Jerusalem Science Contest

Molecular Biology

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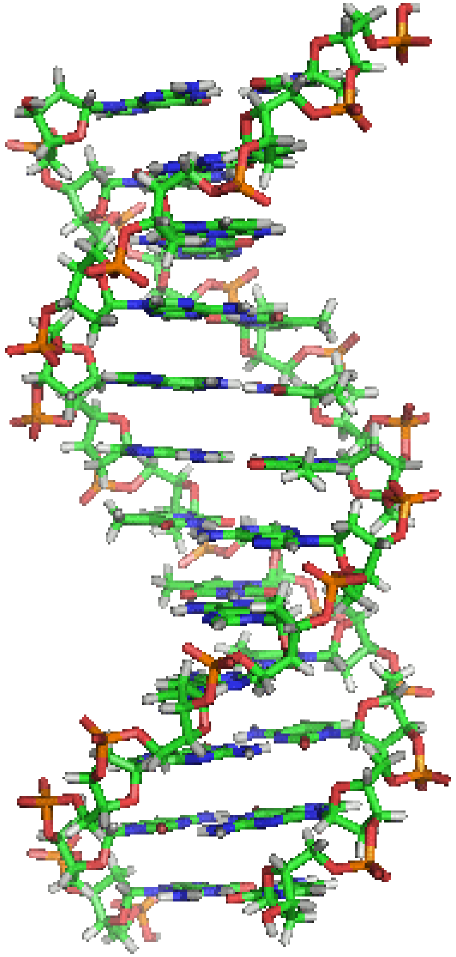
Lecture 1: Discovery of the Genetic Material

Outside reading:

https://www.youthstem2030.org/youth-stem-matters/read/the-story-of-dna-discovery



What Exactly IS Molecular Biology?

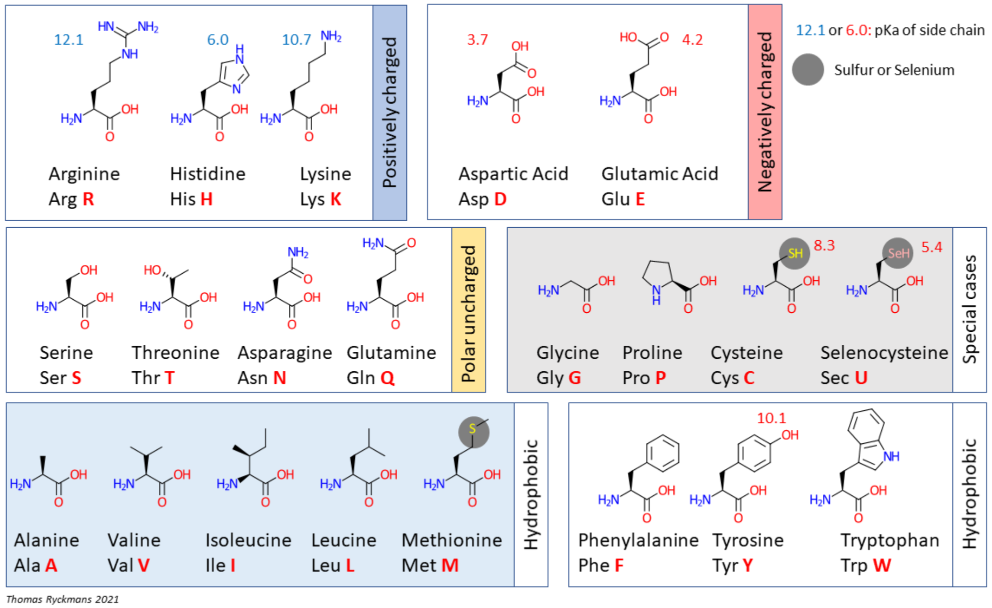
- Must be something to do with molecules and biology…
- But ALL of biology is molecules, so what does it really mean?
- Molecular biology is the study of how cells process information to be able to perform life functions
- Most essential function of cells is to build new cells: replication

History of Molecular Biology

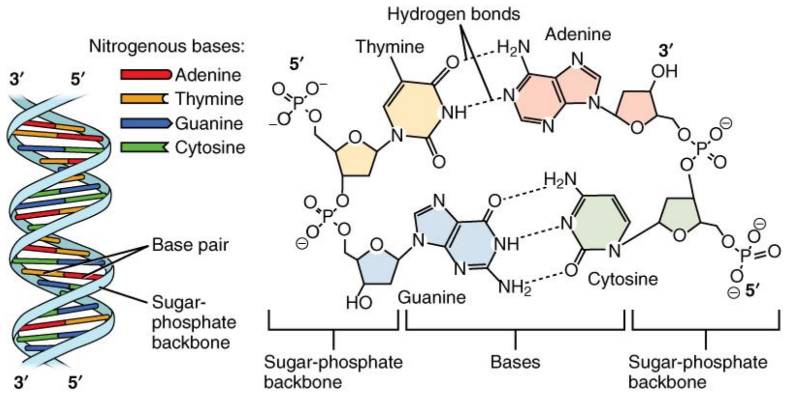
- The field of molecular biology began with trying to understand inheritance: how is biological information passed on to the next generation?

- Focused on the large <u>polymer</u> molecules: DNA, RNA, protein

- These are molecules that are built up as chains of many smaller "subunit" molecules (deoxyribonucleotides, ribonucleotides, and amino acids)



Amino acids

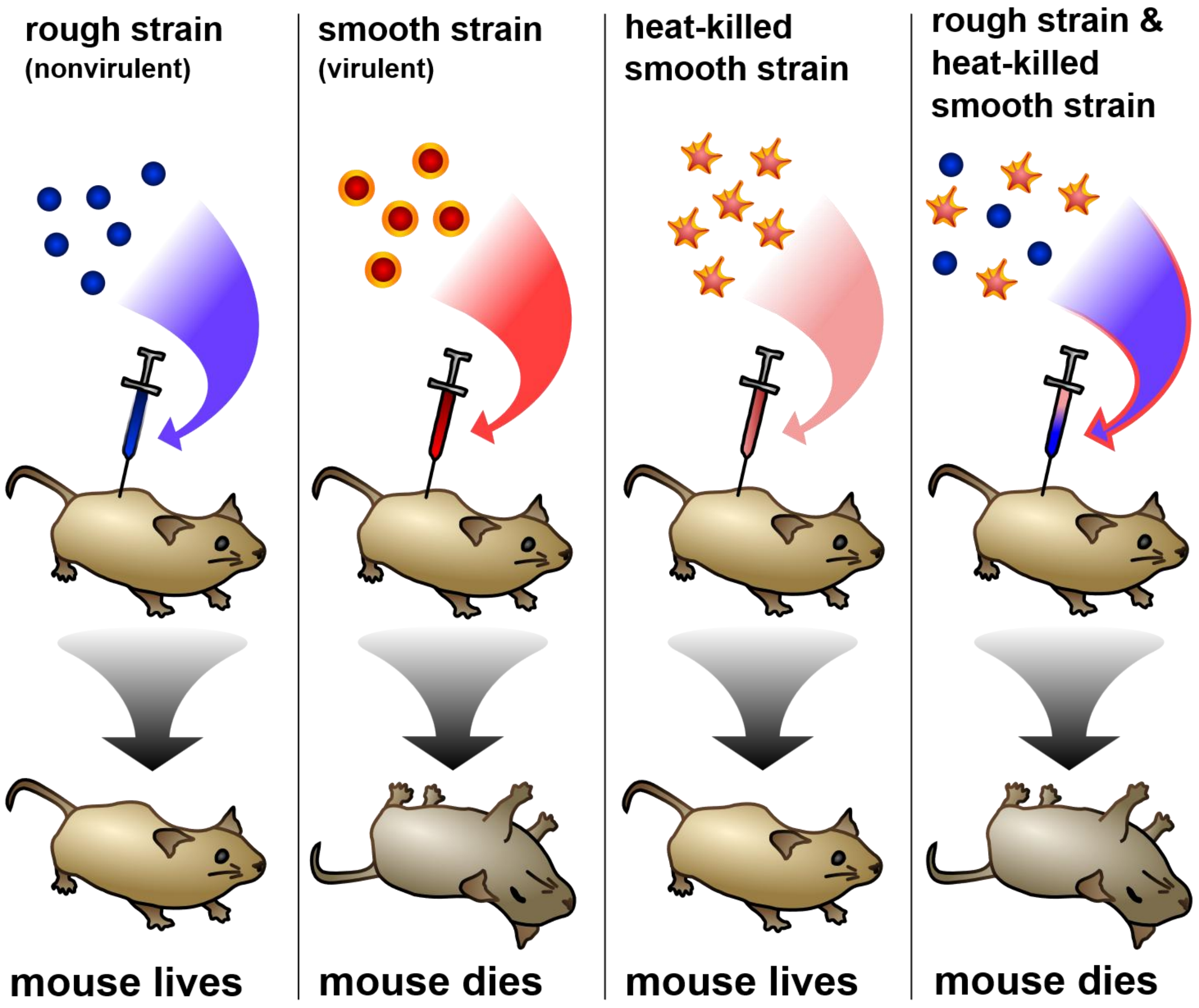


DNA nucleotides

The First Breakthrough: Griffith Experiment (1928)

- Frederick Griffith was trying to develop a vaccine against pneumococcal (bacteria that cause pneumonia) disease in the 1920s
- Studied two related strains of *Streptococcus pneumoniae*: “R” strain (non-virulent; non-lethal in mice) and “S” strain (virulent; lethal in mice)
- Discovered by accident that mixing live “R” strain with dead “S” strain produced bacteria that could kill mice
- “R” strain bacteria were <u>transformed</u> into “S” strain bacteria, presumably by genetic material released from dead “S” strain cells and taken up by the “R” strain cells

The Griffith Experiment

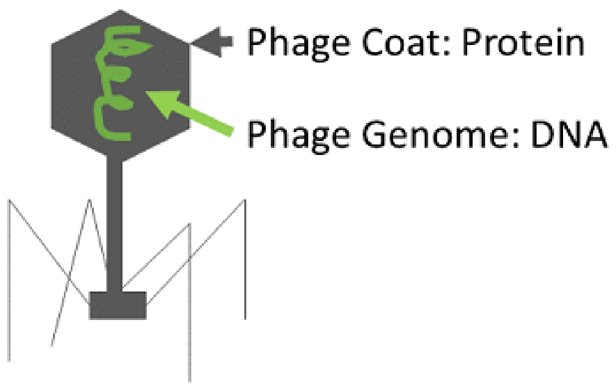


The Next Step: Avery, MacLeod, & McCarty (1944)

- Griffith demonstrated the transfer of genetic information, but did not identify the “transforming factor”
- Oswald Avery, Colin MacLeod, and Maclyn McCarty repeated Griffith’s experiments, with a twist: they replaced heat-killed “S” cells with cell extracts
- They treated the cell extracts with protease (destroys protein), RNase (destroys RNA), or DNase (destroys DNA)
- Protease-treated and RNase-treated extracts could still transform “R” to “S”, but DNase-treated extracts did not
- Concluded that DNA must be the “transforming factor”. In other words, DNA is the molecule of inheritance

Sealing the Deal: Hershey and Chase (1952)

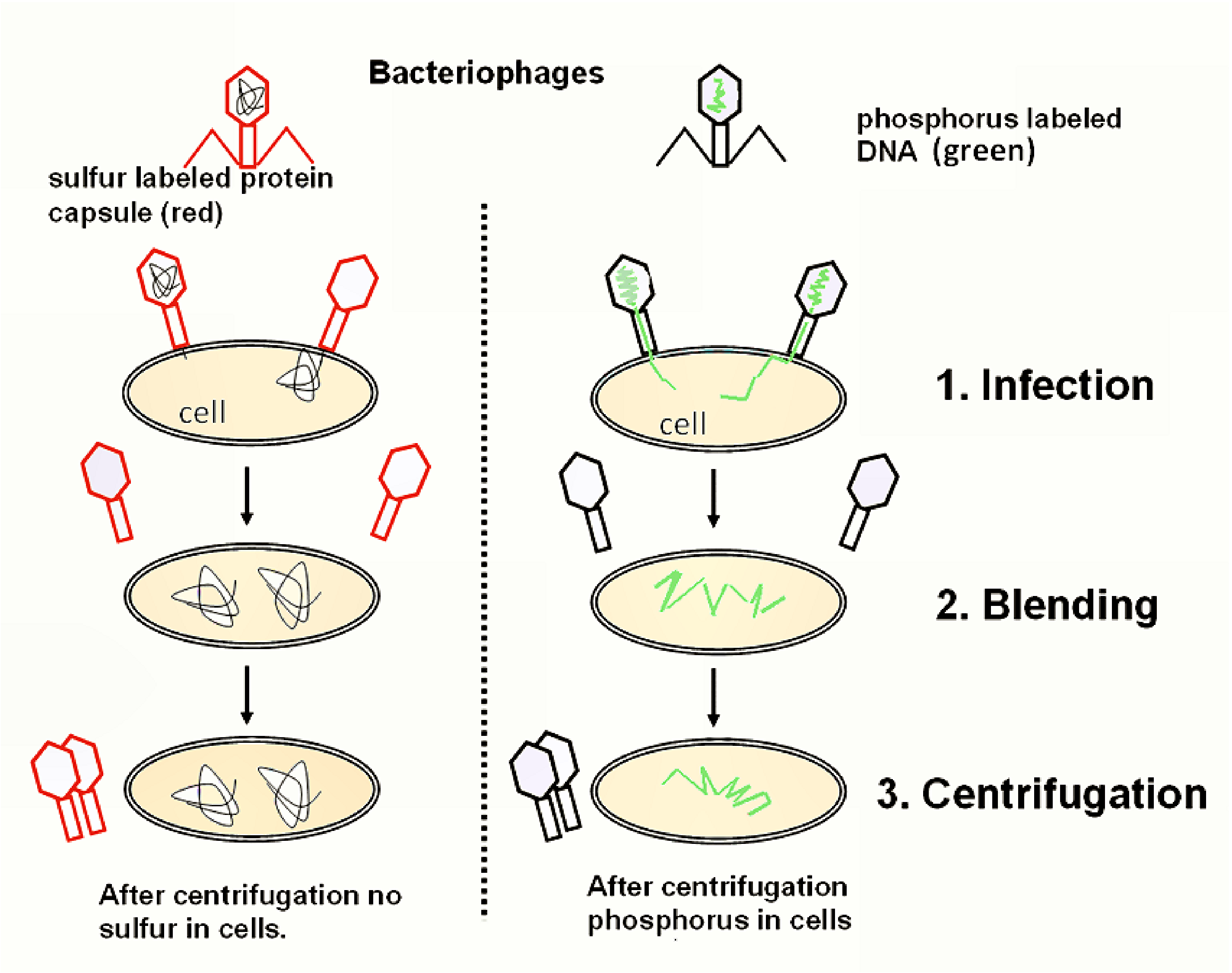
- The results of the Avery, MacLeod, & McCarty experiment were very controversial at the time
- Contradicted the prevailing belief that proteins were the true genetic material
  - Proteins are more complex in makeup than DNA (20 different amino acids, but only 4 different nucleotides)
- Confirmation came from a very different type of experiment, using bacteriophages (viruses that infect and kill bacteria), by Alfred Hershey and Martha Chase
- Virus is essentially a protein shell surrounding a DNA core, so genetic material MUST be one of those two

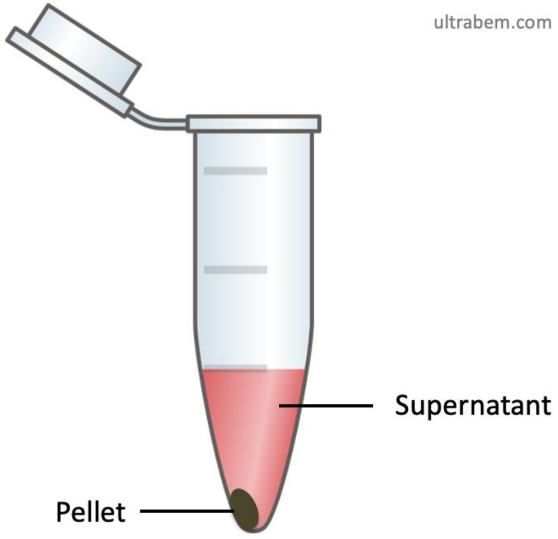


Sealing the Deal: Hershey and Chase (1952)

- Experiment relied on fact that viral proteins contain sulfur but not phosphorus, while DNA contains phosphorus but not sulfur
- Viruses grown in radioactive phosphorus (^{32}P) or radioactive sulfur (^{35}S) were used to infect bacteria. Assumption that genetic material must enter the bacterial cell.
- Samples were then put in a blender to separate bacteria from any pieces of virus that didn't get inside, and centrifuged.
- Found that ^{32}P spun down with bacteria, but ^{35}S remained in supernatant (liquid portion)
- Conclusion: DNA but not protein enters bacteria, so DNA must be genetic material

The Hershey-Chase Experiment





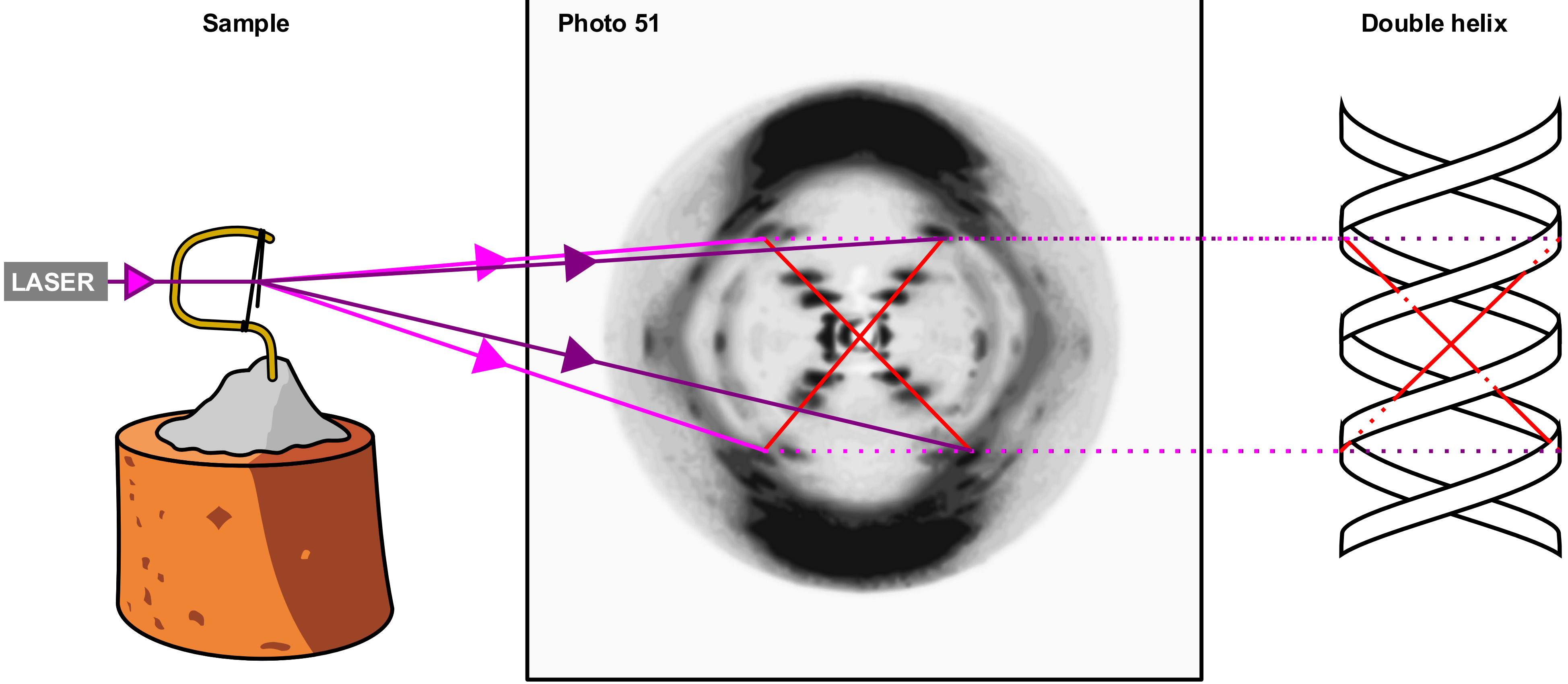
Structure of DNA: A Mechanism for Replication

- The idea that DNA was the hereditary molecule was controversial for a long time, because it was not thought to be complex enough
- A variety of different structures for DNA were proposed, but none could explain how DNA could serve as hereditary molecule
- Erwin Chargaff found that different organisms had different proportions of the 4 nucleotides (A, T, G, C)
    - Chargaff's Rules: A & T were always approximately equal, G & C always approximately equal, but A/T and G/C proportions could differ
- Since base proportions differ, linear sequence can encode information

Structure of DNA: A Mechanism for Replication

- Everything changed in 1953, when James Watson and Francis Crick were visiting Maurice Wilkins in England
- Wilkins showed Watson and Crick a photo of an X-ray diffraction pattern from a DNA crystal (X-ray diffraction is a sensitive way to determine the structure of large biological molecules)
- The photo was from Rosalind Franklin's lab, but shown without her permission
- Watson and Crick recognized the pattern as coming from a helical structure, and were able to build a model for DNA

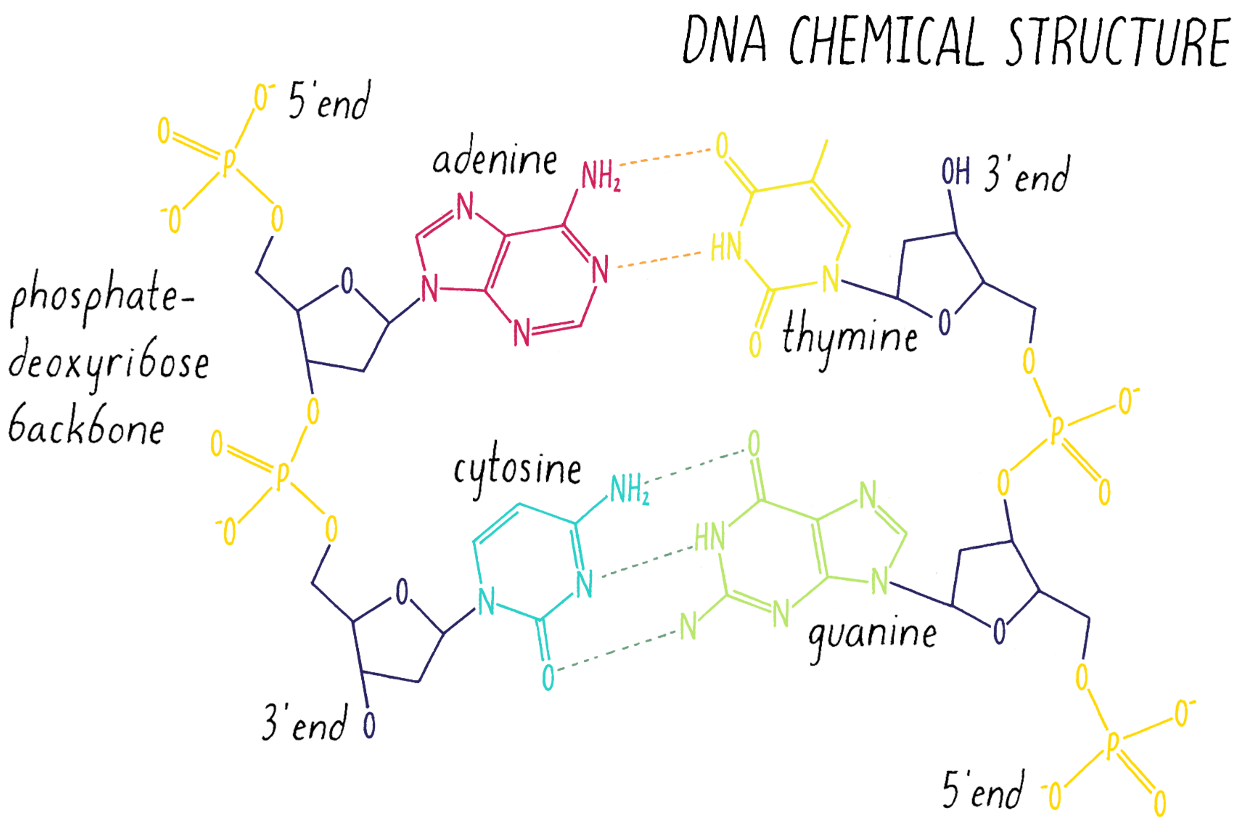
Photo 51: The Game-Changer

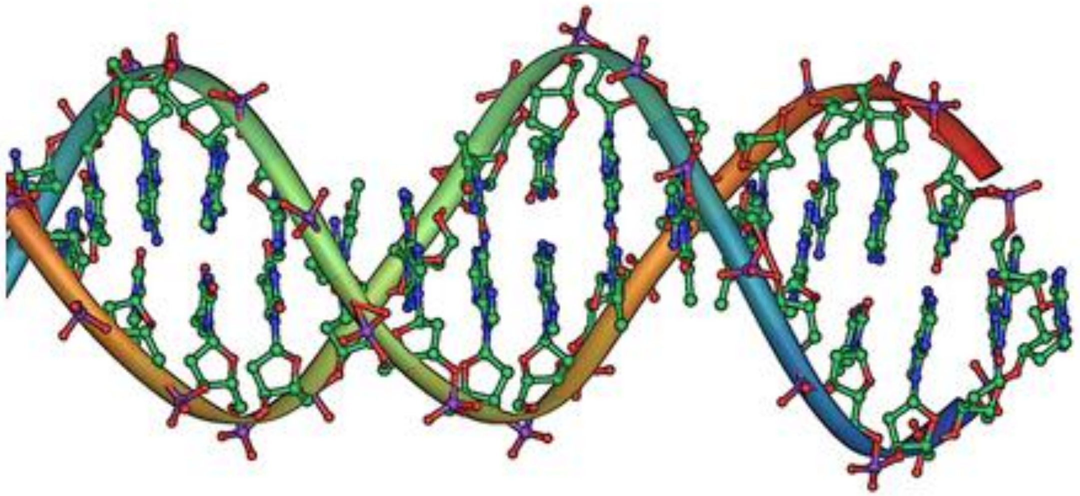


Structure of DNA: A Mechanism for Replication

- Watson and Crick's model was a *double helix*: two strands of DNA coiled around each other like a spiral staircase
- The strands run in opposite directions ("antiparallel"), with the bases (A/T/G/C) pointed inward to form the "stairs" and the sugar-phosphate backbone on the outside, like the railing
- Each base pairs specifically with a "complementary" base, with G binding to C, and A binding to T, explaining Chargaff's Rules
- Structure immediately suggested a mechanism for DNA replication, with each strand serving as a template for copying the other

The DNA Double Helix





Next Lecture: DNA Replication