PNS Chapter 7

Membrane Potential

Carnegie Mellon

18-699 / 42-590
Neural Signal Processing
Spring 2010
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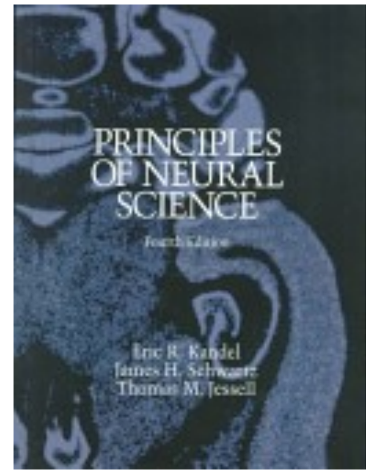
Roadmap



Introduction to neuroscience
- Chapter 1 – The brain and behavior
- Chapter 2 – Nerve cells and behavior

How are neural signals generated?
- Chapter 7 – Membrane potential ←
- Chapter 9 – Propagated signaling: the action potential

How do neurons communicate with each other?
- Chapter 10 – Overview of synaptic transmission
- Chapter 12 – Synaptic integration

Membrane Potential

• Reading assignment from *Principles of Neural Science* (PNS):
  • Chapter 7 – Membrane Potential
  • Chapter 9 – Propagated Signaling: The Action Potential (up to p.158)

• Information carried within & between neurons w/ electrical & chemical signals.

• Transient electrical signals (action potentials) critical for transmitting time-sensitive data rapidly and over long distances.

• Action potentials produced by temporary changes in current flow in/out of cell.

• This is turn changes the electrical potential across the cell membrane – the **membrane potential**.

• Current flow controlled by ion channels in membrane.

Resting and Gated Ion Channels

Resting channels

- Normally open.
- Not influenced by membrane potential.
- Important for maintaining resting membrane potential.

Gated channels

- Normally closed.
- Probability of opening is a function of external factors.
- External factors: mechanical (pressure or strech) forces, changes in membrane potential, or ligand (chemical transmitter) binding

Separation of Charges Across Membrane

• At rest, excess of + charge outside of cell membrane; - charge inside.

• Membrane maintains this separation by blocking diffusion.

• Membrane potential definition:

$$V_m = V_{in} - V_{out}$$

• Resting membrane potential (V_r) = V_m when gated channels are closed.

• V_r typically = -60 mV to -70 mV.

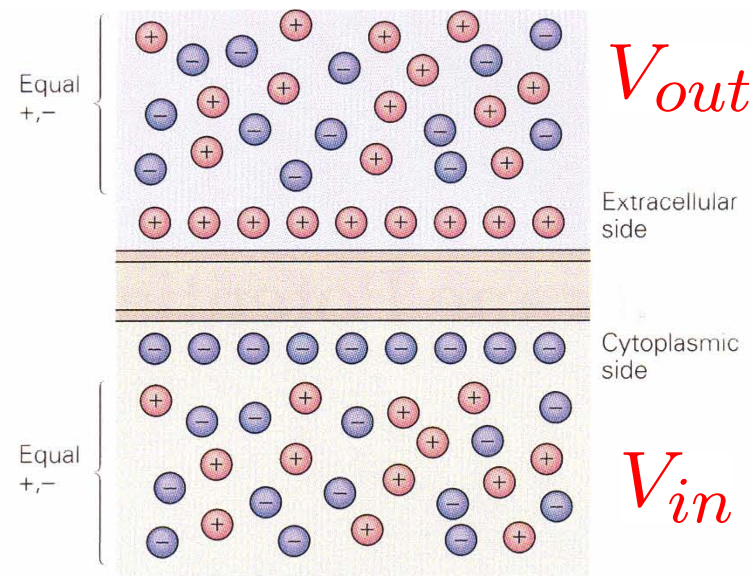


Figure 7-1 The membrane potential results from a separation of positive and negative charges across the cell membrane. The excess of positive charges (**red circles**) outside the membrane and negative charges (**blue circles**) inside the membrane of a nerve cell at rest represents a small fraction of the total number of ions inside and outside the cell.

• Electric current carriers are positive (cations) and negative (anions) ions.

• Direction of current flow defined as direction of net movement of + charge.

Recording the Membrane Potential

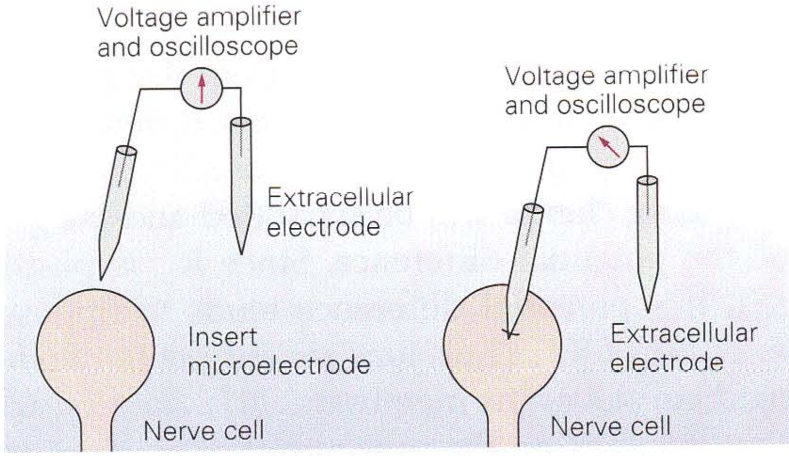


Figure 7-2A The recording setup.

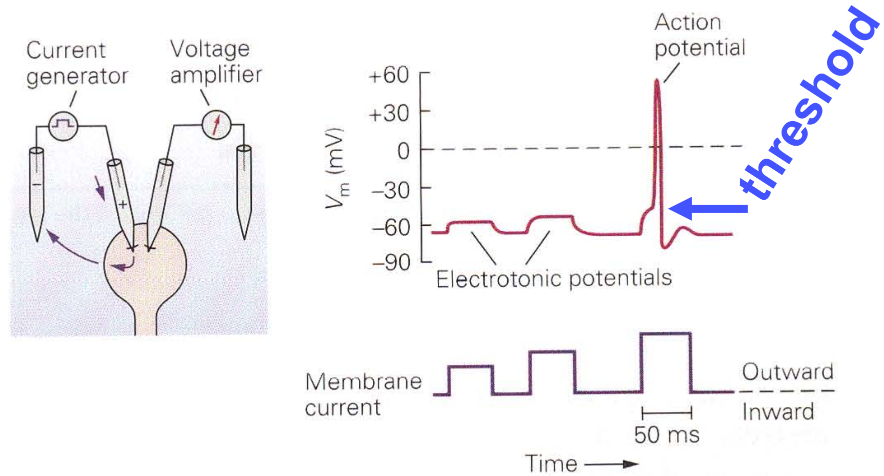


Figure 7-2C Depolarization.

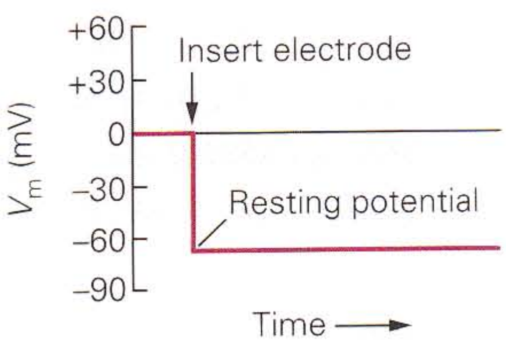


Figure 7-2B Oscilloscope display.

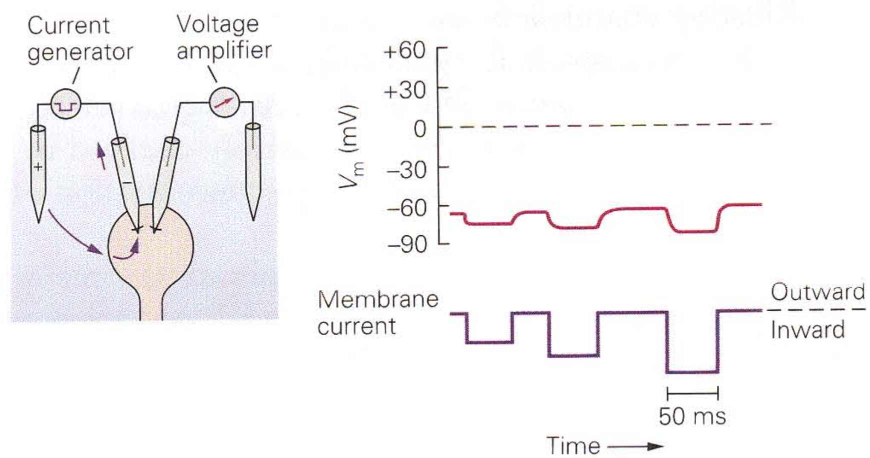


Figure 7-2D Hyperpolarization.

Resting Potential Determined by Resting Ion Channels

- No ion species is distributed equally inside/outside membrane.
- Table shows giant squid axon concentrations; ionic concentrations in vertebrates are 2-3x lower, but concentration gradients similar.

Table 7-1 Distribution of the Major Ions Across a Neuronal Membrane at Rest: the Giant Axon of the Squid

Species of ion	Concentration in cytoplasm (mM)	Concentration in extracellular fluid (mM)	Equilibrium potential[1] (mV)
K^+	400	20	−75
Na^+	50	440	+55
Cl^-	52	560	−60
A^- (organic anions)	385	—	—

[1]The membrane potential at which there is no net flux of the ion species across the cell membrane.

Concentration Gradients & Resting Potential

- For simplicity, we first consider glia.

- Simply because glial membranes are permeable to only K^+, not to all species present (we'll consider this case next).

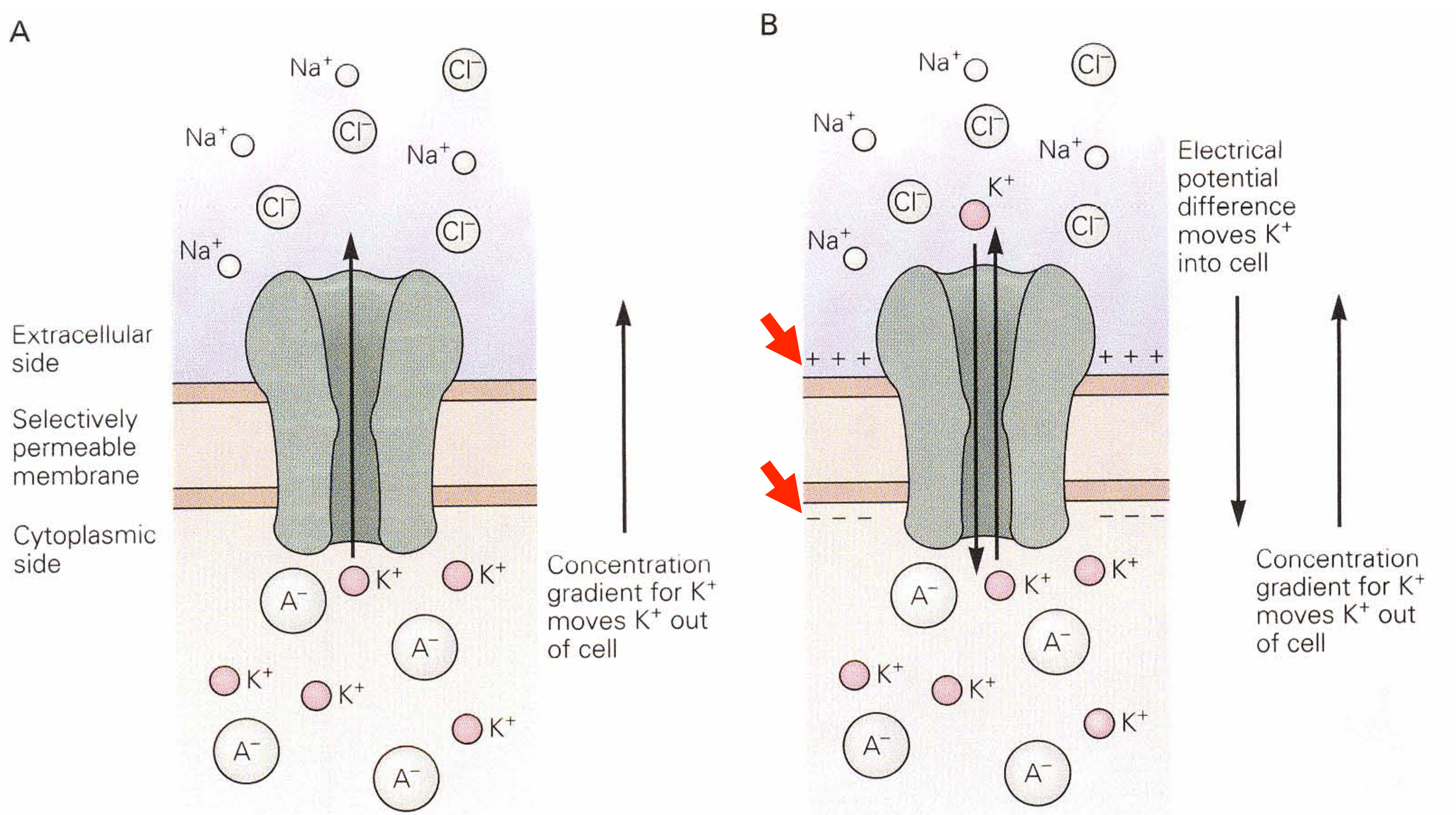
- A high concentration of K^+ and A^- exists inside the cell.

- A high concentration of Na^+ and Cl^- exists outside the cell.

- Intuitively, species that can not transport through the ion channels must stay put (inside or outside of cell).

- Intuitively, species (i.e., K^+) that can transport through the ion channels can potentially do so – but there must be a driving force.

Sketch of Drift and Diffusion Currents



7-3 The flux of K+ across the membrane is deter- by both the K+ concentration gradient and the elec-

charge on the outside of the cell and leaves behind o side an excess of negative charge. This buildup of cha

Concentration Gradients & Resting Potential

1) K^+ diffuse inside→outside cell, down concentration gradient, creating diffusion current.

2) Thus, outside accumulates a slight excess of + charge (K^+) and inside accumulates a slight excess of - charge (lack of $K^{+)}$.

3) Excess charges attract, forming sheet charges along membrane.

4) Sheet charges create electric (E) field, pointing from outside→in (+→-).

5) E-field applies force (drift) on K^+ ions in direction of E-field (outside→in). This creates drift current.

6) At equilibrium (no net current flow), a specific E-field exists such that drift current is equal and opposite diffusion current.

Concentration Gradients & Resting Potential

- The potential difference across the membrane associated with this specific E-field is termed the equilibrium potential (E_K).

- As per previous table, E_K = -75 mV.
  Note: don't be confused, here E is a voltage not an electric field.

- Equilibrium potential for arbitrary ion X given by Nernst equation:

$$E_x = \frac{RT}{zF} ln \frac{[X]_o}{[X]_i}$$

with *R* (gas constant), *T* (temperature in Kelvin), *z* (valence of the ion), *F* (Faraday constant) and $[X]_o$ and $[X]_i$ are chemical concentrations outside and inside of cell.

Calculating Resting Potential

- Since *RT*/*F* = 25 mV at room temperature (25° C), we can write:

$$E_x = \frac{25mV}{z} \; ln \frac{[X]_o}{[X]_i}$$

- Or, including a factor of 2.3 to convert ln → log:

$$E_x = \frac{58mV}{z} \; log \frac{[X]_o}{[X]_i}$$

- And, with z = 1 for K^+:

$$E_x = 58mV \; log \frac{[20]}{[400]} \; = \; -75mV$$

Calculating Resting Potential

- Nernst Equation can be used to find the equilibrium (resting) potential of any ion that is present on both sides of a membrane permeable to that ion.

- See previous table (repeated here for convenience) for equilibrium potentials associated with each ion present in the giant squid axon:

Table 7-1 Distribution of the Major Ions Across a Neuronal Membrane at Rest: the Giant Axon of the Squid

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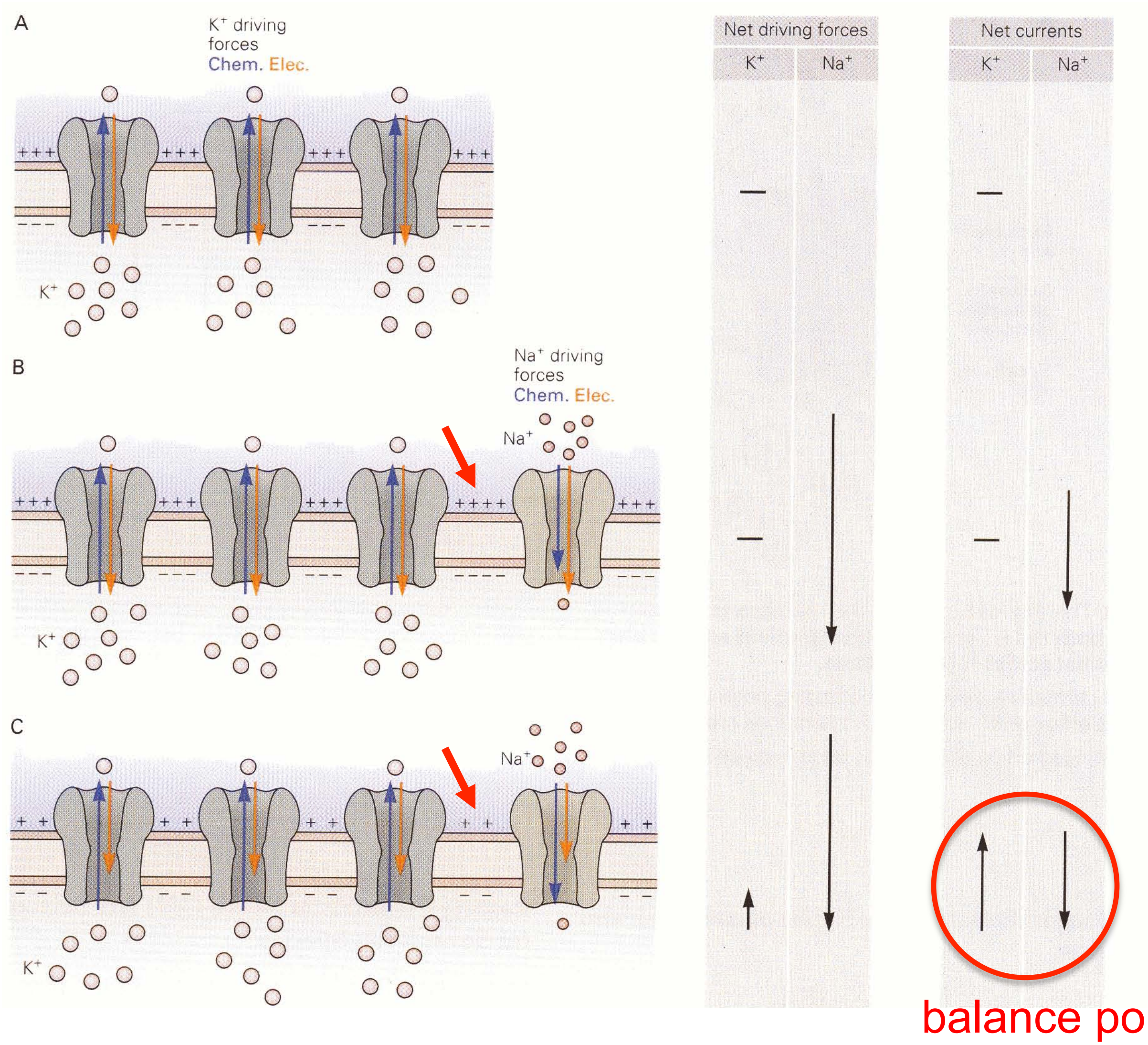
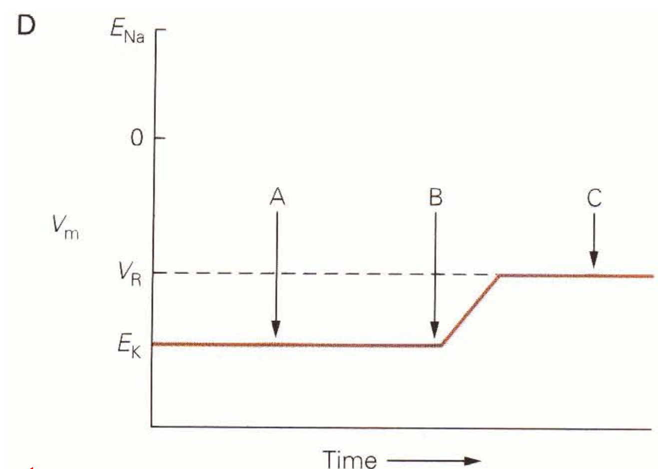
Concentration Gradients & Resting Potential

- Having considered simple glia, we now turn to neurons.
- Neurons at rest are permeable to Na^+ and Cl^- ions, in addition to K^+ ions.
- A^- ions unable to permeate; thus set aside.
- When multiple ion species can permeate membrane, a new resting potential is established such that net current flow is zero (steady state).

Understanding Resting Potential w/ 2 Species



- Why isn't Na^+ flux huge?
- Can these equal and opposite K^+ and Na^+ continue indefinitely?



Why isn't Na^+ influx huge?

• Ion flux is the product of electrochemical driving force and membrane conductance to that ion:

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

• There are relatively few <u>***resting***</u> Na^+ channels (compared w/ resting K^+ channels) so the conductance to Na^+ is quite low.

Na^+ - K^+ Pump

• Now assume that the resting potential has been achieved.

• Passive movement of K^+ out of cell = passive movement of Na^+ into cell.

• But these concentrations gradients will eventually run down, thereby reducing the resting membrane potential!

• Need Na^+ - K^+ pump.

• Moves Na^+ and K^+ against their net electrochemical gradients.
Moves Na^+ out of cell; moves K^+ into cell.

• Pump requires energy (ATP hydrolysis).

• Continuous passive influx of Na^+ and efflux of K^+ through resting channels is counterbalanced by Na^+ - K^+ pump.

• Pump: membrane-spanning protein; 3 Na^+ ions out for every 2 K^+ ions in.

Another Quick Peek at Action Potentials

- Though we will study action potentials in depth soon enough, a quick peek is warranted now.

- If the membrane is depolarized past the "threshold voltage", then voltage-gated Na^+ channels open rapidly.

- Thus Na^+ influx exceeds K^+ efflux → further depolarization → even more voltage-gated Na^+ channels open → …   (positive feedback system)

- Takes V_R very close to E_{Na} = + 55 mV because permeability to Na^+ is predominant.

- Why does membrane ever repolarize, to end action potential?
    - Voltage-gated Na^+ channels gradually *inactivate*.
    - Voltage-gated K+ channels are slow, but eventually open.

Goldman Equation: V_R w/ Multiple Species

- Membrane conductance (1/resistance) is a convenient measure of how readily an ion crosses the membrane.

- Permeability (P, units of cm/s) is another convenient measure; similar to a diffusion constant.

- Membrane potential is easy to calculate w/ Goldman Equation:

$$V_m = \frac{RT}{F} ln \frac{P_K[K^+]_o + P_{Na}[Na^+]_o + P_{Cl}[Cl^-]_i}{P_K[K^+]_i + P_{Na}[Na^+]_i + P_{Cl}[Cl^-]_o}$$

- Species with highest concentration and permeability dominates – consider limit cases:

  At rest, permeability of K^+ dominates.
  At peak of action potential, permeability of Na^+ dominates.

Dynamic range of action potential waveform

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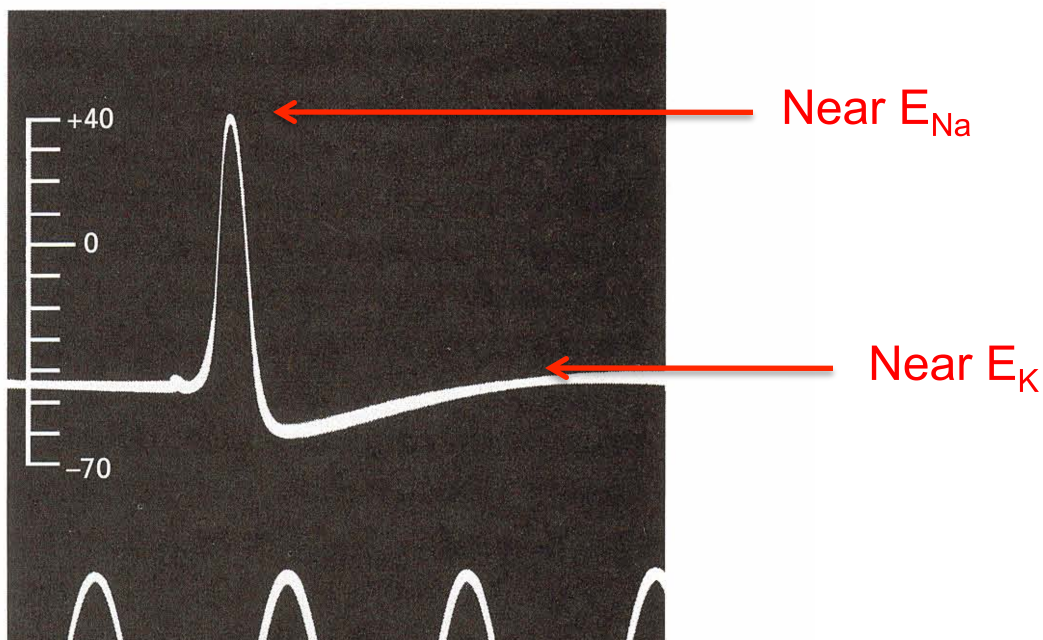

Rest of Chapter 7

• We've covered topics in Chapter 7 up to, but not including, the section titled, "The Functional Properties of the Neuron Can Be Represented in an Electrical Equivalent Circuit".

• If you've had a circuits course, it turns out that a neuron can be thought of as an electrical circuit, where:

- Resistors – represent the ion channels.
- Voltage sources – represent concentration gradients of relevant ions.
- Capacitors – capacity of membrane to store charge.
- Current sources – Na^+-K^+ pump.

• Feel free to read if you are interested in learning more.