*KRCP Lecture 2*

*Neurons and Synapses*

**Scales of Analysis in the Brain**

* **Macroscale**: Lobes, (Brodmann) areas
* **Mesoscale**: Circuits, Cortical columns, Cortical layers
* **Microscale**: Neurons, Glial Cells
* **Nanoscale**: Synapses, Neurotransmitter

**Neurons**

* Basic signaling units that transmit information through the nervous system
* The standard cellular components are found in neurons as well: A cell membrane encases the body (**soma**), which contains the metabolic machinery that maintains the neuron suspended in **cytoplasm**
* Axons also have **dendrites** (branching extensions that receive inputs from other neurons) and an **axon** (single process that extends from the cell body/output side), which sometimes branch to transmit signals to more than one cell
* Transmission occurs at **synapses** (structure where 2 neurons come into close contact so that chemical or electrical signals can be passed from one cell to the next)
* Axons are wrapped in layers of **myelin**, gaps in these sheets are called **nodes of Ranvier**

**Glial Cells**

* Support the neurons
* 4 main types: **astrocytes, microglial cells, oligodendrocytes and Schwann Cells**
* **Astrocytes** connect the neurons with the brain’s vasculature and form the **blood-brain barrier**
* **Oligodendrocytes** form **myelin** in the CNS and **Schwann cells** in the PNS by wrapping their cell membranes around the axon
* **Microglial** cells are phagocytes, which devour and remove damaged cells

**Resting Potential**

* **Electrical potential** across the membrane (voltage across the membrane/inside the neuron vs. outside)
* Voltages depend on the **concentration of potassium, sodium and chloride ions and charged protein molecules**
* Inside is more negatively charged than outside 🡪 voltage difference is **-70mV**
* **Cytoplasm** (inside the cell) and extracellular milieu are separated by the **neuronal membrane** composed of lipids
* Membrane maintains separation of intracellular and extracellular ions and electrical charge, however, it contains **trans membrane proteins**, which act as channels for ions; there are 2 types: **ion channels** and **ion pumps**
* **Ion channels** allow certain ions to flow down their concentration gradient, they are **selectively permeable** (neuronal membrane is more permeable to K+ ions)
* Unlike other cells in the body, neurons are excitable (can change permeability of their membranes) 🡪 due to **gated ion channels**, that open or close based on changes in the voltage
* Normally there are more Na+ and Cl- ions outside the cell and more K+ inside, however they are able to flow down their concentration gradient by ion channels
* **Ion pumps** act against this: they use energy to actively transport K+ and Na+ against their concentration gradient
* 2 forces acting up on each other: **concentration gradient/entropy pressure** (pushing Na+ in and K+ out), pump acts against it & electrical **gradient/electrostatic pressure** (pushing K+ back in the cell because it is more negative there) 🡪 eventually they equal out at -70mV (**equilibrium**)

**Action Potential**

* Internal transmission of output signals
* Made possible by **voltage-gated ion channels** located in the neuronal membrane and found at the **spike-triggering zone** in the **axon hillock** and along the axon
* Multiple input signals are needed at dendrites to produce an AP: **EPSP** depolarize, **IPSP** hyperpolarize; they can sum **spatially** (at different dendrites) or **temporally**
* Passive electrical currents generated by EPSPs flow across the neuronal membrane in the **spike-triggering zone** depolarizing the membrane
* If the depolarization is strong enough an action potential (AP) is triggered; strong enough = at least -55mV (**threshold**)
* When the threshold is reached **voltage-gated Na+ channels** open and Na+ flows into the cell, depolarizing it even more 🡪 more Na+ channels are opened… (**Hodgkin-Huxley Cycle**)
* Next the **voltage-gated K+ channels** open, allowing K+ to flow out of the cell 🡪 membrane potential shifts back toward RP
* Opening of K+ channels triggers closing of Na+ channels 🡪 membrane potential gets even more negative than RP; **hyperpolarized** (**equilibrium potential**)
* K+ channels close 🡪 membrane potential returns to RP
* During hyperpolarization state Na+ channels are unable to open and another AP cannot be generated (**absolute refractory period**), this is followed by the **relative refractory period**, during which the neuron can generate APs but only with larger depolarization currents
* Consequences of **refractory periods**: neuron’s speed for generating APs is limited and AP can only flow in one direction (from axon hillock towards axon terminal)
* APs must travel quickly; solution: **saltatory conduction**: channels are only opened at nodes of Ranvier and therefore APs can travel a lot faster (otherwise **passive conduction**)

**Synapses**

* 2 major kinds of synapses: chemical and electrical
* Most synapses are chemical:

1. Arrival of action potential depolarizes the **terminal membrane**, which causes Ca+ to flow into the cell
2. Ca+ causes **vesicles** to bind the with the cell membrane at the synapse
3. Release of **neurotransmitter** (in the vesicles before) by **exocytosis** into the **synaptic cleft**
4. Neurotransmitter diffuse across the cleft and bind with the **receptor**
5. Binding induces a change in the receptor, which opens specific **ion channels** leading to either **depolarization** (excitation) or **hyperpolarization** (inhibition) of the **postsynaptic cell**

* 2 different kinds of receptors: **Ionotropic** (from an ion channel pore, fast response) and **Metabotropic** (indirectly linked with ion channels in the membrane, slow response)
* 3 ways to end synaptic transmission: neurotransmitters are returned to postsynaptic or glial cell, enzymes inactivate neurotransmitter, neurotransmitter diffuse out of cleft
* Neurotransmitter: are synthesized and located in presynaptic neurons, released when AP depolarizes terminal, postsynaptic neuron contains specific receptors for it
* Some important neurotransmitter:
  + **Acetylcholine** (muscle)
  + **Monoamines**: dopamine (pleasure, addiction) & serotonin (sleep, eating, depression)
  + **Amino acids**: glutamate (main brain excitatory) & GABA (main brain inhibitory)
* **Electrical synapses** operate by passing current directly from one neuron to another via specialized channels in gap junctions that connect the cytoplasm of one cell directly to each other