DNA Structure: Gumdrop Modeling
Teacher Version

DNA is one of the most important molecules in our bodies. It's like a recipe book with the instructions for making us who we are. Because each cell must have a copy of these instructions, cells need to replicate, or make a copy of their DNA, each time they divide. In this 4-part lab, students will get an up-close and personal look at DNA, including the structure of DNA, how that structure is important for DNA replication, and how that DNA is packaged and regulated.

Set-Up (prior to lab)

1. We found it was helpful to assemble "DNA kits" prior to the lab, in order to make sure each group gets the supplies that they need. However, don't do it more than a day or two in advance, or the candies get super hard! The individual baggies contain:

- 6 Mini marshmallows
- 6 Twizzlers
- Either 2 pink, 2 yellow, 1 green, 1 orange -or- 1 pink, 1 yellow, 2 green, and 2 orange DOTs, Mike and Ikes, jelly beans, or similar chewy candy.
    - Note: it's important to have an equal ratio of pink-to-yellow and green-to-orange, since those bases need to pair with each other
- Place the left-over chewy candies, marshmallows, and Twizzlers in a separate bag – the students will need them during the replication portion later on

2. The night before the lab, put the rubbing alcohol in the freezer. If you don't have a freezer at the school, then put it on ice in a small cooler.

3. Cut and color the string for part 4. The string should be approximately 40cm, greeen at one end and blue towards the middle. The location of the color patches is important.

Prerequisites:

Both versions of the lab use a ruler to make basic measurements, which should be understandable for almost any age. However, the advanced lab has a few thought / concept questions which are likely difficult for those below high school science levels.

California Science Content Standards:

- **5. Genetics: The genetic composition of cells can be altered by incorporation of exogenous DNA into the cells.**
    - 5a. Students know the general structures and functions of DNA, RNA, and protein.
    - 5b. Students know how to apply base-pairing rules to explain precise copying of DNA during semi-conservative replication and transcription of information from DNA into mRNA.

Materials:

*** Part 1 & 2 (per group of 2-4 students) – DNA Models

- 1 box DOTS, Mike and Ikes, jelly beans, or similar candy (5 colors per box) *per 3 groups*
- 1 package mini marshmallows *per class*
- 1 box Twizzlers Bites (or similar*) *per 3-4 groups*
- 35 Toothpicks (flat, not round, if possible)
- Scissors

*** Part 3 – Strawberry DNA Extraction (also done in groups)

- Measuring cup
- Measuring spoons
- Rubbing alcohol
- Strawberries (3 per group)
- Salt
- Dish detergent
- Funnel
- Cheesecloth or coffee filter
- Tall cup / glass
- Sealable sandwich bags
- Test tubes (optional)
- Toothpicks

*** Part 4 – DNA Compaction (per group)

- A ruler
- A calculator
- 2 meters of sewing thread
- 2 pieces of white string or yarn, with colored patches
- 2 strips of Scotch tape, wrapped into a circle (sticky side out)

*Other pliable, but firm, candies can be substituted, such as "Circus Peanuts" or small caramels

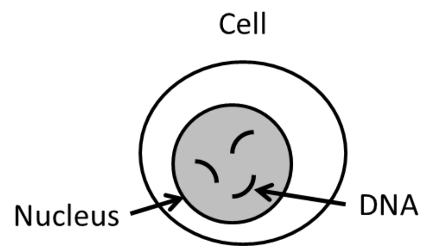
Key Concepts:

- DNA is made of strings of **nucleotides**. A nucleotide is a chemical molecule composed of one phosphate group, one sugar ring, and one nitrogen-containing base.
- DNA has 4 types of **bases**: Adenine, Thymine, Cytosine, and Guanine (A, T, C, and G). These bases have strict binding rules, as A only bonds with T (and vice versa), and C only bonds with G. This is important for DNA replication to work.
- DNA is carefully packaged in the nucleus to compact it, protect it, and control which parts of the DNA are turned on and off in different cells.

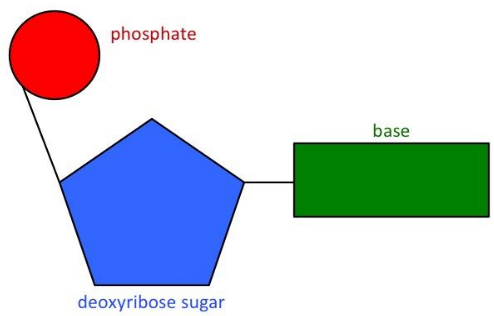
Introductory Mini-Lecture

Before we begin today's lab, let's first start by discussing *what is DNA*? Can anyone give me examples of DNA being talked about… maybe on TV or in movies? *[Possible answers – to* *identify a criminal, to determine if you're at risk for a disease, to establish familial relationships, etc]* All of these things are related to the fact that DNA provides information about living things, like people. Pretty much every cell in your body contains the same set of DNA, half of which came from your mom and half of which came from your dad (which is why you look a little bit like each of them!). Does anyone know where DNA is found in the cell? *[In the nucleus – draw a picture of a cell, similar to below]* The nucleus helps to contain and protect the DNA from harm. But what *is* DNA?

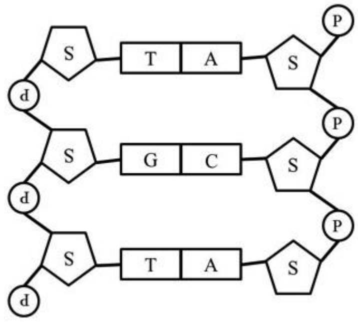
DNA is a chemical molecule inside our bodies, and it contains the instructions for making us who we are. Now, have any of you guys seen DNA before? Why not? [It's too small] But if you were able to zoom in really close on DNA, do you know what it would look like?



The basic building block of DNA is called a **nucleotide**. This building block has three parts: a **phosphate group**, a **sugar**, and a **base**. [Draw a diagram similar to the one below on the board – note the angles between the phosphate, sugar, and base are important!]. There are 4 different flavors of bases, called A, T, C, and G. Because of their shapes, they can only fit together in a certain way – "A" always matches up with "T," and "C" always matches up with "G." As you will see later, this is important when it comes to replicating the DNA.



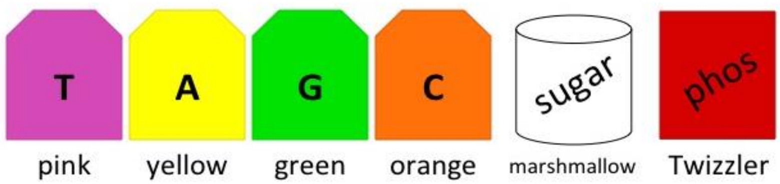
These nucleotides are connected in two long strands, with the phosphate of one nucleotide attaching to the sugar of the next. These two strands wrap around each other, with the bases of one string attached to the bases of the other. You can think of it like a twisted ladder, with the phosphates and sugars forming the sides (or "backbone") and the bases forming the rungs in the middle. This ladder shape is called a ***double helix***. One important thing to remember about this structure is that the two strands of DNA have opposite ***directionality***. Just like the two lanes of a street point in opposite directions, one strand of DNA has the phosphates pointing up, and the other strand has the phosphates pointing down.



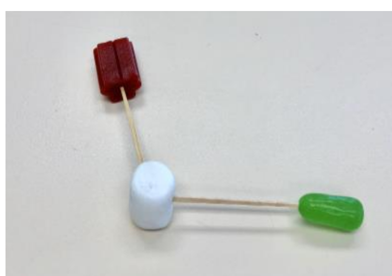
Part 1 – Building a DNA Molecule

In this section, we will build DNA models in order to understand what a **nucleotide** is composed of, and how several nucleotides fit together into a DNA molecule.

1. Separate the two bags of candy you were given. Set one bag aside. Empty out the second bag, and create 6 nucleotides using toothpicks and the following key:



Q1. What are the three parts of a nucleotide? Please draw and label below.
A phosphate, sugar, and base – similar drawing to the one in the lecture section (note that the angle between the three components is important!)



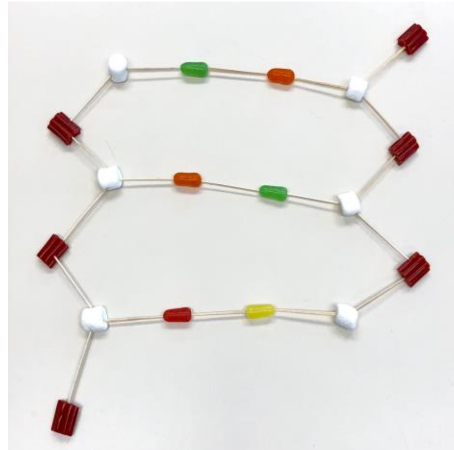
2. Once you have your 6 nucleotides, pick up one of your "A" nucleotides (yellow).

Q2. What is the complementary (matching) base for "A"? What color is that base?
T (thymine); it is pink

3. Use a toothpick to bond the "A" nucleotide with its complementary nucleotide. Note that they should be connected just through the **base**. Also, if one nucleotide has the phosphate pointing *up*, then the paired nucleotide should have the phosphate point *down*, indicating opposite orientations (like the lanes on a street).

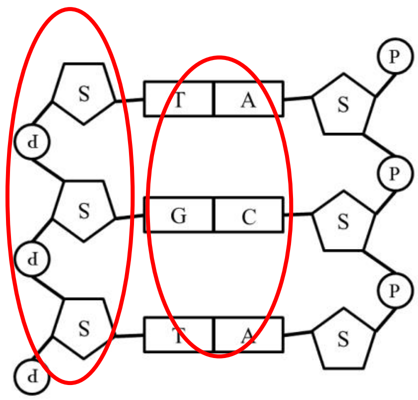
4. Repeat with the remaining nucleotides, creating a total of 3 paired sets.

5. Now connect the three nucleotide pairs together, by attaching the phosphate group (Twizzler) of one nucleotide to the sugar (marshmallow) of the next.



Circle and label the <u>*backbone*</u> *and the* <u>*bases*</u> *of the DNA molecule below*

backbone bases

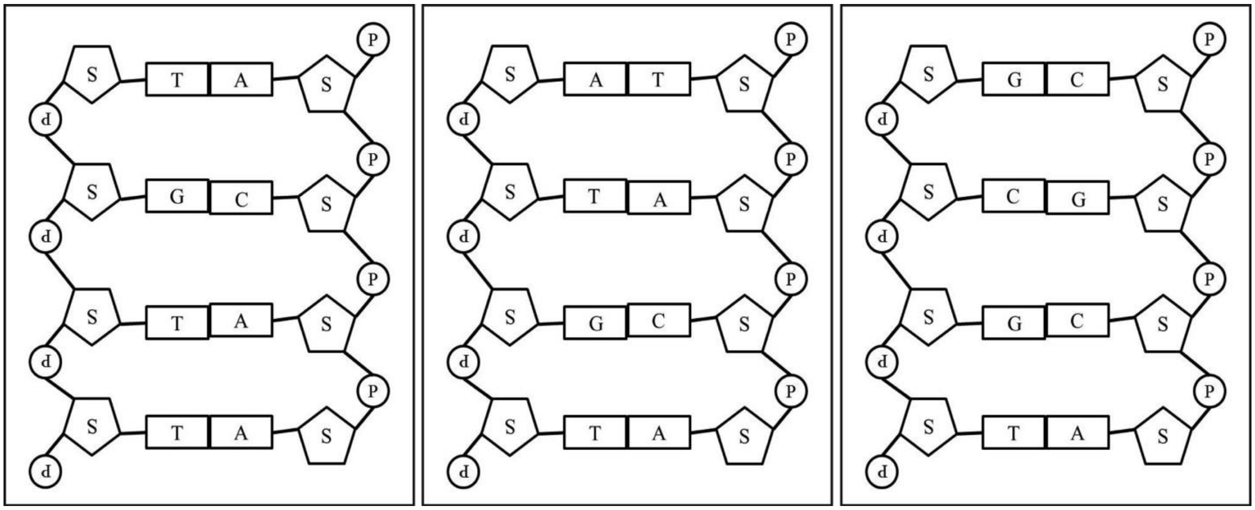


* Your nucleotide pairs do not need to be in this exact order, as long as the A/T and C/G pairing are correct!

Great! You just made a model of a little piece of DNA. Almost all living things have DNA that looks just like this - from people to dogs to cacti! But if DNA contains the recipe for each of these very different creatures, then the DNA from each of them must be different *somehow*, right?

Let's look at an example.

The drawings below show a small section of DNA from three very different organisms: a plant, a mammal, and a bacterium. Each strand of DNA shown contains four nucleotide pairs.



Plant **Mammal** **Bacterium**

Q3. What is different in the DNA of these different organisms? Complete the following table to identify what is different between the DNA of the plant, mammal, and bacterium.

	Compare the plant and mammal DNA.	**Compare the mammal and bacterium DNA**.
Is the arrangement of the sugar and phosphate groups the same in each type of DNA?	*Yes*	*Yes*
Does each type of DNA contain the same four bases (**A**, **C, G, T**)?	*Yes*	*Yes*
Is the order of the bases (read from top to bottom) the same in each type of DNA?	*No*	*No*
Are the base-pairing rules (A/T and C/G) the same in each type of DNA?	*Yes*	*Yes*

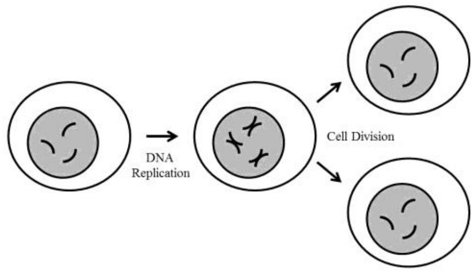
(adapted from http://serendip.brynmawr.edu/sci_edu/waldron/)

Q4. What is the only characteristic that differs between these segments of DNA from a plant, a mammal, and a bacterium?

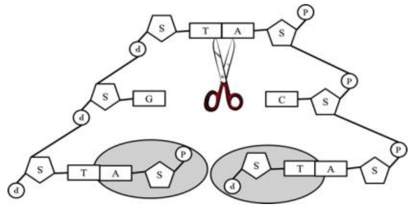
The order, or sequence, of the bases is different

Part 2 – DNA Replication

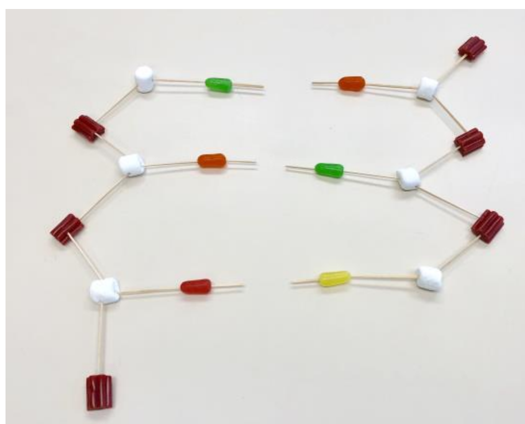
You have now completed a DNA model. However, DNA is not an unchanging molecule! Every time one cell divides into two (for example, to make new skin cells that are needed to heal a cut), both cells need their own copies of the DNA. How does this happen?



To make one DNA molecule into two, the bonds between the bases (the rungs of the ladder) are broken by an enzyme called **DNA helicase** (depicted as scissors below). Once the strands are separated, newly made nucleotides can be brought in and paired up with each individual strand by another enzyme, **DNA polymerase** (depicted as grey ovals), which knows the base pairing rules (A/T and C/G). When they're done, you have two complete copies of DNA, ready to be divided into two new cells!



1. Take the scissors and cut your model through the middle, between the colored bases (be careful!).

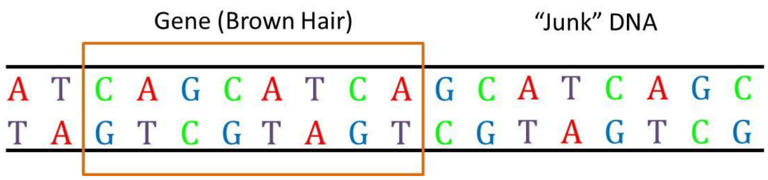


Q5. What part of the replication process do the scissors represent?
Helicase unwinding DNA

2. Using the bag of extra candies, make 6 new nucleotides, each consisting of 1 phosphate, 1 sugar, and 1 base (make sure to pick the right nucleotides that will pair with your DNA strands!)

Fun Facts to discuss while building:

- Only 2% of the human genome is composed of functional units called **genes** (these will be discussed again later). The rest of the DNA in the cell is often referred to as "junk," but is likely important for determining whether genes are turned on or off, and to provide the DNA with structure (but we don't really know!) (http://www.ornl.gov/sci/techresources/Human_Genome/project/info.shtml)



- A human being has 20,000-25,000 genes (the functional units of DNA mentioned above), but a rice plant has over 50,000! Clearly biological complexity is not equivalent to gene number. (http://www.nature.com/scitable/topicpage/eukaryotic-genome-complexity-437)

3. Convert each half-strand of DNA into completed strands by attaching the correctly paired base to each splintered end, making sure to remember the opposite orientation of the phosphate groups!

Q6. What enzyme are you representing now?
DNA Polymerase

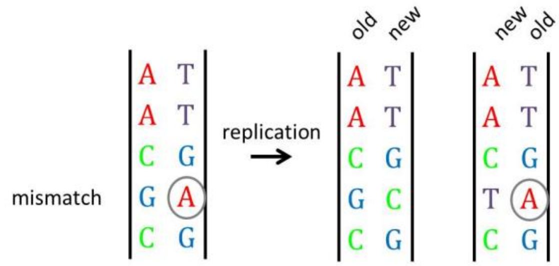
*Q7. You just replicated 3 nucleotide pairs in a matter of a few minutes. However, the DNA polymerase in bacteria can replicate 2,000 nucleotides per **second**! The reason that DNA polymerase needs to travel so fast is because a real bacteria cell doesn't just have 3 nucleotide pairs – it has 5,000,000! How many seconds would it take DNA polymerase to replicate 5,000,000 nucleotides, if it does 2,000 nucleotides per second? How many minutes is this?*
5,000,000 nucleotides / 2,000 nucleotides per second = 2,500 seconds, or 41.7 minutes

Now you have two complete DNA strands, ready to be handed down into new cells!

QS8. Mutations can arise if DNA polymerase makes a mistake and puts in the wrong nucleotide. What happens when you get a mutation? Is it good, or bad, or can it be either?
A mutation is a change in the DNA sequence that can affect the function of that DNA, and possibly the whole organism. Mutations can lead to diseases like cancer or sickle cell anemia, or contribute to natural processes like evolution. If you listen to popular culture, mutations can also give you super-powers! (X-Men, Teenage Mutant Ninja Turtles, etc).

QSA8. What is a mutation? Using your model, can you explain how errors in DNA replication could lead to mutations in later generations of cells?
A mutation is "a relatively permanent change in hereditary information [DNA]" (Merriam-Webster). So it's a change in the DNA sequence which is passed down to future cells. Mutations can arise, for example, when DNA polymerase makes a mistake and incorporates the wrong nucleotide (e.g. an "A" opposite a "G"). Once the two strands of DNA are separated for the next round of replication, one cell will inherit the

correct information, but the other will get the mutated copy, which it will continue to pass along.



Q9. *Mutations often arise when DNA is damaged. Can you think of things in your environment (or in your own body) that can damage DNA?*

UV (sun) light, chemical carcinogens (like those in cigarette smoke), x-rays (from medical treatments or from the natural environment), or oxidative damage (which is caused by oxygen floating around in the cells – a natural byproduct of metabolism. Note that this is why "antioxidants" found in foodstuffs are thought to prevent cancer, by reducing the damage caused by naturally-occurring oxygen-containing molecules in cells).

Part 3 – DNA Extraction

(Adapted from http://genetics.thetech.org/online-exhibits/do-it-yourself-strawberry-dna)

Now that we know what DNA looks like on the molecular (microscopic) level, let's see what real DNA looks like with just your eyes!

We know that DNA is stored in the cell **nucleus**. So how do we get it out? Actually, if you put cells in liquid with lots of salt and detergent, they will **lyse** or pop, releasing the DNA into the liquid around them!

1. Mix together your extraction solution in a measuring cup (make sure to scale up, if necessary, to have at least 4 Tbsp per group). For 3-4 groups:
   1 tsp salt
   2/3 c water
   2 Tbsp dish detergent

2. Place the funnel in the tall glass or cup, and line it with the cheese cloth or coffee filter.

3. Put three strawberries (no stems or leaves!) into a sandwich bag and seal it, squeezing all of the air out of the bag as you do so.

4. Squish the strawberries for about 2 minutes (enough to almost eliminate all clumps).

5. Add 4 Tbsp of the extraction solution to the strawberries. Push out all the air and seal the bag.

6. Squeeze the strawberry mixture for about 1 minute.

   Q10. What are you doing to the strawberry cells right now?
   You're popping them open, or lysing them, and releasing the DNA into the liquid

7. Pour the strawberry mixture into the funnel, and let all of the liquid drain into the cup.

   Q11. Where is the DNA right now?
   In the liquid in the cup

8. Throw away the filter and the strawberry pulp.
   - Optional: Pour the liquid into a test tube until it's about 3/4 full (if you don't have test tubes, just leave the liquid in the cup).

9. Tilt the cup / test tube and *very slowly* pour cold rubbing alcohol along the side, letting it form a layer about 1cm thick on top of the strawberry extract. [It should be enough that you can clearly see through the layer] DO NOT MIX THE ALCOHOL AND THE EXTRACT!

10. Carefully hold the cup up to the light and look through the alcohol layer – can you see anything floating near the surface with the strawberries? [The DNA would rather be in the alcohol than in the strawberry juice, so it will float to the surface and into the alcohol layer – it looks like a clearish, goopy blob]

11. Dip a toothpick into the alcohol, gently touching where the two layers meet. Carefully pull up the skewer – the DNA should stick to it, and be pulled out as well. [If you can see the DNA blob in the alcohol, go ahead and touch it directly. Otherwise, sometimes it helps to "swirl" the toothpick along the interface between the layers, as the DNA will stick better.]

    QS12. What does the DNA look like (long, short, clumpy, smooth, stretchy, brittle, etc)? What color is it?
    It should be long, smooth, and stretchy, clear (or slightly pink), and very goopy / sticky / slimy. It's pretty gross, actually.

    QSA12. What does the DNA look like (long, short, clumpy, smooth, stretchy, brittle, etc)? What color is it? *Looking at your DNA model, why do you think DNA has these properties?*
    It should be long, smooth, and stretchy, clear (or slightly pink), and very goopy / sticky / slimy. It's pretty gross, actually. The reason that it's long and smooth is because the DNA is in long chains (as your model shows). In addition, because the bonds between the sugars and phosphates are at angles, the molecule can stretch and flex, making it difficult to break.

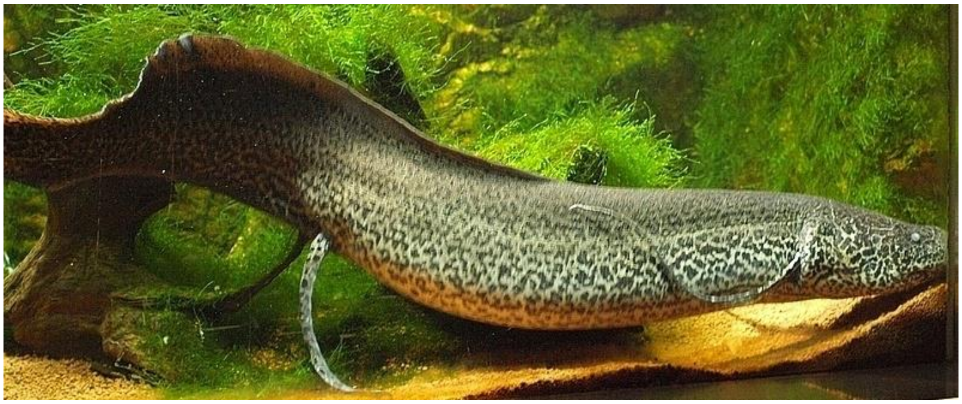
Q13. Based on what you know about DNA structure, if I used this same procedure to extract DNA from human cells or bacteria, do you think it would look the same or different? Why?

It would look the same, because on the macroscopic level (what you can see with your eyes), you're only seeing the chains of DNA, being held together by the sugar / phosphate backbone. This structure is the same in all organisms – it's only the sequence that changes (something that you can't see with this method).

Part 4 – DNA Packaging

If you run out of time, skip part 4 and go straight to the concept questions at the end.

Let's finish up by thinking BIGGER. Your model has 3 nucleotide pairs, but most human cells have *6 billion* of these nucleotide pairs! That's a lot of DNA! Believe it or not, we don't even have the biggest genome on Earth – that belongs to the marbled lungfish (pictured below), which has over 130 billion nucleotide pairs per cell!! In order to fit all that DNA into a cell, it needs to be very tightly **compacted**, or **packaged**.



https://upload.wikimedia.org/wikipedia

1. Take a piece of sewing thread that's 2 meters long. This is how much DNA is in a *single cell* in your body. Roll it into the tiniest little ball that you can, and measure the diameter (how big it is at the widest part of the ball) using the "cm" (centimeter) scale on the ruler.

Fun facts to discuss while rolling / compacting:

- 6 billion can be a hard number to visualize – here's something the students might appreciate
    - According to the web, the average volume of a jelly bean is 3.375 cm3, which is 3.38x10^-6 m3
    - An Olympic swimming pool is 25m x 50m x 2m, or 2500m3
    - Jelly beans in a jar take up about 80% of the space (20% is air), so the effective volume of the pool is (0.8x2500) or 2,000m3
    - 2,000m3/3.38x10^-6 m3 = 600 million jelly beans in a swimming pool
    - So **6 billion jelly beans would fill 10 Olympic swimming pools**! And that's how many nucleotides you have in a single cell!

- If you were to take all of the DNA in your body (~50 trillion cells) and line it up end-to-end, it would stretch from Earth to the Sun and back 300 times!
    - Alternatively, you could take all the DNA from your body and wrap it around the equator 2.5 million times! (http://www.nature.com/scitable/topicpage/dna-packaging-nucleosomes-and-chromatin-310)

Q14. How big is your ball of thread?
Answers vary

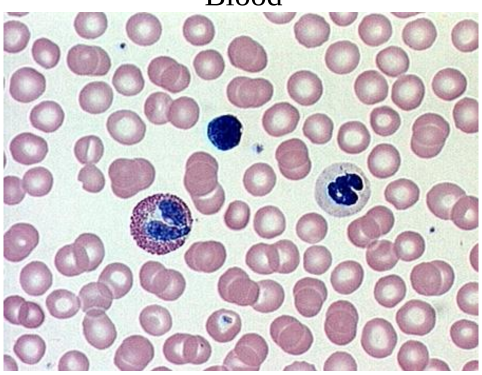
Q15. A cell nucleus is about 0.001cm wide. Were you able to get your ball of thread that small?
No

This packaging not only helps the DNA to fit into the nucleus, it also helps to control which parts of the DNA are **expressed**, or turned on. Think about it – a blood cell and a muscle cell look very different, and have very different jobs to do (see the pictures below), but they have the exact same DNA! This is because different pieces of the DNA, called **genes**, are turned on or off.

Q16. Genes are just pieces of the DNA that "make sense" to the cell. So, for example, if I gave you the following message, would you be able to identify the "gene" in it?

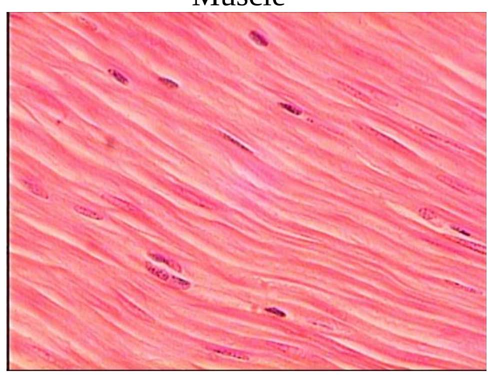
aeoigblerjoisdrjthispieceofdnaisneededforbrownhairplhseroipwahrpoihrs

Blood



http://lifesci.rutgers.edu/~babiarz/bloodtx.htm

Muscle



http://www.gwc.maricopa.edu/class/bio201/Histology/HistoRev22a.htm

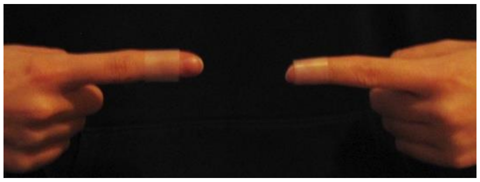
QSA17. Write whether you think each set of genes is "on" or "off" in the two different types of cells above.

	Blood Cell	**Muscle Cell**
Genes for making antibodies	*On*	*Off*
Genes for tight cell-cell connections (Look at the pictures for help!)	*Off*	*On*
Genes for making energy	*On*	*On*

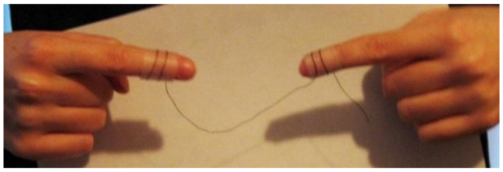
Just like you can use your ability to read to find the hidden message in the question above, genes are able to be recognized by proteins in the cell which know how to look for them! Once they find a gene, they bind to it and start to communicate that message to the rest of the cell ("Hey guys! We're supposed to be an eye cell! This gene says we have green eyes!"). In order for this to happen the gene needs to be **accessible**, or opened up and able to be bound. Let's see how that might happen.

2. Your teacher will give you two pieces of string with colored patches on them – let's say the first patch is a gene for hair color and the patch in the middle is a gene for eye color (see diagram). Lay out one piece flat on the table.

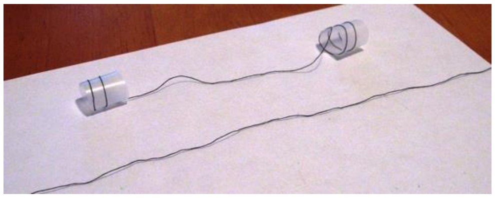
3. Have one person in your group slide a ring of tape (sticky side out!) on each pointer finger, and point the fingers at each other, a few inches apart.



4. Now have a partner take the second piece of string and wrap it 2 times around the tape ring on one finger **<u>making sure to wrap up the first (hair color) gene</u>**. Then take the other end and wrap it 2 times around the other finger **<u>making sure to keep the second (eye color) gene in the middle exposed</u>** in a loop of loose thread.



5. Carefully slide the two tape rings off, and lay the string next to the piece you already have laying on the table.



QS17, QSA18. If you were the cell, which form of DNA would you prefer, based on the concepts that we have discussed so far? List two reasons why your choice (wrapped or unwrapped) is better.

The wrapped one, because 1.) it is more compact; and 2.) it is easier to control accessibility

QS18, QSA19. Draw a diagram of the wrapped DNA and label which gene (represented by the colored patches) is likely turned on, and which is likely turned off.

The gene in the loose DNA between the two tape rings (ie "eye color") is likely on, since that area is accessible (ie the information is "readable). The wrapped areas are likely off as the information can't be read. Imagine trying to read a page of a book – would it be easier to read it when it's flat, or when it's wrapped around a pencil?

QS19, QSA20. Do you think every cell has the DNA wrapped the same way? Why or why not?

No, because different cells require different genes to be accessible, or turned on. In this example, this is what the DNA would look like in an eye cell – the "eye color" gene is exposed, while the "hair color" gene is hidden. An eye cell doesn't care about what color hair a person has – it's unnecessary information!

QSA21. If I took skin cells from two unrelated people and analyzed the DNA, would the sequence be the same? Would the packaging of the DNA be the same? Why or why not?

No, the sequence would be different, since each person's DNA sequence is unique. However, the packaging should be the same, since the organization of the DNA should be the same. Since the function of the skin cell is the same in both people, the same areas of the DNA should be accessed, even if the sequences in those areas are slightly different.

Concept Questions:

QS20,QSA22. Which of the following do you think contain DNA?
*Bananas _X_   Concrete ___   Meat _X_   Metal ___   Plastic ___   Wooden Table _X_*

What do the items you picked have in common?
They were all once alive

QS21,QSA23. The sequence of each person's DNA is different.   *True* / *False*

[Advanced] Can you think of any exceptions to this statement?
Identical twins have exactly the same DNA sequence

QS22,QSA24. Pair these letters with their complementary bases:

A A C T G G T A

T T G A C C A T

QS23,QSA25. DNA is compacted:

a. *To make it fit in the cell nucleus*
b. *To control which parts of the DNA are being used in different cells*
c. *To protect the DNA from damage (like being cut)*
d. *All of the above*

QS24. Imagine that dogs' eyes are normally blue, except when you have DNA that tells the eyes to make a brown color. If this "brown" DNA is mutated, what color eyes do you think that dog will have?
Answer 1 – blue, assuming that the mutation inactivates the "brown" gene
Answer 2 – green / yellow / purple (ie a completely different color) assuming the mutation doesn't inactivate the "brown" gene, but rather changes its function

QSA26. Antibiotics kill bacteria by getting into cells and inactivating specific, essential proteins. However, bacteria can become resistant to antibiotics through acquiring new mutations. Where do these mutations come from? What kinds of genes / proteins do you think are being mutated?
Normally antibiotics bind to specific proteins and make them non-functional. When these proteins don't work, the bacteria die. However, bacteria are always accumulating low levels of mutations naturally (partly because their DNA polymerase enzyme sometimes makes mistakes), and they sometimes acquire random mutations in these essential proteins. Most of the time, these mutations accidentally make the protein inactive and make the bacterium die even without any drug around. Very rarely, however, a bacterium gets lucky and randomly mutates the protein in a way that it still functions normally, but the antibiotic can no longer bind and inactivate it. Now this bacterium is resistant, and will replicate and divide while the other bacteria all die. Eventually the only bacteria that remain will be those that are resistant to the antibiotic.

Alternatively, a bacterium could also become antibiotic resistant by mutating and inactivating small channels or "pumps" on the cell surface. Normally these pumps take in nutrients or chemicals for the bacteria to use, but they also take in antibiotics. By shutting down these pumps, therefore, the bacterium becomes resistant to many different kinds of antibiotics, without having to mutate the individual targets of each drug.

QS25,QSA27. Cancer cells try to turn off genes that would normally prevent them from growing and dividing out of control. What are two ways that we learned about that you could "turn off" a gene?

You could mutate it or you could inappropriately compact that part of the DNA.