

Lecture 2 (FW)

January 26, 2009

DNA is a double helix. Replication. Mitosis

Reading assignment: DNA structure and replication, pp. 81-104.

Cell structure review, pp. 19-26. Mitosis, pp. 31-36.

Lecture 2. **DNA is a double helix of polynucleotides.**

Primary goal: The structure of DNA and how it was discovered. Why is this important? It is the key to understanding the functions of a gene: heredity and governance of the cell.

I. The conundrum

A. DNA seemed too simple to encode information carried by genes. DNA is a polymer of nucleotides, of which there are only 4 kinds, A, G, T and C. Yet, the bacterial transformation, and other kinds of experiments, clearly pointed to DNA.

B. The most complex type of molecule in cells is protein, composed of 20 different kinds of amino acids (monomer) strung together in a polymer (protein or polypeptide).

C. Polymers are molecules in which similar repeating units (monomers) are strung together , held by chemical bonds, like beads on a string. Plastics (acrylamides) and fibers (nylon) are polymers. So are proteins and nucleic acids. There are also polymers of sugar monomers found in cells, called polysaccharides.

II. Would an understanding of the 3D structure of DNA provide a clue about how it could encode and transmit genetic information? The answer to that question, published in 1953, astonished the scientific community, and is the bedrock to the “new biology”.

A. The players:

Jim Watson, A new Ph.D. from Indiana University, who went to Cambridge England (via Copenhagen) on a post-doctoral fellowship. Interested in inheritance, especially in viruses.

Francis Crick, Still grinding away getting a Ph.D. in Cambridge, England, working on the structure of proteins using X-ray crystallography.

Maurice Wilkins. A physical chemist in London interested in protein and DNA structure.

Rosalind Franklin. A Ph.D. research associate of Wilkins who perfected methods for looking at DNA with X-rays.

Linus Pauling. The world’s most celebrated chemist, at Cal Tech, who had made a breakthrough in analysis of protein structure using X- Ray crystallography and model building.

Erwin Chargaff. A biochemist working in New York who analyzed the composition of monomers (A,G, T & C) in different DNAs.

B. The search: what lay behind it?

1. A belief that structure of DNA was the key to understanding how it worked.

2. A belief that model building of DNA was the route to understanding structure; Crick's theory of diffraction of helices; Franklin's X-ray analysis.

3. Model building: placement of the strings and the dangles. What goes outside, what goes inside, and how many strands are there.. The hydrogen bonding of the nucleotide monomers to one another. Chargaff's rule: A=T; G=C.

C. The structure. A double stranded helix of DNA polynucleotides, with nucleotides on the inside, held together by AT and GC hydrogen bonds.

1. The structure is redundant. Once you know the sequence in one strand, you have specified the order in the other. The strands are complementary. They also "run" in opposite directions.

III. Replication.

A. . The proposed structure shows how DNA might be faithfully passed on from parent to daughter cell. Each daughter cell gets one strand of DNA, and the complementary strand is assembled on the template of the parent strand.

B. Replication involves: 1) strand separation 2) initiation of synthesis of a complementary strand on each of the separated parent strands 3) Unwinding 4) Separation of the two new double strands.

C. The double stranded DNA is associated with various proteins. This DNA-protein combination is called chromatin, or chromosomes during actual cell division.

D. Verify how the two strands of DNA are passed on after replication. Draw old and newly synthesized strands and follow them to the next generation.

IV. Mitosis

A. The physical distribution of the genetic material occurs during cell division, called mitosis.

B. Cell division can be divided into several phases. First, there is the actual distribution of the chromosomes, called mitosis. After mitosis there is a phase of growth, called G-1. Then the DNA is replicated, in a phase called S. The chromosomes, located in the nucleus, are not visible during this phase, and are called chromatin. Nevertheless, this is the time when DNA replication occurs. Then there is a pause after S, called G-2, followed by another round of mitosis.

C. Mitosis involves a change in chromatin so that it becomes compact and is called a chromosome. There is also the formation of a mechanical structure composed of microtubules, called the "spindle" or "mitotic apparatus". The tubules attach to the chromosomes and pull the two daughter chromosomes in opposite directions.

D. As a result of mitosis, each daughter cell has a new copy of each chromosome, with its double stranded DNA.

V. Some questions:

1. How could this hypothesis of complementary strands giving rise to a conservative inheritance of DNA be proved? Or disproved

2. Could single stranded DNA (or RNA) also act as a gene? Retroviruses?

3. Could any substance other than DNA or RNA act as an hereditary agent? Prions

4. Chemotherapy for treatment of cancer depends on knowing how DNA replicates. How does chemotherapy work?

Concepts to know: DNA is a double stranded helix composed of hydrogen-bonded, complementary pairs of nucleotides.

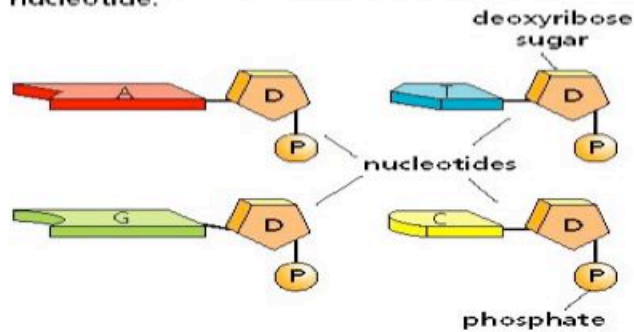
Terms to know: Nucleotide, monomer, polymer, helix, A,T,G,C, mitosis, chromatin, chromosome

Next reading assignment: Recombinant DNA, 240-245; 286-287; 330
PCR, 270-274; 329

(A) Two of DNA's nitrogenous bases, adenine (A) and guanine (G), are larger than the other two, thymine (T) and cytosine (C).

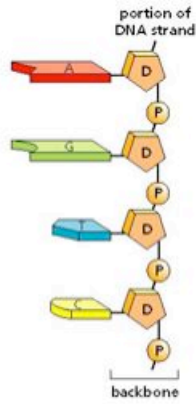


(B) With the addition of deoxyribose (a five-sided sugar molecule) and a phosphate group, each of these nitrogenous bases forms a nucleotide.

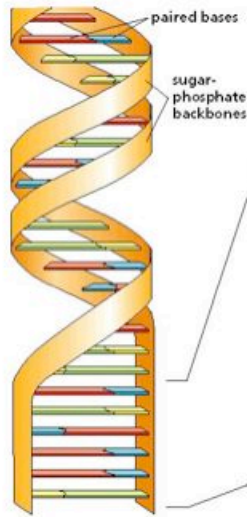


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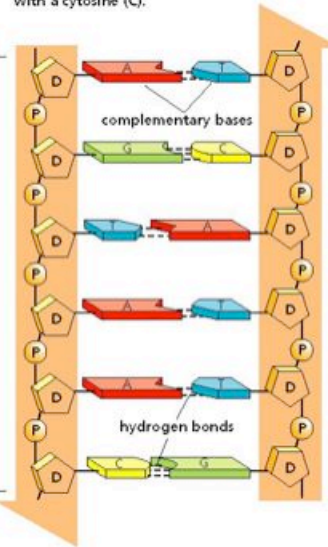
(A) Thousands of nucleotides are strung together by a phosphate-sugar backbone.



(B) Two strands of DNA twist around one another to form a double helix. A straightened portion of this double helix resembles a ladder with the paired (complementary) bases forming the rungs.



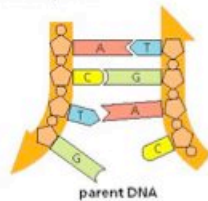
(C) Two nucleotide sequences running in opposite directions pair with one another, with each adenine (A) pairing with one thymine (T), and each guanine (G) pairing with one cytosine (C).



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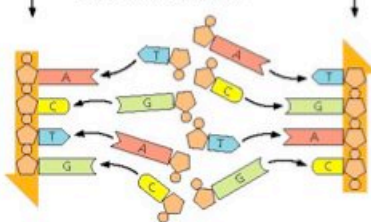
(A) UNWINDING

The two strands of the DNA double helix separate.



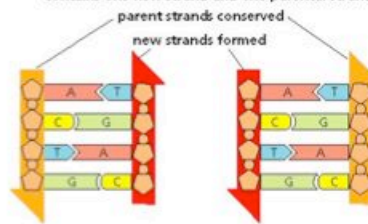
(B) PAIRING

New nucleotides pair with their complementary nucleotides exposed on each strand.



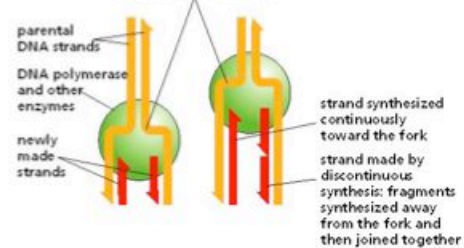
(C) JOINING

Each new row of bases is linked into a continuous strand by joining adjacent sugars and phosphates. Each double helix contains one new strand and one parental strand.

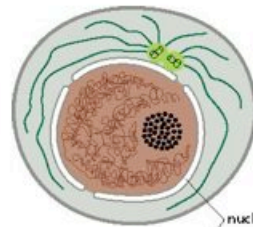


(D) THE REPLICATION FORK

early step
later step
replication fork moves

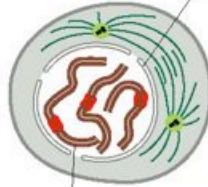


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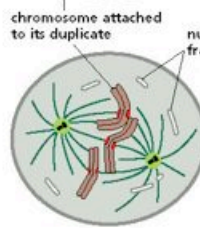
INTERPHASE

The cell increases in size and the chromosomes are duplicated to twice the diploid number, although they are not visible in the nucleus at this stage.



PROPHASE

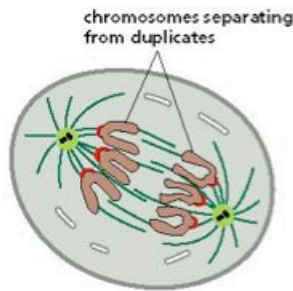
The chromosomes condense and shorten, becoming visible under a microscope as attached pairs.



METAPHASE

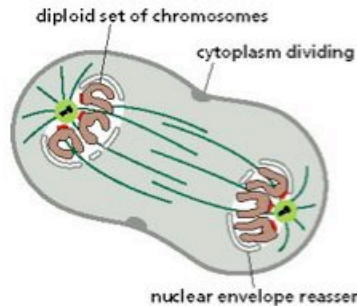
The membrane surrounding the nucleus breaks down; each chromosome and its attached duplicate line up along the midline of the cell.

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ANAPHASE

Each chromosome separates from its duplicate; the chromosome and its duplicate move toward opposite ends of the cell.



TELOPHASE

A complete diploid set of chromosomes arrives at each end of the cell, a nuclear membrane reassembles around each set, forming two nuclei, and the cell begins to separate in half.

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