Cogs17 Neurobiology of Cognition

Lecture 2a: Structure & Function of Cells in the Nervous System

Most cells in the body - including those in the Nervous System - share many basic features, including...

Soma = Cell body **Cytoplasm** = Fluid inside cell **Extracellular Fluid** = Fluid outside cell

Organelles in cells include…

Nucleus – where DNA (mostly instructions for building proteins) stored

Ribosomes - Site of Protein Production

- Proteins serve many functions (structure, transport, metabolism, membrane gates, etc)
- DNA sends "messenger RNA" from Nucleus, mRNA attaches to Ribosomes, instructs protein production

Mitochondria - Produce ATP (Adenosine triphosphate) whose breakdown frees energy to power cell functions

- Tend to cluster where "active" (energy-requiring) processes occur

Membrane - Lipids (fat molecules) w/hydrophobic cilia form double layered wall, 8nm thick

- Permeable to H2O, O2, CO2, some fats; Generally impermeable to charged ions & larger molecules

Glial Cells – The non-neural cells of Nervous System; Many functions, but do NOT participate in Info Transfer

- "Glia" = "Glue", hold the NS together, i.e. physically and chemically buffer and support the Neurons
  - -e.g. Astrocytes– Provide nutrients to Neurons, blood brain barrier, recycle NTs, remove waste, etc.
  - e.g. Microglia - Proliferate in areas of brain damage, remove toxic materials (Like body's immune system)
  - e.g. Myelination - whole Schwann Cells wrap around axon in PNS, arms of an Oligodendrocyte in CNS
  - e.g. Ependymal Cells – Line Ventricles, secrete Cerebral Spinal Fluid, beat cilia to circulate fluid
  - -e.g. Radial Glia - Guide migration and growth of Neurons during development (see below)
- Much smaller than most neurons (average 1/10), much more numerous (10X), so ~ 50% of brain by weight
- Unlike most Neurons, many Glial cells can regenerate (Runaway regeneration = "Glioma" brain tumor)

Neurons - Cells that are specialized for Information Transfer via modified 1) Processes and 2) Membrane

1) Processes = Elongated structures projecting from the "Soma" or cell body = Dendrites and Axon

Dendrites - Site of reception of **incoming** message

- From Greek "Dendron" = Tree, Usually many tapering, dividing branches, sometimes w/extra Spines
- **Receptor Sites** along surface interact w/molecules of **Neurotransmitter (NT)** from other Neurons
- Often have Ribosomes (for protein production, can be important for processing incoming message)

Axon - Site of release of **outgoing** message

- Each Neuron has, *at most, one* Axon, often long, non-tapering, may be Myelinated, end may branch
- Ends in **Presynaptic Terminals** (also called Terminal Buttons or End Bulbs) where **NT is released**
- Mitochondria in Terminals for energy-requiring processes like release/re-uptake of NT, ion pumps

2) **Membrane** As in *all* cells, lipid membrane generally impermeable to charged ions & larger molecules

- Neuron's special **Selective Permeability** controls which chemicals enter/leave; affects electro-chemistry
  - This done via **gates ("channels**") that open or close to let chemicals (charged "ions") pass through

The Nerve Impulse

To understand how Neurons "communicate" we first need to recognize that *Nature seeks a Balance . . .*

-i.e. Any Gradient (inequality) between the chemicals inside vs. outside cell will "seek" an equilibrium

Concentration Gradient - Molecules in area of greater concentration will **Diffuse** to area of lesser conc

Electrical Gradient - Positively charged particles will move away from other positive (& towards negative) and negative will move from negative (& towards positive) = **Electrostatic Pressure**

- In Neurons, the distribution of charged particles (**ions,** w/extra + proton or - electron) in/outside cells is controlled
  - Recall how the Blood-Brain Barrier restricts what chemicals can move from bloodstream into brain
- **Membrane Potential** = Diff in charge in/outside cell, measured in millivolts (mV) using microelectrodes
- Key ions: Sodium **Na+** Potassium **K+** Calcium **Ca++** Cloride **Cl-** as well as some charged Proteins

Resting Potential of most Neurons = **-70 mV** (less positive inside / more positive outside)

- Established in part by energy-requiring **Sodium/Potassium Pump**, actively transports **3 Na+ out** and **2 K+ in**
  - After transport, Na+ gates close, Na+ trapped outside (Extracellular fluid similar to seawater, w/NaCl salt)
  - K+ gates remain semi-open, K+ tends to leak out a bit
- Since Na+ now = 10:1 outside:inside, plus overall high quantity, Na+ "wants" to enter cell (to equalize both the Chemical and Electrical Gradients), but membrane is now impermeable to Na+
- Since K+ now = 1:10 outside:inside, plus lower overall quantity than Na+, K+ "wants" to exit cell to equalize the Chemical Gradient, but inhibited by Electrical Gradient (since outside more +)
- Cell's negatively charged protein molecules are too large to leave, and closed Ca++ gates keep Calcium out
  - Thus, Electrical Gradient also helps maintain more Cl- outside (attracted to more + ions outside)
- Resting cell is thus **Polarized** = Large electro-chemical difference between inside/out = Ready to "fire"

Action Potential = **Depolarization** of Neuron = Cell "Fires" AKA "Spikes"
= Changes in membrane permeability of Axon, propagated via **Ionic Conduction**

- Triggered by NT from other Neuron, electrical stimulation, or other (see more on Synapse, below), typically…
  - Starting at **Axon Hillock** (where Axon joins Soma), **Voltage-activated** Na+ gates open
  - Na+ rushes in, reverses local polarization (depolarizes to +50mV)
- Na+ moving inside causes adjacent Na+ voltage-activated gates to open, & previously-open ones close
  - This depolarization sequence continues along Axon toward Terminal
- As previous Na+ gates close, local K+ gates open wide, K+ leaves (now per both chem & elec gradients)
  - Na+ gates continue to close, and K+ to open, following behind depolarization that is moving along Axon
- When depolarization reaches Terminal, Ca++ gates there open & Ca++ enters cell
  - Ca++ influx leads to Neurotransmitter (**NT**) release
- As Membrane Potential again approaches more pos outside than in from K+ outflow, K+ gates begin to close
  - In time, **Sodium-Potasium Pump** actively restores Resting Potential (via 3Na+ out/2K+ in) => -70mV
  - And **Calcium Pump** actively rejects Ca++ from terminal – Unlike passive ion flow above, pumps req Energy
- During **Refractory Period,** while cell is being re-polarized, it cannot fire (or resists firing)
  - Refractory Period also prevents impulse from being propagated back along Axon toward Soma
    by locking down gates behind, as impulse moves from hillock to terminal
- **All-or-None Law** = In a given cell, an Action Potential always has the same amplitude and velocity,
  regardless of the intensity of the stimulus that triggered it
  - Nonetheless, while the amplitude of the Spike (extent of depolarization) & amt of NT released is fixed
    the "message" such a cell can transmit can be varied through its…
    Frequency of Firing (# spikes per sec) and **Pattern of Firing** (e.g. ||||||| vs. || || || ||)

Myelination and Saltatory Conduction - Increases the speed of the propagation of an Action Potential

- **Glia cells** form insulating sheaths around some axons, with small gaps (**Nodes of Ranvier**) in between sheaths
  - Oligodendrocytes myelinate cells in Central NS (Brain and Spinal Cord), Schwann Cells in Peripheral NS
- **Electrical Conduction** (flow of electrons, like in an insulted wire) occurs along myelinated segment
  - But such signal **degrades** (weakens) as it moves, needs to be re-boosted, periodically, to original strength
- This occurs at Nodes of Ranvier, where electrical signal triggers the slower but stronger Ionic Conduction,
  which in turn triggers Electrical Conduction that moves rapidly under next sheath to next node, etc. etc.
- "**Saltatory**" = "Jumping" Nerve Impulse in effect "jumps" from node to node as it is propagated along axon
  - Increases overall speed of impulse from 1-10 m/sec to 100-120 m/sec!
- **MS** (**Multiple Sclerosis**) - Disease destroys myelin; In such un-insulated axons, electrical signal quickly degrades
  - Plus, since no Na+ gates under sheath, cell cannot resort to Ionic Conduction => cannot fire

Graded Potentials – Releasing NT from a Neuron does NOT always requires an Action Potential !

- e.g. Some **Receptor** cells (e.g. in Retina, Cochlea) react to outside stimulus (light, sound) w/graded potential
  - Loud sound >> large amounts of NT released, Soft sound >> little amount of NT released
- e.g. **Lateral Inhibitors** – cells that suppress neighboring cells so central cell's message can get through
  - Often graded; The more/less excited the principal cell, the more/less inhibition to the neighbors
- e.g. Some Neurons are very small, have short or even no Axon or Dendrites
  - Called **Local Neurons**, these cells communicate only with immediately adjacent cells
  - In these Neurons, extremely rapid Electrical Conduction can cause NT release
  - Since cells so small, Electrical Conduction need not travel far, does not completely degrade

- Unlike Action Potentials, Graded Potentials can **vary in amplitude** in proportion to the input stimulus
  - i.e. React a lot to strong stimulus, less to weak one
- NT Release also tends to be graded (vs. fixed amounts typically released by Action Potential)