Example

The optimum distance for the van der Waals interaction between two carbonyl oxygen atoms is \( r_0 = 0.353 \) nm. The energy for this interaction is -20.78 kJ/mol.

- (a) Derive the force function for the van der Waals interaction \( F_{vdw}(r) \) between two carbonyl oxygen atoms, and compare \( F_{vdw}(r) \) at \( r = 0.3 \) nm, and \( r = 0.4 \) nm. Discuss whether the force is attractive or repulsive at the two distances.
- (b) Estimate the repulsive parameter A and dispersion parameter B for the Lennard-Jones 6-12 potential. Calculate the energy at \( r = 0.4 \) nm, using the parameters.

The environment in cell

- Hydrophilic/hydrophobic environment
- Hydrophilicity and hydrophobicity
- Amphiphilic molecules

Hydrophilic: “water loving”

Hydrophilic forces:
- Electrostatic
- Polar-polar
- Hydrogen bond...
- Molecules contain O, S, N,...
- Or certain Charged, or polar groups
- The strong interaction between the charged ions and polar water. — Energy gain.

NaCl → Na\(^+\) Cl\(^-\)
Water and dye molecules mix well-
Entropy increases (more chaotic)

The environment in cell:
- The structure of macromolecules is strongly
  influenced by their surrounding environment.
- The mass of a cell: 70% Water- biological
  systems-Primarily as aqueous solutions.

Attention:
- H₂O can be part of a solvent to
dissolve NaCl → Na⁺ + Cl⁻
- H₂O can be part of a macromolecule
  (mediating the interaction between
  protein and DNA)

Hydrophobic forces:
- Van der Waals
- steric
- Configurational...
Molecules contain H, C,... non-polar
groups
The environment in cell: **Bio-membrane**

Amphipathic (Amphophilic) Molecules

As amphiphilic molecules, proteins will tend to assemble at the interface. Based on the Gibbs equation:

\[ \Gamma = \frac{1}{R} \frac{\partial G}{\partial n} \]

where \( \Gamma \) is the surface excess of protein at the interface, \( G \) is the free energy of the system in a dilute solution, \( R \) is the gas constant, and \( T \) the absolute temperature, the adsorption or assembly of protein at the air/water interface is directly related to the surface activity of the protein.

**Membrane Protein Diversity**

Channel Protein: Selectively transports a specific molecule or ion over the membrane.

Carrier Protein: Transporters carry a specific molecule or ion across the membrane.

Receptor Protein: Recognizes a specific molecule or ion and triggers a response.

Cell Recognition: Molecules on the cell surface that interact with other cells.

**Types of Transport: Active vs. Passive**

- **Plasma membrane is differentially (selectively) permeable**
  - Allows some material to pass
  - Inhibits passage of other materials

- **Passive Transport**
  - No ATP requirement
  - Molecules follow concentration gradient

- **Active Transport**
  - Requires carrier protein
  - Requires energy in form of ATP
The environment in cell: Non aqueous Environment of Biological Molecules

- A measure of the energy of single charges in a particular medium is its self-energy $E_s$, the energy of a charge in the absence of its counter ion.
  - $E_s = \frac{q^2}{2Dr_s}$
- $r_s$: Stoke's radius-the radius of charge distribution
- $D$: Dielectric const.

The environment in the cell: Non aqueous Environment of Biological Molecules

- $r_s$: a charge distributed over a larger ion or molecule has a lower $E_s$ than an ideal point charge
- ($\mathcal{D} \propto \varepsilon$) Water $\varepsilon \approx 80$; membrane layer $\varepsilon \approx 2-4$, 40-fold lower than in an aqueous solution. The energy of singly charged ions in a lipid bilayer is significantly (40 times) higher than in aqueous solution.
- Lipid membranes are highly efficient barriers against the passage of charged or highly polar molecules, why?

Amphipathic Molecules

What about nucleic acids?

- Answer: Both, amphipathic
- Nucleic acids: hydrophobic bases and negative charged phosphates.
The environment in the cell: Amphiphatic (Amphiphilic) Molecules

- Protein: polypeptide / Amino acid chain
- Some amino acid groups (-R) in a protein are hydrophobic (no charge and non-polar) some are hydrophilic (polar/charged).
- Protein: partially hydrophobic and partially hydrophilic.

Assembly/aggregation

The environment in the cell: Nonaqueous Environment of Biological Molecules

- The interior of a globule protein
  - It is difficult to bury a charge in the interior of a globular protein due to the hydrophobic environment.
  - To estimate the effect of the self energy of amino acids in solution as opposed to being buried in the interior of a protein.
  - De-association constant change. (The large $pK_a$, the easier the de-association will be.)

$$\Delta pK_a = \Delta E_s / 2.303 k_B T$$

$A^+ B^- \rightarrow A^+ B$

The environment in the cell: Nonaqueous Environment of Biological Molecules

- The secondary and the tertiary structures of biomacromolecules are stabilized by hydrogen bond. The hydrophilic environment will dissociate hydrogen bond while the hydrophobic environment will promote the formation of hydrogen bond.
The environment in the cell: Nonaqueous Environment of Biological Molecules

To predict: charged or uncharged.
- A lysine positively charged (protonated) $pK_a = 9$, in water
- $r_s = 0.6 \text{nm}$; in the interior of a protein, $D = 3.5 \kappa e_0$
- From water to the interior: $\Delta E_s = -40 \text{kJ/mol}$.
- $pK_a < 1 \rightarrow$ a lysine buried in the hydrophobic core of a globular protein should be uncharged or it should pair up with a counterion.

Biologically important molecules-
DNA

Biologically important molecules-
DNA

From Gene to An Organism…

- Within the cell – in chromosomes Each very long DNA molecule (~ meters long) is tightly packaged as a chromosome. Humans have two sets of 23 chromosomes in every cell, one set inherited from each parent. A human cell therefore contains 46 of these chromosomal DNA molecules.
From Gene to An Organism…

DNA, Chromosome, Gene, Genome:
- Each DNA molecule that forms a chromosome can be viewed as a set of shorter DNA sequences.
- These are the units of DNA function, called genes, each of which guides the production of one particular component of an organism.
- A set of human chromosomes contains one copy of each of the roughly 30,000 genes in the human “genome” - the term used to refer to the complete genetic instructions for an organism.

From Gene to An Organism…

Throughout the body - in cells...
- Our bodies are formed from between 50 and 100 trillion cells (a trillion is a thousand billion, or a thousand, thousand million).
- These cells are organized into tissues, such as skin, muscle, and bone.
- Each cell contains all of the organism's genetic instructions stored as DNA. However, each cell uses only the instructions from a part of the DNA.

From Gene to An Organism…

For example, a muscle cell uses the DNA that specifies the muscle apparatus, whereas a nerve cell uses DNA that specifies the nervous system. It is as if each cell reads only that part of a book of instructions that it needs.

One of the most important bio-molecules-DNA

- Deoxyribonucleic Acid (DNA): a double helix molecule.
- Containing genetic information, in the form of a chemical code -defining how our own bodies develop, digest food, move, and what we look like…

two- stranded, double helix
Structure of DNA

- Three components:
  - A phosphate group,
  - A pentose sugar (ribose or deoxyribose), and
  - A nitrogenous base (4 kinds in DNA, 3 kinds in RNA, 3 common to both

- Nucleotide subunits connected end-to-end to make nucleic acid
- Sugar of one connected to the phosphate of the next
- Sugar-phosphate backbone

Basic Chain (backbone): deoxyribose (5-carbon sugar) and phosphate linked by phosphatediester bond (covalent bond-strong and stable)
- What about the codes...each part of phosphatediester bond looks the same.

DNA contains:
- Two Nucleotides with purine bases
  - Adenine (A)
  - Guanine (G)
- Two Nucleotides with pyrimidine bases
  - Thymine (T)
  - Cytosine (C)

Biologically important molecules-DNA
- The sequence of A, G, C & T in the sugar chain now directs cellular products and activities...
Chargaff’s Rules

- The amounts of A, T, G, and C in DNA:
  - Identical in identical twins
  - Varies between individuals of a species
  - Varies more from species to species
- In each species, there are equal amounts of:
  - A & T
  - G & C
- All this suggests DNA uses complementary base pairing to store genetic info

Biologically important molecules-DNA

- Base-base coupling- to make coding possible:
  - (Watson-Crick) complementary pairs:
    - G – C: 3 hydrogen bonds (Much stronger)
    - A – T: 2 complementary hydrogen bonds
  - Complementary base pairing-the strongest interaction.

Watson and Crick Model

- Watson and Crick, 1953
  - Constructed a model of DNA
  - Double-helix model is similar to a twisted ladder
    - Sugar-phosphate backbones make up the sides
    - Hydrogen-bonded bases make up the rungs
  - Received a Nobel Prize in 1962

Four Classes of Organics: 4 -Nucleic Acids

- Polymers of nucleotides
- Very specific cell functions
  - DNA (deoxyribonucleic acid)
    - Double-stranded helical spiral (twisted ladder)
    - Serves as genetic information center
    - In chromosomes
  - RNA (ribonucleic acid)
    - Part single-stranded, part double-stranded
    - Serves primarily in assembly of proteins
    - In nucleus and cytoplasm of cell
Protein Synthesis:
From DNA to RNA to Protein

- The mechanism of gene expression
  - DNA in genes specify information, but information is not structure and function
  - Genetic info is expressed into structure & function through protein synthesis
- The expression of genetic info into structure & function:
  - DNA in gene controls the sequence of nucleotides in an RNA molecule
  - RNA controls the primary structure of a protein

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RNA

- RNA is a polymer of RNA nucleotides
- RNA Nucleotides are of four types: Uracil, Adenine, Cytosine, and Guanine
- Uracil (U) replaces thymine (T) of DNA
- Types of RNA
  - Messenger (mRNA) - Takes genetic message from DNA in nucleus to ribosomes in cytoplasm
  - Ribosomal (rRNA) - Makes up ribosomes which read the message in mRNA
  - Transfer (tRNA) - Transfers appropriate amino acid to ribosome when “instructed”

RNA Structure
Comparison of DNA & RNA

<table>
<thead>
<tr>
<th>Feature</th>
<th>DNA</th>
<th>RNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sugar</td>
<td>Deoxyribose</td>
<td>Ribose</td>
</tr>
<tr>
<td>Bases</td>
<td>Cytosine, guanine; adenine, thymine</td>
<td>Cytosine, guanine; adenine, uracil</td>
</tr>
<tr>
<td>Strands</td>
<td>Double-stranded; Pairing across strands</td>
<td>Mostly single stranded</td>
</tr>
<tr>
<td>Helix</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Function</td>
<td>Heredity; cellular control center</td>
<td>Interprets genetic info; protein synthesis</td>
</tr>
<tr>
<td>Where</td>
<td>Chromosomes of cell nucleus</td>
<td>Cell nucleus and cytoplasm</td>
</tr>
</tbody>
</table>

mRNA and Transcription

- tRNA molecules come in 64 different kinds
- All very similar except that
  - One end bears a specific triplet (of the 64 possible) called the anticodon
  - Other end binds with a specific amino acid type
  - tRNA synthetases attach correct amino acid to the correct tRNA molecule
- All tRNA molecules with a specific anticodon will always bind with the same amino acid

Structure of tRNA
Ribosomes

- Ribosomal RNA (rRNA):
  - Produced from a DNA template in the nucleolus
  - Combined with proteins into large and small ribosomal subunits
- A completed ribosome has three binding sites to facilitate pairing between tRNA and mRNA
  - The E (for exit) site
  - The P (for peptide) site, and
  - The A (for amino acid) site

Other Nucleic Acids

- ATP (adenosine triphosphate) is composed of adenine, ribose, and three phosphates
- In cells, one phosphate bond is hydrolyzed – Yields:
  - The molecule ADP (adenosine diphosphate)
  - An inorganic phosphate molecule $P_i$
  - Energy
- Other energy sources used to pull ADP and $P_i$ back together again

ATP
Review

- Hydrophilic/hydrophobic environment
- Hydrophilicity and hydrophobicity
- Amphiphilic molecules
- Macromolecules
- DNA and RNA structures and functions

Key Message

- van der Waals Interaction is responsible for hydrophobic interaction.
- Hydrogen bond plays a very important role in determining the intra molecules interactions and structures.
- Hydrophobic environment will be in favor of the formation of intra molecular hydrogen bond while hydrophilic environment will deteriorate the formation of H bond.
- Amphiphilic molecules tend to assemble at the surface
- **Dielectric constant \( \varepsilon \):** An environmental factor in stabilizing the conformation of a macromolecule