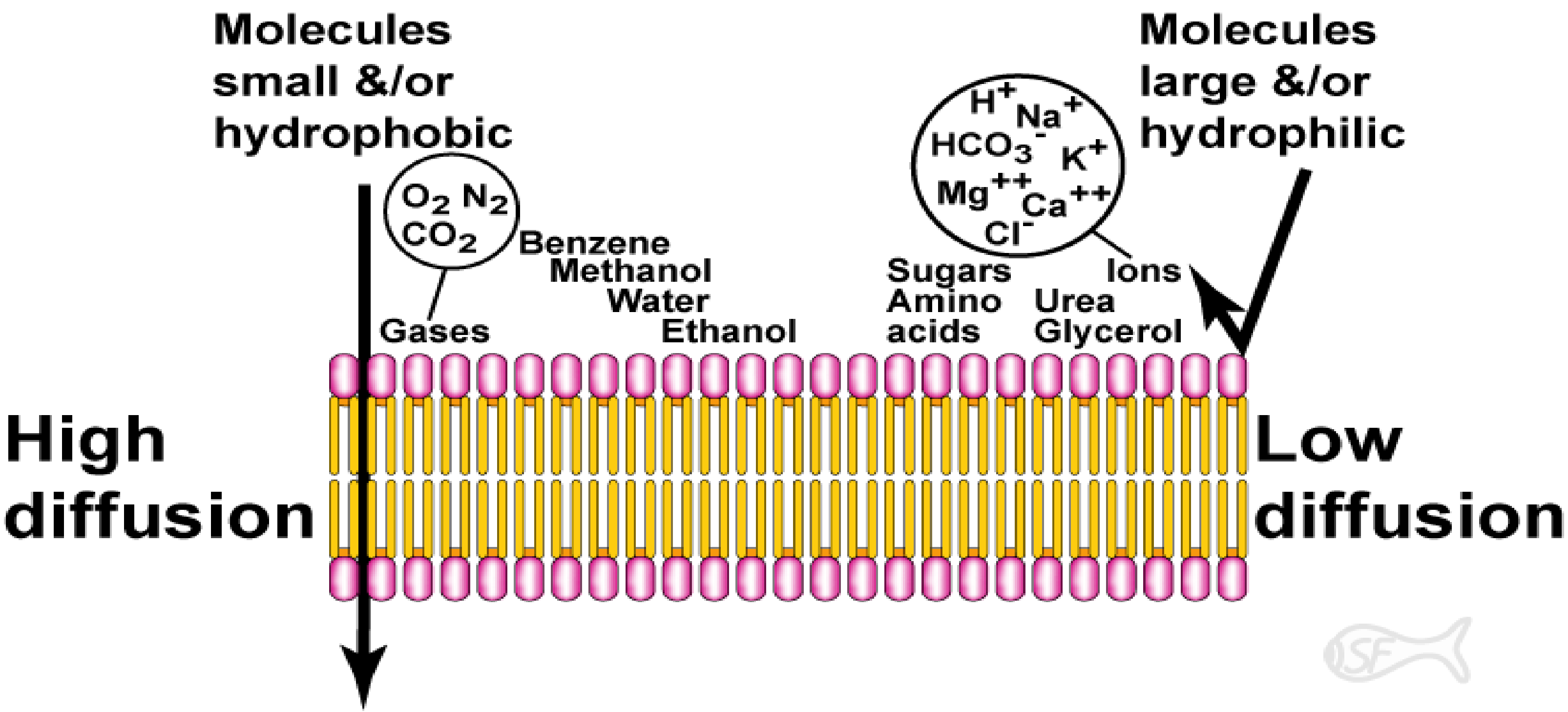
Membrane Biophysics: Carriers & Channels

The membrane lipid barrier:

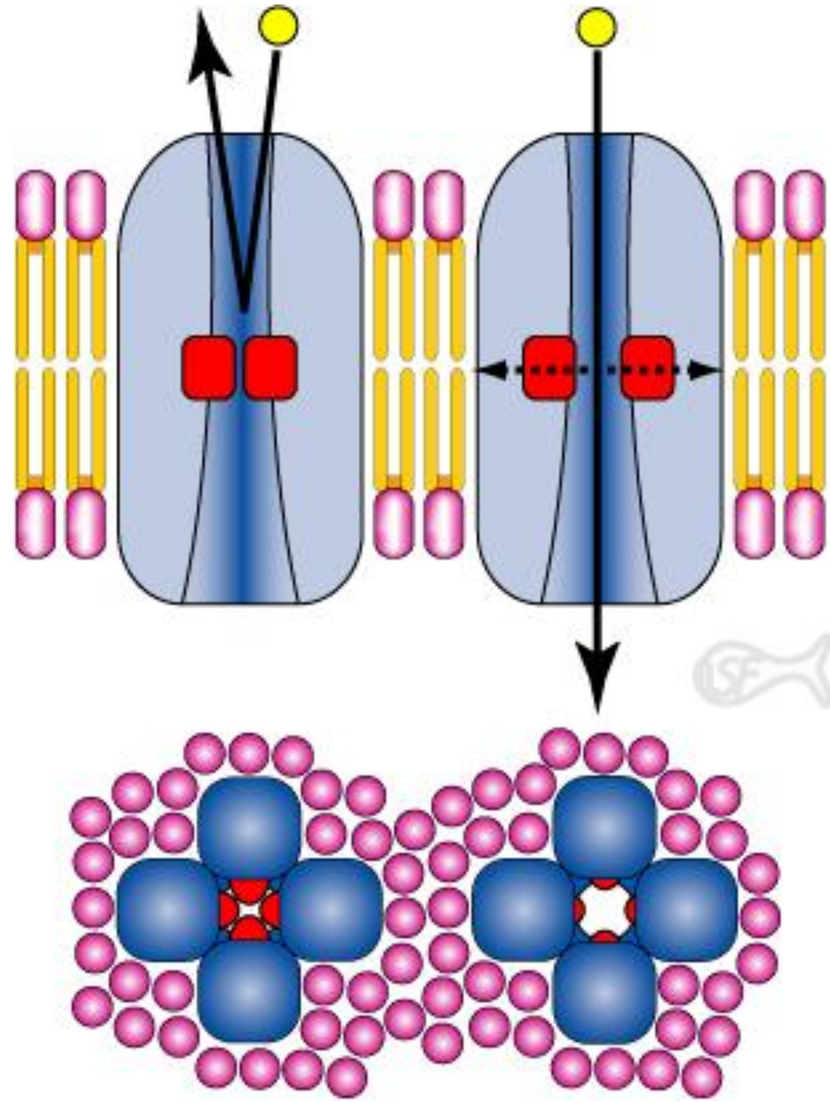
Passive diffusion through the lipid bilayer

- Concentration gradient up, diffusion up
- Molecule lipid solubility up, diffusion up
- Molecular size up, diffusion down
- Molecule electrically charged, diffusion blocked



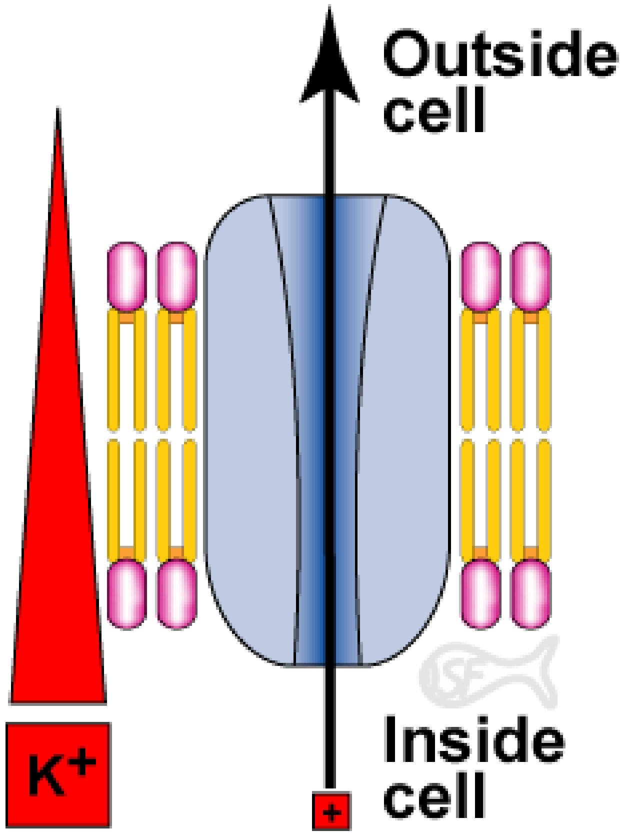
Most channel transporters are gated

- **Opening & closing of the gate mechanism**
  - Ligand gated
  - Voltage gated
  - Mechanically gated
  - Other types later in the course



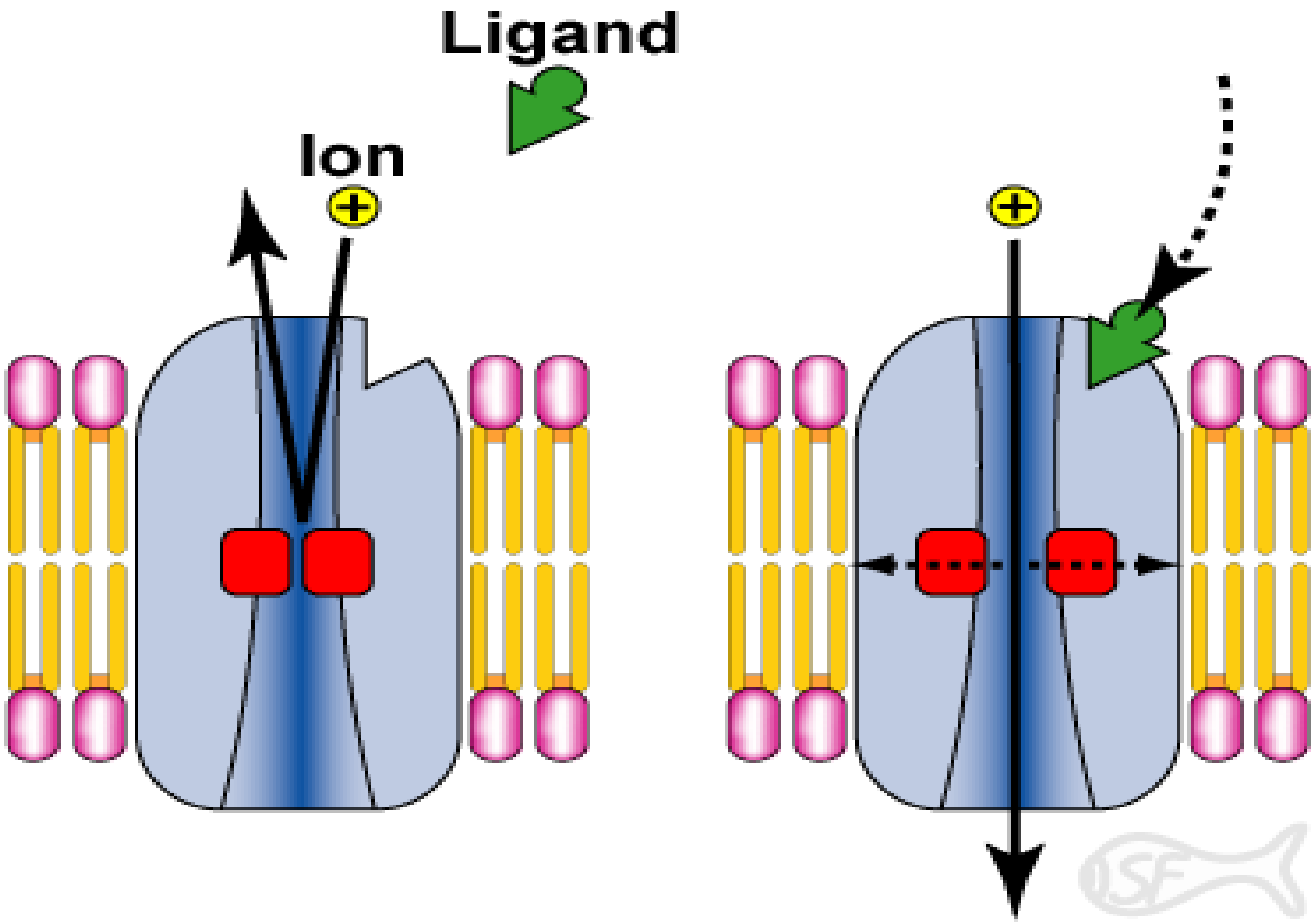
Leak channels

- Open all the time
- Best known type are K^+ channels
- K^+ going down concentration gradient out of the cell
- Increases inside negativity of the cell
- Gradient created by the Na^+-K^+ pump



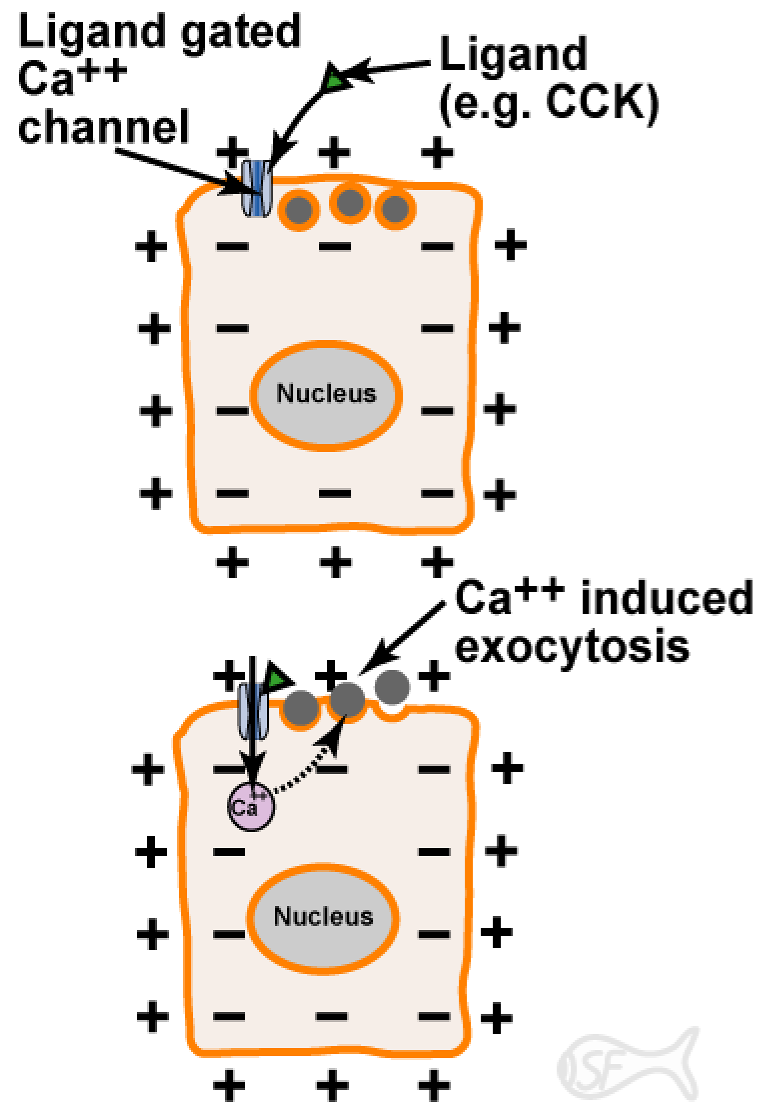
Ligand gated channels

- Binding of ligand changes conformation of the channel
- Gate opens to allow an ion (+ or -) to enter or exit the cell



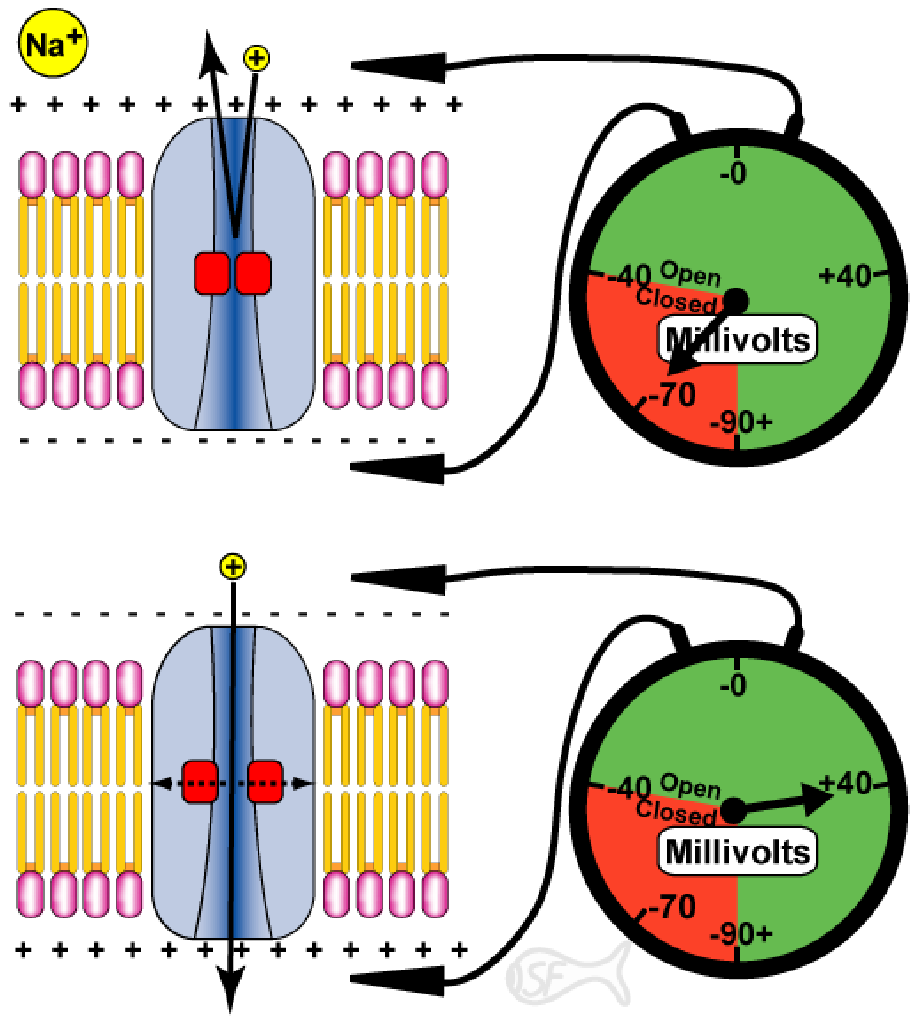
Hormones can trigger secretion

- Example- Pancreatic cells secrete digestive enzymes into the small intestine
- Ligand opens gate on Ca^{++} channel
- Membrane potential & Ca^{++} gradient sum
- Ca^{++} entering triggers fusion of vesicles with membrane

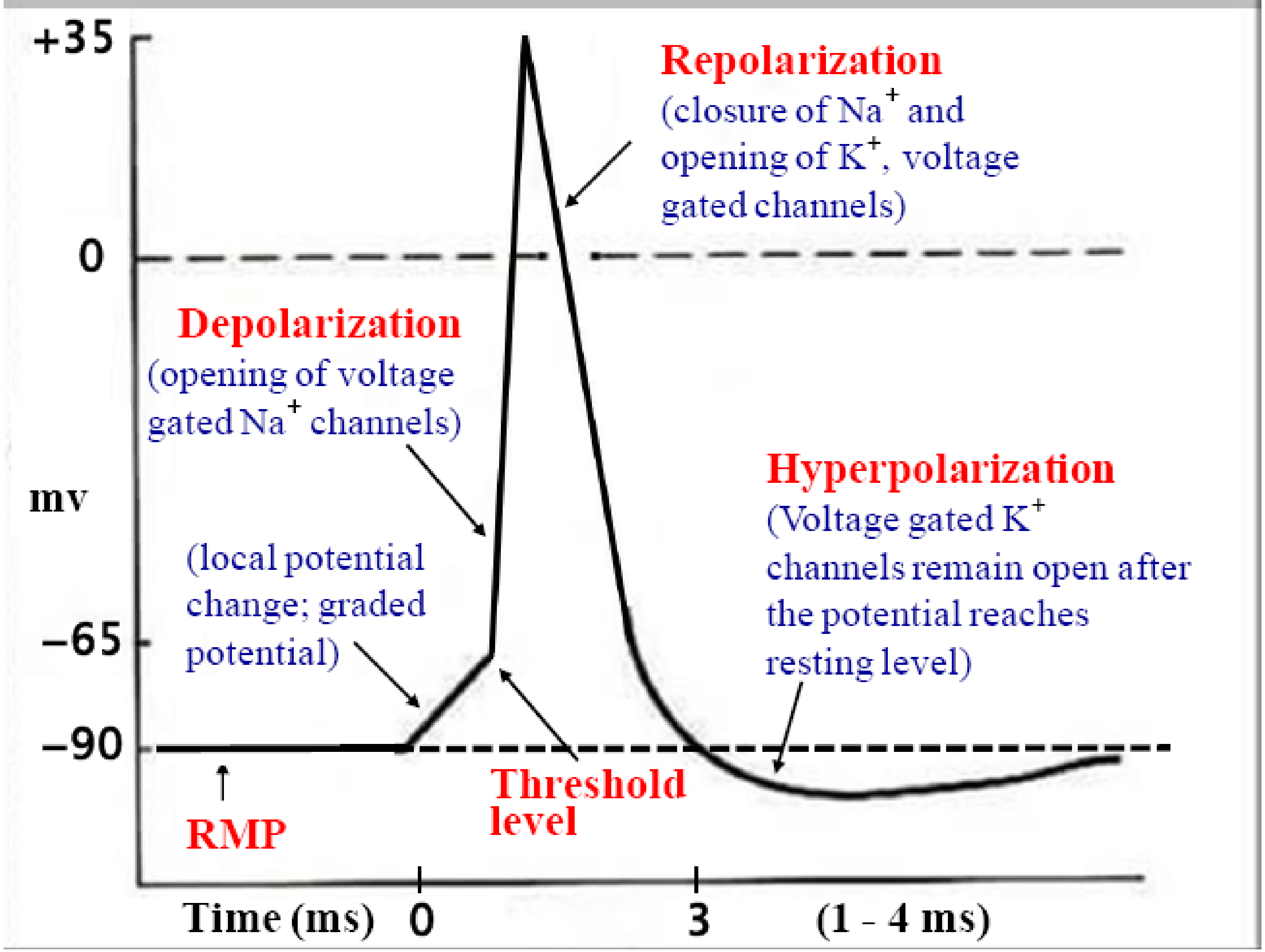


Voltage gated channels

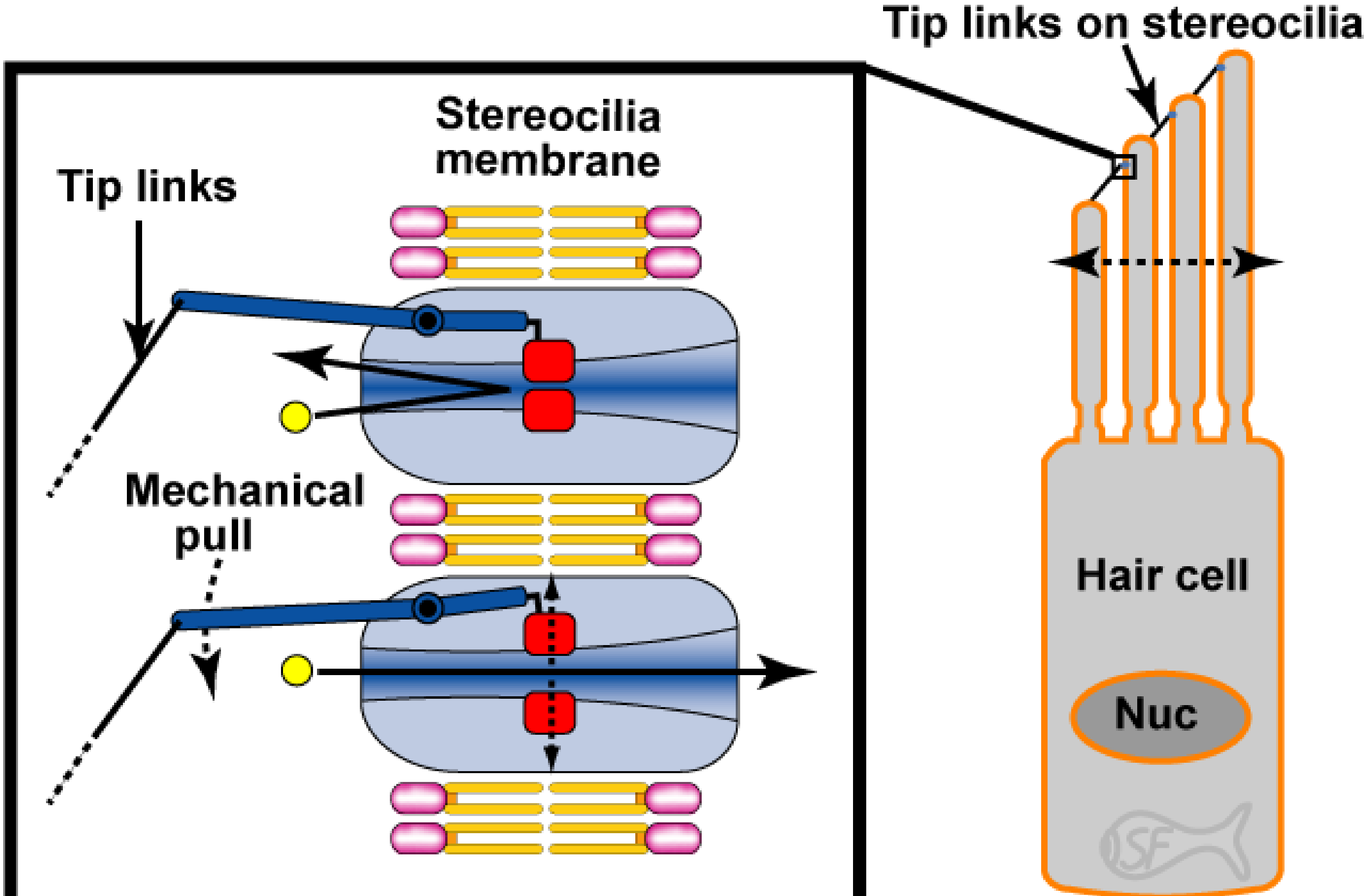
- Are sensitive to voltage across the cell membrane
- When the voltage changes to a trigger level, it opens
- The gate will close again when the voltage returns to the trigger level
- The voltage gated Na^+ channel serves as a good example



Action potential



Mechanically gated channels: hair cells in the ear



Membrane Potential

- Difference in electrical potential across cell membrane
- Generated in all cells
- Produced by separation of charges across cell membrane
  - Ion solutions
    - Extracellular fluid
    - Cytoplasm
  - Cell membrane
    - Impermeable barrier
  - Ion channels
    - Permit passage of ions through cell membrane
    - Passive (leaky channels) = with gradient
    - Active = against gradient
- Resting membrane potential

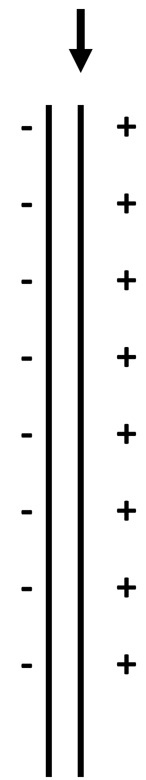
Nernst Equation

- Calculates the equilibrium potential for each ion

$$E = \frac{RT}{zF} \log \frac{[\text{ion outside cell}]}{[\text{ion inside cell}]}$$

  - R = gas constant,
  - T = temperature,
  - F = Faraday constant,
  - z = charge of the ion
  - Assumptions:
    - Membrane is permeable to ion
    - Ion is present on both sides of membrane

Cell Membrane



Cytoplasm

- **[Na+] = 15 mM**
- **[K+] = 150 mM**
- **[Cl-] = 9 mM**
- **[A-] = 156 mM**

Extracellular Fluid

- **[Na+] = 145 mM**
- **[K+] = 5 mM**
- **[A+] = 5 mM**
- **[Cl-] = 125 mM**
- **[A-] = 30 mM**

Resting Membrane Potential

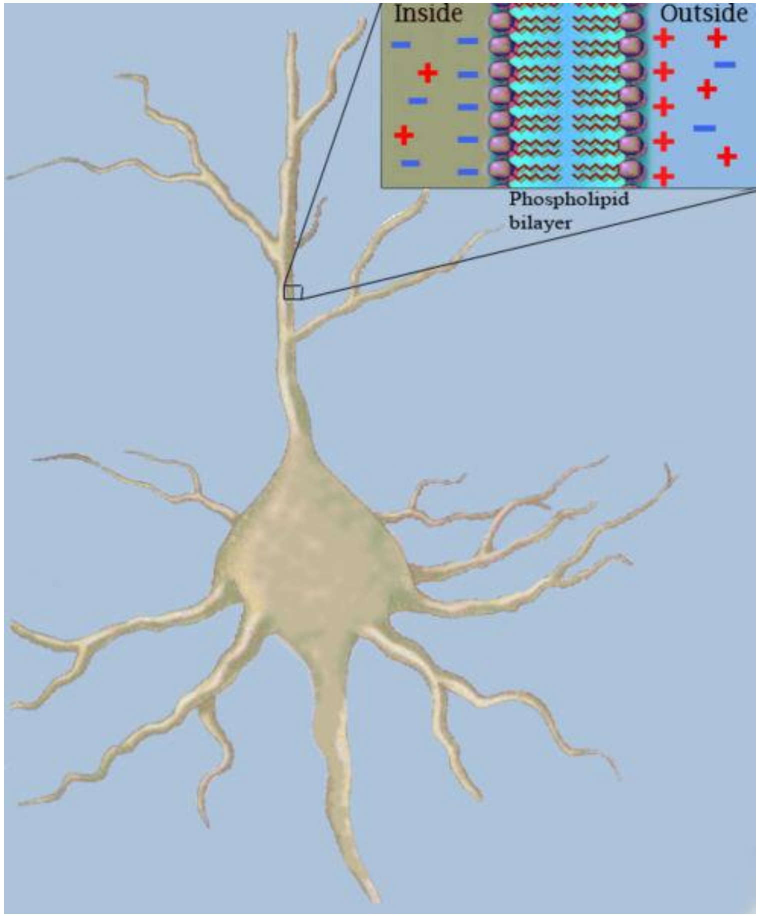
- Actually 4 ions (K^+, Na^+,Cl^-, Ca^{2+}) that strongly influence potential
- *Goldman-Hodgkin-Katz Equation*
  - Takes into account all ionic species and calculates the membrane potential

$$E_m = \frac{RT}{F} \ln \left(\frac{\sum_i^N P_{M_i^+}[M_i^+]_{\mathrm{out}} + \sum_j^M P_{A_j^-}[A_j^-]_{\mathrm{in}}}{\sum_i^N P_{M_i^+}[M_i^+]_{\mathrm{in}} + \sum_j^M P_{A_j^-}[A_j^-]_{\mathrm{out}}} \right)$$

    - P = permeabili
      - Proportior
    - Not specific to the resting membrane potential
    - Can replace p with conductance (G) and [ion]in/[ion]out with Eion
  - Greater the membrane permeability = greater influence on membrane potential
- Permeability: P_K: P_{Na}: P_{Cl} = 1 : 0.04 : 0.45
  - Cl- typically not pumped, so at equilibrium
  - K^+ dominates because greatest conductance
  - Resting membrane potential usually very negative -70 mV

Membranes as Capacitors

- Capacitor
  - Two conductors separated by an insulator
  - Causes a separation of charge
    - Positive charges accumulate on one side and negative charges on the other
- Plasma Membrane
  - Lipid bilayer = insulator
  - Separates electrolyte solutions = conductors
  - ❖ **Ionic gradient as a battery**



PASSIVE ELECTRICAL PROPERTIES

- Membrane Capacitance (C)
  - Limits the conduction velocity
    - $\Delta V = I_c \times \Delta t / C$, where I_c = current flow across capacitor, t = time, and C = capacitance
    - Takes time to unload the charge on a capacitor when changing potential.
  - Function of surface area of plates (A), distance between plates (d) and insulator properties (ε)

$$C = \frac{\varepsilon A}{d}$$

  - Lipid bilayer = great insulator properties and very thin = high capacitance

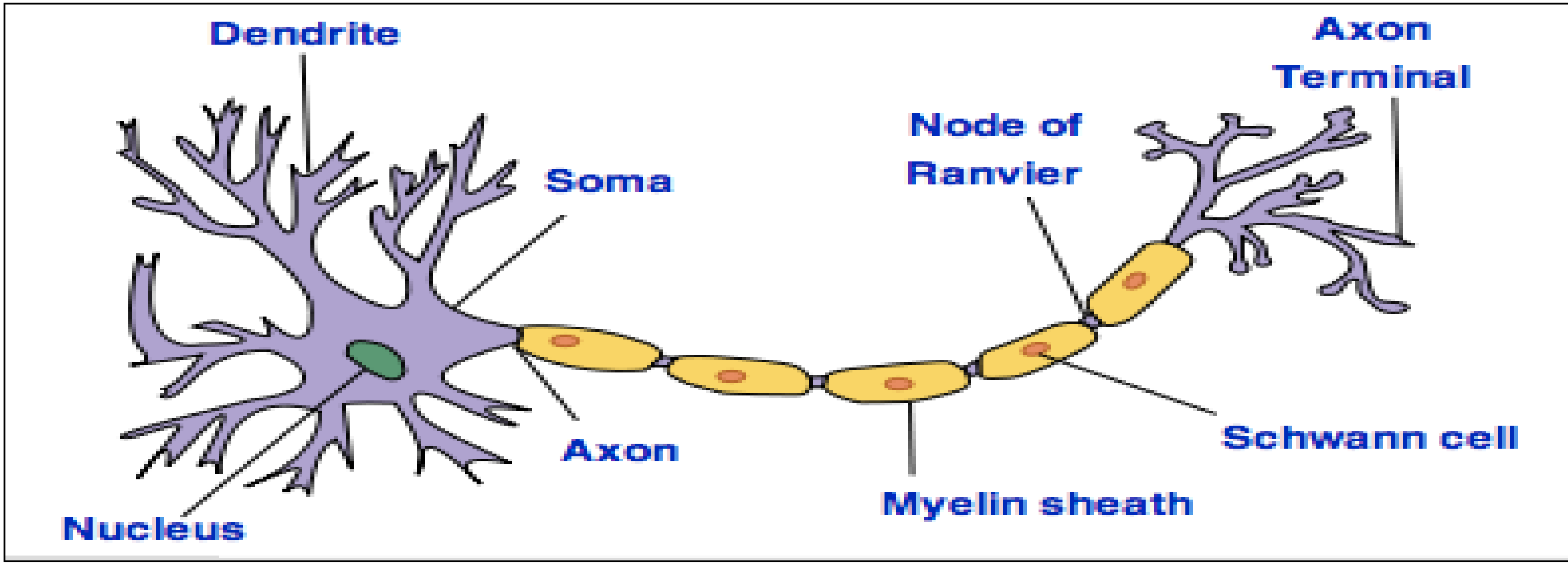
Increasing Conduction Velocity

- Myelination of axons
  - Wrapping of glial membranes around axons
  - Increases the functional thickness of the axonal membrane
    - 100x thickness increase
    - Decreases capacitance of the membrane

$$C = \frac{\varepsilon A}{d}$$

  - Same increase in axonal diameter by myelination produces larger decrease in $r_a C_m$
    - More effective increase of conduction velocity

Myelin



- Lipid-rich substance
- Produced by Schwann cells and Oligodendrocytes that wrap around axons
- Gaps between = Nodes of Ranvier

Action Potential Propagation

- Myelin decreases capacitance
  - Depolarization current moves quickly
  - Current flow not sufficient to discharge capacitance along entire length of axon

- Myelin sheath interrupted every 1-2 mm
  - Nodes of Ranvier
    - Exposed bare membrane (~2 um)
      - Increases capacitance
      - Depolarization current slows
    - High density of Na+ channels
      - Intense depolarization
      - Regenerates full depolarization of amplitude
      - Prevents action potential from dying out

- Saltatory Conduction
  - Action potential “hops” from one node of Ranvier to the next, down the axon
    - Fast in myelinated regions
    - Slow in bare membrane regions

Demyelination

- **Loss of the myelin sheath that insulates axons**
- Examples:
  - Multiple sclerosis →
  - Acute disseminated encephalomyelitis
  - Alexander's Disease
  - Transverse myelitis
  - Chronic inflammatory demyelinating neuropathy
  - Central pontine myelinosis
  - Guillain-Barre Syndrome
- **Result:**
  - Impaired or lost conduction
  - Neuronal death
  - Symptoms vary widely and depend on the collection of neurons affected

- **Symptoms vary greatly**
  - Changes in sensation
  - Neuropathic pain
  - Muscle weakness, spasms, or difficulty moving
  - Difficulty with coordination and balance
  - Speech, swallowing or visual problems
  - Fatigue
  - Cognitive impairment