RES.TLL-004 STEM Concept Videos, Fall 2013

Transcript ï Chirality

Have you ever wondered why the word Ambulance is printed as its mirror image on the front an Ambulance truck? The word is written this way so that drivers can read the word in their rearview mirror signaling them to pull over if necessary. In chemistry and biology, molecules can also be mirror image of each other and have very different functions.

This video is part of the Structure-Function-Properties video series. The structure, function and properties of a system are related and depend on the processes that define or create the system.

Hi, my name is Brad Pentelute, and I am a professor of chemistry at MIT. My research focuses on the biological properties of mirror-image proteins and how these macromolecules may be used in pharmaceutical applications and therapeutics.

Before watching this video, you should be familiar with: Molecular Geometry, the structure of the 20 naturally occurring amino acids, as well as have an understanding of what a protein is and its three-dimensional structure

After watching this video, you will be able to:

1. Identify chiral objects and molecules.
2. Understand how chirality plays a role in the function of biological compounds.

Let's begin by talking about chirality. In this video, you'll see that chirality is an important feature in biological molecules because molecular structure is often closely related to biological function.

A molecule is chiral if it is not superimposable with its mirror image. But, before we talk about chirality in molecules, let's first look at a couple of ordinary objects to learn exactly what we mean by the term, chirality.

Let's look at a common example of chirality in this left and right glove. Gloves are mirror images of one another. The gloves look identical but we know from experience that they are not the same. They have different shapes. One fits only your left hand and the other fits only your right hand. If we try to lay the right glove on top of the left glove and align their key features, we see that they are not superimposable at all. Because left and right gloves are non-superimposable mirror images, we can say that gloves are chiral. Are there other objects that you can think of that are chiral? Please pause the video here to think of a few examples.

You may have suggested such objects as your left or right ears, a drinking fountain, or a screw.

Let's look at this airplane. Is it chiral? If we take the airplane and compare it to its mirror image, we can see that the two images are identical and are superimposable. Therefore, the airplane is not chiral. Can you describe what characteristic of the airplane makes it achiral? Please pause the video and give a possible answer.

There is a plane of symmetry through the center of the airplane itself. If one half of an object can be reflected onto its other half, then the object is never chiral. Can you think of another object with an internal plane of symmetry? Please pause the video and try to think of other achiral objects and where the internal plane of symmetry would be.

Objects such as a chair, a drinking glass, and a fork have an internal plane of symmetry and hence are achiral. The planes of symmetry are here, here, and here.
Notice that there is no way to divide a right-handed glove into two equal halves, which is why the glove is chiral.

Finally, another everyday object that I want to show you is this fan. First, let's think. Do you think a fan is chiral? Please pause the video and discuss this with a friend.

Is the fan chiral? Yes, it is. Each blade is hung with a tilt that makes the fan chiral! The function of the tilted blades pushes air forward to create a wind chill effect to cool you. However, the tilted blades also cause the fan to be non-superimposable with its mirror image. As you can see, the mirror image has blades that tilt in the opposite direction.
All objects can be classified as chiral or achiral, including molecules.

As with objects, a molecule is chiral if it is non-superimposable with its mirror image. The mirror image of a chiral molecule is called its enantiomer. Enantio is Greek for opposite and the term enantiomer describes the relationship between the two molecules.

Enantiomers have identical molecular formulas and have the same chemical connectivity but differ in the three-dimensional spatial arrangement of the atoms in the molecule.

Let's look at this model of the molecule, bromo-chloro-iodo methane. The green ball represents a chlorine atom, the orange ball represents a bromine atom, the purple ball represents an iodine atom and the white ball represents a hydrogen atom.

If we take our molecule and hold it in front of a mirror, we see the molecule and its image in the mirror. But, now let's look at 3-D models of both our original molecule and its mirror image. We see that the two are not superimposable, regardless of how one rotates the molecules. Hence, this tells us that bromo-chloro-iodo methane is a chiral molecule.

A quick way to know if a molecule is chiral is to check and see if it has a chiral center. A chiral center is a tetrahedral atom attached to four different atoms or groups. The tetrahedral atom is usually carbon.

Let's make a model of the organic compound, 2-chlorobutane. The number 2 in front of the compound name means that chlorine is on the second carbon atom. This carbon is attached to four different groups, chlorine, hydrogen, a -CH3 group and a
-CH2CH3 group and that means that it's a chiral center.
What would happen to the chirality of this compound if we substituted the hydrogen atom with a second chlorine atom? Would the resulting molecule be chiral? Please pause the video here.

This new molecule, called 2, 2 di-chlorobutane is not chiral. The second carbon with two chlorine atoms no longer has four different groups attached. You can even see that this molecule has an internal plane of symmetry and therefore can be superimposable on its mirror image.

When we do have a chiral molecule, sometimes its enantiomer has an entirely different function. For example, the enantiomers of Carvone are the flavors of caraway and spearmint. One enantiomer of Carvone fits into a specific receptor in your nose only in the way a left-handed glove fits your left hand. The other enantiomer of carvone fits into an entirely different receptor, resulting in the different odor. Many drugs such as the pain reliever, ibuprofen has biological activity while its enantiomer is inert or toxic.

As with simple molecules, it is possible for proteins to exist that are mirror images of each other. However, this doesn't occur in nature. Naturally occurring proteins are composed of L-amino acids only. It is not clear why nature selected for this particular enantiomer. Selection of L-amino acids has structural consequences for a proteins three-dimensional shape.

Pause the video here and discuss with a friend the general structure of amino acids. What are the groups attached to the central carbon? Which if any of the amino acids are achiral?

An amino acid contains both an amino group and a carboxylic acid group. It also contains a hydrogen atom and a sidechain. The central atom is carbon.   Of the 20 naturally occurring amino acids, glycine is the only achiral amino acid. Its sidechain is a second hydrogen atom. The remaining 19 amino acids have the L configuration.

Let us recall that naturally occurring amino acids have an L-configuration and combine to form L-proteins. However, scientists can now chemically synthesize proteins made up entirely of D-amino acids. These synthetic macromolecules are also known as D-proteins. Interestingly, these proteins fold into three- dimensional structures, which mirror those of the naturally occurring L-protein counter-part.

Snow fleas are a species of dark blue insect. They are often seen bouncing around on the snow in the winter. Ice fish live in the Antarctic. These fish live in the ocean at subzero temperatures. What do the snow flea and the arctic fish have in common? They can both survive in subfreezing temperatures. How do they do this?   Both creatures make a class of proteins called Antifreeze proteins. These proteins protect these organisms and others, including moths, beetles, plants and even bacteria by binding to water and stopping the growth of ice crystals in their bodies.

Is water chiral? Please pause the video here and try to answer this question.

Here you can see the chemical structure of water. As you can see, it has two planes of symmetry, and water is superimposable with its own mirror image.

The antifreeze protein is comprised of 81 amino acids folded into six helices. Each helix is connected by amino acids that form a short connecting loop. The helices in the antifreeze protein are left-handed. Do you think the helices are chiral? Pause the video and discuss this with a friend.

The helix winds up in the direction of your left thumb when your fingers are curled in to make a fist. These helices do not have an internal plane of symmetry, and are not superimposable with their mirror images. They are chiral.

The antifreeze protein was the first protein whose mirror image was chemically synthesized. The mirror image protein is composed of entirely D-amino acids. The helices are right-handed, opposite to that of the naturally occurring protein. They wind up in the direction of your right thumb when your fingers are curled in to make a fist. In proteins, we see chirality in the amino acid units and in the secondary structure as well.

Do you think the D-form of the antifreeze protein will have a function the same as or different from the natural L-form? Please pause the video here and discuss with a friend. Interestingly, the mirror image protein has the same antifreeze properties. This is because its binding partner, water is achiral. So the mirror image protein can still bind water.

Hopefully by now you have the tools to recognize chiral objects and molecules, and the role that chirality can play in recognition and specificity between biological systems. In this video, we saw that an object or molecule is chiral if it cannot be superimposed onto its mirror image. Objects or molecules that have an internal plane of symmetry are never chiral. We also talked about enantiomers, which are the mirror image of a chiral molecule. Since the spatial orientation of the atoms in enantiomers are different, chiral compounds can and often do have distinct functions. But, as you saw with the antifreeze protein, sometimes there are exceptions to the rule!