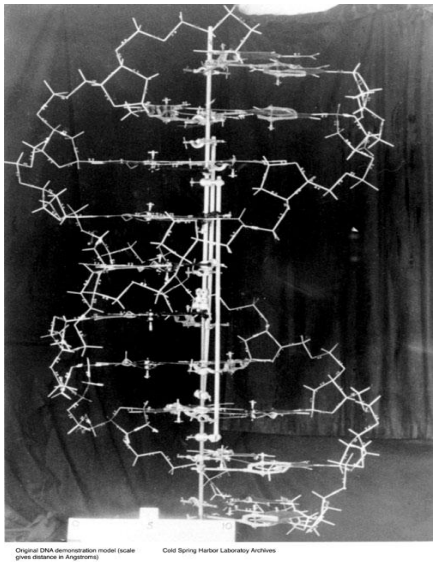
Molecular Biology
Part II

Discovery of DNA

- DNA Sequences
  - Chargaff and Vischer, 1949
    - DNA consisting of A, T, G, C
      - Adenine, Guanine, Cytosine, Thymine
  - Chargaff Rule
    - Noticing #A≈#T and #G≈#C
      - A "strange but possibly meaningless" phenomenon.
- Wow!! A Double Helix
  - Watson and Crick, *Nature,* April 25, 1953
  -
  - Rich, 1973
    - Structural biologist at MIT.
    - DNA's structure in atomic resolution.



Original DNA demonstration model (scale gives distance in Angstroms) Cold Spring Harbor Laboratory Archives

Watson and Crick walk along the Backs Cold Spring Harbor Laboratory Archives

Crick Watson

Watson & Crick – *"…the secret of life"*

- Watson: a zoologist, Crick: a physicist
- *"In 1947 Crick knew no biology and practically no organic chemistry or crystallography.."* – www.nobel.se
- Applying Chagraff's rules and the X-ray image from Rosalind Franklin, they constructed a "tinkertoy" model showing the double helix
- Their 1953 *Nature* paper: *"It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material."*

Watson & Crick with DNA model

Rosalind Franklin with X-ray image of DNA

The Story of Double helix

The discovery of double helix by James Watson and Francis Crick in 1953 was preceded by several other important discoveries in Biology:

1) Erwin Chargaff (Columbia University) found experimentally that in DNA the number of adenine residues equals the number of thyamine residues and that the number of guanine equals the number of cytosines. This is sometimes stated as A=T and C=G. But this does not mean that A+T equals C+G. In fact, the AT and CG contents of different species vary considerably. For example, the malaria parasites are very AT rich.

The Story of Double Helix

b) Rosalind Franklin of King's College, London in 1952 discovered using X-ray diffraction analysis that DNA has a helical structure. In fact, she showed that DNA exists in two forms, the A-form and the B-form. The Watson-Crick structure was the B-form of which she obtained an amazingly clear X-ray photograph.

Her research was based on earlier X-ray diffraction work pioneered by Maurice Wilkins who was her boss at the King's college. The two did not get along very well.

The photograph was shown to Watson by Wilkins without Dr. Rosalind Franklin's knowledge.

The Story of Double Helix

Francis Crick and James Watson were colleagues at Cambridge University. Crick provided the mathematical insight and Watson was a very aggressive young scientist who provided the power of his imagination, intuition and modeling skill. To break the secret of DNA they were racing against time because Linus Pauling the towering Nobel Laureate chemist from Caltech also came close to discovering the DNA structure (By the way, it was Rosalind Franklin who had the courage and technical skill to point out the error in Pauling's model.)

The X-ray photograph of Rosalind Franklin provided the final clue that Watson and Crick needed to complete their model of DNA structure. Watson and Crick published a paper giving the correct double helix structure of DNA which earned them Nobel prize in 1962 which was shared by Wilkins.

Rosalind was not a co-author of the paper neither was she informed of the fact that her data was being used before the publication of their paper.
Rosalind Franklin died a sad and horrible death from cancer in 1959.

The Story of Double Helix

Further Reading:

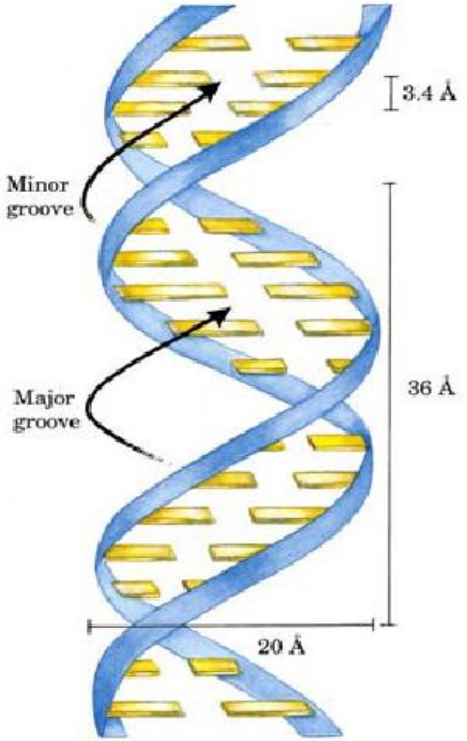
1) "Rosalind Franklin: The Dark Lady of DNA ", Brenda Maddox, Harper Collins, 2002.

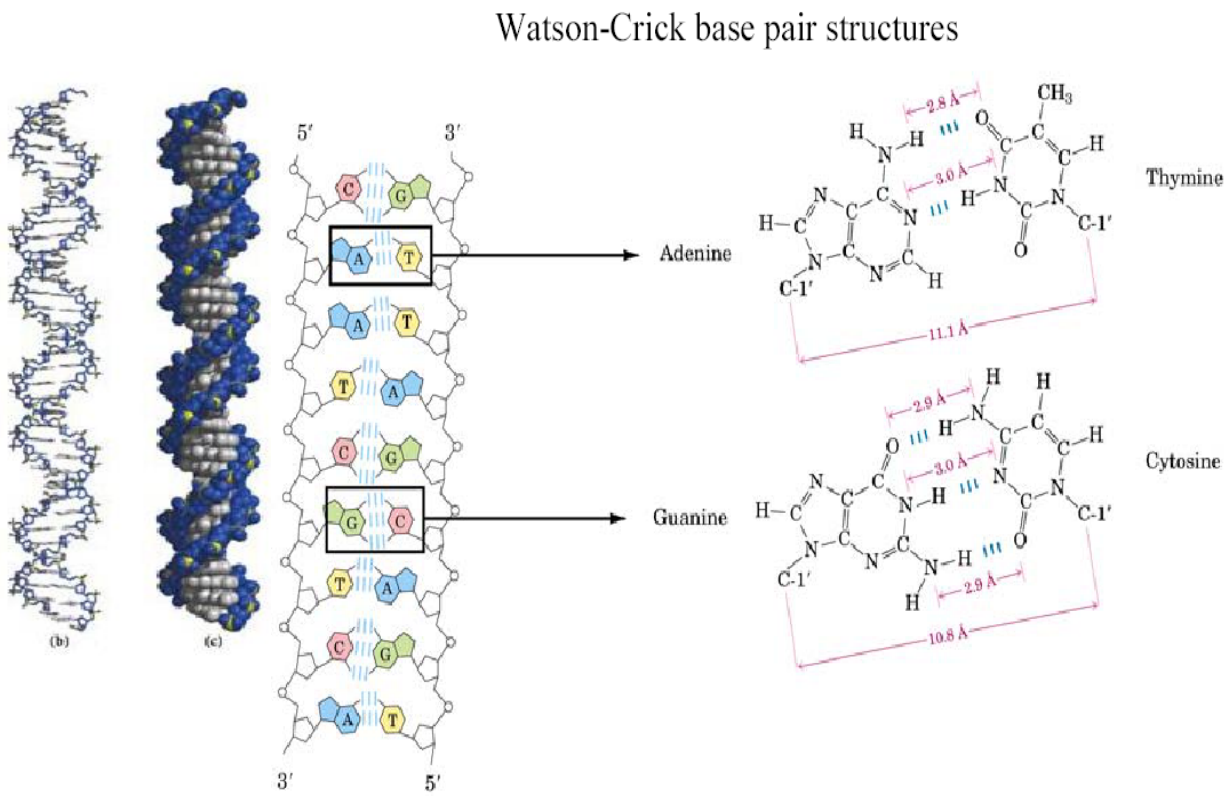
2) "The Double Helix: A Personal Account of the Discovery of the Structure of DNA" by James D. Watson and Lawrence Bragg, Atheneum, London (1968)

3) " Rosalind Franklin and DNA" by Anne Sayre, W.W.Norton, New York,1975.

4) "The Double Helix: A New Critical Edition",by G.S. Stent Weidenfeld and Nicholson, London,1981.

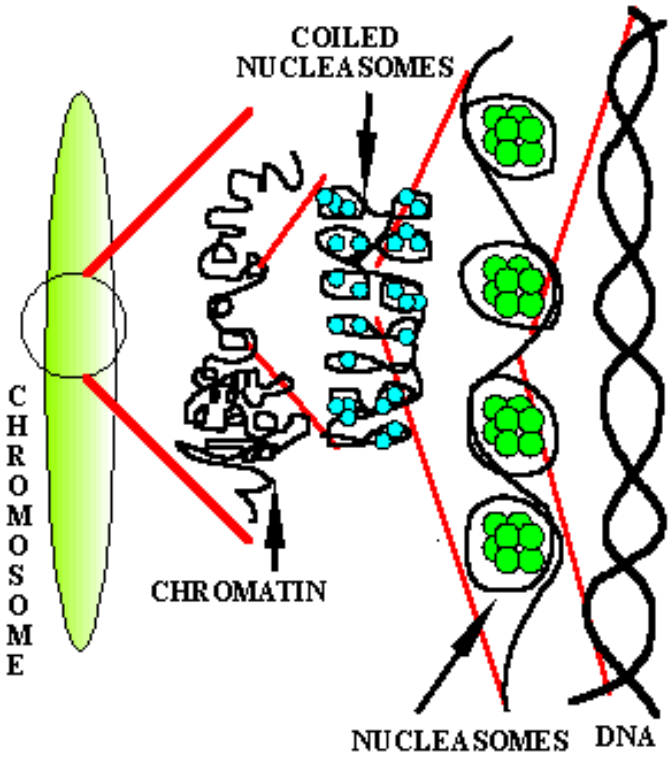
DNA: The Basis of Life



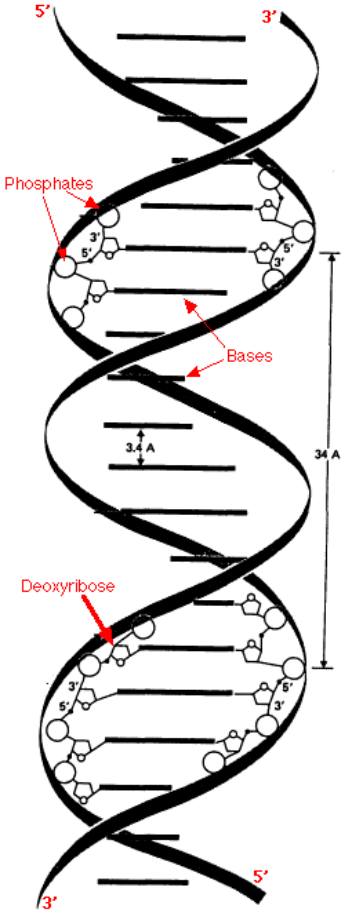


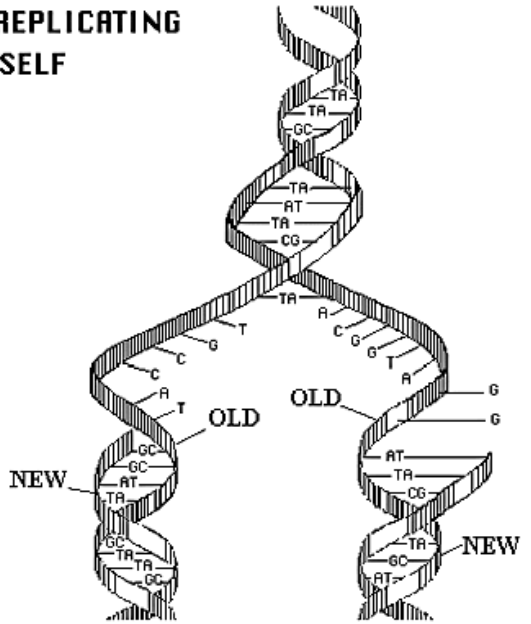
DNA: The Basis of Life

- Humans have about 3 billion base pairs.
  - How do you package it into a cell?
  - How does the cell know where in the highly packed DNA where to start transcription?
    - Special regulatory sequences
  - DNA size does not mean more complex
- Complexity of DNA
  - Eukaryotic genomes consist of variable amounts of DNA
    - Single Copy or Unique DNA
    - Highly Repetitive DNA



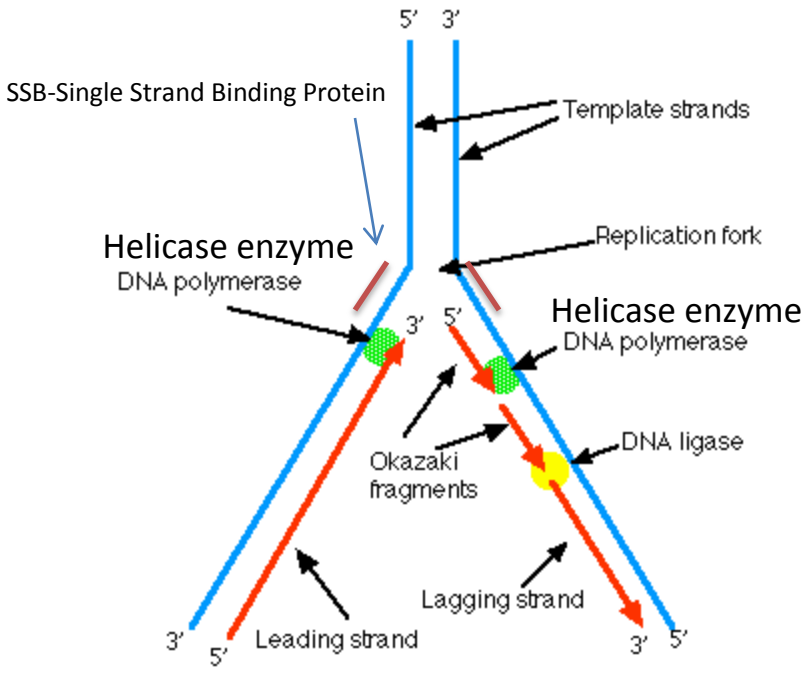
DNA Replication





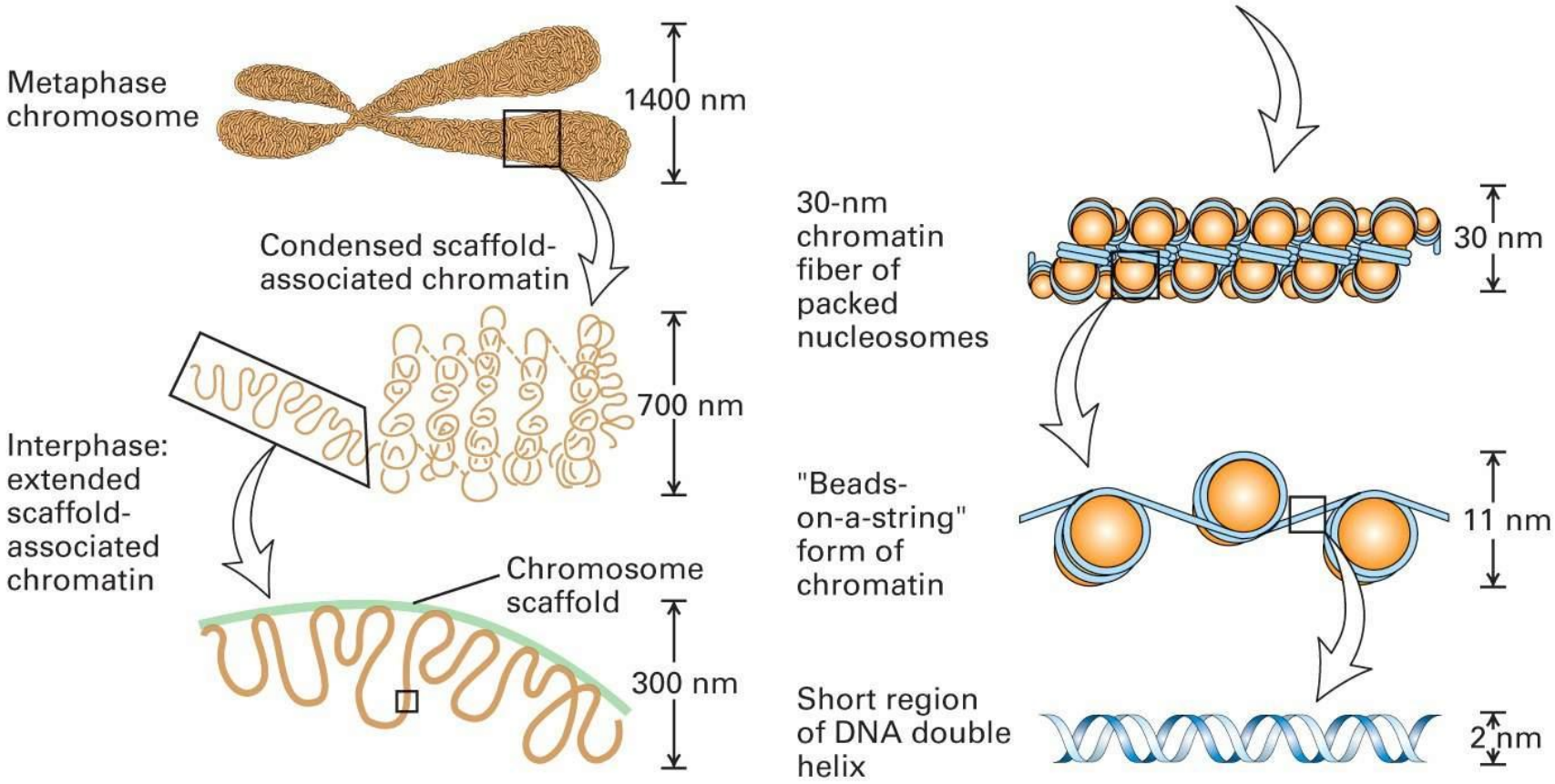
DNA - replication

- DNA can replicate by splitting, and rebuilding each strand.
- The rebuilding of each strand uses slightly different mechanisms due to the 5’ 3’ asymmetry, but each daughter strand is an exact replica of the original strand.



http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/D/DNAReplication.html

Superstructure



Lodish et al. *Molecular Biology of the Cell* (5th ed.). W.H. Freeman & Co., 2003.

Superstructure Implications

- DNA in a living cell is in a highly compacted and structured state
- Transcription factors and RNA polymerase need ACCESS to do their work
- Transcription is dependent on the structural state – SEQUENCE alone does not tell the whole story

Chromosomes

Organism	Number of base pair	number of Chromosomes
Prokayotic		
Escherichia coli (bacterium)	$4x10^6$	1
Eukaryotic		
Saccharomyces cerevisiae (yeast)	$1.35x10^7$	17
Drosophila melanogaster(insect)	$1.65x10^8$	4
Homo sapiens(human)	$2.9x10^9$	23
Zea mays(corn)	$5.0x10^9$	10