Voltage-Gated Ion Channels and the Action Potential

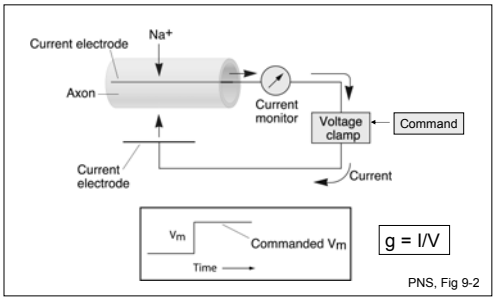
jdk3

Principles of Neural Science, chaps 8&9

Voltage-Gated Ion Channels and the Action Potential

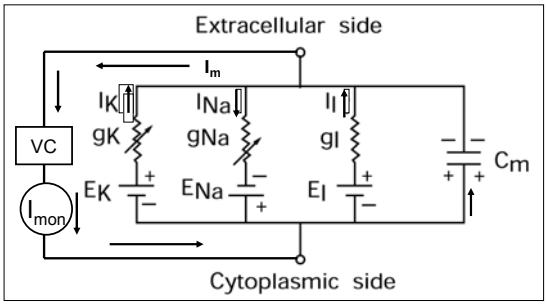
- The Action Potential
  - Generation
  - Conduction
- Voltage-Gated Ion Channels
  - Diversity
  - Evolutionary Relationships

Electronically Generated Current Counterbalances the Na^+ Membrane Current

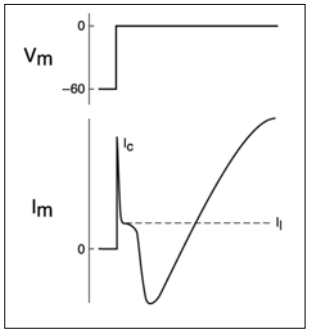


PNS, Fig 9-2

Equivalent Circuit of the Membrane Connected to the Voltage Clamp

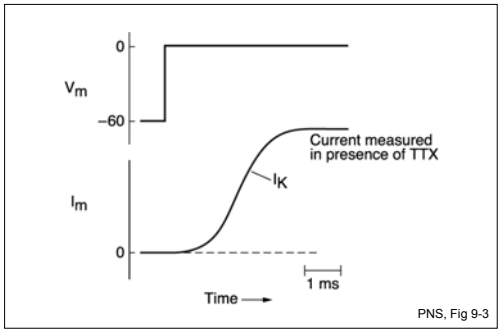


For Large Depolarizations, Both I_{Na} and I_K Are Activated



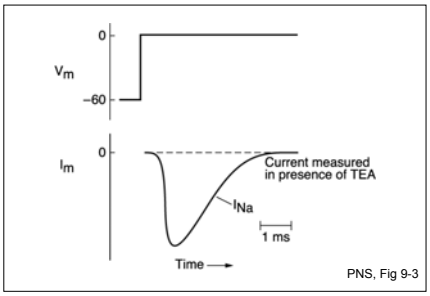
PNS, Fig 9-3

I_K is Isolated By Blocking I_{Na}



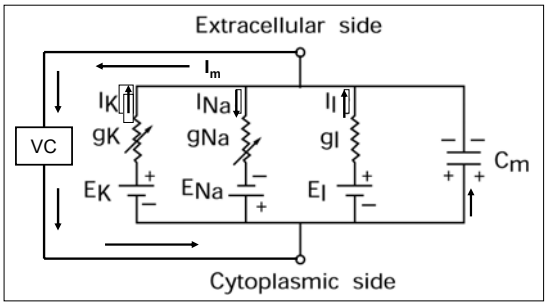
PNS, Fig 9-3

I_{Na} is Isolated By Blocking I_K

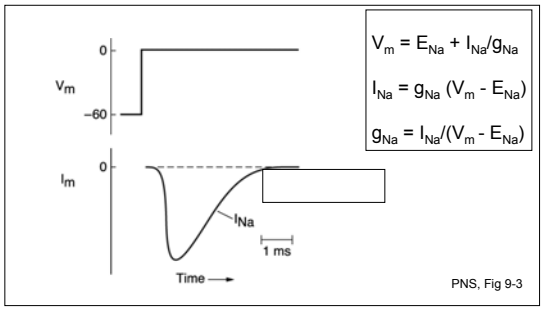


PNS, Fig 9-3

V_m = the Value of the Na Battery Plus the Voltage Drop Across g_{Na}

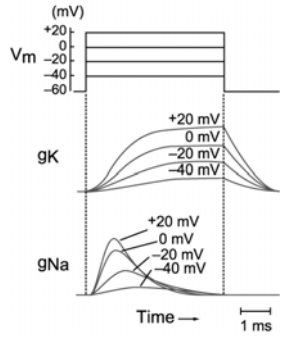


Calculation of g_{Na}



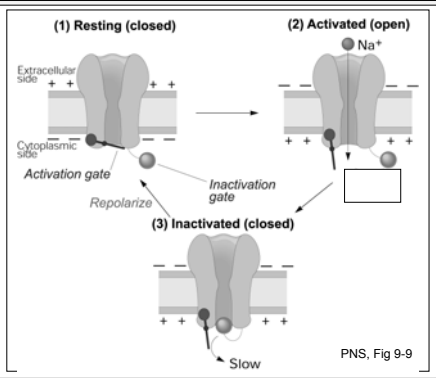
PNS, Fig 9-3

g_{Na} and g_K Have Two Similarities and Two Differences



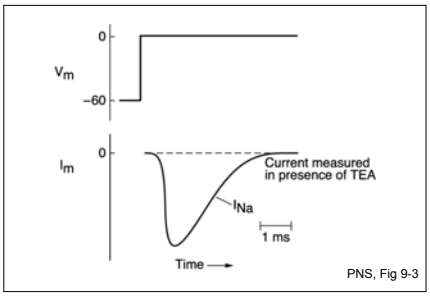
PNS, Fig 9-6

Voltage-Gated Na^+ Channels Have Three States



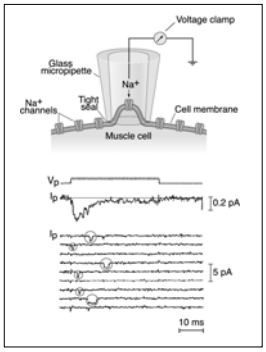
PNS, Fig 9-9

Total I_{Na} is a Population Phenomenon



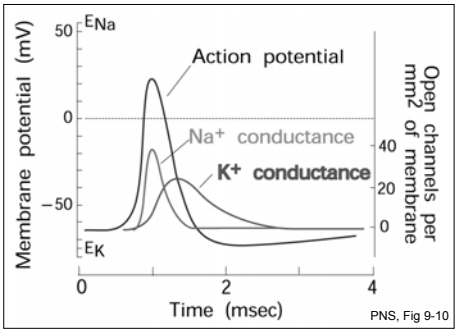
PNS, Fig 9-3

Na^+ Channels Open in an All-or-None Fashion



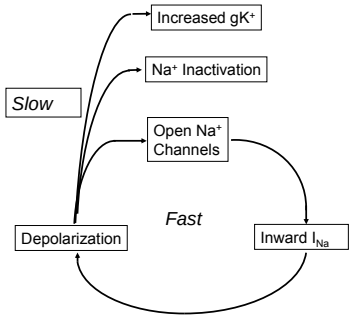
PNS, Fig 9-12

The Action Potential is Generated by Sequential Activation of g_{Na} and g_K

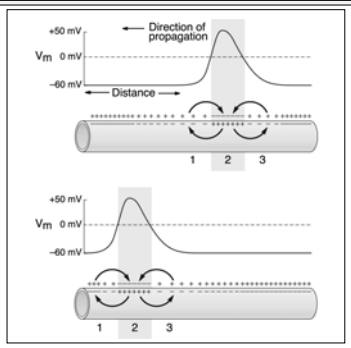


PNS, Fig 9-10

Negative Feedback Cycle Underlies Falling Phase of the Action Potential

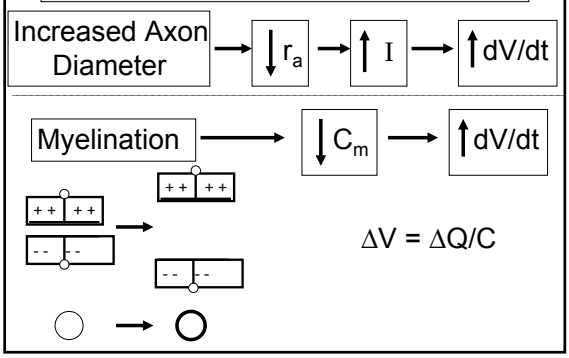


Local Circuit Flow of Current Contributes to Action Potential Propagation

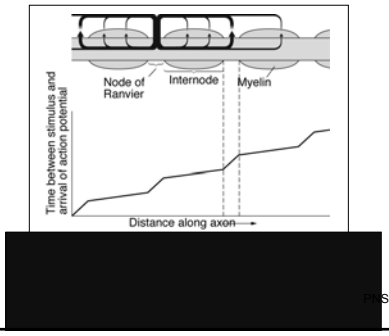


PNS, Fig 8-6

Conduction Velocity Can be Increased by Increased Axon Diameter and by Myelination



Myelin Speeds Up Action Potential Conduction

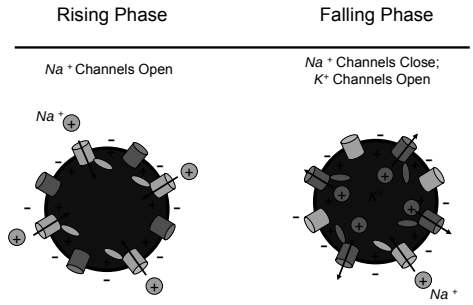


PNS, Fig 8-8

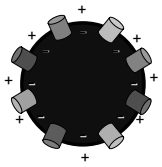
Voltage-Gated Ion Channels and the Action Potential

- The Action Potential
  - Generation
  - Conduction
- Voltage-Gated Ion Channels
  - Diversity
  - Evolutionary Relationships

Opening of Na^+ and K^+ Channels is Sufficient to Generate the Action Potential



However, a Typical Neuron Has Several Types of Voltage-Gated Ion Channels



Functional Properties of Voltage-Gated Ion Channels Vary Widely

- Selective permeability
- Kinetics of activation
- Voltage range of activation
- Physiological modulators

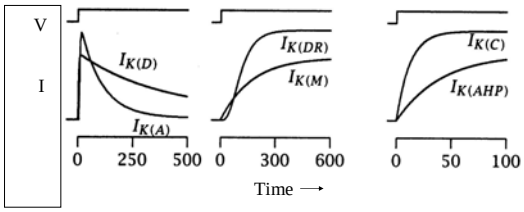
Voltage-Gated Ion Channels Differ in their Selective Permeability Properties

Cation Permeable	Anion Permeable
Na^+	Cl^-
K^+	
Ca^{++}	
Na^+, Ca^{++}, K^+	

Functional properties of Voltage-Gated Ion Channels Vary Widely

- Selective permeability
- Kinetics of activation
- Voltage range of activation
- Physiological modulators

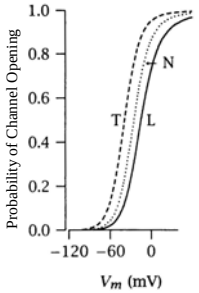
Voltage-Gated K^+ Channels Differ Widely in Their Kinetics of Activation and Inactivation



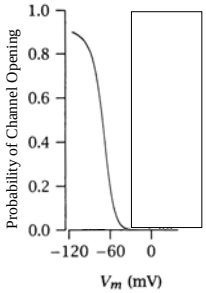
Functional properties of Voltage-Gated Ion Channels Vary Widely

- Selective permeability
- Kinetics of activation
- Voltage range of activation
- Physiological modulators

Voltage-Gated Ca^{++} Channels Differ in Their Voltage Ranges of Activation



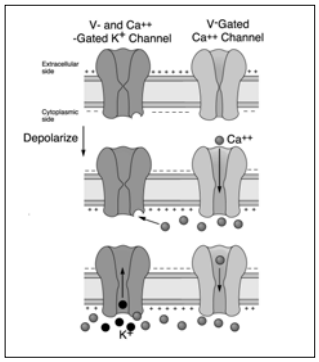
The Inward Rectifier K^+ Channels and HCN Channels Are Activated by Hyperpolarization



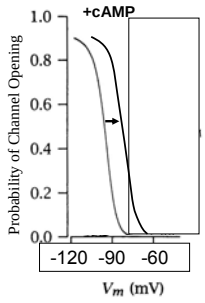
Functional properties of Voltage-Gated Ion Channels Vary Widely

- Selective permeability
- Kinetics of activation
- Voltage range of activation
- Physiological modulators: *e.g.*, phosphorylation, binding of intracellular Ca^{++} or cyclic nucleotides, etc.

Physiological Modulation



HCN Channels That Are Opened by Hyperpolarization Are Also Modulated by cAMP



Voltage-Gated Ion Channels Belong to Two Major Gene Superfamilies

I. Cation Permeant

II. Anion Permeant

Voltage-Gated Ion Channel Gene Superfamilies

I) Channels With Quatrameric Structure Related to Voltage-Gated, Cation-Permeant Channels:

A) Voltage-gated:

- K^+ permeant
- Na^+ permeant
- Ca^{++} permeant
- Cation non-specific permeant

Voltage-Gated Ion Channel Gene Superfamily

I) Channels With Quatrameric Structure Related to Voltage-Gated, Cation-Permeant Channels:

A) Voltage-gated:

- K^+ permeant
- Na^+ permeant
- Ca^{++} permeant
- Cation non-specific permeant (HCN)

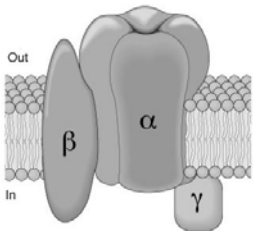
Structurally related to-

B) Cyclic Nucleotide-Gated (Cation non-specific permeant)

C) K^+-permeant leakage channels

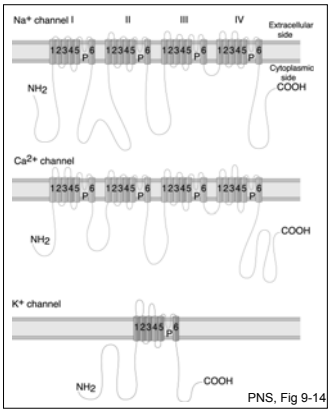
D) TRP Family (cation non-specific); Gated by various stimuli, such as osmolarity, pH, mechanical force, ligand binding and temperature

The α-Subunits of Voltage-Gated Channels Have Been Cloned



PNS, Fig 6-9

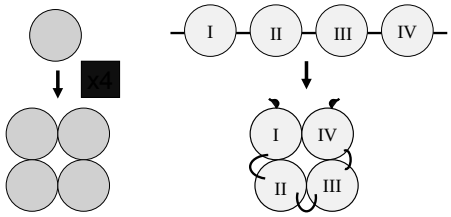
Voltage-Gated Cation-Permeant Channels Have a Basic Common Structural Motif That is Repeated Four-fold



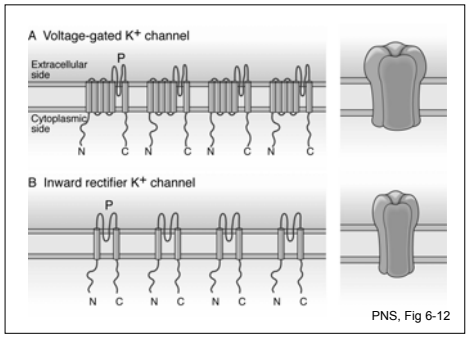
PNS, Fig 9-14

Four-Fold Symmetry of Voltage-Gated Channels Arises in Two Ways

K^+ Channels, HCN Channels Na^+ or Ca^{++} Channels

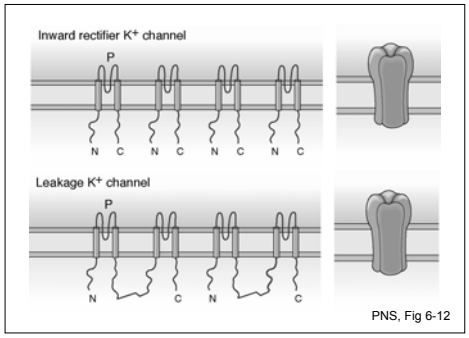


Inward Rectifier K^+ Channels Have Only Two of the Six Alpha-Helices per Subunit



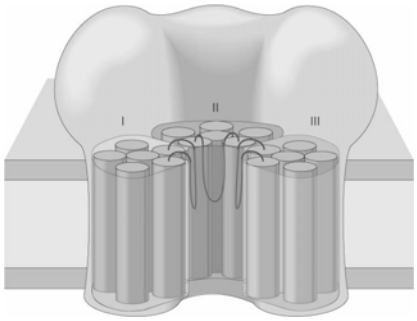
PNS, Fig 6-12

Leakage K^+ Channels Are Dimers of Subunits With Two P-Loops Each



PNS, Fig 6-12

P-Loops Form the Selectivity Filter of Voltage-Gated Cation-Permeant Channels



PNS, Fig 9-15

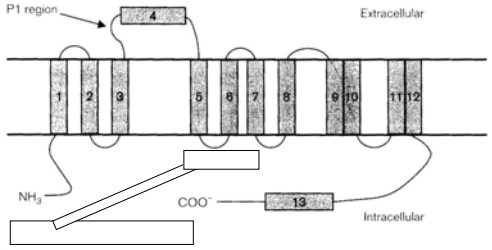
Voltage-Gated Ion Channel Gene Superfamilies

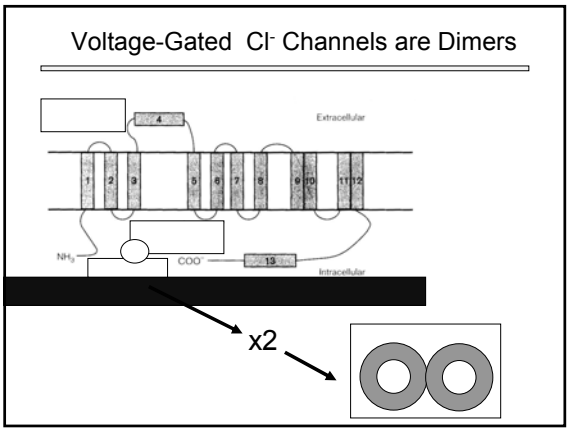
II) "CLC" Family of Cl^--Permeant Channels (dimeric structure):

Gated by:

- •Voltage - particularly important in skeletal muscle
- •Cell Swelling
- •pH

Voltage-Gated Cl^- Channels Differ in Sequence and Structure from Cation-Permeant Channels




Voltage-Gated Cl- Channels are Dimers
Extracellular
1
2
3
4
5
6
7
8
9
10
11
12
13
NH3
COO-
Intracellular
x2