

Lecture 4 -- Neuroexcitability II -- Koester

The Action Potential: Generation and Conduction *Voltage-Gated Ion Channels: Diversity and Evolutionary Relationships*

I. From V_m and I_{Na} , one can calculate g_{Na}

- A. $V_m = E_{Na} + I_{Na}/g_{Na}$ - from the circuit
- B. $I_{Na} = g_{Na} (V_m - E_{Na})$ - generally useful form of the equation
- C. $g_{Na} = I_{Na} / (V_m - E_{Na})$ - used to calculate g_{Na}

II. Voltage-activated g_{Na} and g_K have:

A. Similarities:

- 1. More depolarization causes a greater conductance increase
- 2. More depolarization causes a faster conductance increase

B. Differences:

- 1. g_{Na} activates faster – allowing net influx of positive charge
- 2. g_{Na} inactivates with maintained depolarization, contributing to repolarization
 - a) Na channels have activation and inactivation gates
 - b) Recovery from inactivation at V_{rest} takes time

III. Generation of the action potential

- A. Positive feedback causes upstroke
- B. Negative feedback causes falling phase and (subsequently) the refractory period

- 1. g_{Na} inactivation
- 2. Increased g_K

IV. Conduction of the action potential:

- A. Local circuit flow of current
- B. Two phases of spread of the action potential:

- 1. Active
- 2. Passive
 - a. r_a limits current flow, thereby slowing the rate of discharging of c_m
 - b. Spread of depolarization limited by r_a and c_m
 - b1. Increased axon diameter reduces r_a
 - b2. Myelination reduces c_m , and increases effective r_m

V. Functional analysis reveals wide diversity of channel types in the nervous system, based on differences in:

A. Selectivity

- B. Kinetics of activation
- C. Voltage-range of activation
- D. Physiological modulators (e.g., $[Ca^{++}]_i$, cyclic nucleotides, etc.)

VI. Voltage-gated ion channels belong to two major gene superfamilies:

A. Cation permeant (4-fold symmetry; similar secondary, tertiary and quaternary structures):

1. Voltage-gated

- a. K^+ permeant
 - a1. Six transmembrane helices
 - a2. Two transmembrane helices (inward rectifiers = hyperpolarization-activated)
- b. Na^+ permeant
- c. Ca^{++} permeant
- d. Cation – non-specific permeant (HCN = hyperpolarization-activated)

2. *Cyclic nucleotide-gated*

3. *TRP family*

4. *TWIK = K^+ permeant leakage channels*

B. Anion (Cl^-) permeant (channels form from single proteins, which combine as dimers to give double-barrelled structure):

- 1. Voltage-gated
- 2. *Cell swelling-gated*
- 3. *pH-gated*

Relevant reading: chapter 9 in “Principles”