

**The Structure of DNA:
Molecular biology = biology + chemistry + physics**

1/31/00

Physicists enter biology I

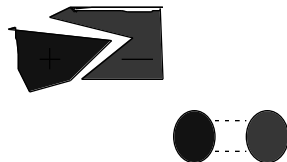
- 1935: physicist Max Delbrück publishes a paper proving that the “gene” is a physical entity which follows quantum mechanical behavior.
 - Uses a quantitative method to study dose-response curves of mutating DNA by x-rays;
 - Induction of mutations by x-rays shows the same behavior as absorption of energy by molecules;
 - Therefore, the gene must be a molecule.
 - Paper pretty much ignored by biologists and physicists alike.

Physicists enter biology II

- 1944: Schrödinger publishes *What is Life?* in which he cites Delbrück's model
 - Uses a statistical mechanical model to show that the gene must be a very large molecule;
 - Describes the gene as an “aperiodic solid”;
 - Asserts that the gene must work by encoding information, like a molecular morse code;
 - Lots of people read *What is Life?*

Physicists enter biology III

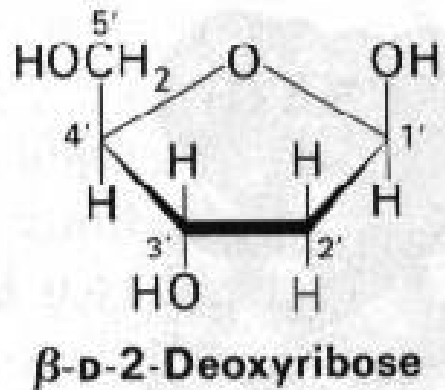
- 1948: Linus Pauling, a physical chemist, writes that complementary non-covalent interactions must be the explanation for biological recognition and replication
 - Two different molecule can “recognize” each other via hydrogen bonds or opposite charges;
 - In this way, one molecule could serve as a template for another



Summary: how could physics/physical chemistry solve the gene problem?

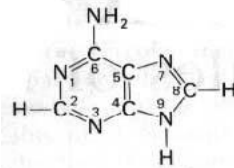
- What is the molecular structure of the gene?
- What types of complementary interactions allow for self-replication of the gene?
- How can the gene molecule encode information (how is it an “aperiodic solid”)?

Back to DNA: the sugar group

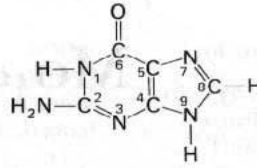


DNA: the bases

Purines:

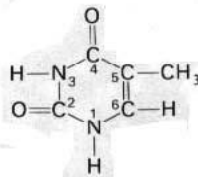


Adenine
(A)

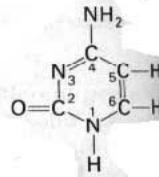


Guanine
(G)

Pyrimidines:

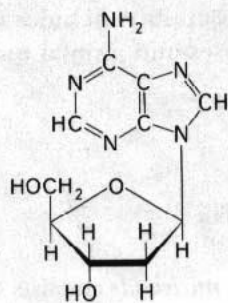


Thymine
(T)

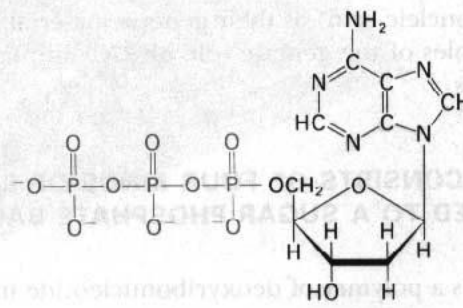


Cytosine
(C)

Sugar + base + phosphate = nucleotide

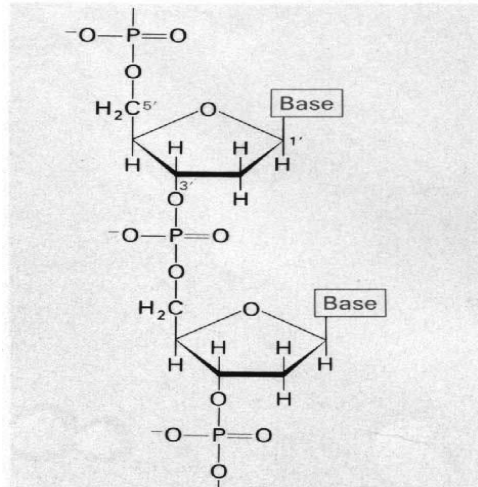


Deoxyadenosine
(A nucleoside)



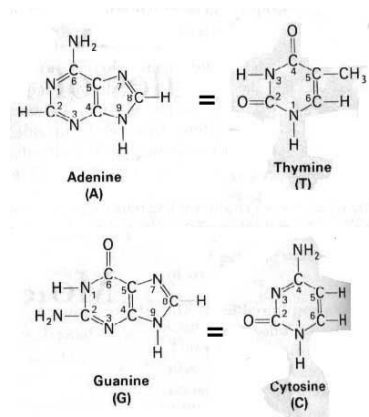
Deoxyadenosine 5'-triphosphate
(dATP)
(A nucleotide)

Nucleotides linked by 3' → 5' phosphodiester bonds



- DNA has a negatively charged phosphate backbone
- The chain has a polarity or direction
- Bases all face same side of the chain

Chargaff's rules: [A] = [T] and [G] = [C]



- Biochemist Erwin Chargaff performed chemical digestion and analysis of DNA
- Found that DNA always has same number of A bases as T, and same number of G bases as C

How is DNA structured in the gene?

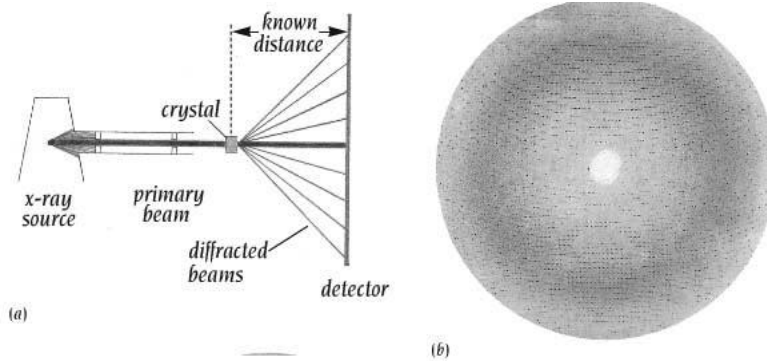
The structure must:

- The rules for covalent bonding laid out by Pauling;
- Explain Chargaff's rules;
- Provide a mechanism for replication (complementarity);
- Provide a mechanism for encoding information.
- To find the solution, use: *x-ray crystallography*

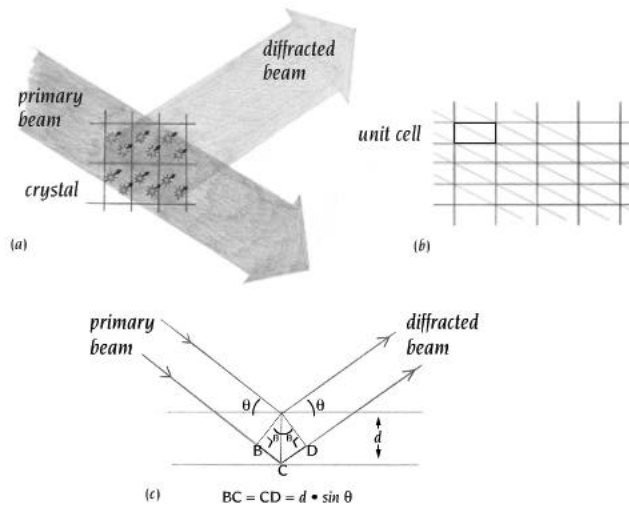
Molecular structures can be determined by *x-ray crystallography*

- A crystal is a solid which is an infinite repeat of units on a lattice.
- When x-rays strike this lattice, they *diffract* from the crystal faces.
- The patterns of diffraction contain information about molecular structures.
- This technique was developed by William and Lawrence Bragg at the turn of the century and applied masterfully by Pauling to study organic molecules in detail.

Layout of an x-ray crystallography experiment

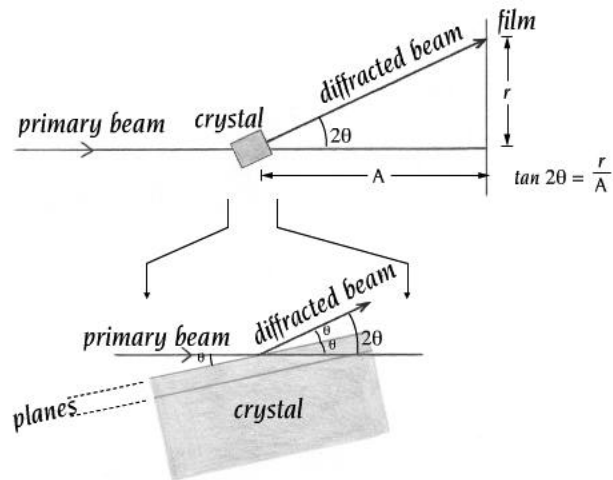


Rules for diffraction given by Bragg's Law



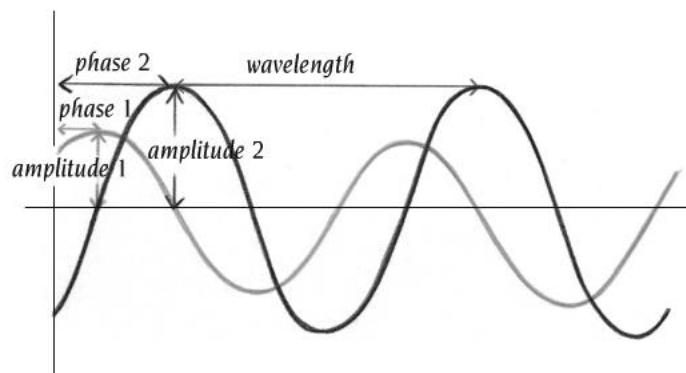
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Position of spots on film gives diffraction angle



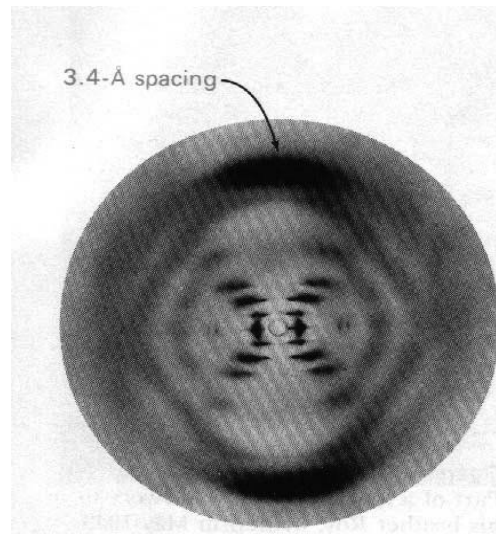
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Intensities of the spots depend on interference of wave and phases of waves



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DNA fibers produce a diffraction pattern characteristic of a *helix*



Watson and Crick noticed that A,T and G,C can form hydrogen bonded base pairs

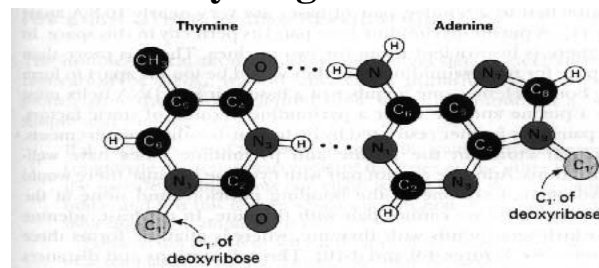
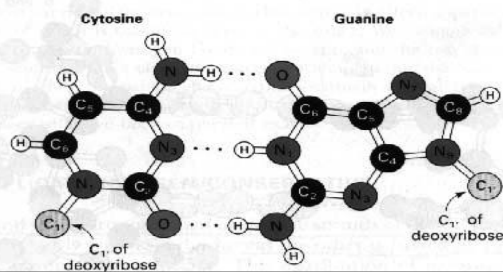
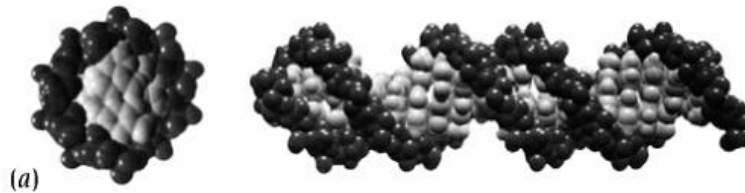


Figure 4-9
Model of an adenine-thymine base pair.

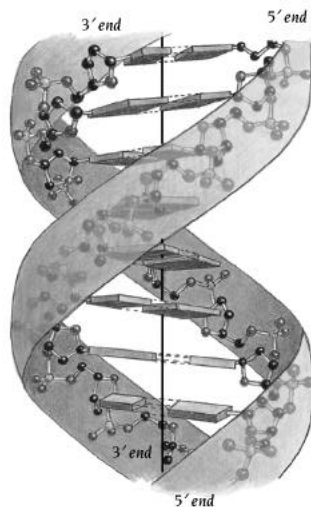


Structure of DNA is a double helix



- Two helical polynucleotide chains running in opposite directions coiled around a common axis.
- The bases are on the inside; phosphate and deoxyribose units on the outside.
- The two chains are held together by hydrogen bonds between pairs of bases (A with T, G with C).
- The sequence of bases along a polynucleotide chain is not restricted in any way.

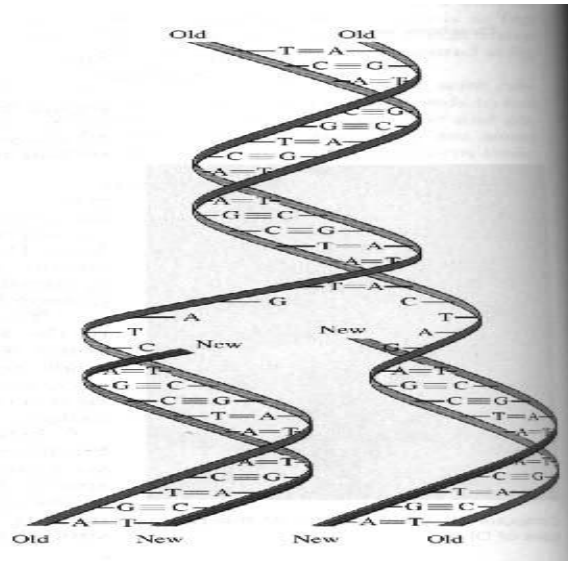
DNA: the statistics



- Adjacent bases are separated by 3.4 Å.
- Adjacent bases are related by a rotation of 36° (the helical structure repeats after 10 residues)
- The diameter of the helix is 20 Å.

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The double helix offers a simple solution to the replication question

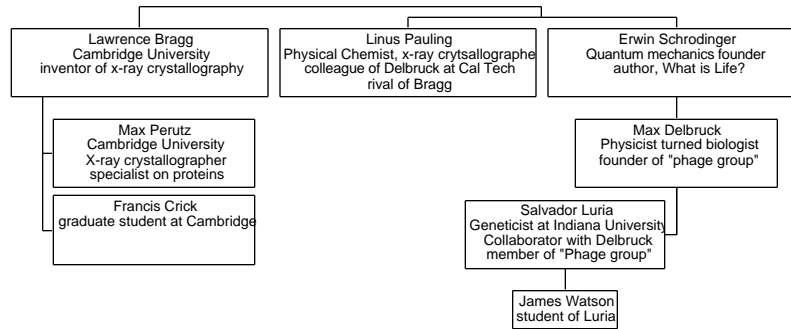


Each strand in DNA is a template

- Each chain is the complement of the other; if the order of bases on one chain is known, the order on the other can be derived from base-pairing considerations.
- DNA replication is semi-conservative; after replication, each new DNAmolecular contains one “new” strand and one “old” strand.
- *In vivo*, DNA replication is carried out by enzymes: *DNA polymerases*.

Everyone was connected to everyone else

Key Parts of the Molecular Biology community



•Delbrück, Luria, and Watson were all supported by the Rockefeller Foundation (+ Warren Weaver)