Medical Neuroscience | Tutorial Notes

Ionic Basis of the Action Potential

MAP TO NEUROSCIENCE CORE CONCEPTS[1]

NCC2. Neurons communicate using both electrical and chemical signals.

LEARNING OBJECTIVES

After study of the assigned learning materials, the learner will:

1. Use the Goldman (and Nernst) equations to predict the membrane potential of neurons given knowledge of the concentration gradients of ions and their relative permeabilities across the neuronal plasma membrane.
2. Describe the ionic basis of the action potential in terms of the voltage- and time-dependant changes in ionic permeabilities that occur across the neuronal plasma membrane.
3. Describe the driving force for current flow across the plasma membrane.
4. With careful precision, relate the time course of changes in Na^+ and K^+ conductance to changes in membrane potential during the action potential.
5. Characterize the refractory period for action potential generation.

TUTORIAL OUTLINE

I. Introduction: changes in membrane permeability underlie the neuronal action potential

- A. let's review the changes in membrane permeability that, in principle, underlie the neuronal action potential (see **Figure 2.7B**[2])
  1. at rest the neuronal membrane is permeable to K^+, but not to Na^+ ($P_{K+}>>P_{Na+}$); thus, the resting membrane potential approaches E_K
  2. for a very brief interval (about 1 msec), the membrane may become highly permeable to Na^+ ($P_{K+}<<P_{Na+}$); thus, at the peak of the action potential, the membrane potential approaches E_{Na}
- B. view an online animation that accompanies *Neuroscience, 5th. Ed.*, Chapter 2: Animation 2.2 Electrochemical Equilibrium [click here]

II. Ionic currents across neuronal membranes

[1] Visit **BrainFacts.org** for *Neuroscience Core Concepts* (©2012 Society for Neuroscience) that offer fundamental principles about the brain and nervous system, the most complex living structure known in the universe.
[2] Figure references to Purves et al., *Neuroscience, 5th Ed.*, Sinauer Assoc., Inc., 2012. [click here]

A. voltage clamp method (see **Box 3A**, p. 42)

1. necessary to study permeability changes without evoking action potentials (because action potentials involve explosive changes in membrane potential, it is difficult to control and study membrane permeability when they occur)
2. method of recording neural activity that allows experimenters to measure *current flow* across a membrane without changing the membrane potential

B. *membrane permeability is voltage dependent* (see **Figure 3.1**)

1. depolarization of the membrane to near 0 mV induced two types of currents that could be distinguished based on their direction of flow across the membrane and their distinct time courses
   - **a. transient inward current**
   - **b. delayed outward current**

C. these *currents are carried by Na^+ and K^+*

1. based on the Nernst equation, Hodgkin and Huxley knew the equilibrium potentials for Na^+ and K^+
2. remember, at an equilibrium potential, there is no net current flow (the concentration gradient is exactly counterbalanced by the electrical gradient)
3. so, adjusting the membrane potential to the equilibrium potential of a given ion should remove the contribution of that ion to the total current flowing across the membrane (see **Figures 3.2** & **3.3**)
   - a. with increasing depolarization of the plasma membrane, both the transient inward and delayed outward currents changed in magnitude
   - **b. transient inward current**
     - (1) depolarization to small positive potentials (e.g., +26 mV) reduced the size of transient inward current
     - (2) at +52 mV (very near E_{Na} for the experimental system) the transient inward current *disappeared*
     - (3) at even more depolarizing potentials (+65 mV), the inward current *reversed*
     - (4) the behavior of the inward current was nearly identical to what was predicted for a **Na^+ current**, given the known concentrations of Na^+ inside and outside of the axon
     - (5) the identity of this current was confirmed in ion-substitution experiments where Na^+ was removed from the extracellular medium (see **Figure 3.4**)
   - c. **delayed outward current**
     - (1) as depolarization increased, the delayed outward current steadily increased in magnitude

(2) removal of Na^+ from the extracellular medium did not affect the delayed outward current

(3) this behavior is consistent with a **K^+ current**, which further experiments confirmed (see **Figure 3.5**)

III. Reconstruction of the action potential

A. effect of voltage on Na^+ and K^+ conductance

1. **conductance**: the reciprocal of membrane resistance; the electrical term used to describe the opening and closing of ion channels (symbolized as *g*)

2. easily determined by rearranging Ohm's law and substituting a "**driving force**" term for voltage

$$I = g\ V$$

A "driving force" term can be substituted for *V* to account for the difference between the membrane potential and Nernst equilibrium potential for a given ion; thus

$$I_{ion} = g_{ion}\ (V_m - E_{ion})$$

I_{ion}	Ionic current
$\boldsymbol{g_{ion}}$	**Ionic conductance**
V_m	Membrane potential
E_{ion}	Nernst equilibrium potential

3. Hodgkin and Huxley recorded membrane currents under voltage clamp conditions and calculated membrane conductance for Na^+ and K^+

a. **both conductances are voltage-dependent** (implies that the mechanism responsible for conductance must be capable of sensing changes in membrane potential)

b. **both conductances change over time** (see **Figure 3.6**)

i. after activation, the Na^+ conductance **inactivates**, which means the current stops flowing despite the persistence of an electrochemical driving force

ii. not so for the K^+ conductance; current flows as long as there is an electrochemical driving force

B. The Hodgkin-Huxley model of the action potential (see **Figures 3.8** & **3.9**)

1. ACTION POTENTIAL IS EXPLAINED BY VOLTAGE-DEPENDENT AND TIME- DEPENDENT CHANGES IN THE PERMEABILITY OF THE NEURONAL MEMBRANE TO Na^+ AND K^+

2. this model also explains the *threshold* for the generation of an action potential (see **Box 3B**) and the *all-or-none* (regenerative) character of the action potential (see **Figure 3.9**)

3. model also explains the *refractory period* of the action potential

a. when the Na^+ conductance is inactive, it is not possible for the local region of membrane to generate another action potential; this period of Na^+ inactivation is called the *absolute* refractory period

b. after Na^+ de-inactivation (removal of Na^+ inactivation), it is possible to generate an action potential, but the prolonged activation of the K^+ conductance means that it will be more difficult to elicit another action potential; this period of K^+ conductance activation after Na^+ de-inactivation is termed the *relative* refractory period

4. Hodgkin-Huxley model holds for the vast majority of neurons in the CNS

C. Review the content of this tutorial by viewing an online animation that accompanies *Neuroscience, 5th. Ed.*, Chapter 2: **Animation 2.3 The Action Potential** [click here]

STUDY QUESTION

The regenerative nature of the action potential is explained by a fast positive cycle turning at a faster rate than a slower, negative cycle. Given these facts, why is the action potential a "spike"? That is, what single factor best explains the short duration of the typical, neuronal action potential?

A. Depletion of extracellular sodium.
B. Depletion of intracellular potassium.
C. Potassium channel inactivation.
D. Sodium channel inactivation.