BIOL 300 – Foundations of Biology
Summer 2017 – Telleen
Lecture Outline

DNA: Life's Information Molecule
I. The importance of an information molecule

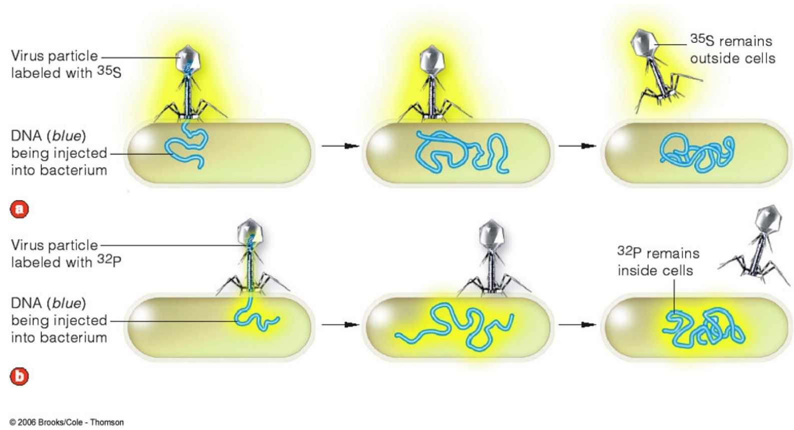
A. Biologists first began to search for a replicable and transmittable information molecule in the early 1900s
B. Each life form clearly passes on specific information to its descendents
C. Clues to the biochemical nature of this information molecule came from several lines of evidence:
    1. Gregor Mendel's discovery of the laws governing the transmission of inherited traits from one generation to the next (1850s-60s)
    2. Detailed descriptions of the behavior of chromosomes (late 1800s)
    3. Studies that inventoried the biochemical contents of nuclei of complex cells
D. From these discoveries, biologists deduced that the information molecule must be closely associated with chromosomes
E. Logic told them that it must have the following characteristics:
    1. It must contain, in a stable form, all the information for an organism's cell structure, function, development, and reproduction. In particular, it must specify how and when to make proteins, which are the work horses of the cell
    2. It must be able to replicate accurately so that all progeny cells will contain the same genetic information as the parent cell
    3. It must be capable of variation. Without variation there would have been nothing for natural selection to work upon and evolution would not have happened

II. Early guesses about the information molecule

A. The science of biochemistry was much more advanced than molecular biology in the early 1900s
    1. Biochemists study all biomolecules, but focus mostly on proteins because they are the most ubiquitous structural molecules in cells and they catalyze most cellular reactions. They are abundant and easily purified while having rich and complex chemistries
    2. Biochemists assumed that the information molecule must be some type of protein
B. At the time, much less was known about DNA (deoxyribonucleic acid), a homogenous and chemically inert molecule that co-purifies with protein when chromosomes are extracted from nuclei
    1. Unlike proteins, all DNA molecules have the same 3-D conformation (long thin rods) and are negatively charged
    2. It was difficult to get DNA to react with anything except strong acids, and few biochemists paid attention until several seminal experiments

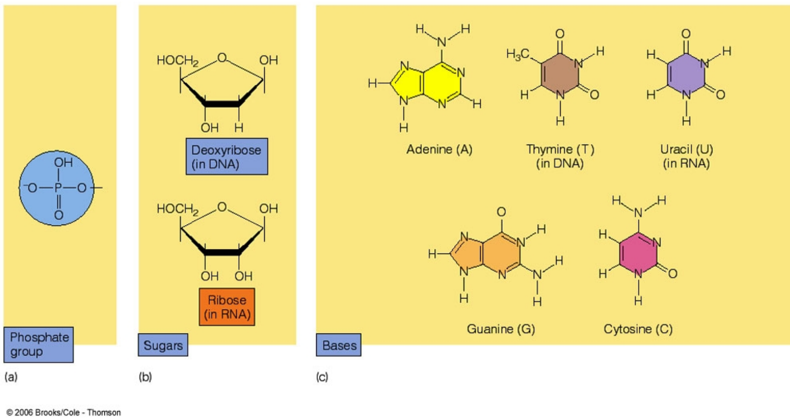
were conducted between 1928 and 1952 that showed that DNA is the information molecule

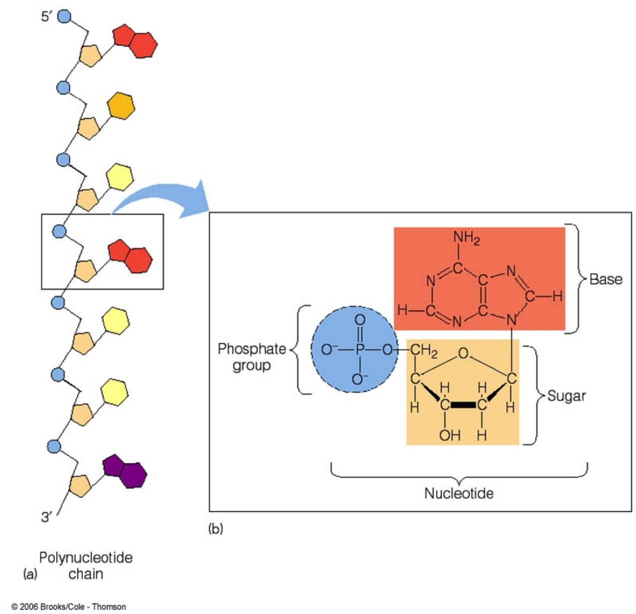
3. Experiments showing DNA is the information molecule:
    a. Frederick Griffith leading to experiments by the Rockefeller Institute (pneumonia causing effect carried on DNA)
    b. Alfred Hershey and Martha Chase (Phage DNA is responsible for replication in bacteria, not protein)



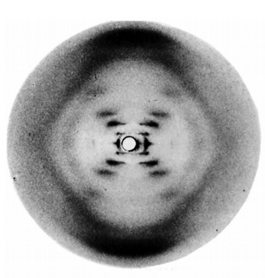
C. DNA Chemistry
1. As evidence mounted that DNA is the genetic material during the late 1940s and 1950s, the race was on to solve the molecular structure of the DNA molecule
    a. It was assumed that the structure would reveal the "secret of life"
2. James Watson and Francis Crick solved the structure in 1953 and were awarded the Nobel Prize
    a. In building their molecular model of DNA, Watson and Crick didn't actually perform any experiments, but instead successfully put together three lines of experimental evidence produced by others
    b. They also had to make sure their model incorporated and explained all of the known experimental evidence that had been gathered about DNA
3. Lines of Evidence:
    a. DNA is made up of chains of subunits called nucleotides
        1. The basic structure of an individual nucleotide is one nitrogenous base (adenine (A), guanine (G), cytosine (C), or thymine (T)) linked to a single five carbon sugar (in this case deoxyribose) that is in turn linked to a single phosphate group.
        2. The sugar is called deoxyribose because the 2' carbon carries a hydrogen (-H) instead of a hydroxyl (-OH). In RNA, which we'll discuss later, the hydroxyl group is present and the sugar is called ribose.

3. Nucleotides are then linked together, with each phosphate being linked to the sugar of the next nucleotide. A strand of DNA is negatively charged because of the phosphates in the backbone



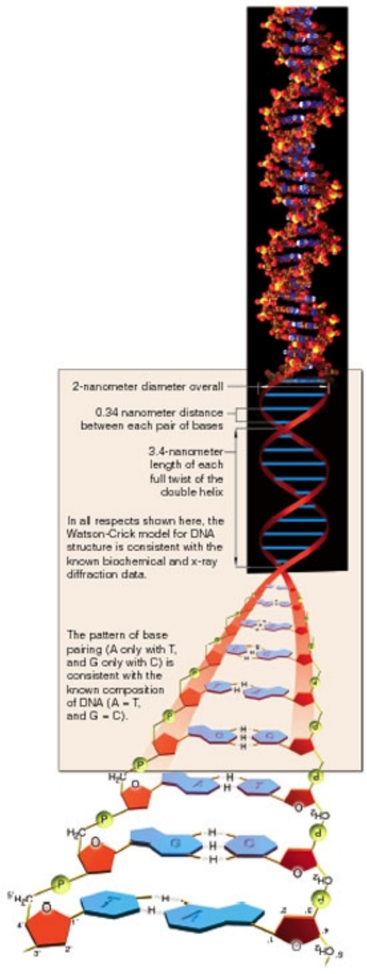


b. The amount of A always equals the amount of T and the amount of C always equals the amount of G
   1. Erwin Chargaff chemically analyzed DNA from a number of different organisms
   2. He quantified the nucleotides and always found adenine and thymine in equal amounts and cytosine and guanine in equal amounts
   3. These results came to be known as Chargaff's Rules, although no one had been able to explain them
c. DNA is a highly ordered, helical structure
   1. This information came from X-ray diffraction photographs taken by Rosalind Franklin
   2. Franklin's photos became one of the basic criteria by which Watson and Crick ultimately evaluated most of their early models
   3. Franklin died of cancer at the age of 38, before she could share in the Nobel Prize



Rosalind Franklin.
Franklin's photographs (left) of DNA were instrumental to Watson and Crick in building their models.

D. The Molecular Structure of DNA

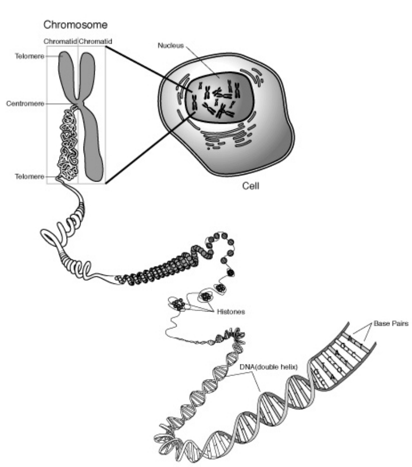


1. Watson and Crick were unsure of some of the specifics of the chemistry involved, but made excellent informed guesses. Their model, now called the Double Helical or Watson-Crick Model of DNA, has the following features:
   a. As predicted by Franklin, the DNA molecule consists of two nucleotide chains wound around each other in a double helix
   b. The two chains are anti-parallel. The strands show opposite polarity: The two strands are oriented in opposite directions with one strand oriented 5’ to 3’ (with respect to the numbering of the carbons in the sugar) while the other chain runs 3’ to 5’
   c. The sugar-phosphate backbones of the two strands are on the outside of the DNA molecule, while the bases face each other on the inside
   d. The bases of the two strands are bonded together by relatively weak hydrogen bonds
   e. A bonds only with T and G bonds only with C. This is due to spatial considerations based on the size and shape of the bases and locations of the atoms within them. This aspect explains Chargaff’s Rule
   f. The weakness of the hydrogen bonds makes it possible for the strands to come apart under certain conditions
   g. The specific A-T and C-G base pairs are called complementary base pairs, and the nucleotide sequence of one strand dictates what the sequence on the other strand will be.

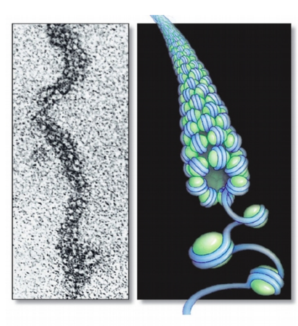
      For example: 5’ – TATTCCGA – 3’ the other strand must be:
      3’ – ATAAGGCT –5’

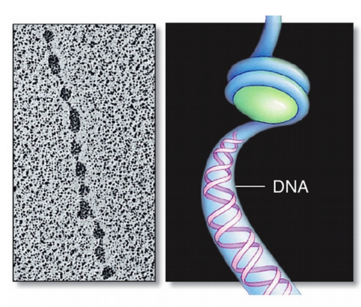
E. Chromosomes are complexes of DNA and Proteins

1. DNA is wound around proteins called histones.
2. The resulting “string of beads” is then wound up into an thread, which is also wound up, and so on, until you get the final chromosome structure



http://www.accessexcellence.org/AB/GG/chromosome.html


(c) At a deeper level of structural organization, the chromosomal proteins and DNA are organized as a cylindrical fiber.



(d) Immerse a chromosome in saltwater and it loosens up to a beads-on-a-string organization. The “string” is one DNA molecule. Each “bead” is a nucleosome.

F. How DNA holds information

1. In retrospect, it is not at all surprising that the molecule that carries genetic material is highly stable and inert since it is the master copy of all the information necessary for a cell's growth, reproduction, and function.
2. DNA carries information by way of its nucleotide sequence, which spells out the code for various proteins that perform most of the dynamic processes in the cell.
3. Each protein needed by the cell is encoded by a DNA sequence called a gene, and the overall length and sequence of a gene defines the amino acid sequence and length of a polypeptide (protein) for which is codes
4. Because DNA is a nucleic acid with very different chemistry than a polypeptide, it must be decoded.
5. During this process, a single stranded messenger RNA (mRNA) is made which copies one strand of the DNA. This is called transcription
6. mRNA is then "read" by a protein/RNA complex called a ribosome which translates the nucleic acid code into protein.

G. The Central Dogma of Molecular Genetics

1. States that the information flow of genetic information starts in DNA, which is transcribed into RNA, which is translated into Protein, which carries out the biochemical functions necessary to maintain life.
2. While this is generally true, there are some exceptions: Notably that RNA can be converted back to DNA in some instances. RNA can also regulate the processes of transcription and translation.

H. Mutations in DNA

1. A change in the sequence of a gene (a mutation) can change the protein sequence coded by the gene
2. Most often, this disrupts the protein, but it can also cause a change in function of the protein

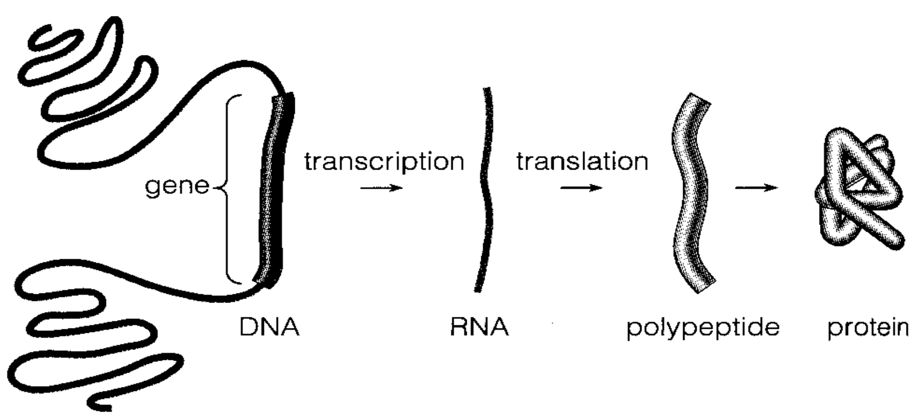


Figure 3.1 The central dogma of molecular genetics.