Interneuron Communication

- Axons are like telephone lines in that they simply carry messages from one place to another.
- They take no part in the creation of the conversation at one end of the line.
- Or the comprehension of the information at the other end.
- Cell bodies are analogous to humans at the two ends of the lines.
- Processes within the soma and dendrites create the information to be transmitted along the axon in nerve impulse code.
- Let's begin by exploring the process of interneural communication. 

Interneuron Communication (continued)

- Axodendritic synapse
- Axosomatic synapse
- Axoaxonic synapse

Interneuron Communication (continued)

- The neuron B in the slide receives impulses from the neuron A.
- And neuron B would send impulses to the next neuron C.
- The junction between the cells are synapses.
- The neuron A is the presynaptic neuron.
- The neuron B is the postsynaptic neuron.
- Neuron B sends an impulse to neuron C.
- Then neuron B is the presynaptic neuron.
- And neuron C is the postsynaptic neuron.

Presynaptic Events

- Image a nerve impulse in the axon of the first cell.
- On reaching the telodendria, the single impulse becomes many impulses, one for each telodendron.
- Thus, picture a nerve impulse racing down each of the telodendria, heading for the terminal buttons at its tip.
- When the impulse reaches the terminal button, it will run out of the membrane to depolarize and flicker out of existence.
- As it depolarizes the membrane of the terminal button, however, it triggers the next step in the process of passing information to the postsynaptic cell. 

Interneuron Communication (continued)
Presynaptic Events (continued)

- Let's examine what happens at the terminal button.
  - The term synapse refers to an area that includes parts of the two connecting cells plus the gap between them.
  - The part of the synapse called the synaptic gap or cleft is the fluid-filled space between cells.
  - Despite the fact that the distance between neighboring cells is greater at the synapse than anywhere else, the gap is hardly more than a few molecules wide.
- Just above the synaptic cleft is the presynaptic membrane, the part of the terminal buttons closest to the gap.\(^\text{ex}\)

Presynaptic Events (continued)

- Below the gap is the postsynaptic membrane, which is part of either the dendrite or the soma of the postsynaptic neuron.
- These three components – presynaptic membrane, synaptic cleft, and postsynaptic membrane – make up the synapse.
- When neuroanatomists look for synapses in nerve tissue one outstanding feature that helps them find what they are looking for is the cluster of tiny bubblelike vesicles, synaptic vesicles, that are always present in the terminal buttons.
- These synaptic vesicles are storage bottles for chemicals called neurotransmitters.\(^\text{ex}\)

Synapse

- Presynaptic membrane
- Synaptic cleft
- Postsynaptic membrane
- Synaptic vesicles\(^\text{ex}\)

Presynaptic Events (continued)

- These synaptic vesicles cluster near the presynaptic membrane,
- and in some cases, they even meld with the membrane and spill their contents into the synaptic gap.
- Transmitter molecules diffuse across the gap and trigger activity in the postsynaptic neuron.
- Secretion of neurotransmitter from the presynaptic membrane must be carefully controlled because it is the carrier of information.
- The postsynaptic neuron should be stimulated by transmitter only when the presynaptic cell has fired.\(^\text{ex}\)

Presynaptic Events (continued)

- Any transmitter released between impulses is unrelated to true information
- And resembles the static that interferes with the reception of AM radio stations.
- Furthermore, if two impulses arrive at the terminal button in quick succession, then twice as much neurotransmitters should be secreted.
- The arrival of an impulse in the terminal button opens not only the sodium gates in the membrane but opens calcium channels as well.
- Calcium ions (Ca\(^{2+}\)) act as go-between, allowing vesicles to bind themselves to the inside of the presynaptic membrane preparatory to opening into the gap.\(^\text{ex}\)

Presynaptic Events (continued)

- The closer a vesicle is to a group of calcium channels, the more likely the vesicle is to release its transmitter.
- If two impulses arrive in quick succession, twice as much calcium will be admitted, and the amount of transmitter released is doubled.
- To summarize:
  - A single impulse in a presynaptic axon becomes many impulses as the axon branches into telodendria.
  - Each impulse dies as it runs out of the membrane at the terminal buttons.
  - But as it depolarizes the presynaptic membrane of the terminal button, calcium channels are opened.\(^\text{ex}\)
Presynaptic Events (continued)

- Calcium ions rush into the terminal button and react with both the membrane of a nearby synaptic vesicle.
- And the presynaptic membrane of the neuron itself, binding the two together
- so that the vesicle can open and release it molecules of neurotransmitter into the synaptic cleft.
- Each vesicle releases about 10,000 molecules of neurotransmitter.**

Postsynaptic Potentials

- Once released from vesicles, neurotransmitter molecule quickly diffuse into the fluid and reach the postsynaptic membrane of soma or dendrite.
- The postsynaptic membrane is pierced by large protein molecules forming ion channels.
- Each channel is formed by one immensely long protein molecule that twists and turns, curling into complex helixes and twining back through itself to create, in outline a solid shape.
- The portion of the molecule on the outside of the membrane, poking into the synaptic cleft, has three cusps in which the twists of the molecules have created shaped depressions.***

Postsynaptic Potentials (continued)

- These sockets are called receptor sites because their shape matches that of a neurotransmitter molecule.**

Postsynaptic Potentials (continued)

- Each type of neurotransmitter in the nervous system has a different shape to its molecule and requires a differently shaped receptor site protein molecule to receive it.
- When the protein molecule has empty receptor sites its ion channel is closed, preventing the flow of sodium ions.
- When neurotransmitters bind with the receptor sites it twists the protein molecule a little further
- Opening the ion channel through its center and allowing sodium ions to flow inward.
- The neurotransmitter finds the receptor sites strictly by chance,***

Postsynaptic Potentials (continued)

- The molecules float about, bouncing off each other or off nonreceptive parts of the membrane.
- But, the distance are unimaginably small and the channels so closely packed that the whole trip from release to binding take some molecules less than 1 ms.
- The 10,000 molecules from one vesicle open about 2,000 channels.
- As soon as channels begin to open, sodium molecules flow inward, creating a transmembrane current.
- This current has a very short life (about 15 ms)
- Because the neurotransmitter molecules that initiated it remain in the receptor sites for only a brief moment.**

Postsynaptic Potentials (continued)

- Their binding is easily reversed, freeing them to float away and, perhaps, bind to another channel.
- As soon as a receptor is empty once more, the channel it controls closes immediately.
- Thus shutting off the current.
- Because these small transmembrane currents tend to excite the neuron, they are called excitatory postsynaptic potentials (EPSPs).**
EPSP Versus Action Potential

- I did not say that the neurotransmitter set off a nerve impulse in the postsynaptic cell.
- It is an EPSP that occurs when ion channels open, not an impulse.
- There is a great difference between nerve impulses and EPSPs.
- EPSP is
  - A small transmembrane current of inward-flowing sodium ions and outward-flowing potassium ions that occurs at the postsynaptic membrane.
  - Just like the transmembrane currents that make up the action potential, it is accompanied by electrotonic currents that spread across the surrounding cell membrane.

EPSP Versus Action Potential (continued)

- The major difference between EPSPs and impulses lies in the nature of the channels through which they flow.
  - Gates on the sodium channels of the axon are held close by a voltage between the inside and outside of the membrane.
  - When depolarization occurs, gates open and transmembrane currents flow.
  - Thus channels used by the action potential are voltage-regulated.
  - Ion channels in the membrane of the dendrites and soma, however, are opened not by a voltage drop but by a neurotransmitter.
  - Thus, the channels responsible for EPSPs are transmitter-regulated.

EPSP Versus Action Potential (continued)

- This difference in channel-gate regulation creates another difference between EPSPs and action potentials.
  - When a transmembrane current flows through the membrane of the axon,
  - it accompanying electrotonic current depolarize the adjoining membrane and open the channel there
  - to produce another set of transmembrane currents.
  - The action potential is self-propagating.
  - EPSPs cannot propagate themselves.
  - As transmembrane current flows, the accompanying electrotonic currents depolarize the neighboring area of the dendrite but with no effect.

EPSP Versus Action Potential (continued)

- The channels of dendritic and somatic membrane can only be opened with a transmitter.
- Consequently, an EPSP flowing at a synapse influences the distant axon hillock only with the spread of its electrotonic currents
- And these grow weaker the farther they spread.
- Sometimes this spread of electronic current is spoken of as a form of conduction
- But in acknowledging the fact that it decreases in strength as it travels, it is called decremental conduction.

EPSP Versus Action Potential (continued)

- The arrival of an action potential at the terminal button can cause one of two electrical changes on the postsynaptic side.
  - The first possibility is a depolarization shift of the postsynaptic membrane potential from its resting -70 mV to a slightly less negative value (say -68 mV)
  - Since this shifts is in the direction of (-50 to -60mV) the action potential threshold
  - And therefore makes the action potential more likely this is an EPSP.
**EPSP Versus Action Potential (continued)**

- An EPSP is different from an action potential in three significant ways.
  - 1) The shift is only a matter of a few mV instead of 110 mV.
  - 2) An EPSP lasts for 15 msec, while the action potential is much more transient.
  - 3) An EPSP is decremental, while the action potential is nondecremental.
    - An EPSP is localized to the portion of the membrane directly across from the presynaptic membrane.
    - The degree of the potential shift falling off steeply as one move away from the receptor site.

**EPSP**

- If an EPSP is so weak, how does the postsynaptic membrane ever reach threshold?
  - Often the threshold is not reached.
    - The neuron carrying the action potential on the presynaptic side fails to transmit the action potential to the neuron on the postsynaptic side.
    - Despite the fact that the two neurons have synaptic contact.
  - Successful transmission of action potential, however, is helped considerably by two types of summation.
    - In which subthreshold EPSPs in combination can build upon each other in order to reach a threshold for an action potential.

**EPSP (continued)**

- In an example of the first type, called **spatial summation**.
  - Two subthreshold EPSPs at adjacent locations on a postsynaptic membrane can overlap at a location in the middle.
  - The combined amounts of EPSP in the area of overlap could be sufficient to reach threshold.
  - Where the original EPSPs alone could not.
- In the second type of summation, called **temporal summation**.
  - The method of combination works on the basis of successive, rather than simultaneous, EPSPs.
  - Two action potential, one arriving at the terminal button very quickly after another, could produce two subthreshold EPSPs.
  - With the second EPSP appearing before the first has completely died away.

**Inhibitory Postsynaptic Potential**

- The EPSP shift, however, is only one of the two possible influences on the postsynaptic membrane.
- The other one is a hyperpolarizing shift from -70 mV to more negative values (say -72 mV).
- Since the shift is away from the threshold (~50 mV), it is called an inhibitory postsynaptic potential (IPSP).
- Creating a bias away from the firing of the receiving cell.
- The IPSP shares the localized character,
  - relatively long time course,
  - and the summation capability (spatial or temporal) of the EPSP.
- But the direction of the potential change is opposite.

**IPSP (continued)**

- The receiving membrane of a given cell may undergo potential changes of both EPSP and IPSP at different places and at different moments in time.
- Electron-microscopic pictures of neurons reveal as many as 40,000 synapses, some excitatory and some inhibitory, on the surface of one neuron.
- The net effects of the EPSP and IPSP combinations determine the likelihood of firing in the cell.
Chemical Bases for EPSP & IPSP (continued)

- There are two basic ways that these effects can be accomplished.
  - One way involves a specific alteration in the ionic channels in the membrane, so as to allow specific ions to move in or move out of the neuron.
  - Those receptor sites are directly tied to an ion channel are called 
    *ionotropic* receptor sites.
  - It is conceivable that a shift in the potential toward depolarization could result from a movement of Na⁺ ions into the cell and a relatively smaller amount of K⁺ ions to move out of the cell.
  - A slight permeability to K⁺ ion alone (and consequently a movement of K⁺ ions out of the cell has been proposed as a mechanism for hyperpolarization.²⁸

Chemical Bases for EPSP & IPSP (continued)

- A second way does not involve any direct action upon ions but rather a series of metabolic changes in the proteins inside the membrane.
- In this case, the neurotransmitter activates an enzyme
  - That converts *adenosine triphosphate* (ATP),
  - Into another chemical, *cyclic adenosine monophosphate* (cAMP)
- The cAMP then acts as a kind of *second messenger* (the neurotransmitter being the first messenger)
- Since it then alters the proteins (protein Kinase PKC) within the cell that establish the permeability of specific ions.²⁹

Chemical Bases for EPSP & IPSP (continued)

- Therefore, the depolarization and hyperpolarization occur in an indirect, rather than direct, manner.
  - The second process, dependent as it is upon more complex metabolic changes, is slower than the purely ionic process.
  - But the advantage lies in its longer-lasting effects,
  - Extending in time from seconds to minutes
  - An important factor in achieving long-term synaptic changes related to learning and memory.³⁰
Chemical Bases for EPSP & IPSP (continued)

- Therefore, a particular neuron influences all other for which it has synaptic communication via the same set of neurotransmitters.
- What is more important is not the neurotransmitter but the receptor site which will determine if a neurotransmitter is excitatory or inhibitory.
- It is the ion channel that the receptor site is tied to that determines whether an EPSP or an IPSP is produced.

Triggering Nerve Impulse (continued)

- Functionally, most large nerve cells are split into two parts, and each part performs a different task.
- The axon and dendrites constitute the communication unit.
- The job is to carry information from the part of the nervous system in which the soma is located to some distant part where the postsynaptic cells use the information.
- For example, cell B might have its soma in the thalamus
- And its axon might extend out of the thalamus to make contact with cell C whose soma lies several inches away in the cerebral cortex.

- The axon is like a telephone line connecting two computers.
Triggering Nerve Impulse (continued)

- It delivers the computations (output) of the first computer to the second computer.
- Which will use this information in its own computations.
- Without stretching the analogy too far, the brain can be thought of as a highly interconnected collection of biological computers.
- Each with a particular function.
- Some of these structures process data coming directly from sense organs.
- But most of them process input that is the output from other such computing devices elsewhere in the brain.

Triggering Nerve Impulse (continued)

- If communication is the function of the axon of the neuron.
- Then computing is the job of the other unit, the cell body and dendrites.
- Each soma-dendrite unit receives input from thousands of terminals scattered over most of its surface.
- These terminals come from hundreds of presynaptic cells.
- Each of whose soma could be located in any one of a dozen or more places around the nervous system.

Triggering Nerve Impulse (continued)

- It is at the hillock that our microscopic biological computer does its most important adding and subtracting.
- Because each individual EPSP is too tiny to reach the axon threshold and trigger an action potential by itself.
- The generation of an impulse has to wait that moment when a number of EPSPs all arise more or less simultaneously.
- Electrotonic currents from different EPSPs can add together in a process called summation.
- If there is sufficient summation, axon threshold is reached, and the sodium gate at the axon hillock are opened to initiate an action potential.

Summation

- As you can see, the temporal pattern is very important in determining how big the summated potential will be.
- This means that when an impulse does finally occur in the axon of the postsynaptic cell it is a signal that the soma has received a particular pattern of presynaptic impulses.
- It is into patterns of this sort that information is coded in the nervous system.
- Thoughts, perceptions, emotions are apparently all patterns of nerve impulses in the 10 billion or so neurons of the nervous system.