MCB 150

The Molecular and Cellular Basis of Life

The Central Dogma and The Structure of DNA

Today's Learning Catalytics Session ID is:
10012002

Handouts will be good for 3 (or 4?) lectures

- DNA encodes the genetic information that directs the cell how to make proteins and RNAs.
- Information carried in our genes does not pass directly from DNA to proteins.
- Instead, the information carried in the nucleotide sequence of our genes is first copied into an RNA intermediate (**transcription**).
- The nucleotide sequence information in the RNA is then used to build proteins (**translation**).
- The flow of genetic information from DNA to RNA to Protein is referred to as the Central Dogma of Molecular Biology.

Discovering the **function** of DNA:

- By 1940s, hereditary material known to reside on one or more chromosomes
- Chromosomes are composed of chromatin, which is a complex of DNA and protein.
- We knew proteins were made of 20 amino acids, and DNA was made of 4 nucleotides.
- So… seemed logical that protein is genetic material because of diversity needed, *but found to be DNA*
- Next step: Deduce 3D structure of DNA, then figure out how it is copied and turned into protein.

Discovering the **structure** of DNA:

- Chargaff's Rules (1949)
  - amount of each dNTP varies between organisms, but
  - [dA] = [dT] and [dC] = [dG] in ALL organisms

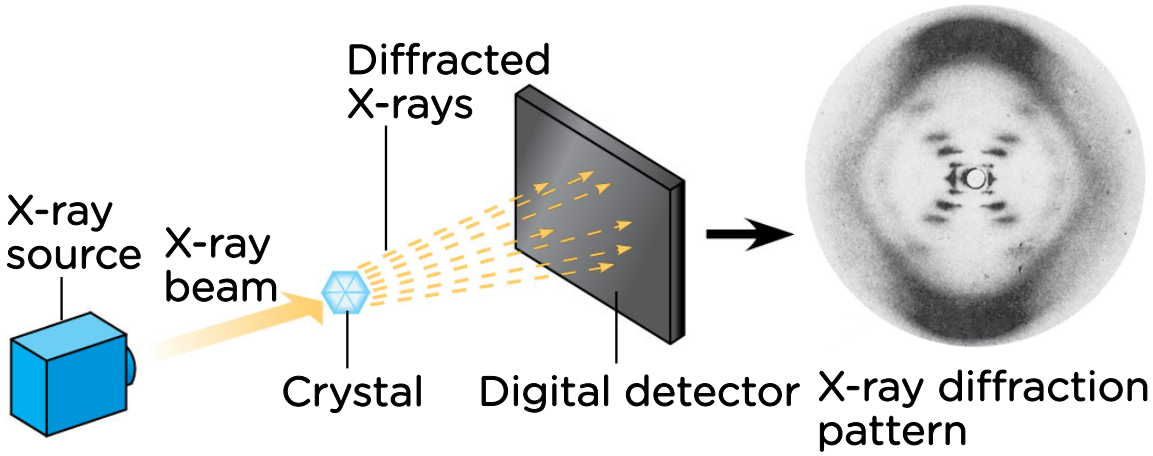
	Number of Each Type of Nucleotide*				Nucleotide Ratios**		
Source of DNA	**A**	**T**	**G**	**C**	**A/T**	**G/C**	**(A + T)/(G + C)**
Bovine thymus	28.4	28.4	21.1	22.1	1.00	0.95	1.31
Bovine liver	28.1	28.4	22.5	21.0	0.99	1.07	1.30
Bovine kidney	28.3	28.2	22.6	20.9	1.00	1.08	1.30
Bovine brain	28.0	28.1	22.3	21.6	1.00	1.03	1.28
Human liver	30.3	30.3	19.5	19.9	1.00	0.98	1.53
Locust	29.3	29.3	20.5	20.7	1.00	1.00	1.41
Sea urchin	32.8	32.1	17.7	17.3	1.02	1.02	1.85
Wheat germ	27.3	27.1	22.7	22.8	1.01	1.00	1.19
Marine crab	47.3	47.3	2.7	2.7	1.00	1.00	17.50
Aspergillus (mold)	25.0	24.9	25.1	25.0	1.00	1.00	1.00
Saccharomyces cerevisiae (yeast)	31.3	32.9	18.7	17.1	0.95	1.09	1.79
Clostridium (bacterium)	36.9	36.3	14.0	12.8	1.02	1.09	2.73

*The values in these four columns are the average number of each type of nucleotide found per 100 nucleotides in DNA.

**The A/T and G/C ratios are not all exactly 1.00 because of experimental error.

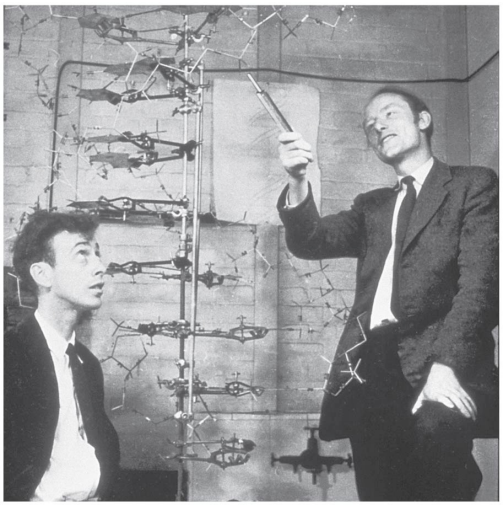
Discovering the **structure** of DNA:

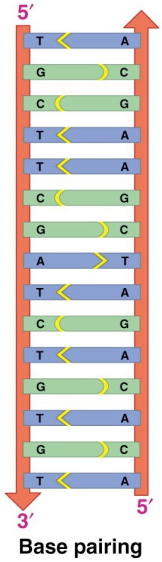
- Rosalind Franklin & Maurice Wilkins
  - x-ray diffraction suggested helix of two strands, with a uniform width that stacks bases, with sugar-phosphate on outside

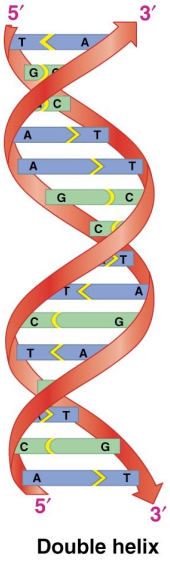


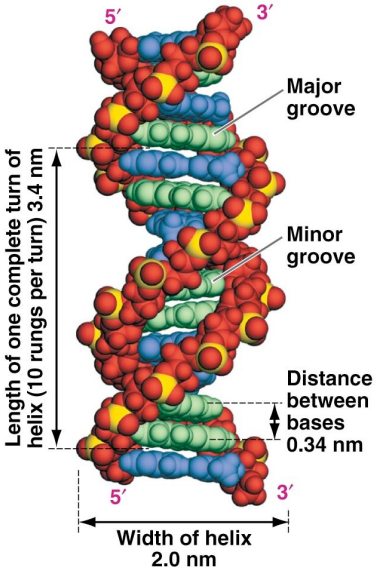
Discovering the **structure** of DNA:

- James Watson & Francis Crick
  - created a scale model that fit all the available data:



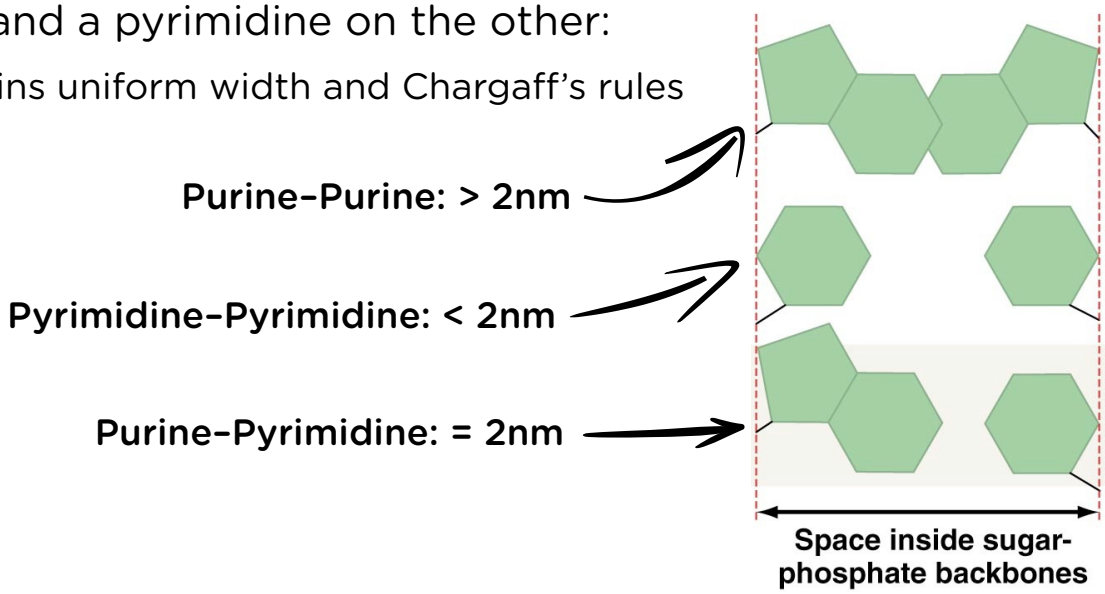






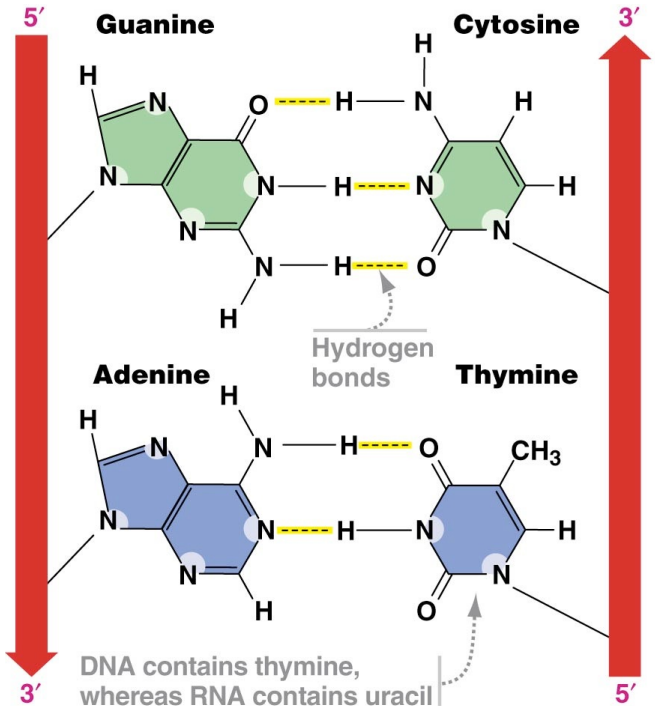
If DNA contains more than one chain of nucleotides, what forces hold them together?

- If it's hydrogen bonds forming between a purine on one strand and a pyrimidine on the other:
  - Explains uniform width and Chargaff's rules

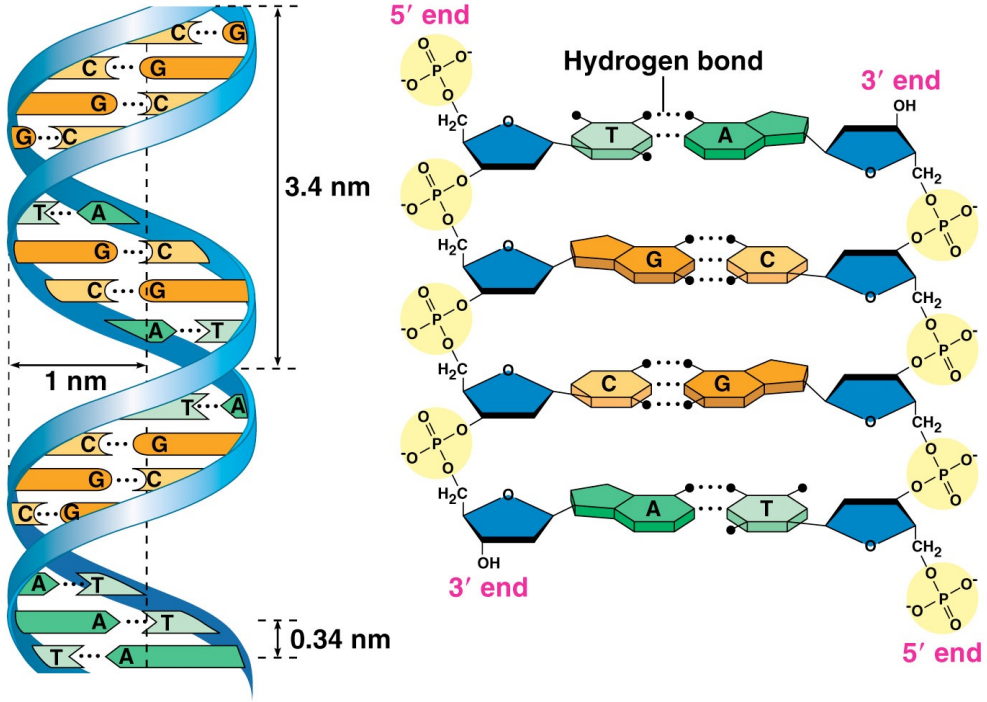


If purines are opposite pyrimidines:

- Only G can "fit" opposite C and A opposite T in order for groups to be precisely positioned for H-bonds to form between them
  - Called Watson-Crick or complementary base pairing



Double-stranded DNA is **antiparallel & complementary**:



The information content of DNA resides in the sequence of its bases

- Only have 4 to choose from
- But, potential for different combinations is staggering when the size of chromosomes is considered
  - If chain has 2 nucleotides, 4x4=16 possibilities (4^2)
  - If chain has 3 nucleotides, 4x4x4=64 (4^3)
  - If chain has *n* nucleotides, 4^n possibilities
- Some human chromosomes have 250 million bases
  - $4^{250,000,000}$ possibilities!
- How is this information copied?

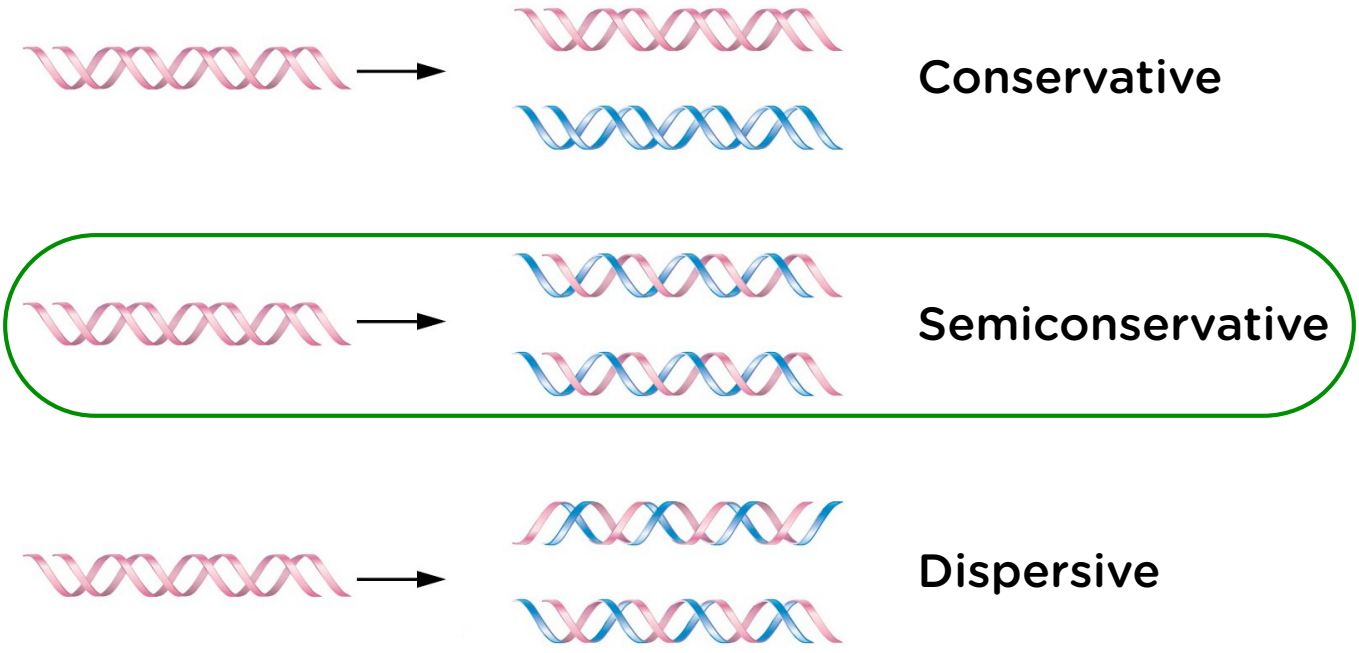
Watson & Crick's model of DNA double helix

- Placed a great deal of importance on complementary bases
- Suggested a copying mechanism

> Each DNA strand in a double helix contains all the information needed to make a new identical double helix

If "parental" double helix is unwound, all that is necessary to build 2 identical "daughter" helices is to add complementary bases to the now-single-stranded DNA chains (templates)

How (if at all) are the parent strands maintained?

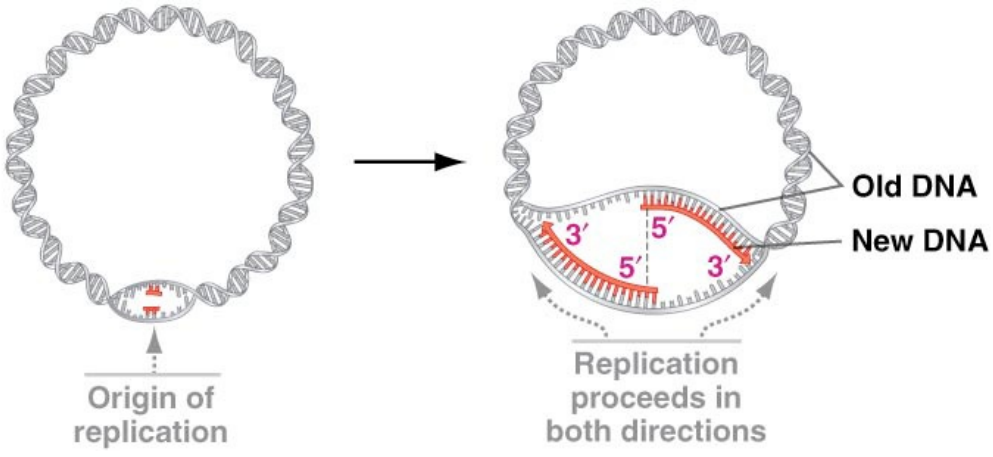


Order of events for DNA Replication:

1. Determine where to start
2. Separate the strands
3. "Prime the pump"
4. Synthesize DNA
5. Clean up

The "start signal" for DNA Replication is the Origin of Replication (*ori* for short)

- The *ori* is a specific sequence of bases in the DNA



Strands will be separated at the *ori*, and synthesis of new DNA will occur from **both** parent strands in **both** directions away from the *ori*

Circular bacterial chromosomes typically have a few million base pairs and a single *ori*: