# Cells of the Nervous System

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# Glia

- "*Glue*"
- Can undergo division
- Physical and metabolic support for neurons

# Astrosit

- Maintain blood-brain barrier
- Provide structural support
- Regulate ion, nutrient and dissolved gas concentrations
- Absorb and recycle neurotransmitters
- Form scar tissue after injury
- Release neurotrophic factors

# Oligodendrocyte

- Myelinate central nervous system axons
  - One oligodendrocyte → 40 myelin sheaths
- Provide structural framework

# Schwann Cells

- Surrounds axons in peripheral nervous system

- Responsible for miyelination of peripheral axons
  - one cell one myelin sheat

- Participate in repair process after injury

# Microglia

- Remove cell debris, wastes and pathogens by phagocytosis

# Ependymal Cells

- Line ventricles (brain) and central canal (spinal cord)
- Assist in producing, circulating and monitoring of cerebrospinal fluid

# Satellite cells

- Surround neuron cell bodies in ganglia – peripheral nervous system

- Regulate $O_2$, $CO_2$, nutrient and neurotransmitter levels around neurons in glia

# Neuron

- **Neurons** are nerve cells that transfer information within the body
- Neurons use two types of signals to communicate: electrical signals (long-distance) and chemical signals (short-distance)

# Neuron Structure and Function

- Most of a neuron’s organelles are in the **cell body**
- Most neurons have **dendrites**, highly branched extensions that receive signals from other neurons
- The **axon** is typically a much longer extension that transmits signals to other cells at synapses
- The cone-shaped base of an axon is called the **axon hillock**

# Neuron Structure and Function

- A **synapse** is a junction between an axon and another cell
- The synaptic terminal of one axon passes information across the synapse in the form of chemical messengers called **neurotransmitters**
- Information is transmitted from a presynaptic cell (a neuron) to a postsynaptic cell (a neuron, muscle, or gland cell)

# Information Processing

- Nervous systems process information in three stages: sensory input, integration, and motor output
  - **Sensory neurons** transmit information about external stimuli such as light, touch, or smell
  - **Interneurons** integrate (analyze and interpret) the information
  - **Motor neurons** transmit signals to muscle cells, causing them to contract

# Information Processing

- Interpreting signals in the nervous system involves sorting a complex set of paths and connections
- Processing of information takes place in simple clusters of neurons called **ganglia** or a more complex organization of neurons called a **brain**

# Information Processing

- Many animals have a complex nervous system that consists of
  - A **central nervous system (CNS)**, where integration takes place; this includes the brain and a nerve cord
  - A **peripheral nervous system (PNS)**, which carries information into and out of the CNS

# Membrane Potentials

- Extracellular fluid
  - $Na^+$, $Cl^-$
- Intracellular fluid
  - $K^+$, phosphate compounds, proteins with negatively charged side chains

# Potential Difference (Electrical Potential)

- Separated electrical charges of opposite sign have the potential to do work if they are allowed to come together

- The units are volts
  - In biological systems mV

# Membrane Potential

- Electrical charge difference across the membrane

- Membrane potential (Vm)

$$V_{\mathrm{m}} = V_{\mathrm{in}} - V_{\mathrm{out}}$$

- Resting membrane potential (Vr) :The membrane potential of a cell at rest

  - Vout = 0 (reference)
  - Vm = Vin ≈ -70 mV

  (Vm in neurons = -40 to -90)

# Resting membrane potential

- The resting membrane potential is the result of the passive flux of individual ion species through several classes of resting channels

- The magnitude of the resting membrane potential depends mainly on two factors:
  - differences in specific ion concentrations in the intracellular and extracellular fluids
  - differences in membrane permeabilities to the different ions, which reflect the number of open channels for the different ions in the plasma membrane

# Membrane Potential

- electrochemical driving force (the sum of the electrical and chemical driving forces)
- the conductance of the membrane to the ion

*ion flux =(electrical driving force +chemical driving force) × membrane conductance*

# Membrane Potential

- *Equilibrium potential*: The membrane potential at which electrical and chemical fluxes become equal in magnitude but opposite in direction
  - The larger the concentration gradient, the larger the equilibrium potential
- *Nernst equation*

# Membrane Potential

- The resting potential of a cell is determined by the proportions of different types of ion channels that are open, together with the value of their equilibrium potentials

- Goldman-Hodgkin-Katz Equation

$$V_m = 61 \log \frac{P_K [K_{out}] + P_{Na} [Na_{out}] + P_{Cl} [Cl_{in}]}{P_K [K_{in}] + P_{Na} [Na_{in}] + P_{Cl} [Cl_{out}]}$$

- $P_{ion}$ = relative membrane permeability

# Resting membrane potentail

- Resting potential is generated largely because of the movement of K+ out of the cell down its concentration gradient through K+ leak channels

- Inside of the cell becomes negative with respect to the outside

- Resting membrane potential is not equal to the K+ equilibrium potential because a small number of open leak channels for Na+ does pull the membrane potential slightly toward the Na+ equilibrium potential

# Na+/K+ Pumps

- The concentrations of intracellular sodium and potassium ions do not change, because of the action of the Na+/K+-ATPase pump.
  - In a resting cell, the number of ions the pump moves equals the number of ions that leak down their electrochemical gradient

- Electrogenic pump
  - Moves three Na+ out of the cell for every two K+ that it brings in
  - Unequal transport of positive ions makes the inside of the cell more negative than it would be from ion diffusion alone
  - Very small contribution

# Graded potentials and Action potentials

- All cells have a resting membrane potential due to the presence of ion pumps, ion concentration gradients, and leak channels in the cell membrane

- What makes a cell excitable?
  - Gated ion channels
  - Gated channels give a cell the ability to produce electrical signals (*excitability*) that can transmit information between different regions of the membrane (*excitable membranes*-neurons and muscle cells)

- Graded potentials → short distance signaling
- Action potentials → long-distance signaling

- Polarized:
  - outside and inside of a cell have a different net charge
- Depolarization:
  - reduction in charge separation
  - less negative potential
- Overshoot:
  - reversal of the membrane potential polarity—when the inside of a cell becomes positive relative to the outside.
- Repolarization:
  - returning of membrane potential to the resting value
- Hyperpolarization:
  - increase in charge separation
  - more negative membrane potential

# Graded Potentials

- Graded potentials are changes in membrane potential that are confined to a relatively small region of the plasma membrane.
  - the magnitude of the potential change can vary
  - Receptor potential, synaptic potential, pacemaker potential

- Charge flows between the place of origin of the potential and adjacent regions of the plasma membrane, which are still at the resting potential

# Graded potentials

- Can be either depolarizing or hyperpolarizing

- Magnitude is related to the magnitude of the initiating event (graded)

- Charge is lost with the distance
  - Leak channels (predominantly K+)

# Action Potential

- Large alterations in the membrane potential (up to 100 mV)
- Very rapid (1-4 msec)
- Voltage-gated Na+ and K+ channels that mediate most neuronal action potentials

# Voltage-gated channels

- Have sequences of charged amino acids that make the channels reversibly change their conformation in response to changes in membrane potential

- At negative potential (during resting) stay closed
- At positive potentials (depolarization) open

- Voltage-gated Na+ channels respond faster and have *inactivation gates*

- Voltage-gated Na+ Channel inactivation gate
  - Blocks channel shortly after depolarization
  - Opens at repolarization state

- Positive feedback loop
  - Step 3, opening of voltage gated Na+ channels causes more Na+ to enter and more voltage gated Na+ channels to open

- Membrane depolarization comes close to but does not reach to $E_{Na}$
  - Na+ channels get inactivated and also voltage gated K+ channels open

- The threshold of most excitable membranes is about 15 mV less negative than the resting membrane potential (−55 mV)

- Cellular accumulation of $Na^+$ and loss of $K^+$ are prevented by the continuous action of the membrane $Na^+/K^+$ ATPase pumps

# The Action Potential

- Graded changes in current cause graded changes in voltage.
- If voltage is depolarized beyond a threshold (about -50 mV), an action potential is triggered.

# An Action Potential is “All-or-None”

- At a brief moment in time (~1 ms), an action potential either occurs or it does not
- The shape of an action potential is always the same
- The magnitude of the action potential does not change

- All or None
  - After passing the threshold, all the stimuli triggers same action potentials at the same amplitude
    - All voltage-gated Na+ channels open
  - How do you differentiate between a weak and strong stimuli?
    - Number and patterns of action potentials transmitted per unit of time (frequency)

# Firing Rate Depends on Current Magnitude

- The frequency of action potentials (“firing rate”) depends on the magnitude of depolarizing current

# Refractory Periods

- Absolute refractory period
  - During the action potential a second stimulus can not produce another action potential
    - Voltage-gated Na+ channels are already open or in inactive state
- Relative refractory period
  - Coincides with the after hyperpolarization
  - A stimulus stronger than normal can produce action potential
    - Fewer Na+ channels available and some of the K+ channels are still open
- Limits the number of action potentials
- Helps separation of action potentials from each other
- Determines direction of action potential propogation

# Action Potential Propagation

- Sequential opening and closing of voltage-gated Na+ and K+ channels along the membrane
  - The difference between the potentials causes current to flow, and depolarizes the adjacent membrane
  - The new action potential produces local currents of its own that depolarize the region adjacent to it, producing another action potential at the next site …
- Because the membrane area behind  is refractory, the direction of action potential propagation is away from a region of membrane that has recently been active

# Velocity of Action Potential

- Fiber diameter ↑ Velocity ↑
  - Less internal resistance to local current
- Myelination ↑ Velocity ↑
  - Less charge flow between intracellular and extracellular fluid compartments (leakage)
  - Action potentials only at the nodes
    - More charge arrives at the node
    - Metabolically more efficient

# Velocity of Action Potential

- 0.5 m/sec → 100 m/sec
  - small diameter, unmiyelinated fiber = 0.5 m/sec
    - 4 sec from toe to brain
  - large diameter, myelinated fiber = 100 m/sec
    - 0.02 sec from toe to brain