8: Functional Groups

Functional Groups

A functional group is a specific group of atoms within a molecule that is responsible for a characteristic of that molecule. Many biologically active molecules contain one or more functional groups. In Bis2a we will discuss the major functional groups found in biological molecules. These include: Hydroxyl, Methyl, Carboxyl, Carbonyl, Amino and Phosphate.

The functional groups shown here are found in many different biological molecules. "R" represents any other atom or extension of the molecule. The charges discussed, but not depicted, here at are pH 7. Attribution: Marc T. Facciotti
A functional group may participate in a variety of chemical reactions. Some of the important functional groups in biological molecules are shown above; they include: hydroxyl, methyl, carbonyl, carboxyl, amino, phosphate, and sulfhydryl (R-S-H). These groups play an important role in the formation of molecules like DNA, proteins, carbohydrates, and lipids. Functional groups can sometimes be classified as having polar or non-polar properties depending on their atomic composition and organization. The term polar describes something that has a property that is not symmetric about it - it can have different poles (more or less of something at different places). In the case of bonds and molecules, the property we care about is usually the distribution of electrons and therefore electric charge between the atoms. In nonpolar bonds or molecules electrons and charge will be relatively evenly distributed. In a polar bond or molecule, electrons will tend to be more concentrated in some areas than others. An example of a nonpolar group is the methyl group (see discussion in Atoms to Bonds for more detail). Among the polar functional groups is the carboxyl group found in amino acids, some amino acid side chains, and the fatty acids that form triglycerides and phospholipids.

### Non-Polar Functional Groups

#### Methyl R-CH₃

The methyl group is the only non-polar functional group in our class list above. The methyl group consists of a carbon atom bound to 3 hydrogen atoms. In this class we will treat these C-H bonds as effectively nonpolar covalent bonds. This means that methyl groups are unable to form hydrogen bonds and will not interact with polar compounds such as water.
The amino acid isoleucine on the left and cholesterol on the right. Each has a methyl group circled in red.

Attribution: Created by Marc T. Facciotti (Own work adapted from Erin Easlon)

The methyl groups highlighted above are found in a variety of biologically relevant compounds. In some cases, the compound can have a methyl group but still be a polar compound overall due to the presence of other functional groups with polar properties (see Polar Functional Groups discussed below).

As we learn more about other functional groups, we will add to the list of non-polar functional groups. Stay alert!

Polar Functional Groups
Hydroxyl R-OH

A hydroxyl (alcohol group) is an –OH group covalently bonded to a carbon atom. The oxygen atom is much more electronegative than either the hydrogen or the carbon, which will cause the electrons in the covalent bonds to spend more time around the oxygen than around the C or H. Therefore, the O-H and O-C bonds in the hydroxyl group will be polar covalent bonds. The figure below depict the partial charges $\delta^+$ and $\delta^-$ associated with hydroxyl group.
The hydroxyl functional group shown here consists of an oxygen atom bound to a carbon atom and a hydrogen atom. These bonds are polar covalent, meaning the electron involved in forming the bonds are not shared equally between the C-O and
O-H bonds.

Attribution: Created Marc T. Facciotti (Own work)

The hydroxyl functional groups can form hydrogen bonds, shown as a dotted line. The hydrogen bond will form between the $\delta^-$ of the oxygen atom and a $\delta^+$ of the hydrogen atom. Dipoles shown in blue arrows. Attribution: Marc T. Facciotti (original work)

Hydroxyl groups are very common in biological molecules. Hydroxyl groups appear on carbohydrates (A), on the R-groups of some amino acids (B), and on nucleic acids (C). Can you find any hydroxyl groups in the phospholipid in (D)?
Hydroxyl groups appear on carbohydrates (A glucose), on some amino acids (B Serine), and on nucleotides (C Adenosine triphosphate). D is a phospholipid.

**Carboxyl R-COOH**

Carboxylic acid is a combination of a carbonyl group and a hydroxyl group attached to the same carbon, resulting in new characteristics. The carboxyl group can ionize, which means it can act as an acid and release the hydrogen atom from the hydroxyl group as a free proton (H⁺). This results in a delocalized negative charge on the remaining oxygen atoms. Carboxyl groups can switch back and forth between protonated (R-COOH) and deprotonated (R-COO⁻) states depending on the pH of the solution.

The carboxyl group is very versatile. In its protonated state, it can form hydrogen bonds with other polar compounds. In its deprotonated states, it can form ionic bonds with other positively charged compounds. This will have several biological consequences that will be explored more when we discuss enzymes.

Can you identify all the carboxyl groups on the macromolecules shown above?

**Amino R-NH₃**

The amino group consists of a nitrogen atom attached by single bonds to hydrogen atoms. An organic compound that contains an amino group is called an amine. Like oxygen, nitrogen is also more electronegative than both carbon and hydrogen which results in the amino group displaying some polar character.

Amino groups can also act as bases, which means that the nitrogen atom can bond to a fourth hydrogen atom as shown in the image below. Once this occurs, the nitrogen atom gains a positive charge and can now participate in ionic bonds.
The amine functional group can exist in a deprotonated or protonated state. When protonated the nitrogen atom is bound to three hydrogen atoms and has a positive charge. The deprotonated form of this group is neutral.

Attribution: Created Erin Easlon (Own work)

**Phosphate R-PO₄⁻**

A phosphate group is an phosphorus atom covalently bound to 4 oxygen atoms and contains one P=O bond and three P-O⁻ bonds. The oxygen atoms are more electronegative than the phosphorous atom resulting in polar covalent bonds. Therefore these oxygen atoms are able to form hydrogen bonds with nearby hydrogen atoms that also have a δ⁺ (hydrogen atoms bound to another electronegative atom). Phosphate groups also contain a negative charge and can participate in ionic bonds.

Phosphate groups are common in nucleic acids and on phospholipids (the term "phospho" referring to the phosphate group on the lipid). Below are images of a nucleotide monophosphate(A) and a phosphoserine (B).

A nucleotide on the left and phosphoserine on the right. Each has a phosphate group circled in red. Attribution: Created by Marc T. Facciotti (Own work)

**Water**

Water is a unique substance whose special properties are intimately tied to the processes of life. Life originally evolved in a watery environment, and most of an organism's cellular chemistry and metabolism occur inside the water-solvated contents of the cell. Water solvates or "wets" the cell and the molecules in it, plays a key role as reactant or product in innumerable number of biochemical reactions, and mediates the interactions between molecules in and out of the cell. Many of water's important properties derive from the molecule's polar nature induced by the polar covalent bonds between hydrogen and oxygen, combined with the fact that these bonds are at an angle, resulting in a net dipole from the more O-rich pole to the more H rich pole of the molecule. In contrast, in CO₂ the bonds between O and C are polar, but there
is no net dipole (asymmetry of charge) from one end of the molecule to the other, because the bonds extend at and 180° angle from each other (O=C=O). Thus CO₂ is not a polar molecule, even though it has polar bonds.

In Bis2a, the ubiquitous role of water in nearly all biological processes is easy to overlook by getting caught up in the details of specific processes, proteins, the roles of nucleic acids, and in your excitement for molecular machines (it'll happen). However water plays key roles in all of those processes and we will need to continuously stay aware of the role that water is playing if we are to develop a better functional understanding. Be on the lookout and also pay attention when your instructor points this out.

In a liquid state, individual water molecules interact with one another through a network of dynamic hydrogen bonds that are constantly forming and breaking (H bonds are relatively weak bonds). Water also interacts with other molecules that have charged functional groups and/or functional groups with hydrogen bond donors or acceptors. A substance with sufficient polar or charged character may dissolve or be highly miscible in water is referred to as being hydrophilic (hydro- = “water”; -philic = “loving”). By contrast, molecules with more non-polar character such as oils and fats do not interact well with water and separate from it rather than dissolve in it, as we see in salad dressings containing oil and vinegar (an acidic water solution). These nonpolar compounds are called hydrophobic (hydro- = “water”; -phobic = “fearing”). We will consider the some of the energetic components of these types of reactions in other another chapter.

Water's Solvent Properties

Since water is a polar molecule with slightly positive and slightly negative charges, ions and polar molecules can readily...
dissolve in it. Therefore, water is referred to as a solvent, a substance capable of dissolving other polar molecules and ionic compounds. The charges associated with these molecules will form hydrogen bonds with water, surrounding the particle with water molecules. This is referred to as a sphere of hydration, or a hydration shell and serves to keep the particles separated or dispersed in the water.

When ionic compounds are added to water, the individual ions interact with the polar regions of the water molecules and the ionic bonds are likely disrupted in the process called dissociation. Dissociation occurs when atoms or groups of atoms break off from molecules and form ions. Consider table salt (NaCl, or sodium chloride). When dry, a block of NaCl is held together by ionic bonds and it is difficult to dissociate. When NaCl crystals are added to water, however, the molecules of NaCl dissociate into Na\(^+\) and Cl\(^-\) ions, and spheres of hydration form around the ions. The positively charged sodium ion is surrounded by the partially negative charge of the water molecule’s oxygen. The negatively charged chloride ion is surrounded by the partially positive charge of the hydrogen on the water molecule. One may imagine a model in which the ionic bonds in the crystal are “traded” for many smaller scale ionic bonds with the polar groups on water molecules.

When table salt (NaCl) is mixed in water, spheres of hydration are formed around the ions. This figure depicts a sodium ion (dark blue sphere) and a chloride ion (light blue sphere) solvated in a "sea" of water. Note how the dipoles of the water molecules surrounding the ions are aligned such that complementary charges/partial charges are associating with one another (i.e. the partial positive charges on the water molecules align with the negative chloride ion whereas the partial negative charges on the oxygen of water align with the positively charged sodium ion. Attribution: Ting Wang - UC Davis (original work modified by Marc T. Facciotti)

Note: Possible discussion

Consider the model of water dissolving a salt crystal presented above. Describe in your own words how this model can be used to explain what is happening at the molecular level when enough salt is added to a volume of water that the salt no longer dissolves (the solution reaches saturation). Work together to craft a common picture.