Canada, Motorola, the Defense Advanced Research Projects Agency (DARPA), the Office of Naval Research, the National Science Foundation, and the Air Force Office of Scientific Research.

Timeline: 3 - 5 years
Funding: Government; Corporate
TRN Categories: Biological, Chemical, DNA and Molecular Computing
Story Type: News
Related Elements: Technical paper, " Metallic Conduction through Engineered DNA: DNA Nanoelectric Building blocks" appeared in the journal *Physical Review Letters*, April 16, 2001

TRN

Materials

DNA Part Makes Transistor

Technology Research News, June 4/11, 2003

Researchers from the University of Lecce in Italy and the University of Bologna in Italy have produced a transistor made from a derivative of one of the four bases that make up DNA.

The field-effect transistor, which carries electricity from a source electrode to a drain electrode when turned on by a gate electrode, is made from a group of guanosine bases the researchers coaxed to self-assemble into orderly ribbons. The researchers used beams of electrons to etch metal electrodes 20 nanometers apart. They then coaxed a layer of guanosine to form between the electrodes.

The researchers measured a maximum voltage gain of 0.76 for their tiny transistor, which is relatively high for a molecular device, though low compared to standard transistors. Gain is critical for keeping signals from fading. The transistor also operates well at room temperature.

The device, at a few hundred nanometers, is close to the size of today's silicon transistors. The self-assembling nature of the molecular layer means guanosine-based transistors could be manufactured in large numbers at low cost, according to the researchers.

The researchers are working on improving the device's electrical properties and long-term stability.

The work appeared in the April 9, 2003 issue of *Nano Letters*.

TRN

DNA Device Detects Light Signals

By Eric Smalley, Technology Research News
June 13/20, 2001

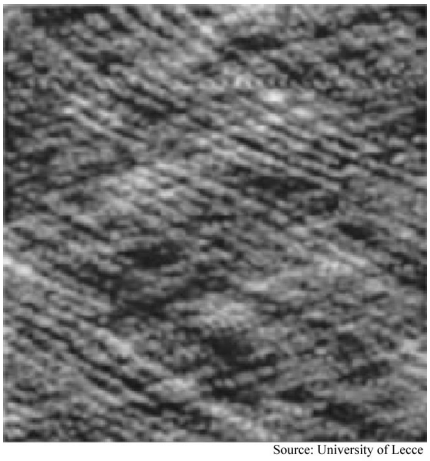
DNA is famous for its ability to assemble itself into very long strings of code made up of four bases. With a nod to nature's choice of materials, a team of researchers in Italy is tapping the self-assembly talent of one of the bases to form a thin film that produces an electric current when light shines on it.

The researchers have built a device that uses a film of guanosine in place of the inorganic silicon or gallium arsenide semiconductor material usually used in photodiodes. Photodiodes are the light-sensing elements of photodetectors, which are used to convert light pulse signals to electrical signals in communications networks.

The guanosine films are cheaper and have a better light sensitivity than the inorganic semiconductor used in

commercial photodiodes, said Ross Rinaldi, a physics professor at the University of Lecce in Italy.

The researchers produced the film by depositing a tiny drop of water containing about 100,000 guanosine molecules between a pair of very closely spaced gold electrodes. As the water evaporated, the guanosine molecules assembled themselves into ribbons that interconnected to form a film with semiconductor properties. The film formed a contact between the electrodes in the researchers' prototype photodiode.



Source: University of Lecce

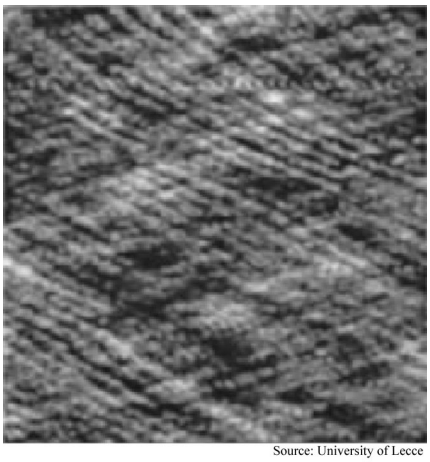
Molecules of the DNA base guanosine combine to form ribbons, yielding an orderly semiconductor film.

The researchers chose guanosine because it has good self-assembly properties and is oxidized the least of the four DNA bases, "insuring good conductivity properties in the ordered film," said Rinaldi. Oxidation results when oxygen in air combines with material on a surface. Oxidation turns semiconductors into insulators, which block electron flow.

The devices use relatively short 100-nanometer long spans of the film. As a result, the gold electrodes have to be produced using electron beam lithography rather than the simpler, less expensive photolithography process of commercial chipmaking, said Rinaldi.

The researchers are working on avoiding this by making longer films. "We are working to extend the ordering lengths of the biomolecular layer towards the 250 nanometer range, thus reducing the spatial resolution required for the contacts fabrication," she said.

This would make it possible to mass-produce the guanosine photodiodes using standard photolithography to make the electrodes and modified inkjet printer nozzles to make the guanosine films, said Rinaldi.



Source: University of Lecce

Molecules of the DNA base guanosine combine to form ribbons, yielding an orderly semiconductor film.

Rinaldi's research colleagues were Emanuela Branca and Roberto Cingolani of the University of Lecce, and Salvatore Masiero, Gian Piero Spada and Giovanni Gottarelli of the University of Bologna. They published the research in the May 28, 2001 issue of the journal *Applied Physics Letters*. The research was funded by the Italian National Institute for Condensed Matter Physics.

Timeline: 5 years
Funding: Government
TRN Categories: Materials Science and Engineering; Biological, Chemical, DNA and Molecular Computing
Story Type: News
Related Elements: Technical paper, "Photodetectors fabricated from a self-assembly of a deoxyguanosine derivative," *Applied Physics Letters*, May 28, 2001

TRN

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