Localization of Certain Neurons
Neurotransmitters
Nerve Conduction

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Clarification: Types of Neuron

- There may be none, one, or many dendrites composing part of a neuron.

- No dendrite = a *unipolar* neuron

- One dendrite = *bipolar* neuron

- More than one dendrite = *multipolar* neuron.
**Structural Classes of Neurons**

- **Multipolar neuron**
  - Has many dendrites and one axon.
  - Multipolar neurons are found as motor and interneurons.

- **Bipolar neuron**
  - Has one dendrite and one axon attached to the cell body.
  - Bipolar neurons are rare, found only in ear and eye.
Unipolar neurons have one process from the cell body, an axon. It branches to connect to receptors and the spinal cord or brain.

Unipolar neurons are most of the body’s sensory neurons. The dendrites are found at the receptor and the axon leads to the spinal cord or brain.
Localization of Neuron types

• **Unipolar:**
  – found in most of *body's sensory neurons*
  – *dendrites are the exposed branches connected to receptors*
  – *axon carries the action potential in to the CNS*
  – *Examples: posterior root ganglia + cranial nerves*
  – *Usually: have peripheral + central connections*
Localization of Neuron types

- **Bipolar**: retina, sensory cochlear, vestibular ganglion
- **Multipolar**: (fibers) brain + spinal cord
  - found as *motor neurons* and *interneurons*
  - neuronal tracts $\rightarrow$ CNS
  - peripheral nerves $\rightarrow$ PNS
Size of Neurons + their localization

- **Golgi I:**
  - Fiber tracts: brain + spinal cord (PNS + motor)
  - (i.e., Pyramidal tract + Purkinje cells)

- **Golgi II:**
  - Cerebral + cerebellar cortex
  - Often inhibitory
  - Out number Golgi I
  - Star-shaped appearance 2° short dendrites
Histology of the Nervous System
A review of Cell types

1) Neurons - the functional cells of the nervous system
2) Neuroglia (glial cells) - Long described as supporting cells of the nervous system, there is also a functional interdependence of neuroglial cells and neurons
   a) astrocytes - anchor neurons to blood vessels, regulate the micro-environment of neurons, and regulate transport of nutrients and wastes to and from neurons
   b) microglia- are phagocytic to defend against pathogens and monitor the condition of neurons
   c) ependymal - line the fluid-filled cavities of the brain and spinal column and play a role in production, transport, and circulation of the CSF.
2) **Neuroglia** (glial cells, continue)
   
   d) **oligodendrocyte** – produce myelin sheath in the CNS, which insulates and protects axons
   
   e) **Schwann cells** – produce myelin sheath in PNS, insulates axons, maintains their micro-environment, enables regeneration and re-establishment with receptors or effectors
   
   f) **satellite** – surrounds cells bodies of neuron in ganglia, maintain micro-environment and provide insulation for the ganglion cells

http://images.google.com/imgres?imgurl
Neurotransmitters

• Substances that produce a chemical response or reaction
• Typically 1 principal neurotransmitter released per neuron site (not always)
• Different types of neurotransmitters
• Each neurotransmitter may have a different effect on different CNS locations.
• Most major neurotransmitters composed of amino acids except acetycholine (ACh)

• Approximately 60 neurotransmitters identified, some common ones discussed in this lecture
Classification of Neurotransmitters

Action:
- rapid Excitation vs. Inhibition
- neuromodulator of postsynaptic activity

Size of transmitter
- Small molecules $\rightarrow$ short lasting effects
- Large molecules $\rightarrow$ long lasting effects
Small molecular transmitters

• Acetylcholine
• Monoamine:
  – Norepinephrine
  – Dopamine
  – Serotonin
  – Glutamate
  – GABA
Acetylcholine

- PNS + CNS
  - Reticular formation, forebrain, cortex
  - Circadian cycles
  - Stereotypical movements

- Pathology:
  - MG, Alzheimer’s
ACh

- Controls activity in brain areas connected with **attention, learning and memory**. People with Alzheimer's disease typically have **low levels of ACh** in the cerebral cortex, and drugs that boost its action may improve memory in such patients.
Dopamine

- Cortex, midbrain (Substantia Nigra)
- Voluntary movement
- Pathology:
  - Parkinson’s Disease
Dopamine

• Controls arousal levels in many parts of the brain and is vital for giving physical motivation. When levels are severely depleted, as in Parkinson’s Disease, individuals may find it impossible to move forward voluntarily. Low dopamine may also be implicated in mental stasis. Some drugs (LSD + hallucinogens) are thought to work on the dopamine system.
Norepinephrine

- Pons + medulla + limbic + thalamus + cortex
- Sleep, sustained memory + vigilance
Serotonin

- GI tract, blood, brainstem
  - subcortical + cortical regions
- Arousal, sleep, pain control
- Pathology: depression
“I feel good……”

• The neurotransmitter, Serotonin, is enhanced by Prozac, and has become known as the 'feel-good' drug. It has a profound effect on mood and anxiety -- high levels of it, or sensitivity to it, are associated with serenity and optimism.
GABA

- CNS (inhibitory)
- Pathology:
  - Huntington’s chorea
Glutamate

• This neurotransmitter is the brain's major excitatory neurotransmitter. It is vital for creating the links between neurons that are the basis of learning and long-term memory.
Noradrenaline

• This neurotransmitter is mainly excitatory that induces physical and mental arousal and elevated mood. Production is centered in an area of the brain called the locus coreuleus, which is considered to be one of the brain's 'pleasure' centers.
Communication of Neurons

• Nerve impulses allow nerve cells to ‘communicate’ via action potentials
• Neurotransmitters (chemicals) activate ‘electrical’ action potentials
• Charged particles move in/out cell membrane
• Propogates an axon potential down axon in pre-synaptic cell → releases neurotransmitter
• Excitation of post-synaptic cell +/- results
General Action

Action potential ➔
- presynaptic vesicles fuse with cell membrane
- neurotransmitter released ➔ presynaptic cleft
- mitochondria ➔ ATP (adenosine triphosphate)
- Postsynaptic membrane ➔
  • Selectively opens or closes ion channel
- Postsynaptic resting potential:
  • raised (E) or lowered (I)
More General Principles → Nerve Impulses

• Membrane permeability → ion concentration
• Whereby,
  – The greater the gradient across the membrane
  – The greater the flow of ions from
    • High → Low concentrations
• Cell Membrane channels are gated:
  – Open vs. Closed to Na+ or K+
• Determined by:
  – electrical potentials + neurotransmitter release
  – strength of stimulus
Resting state:

- Cell is not excited nor conducting impulse
- Distribution of (+) and (-) ions unequal on each side of membrane
  - “polarized” → resting state
- **That is**, there is a **difference** in:
  - electrical charges on
  - inner + outer sides of membrane
Whereby,
(at resting state)

- Outside Cell Membrane: + charged
- Inside Cell Membrane: - charged
  - (~ -70 mV to -80 mV at resting state)
Resting membrane potential

- Potential **inside** cell membrane:
  - -70 to -80 mV
- Maintained by unequal distribution of:
  - (Na+) sodium ions
  - (K+) potassium ions
  - (Cl-) chloride ions
    - (contribute to hyper-polarization)
Action Potentials

http://www.youtube.com/watch?v=SCasruJT_DU
Because of their size + charge…..

- K+ (potassium) ions move freely through membrane pores/gates: in → out pores
- Na+ (sodium) ions have restricted access
- Action potential increases permeability of Na+
- There is selectivity in opening/closing Na+ and K+ gates
- Remember: Plasma membrane is semi-permeable to K+
  - Physico-chemical ion selectivity channels
  - (i.e., K+ weaker fields → Na+, larger ion size, gate permeability)
Distribution: Sodium vs. Potassium ions

- Is constantly adjusted by:
  - Sodium-Potassium Pump
    - Inside cell: Low Na+ and High K+
    - Outside cell: High Na+ and Low K+

- Active transport:
  - Transports Na+ $\rightarrow$ out
  - Transports K+ $\rightarrow$ in

- Gate selectivity $\rightarrow$ open vs. close for particular ions
Sodium-Potassium Pump

Maintains concentrations:
  – Pumps Na⁺ → out of cell
  – Transports K⁺ → into cell
  – ATP provides energy → ADP

Because, there is cell membrane selectivity due to pore size:
  • K⁺ ions move easily
  • Na⁺ has restricted access

Membrane not permeable to (-) ions in cell
  – however, negative anions (-Cl, -Proteins)
  – attract to K⁺ and Na⁺
The sodium-potassium pump moves sodium ions out of cells and potassium ions into cells.

**a** Sodium ions within the cell fit precisely into receptor sites on the channel protein.

**b** The channel changes shape, pumping the sodium ions across the membrane. Potassium ions outside the cell move into receptor sites.

**c** Sodium ions are released and cannot reenter through this channel. At the same time, potassium ions are pumped across the channel into the cell.

**d** Potassium ions are released inside the cell. Sodium ions outside the cell, along with sugar molecules, later enter the cell through coupled channels.
Nerve Excitability

• The nerve cell will respond to various stimuli such as:
  – Temperature
  – Electrical impulse
  – Nerve stimulation

• However, action potentials are initiated via:
  – chemical or electrical actions
  – neurotransmitters vs. ionic activity, respectively
a. Neurotransmitter molecules in synaptic vesicles of presynaptic neuron

b. Synaptic vesicles fuse with presynaptic membrane; neurotransmitter molecules diffuse across synapse, bind to receptor sites of ion channels, and relay message to postsynaptic neuron.
As a result.....

• An action potential is elicited
• Nerve cell becomes hyperpolarized
  – inside → more negative
  – usu. returns to resting potential
• Nerve cell becomes depolarized
  – inside → more positive
  – a spike is triggered > 10 mV (-70 to –60 mV)
  – Na+ moves into cell: until +30 to +40 mV
Na+ flow continues, but stops when.. 

- until there is **charged** cell interior to:
  - +30 mV → +40 mV
  - then flow of K+ inside cell
- Cell returns to **absolute refractory period**
  - interior drifts to -80 mV → -90 mV
  - followed by a **relative refractory period**
  - at this stage, gates are closed to Na+
- Please note:
  - another action potential **can’t be fired** until membrane potential returns → **resting potential**
Sodium channel

1. Open
2. K^+ channels open, K^+ begins to leave cell
3. Refractory
   - Na^+ channels become refractory, no more Na^+ enters cell
4. K^+ continues to leave cell, causes membrane potential to return to resting level
5. K^+ channels close, Na^+ channels reset
6. Extra K^+ outside diffuses away

Membrane potential (mV)

+40
0
-70
Threshold of excitation
To recap.....

- **Resting state:**
  - Membrane permeable to K+, not to Na+
- **Stimulus elicits action potential**
  - Gates 1\(^{st}\) wide open to Na+
  - Gates then open to K+
  - Gates closed to Na+ (at +30 to +40 mV)
  - repolarization occurs
Excitatory vs. Inhibitory Action Potentials

• A nerve impulse is either:
  – Excitatory (E)
  – Inhibitory (I)
  – to the post-synaptic neuron

• A nerve impulse in the synaptic cleft is also modulated by ‘neuromodulators’
Excitatory Impulses (EPSPs)

- Lowers Post-synaptic membrane potential for a new impulse → excites
Inhibitory Impulses (IPSPs)

• Makes post-synaptic membrane hyperpolarized (inside more negative)
• It is more difficult to elicit an impulse
Conduction Velocity

• Myelinated neurons
  • ~ axonal diameter size X 6m/sec
  • ~ 120 m/sec
  • ~ fast long distance travel $\rightarrow$ excitation
  • ~ via saltatory conduction: node $\rightarrow$ node
• Unmyelinated neurons
  • ~ 0.5 to 1m/sec
  • ~ short diffuse travel $\rightarrow$ excitation
  • ~ travel down length of axonal membrane
Classic Neurotransmission

• Rapid excitation vs. inhibition
  – Fast EPSP or fast IPSP
• Receptor mechanism: ion channel receptors
• Examples:
  – L-glutamate: ionotropic
  – GABAA
  – ACH (nicotonic)
• Systems: direct relay: sensory or motor
Neuromodulators

• Modulates neural excitation
  – Open vs. closing of gates: K+ or Na+
  – Modulates excitation vs. inhibition
• For example: Slow IPSP or slow EPSP
• G-proteins receptors
• Examples:
  – GABAB, ACh 9 (muscarinic)
  – Neuropeptides, monamines
• Diffuse systems, indirect regulation, consciousness
Too Much excitation

- Focal seizures
- Tonic spasms
- Muscle cramp
- Paresthesia
- Paroxysmal pain
TIA\textsubscript{s} • Migraine • Transient mononeuropathy • Syncope
Mechanisms for transient disorders

• Energy failure:
  – Hypoxia, hypoglycemia
  – Seizures
  – Spreading cortical depression
  – Trauma
Ion channel disorders

- Channel protein mutations
- Immune blockades
- Drugs
- Toxins
Other

- Electrolyte disorders
- Demyelination
- Transmission of disease via action potentials:
  - Rabies
  - Poliomyelitis
  - Herpes simplex (cold sores)
  - Herpes zoster (shingles)
Transmission of disease via action potentials

- Rabies
- Poliomyelitis
- Herpes simplex (cold sores)
- Herpes zoster (shingles)
The image illustrates the process of an action potential in a neuron, focusing on the sodium channel's states.

1. **Closed State**: Sodium channels are closed, preventing sodium ions from entering the cell.
2. **Open State**: Sodium channels open, allowing sodium ions to enter the cell. This event is accompanied by a rapid change in membrane potential, leading to an increase in membrane potential.
3. **Refractory Period**: Sodium channels remain open, and potassium channels begin to open, leading to a decrease in membrane potential. During this time, no more sodium ions enter the cell.
4. **Refilling the Cell**: Potassium channels continue to open, allowing potassium ions to leave the cell and help restore the resting membrane potential.
5. **Reset**: Sodium channels close, and potassium channels close, returning the cell to its resting state.
6. **Extra K+ Outside Diffuses Away**: Extra potassium ions outside the cell eventually diffuse away, completing the cycle.

The graph shows the changes in membrane potential over time, with the threshold of excitation marked. The graph illustrates the voltage changes from a resting potential of -70 mV to a peak at +40 mV, and back to the resting potential.