I. From $V_m$ and $I_{Na}$, one can calculate $g_{Na}$
   A. $V_m = E_{Na} + \frac{I_{Na}}{g_{Na}}$ - from the circuit
   B. $I_{Na} = g_{Na} (V_m - E_{Na})$ - generally useful form of the equation
   C. $g_{Na} = \frac{I_{Na}}{V_m - E_{Na}}$ - 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 diversity 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. **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. **Non-Voltage-gated**

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

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

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