Lecture 07. Ion Channel Structure and Function

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Reading

Bear pp. 73-75; 92-96; and Box 4.6

Lecture Objectives:

1. To learn how single channels underlie the flow of the currents through the neuronal membrane.

2. To examine the molecular and crystal structure of ion channel proteins to understand how they give rise to channel properties such as selectivity, high ion throughput, and voltage sensitivity.

3. To learn about the diversity of ion channels and the importance of that diversity.

Lecture Outline

We now know much about the physiology and molecular structure of single ion channels. In fact, two relatively recent Nobel prizes have been awarded for studies examining the structure and function of ion channels at the level of individual channels. In this lecture, we will look more closely at the channels and how their properties give rise to the electrical properties of the neuron as a whole.

1. **Some expected properties of channels were predicted even before the channels could be studied at the single channel level:**

A. Ions must be able to flow through the channels fast to account for the very rapid potential changes during an action potential (which last about 1millisecond).

B. There must be some differences in which ions can pass through particular channels. For example, there seem to be currents that are carried by potassium and others by sodium, suggesting that somehow the channels "select" which ions pass through them.

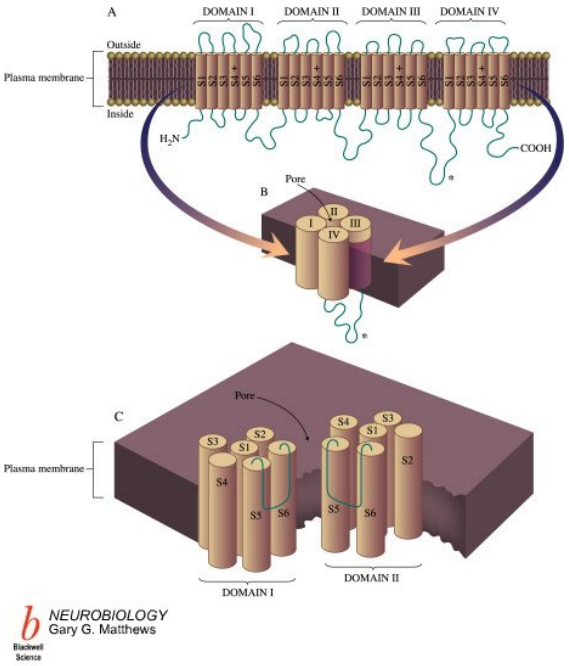
C. The channels must somehow be able to sense the potential across the membrane and open or close in response to it based upon the voltage clamp data. We have seen a crude model of how this might occur for the sodium channel, but need to explore what parts of the channel accomplish this.

2. **The invention of Patch clamp recording to measure currents through individual channels.**

A. The patch clamp method, described in 1976, resulted in a Nobel Prize for Sakmann and Neher in 1991. You will learn how it works.

3. **Molecular structure of ion channels.**

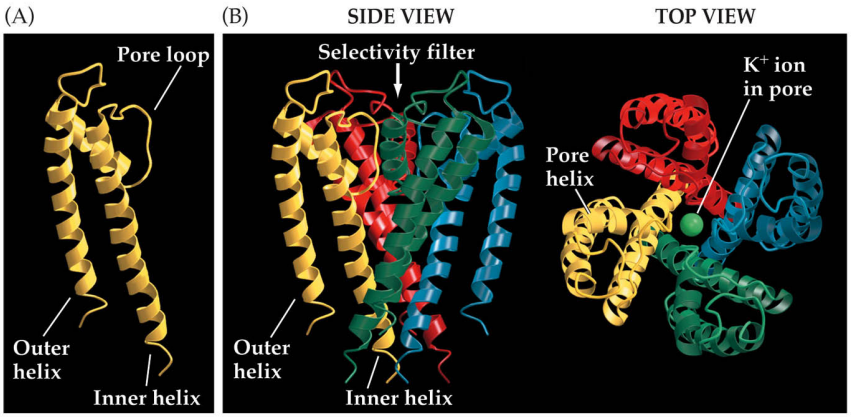
A. Structure of the voltage gated sodium channel.



One polypeptide with four domains, each with 6 membrane spanning regions, surrounding a central pore. Details of the functional domains inferred by mutagenesis studies reveal probable location of pore, voltage sensor, m and h gates.

B. Structure of the first crystallized potassium channel led to a direct visualization of the channel in the membrane and another Nobel prize (in chemistry to Rod Mackinnon in 2003).

4. **There is a great diversity of ion channels, even within those selective for a particular ion. The ion channels that form gene families that arose via gene duplication. Why are there so many channel types?**



A. Diversity of channels allows for fine tuning of the firing properties of individual neurons by incorporating different ion channel combinations and placing them at different locations in the neuron.

B. Neurons

have many different firing properties that reflect these differences in the ion channels in their membranes. For example, some neurons fire rhythmic bursts of action potentials without any input, others fire in brief bursts even to a sustained depolarizing input, and still others can follow a sustained depolarization with firing at high frequencies.

Study Questions:

1. How could channels that have only an open and closed state give rise to a whole cell membrane potential that appears to change continuously?

2. Why is a K channel so much more selective to K than Cl? Why is it more selective to K than to Na?

3. How does a voltage change across the membrane open an ion channel?

4. Why are there so many ion channel proteins?