DNA, the molecule of heredity

“DNA neither cares nor knows. DNA just is. And we dance to its music.”

- Richard Dawkins

River Out of Eden: A Darwinian View of Life (1995), 133
Principles of Biology

• Chapter ‘Mendel's Principles’ (overview only)
• Chapter ‘Chromosome Theory’ (http://www.nature.com/scitable/topicpage/developing-the-chromosome-theory-164)
• Chapter ‘DNA’
• Chapter ‘Nucleic Acids’
Objectives

• Describe the research that led to the identification of DNA as the carrier of genetic information.

• Explain the contributions of Watson, Crick, Wilkins and Franklin in the discovery of the structure of the DNA molecule

• **Key Terms**: adenine, antiparallel, bacteriophage, Chargaffs rule, chromosome, cytosine, deoxyribonucleic acid (DNA), double helix, gene, guanine, nitrogenous base, nucleotide, purine, pyrimidine, radioactive isotope, sugar-phosphate backbone, thymine, transformation, transforming principle
Biological information

Biological (genetic) information must serve two functions

• Direct the expression of proteins (as proteins mediate the structure and function of cells).

• Be passed on to subsequent generations
Evolution through natural selection

• Darwin proposed a **process for change (evolution)**, but not a physical mechanism.

• How does **heredity** operate?

Darwin could not explain mechanism of inheritance.

Mendel was an experimentalist who examined the scientific basis of inheritance using plant breeding models.

Mendel (seated, left) was born to Austrian farmers. He was educated in Mathematics and Physics. He became an Augustinian monk (and later, the abbot) of a monastery in Brno (Czech Republic).
Mendel concluded that traits are encoded by ‘heritable factors’.

- Heritable factors are passed on to the next generation in defined ratios.
- Factors may be dominant, recessive or co-dominant.
- The heritable factors were later called genes.
Friedrich Meischor discovers DNA

- DNA is insoluble in alkalis and is found in the nuclei of cells
- DNA containing carbon, hydrogen, oxygen, nitrogen and phosphorus, but not sulphur.
- He called DNA – nuclein.

Chromosomes, sex and genes

“… the association of paternal and maternal chromosomes in pairs and their subsequent separation … may constitute the physical basis of the Mendelian law of heredity.” - Sutton

W. Flemming

T. Boveri

W. Sutton, C. E. McClug, N. Stevens

T. H. Morgan

Discovers mitosis and chromosomes in nuclei

Nucleus is important for fertilisation

Sex is determined by chromosomes

Genes depend on sex, hence genes are carried on chromosomes
Total of 4 pairs of chromosomes. Female flies have two similar X chromosomes; males have an X and a Y chromosome.
The Griffiths experiment

Frederick Griffith’s experiment described a “**transforming principle**” that can change nonvirulent R strain bacteria into virulent S strain bacteria.
The information that determines a bacteria’s strain and virulence must be encoded in a \textit{nonliving chemical}, as this information can be \textit{transferred from dead to living bacteria}.

Griffiths’ Conclusion
Avery's Bioassays

Let's take a closer look at Avery's experiment. The first step in Avery's bioassay involved killing the bacteria and breaking open the cell contents by homogenization.

S strain (virulent) is heat-killed → Homogenous S strain cell contents

To begin: Examine the first step in the experiment, then click the Next button to continue.
The Hershey-Chase experiment used bacteriophage viruses (phages) to show that DNA, not protein, was the essential component for transfer of genetic information.
In two separate experiments, either the DNA core or the protein coat of phage was radioactively labeled.

The labeled phages were used to infect bacteria, and the infected cells were then separated by centrifugation.

The pellet contained the cell contents, while the supernatant contained phage particles that did not enter the cell.

Only radioactively labeled DNA was found in the pellet, indicating that DNA entered the cell.
• The structure of DNA deduced from X-ray crystallography = scatter pattern of X-rays passing through a crystal of DNA molecules

• X-ray crystallography reveals repeating patterns in DNA with dimensions of: 0.34 nm, 3.4 nm and 2.0 nm

▲ Figure 16.6 Rosalind Franklin and her X-ray diffraction photo of DNA. Franklin, a very accomplished X-ray crystallographer, conducted critical experiments resulting in the photograph that allowed Watson and Crick to deduce the double-helical structure of DNA. Franklin died of cancer in 1958, when she was only 38. Her colleague Maurice Wilkins received the Nobel Prize in 1962 along with Watson and Crick.
On this spot, on February 28, 1953, Francis Crick and James Watson made the first public announcement of the discovery of DNA with the words “We have discovered the secret of life”. Throughout their early partnership Watson & Crick dined in this room on six days every week.
DNA, the thread of life

“It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.”

- Watson and Crick

Nature, 171, 737-8

The Nobel Prize in Physiology or Medicine 1962 was awarded jointly to Francis Harry Compton Crick, James Dewey Watson and Maurice Hugh Frederick Wilkins "for their discoveries concerning the molecular structure of nucleic acids and its significance for information transfer in living material".
Nucleic acids

One of four classes of large biological molecules essential to cellular structure and function

1. Nucleic acids: include both DNA & RNA
2. Carbohydrates
3. Lipids
4. Proteins
Nucleic acids

Polymers consist of multiple repeating subcomponents.

**Nucleotides**: repeating subcomponents that exist in a variety of forms rather than repeated monomer subcomponents.

**Polynucleotides**: polymers consisting of multiple nucleotides.
Three main components of nucleotides

- Phosphate
- Sugar
- Nitrogenous base

Phosphate unit links nucleotides together in the polynucleotide chain.

Sugar connects phosphate backbone with base.

Nitrogenous base structure identifies nucleotides as guanine, thymine, adenine, cytosine or uracil.
Pyrimidine and purine

Nucleotides found in DNA and RNA have one of two basic structures that determine which nucleotide it can bind to.

- **Pyrimidine**: four-carbon ring connected by nitrogen atoms at the 1 and 3 position.

- **Purine**: pyrimidine ring connected to an imidazole ring; the overall structure is a double ring.
Nucleotides and bases

• **Nucleotides** are the individual units of DNA.

• A DNA nucleotide is composed of a nitrogenous **base**, the sugar **deoxyribose**, and one or more phosphate groups.

• The four bases in DNA are **adenine**, **thymine**, **cytosine**, and **guanine**. Adenine and guanine are **purines**, and cytosine and thymine are **pyrimidines**.

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A-T and G-C are called complementary base pairs

Erwin Chargaff: in all organisms, their DNA is composed of equal proportions of A/T and C/G. "That...such giant shadows are cast by such pygmies only shows how late in the day it has become".
Other structural characteristics of DNA

Two polynucleotide strands with sugar-phosphate backbones linked by purine-pyrimidine pairs.
Each strand has directionality

That is, the 5’ to 3’ direction of one strand is opposite to the complementary strand, oriented in a 3’ to 5’ direction.

**Antiparallel**: two complementary strands running in opposite directions.
RNA

• Can form a double helix.
• Complementary base pairing occurs along different portions than DNA.
• **Hairpin**: secondary structure formed by a stem-loop.
RNA

• Multiple roles vary depending on RNA type: mRNA, tRNA, rRNA.
• Each form specialized to its function.
• Without RNA, cell would have no way to make proteins, which serve as enzymes, structural components and membrane components.
• Without DNA, RNA would have no information with which to produce these important cellular components.
By now, you should be able to:

• Describe Mendel's contribution to our understanding of the rules of heredity.
• Describe the two landmark experiments that led to the conclusion that DNA was the molecule of heredity (transforming principle; Harvey-Chase experiment).
• Explain the role of Chargaff’s rule, X-ray crystallography and model building in elucidating the structure of DNA.
• Describe the structure of DNA as a polymer of nucleotides, in terms of the base-pairing rules.
• Explain how the double helical structure of DNA satisfies the 3 X-ray crystallographic measurements: 2.0 nm, 0.34 nm and 3.4 nm.