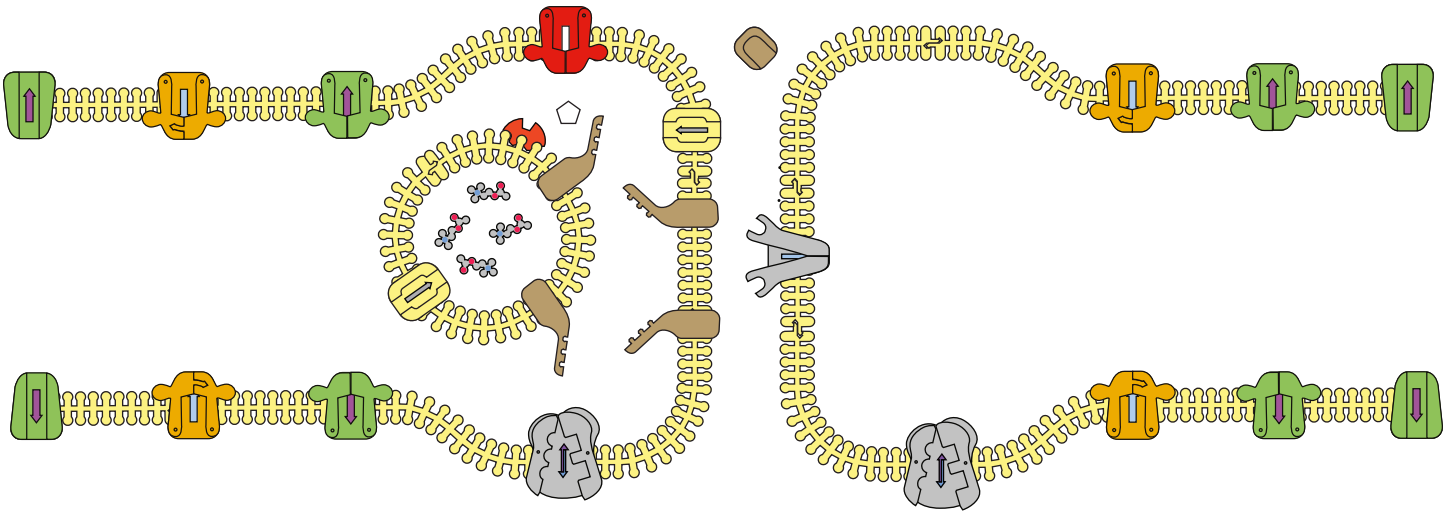
# Part III: Modeling Neurotransmission – A Cholinergic Synapse

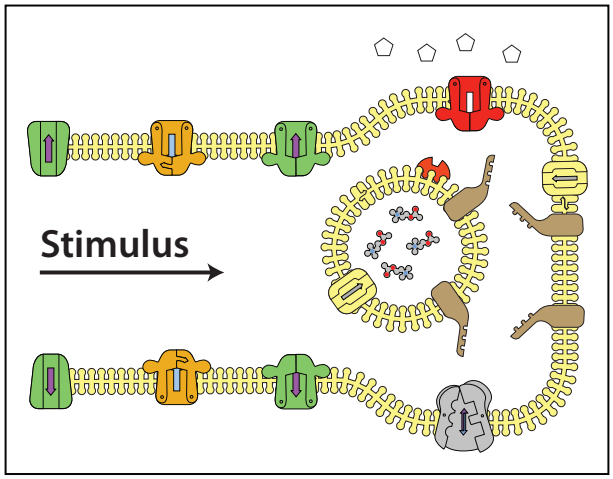
Signaling through the nervous system is dependent on the flow of information through chains of neurons functionally connected by **synapses.** The neuron that conducts impulses toward the synapse is the **presynaptic neuron**, and the neuron that transmits the signal away from the synapse is the **postsynaptic neuron**. Chemical synapses are specialized for release and reception of chemical neurotransmitters. For the most part, neurotransmitter receptors in the membrane of the postsynaptic cell are either **1.) channel-linked receptors**, which mediate fast synaptic transmission, or **2.) G protein-coupled receptors**, which oversee slow synaptic responses. **Channel-linked receptors** are **ligand-gated ion channels** that interact directly with a neurotransmitter and are called **ionotropic receptors.** Alternatively, **metabotropic receptors** do not have a channel that opens or closes but rather, are linked to a G-protein. Once the neurotransmitter binds to the metabotropic receptor, the receptor activates the G-protein which, in turn, goes on to activate other molecules.

Model the **ionotropic cholinergic synapse** shown below. Be sure to label all of the following: voltage-gated sodium channel, voltage-gated potassium channel, neurotransmitter, synaptic vesicle, presynaptic cell, postsynaptic cell, potassium leak channel, sodium-potassium pump, synaptic cleft, acetylcholine receptor, acetylcholinesterase, voltage-gated calcium channel, synaptotagmin, SNAP/SNARE proteins, reuptake channel, and vesicular transporter.

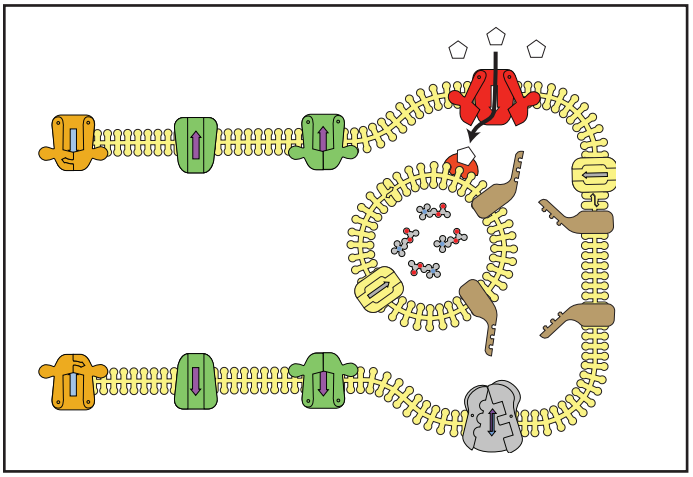


When a nerve impulse (action potential) reaches the axon terminal, it sets into motion a chain of events that triggers the release of neurotransmitter. You will next model the events of neurotransmission at a **cholinergic synapse**. Cholinergic synapses utilize **acetylcholine** as the chemical of neurotransmission.

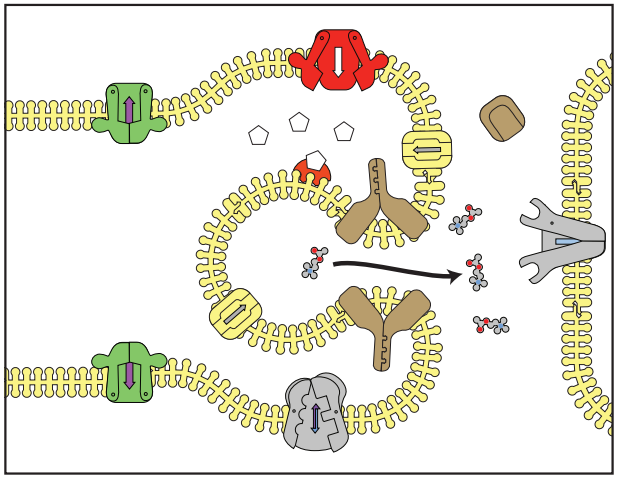
# Part III: Modeling Neurotransmission – A Cholinergic Synapse



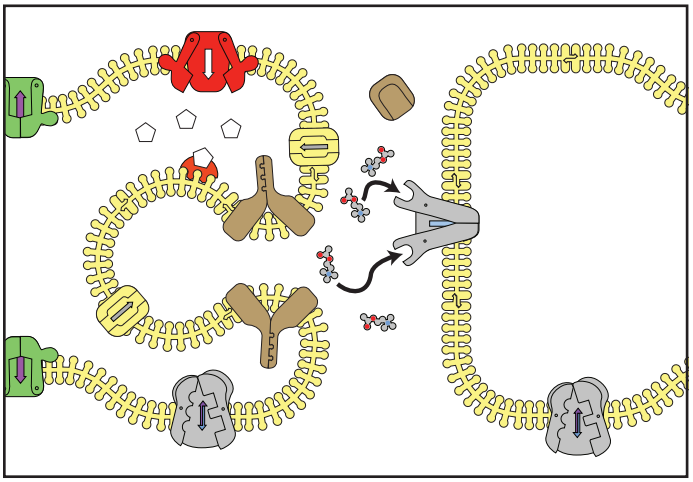

**Step 1 -** Action potential arrives at the terminal end of the presynaptic cell.



**Step 2 -** Calcium channels open in the presynaptic axon terminal. Open the calcium channels (red) and move some calcium ions to the interior of the neuron. Calcium ions bind to synaptotagmin.

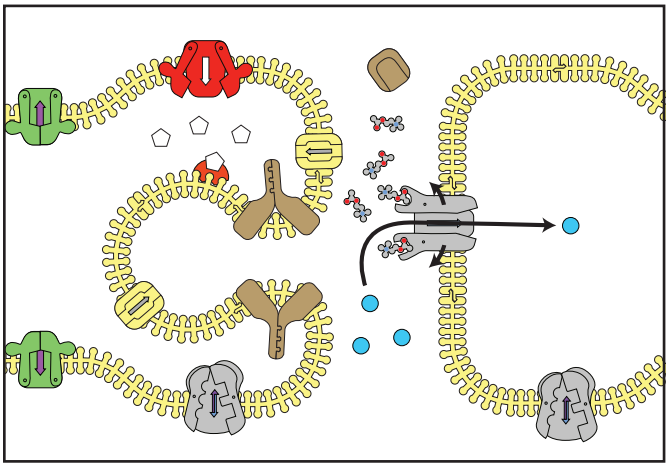


**Step 3 -** Bound $Ca^{2+}$ triggers SNAP/SNARE protein interaction to bring the vesicle in position for fusion with the presynaptic cell membrane. Acetylcholine is released into the synaptic cleft.

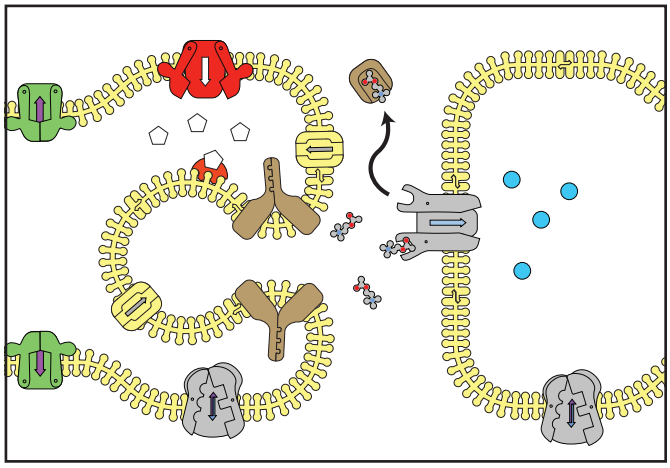


**Step 4 -** Acetylcholine traverses the synaptic cleft to bind to the acetylcholine receptor embedded in the postsynaptic membrane. Both binding sites must be occupied by acetylcholine for the channel to open.

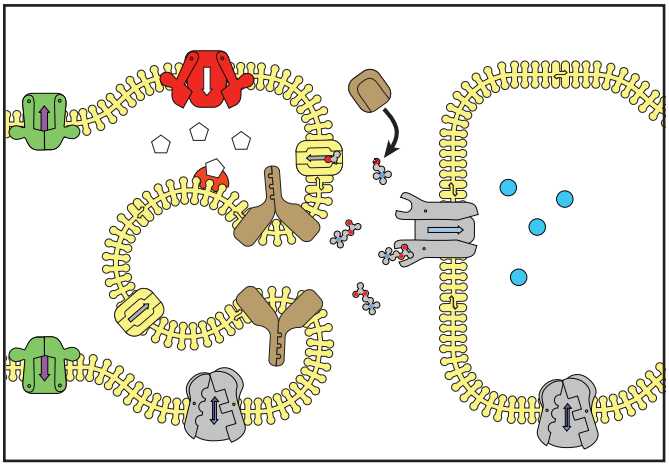
# Part III: Modeling Neurotransmission – A Cholinergic Synapse



**Step 5 -** The acetylcholine receptor opens to allow sodium ions to follow their concentration gradient into the postsynaptic cell. Depolarization of the postsynaptic cell occurs and an action potential may be generated in the post synaptic cell. Note: the receptor also allows passage of $Ca^{2+}$ and $K^{+}$.



**Step 6 -** The enzyme acetylcholinesterase breaks the neurotransmitter down into acetic acid and choline.



**Step 7 -** An uptake transporter moves choline back into the presynaptic cell for use in the synthesis of more acetylcholine in the presynaptic cell. A vesicular transport protein moves synthesized acetylcholine into the vesicle.

# Part III: Modeling Neurotransmission – A Cholinergic Synapse

3b. Identify the ion that triggers the SNAP/SNARE proteins to cause the synaptic vesicle to "fuse with the presynaptic cell membrane.

3c. What molecule is released into the synaptic cleft in this model?

3d. Why is it important that acetylcholinesterase is present in the synaptic cleft?

3e. What is transported through the uptake transporter of the presynapctic cell?

3f. What type of channel is the acetylcholine receptor in the postsynaptic cell? What implication does this have for the speed at which a signal is conducted?

3g. What happens in the postsynaptic cell when acetylcholine binds to the receptor?

3h. Identify the cholinergic synapse modeled excitatory or inhibitory. Explain your choice.