**http://biology.clc.uc.edu/courses/bio104/dna.htm**

**DNA Structure and Function**

|  |  |
| --- | --- |
| **DNA** stands for [**deoxyribonucleic acid**](javascript:WordStem('Deoxyribonucleic Acid (DNA)')). DNA is pretty unusual in that it is about the only common molecule capable of directing its own synthesis.  The processes of mitosis and meiosis were discovered in the 1870s and 1890s. It was observed that, as cells divided, chromosomes moved around in a cell, and people began to wonder what their function was. It was determined that chromosomes were made of protein and DNA, about which people knew almost nothing. People began to suspect that chromosomes had something to do with genetics, but couldn’t explain what/how. When enough evidence was accumulated to confirm that chromosomes did, indeed, have something to do with genetics, most people thought that in some way the protein in the chromosomes served as the genetic material. People knew that DNA was also in the chromosomes, but because its structure was unknown and people didn’t know much about it, few people thought it was the genetic material. | **Onion Root Tip Mitosis Mitosis in onion root tip** |

[[](javascript:DeadMouse%20=%201;%20Duckie('griffith%20js.htm'))](javascript:DeadMouse%20=%201;%20Duckie('griffith%20js.htm'))In 1928, **[Frederick Griffith](javascript:DeadMouse%20=%201;%20Duckie('griffith%20js.htm'))** performed an experiment using [**pneumonia**](javascript:WordStem('Pneumonia')) bacteria and mice. This was one of the first experiments that hinted that DNA was the genetic code material. Click on the “mouse button” to study his experiment. He used two strains of *Streptococcus pneumoniae*: a “**smooth**” strain which has a polysaccharide coating around it that makes it look smooth when viewed with a microscope, and a “**rough**” strain which doesn’t have the coating, thus looks rough under the microscope. When he injected live S strain into mice, the mice contracted pneumonia and died. When he injected live R strain, a strain which typically does not cause illness, into mice, as predicted they did not get sick, but lived. Thinking that perhaps the polysaccharide coating on the bacteria somehow caused the illness and knowing that polysaccharides are not affected by heat, Griffith then used heat to kill some of the S strain bacteria and injected those dead bacteria into mice. This failed to infect/kill the mice, indicating that the polysaccharide coating was not what caused the disease, but rather, something within the living cell. Since Griffith had used heat to kill the bacteria and heat denatures protein, he next hypothesized that perhaps some protein within the living cells, that was denatured by the heat, caused the disease. He then injected another group of mice with a mixture of heat-killed S and live R, and the mice died! When he did a necropsy on the dead mice, he isolated live S strain bacteria from the corpses. Griffith concluded that the live R strain bacteria must have absorbed genetic material from the dead S strain bacteria, and since heat denatures protein, the protein in the bacterial chromosomes was not the genetic material. This evidence pointed to DNA as being the genetic material. [**Transformation**](javascript:WordStem('Transformation')) is the process whereby one strain of a bacterium absorbs genetic material from another strain of bacteria and “turns into” the type of bacterium whose genetic material it absorbed. Because DNA was so poorly understood, scientists remained skeptical up through the 1940s.

[[](javascript:Ecoli%20=%201;%20Duckie('hershey-chase%20js.htm'))](javascript:Ecoli%20=%201;%20Duckie('hershey-chase%20js.htm'))In 1952, **[Alfred Hershey and Martha Chase](javascript:Ecoli%20=%201;%20Duckie('hershey-chase%20js.htm'))** did an experiment which is so significant, it has been nicknamed the “Hershey-Chase Experiment”. Click on the “virus button” to study their experiment. At that time, people knew that viruses were composed of DNA (or RNA) inside a protein coat/shell called a **capsid**. It was also known that viruses replicate by taking over the host cell’s metabolic functions to make more virus. We are used to thinking and talking about viruses which invade our bodies and make us sick, but there are other, different kinds of viruses that infect other kinds of animals, still other viruses which infect plants, and even some viruses that infect bacteria. A virus which infects a bacterium is called a [**bacteriophage**](javascript:WordStem('Bacteriophage')) because the host bacterium cell is killed as the new virus particles leave the bacterial cell. In order to do all this, the virus must inject whatever is the viral genetic code into the host cell. Thus, people realized that the viral genetic code material had to be either its DNA or its protein capsid. Hershey and Chase sought an answer to the question, “Is it the viral DNA or viral protein coat (capsid) that is the viral genetic code material which gets injected into a host bacterium cell? To try to answer this question, Hershey and Chase performed an experiment using a bacterium named [***Escherichia coli***](javascript:WordStem('%3cI%3eEscherichia coli%3c/I%3e')), or *E. coli* for short (named after a scientist whose last name was Escher) and a virus called T2 that is a [**bacteriophage**](javascript:WordStem('Bacteriophage')) that infects *E. coli*. Isolated T2, like other viruses, is just a crystal of DNA and protein, so it must live inside *E. coli* in order to make more virus like itself. When the new T2 viruses are ready to leave the host *E. coli* cell (and go infect others), they burst the *E. coli* cell open, killing it (hence the name “bacteriophage”). The results that Hershey and Chase obtained indicated that the viral DNA, not the protein, is its genetic code material.

Hershey and Chase used radioactive chemicals to distinguish between (“label”) the protein capsid and the DNA in T2 virus so they could tell which of those molecules entered the *E. coli* cells. Since some amino acids contain sulfur in their side chains, if T2 is grown in *E. coli* with a source of radioactive sulfur, the sulfur will be incorporated into the T2 protein coat making it radioactive. Since DNA has lots of [**phosphorus**](javascript:WordStem('Phosphorus')) in its phosphate (–PO4) groups, if T2 is grown in *E. coli* with a source of radioactive phosphorus, the phosphorus will be incorporated into the viral DNA, making that radioactive. Hershey and Chase grew two batches of T2 and *E. coli*: one with radioactive sulfur and one with radioactive phosphorus to get batches of T2 “labeled” with either radioactive S or radioactive P. Then, these radioactive T2 were placed in separate, new batches of *E. coli*, but were left there only 10 minutes. This was to give the T2 time to inject their genetic material into the bacteria, but not reproduce. In the next step, still in separate batches, the mixtures were agitated in a kitchen blender to knock loose any viral parts not inside the *E. coli* but perhaps stuck on the outer surface. Hopefully, this would differentiate between the protein and DNA portions of the virus. Then, each mixture was spun in a centrifuge to separate the heavy bacteria (with any viral parts that had gone into them) from the liquid solution they were in (including any viral parts that had not entered the bacteria). The centrifuge causes the heavier bacteria to be pulled to the bottom of the tube where they form a **pellet**, while the light-weight viral “left-overs” stay suspended in the liquid portion called the [**supernatant**](javascript:WordStem('Supernatant')). In the subsequent step, the pellet and supernatant from each tube were separated and tested for the presence of radioactivity. Radioactive sufur was found in the supernatant, indicating that the viral protein did not go into the bacteria. Radioactive phosphorus was found in the bacterial pellet, indicating that viral DNA did go into the bacteria.

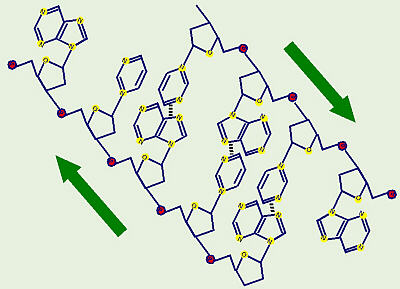
Based on these results, Hershey and Chase concluded that DNA must be the genetic code material, not protein as many poeple believed. When their experiment was published and people finally acknowledged that DNA was the genetic material, there was a lot of competition to be the first to discover its chemical structure.

What was known is that DNA contains a **nitrogenous base**. There are two kinds of these, which include:

|  |  |  |
| --- | --- | --- |
| **Pyrimidine (6-member ring of C & N)** |  | **Purine (that + 5 member ring of C & N)** |
| cytosine | guanine |
| thymine in DNA uracil in RNA | adenine |
| **Pyrimidine** | **Purine** |

|  |  |  |
| --- | --- | --- |
| **Nucleoside nucleoside** | Each nitrogenous base is connected to a molecule of ribose sugar (–1 oxygen in DNA) to form a **nucleoside** like the *adenosine* in ATP.  Each nucleoside is joined to a PO4 (phosphate group) to form a **nucleotide** like adenosine monophosphate (which can be turned into ATP by adding phosphate groups).  People also knew that nucleotides were somehow linked by dehydration synthesis to form DNA, but the exact structure/arrangement was unknown. | **Nucleotide nucleotide** |
|  | **Nucleotide deoxy nucleotide** |  |

In the early 1950s, Rosalind Franklin, an Englishwoman, was doing research which involved bouncing x-rays off crystals of various substances (a process which is called **x-ray crystallography**), including DNA, then exposing photographic film to the x-rays. She was studying the scatter patterns made by the x-rays bouncing off the crystals of various substances (Unfortunately, she died of cancer soon afterwards, or she might have been more famous). Other people like Linus Pauling were also attempting to figure out the structure of DNA.

James Watson, a young American scientist was in England working with Francis Crick, another young researcher. Someone else showed them Franklin’s photographs of DNA x-ray crystallography, and from her pictures, they were able to determine that the structure of DNA was organized into a double spiral or double helix. Based on Franklin’s data, in 1953, Watson and Crick published a paper in which they proposed and described an hypothetical structure for DNA. Subsequent research by many other people has since upheld their hypothesis, and based on subsequent examination of Franklin’s lab notes and calculations, she was probably within a couple days of coming to the same conclusion when their paper was published. For their discovery, Watson and Crick received the Nobel prize in 1962. In the intervening time, Rosalind Franklin had died in 1958 of ovarian cancer, probably due in large part to her work with x-rays. Since the Nobel prize is not awarded posthumously, people have often wondered if the Nobel committee would have included Franklin if she had still been alive.

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| **Double Helix Double Helix** | DNA is a double helix. The outer edges are formed of alternating ribose sugar molecules and phosphate groups. The two strands go in opposite directions (1 “up” and 1 “down”). The nitrogenous bases are “inside” like rungs on a ladder. Adenine on one side pairs with thymine (uracil in RNA) on the other by hydrogen bonding, and cytosine pairs with guanine. Note that the C-G pair has three hydrogen bonds while the A-T pair has only two, which keeps them from pairing wrong. This dictates side-to-side pairing, but says nothing about the order *along* the molecule. Watson and Crick said this variability along the molecule can account for the variety in the genetic code. Their model also accounts for how DNA can replicate itself. They said the molecule “unzips” and new matching bases are added in to create two new molecules. They called this **semiconservative replication** because each new molecule has one “old” and one “new” strand of DNA. | **DNA Replication DNA Replication** |

DNA codes for protein synthesis by first coding for RNA. First, the DNA code is [**transcribed**](javascript:WordStem('Transcription')) to RNA code, which is still in the “language” of nitrogenous bases, except that adenine on the DNA pairs with uracil (in place of thymine) on the RNA. The RNA code is then [**translated**](javascript:WordStem('Translation')) to protein code, which is a different “language.” This process involves ribosomes and two kinds of RNA: **mRNA** and **tRNA**. The mRNA codes for the gene in question and is copied off the DNA, while tRNA matches a specific group of nucleotides with a specific amino acid. A “unit” of three nucleotides on the tRNA codes for one amino acid. Each of these “units” is called an **anticodon**. These match up with corresponding three-nucleotide sequences on the mRNA called **codons**, and in this manner the amino acids are organized into the correct sequence to build a protein. The ribosome works with the mRNA and tRNA to hook the amino acids together to form a protein.

Here is a list of the mRNA codons and the corresponding amino acids for which they code.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | | **Second Base** | | | |  | |
| **U** | **C** | **A** | **G** |
| **F   i r s t  B a s e** | **U** | UUU  Phe | UCU  Ser | UAU  Tyr | UGU  Cys | **U** | **T   h i r d  B a s e** |
| UUC  Phe | UCC  Ser | UAC  Try | UGC  Cys | **C** |
| UUA  Leu | UCA  Ser | UAA  Stop | UGA  Stop | **A** |
| UUG  Leu | UCG  Ser | UAG  Stop | UGG  Trp | **G** |
| **C** | CUU  Leu | CCU  Pro | CAU  His | CGU  Arg | **U** |
| CUC  Leu | CCC  Pro | CAC  His | CGC  Arg | **C** |
| CUA  Leu | CCA  Pro | CAA  Gln | CGA  Arg | **A** |
| CUG  Leu | CCG  Pro | CAG  Gln | CGG  Arg | **G** |
| **A** | AUU  Ile | ACU  Thr | AAU  Asn | AGU  Ser | **U** |
| AUC  Ile | ACC  Thr | AAC  Asn | AGC  Ser | **C** |
| AUA  Ile | ACA  Thr | AAA  Lys | AGA  Arg | **A** |
| AUG  Met     or Start | ACG  Thr | AAG  Lys | AGG  Arg | **G** |
| **G** | GUU  Val | GCU  Ala | GAU  Asp | GGU  Gly | **U** |
| GUC  Val | GCC  Ala | GAC  Asp | GGC  Gly | **C** |
| GUA  Val | GCA  Ala | GAA  Glu | GGA  Gly | **A** |
| GUG  Val | GCG  Ala | GAG  Glu | GGG  Gly | **G** |

**Transcription and Translation Practice**

Here is a DNA gene for some fictitious protein. **Transcribe** the DNA code to RNA code, then **translate** the RNA code to an amino acid sequence. It is set up to only accept a 3-letter code, so use the codes “sta” for START and “sto” for stop.

Top of Form

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What would the RNA codons be?  


What would the amino acid sequence be? Remember to use codes “sta” for START and “sto” for stop.  


http://biology.clc.uc.edu/graphics/steincarter/moon/32x64.gifhttp://biology.clc.uc.edu/graphics/steincarter/moon/32x64.gif

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[**Mutations**](javascript:WordStem('Mutation')) can be caused by a change in the sequence of the nucleotides. Some mutations have more effect than others, depending on where in the code they are and how important that area is to the code. While mutations in some areas of some genes have little effect, sickle cell anemia is caused by a mutation in only one nucleotide. This changes the codon at that location to code for a different amino acid, and that, in turn, significantly changes the shape of the hemoglobin molecules in that person’s blood.

When some viruses (especially *Herpes* viruses, including Chicken Pox and Cold Sores) infect us, they insert their DNA into our cells’ DNA, and stay resident in our cells for the rest of our lives. These can potentially become active again either making a person sick again (like Shingles in a person who has had Chicken Pox) or just being shed from a person’s body (to infect others) without obvious symptoms of illness (like Mononucleosis). Some kinds of cancer may be caused this way. For example, there is some pretty strong evidence linking genital warts ([**human papillomavirus, HPV**](http://www.merck.com/pubs/mmanual/section13/chapter164/164l.htm)) and cervical cancer.

The AIDS virus does things “backwards.” This virus contains RNA rather than DNA, yet when it gets into someone’s cells, it can do **reverse transcription** and code from its RNA to make DNA which, then, can code to make more virus.

**Genetic Engineering — Is It Good or Bad?**

We now have the knowledge and ability to transfer genes from one organism to another, which seems to have some benefits associated with it, but may also have many yet-to-be-discovered problems associated with it. Because this is all so new, not enough time has elapsed to allow scientists to study/look for any possible long-term effects of genetically-modified organisms (**GMOs**).

* Many medicines are now made by GMOs. For example, insulin was formerly extracted from the pancreas of animals after they were slaughtered for meat. However, now most insulin is produced by bacteria with the insulin gene spliced onto their chromosome. Using this method of production, drug companies can make more insulin, faster. In theory, insulin produced in this way should be more “pure” — someone who could not use pig insulin due to a pork allergy may be able to tolerate insulin made in this way (but someone could, potentially, be allergic to some component of the bacteria present in the refined insulin). In the relatively short time that this form of insulin has been available, there is no doubt that it has saved many people’s lives — let’s hope that some unforseen, long-term, deleterious effects are not discovered later on.
* Experimentation is being done to investigate the possible use of genetically-engineered viruses to treat genetic diseases such as cystic fibrosis. In this “treatment,” a kind of virus that infects our lungs is used. The genes that enable it to infect our cells are kept while the genes which make us sick are (hopefully) all removed, and the missing human (normal) gene that relieves cystic fibrosis is then inserted into the virus’ genome. These viruses are then sprayed into the lungs of a person with CF and allowed to “infect” the cells in that person’s lungs. When the normal gene is inserted into the genetic make-up of the cells lining that person’s lungs, those cells function normally and the CF symptoms are alleviated. However, this treatment doesn’t last because only that layer of cells is “infected,” and when those cells die and are replaced by new cells, the new cells do not contain the genetic code to overcome the CF gene, and the person must inhale more genetically-engineered virus. While this seems to be a promising, life-giving, technique, no data are yet available on long-term effects and safety.
* *Bacillus thuringiensis* (BT) is a species of bacterium that infects and kills a number of species of caterpillars (Remember that caterpillars turn into butterflies or moths when they grow up.). There is a species of moth whose caterpillar is a “pest” in corn plants, and insects of any kind are more successful when we humans plant huge **monocultures** of their favorite foods. For a number of years, now, people have realized that in certain situations, by judiciously applying BT, “pest” species of caterpillars can be infected and killed without the use of man-made, chemical insecticides. More recently, a major US chemical company came up with the idea of creating genetically-engineered corn containing BT genes, which was good news to agri-business firms who plant huge areas of land with monocultures of corn. Because corn is wind-pollinated and therefore makes lots of pollen which, in this case, contains BT genes, many scientists are concerned about the effects of this corn on local butterfly populations. Some research has indicated that when this pollen settles on nearby caterpillar host plants and is, therefore, consumed by caterpillars, this might cause an increase in mortality (therefore fewer “good” butterflies such as Monarchs). It is assumed that these BT genes in corn should, they think, have no adverse effects on people or cattle who consume this corn, but no long-term testing has been done. Also, this company has convinced the government that this corn should be marketed without any labeling indicating that it is genetically-engineered — they’re scared that if you are given a choice, you won’t buy/eat their corn if you know it is genetically engineered. Additionally, to increase their profits, this company has also put “suicide” genes into this corn so that farmers cannot save seed from one year to plant the next year, and have to buy more seed from them, instead. For big agri-businesses, this is of small consequence, but for small, family farmers this is total disaster. To save money, the latter often save seed from one year to plant the next, and even if they don’t plant this genetically-engineered corn, if their corn is pollinated by genetically-engineered corn from a neighboring field, it will not produce viable seed.
* This same chemical company came up with the idea of “transplanting” what they think is the cold-tolerance gene from a species of cold-water-inhabiting fish into tomatoes, thereby hoping to “invent” cold-tolerant tomatoes, and again, has convinced the government that these tomatoes should not be labeled in any way to indicate that they have fish genes in them, and that you should not have a choice about what you eat. At the very least, this would be a problem for someone who is a vegetarian and chooses to not eat fish. A more serious consequence, however, would be that a person who is severely allergic to fish could also have an allergic reaction to these tomatoes and end up in the hospital (or worse. . .). Again, no tests were done before the government approved these tomatoes and no data are available on the long-term effects on humans (or anything else).
* This same chemical company manufactures a widely-used herbicide, and came up with the idea to genetically engineer cotton, soybeans, and other crop plants so they would be immune to the effects of that herbicide. That way, farmers can (have to?) buy their seed from that company, then spray their fields with herbicide also purchased from that company to (hopefully) kill all local plants except the immune crop, simultaneously putting all their money in the corporation’s pockets. Preliminary research has shown that these resistant genes have already begun to “jump” into local weeds, thereby making them resistant to that herbicide, and again, no data are available on long-term effects on humans, other animals, or the environment in general.
* Interestingly, while this corporation has convinced the US government that their GMOs are “safe” to sell, plant, and consume and that consumers should not be allowed to know what they’re eating, the same is not true elsewhere. From what I’ve heard, in many other countries around the world, it is illegal to purchase and plant this company’s seed, and in many places, foods containing GMOs must be labeled as such.

For more information on genetically-modified foods, see [**Dr. Fankhauser’s Web page on that topic**](http://biology.clc.uc.edu/fankhauser/Society/Gen_Engnrg7Oct99.html).

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**There is a large number of Web pages with information relating to the Watson-Crick-Franklin-Wilkins story. Here is a small sample of the many that were found via a search:**

* [**http://news.bbc.co.uk/2/hi/science/nature/2895681.stm**](http://news.bbc.co.uk/2/hi/science/nature/2895681.stm)
* [**http://www.nature.com/nature/dna50/index.html**](http://www.nature.com/nature/dna50/index.html)
* [**http://www.kcl.ac.uk/dna/scientists/franklin.html**](http://www.kcl.ac.uk/dna/scientists/franklin.html)
* [**http://www.americanfieldguide.com/wgbh/evolution/library/06/3/image\_pop/l\_063\_01.html**](http://www.americanfieldguide.com/wgbh/evolution/library/06/3/image_pop/l_063_01.html)
* [**http://www.phschool.com/science/science\_news/articles/happy\_anniv.html**](http://www.phschool.com/science/science_news/articles/happy_anniv.html)
* [**http://news.bbc.co.uk/onthisday/hi/dates/stories/april/25/newsid\_2932000/2932793.stm**](http://news.bbc.co.uk/onthisday/hi/dates/stories/april/25/newsid_2932000/2932793.stm)
* [**http://osulibrary.orst.edu/specialcollections/coll/pauling/dna/pictures/franklin-typeBphoto.html**](http://osulibrary.orst.edu/specialcollections/coll/pauling/dna/pictures/franklin-typeBphoto.html)
* [**http://www.ba-education.demon.co.uk/for/science/dnamain.html**](http://www.ba-education.demon.co.uk/for/science/dnamain.html)
* [**http://www.strangescience.net/rfranklin.htm**](http://www.strangescience.net/rfranklin.htm)