Lecture 4

Neuroexcitability II

The Action Potential: Generation and Conduction
Voltage-Gated Ion Channels: Functional 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. <u>Generation</u> 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. <u>Conduction</u> 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. <u>Functional diversity</u> of voltage-gated 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. <u>Cation permeant</u> (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. Non-Voltage-gated

2. Cyclic nucleotide-gated
3. TRP family – activated by various second messenger pathways
4. permeant leakage channels

B. <u>Anion (Cl^-) pemeant</u> (channels form from single proteins, which combine as dimers to give double-barreled structure):

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