

DNA Nanotechnology



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General Description

Facilitated activity

“DNA Nanotechnology” is a cart demonstration exploring deoxyribonucleic acid, a nanoscale structure that occurs in nature. Visitors learn that nanoscientists study DNA to understand its biological function, and that they also use it to make other nanoscale materials and devices. They extract a sample of DNA from split peas and put it in an Eppendorf tube to take home.

Program Objectives

Big idea: Researchers in the field of nanotechnology use DNA, a nanoscale structure present in the cells of every living thing, to make tiny shapes and patterns.

Learning goals:

As a result of participating in this program, visitors will learn that:

1. DNA is in the cells of every living thing.
2. DNA helps cells to grow and do their jobs.
3. DNA is a nanoscale material: it's only two nanometers across.
4. Nano is very, very small.
5. Nanoscientists learn about and make things that are too small to see.
6. Researchers in the field of nanotechnology use DNA to create new materials and technologies.

NISE Network Main Messages:

- 1. Nanoscale effects occur in many places. Some are natural, everyday occurrences; others are the result of cutting-edge research.
- 2. Many materials exhibit startling properties at the nanoscale.
- 3. Nanotechnology means working at small size scales, manipulating materials to exhibit new properties.
- 4. Nanoscale research is a people story.
- 5. No one knows what nanoscale research may discover, or how it may be applied.
- 6. How will nano affect you?

DNA Nanotechnology

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Time Required

Set-up	Program	Clean Up
30 minutes	15 minutes	15 minutes

Background Information

Definition of terms

Nano is the scientific term meaning one-billionth ($1/1,000,000,000$) It comes from a Greek word meaning “dwarf.”

A *nanometer* is one one-billionth of a meter. One inch equals 25.4 million nanometers. A sheet of paper is about 100,000 nanometers thick. A human hair measures roughly 50,000 to 100,000 nanometers across. Your fingernails grow one nanometer every second.

(Other units can also be divided by one billion. A single blink of an eye is about one-billionth of a year. An eyeblink is to a year what a nanometer is to a yardstick.)

Nanoscale refers to measurements of 1 – 100 nanometers. A virus is about 70 nm long. A cell membrane is about 9 nm thick. Ten hydrogen atoms are about 1 nm.

At the nanoscale, many common materials exhibit unusual properties, such as remarkably lower resistance to electricity, or faster chemical reactions.

Nanotechnology is the manipulation of material at the nanoscale to take advantage of these properties. This often means working with individual molecules.

Nanoscience, *nanoengineering* and other such terms refer to those activities applied to the nanoscale. “Nano,” by itself, is often used as short-hand to refer to any or all of these activities.

Program-specific background

DNA

DNA stands for *deoxyribonucleic acid*. DNA is present inside the cells of every living thing. It contains the chemical instructions and genetic information to help organisms develop and function.

DNA is only two nanometers across, but if you could unravel all the strands from just one cell and line them up end to end, you'd have a thread two meters long!

Most of our DNA—99.5%—is the same as every other person's, but a small amount is unique. Only identical twins have exactly the same DNA as another person.

The human *genome* (all of our genetic material) is contained in 46 long, thin "threads" called *chromosomes*. Each person inherits 23 chromosomes from each of our parents, for a total of 46 chromosomes.

Human DNA is made of two long strands that are twisted together, in a structure called a *double helix*. It looks like a long, spiral ladder.

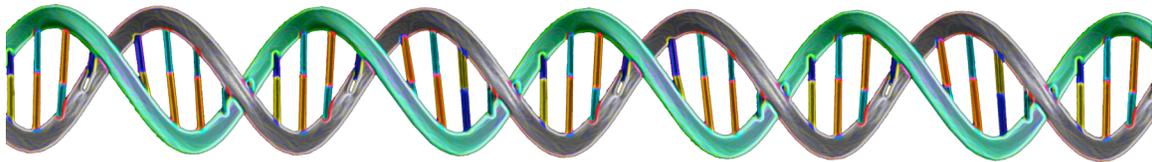


Illustration of DNA by James J. Caras, National Science Foundation

The sides of the ladder are made of units called *nucleotides*. The rungs of the ladder are made of four different types of molecules, called *chemical base pairs*:

- Adenine (A) and Thymine (T)
- Guanine (G) and Cytosine (C)

The base pairs always join in the same way. A and T always join together, and G and C always join together.

Humans have over 3 billion chemical base pairs in our DNA. The instructions that help our bodies grow and live are carried in the sequence of the base pairs, and are called *genes*.

Our genes contains the chemical instructions to make the tens of thousands of different proteins that our bodies need in order to grow and function. To build a new protein, the specific gene that is responsible unwinds from its chromosome. A single-stranded copy of its instructions is made. This copy is called RNA, short for *ribonucleic acid*.

RNA leaves the nucleus of the cell to locate *ribosomes*, which assemble proteins, and *amino acids*, which are the building blocks of proteins. RNA provides a template for the protein production, instructing the ribosomes to join the amino acids in a particular order.

DNA nanotechnology

DNA nanotechnology uses DNA and other nucleic acids as structural materials, taking advantage of their ability to self-assemble in order to create new, nanoscale structures. Applications of DNA nanotechnology include DNA computing, where DNA arrays perform computation as they assemble, and nanoarchitecture, where DNA is used as a template to assemble other molecules.

In nature, molecules and cells organize themselves into functional structures through a process called *self-assembly*. DNA is an example of a biological structure that self-assembles.

Self-assembly is an important area of research in nanotechnology. Self-assembly could make the manufacturing of nanomaterials fast and cheap and allow the creation of smaller structures than is possible with traditional technology.

In nanotechnology, self-assembly relies on chemical and physical forces to guide molecules into arranging themselves into predictable, ordered structures. The final structure is determined by properties of the molecules that are used, as well as the controlled environment in which they grow.

Self-assembly is a “bottom up” manufacturing technique, meaning that it begins with small pieces and builds them up to a larger structure. This is in contrast to “top down” techniques, where larger blocks of materials are pared down to create a smaller structure.

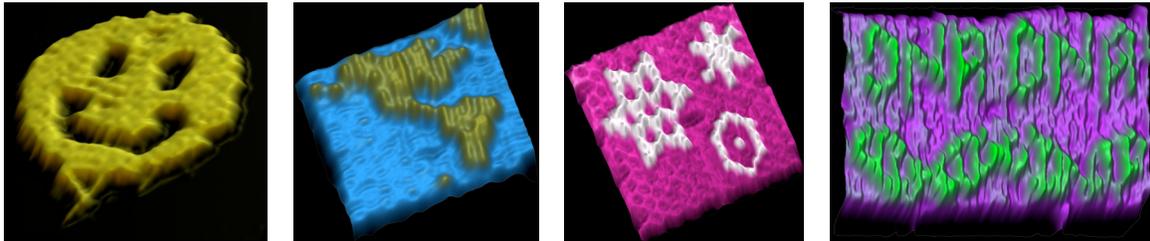
DNA is an important material in self-assembly research for many reasons. Researchers now have a good understanding of how DNA forms; they can predict the shape that a given molecule of DNA will take in solution; and they can easily get DNA molecules of any sequence they need.

Taking advantage of DNA's ability to self-assemble in controllable ways, researchers have created a variety of structures with DNA:

- Three-dimensional structures with branches and junctions that can be combined to create larger complexes (Ned Seeman)
- Three-dimensional polyhedrons, including cubes and octahedrons, with DNA junctions at their vertices (William Shih)
- Two-dimensional tiles with sticky ends that can be combined into different patterns, including lattice patterns and hollow tubes (Erik Winfree)
- Two-dimensional structures created by folding long strands of DNA using shorter strands (Paul Rothemund)

Paul Rothemund at the California Institute of Technology is researching the potential of DNA to help build smaller, faster computers and other examples of nanotechnology. Together with a team of other researchers, he is working on a project to use biological materials such as DNA to create nonbiological shapes and patterns.

Rothemund designed and self-assembled nanoscale shapes and patterns made from DNA. Examples include a smiley face, a map of North America, snowflakes, and a picture of a double helix DNA strand.



Smiley face

Map

Snowflakes

DNA

Courtesy Paul W.K. Rothemund, California Institute of Technology

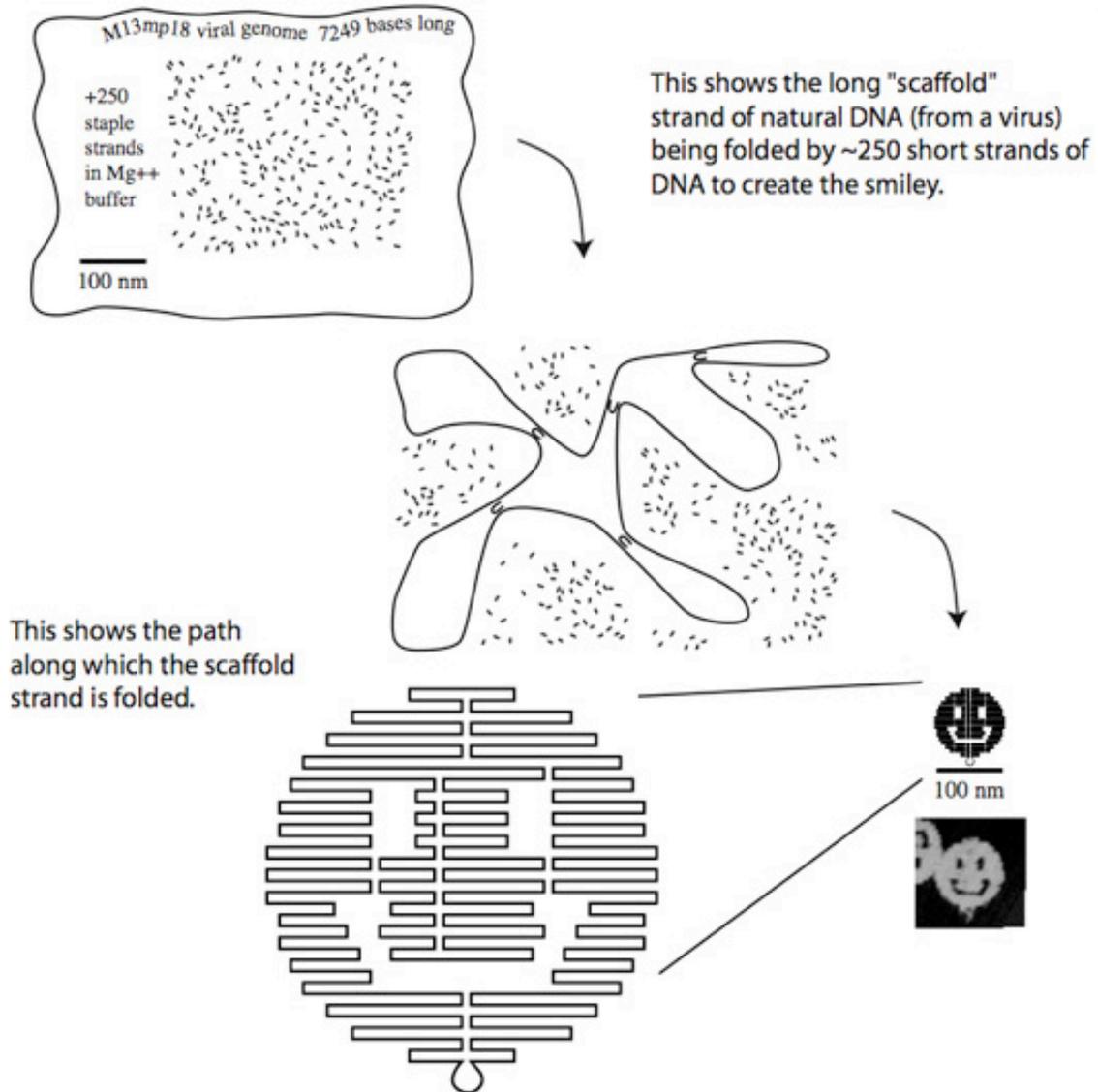
To create these shapes and patterns, Rothemund used a process he calls “DNA origami.” A long, single-stranded genome was used as a “scaffold.” Many short strands of synthetic DNA, or “staples,” were used to fold the long strand into a shape, such as a smiley face. Rothemund then used staple strands to decorate some of these shapes with patterns, such as the map of North America.

To create the smiley face Rothemund first designed the geometrical shape, then figured out how the scaffold strand could be folded in stacks to fill in the shape. Then, using a computer, he figured out the sequence of short staples necessary to fold the scaffold in the right places. Each staple has a left half that joins the long strand in a specific place and a right half that joins it further down the strand.

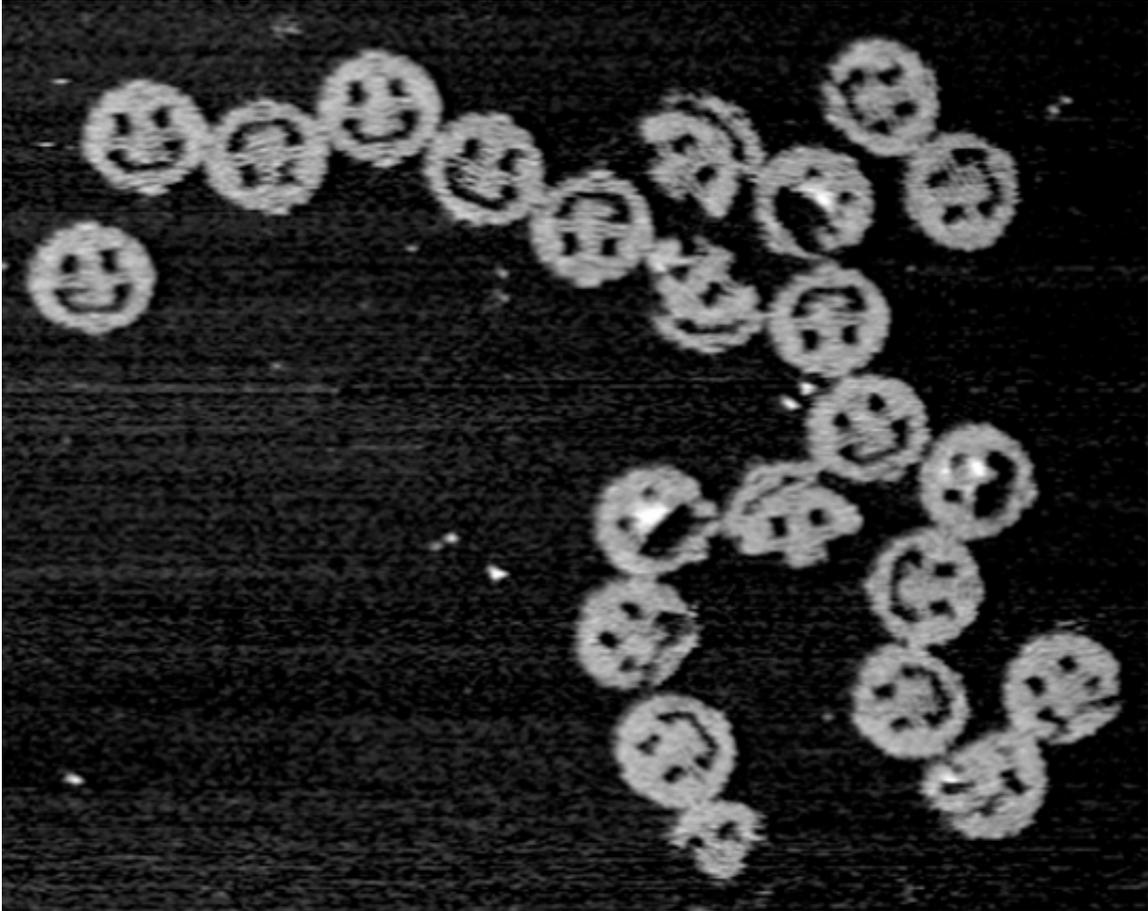
Next, long, scaffold strands and short, staple strands of DNA were combined in a buffer solution. The solution was heated to almost boiling, then cooled. As the mixture cooled, the short strands bonded to the long strands, folding them up into

tiny, 100 nm shapes.

The result was 50 billion DNA smiley faces floating around in single drop of solution! About 72% of the faces were well formed.



**Creating a 100 nm smiley face with the process of DNA origami.
Courtesy Paul W.K. Rothemund, California Institute of Technology.**



**DNA smiley faces. Each face is about 100 nm across.
Courtesy Paul W.K. Rothemund, California Institute of Technology.**

The patterned shapes Rothemund created with the DNA origami technique have a spatial resolution of about 6 nm, and are composed of about 200 individual pixels. They are 10 times more complex than previously-created arbitrary patterns.

DNA origami is limited by the length of single-stranded DNA that is available. On its own, this technique can't be used to create large structures.

To make bigger things out of DNA, Rothemund is collaborating with a scientist named Erik Winfree (also at Caltech) on a process called algorithmic self-assembly of tiles. In this process, square tiles of DNA join together to make larger, two-dimensional structures. DNA origami is used to start the process.

Rothemund predicts that in 5-10 years it will be possible to use a process called molecular programming to create circuits and computer memory. Further in the future, Rothemund envisions that molecular programming might allow us to build technologies from the bottom up.

The process of molecular programming would include the following steps:

1. A device (such as a cell phone) is designed using a computer.
2. A compiler turns the design into molecules that can be sent to a synthesizer.
3. The synthesizer packs the molecules into a seed.
4. The seed is watered and fed.
5. The seed grows. It does a developmental computation and builds the device as designed.

Materials

Materials to present the program

- Powerpoint or hard copies of images
- Prepared strips of paper and adhesive envelope labels
- Pea mixture in labeled squirt bottles
- Buffer solution in labeled dropper bottles
- Alcohol in labeled squirt bottles
- Glass vials (or test tubes and a holder)
- Eppendorf tubes (1.5 ml or 2 ml)
- String or yarn
- Scissors
- DNA extraction protocol handout
- Safety glasses
- Paper towels (for spills)

Materials to prepare the pea mixture

- Dried split peas
- Cold water
- Blender
- 1 c measuring cup
- Mixing bowl or other container
- Strainer that fits into the mixing bowl
- Labeled squirt bottles (~500 ml)
- Funnel (optional)

Materials to prepare the buffer solution

- Cold water
- Dishwashing liquid (detergent)
- Salt
- 1/2 c measuring cup
- 1 t measuring spoon
- 1/8 t measuring spoon
- Mixing bowl or other container
- Spoon
- Labeled dropper bottles (~100 ml)
- Funnel (optional)

Materials to prepare the alcohol

- Isopropyl alcohol (at least 70%)
- Labeled squirt bottles (~250 ml bottles)
- Funnel (optional)

Materials to prepare the DNA origami demo

- Strips of paper or register tape
- Self-adhesive envelope labels
- Marker

Set Up

Time: 30 minutes

Step 1:

Prepare materials for the DNA origami demonstration. The instructions below are for a simple, two-fold model.

Scaffold DNA strands

1. Cut a strip from a sheet of office paper, around an inch wide and 11 inches long.
2. Mark one side of the long strip with the letter A in two places: about 1 inch from the end and 4 inches from that same end.
3. Flip over the long strip. Mark the back side of the other end of the strip with the letter G in two places: about 1 inch and 4 inches from the end.

DNA staples

1. Mark one self-adhesive envelope label with the letter T at each end.
2. Mark a second label with the letter C at each end.

The letters represent the DNA base pairs. A bonds with T; G bonds with C.

When you perform the demo, you'll make two folds in the paper strip, sticking it together with the adhesive label. You'll use the label marked with Ts to fold the paper strip at the points marked A. You'll use the label marked with Cs to fold the paper strip at the points marked G. The result will be a floppy S shape.

Step 2:

Prepare materials for the DNA extraction. These instructions create adequate materials for 100 visitors.

Note: Prepare the pea mixture the same day you're doing the activity.

Pea mixture

1. Put the following ingredients into a blender:
 - 2 c dried split peas
 - 4 c cold water
2. Blend on high for about a minute.
3. Pour the mixture through a strainer into another container.
4. Discard the solids in the strainer and save the liquid in the container. The liquid is the pea mixture you'll use in the activity.
5. Pour the mixture into labeled squirt bottles (~250 ml).

Buffer solution

1. Put the following ingredients in a small container:
 - 1/2 c water
 - 2 t dishwashing liquid
 - 1/8 t salt
2. Gently stir to mix.
3. Pour the solution into labeled dropper bottles (~100 ml).

Alcohol

- Pour the alcohol into labeled squirt bottles (~250 ml).

Step 3:

Set up all the materials in your presentation space. You'll need access to a sink to empty and rinse the vials or tubes you use for the activity.

Program Delivery

Time: 15 minutes

Safety:

The presenter and visitors should wear safety glasses while doing this activity.

Visitors should not taste or consume any of the materials used in this activity.

Procedure and Discussion:

Today's program is about DNA:

- We're going to learn what DNA is and what its job is in nature.
- Then, I'll tell you about a totally different way DNA is being used in an area of research called nanotechnology.
- And at the end, you can extract some real DNA from split peas and put it in a tube to take home.

Introduction to DNA

DNA stands for *deoxyribonucleic acid*. DNA is inside every cell of every living thing. It tells cells how to grow and do their jobs.

DNA is so tiny that you usually can't see it! It's much too small to see without special tools.

Here's a picture of what human DNA looks like.

<Image of DNA>

It's kind of like a long, spiral ladder. This shape is called a double helix. The rungs of the ladder hold it together.

The rungs are made of pairs of chemicals known by the letters A, T, G, and C. They always join together in the same way: A with T and G with C. The order of these pairs in the ladder is what contains the genetic information that helps your body to grow and live.

Most of our DNA is the same as every other person's, but a small amount is unique. Your DNA is different from everyone else's in the whole world—unless you have an identical twin!

So DNA is really important in nature.

DNA nanotechnology

DNA is also really important in technology, especially a new area of technology called nanotechnology.

I mentioned before that DNA is small. It's so small it's measured in nanometers. Has anyone ever heard of a nanometer?

A nanometer is a billionth of a meter.

A meter is about as long as the distance from my chin to my hand [hold arm straight out].

A nanometer is a **billionth** of that distance! That's really small. It's way too small to see. A nanometer is so small that your fingernails grow one nanometer every second!

DNA is only two nanometers across, so it's super tiny.

In the field of nanotechnology, researchers learn about things that are too small to see—like atoms and molecules and DNA—and make new materials and devices that are super small.

There's a special field of nanotechnology called DNA nanotechnology where researchers are figuring out how to use DNA to build other tiny structures. DNA is a useful building material because it can assemble itself into structures.

DNA origami

Here are some cool example of nanostructures made from DNA. Can you tell what these are?

<Image of DNA origami shapes>

Here we have a smiley face, a map of North America, some snowflakes, and a picture of a double helix DNA strand!

A scientist named Paul Rothemund at the California Institute of Technology got DNA to self-assemble into these structures using a process he calls DNA origami.

To create the smiley face, Rothemund used a long, scaffold strand of DNA. He folded it up into the smiley face shape using short, staple strands of DNA.

<Diagram of DNA origami process>

Each staple has a left half that binds to the long strand in one place and a right half that binds to it in a different place further down the strand. When the short staple binds itself to the long strand, it folds the longer stand.

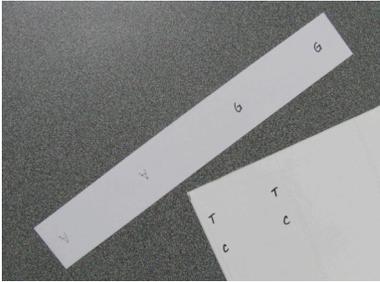
When all the short staples are joined to the long strand, the long strand is folded up into a new shape.

Here's a demonstration of how this works. This long strip of paper represents a long, scaffold strand of DNA. These short labels represent the staples.

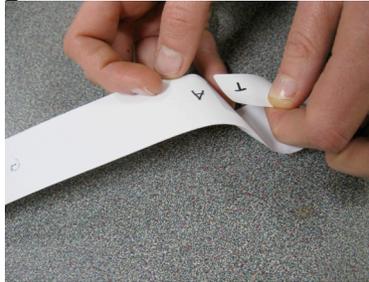
You can see I've marked my paper with the letter A on one side, here and here, and the letter G on the other side, here and here. I've marked one of my labels with the letter T and the other with the letter C.

These letters represent chemical base pairs that hold DNA together. A always joins with T and G always joins with C.

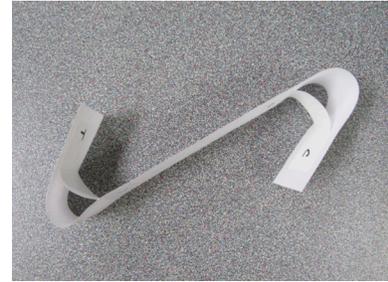
Demonstration of DNA origami



Strip of paper marked with As and Gs, and labels marked with Ts and Cs



Stick Ts on label to As on paper strip, making a first fold



Stick Cs on label to Gs on paper strip, making a second fold

So here's my T staple. Where are the two T ends going to bond with my scaffold DNA? Here at the As.

How about the staple that ends in C? It's going to bond here at the Gs.

Now we've made a new shape, kind of a floppy S.

This is a model of the process of DNA origami that Rothemund used to fold up a long strands of DNA into smiley faces. Of course, this is a lot simpler!

To make his smiley faces, Rothemund took long, scaffold strands and short, staple strands of DNA and combined in a salt solution. He heated it up, then let it cool. As the solution cooled, the short strands bonded to the long strands, folding them up into tiny shapes.

The result was 50 billion DNA smiley faces floating around in single drop of salt water!

<Image of field of smiley faces>

Each smiley face is about 100 nanometers across, or around 50 times bigger than a single strand of DNA. Around 1,000 of these smiley faces could line up across a human hair!

Other researchers at Caltech have used DNA origami to make a nanoscale switch that really works. They used the DNA to attach a switch to a tiny tube called a carbon nanotube.

In the future, it might be possible to use DNA to self-assemble technological devices such as cell phones or laptop computers!

DNA extraction activity

Now, let's extract some real DNA so you can get a look at what this stuff is like.

In this activity, we're going to get our DNA from split peas. Split peas are a plant seed, so they have DNA in them.

In this container I have a murky liquid that I made by mixing dried split peas and water together in a blender.

The first thing we're going to do is extract, or remove, the DNA from the pea cells.

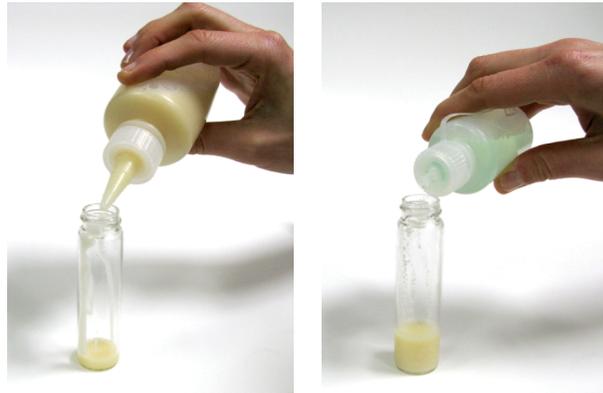
I already started that process when I put the peas in the blender. The blender separated the cells.

Now you're going to add something called buffer solution that breaks down the cell walls and pulls out the DNA. The buffer solution is made of water, dishwashing liquid, and a little bit of salt.

[Walk visitors through Step 1 of the protocol. Offer them the handout to follow.]

Break down the cell membrane

1. Squirt about a teaspoon or so of pea mixture into a vial.
2. Squeeze about 10 drops of buffer solution into the vial.
3. Swirl or rock the vial to combine the buffer solution and pea mixture.



Now we're going to let the vial sit for a bit to give the buffer solution time to work. The buffer solution breaks down the cell membrane and pulls out the DNA.

The outside of the cell is called the cell membrane. The dishwashing liquid in buffer solution breaks down the fatty parts of the cell membrane. (When you wash dishes, it helps to break down the grease on your plates!).

The salt in the buffer solution causes the contents of the cell—including the DNA—to come out.

Now the DNA is accessible inside the pea mixture, but it's still too small to see.

So we're going to add some alcohol. That will make the DNA precipitate, or clump together. When enough DNA has clumped together, we'll be able to see it.

[Walk visitors through Step 2 protocol. They can also follow their handout.]

Precipitate the DNA

1. Tilt the vial and squirt about a half teaspoon of alcohol down the inside.
2. The alcohol will form a clear layer on top of the pea mixture.
3. DNA will gradually rise out of the pea layer into the alcohol. It's white and looks like mucus.
4. Very gently swirl or rock the tube to help the DNA rise and clump together.



Now we have a layer of pea mixture at the bottom and a clear layer of alcohol at the top.

If you look closely, you can see DNA rising from the pea layer into the alcohol layer. It's the whitish, slimy-looking stuff.

The alcohol makes the DNA precipitate, or clump together, so we can see it. Each individual piece of DNA is still too small to see, but when enough of it sticks together we can see the clump. There are millions of strands of DNA in the glob you see.

You can put your DNA into a tube to take home. If you like, you can put the tube on a piece of yarn and wear it as a necklace or a bracelet.

Put the DNA in a tube

1. Carefully pour the top layer (alcohol and DNA) from the vial into an Eppendorf tube.
2. Slip a length of yarn over the connector between the cap and tube.
3. Snap the cap shut.



Make a necklace

1. Tie the yarn around your neck or wrist. Be sure not to make it too tight!
2. Remember to look at it later. The DNA will continue precipitating so it will be even easier to see later on.



There you go! You extracted DNA.

Wrap-up

So now we've learned a little bit about what DNA is, how it's being used in nanotechnology to create new, tiny, very cool structures, and we extracted some real DNA from split peas.

We're done! I'm happy to answer questions.

Tips and Troubleshooting:

Children and individuals with limited dexterity may need help manipulating their vials and using the dropper bottles. You or a partner can assist them with the dropper bottles, describing what you're doing and asking them to observe the results.

Common Visitor Questions

Is this how scientists extract DNA in labs?

They use a similar process but different chemicals.

Why do scientists extract DNA?

Scientists extract DNA to study specific genes. They might do this in order to diagnose or treat a disease.

Can you extract DNA from other things?

Yes. The cells of every living thing contain DNA. You could use a similar protocol (set of instructions) to extract DNA from kiwifruit, strawberries, bananas, chicken liver, or eggs.

How can scientists see DNA? Do they use microscopes?

DNA is too small to see using even the most powerful optical microscopes. Scientists use a technique called x-ray crystallography to create an image of DNA molecules.

How do scientists use DNA to identify criminals?

Investigators can create a DNA profile by lining up pieces of DNA in a pattern. They can compare the pattern of a suspect's DNA to the pattern of DNA left at a crime scene, to see if they match.

How could you make something big like a cell phone using nanotechnology, since DNA and other nanostructures are so small?

Scientists at the California Academy of Sciences, including Paul Rothmund and Erik Winfree, are working on a project in molecular programming, which would use biological and chemical processes to execute molecular algorithms and build new technologies.

Currently, they've developed a way to get small tiles to join together into bigger structures. This process called algorithmic self-assembly of tiles. In this process, square tiles of DNA join together to make larger, two-dimensional structures. DNA origami is used to seed the self-assembly of these tiles into predetermined structures.

Rothmund predicts that in 5-10 years it will probably be possible to use molecular programming to create circuits and computer memory. Further in the future, molecular programming might allow us to build technologies from the bottom up.

Going Further...

Here are some resources you can share with your visitors:

The Genetic Science Learning Center at the University of Utah provides information and resources related to DNA:

- <http://learn.genetics.utah.edu>

Nature has a number of relatively accessible articles on DNA nanotechnology:

- Rothmund, P.W.K. 2006. *Nature* 440: 297-302.
- Seeman, N.C. 2003. *Nature* 421: 427-431.
- Shih, W., Quispe, J., and Joyce, G. 2004. *Nature* 427: 618-621.
- Winfree, E., Liu, F., Wenzler, L., Seeman, N.C. 1998. *Nature* 394: 539-544.

Paul Rothmund presents his DNA origami research in two talks on **TED.com**:

- http://www.ted.com/index.php/talks/paul_rothemund_casts_a_spell_with_dna.html
- http://www.ted.com/index.php/talks/paul_rothemund_details_dna_folding.html

Wikipedia (www.wikipedia.com) has articles on DNA, DNA nanotechnology, DNA origami, and other related topics.

Clean Up

Time: 15 minutes

Labware can be washed in water. Leftover split pea mixture can be poured down the sink. (It won't keep to use another day.) The buffer solution and alcohol can be saved and used later.

Universal Design

This program has been designed to be inclusive of visitors, including visitors of different ages, backgrounds, and different physical and cognitive abilities.

The following features of the program's design make it accessible:

- [x] 1. Repeat and reinforce main ideas and concepts
 - The activity is organized into discrete chunks.
 - An overview of the activity is provided at the beginning and end of the program. The different parts of the activity are called out during the program.
 - Learning objectives are repeated throughout the presentation.
- [x] 2. Provide multiple entry points and multiple ways of engagement
 - Program content is communicated through conversation as well as a demonstration and hands-on activity.
 - Concise key phrases are used to support main ideas.
- [x] 3. Provide physical and sensory access to all aspects of the program
 - Main ideas are presented through multiple senses (sight, hearing, and touch).

To give an inclusive presentation of this program:

- Ask the audience questions, and check in with them along the way to make sure they're engaged and following you.
- Use descriptive language to describe objects and images.

- Provide a handout with the activity protocol, so visitors can follow written text as well as your verbal instructions.
- Help individuals with limited dexterity to use the dropper bottles, or assist a companion in working with them. Describe what you/they are doing and ask them to observe the results so they remain engaged in the activity.
- Make sure your audience knows about any special accommodations you offer.

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Any opinions, findings, and conclusions or recommendations expressed in this program are those of the author and do not necessarily reflect the views of the Foundation.