Chemistry of nerve gas:
How neurotransmitters work at specific receptors

Target audience: 9-12
Background and Notes:

In the body, most molecules contain covalent bonds. However, the interaction of molecules or compounds within the body involves intermolecular forces such as hydrogen bonding (e.g. water to water) and dipole-dipole between large molecules (e.g. sucrose to sucrose). Intermolecular forces are also formed between most drugs and their targets (e.g. proteins such as receptors or enzymes) in the body. These intermolecular forces are not nearly as strong as the covalent bonds that hold the atoms together in molecules.

Most intermolecular forces between drugs and proteins are easily broken (i.e. reversible binding). Some interactions are so strong they cannot be broken. In the latter case, these are covalent interactions between molecules and are irreversibly bound. These enzymes function like a key that fits into a lock and perform biological functions. Acetylchoine and the enzyme, acetylcholinesterase, enable muscles to contract and relax. Normally, acetylcholine, a neurotransmitter, when released into the synapse for a muscle elicits the contraction of a muscle and is subsequently broken down by the enzyme, acetylcholinesterase, and relaxation of the muscle can occur. However, sarin, a nerve gas, irreversibly binds to acetlycholinesterase blocking it from breaking down the acetylchoine, thereby causing muscles to remain contracted. There exists a structural similarity between the active sites of the acetylcholine and the sarin molecule, that enables the sarin molecule to fit into the acetylcholinesterase molecule. If the muscle is the diaphragm, it would remain contracted and the person would not be able to breathe. By understanding the function of the acetylcholine system and the interference of a nerve gas, students will be able to connect bonding and intermolecular force to real life situations.

Acetylcholine causes intestinal smooth muscle contractions, resulting in diarrhea and not constipation. This is part of its action within the parasympathetic nervous system.

One of the reasons that nerve gas is so poisonous is its ability to get into the human body quickly in many ways: absorption through the skin, inhalation into the lungs, and entrance through the eyes. Once in the body, the drug easily reaches the brain, diffusing readily through the brain's protective membrane (the blood-brain barrier). The brain capillaries provide protection to the brain because the endothelial cells are packed tightly together. Therefore, only compounds that are highly lipophilic or non-polar, such as nerve gas, can enter the brain by diffusing through the capillary membranes. Lipophilic compounds also penetrate eyes and skin readily, passing easily through the lipid membranes of those tissues.

The peripheral nervous system includes neurons that connect the brain and spinal cord to muscles, organs and skin to send sensory and motor information. The somatic nervous system is responsible for controlling voluntary movement.

Nerve gases are extremely toxic; a small droplet can kill a person. They exist in both liquid and gaseous forms. Inside closed containers, the nerve gases are in liquid form. However, they when exposed to air, these gases vaporize and can reach many people in a short period of time. These gases are heavier than air and tend to remain close to the ground where people can be exposed and harmed by them.

Knowledge and skills:

- Students will model enzyme action, using acetylcholine at a neuro-muscular synapse.
- Students will be able to diagram the actions of a neuro-muscular synapse, including acetylcholine release, acetylcholine binding to its receptor, an electrical (ion) current in the membrane, and the break down of acetylcholine by the enzyme, acetylcholineesterase.
- Students will use diagrams to show how sarin affects the nervous system.
- Students will understand the consequences of an irreversible reaction between sarin and its target.

Fundamental understanding:

- Students will understand the connections between bonding, intermolecular forces and the way that molecules act in the body.

Essential Questions:

- How does chemical bonding and intermolecular forces relate to biological function?

National standard (s):

- National content standard C: As a result of activities students should develop an understanding of the cell, molecular basis of heredity, biological evolution, interdependence of organisms, matter, energy and organization in living systems and behavior of organisms.

State standard(s):

- 1.02 and 1.07 Objectives for North Carolina Chemistry Standard Course of Study Objective: Bond Polarity and molecular polarity, including intermolecular forces in order to explain polarity
- 1.01a Objectives for North Carolina Biology Standard Course of Study Chemical processes and regulatory mechanisms of cells
- 1.01b Objectives for North Carolina Biology Standard Course of Study Objective: Bonding patterns.

Purpose: to demonstrate the interaction of molecules using pop beads.

Safety Precautions: None

Materials:

- **Equipment:**
  Brown paper bags prepared with simulated acetylcholine and sarin gas and cards with symptoms of nerve gas poisoning. One bag per student

Procedure:

1. Have students stand up by their desk. Tell them that they are the acetylcholinesterase and that they will be breaking the acetylcholine into choline and acetate. Each student will have one bag. Warn them: Do not look into the bag just reach in when I tell you.
2. Upon signal from instructor, student will reach into bag without looking and pull out one pair of beads.
3. They will pull the beads apart and place on their desk. If the beads come apart, they need to reach in and pull out another pair, when you them to reach in. This is normally what happens to the acetylcholine, so it will leave the muscle and allow the muscle to relax. If the beads are glued together, they have bonded to sarin and can no longer carry out their enzymatic action and the muscle continues to contract for at least 15- 20 minutes before the sarin is released. The student will next read their card to the class to determine cause of death.
4. Students who have died because of sarin gas which has inactivated their enzymes should then sit down.
5. The activity continues until all students are sitting i.e the entire class will ultimately pass away.

Discussion of Results:

With this activity you should be able to make a link between the similarities and differences of nerve gas and insecticides. The nerve gases are covalently bonded to the enzyme and will not be removed. Most insecticides are bonded by intermolecular forces (usually hydrogen bonding) to acetylcholinesterase and these interactions can be more easily broken.

Also, students could enter into a discussion about chemical warfare and the ethical issues surrounding this current issue. This activity could lead to a historical discussion about the use of nerve gas and chemical warfare.

Recommendations for Assessment:

Draw and label the neuro-muscular synapse. Write an explanation about the significance of the pop beads and what they represent i.e. the acetyl and choline moieties. Discuss the ethical issues surrounding this topic, including other types of biological weapons.

Extension:

Research the treatments for nerve gas poisoning. Research the different countries that have signed treaties against the use of nerve gas.

References and Resources:
College or High School Biology Textbook
Schwarz-Bloom, Rochelle, Pharmacology Education Project,
http://www.duke.edu/~schwa001/scienceeducation.htm

Teacher Notes:

Materials to purchase:

1. pop beads (three colors would be preferred),
2. crazy glue,
3. small brown paper bags (1/student)
4. (Other possibilities: nuts and bolts, legos)

To set up the activity:

1. Prepare a classroom set of bags with pairs of pop beads. One bag per student.
2. There should be AT LEAST 11 pairs of beads (two different colors – acetyl group represented by one color and the other color represents the choline moiety) in each bag. Ten of the eleven pairs should be unglued but connected, one pair will be glued with super glue.
3. If you have the resources, have more pairs of acetylcholine beads. Also it would be helpful if you have three colors of beads. For example: blue represents choline, red represents acetate and green represents the sarin nerve gas.
4. Each bag should have one 3" x 5" card which lists death by different forms of continuous muscle contractions.
    a. breathing, diaphram permanently contracted
    b. diarrhea: intestines permanently contracted, dehydration
    c. sweating: dehydration
    d. salivating: dehydration