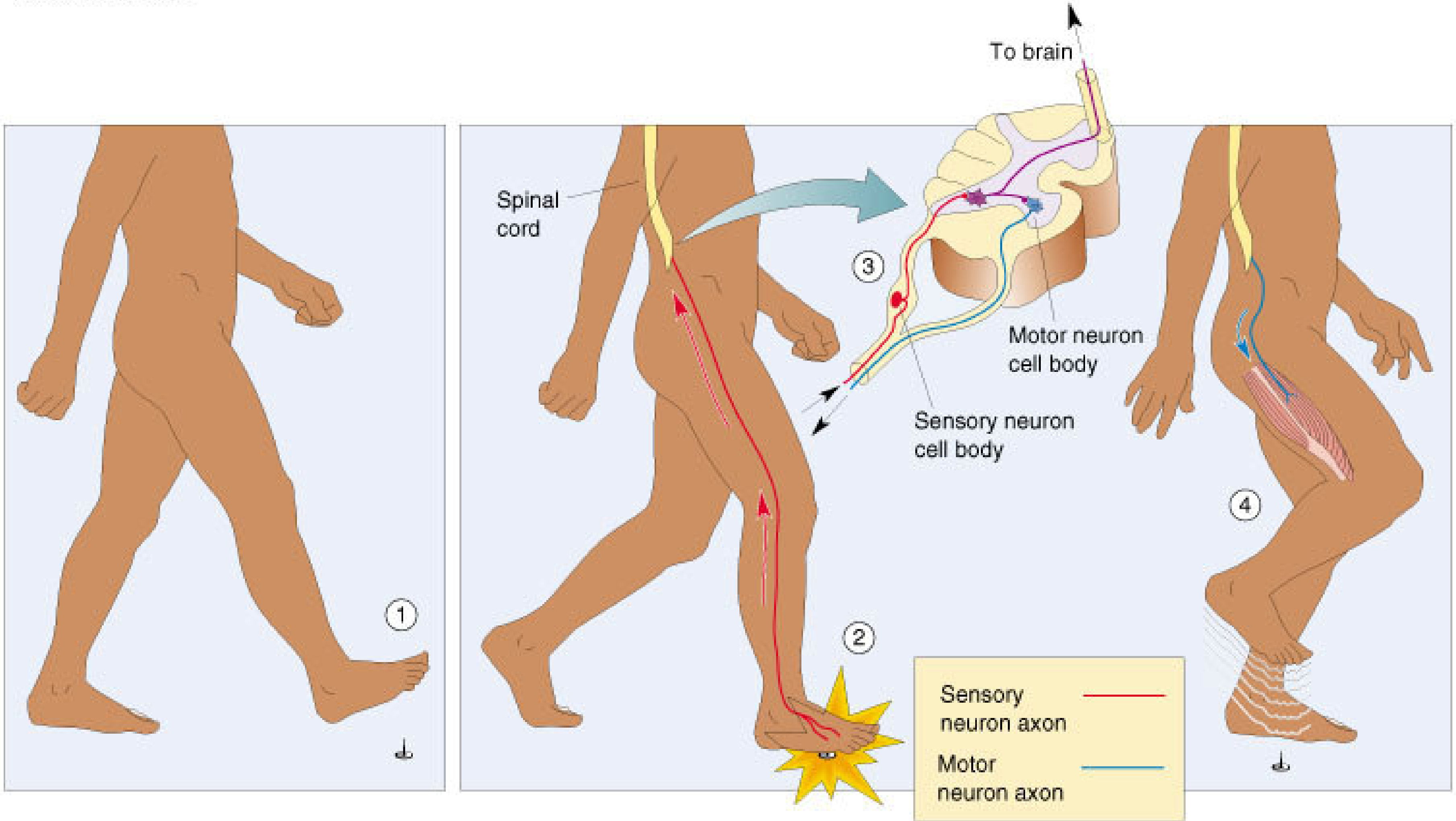
- **The Neuronal Membrane at Rest**
- **The cast of chemicals**
- **The movement of ions**
- **The ionic basis of the resting membrane potential**

Figure 3.1

A simple reflex. 1- A person steps on a thumbtack. 2- The breaking of the skin is translated into signals that travel up sensory nerve fibers (the direction of information flow, indicated by the arrows). 3- In the spinal cord, the information is distributed to interneurons. Some of these neurons send axons to the brain, where the painful sensation is registered. Others synapse on motor neurons, which send descending signals to the muscles. 4- The motor commands lead to muscle contraction and withdrawal of the foot.



INTRODUCTION

- Fig 3.1
- In a copper telephone wire

-about half the speed of light

- In a nerve fiber

-far less conductive

-not especially well insulated

- the nerve impulse, or **action potential**

- Information is encoded in the frequency of action potentials and in the distribution & number of neurons firing action potentials in a given nerve.

  - Morse code

- excitable membrane
- the **resting membrane potential**

  (resting potential)

THE CAST OF CHEMICALS

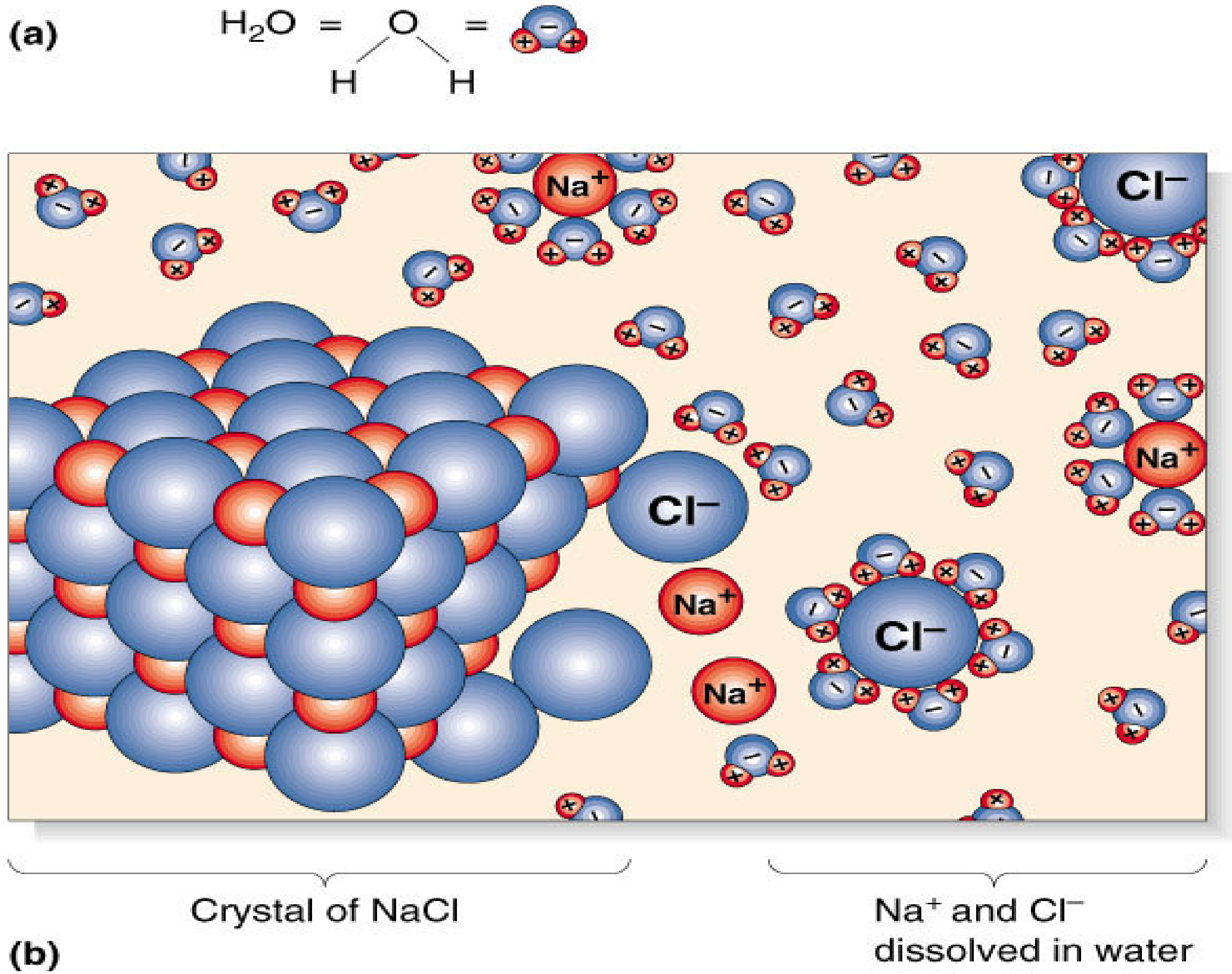
- **Cytosol and Extracellular Fluid**
- **Water**.

  polar covalent bonds.
- **Ions**

  ionic bond, clouds of water

  monovalent, divalent
- **cations, anions**
- Na^+ (sodium), K^+ (potassium), Ca^{2+} (calcium)
- monovalent anion Cl^- (chloride)

Figure 3.2
Water is a polar solvent. (a) Representations of the atomic structure of the water molecule. The oxygen atom has a net negative electrical charge, and the hydrogen atoms have a net positive electrical charge, making water a polar molecule. (b) A crystal of sodium chloride (NaCl) dissolves in water because the polar water molecules have a stronger attraction for the electrically charged sodium and chloride ions than the ions do for one another.



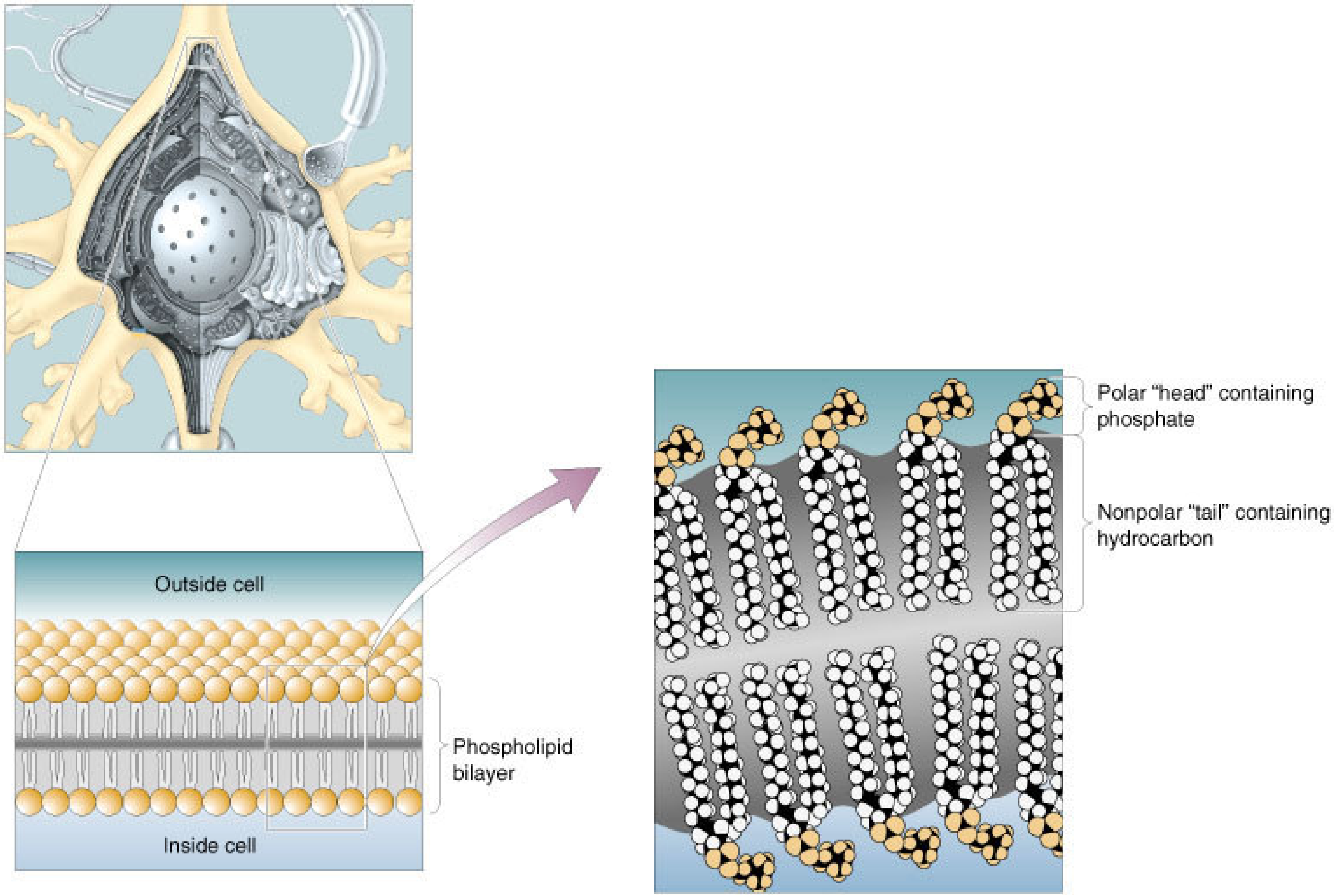
The Phospholipid Membran e

- "water-loving," or *hydrophilic*

  -nonpolar covalent bonds
- "water-fearing," or *hydrophobic*

  -lipid
- **The Phospholipid Bilayer**

Figure 3.3
The phospholipid bilayer. The phospholipid bilayer, the core of the neuronal membrane, forms a barrier to water-soluble ions.



Protein

- *enzymes*
- *cytoskeleton*
- *receptors*
- *special proteins* that span the phospholipid bilayer

-protein structure-

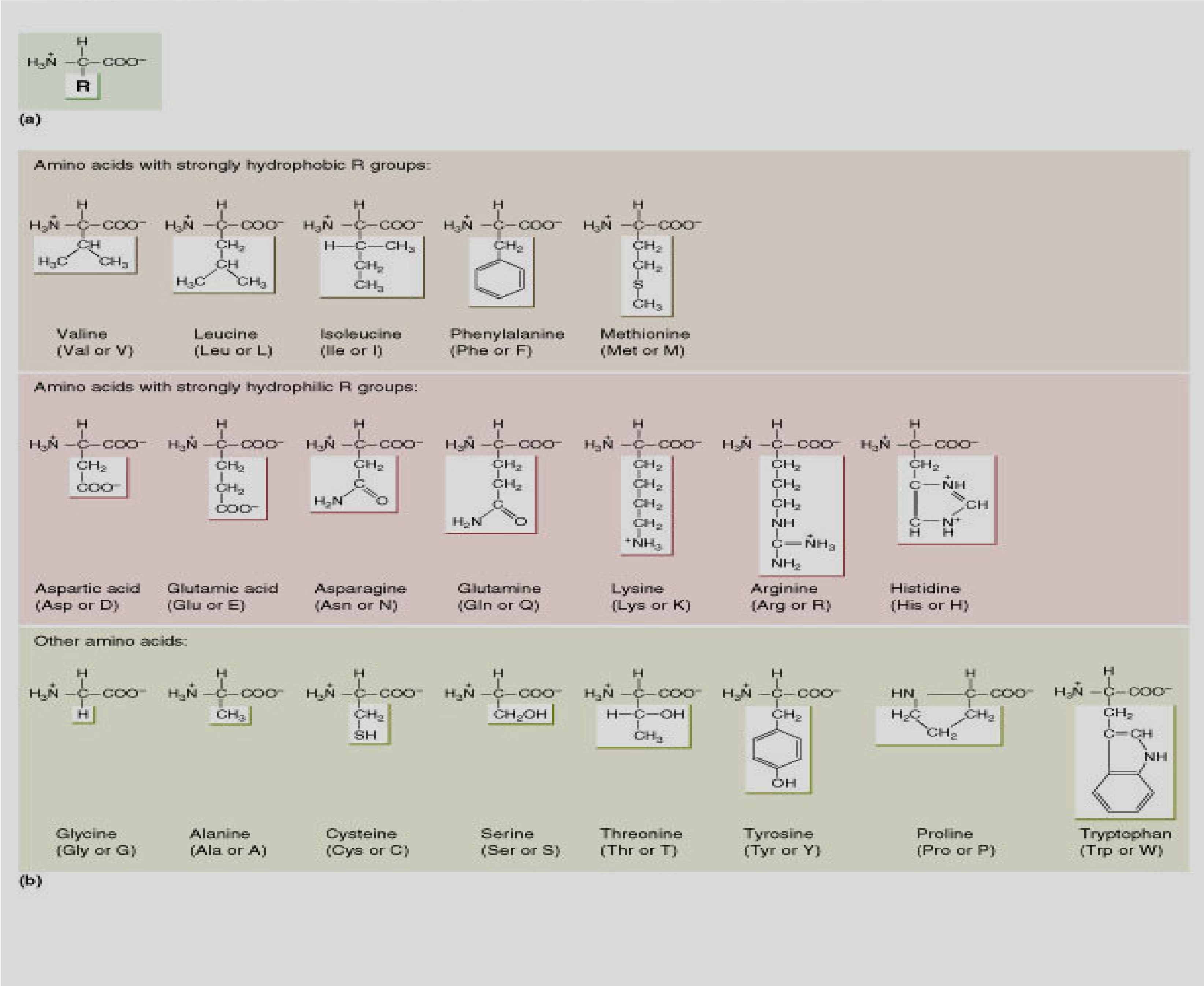

(a)
Amino acids with strongly hydrophobic R groups:
Valine (Val or V)
Leucine (Leu or L)
Isoleucine (Ile or I)
Phenylalanine (Phe or F)
Methionine (Met or M)
Amino acids with strongly hydrophilic R groups:
Aspartic acid (Asp or D)
Glutamic acid (Glu or E)
Asparagine (Asn or N)
Glutamine (Gln or Q)
Lysine (Lys or K)
Arginine (Arg or R)
Histidine (His or H)
Other amino acids:
Glycine (Gly or G)
Alanine (Ala or A)
Cysteine (Cys or C)
Serine (Ser or S)
Threonine (Thr or T)
Tyrosine (Tyr or Y)
Proline (Pro or P)
Tryptophan (Trp or W)
(b)

Figure 3.5
The peptide bond and a polypeptide. (a) Peptide bonds attach amino acids together. The bond forms between the carboxyl group of one amino acid and the amino group of another. (b) A polypeptide is a single chain of amino acids.

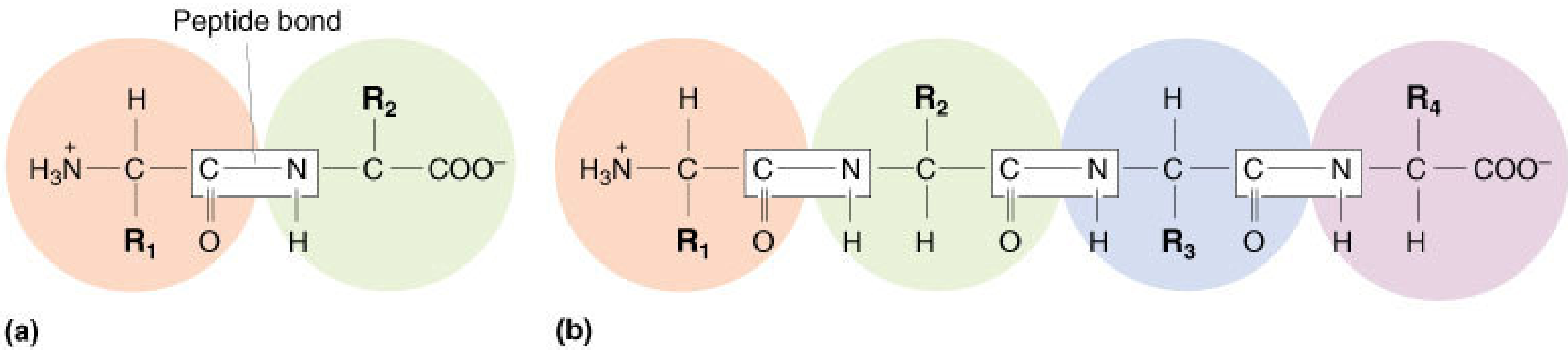
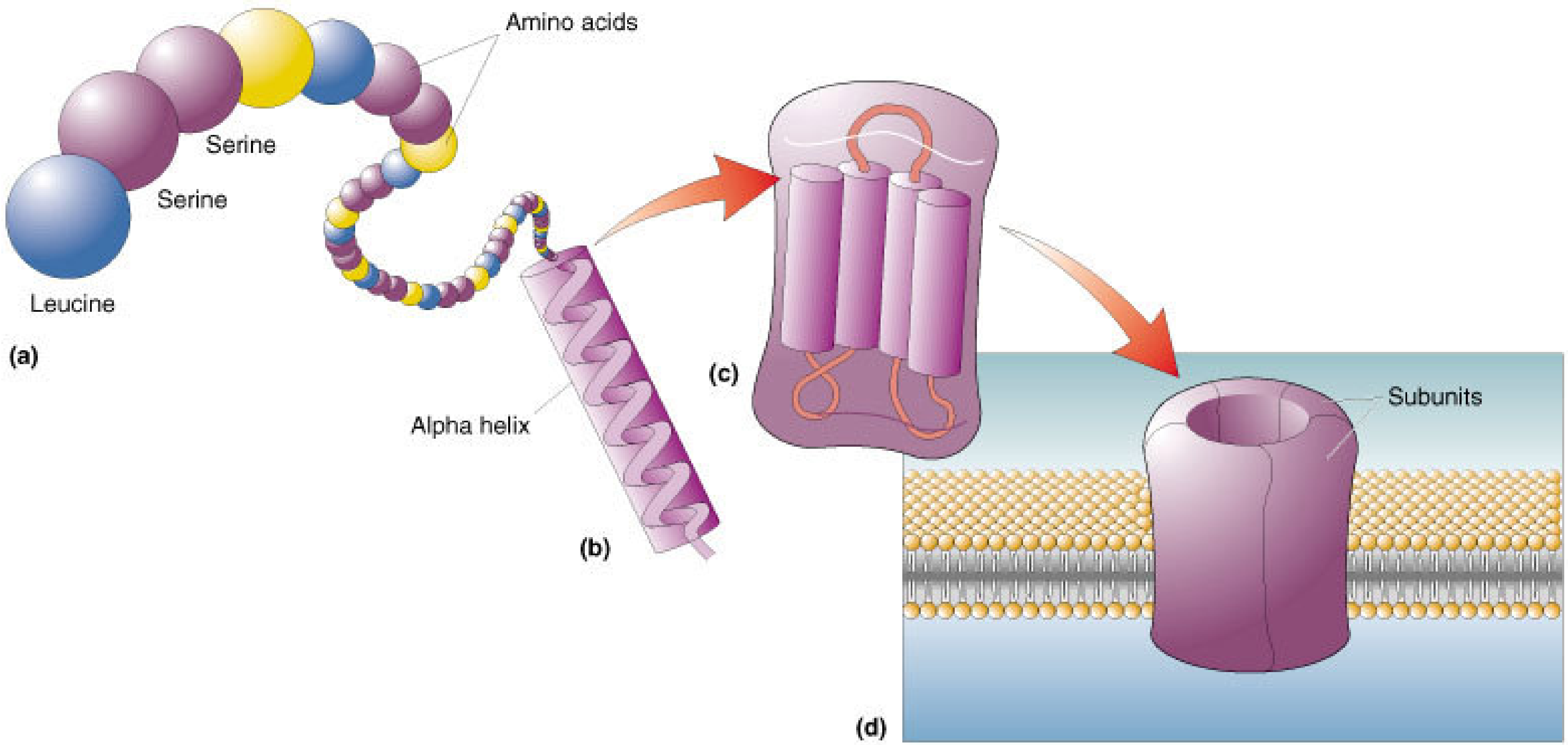


Figure 3.6

Protein structure. (a) Primary structure: the sequence of amino acids in the polypeptide. (b) Secondary structure: coiling of a polypeptide into an alpha helix. (c) Tertiary structure: three-dimensional folding of a polypeptide. (d) Quaternary structures various polypeptides bonded together to form a larger protein.



Channel Proteins.

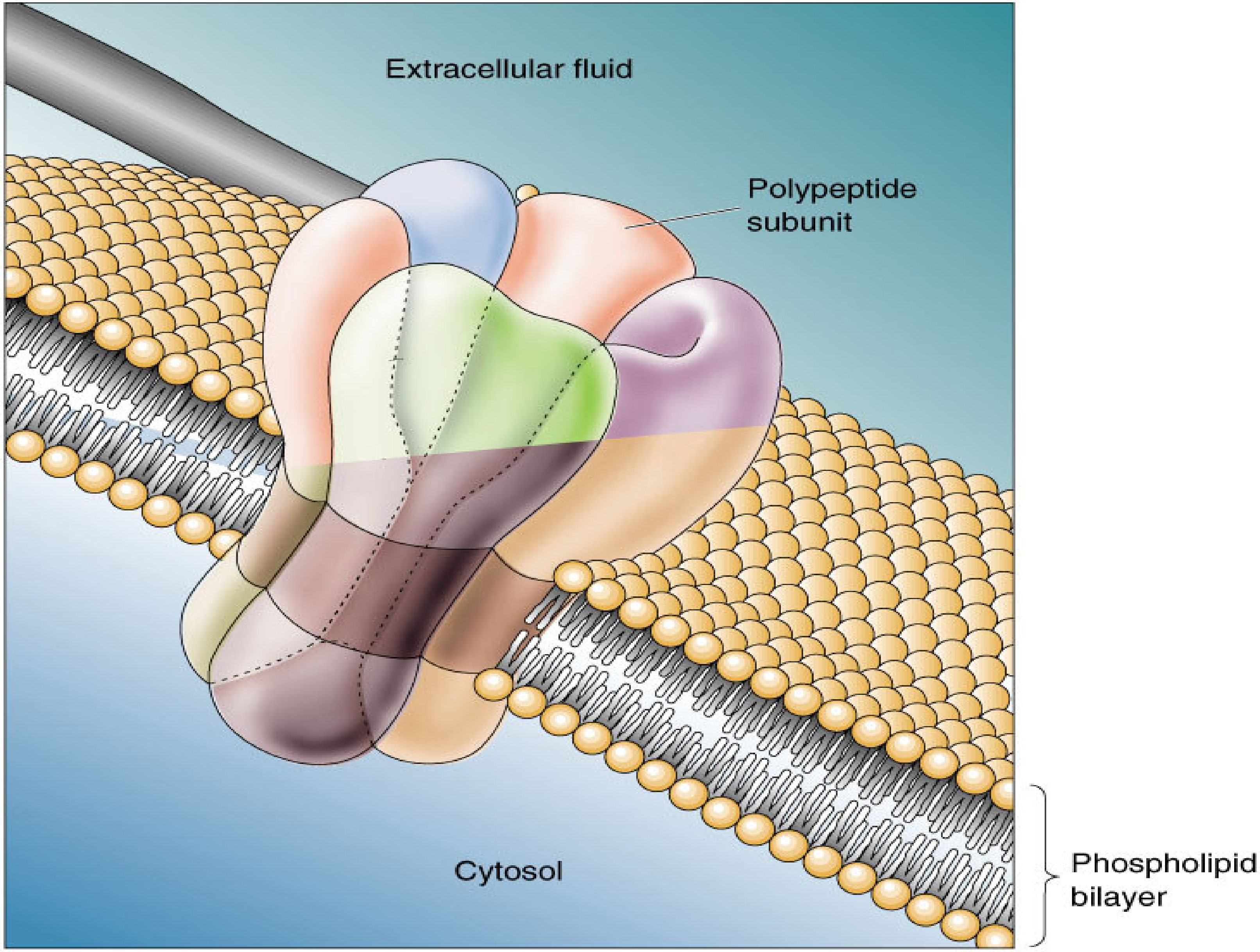
Ion channels, a pore

- ion selectivity

  - the nature of the R groups lining it
- gating
- *Understanding ion channels in the neuronal membrane is key to understanding cellular neurophysiology*

- **Ion pumps**

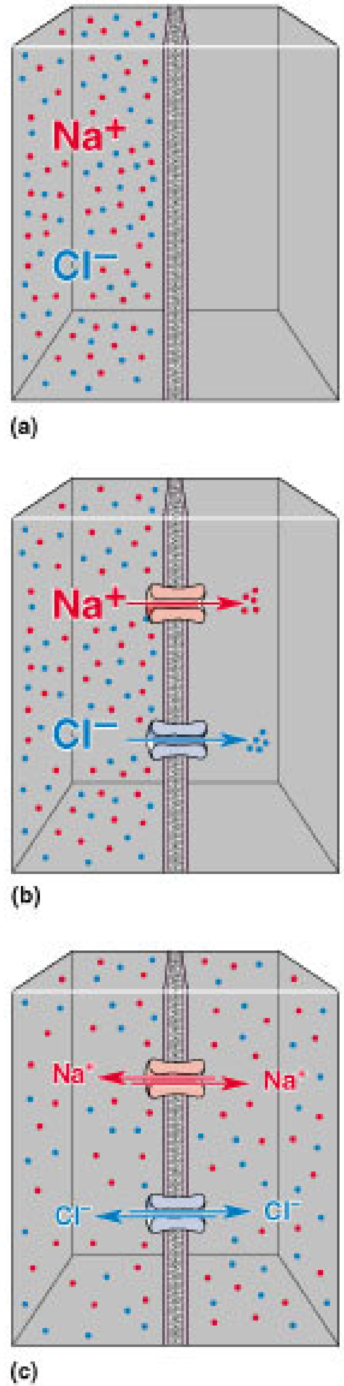
Figure 3.7
A membrane ion channel. Ion channels consist of membrane-spanning proteins that assemble to form a pore. In this example, the channel protein has five polypeptide subunits. Each subunit has a hydrophobic surface region (shaded) that readily associates with the phospholipid bilayer.



THE MOVEMENT OF IONS

Diffusion

- concentration gradient
- Driving ions across the membrane by diffusion
- happens when (1) the membrane possesses channels permeable to the ions, (2) there is a con. gradient across the membrane


Na+
Cl−
(a)
Na+
Cl−
(b)
Na+
Na+
Cl−
Cl−
(c)

Electricity

- Another way to induce a net movement of ions in a solution is to use an electrical field

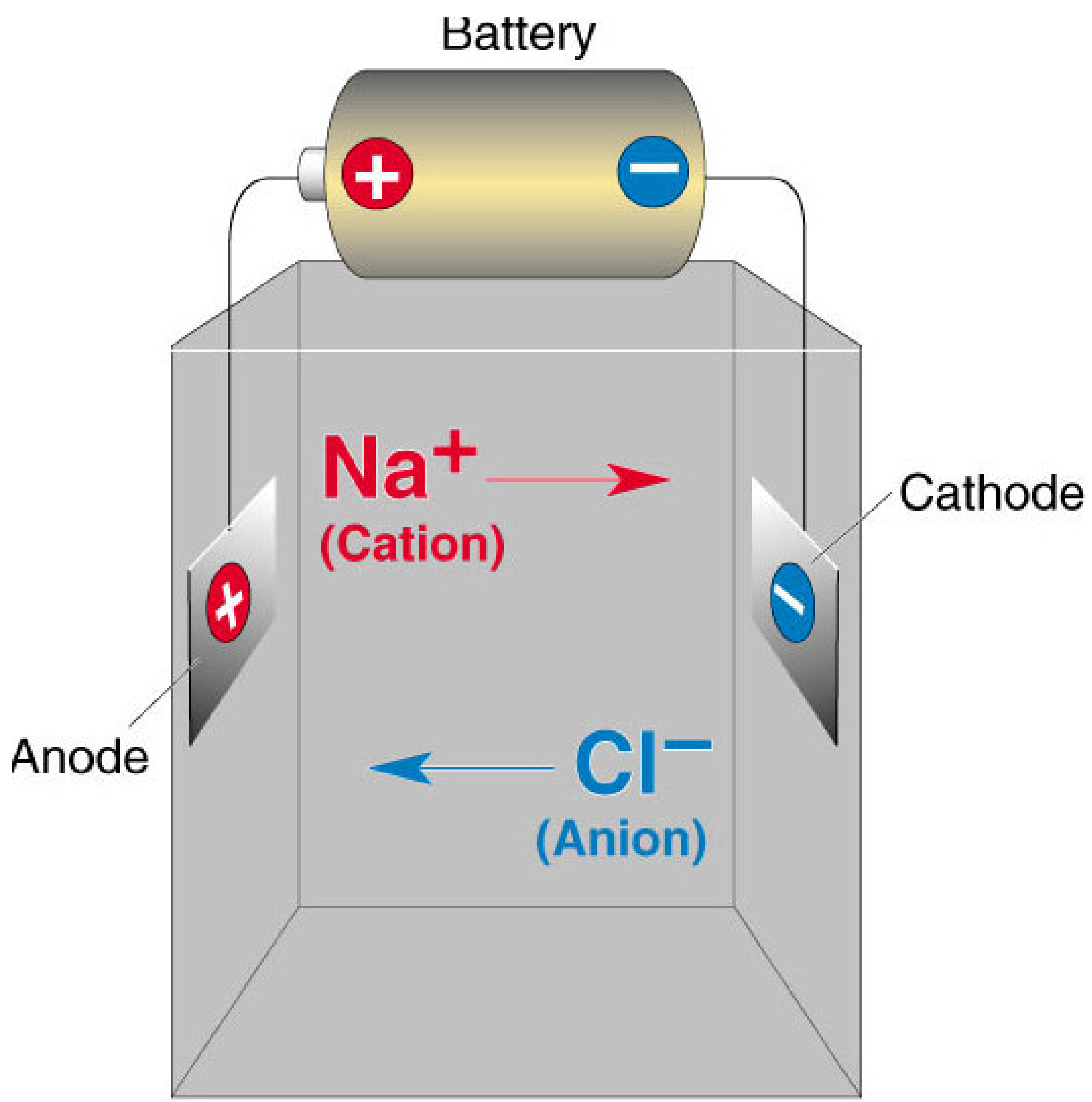
- The movement of electrical charge:

  electrical current, symbol I, amperes (amps)

- the direction of positive-charge movement

- Two important factors determine how much current will flow:

  electrical potential and electrical conductance.


Battery
Na+
(Cation)
Cathode
Anode
Cl−
(Anion)

Electrical potential

- voltage

  - the force exerted on a charged particl
e
- the difference in charge between the an
ode and the cathode, symbol V, volts

Electrical conductance

- the relative ability of an electrical charge to migrate from one point to another: symbol g, siemens(s)
- Conductance depends on the number of parti cles available to carry electrical charge and on the ease with which these particles can travel thr ough space.
- **Electrical resistance**, the relative inability of an electrical charge to migrate: R, ohms(Ω) r =1/g

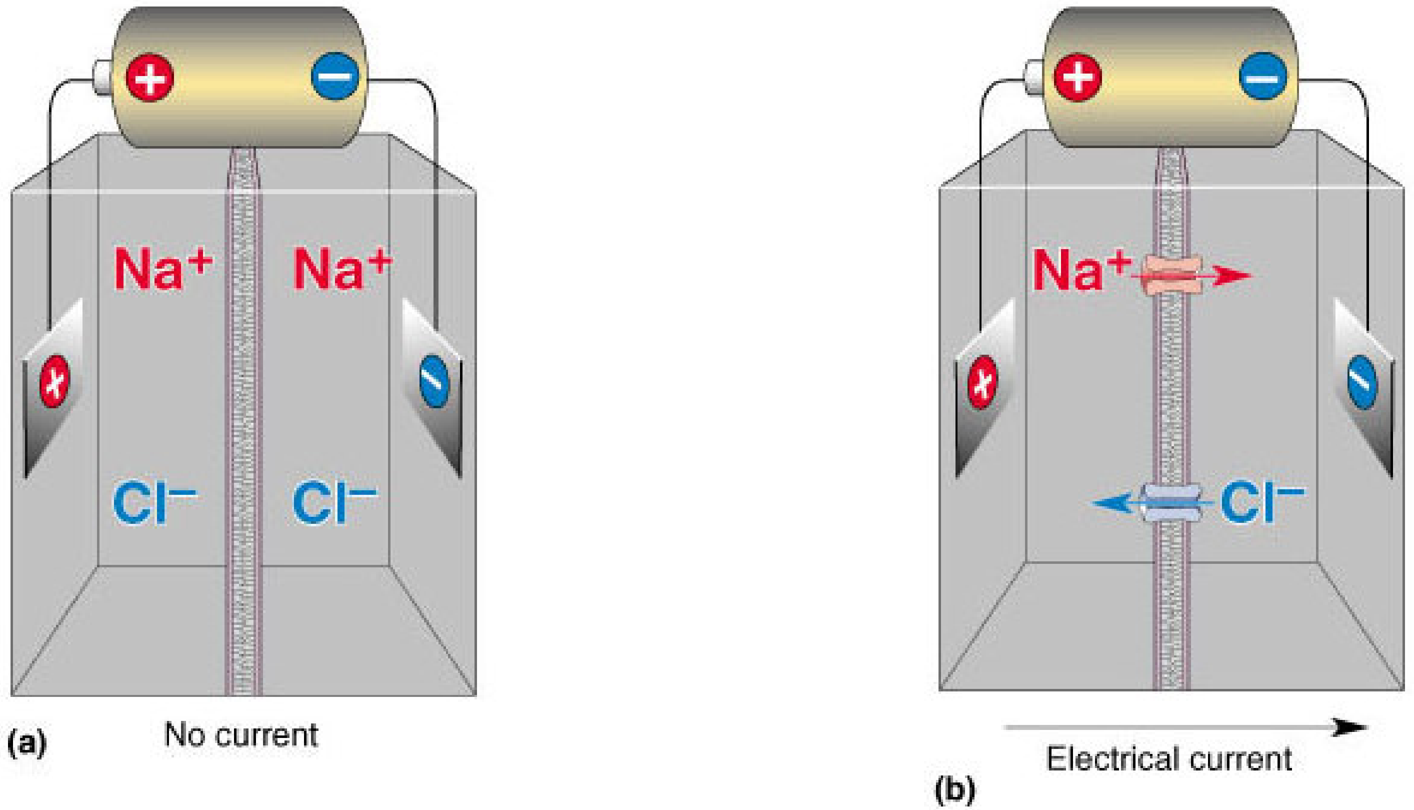
ELECTRICITY

Ohm's law $I = gV$

-Driving an ion across the membrane electrically requires that (1) the membrane possesses channels permeable to that ion and (2) there is an electrical potential difference across the membrane.

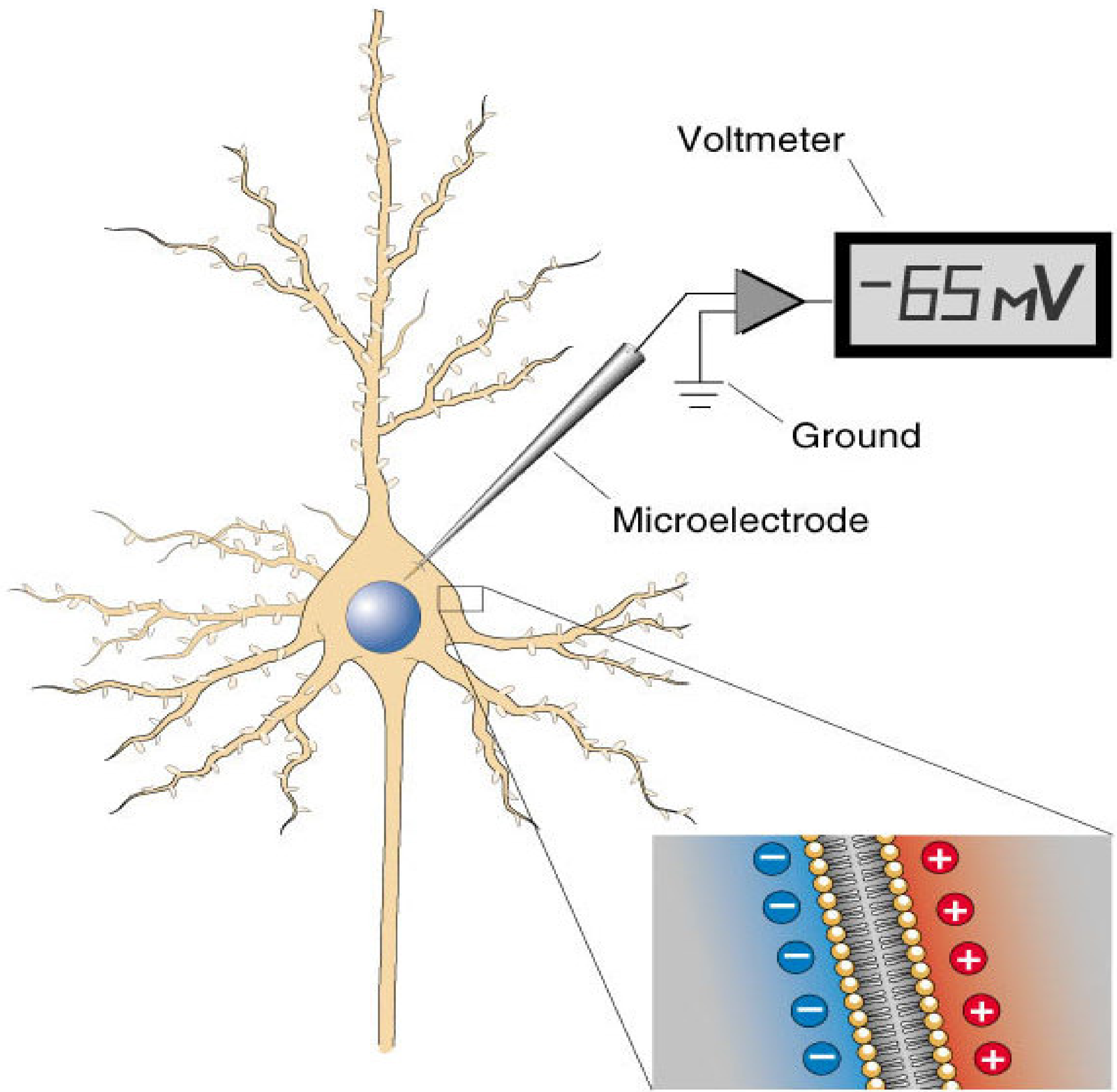
ELECTRICITY

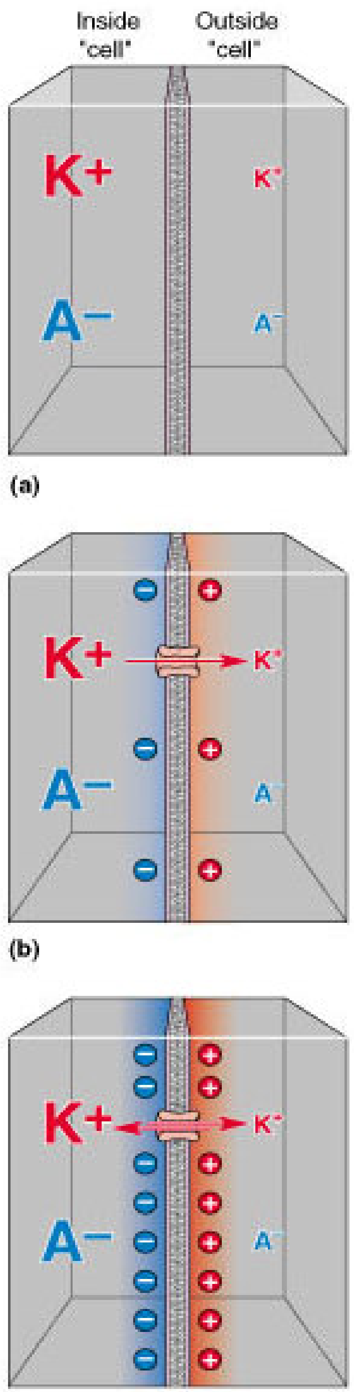
The movement of any ion through its channel depends on the concentration gradient and the difference in electric
al
potential across the membrane.


Na+
Na+
Cl−
Cl−
(a)
No current
Na+
Cl−
Electrical current
(b)

IONIC BASIS OF THE RESTING ME MBRANE POTENTIAL

- The membrane potential is the voltage across the neuronal membrane at any moment: symbol V
- microelectrode
- Equilibrium Potentials
- ionic equilibrium potential (equilibrium potential)
- E_{ion} -80 mV
- an ionic concentration gradient and selective ionic permeability


Voltmeter
-65 mV
Ground
Microelectrode


Inside "cell"
Outside "cell"
K+
K+
A−
A−
(a)
K+
K+
A−
A−
(b)
K+
K+
A−
A−

1. *Large changes in membrane potential are*

    caused by minuscule changes in i onic

    concentrations

-a cell with a 50-μm diameter containing

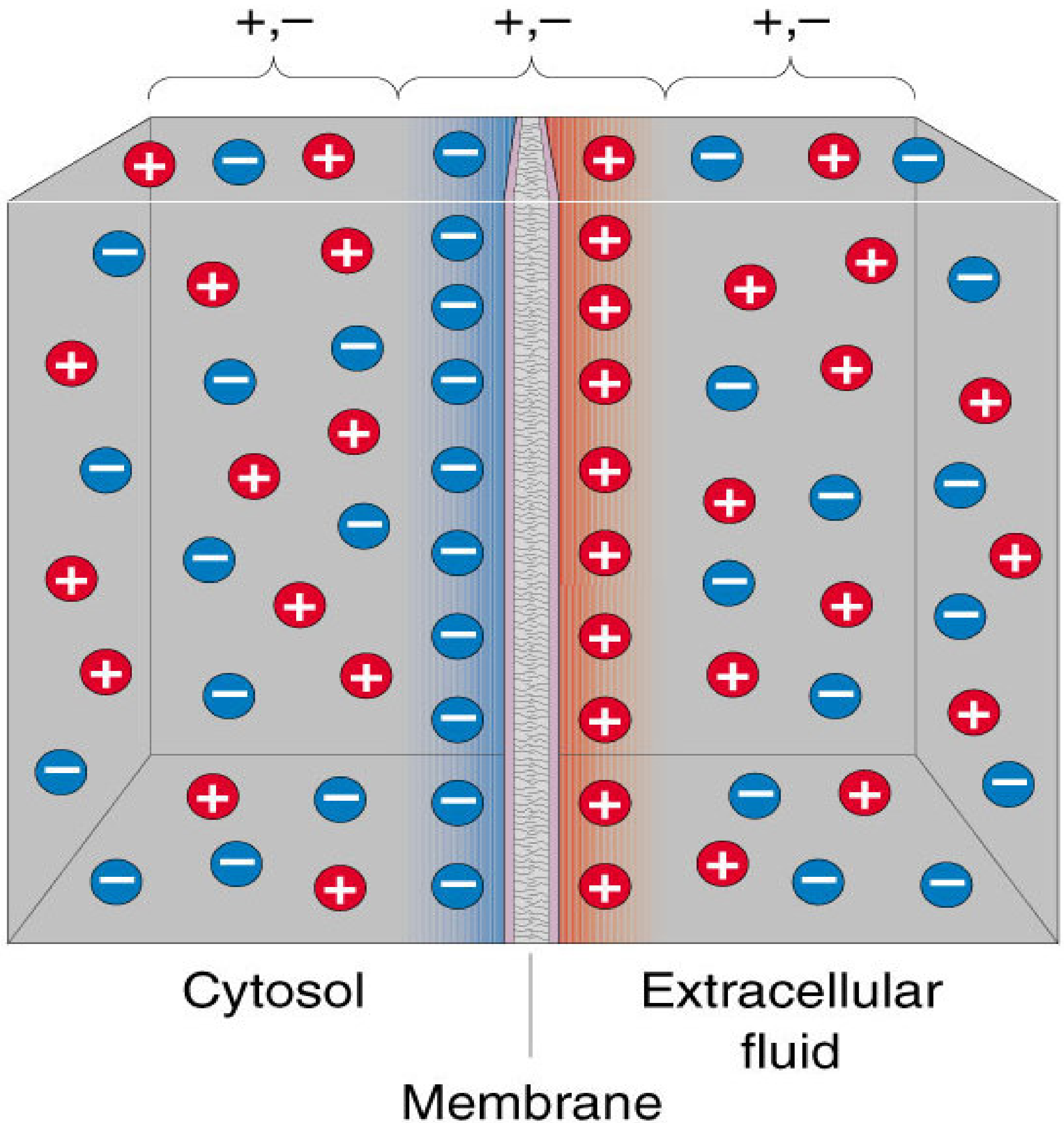
100 mM K^+ ; from 0 to - 80 mV

-from 100 mM to 99.99999 mM

: a negligible drop in concentration

2. *The net difference in electrical charge occurs at the inside and outside surfaces of the membrane.*

- the membrane is said to store electrical charge, a property called capacitance


+,−
+,−
+,−
Cytosol
Membrane
Extracellular fluid

3. *Ions are driven across the membrane a t a*

rate proportional to the difference

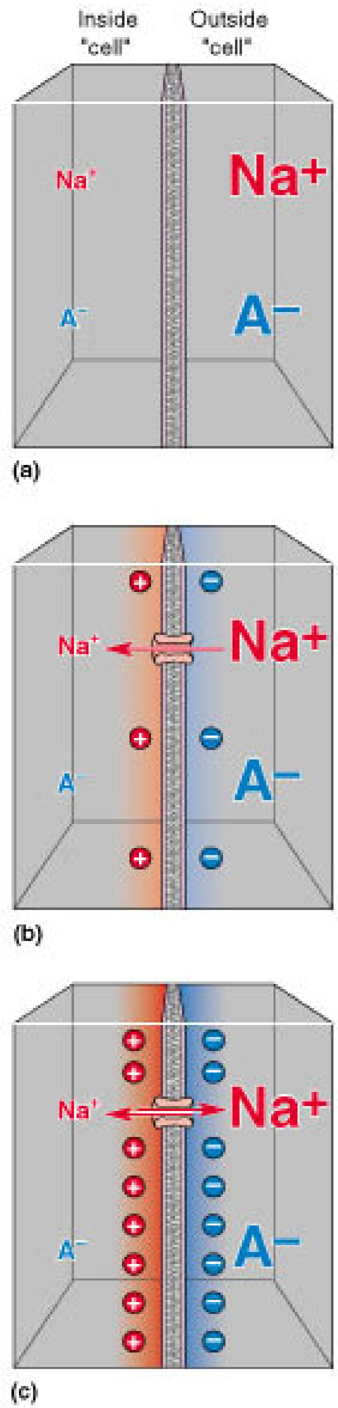
between the membrane potential and

the equilibrium potential

- $(V_m - E_{ion})$
- ionic driving force

4. *If the concentration difference across the membrane is known for an ion, an equilibrium potential can be calculated for that ion.* -Nernst equation

- (Figure 3.14)


Inside "cell"
Outside "cell"
Na+
Na+
A−
A−
(a)
(b)
(c)

- **The Nernst Equation.**

  E_K

  E_{Na}

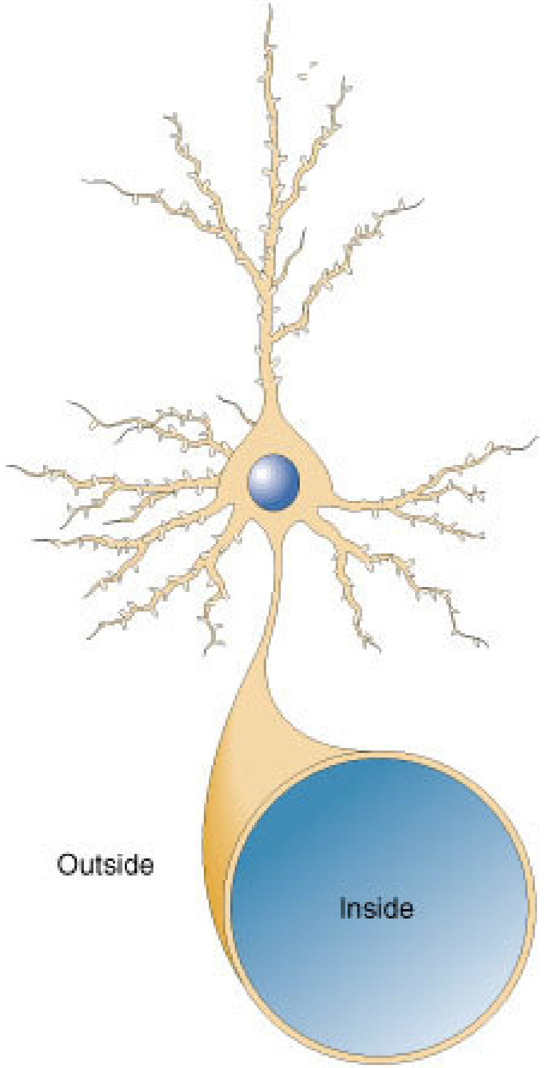
  E_{Ca}

The Distribution of ions Across the Membrane

- Figure 3.15
- K^+ is more concentrated on the inside than the outside.

  Na^+ and Ca^{2+} are more concentrated on the outside than the inside.

Figure 3.15
Approximate ion concentrations on either side of a neuronal membrane. Eion is the membrane potential that would be achieved at body temperature if the membrane were selectively permeable to that ion.



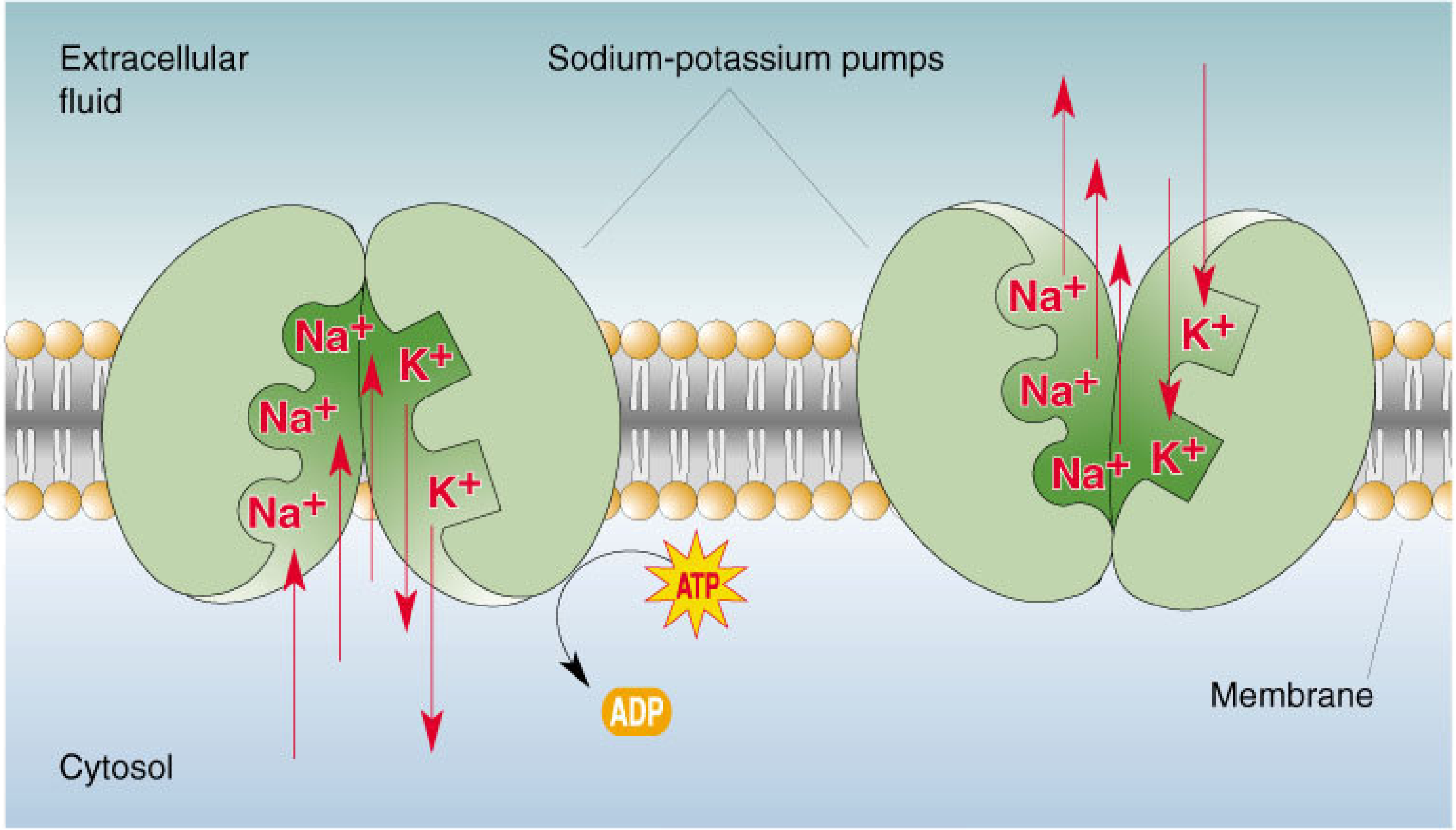
Outside	Inside	Ratio Outside:Inside	E_{ion} (at 37°C)
$[K^+]_o$ = 5 mM	$[K^+]_i$ = 100 mM	1:20	−80 mV
$[Na^+]_o$ = 150 mM	$[Na^+]_i$ = 15 mM	10:1	62 mV
$[Ca^{2+}]_o$ = 2 mM	$[Ca^{2+}]_i$ = 0.0002 mM	10,000:1	123 mV
$[Cl^-]_o$ = 150 mM	$[Cl^-]_i$ = 13 mM	11.5:1	−65 mV

Ion Pump

- **sodium-potassium pump**
- 70% of the total amount of ATP utilized by the brain

- **calcium pump**
- intracellular Ca^{2+} (0.0002mM)
- calcium-binding proteins and organelles (mitochondria and endoplasmic reticulum)

Figure 3.16
The sodium-potassium pump. This ion pump is a membrane-associated protein that transports ions across the membrane against their concentration gradients at the expense of metabolic energy. (ADP 5 adenosine diphosphate.)



Relative Ion Permeabilities of the Membrane at Rest

- Goldman equation

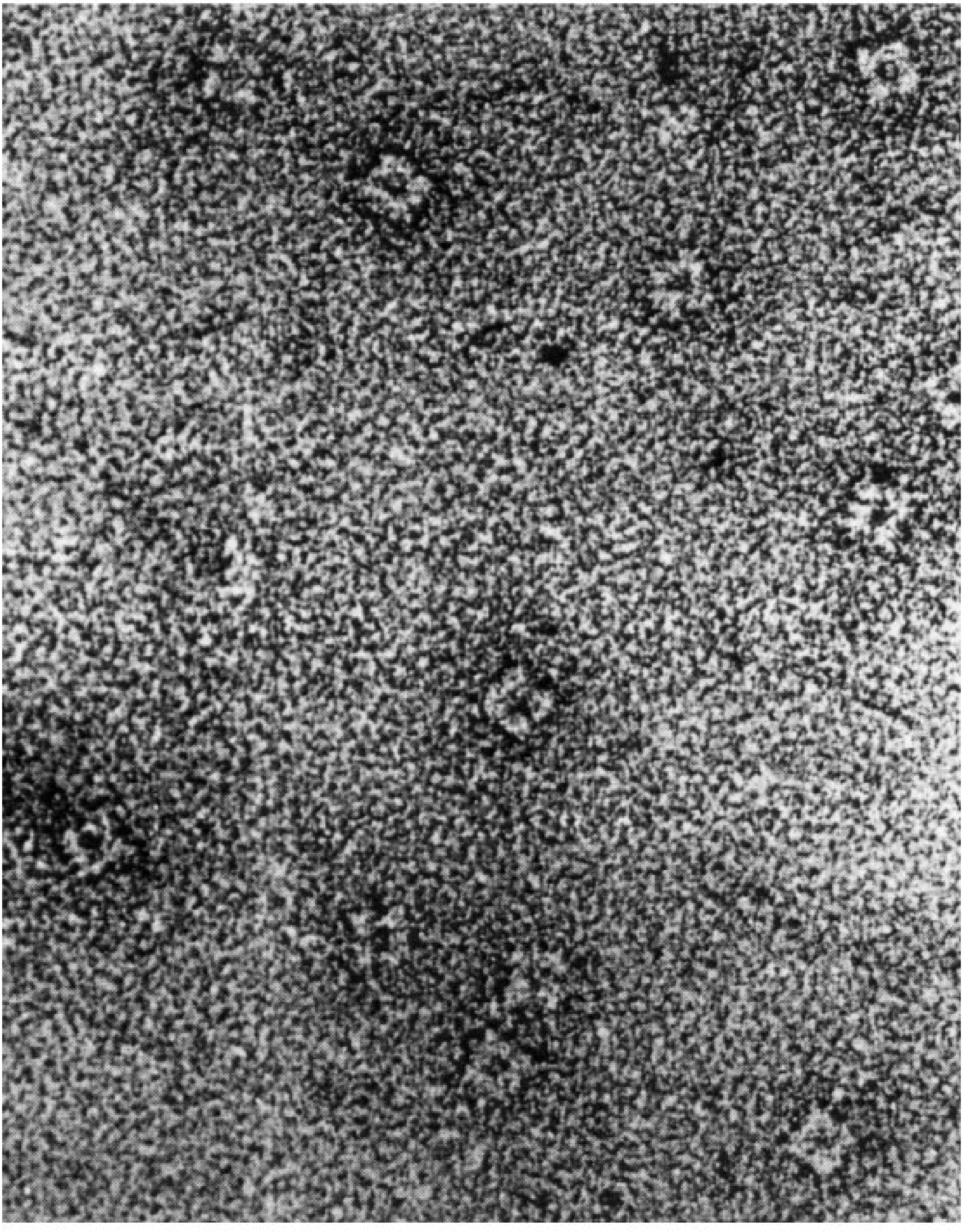
Potassium Channels

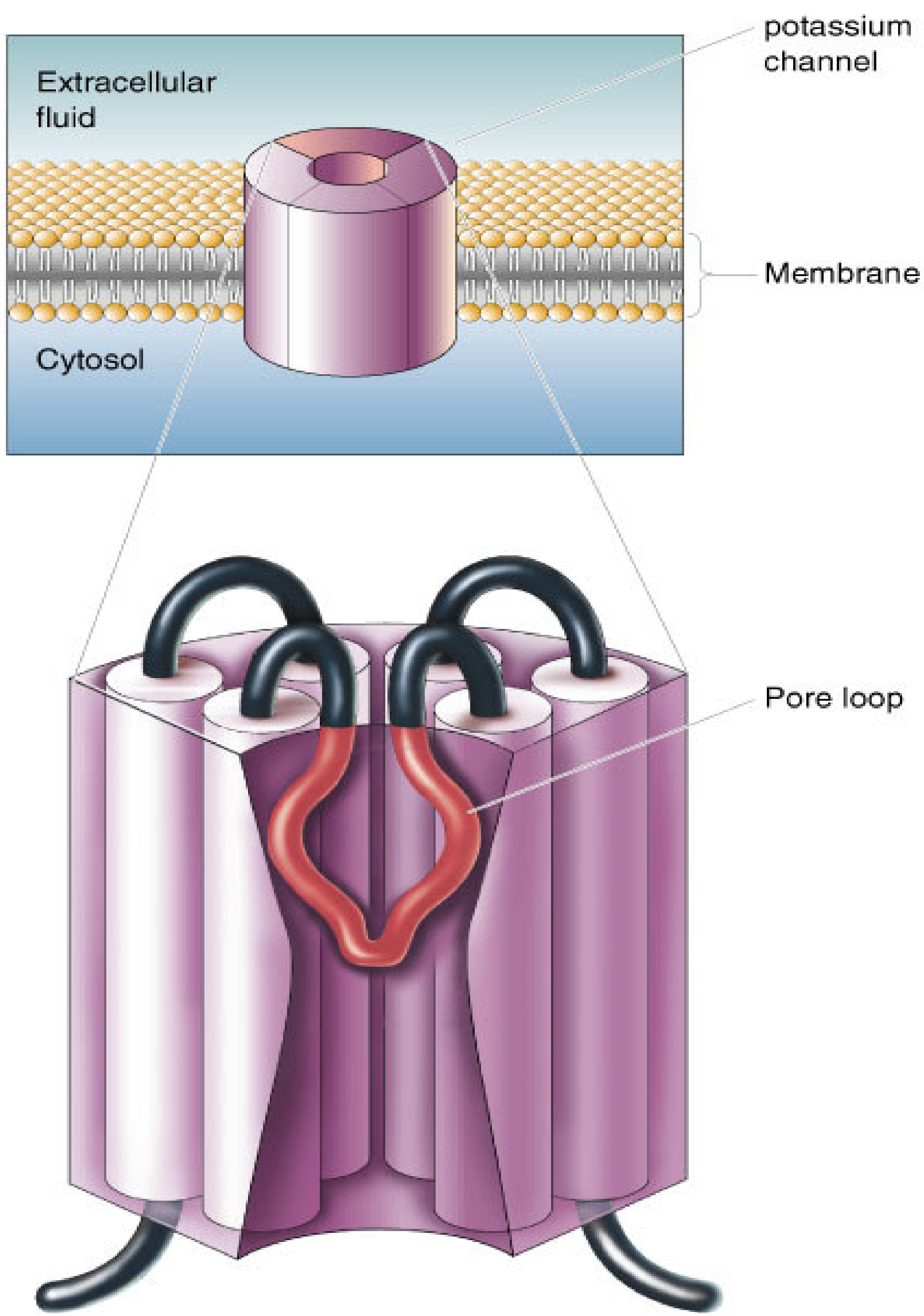
- *Shaker*
- *Shaker* potassium channel
- a very large number of different potassium channels
- pore loop, *selectivity filter*

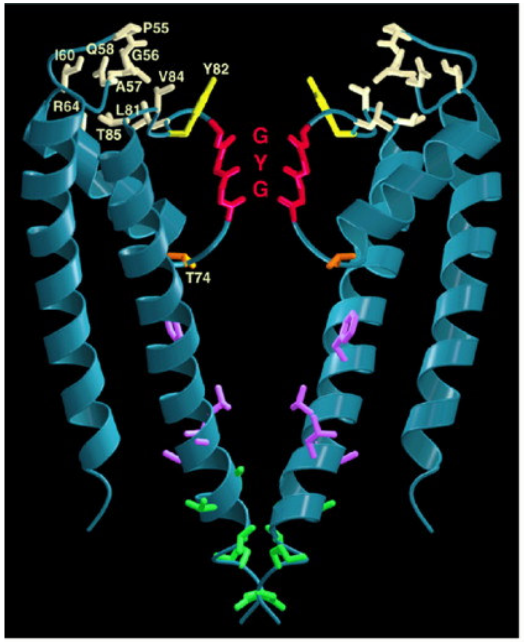
Potassium Channels

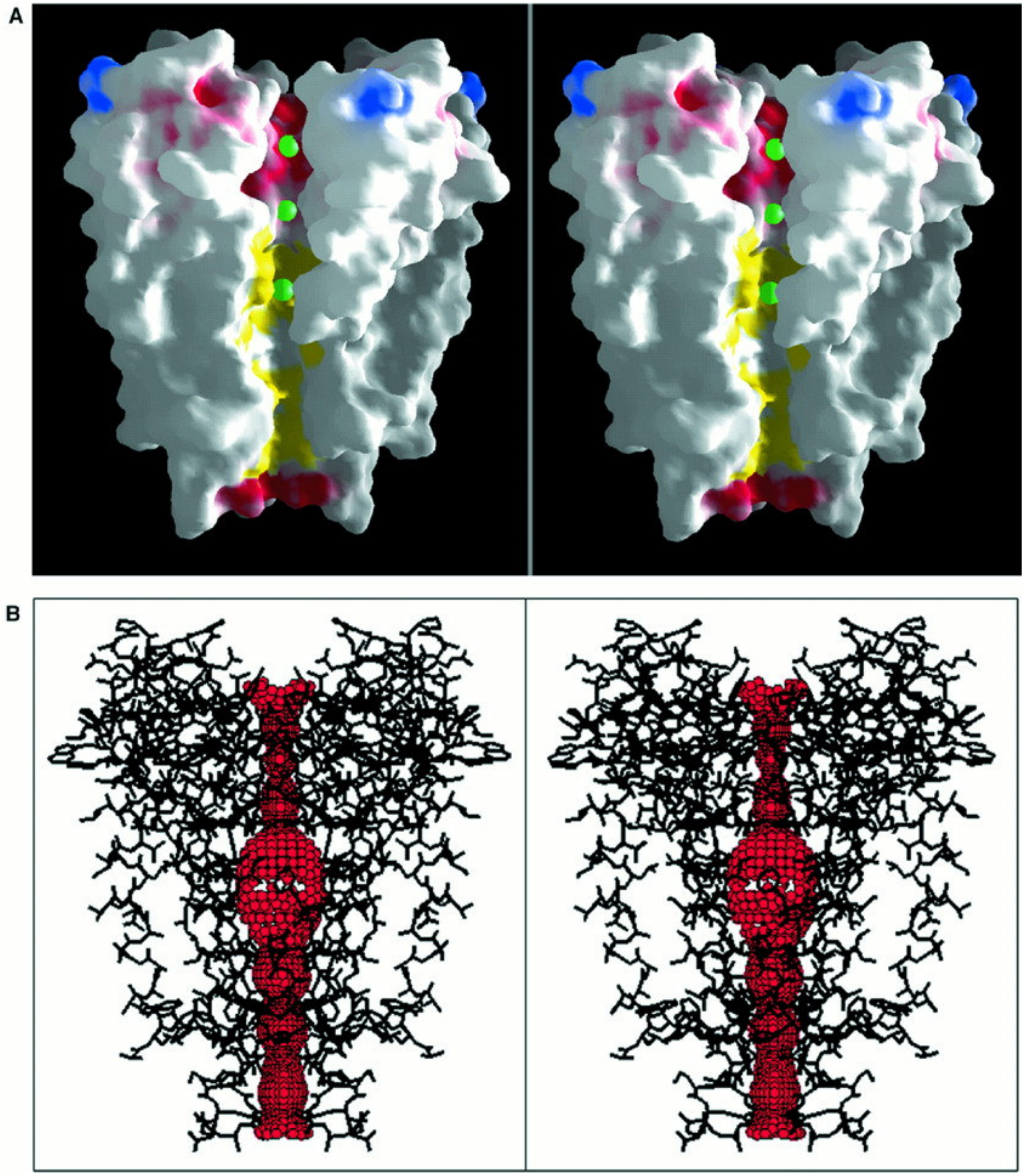
- strain of mice called *Weaver*
  - mutation of a single a.a. in the pore loop
    of a potassium channel the cerebellum
  - Na^+ as well as K^+ ions can pass through
  - less negative membrane potential

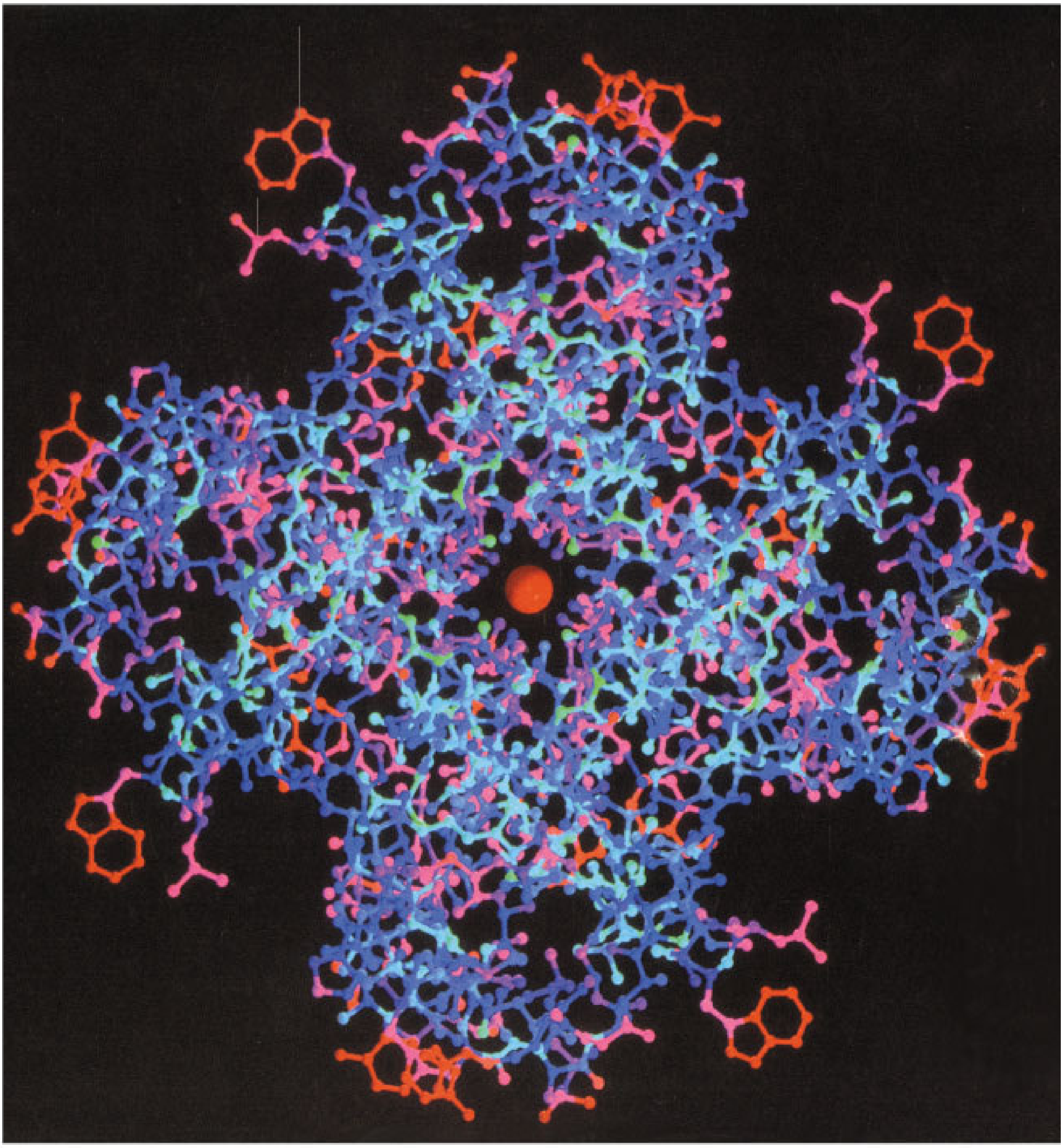
- inherited neurological disorders, epilepsy




Extracellular
fluid
Cytosol
potassium
channel
Membrane
Pore loop


P55
I60
Q58
G56
A57
V84
Y82
R64
L81
T85
G
Y
G
T74

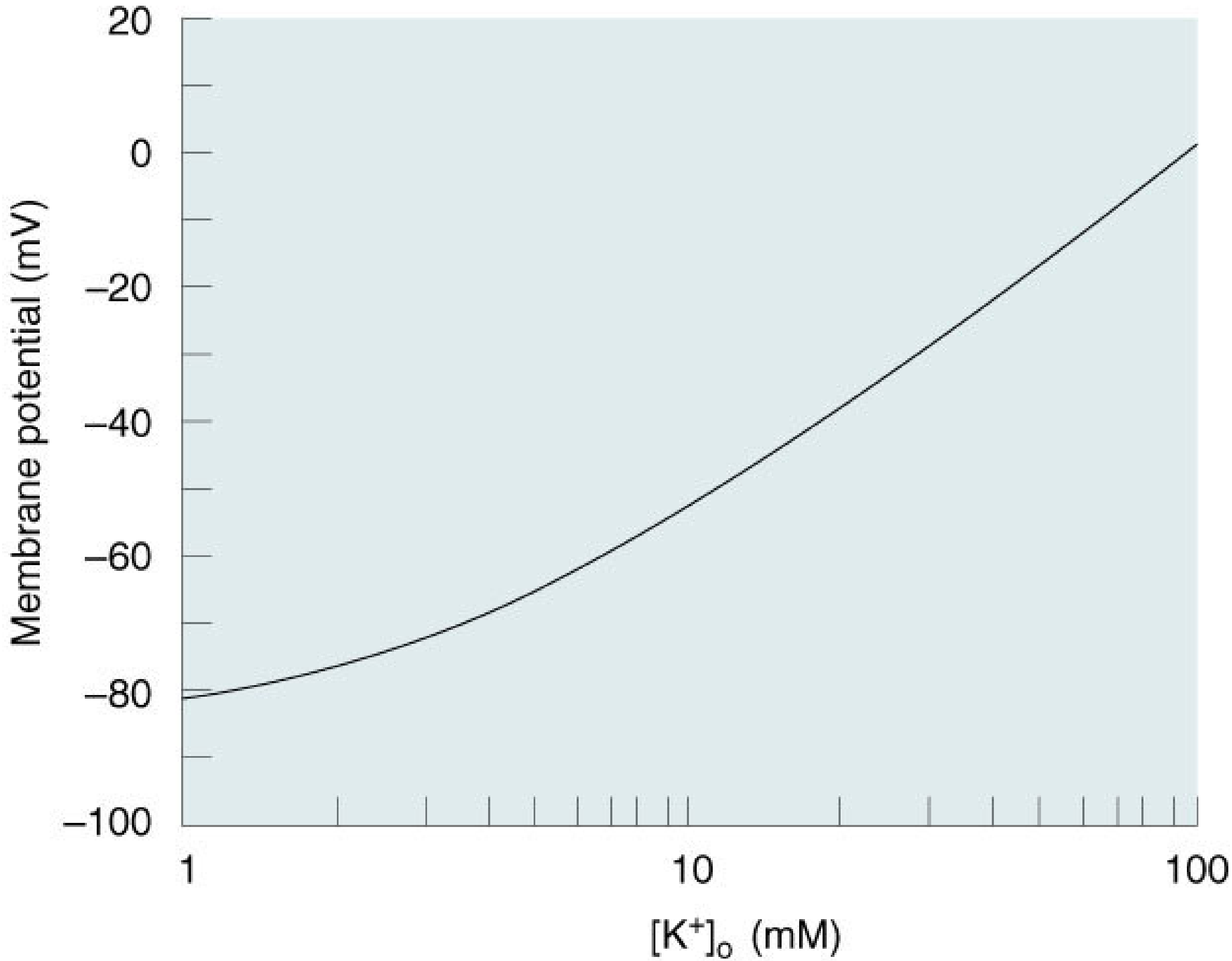

A
B



Regulating the External Potassium Concentration

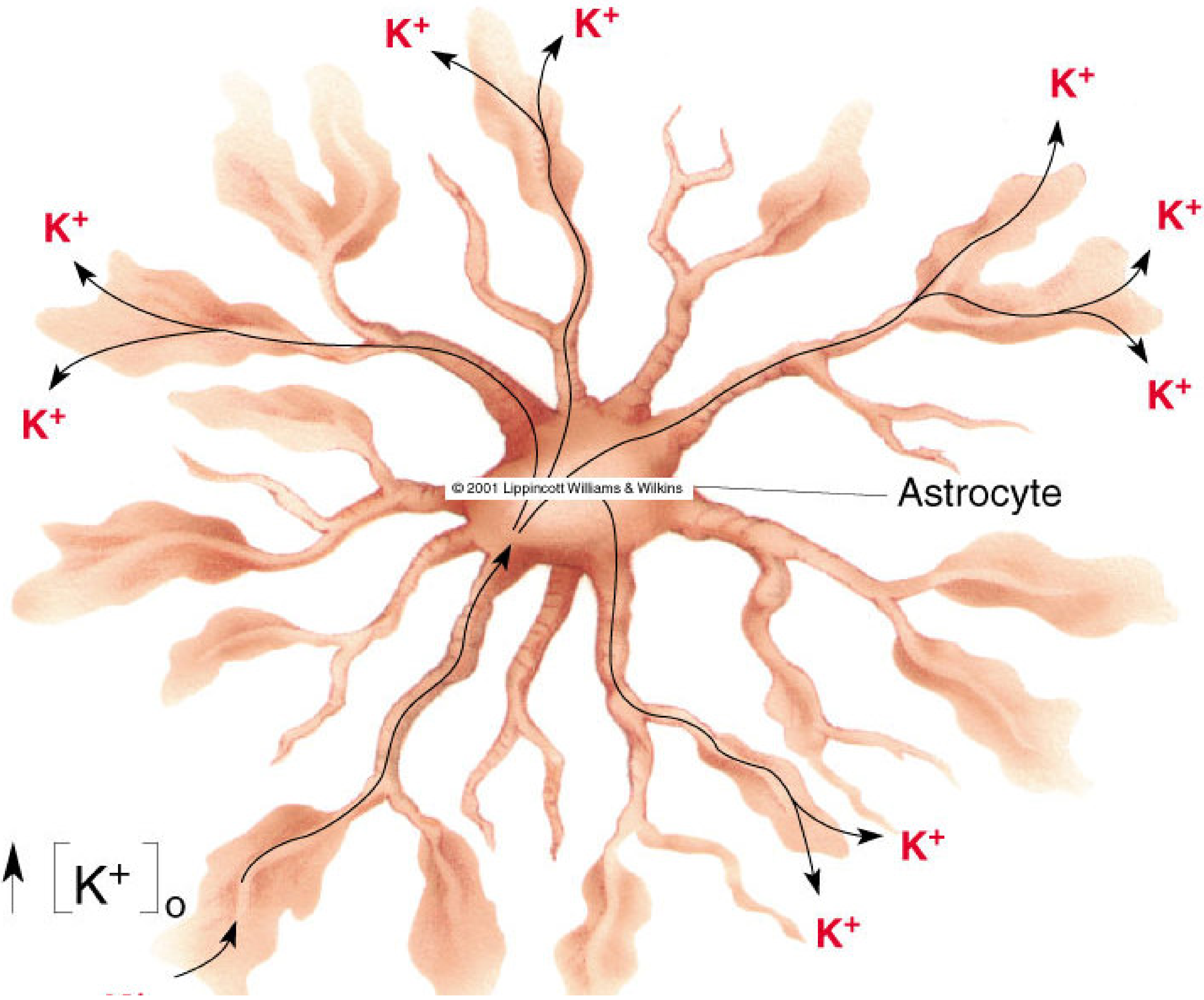
- Figure 3.19
- Increasing extracellular potassium depolarizes neurons.
- **blood-brain barrier** that limits the movement of potassium into the extracellular fluid of the brain

Figure 3.19
The dependence of membrane potential on external potassium concentration. Because the neuronal membrane at rest is mostly permeable to potassium, a tenfold change in [K1]o from 5 to 50 mM causes a 48-mV depolarization of the membrane. This function was calculated using the Goldman equation (Box 3.3).



- Glia, particularly astrocytes,
- potassium spatial buffering (Figure 3.20)

- elevations of K^+ in the blood can have serious consequences for body physiology, e.g. muscle cells


K+
K+
K+
K+
K+
K+
K+
K+
K+
Astrocyte
© 2001 Lippincott Williams & Wilkins
[K+]o

The rest is silence.

-Hamlet's last words.

William Shakespeare