

The image shows the cover of a textbook chapter. The background is a vibrant green with a blurred image of leaves and water droplets. Overlaid on this is a white hexagonal grid pattern, with some hexagons containing small icons like a leaf and a recycling symbol. The title 'Foundations of Biochemistry' is written in a large, bold, black font, and '1.3 Chemical Foundations' is written below it in a smaller, bold, black font. At the bottom left is the Western Oregon University logo, which consists of a stylized torch and the text 'Western Oregon UNIVERSITY'. To the right of the logo is a small block of text: 'If you have a disability that may require some accommodation in order to participate in a WOU activity, please notify Disability Services at 503-838-8250 or ods@wou.edu at least 72 hours in advance.' At the bottom right, there is a red triangular graphic with the text 'TOGETHER WE SUCCEED' in white.

**Foundations of
Biochemistry**
1.3 Chemical Foundations

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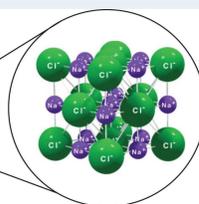
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In this section, we will explore major chemistry foundations that will help us with our discussions of biochemistry.



Intermolecular Forces

Bond Type	Dissociation Energy (kcal/mol)
Ionic Bond Lattice	250-4000 kcal/mol
Hydrogen Bond	1-12 (water H-bonds are ~5)
Other Dipole-Dipole Interactions	0.5-2
London Dispersion Forces	< 1.0



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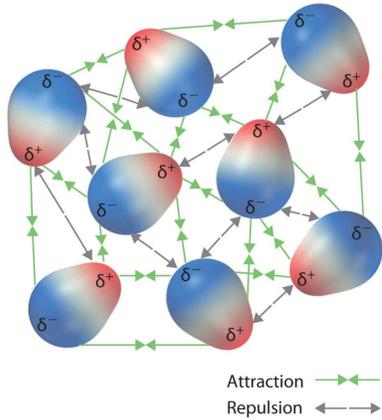
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Recall that major intermolecular forces between molecules includes ionic interactions (where fully charged ions are attracted to each other), dipole-dipole interactions (where partial charges from one molecule that have permanently formed in covalent bonds due to the unequal sharing of electron pairs are attracted to partial charges from another molecule), and London Dispersion Forces (which form from the momentary dipoles that are created in covalent bonds that share electrons more equally). Also recall that Hydrogen bonding is a special form of dipole-dipole interaction that is stronger than other common dipoles. This occurs between a partial positive charge forms on H (when it is covalently bonded to N or O in biological systems) and is attracted to a partial negative charge of an O or N atom from another molecule or bond. For a complete review of intermolecular forces, please watch the separate review video that is posted in Canvas.



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Attraction \longleftrightarrow
 Repulsion \longleftrightarrow

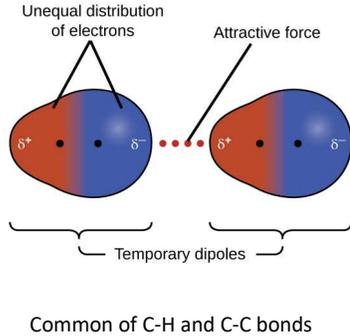
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dipole-dipole interactions (where partial charges from one molecule that have permanently formed in covalent bonds due to the unequal sharing of electron pairs are attracted to partial charges from another molecule)

 **Intermolecular Forces**

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Common of C-H and C-C bonds

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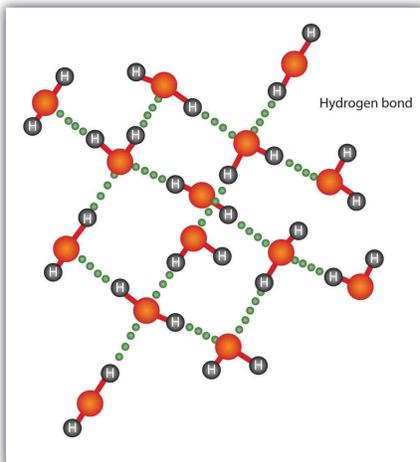
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and London Dispersion Forces (which form from the momentary dipoles that are created in covalent bonds that share electrons more equally).



Intermolecular Forces

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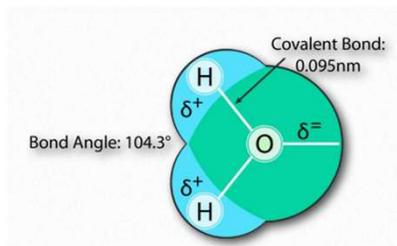
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Hydrogen bonding is a special form of dipole-dipole interaction that is stronger than other common dipoles. This occurs between a partial positive charge forms on H (when it is covalently bonded to N or O in biological systems) and is attracted to a partial negative charge of an O or N atom from another molecule or bond. For a complete review of intermolecular forces, please watch the separate review video that is posted in Canvas.



1.3 Chemical Foundations



Mixing of Water with Nonpolar Substances



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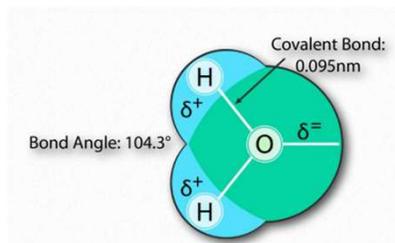
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Let's consider mixing a hydrophilic molecule (water) with permanent hydrogen bonding dipoles and a hydrophobic molecule (oil) that only has London Dispersion Forces.



1.3 Chemical Foundations



Mixing of Water with Nonpolar Substances

$$\Delta G = \Delta H - T\Delta S$$



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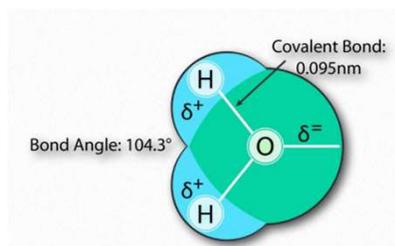
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The non-polar molecules of the oil don't really interact with water. They are not strong enough to disrupt the normal hydrogen bonding of the water. In fact, around each non-polar molecule, water gets very organized, aligning itself regularly. This would cause entropy to decrease, causing the Temperature Delta S term of the Gibb's free energy equation to become positive (a negative of a negative)



1.3 Chemical Foundations



Mixing of Water with Nonpolar Substances

$$\Delta G = \Delta H - T\Delta S$$



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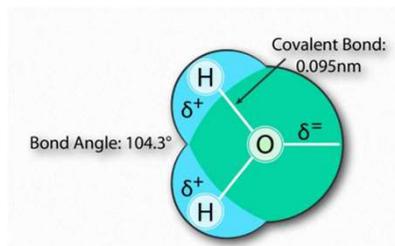
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Since mixing a non-polar substance with water doesn't generally have any significant heat component, the overall ΔG is positive. This means, then, that dissolving a non-polar compound in water is not favorable and does not occur to any significant extent. The oil stays separated from the water.



1.3 Chemical Foundations



Mixing of Water with Nonpolar Substances



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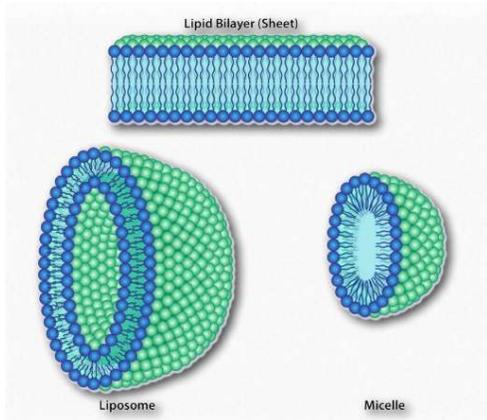
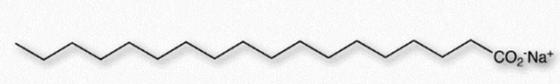
Further, when the nonpolar material associates with itself and not water, then the water molecules are free to mix, without being ordered, resulting in an increase of entropy. Entropy therefore drives the separation of nonpolar substances from aqueous solutions.



Mixing Water with Amphipathic Molecules

Soap ions arrange themselves into micelles

Biological phospholipids form a lipid bilayer

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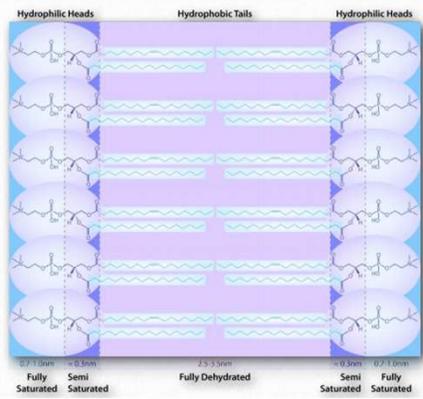
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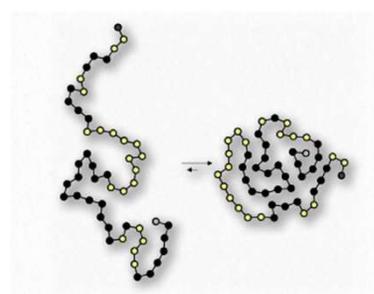
Since we know fatty acids dissolve in water, there must be something else at play. There is. Just like the nonpolar molecules in the first example associated with each other and not water, so too do the non-polar portions of the soap ions associate with each other and exclude water. The result is that the soap ions arrange themselves as micelles

 Water is important in the shape of Biological molecules

Lipid Bilayer



Protein Folding



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Interactions with water also help to drive the formation of lipid bilayers and the folding of proteins and other biological molecules.

Hydrogen Bonding

Between a Proton of a Hydroxide and the Oxygen of Water

Between Oxygen of Water and the Proton of an Amine

Between a Proton on Water and a Carbonyl Group

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The importance of hydrogen bonds in biochemistry is hard to overstate. Linus Pauling himself said,

“ . . . I believe that as the methods of structural chemistry are further applied to physiological problems it will be found that the significance of the hydrogen bond for physiology is greater than that of any other single structural feature.”

We are after all about 70% water! In the body, it forms the biological solvent in which all molecules must move through.



Buffers in Biological Systems

Weak Acid pKa Values

Name	Chemical Structure of Acid	Chemical Structure of Salt	pKa
Acetic Acid	CH ₃ COOH	CH ₃ COO ⁻	4.76
Formic Acid	HCOOH	HCOO ⁻	3.75
Lactic Acid	CH ₃ CHOHCOOH	CH ₃ CH(OH)COO ⁻	3.86
Pyruvic Acid	CH ₃ COCOOH	CH ₃ C(O)COO ⁻	2.50
Oxalic Acid (1)	HOOC—COOH	HOOC—COO ⁻	1.23
Oxalic Acid (2)	HOOC—COO ⁻	OOCCOO ⁻	4.19
Carbonic Acid (1)	H ₂ CO ₃	HCO ₃ ⁻	6.37
Carbonic Acid (2)	HCO ₃ ⁻	CO ₃ ²⁻	10.20
Malic Acid (1)	HOOC—CH ₂ —CHOH—COOH	HOOC—CH ₂ —CHOH—COO ⁻	3.40
Malic Acid (2)	HOOC—CH ₂ —CHOH—COO ⁻	OOCC—CH ₂ —CHOH—COO ⁻	5.26
Malonic Acid (1)	HOOC—CH ₂ —COOH	HOOC—CH ₂ —COO ⁻	2.83
Malonic Acid (2)	HOOC—CH ₂ —COO ⁻	OOCC—CH ₂ —COO ⁻	5.69
Phosphoric Acid (1)	H ₃ PO ₄	H ₂ PO ₄ ⁻	2.14
Phosphoric Acid (2)	H ₂ PO ₄ ⁻	HPO ₄ ²⁻	7.20
Phosphoric Acid (3)	HPO ₄ ²⁻	PO ₄ ³⁻	12.40
Succinic Acid (1)	HOOC—CH ₂ —CH ₂ —COOH	HOOC—CH ₂ —CH ₂ —COO ⁻	4.21
Succinic Acid (2)	HOOC—CH ₂ —CH ₂ —COO ⁻	OOCC—CH ₂ —CH ₂ —COO ⁻	5.63

- $\text{pH} = -\text{Log}[\text{H}^+]$
- $\text{pOH} = -\text{Log}[\text{OH}^-]$
- $\text{pH} + \text{pOH} = 14$



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Water can ionize to a slight extent (10^{-7} M) to form H^+ (proton) and OH^- (hydroxide). We measure the proton concentration of a solution with pH, which is the negative log of the proton concentration. If the proton concentration, $[\text{H}^+] = 10^{-7}$ M, then the pH is 7. We could just as easily measure the hydroxide concentration with the pOH by the parallel equation, In pure water, dissociation of a proton simultaneously creates a hydroxide, so the pOH of pure water is 7, as well. This also means that $\text{pH} + \text{pOH} = 14$. The presence of acids or bases within a solution, can therefore have profound effects on the pH of a system. Thus, the importance of buffers within biological systems that can stabilize solution pH is critical for maintaining life. Within biological systems, weak acids often behave as this buffering system.



Calculating pH Change

$$\text{HA} \rightleftharpoons \text{H}^+ + \text{A}^-$$

Acid
Salt

pH = pKa + log ([Ac⁻]/[HAc])

Clearing Confusion - Students are often puzzled and expect that

$[\text{H}^+] = [\text{A}^-]$

because the dissociation equation shows one of each from HA. This is, in fact, true ONLY when HA is allowed to dissociate in pure water. Usually the HA is placed into solution that has protons and hydroxides to affect things. Those protons and /or hydroxides change the H⁺ and A⁻ concentration unequally, since A⁻ can absorb some of the protons and/or HA can release H⁺ when influenced by the OH⁻ in the solution. Therefore, one must calculate the proton concentration from the pH using the Henderson Hasselbalch equation.

$\text{pH} = \text{pK}_a + \log ([\text{Ac}^-]/[\text{HAc}])$



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pKa

For a general acid, HA, which dissociates as

$$\text{HA} \rightleftharpoons \text{H}^+ + \text{A}^-$$

then,

$$K_a = \frac{[\text{H}^+][\text{A}^-]}{[\text{HA}]}$$

and

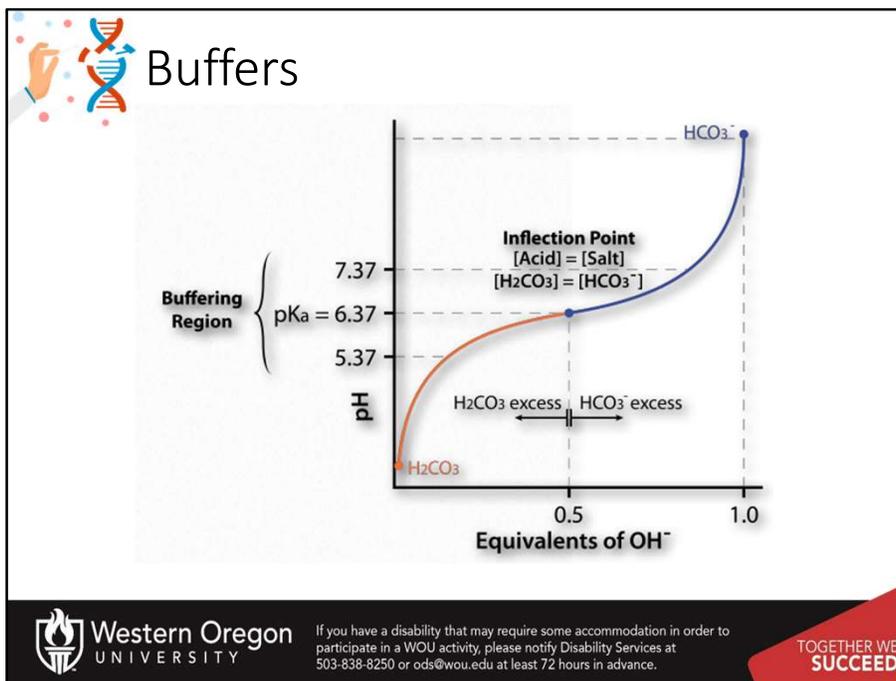
$$\text{pKa} = -\text{Log } K_a$$

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Recall that the ***K_a is the acid dissociation constant*** and is a measure of the strength of an acid. For a general acid, HA, which dissociates as HA to H⁺ and the conjugate base, then the K_a is equal to the concentration of the products of the dissociated acid over the reactants (or concentration of acid). Thus, the stronger the acid, the more protons that will dissociate from it when added to water and the larger the value its K_a will have. Large values of K_a translate to lower values of pK_a. As a result, the lower the pK_a value is for a given acid, the stronger the acid.



Let's get back to buffers! A **buffer** is a solution that can resist pH change upon the addition of an acidic or basic components. It is able to neutralize small amounts of added acid or base, thus maintaining the pH of the solution relatively stable. It is essentially a substance that can act as both an acid or a base depending on the circumstances. This is important for processes and/or reactions which require specific and stable pH ranges. In biological systems, maintaining pH values is critical for maintaining life. The normal physiological pH of mammalian arterial blood is strictly maintained at 7.40; A decrease of more than 0.05 units from the normal pH results in acidosis.

Now, how does this translate into stabilizing pH? Figure 1.34 shows a titration curve. In this curve, the titration begins with the conditions at the lower left (very low pH). At this pH, the H_2CO_3 form predominates, but as more and more OH^- is added the pH goes up, the amount of HCO_3^- goes up and (correspondingly), the amount of H_2CO_3 goes down. Notice that the curve "flattens" near the pKa (6.37).

Flattening of the curve tells us is that the pH is not changing much (not going up as fast) as it did earlier when the same amount of hydroxide was added. The system is resisting a change in pH (not stopping the change, but slowing it) in the region of about one pH unit above and one pH unit below the pKa. Thus, the buffering region of the carbonic acid/bicarbonate buffer is from about 5.37 to 7.37. It is maximally strong at a pH of 6.37.

This is consistent with the Henderson Hasselbalch equation and the titration curve. If a buffer has more than one pKa, then each pKa region will display the behavior.



Organic Functional Groups

- Name common ones
- Identify them from structures
- Understand biological reactions for common ones, especially the carboxylic acid series of reactions.



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Another key chemistry area that you will need to review is basic organic chemistry, as all biological molecules are organic in nature. Thus, it is very useful to have good working vocabulary for naming common organic functional groups, being able to identify these groups from larger molecular structures, and understanding the common reactions for the major functional groups, especially the reactivity of carboxylic acids and amines

	alkane	$\begin{array}{c} \text{H} & \text{H} \\ & \\ \text{H}-\text{C}-\text{C}-\text{H} \\ & \\ \text{H} & \text{H} \end{array}$	ketone	$\begin{array}{c} \text{O} \\ \\ \text{H}_3\text{C}-\text{C}-\text{CH}_3 \end{array}$
	alkene	$\begin{array}{c} \text{H} & & \text{H} \\ & \backslash & / \\ & \text{C}=\text{C} \\ & / & \backslash \\ \text{H} & & \text{H} \end{array}$	aldehyde	$\begin{array}{c} \text{O} \\ \\ \text{H}_3\text{C}-\text{C}-\text{H} \end{array}$
	alkyne	$\text{H}-\text{C}\equiv\text{C}-\text{H}$	carboxylic acid	$\begin{array}{c} \text{O} \\ \\ \text{H}_3\text{C}-\text{C}-\text{OH} \end{array}$
	aromatic		ester	$\begin{array}{c} \text{O} \\ \\ \text{H}_3\text{C}-\text{C}-\text{O}-\text{CH}_3 \end{array}$
	alkyl halide	$\begin{array}{c} \text{H} \\ \\ \text{H}-\text{C}-\text{Cl} \\ \\ \text{H} \end{array}$	amide	$\begin{array}{c} \text{O} \\ \\ \text{H}_3\text{C}-\text{C}-\text{N}-\text{CH}_3 \\ \\ \text{H} \end{array}$



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You should be able to identify the major functional groups on these next two slides....



alcohol	$\begin{array}{c} \text{H} \\ \\ \text{H}_3\text{C}-\text{C}-\text{OH} \\ \\ \text{H} \end{array}$	thioester	$\begin{array}{c} \text{O} \\ \\ \text{H}_3\text{C}-\text{C}-\text{S}-\text{CH}_3 \end{array}$
thiol	$\begin{array}{c} \text{H} \\ \\ \text{H}_3\text{C}-\text{C}-\text{SH} \\ \\ \text{H} \end{array}$	acyl phosphate	$\begin{array}{c} \text{O} \\ \\ \text{H}_3\text{C}-\text{C}-\text{O}-\text{P}(\text{O})_2\text{O}^- \end{array}$
amine	$\begin{array}{c} \text{H} \\ \\ \text{H}_3\text{C}-\text{C}-\text{NH}_2 \\ \\ \text{H} \end{array}$	acid chloride	$\begin{array}{c} \text{O} \\ \\ \text{H}_3\text{C}-\text{C}-\text{Cl} \end{array}$
ether	$\text{H}_3\text{C}-\text{O}-\text{CH}_3$	phosphate monoester	$\begin{array}{c} \text{O} \\ \\ \text{O}^--\text{P}-\text{OCH}_3 \\ \\ \text{O}^- \end{array}$
thioether	$\text{H}_3\text{C}-\text{S}-\text{CH}_3$	phosphate diester	$\begin{array}{c} \text{O} \\ \\ \text{O}^--\text{P}-\text{OCH}_3 \\ \\ \text{OCH}_3 \end{array}$
phenol		nitrile	$\text{R}-\text{C}\equiv\text{N}$

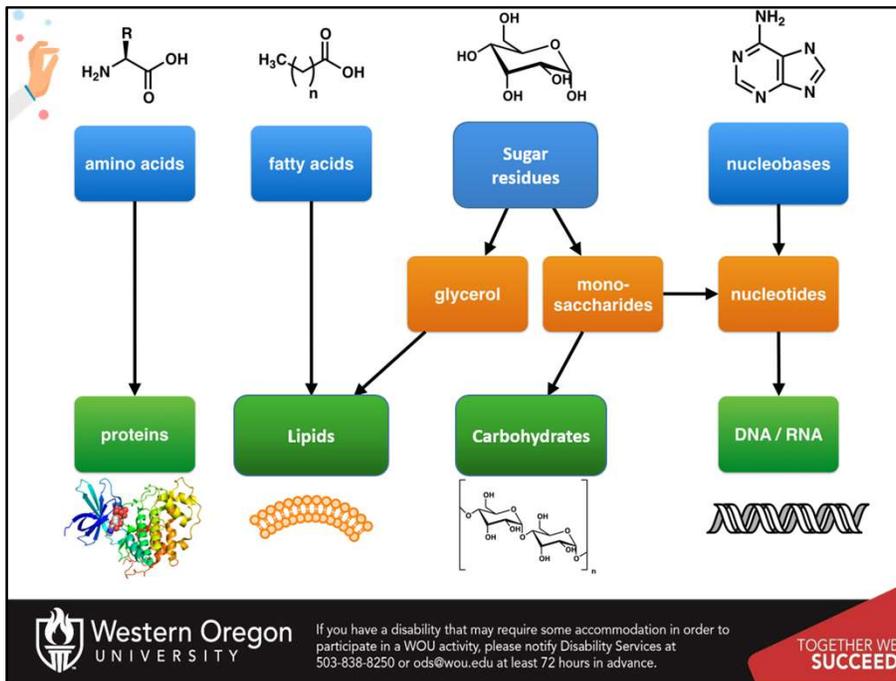


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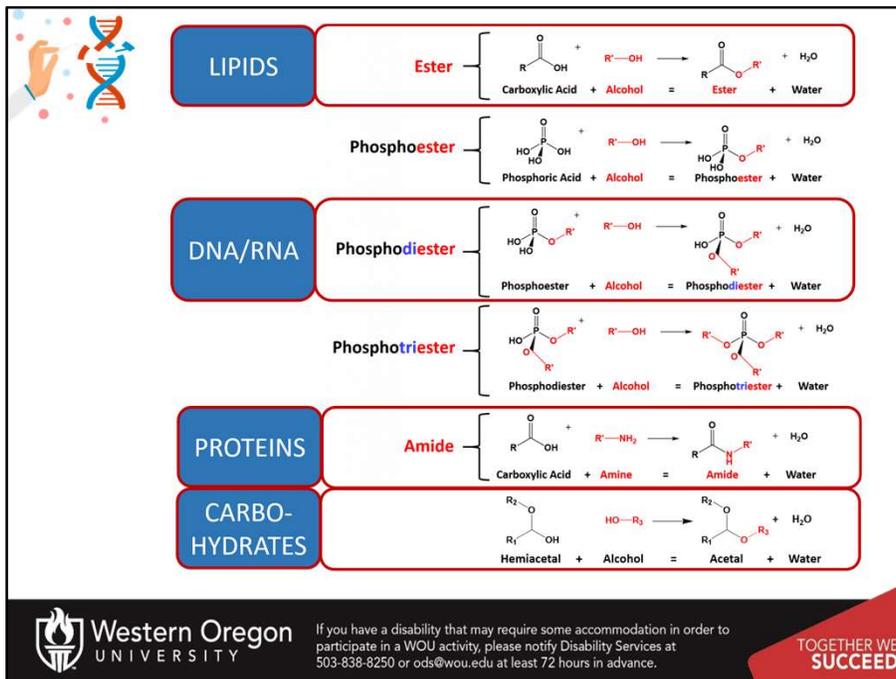
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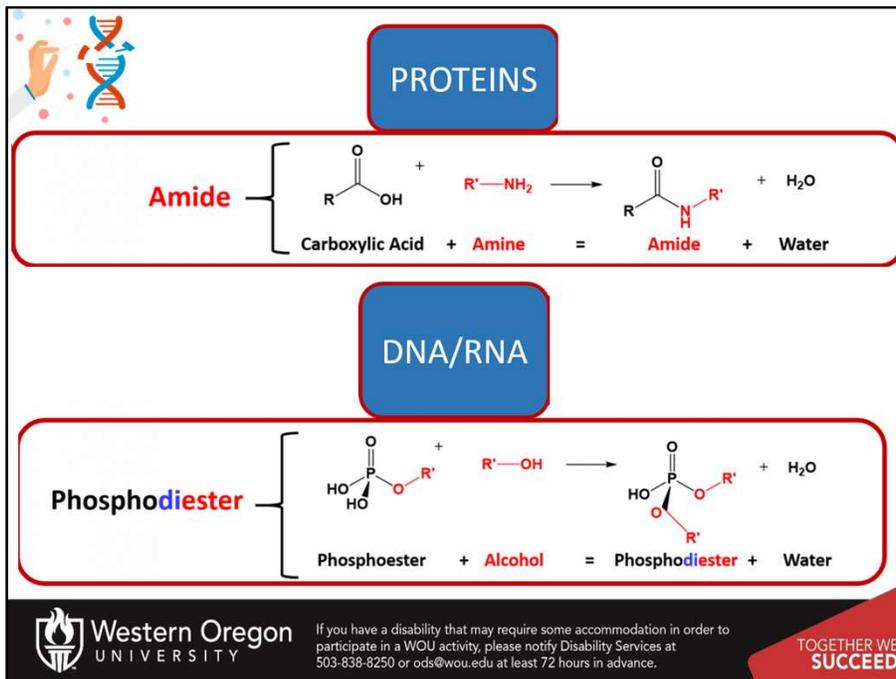
Nitriles are rare and are the least important.



All of the major macromolecules are put together using dehydration synthesis. The two major macromolecules that we will focus on this term are proteins and nucleic acids (DNA & RNA).



The major dehydration synthesis reactions for each of the major macromolecules is noted here. They are all related to the formation of an ester bond, with the loss of the hydroxyl from the carboxylic acid functional group and a proton from the alcohol donor in this case. The oxygen from the alcohol mediates attack on the carbonyl carbon and the alcohol functional group of the carboxylic acid is displaced to form the water molecule. This reaction requires the activity of an enzyme.



For proteins and nucleic acids, the reactions are similar, however, in the case of proteins the amine nitrogen mediates the attack at the carbonyl carbon of the carboxylic acid to displace the alcohol from the carboxylic acid and release the water molecule. This forms an amide linkage between the two amino acids. For nucleic acids, phosphoric acid functional groups are used instead of carboxylic acids which will form the phosphoester linkages inherent to the DNA and RNA backbones. Two phosphoester linkages (a phosphodiester) are required to link two nucleotides together. In the next section, we will discuss the foundations of evolution and genetics, before we begin to explore biochemistry in detail.