Objectives:
The student should be able to:
1. Describe a graded potential.
2. State how stimulus polarity and magnitude affect a graded potential.
3. Define spatial and temporal summation of graded potentials.
4. List the sequence of membrane permeability changes responsible for an action potential.
5. Define absolute and relative refractory periods.
6. Describe how some anesthetics can block nerve activity.

Outline:
I. Graded potentials
   A. Opposite charges attract one another, and therefore will dissipate to electroneutrality.
   B. A local perturbation in membrane potential:
      1. affects the membrane potential at some distance from the site of the perturbation;
      2. decrements over time and distance;
      3. produces local currents because of the charge movement.
   C. Features of a graded potential:
      1. change from the resting membrane potential can be either more positive (depolarization) or negative (hyperpolarization);
      2. depends upon the initial stimulus magnitude;
      3. decrements over distance and time;
      4. summates with other stimuli in time and space (both positive and negative).
   D. If a depolarizing graded potential is sufficiently large, it will produce an action potential (below).
II. Action potentials

A. There is a threshold potential for stimulation of an action potential
   1. voltage-gated sodium channels are normally closed at resting membrane potentials (low sodium permeability);
   2. near the threshold potential some channels begin to open, allowing sodium to flow in and further depolarize the membrane;
   3. more sodium channels open, further depolarizing the membrane and opening most or all of the sodium channels (regeneration);
   4. the membrane potential will approach the sodium equilibrium potential because of the high membrane permeability to sodium relative to potassium.

B. Changes in membrane permeability are responsible for the shape of the action potential.
   1. sodium channels open in response to a suprathreshold stimulus, causing the membrane potential to “spike” near the sodium equilibrium potential because the potassium permeability is low relative to the sodium permeability;
   2. sodium channels also exhibit a rapid voltage-dependent inactivation that occurs at potentials more positive than the resting membrane potential;
   3. sodium channel inactivation begins to decrease the sodium permeability;
   4. at the same time sodium channels are inactivating the potassium channels begin a voltage-gated activation, increasing the potassium permeability;
   5. the increased potassium permeability combined with the decreased sodium permeability returns the membrane potential to rest or even hyperpolarized potentials;
   6. at the resting potential potassium channels close once again and the spontaneous inactivation of the sodium channels “resets.”

C. The membrane becomes refractory to another action potential during and for a time following an action potential.
   1. sodium channel inactivation is “reset” only at membrane potentials at or hyperpolarized below the resting membrane potential;
   2. it takes a period of time several times longer than the action potential for the sodium channels to reset;
   3. during and immediately following the action potential the membrane is in a absolute refractory period because no amount of stimulus can open the inactivated sodium channels;
   4. as time progresses more and more sodium channels are reset, so that some may be opened;
   5. initially a greater than threshold stimulus is required to generate an action potential because not all the sodium channels have reset (relative refractory period);
   6. as more time elapses the stimulus intensity required to produce an action potential returns to the normal threshold level.
D. In some cell types other ions may participate in the action potential, *e.g.*, calcium moving similarly to sodium from a high concentration outside the cell to a low concentration inside through a regenerative calcium channel.

E. The initial stimulus for the threshold depolarization may:
   1. arise from voltage-gated changes in membrane permeability;
   2. arise from ligand-gated changes in membrane permeability (*e.g.*, increased sodium influx);
   3. be inhibited by hyperpolarizing changes in membrane permeability.

F. Many anesthetics block the opening of the sodium channel or the flux of sodium through the channel, preventing a threshold stimulus from initiating an action potential.