Chem 452 - Lecture 1
Introduction to Biochemistry
Part 2

Question of the Day: Watson and Crick made the following observation in their landmark article, which was published in 1953 in the journal Nature, "It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material." What are they talking about?

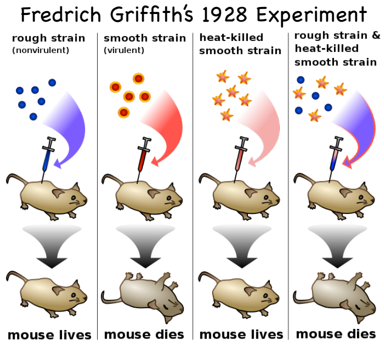
DNA function

- In the 1940's DNA was discovered to comprise the genetic material of a cell.

Ostwald Avery, Colin MacLeod and Maclyn McCarty identified the "transforming principle" in Griffith's experiments was DNA

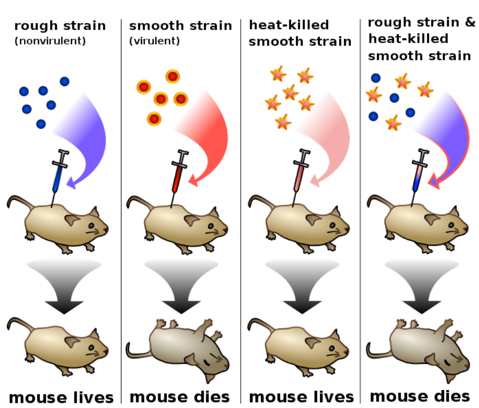
(Wikipedia entry)

Fredrich Griffith's 1928 Experiment



DNA function

Injecting mice with strains of pneumococcus bacteria.



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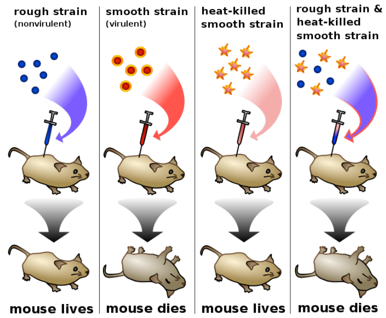
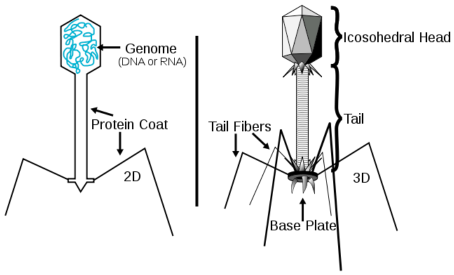


DNA function

- DNA's genetic role was confirmed in 1952 by Hershey and Chase.

The experiments of Alfred Hershey and Martha Chase demonstrated that DNA was the infectious component of bacteriophages

(Wikepedia entry)



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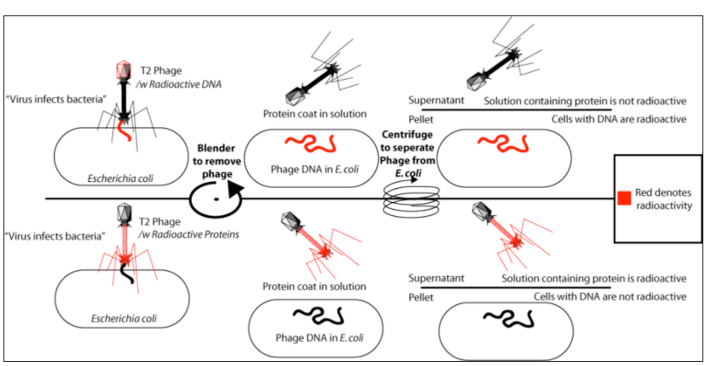
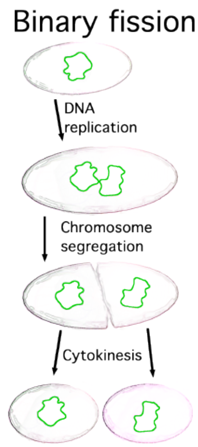


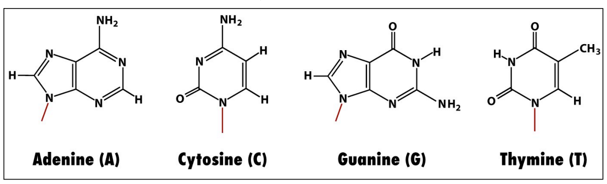
DNA function

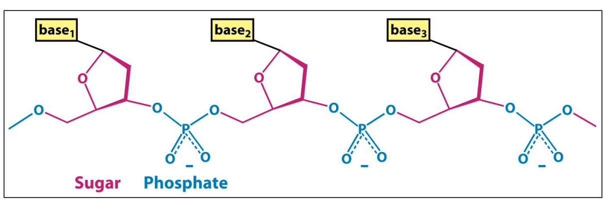
- One consequence of being the genetic material is that DNA has to be able to replicate itself in order to be passed down from generation to generation



DNA structure

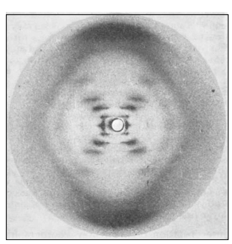
- Molecular components





DNA's structural evidence

- X-ray fiber data (Maurice Wilkins and Rosalind Franklin)
- Evidence that DNA is helical.
- 3.4 Å nucleotide repeat
  - This repeat seems to be limited to central region; "...suggests the bases arranged like a pile of pennies in the central regions of the helical system"
- 34 Å axial repeat
- See also a 20 Å spacing at right angles to the 34 Å repeat.



Wilkins *et al.*, "Molecular Structure of Deoxypentose Nucleic Acids" *Nature 1953, 171, 738-970.*

DNA's structural evidence

- Chargaff's Rules (Erwin Chargaff)

Table 3-2 Data Leading to the Formulation of Chargaff's Rules

Source	Adenine to Guanine	Thymine to Cytosine	Adenine to Thymine	Guanine to Cytosine	Purines to Pyrimidines
Ox	1.29	1.43	1.04	1.00	1.1
Human	1.56	1.75	1.00	1.00	1.0
Hen	1.45	1.29	1.06	0.91	0.99
Salmon	1.43	1.43	1.02	1.02	1.02
Wheat	1.22	1.18	1.00	0.97	0.99
Yeast	1.67	1.92	1.03	1.20	1.0
Hemophilus influenzae	1.74	1.54	1.07	0.91	1.0
E-coli K2	1.05	0.95	1.09	0.99	1.0
Avian tubercle bacillus	0.4	0.4	1.09	1.08	1.1
Serratia marcescens	0.7	0.7	0.95	0.86	0.9
Bacillus schatz	0.7	0.6	1.12	0.89	1.0

SOURCE: After E. Chargaff et al., *J. Biol. Chem.* 177 (1949).

DNA's structural evidence

- Using other people's experimental results, James Watson and Francis Crick proposed the now accepted model for the 3-dimensional structure of DNA

Francis Crick James Watson

DNA proposed structures

- While Watson and Crick were working on their model for DNA, Pauling and Corey's published an alternative model
- They proposed a triple helix with the ribose phosphate backbone on the inside and the nucleotide bases extending outward from the core.

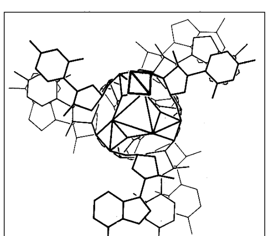
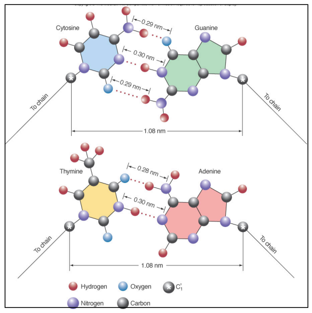


FIGURE 6 Plan of the nucleic acid structure, showing several nucleotide residues.

Pauling, L. & Corey, R. "A Proposed Structure for the Nucleic Acids", *Proceedings of the National Academies of Science 1953, 39, 84-97.*

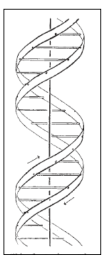
DNA proposed structures

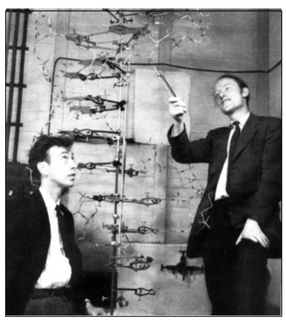
- Watson and Crick proposed specific base pairing to account for both Chargaff's Rules and the 20 Å spacing that Wilkin's and Franklin observed.



DNA proposed structures

- Watson & Crick proposed a double-helix





Watson, J. and Crick, F. "A Structure for Deoxribonucleic Acid" *Nature* 1953, *171*, 737-738.

DNA proposed structures

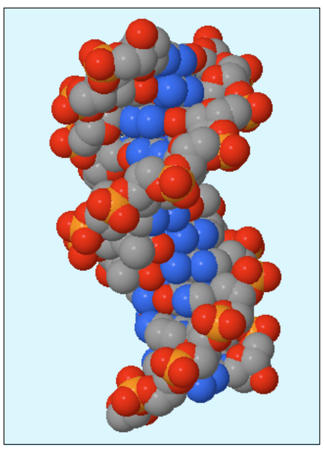
- Watson & Crick proposed a double-helix
  - X-ray structure is a salt and not a free acid. (Negatively charged)
    - Not clear what forces would hold Pauling and Corey's model together.
  - Bases are paired
    - Adenine (a purine) to Thymine (a pyrimidine)
    - Guanine (a purine) to Cytosine (a pyrimidine)

DNA proposed structures

- Watson & Crick's DNA structure also made biological sense:
  - "However, if only specific pairs of bases can be formed, it follows that if the sequence of bases on one chain is given, then the sequence on the other chain is automatically determined?"
  - "It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material."

DNA structure

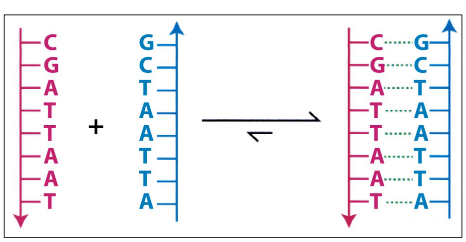
- The rules of chemistry help us to understand the 3-dimensional structures that are formed by biological macromolecules



B-DNA

DNA structure

- The duplex (double-helical) structure of DNA forms spontaneously in aqueous solutions.



DNA structure

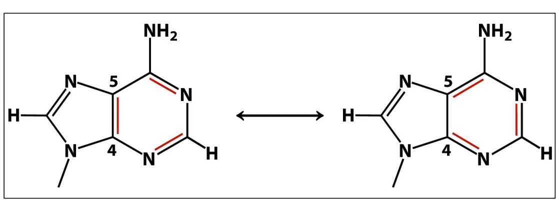
- What interactions (bonds) are involved in holding macromolecules together?

DNA structure

- Interatomic interactions (bonding)
- Thermodynamics
  - What can it tell about duplex formation.
- Acid/Base chemistry
  - We live in an aqueous world

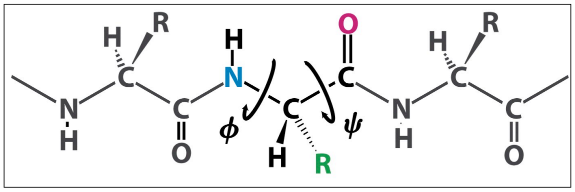
Intermolecular Interactions (Bonds)

- Covalent bonds
  - Determine the local shape.



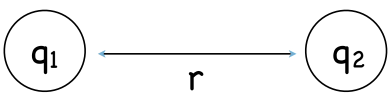
Intermolecular Interactions (Bonds)

- Covalent bonds
  - Rotation about single bonds allow for multiple conformations.



Intermolecular Interactions (Bonds)

- Non-covalent interactions (bonds)
  - Charge/Charge



$$F \approx \frac{q_1 q_2}{Dr^2}$$ Coulomb's Law

$$E = \frac{k q_1 q_2}{Dr}$$

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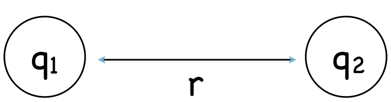


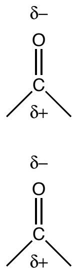
$$F \approx \frac{q_1 q_2}{Dr^2}$$ Coulomb's Law

$$E = \frac{k q_1 q_2}{Dr}$$

Vacuum:	D=1
Benzene:	D=2
Water:	D=80

Intermolecular Interactions (Bonds)

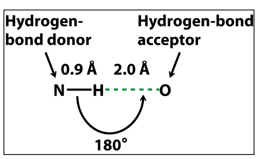
- Non-covalent interactions (bonds)
  - Dipole/Dipole

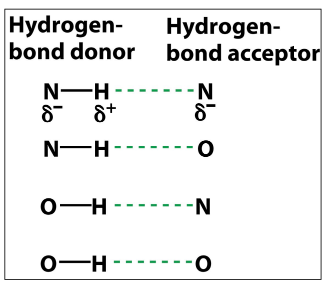


$$E \approx \frac{q_1 q_2}{Dr^2}$$

Intermolecular Interactions (Bonds)

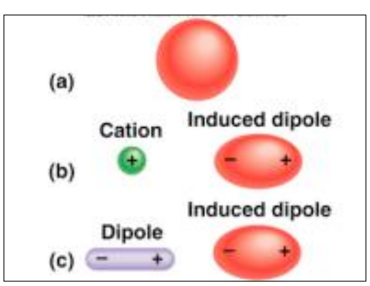
- Non-covalent interactions (bonds)
  - Hydrogen Bonds

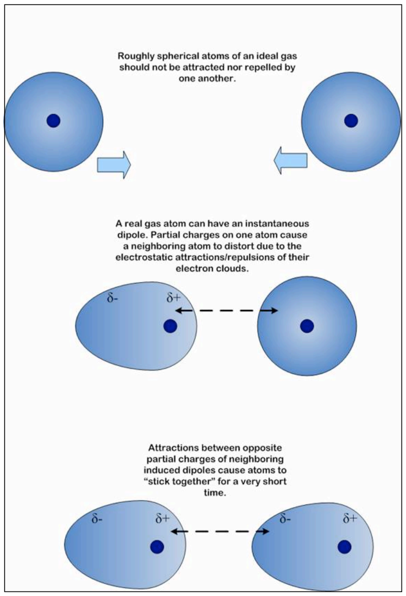




Intermolecular Interactions (Bonds)

- Non-covalent interactions (bonds)
  - van der Waals Interaction





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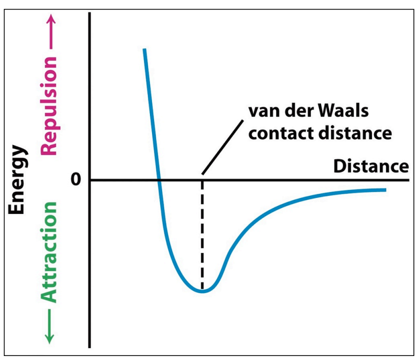

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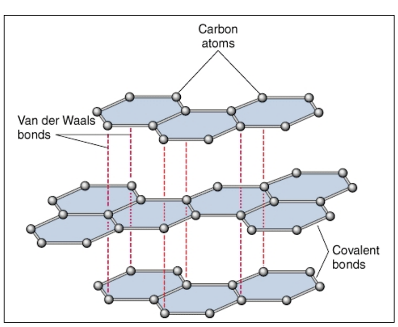
Graphite



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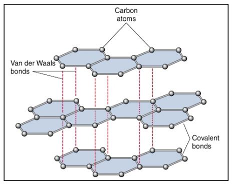
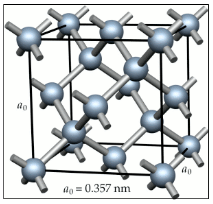
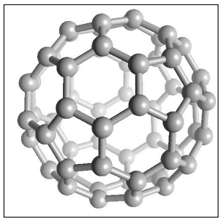


Diamond





Buckminsterfullerene(Buckey balls)

Intermolecular Interactions (Bonds)

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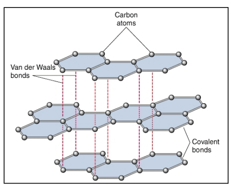

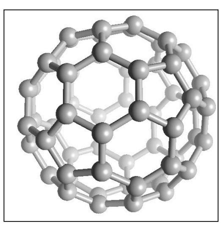

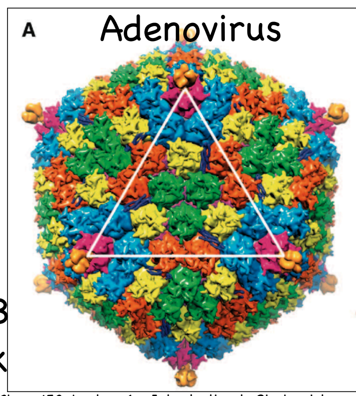

Adenovirus

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Intermolecular Interactions (Bonds)

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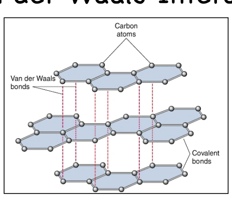

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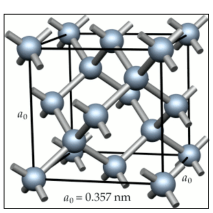
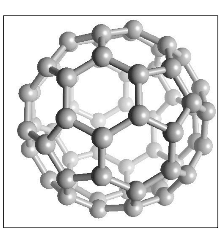




Buckminsterfullerene(Buckey balls)

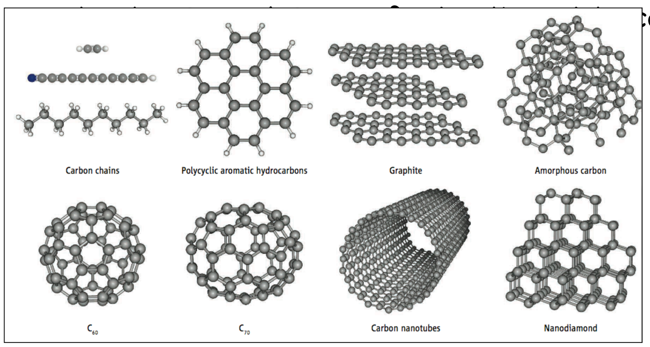
Intermolecular Interactions (Bonds)

- "Hydrogen-poor conditions in a planetary nebula enable the detection of carbon-cage molecules C_{60} and C_{70}, confirming the existence of...

Fullerenes in Space!!!

Intermolecular Interactions (Bonds)

- "Hydrogen-poor conditions in a planetary nebula enable the detection of carbon-cage



Ehrenfreund, P., and Foing, B. H. (2010) Astronomy. Fullerenes and cosmic carbon, *Science* ***329***, 1159-1160.

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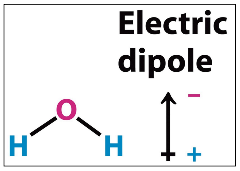
Water

- Water (The solvent)
  - Behavior is strongly influenced by non-covalent interactions



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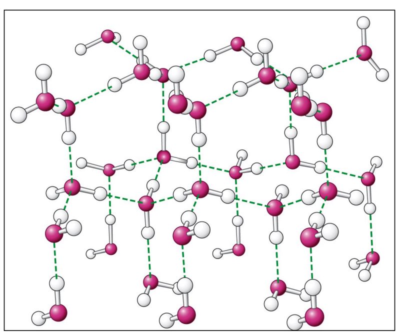
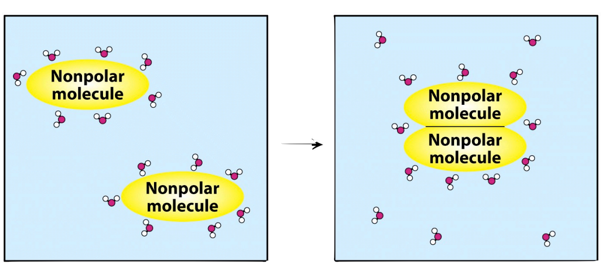


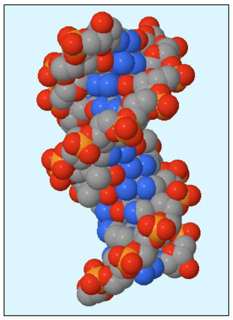
Water

- The Hydrophobic Effect



DNA structure

- What interactions (bonds) are involved in holding macromolecules together?



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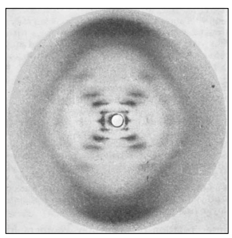

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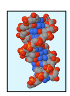
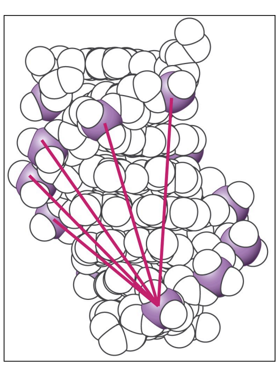
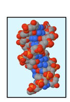


DNA structure

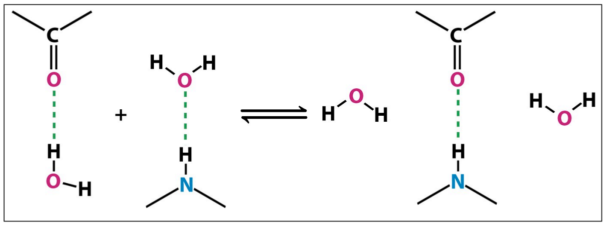
- Charge/Charge Interactions?





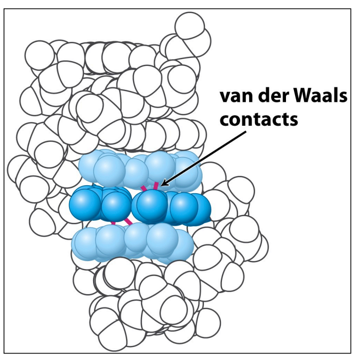
DNA structure

- Hydrogen Bonds?



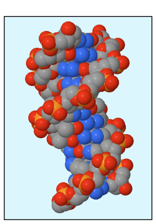
DNA structure

- vander Waals Interactions?



Questions

- What interactions drive the formation of the DNA double helix?
- What interactions stabilize that structure once it is formed?



Thermodynamics

- Systems and Surroundings
  - System + Surroundings = Universe
- First Law
  - $\Delta E_{total} = 0$
    - The total energy of the Universe is fixed!!
  - $\Delta E_{system} = q + w$
    - q = heat absorbed by the system
    - w = work done on the system

Thermodynamics

- Systems and Surroundings
  - System + Surroundings = Universe
- Second Law
  - Entropy (S) is a measure of disorder.
  - $\Delta S_{system} = q_{system}/T$
  - For any spontaneous process, the entropy of the Universe increases!!
    - $\Delta S_{universe} > 0$
    - $\Delta S_{universe} = \Delta S_{system} + \Delta S_{surroundings}$

Thermodynamics

- $\Delta S_{universe}$
  - The Change in Entropy for the Universe ($\Delta S_{universe}$) can be used as a tool to predict whether reactions or processes are spontaneous or not.

$\Delta S_{universe} > 0$, the reaction or process is spontaneous as written

$\Delta S_{universe} < 0$, the reaction or process is not spontaneous as written, it is, however, spontaneous in the reverse direction.

$\Delta S_{universe} = 0$, the reaction or process is at equilibrium.

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With ΔS, you must look at the whole universe to determine if a reaction is spontaneous.

Thermodynamics

- Gibb's Free Energy (ΔG_{system})

$$\Delta H_{system} = q_P \text{ (at constant } P)$$

$$\Delta S_{surroundings} = \frac{q_{surrounding}}{T} = -\frac{q_{system}}{T} = \frac{-\Delta H_{system}}{T} \text{ (at constant } P \,\&\, T)$$

$$\Delta S_{universe} = \Delta S_{system} + \Delta S_{surroundings}$$

$$\Delta S_{universe} = \Delta S_{system} - \frac{\Delta H_{system}}{T}$$

$$-T\Delta S_{universe} = -T\Delta S_{system} + \Delta H_{system}$$

$$\Delta G_{system} = \Delta H_{system} - T\Delta S_{system} \text{ (at constant } P \,\&\, T)$$

Thermodynamics

- Gibb's Free Energy (ΔG)

$\Delta G_{system} < 0$, the reaction or process is spontaneous as written

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Thermodynamics

- Gibb's Free Energy (ΔG)

$\Delta G_{system} < 0$, the reaction or process is spontaneous as written

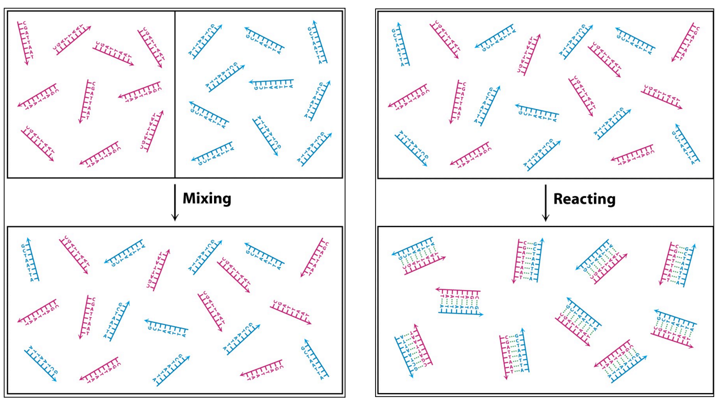
$\Delta G_{system} > 0$, the reaction or process is not spontaneous as written, it is, however, spontaneous in the reverse direction.

$\Delta G_{system} = 0$, the reaction or process is at equilibrium.

When using ΔG, you only need to look at the system to determine if a reaction is spontaneous.

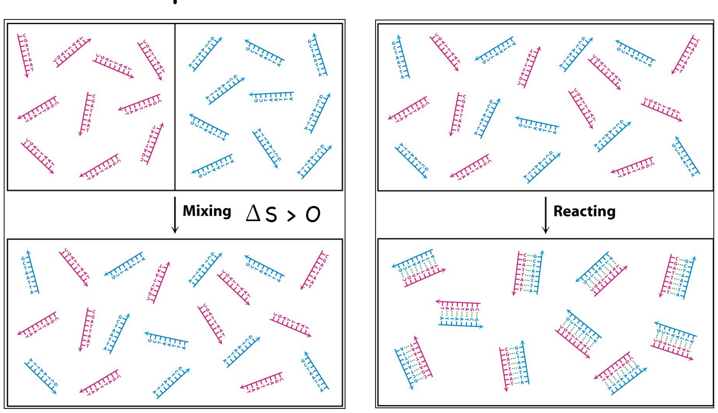
Thermodynamics

- DNA duplex formation



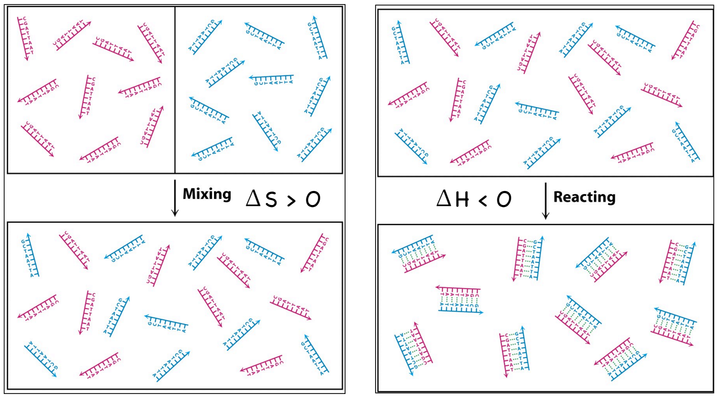
Thermodynamics

- DNA duplex formation



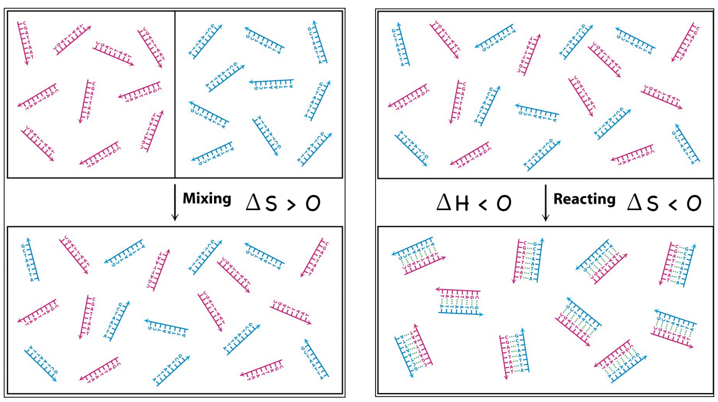
Thermodynamics

- DNA duplex formation



Thermodynamics

- DNA duplex formation



Problem

Given the following values for the changes in enthalpy (ΔH) and entropy (ΔS), which of the following processes can occur at 298 K without violating the Second Law of Thermodynamics?

A) ΔH = -84 kJ/mol and ΔS = +125 J/mol

B) ΔH = -84 kJ/mol and ΔS = -125 J/mol

C) ΔH = +84 kJ/mol and ΔS = +125 J/mol

D) ΔH = +84 kJ/mol and ΔS = -125 J/mol

$$\Delta G_{system} = \Delta H_{system} - T\Delta S_{system}$$

Looking ahead to Monday, 10. Sept.

- Acids and Bases
- The genomic revolution
- Protein Structure
- **Question of the Day:** This week, big news was made in the field of genomic. It was not only reported in the journals Nature and Science, but was also picked up by the New York Times and the Eau Claire Leader-Telegram. What was this news?