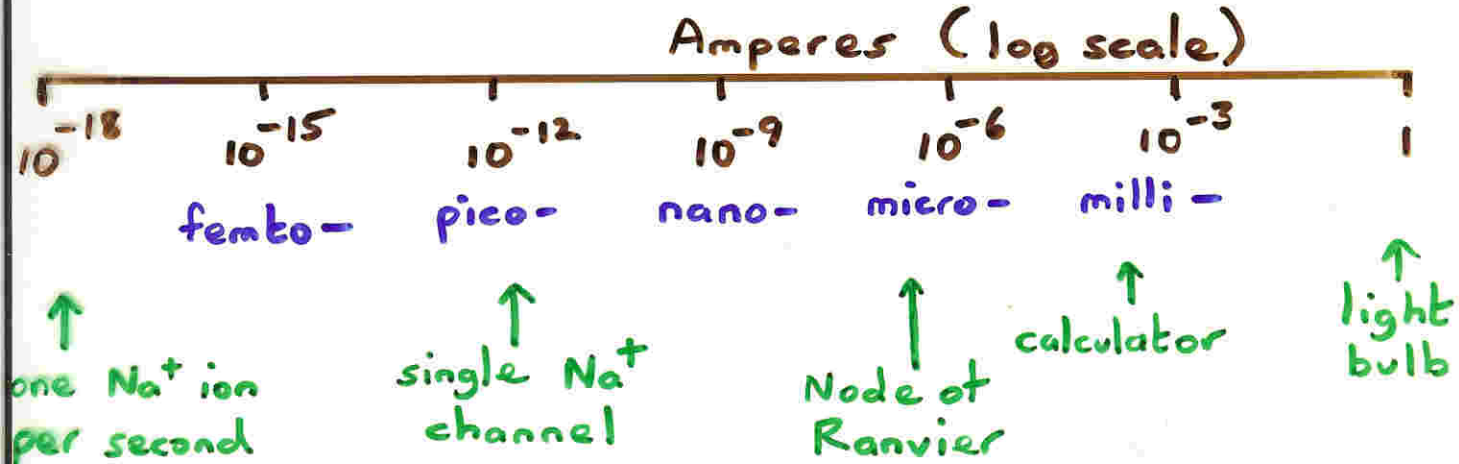
Ion Channels

Protein molecules in lipid membrane forming aqueous pore through which ions can permeate.

Total current given by number of channels open × current through each channel.

Single channel currents

Typically a few pA (10^{-12} A)



Action potential at single node involves roughly 1 million Na^+ channels.

Each channel lets through about 1 million Na^+ ions / second: too fast to be transport protein.

Ways to study ion channels

① Functional studies – record currents through single channels by patch clamp (Neher & Sakmann, 1976)

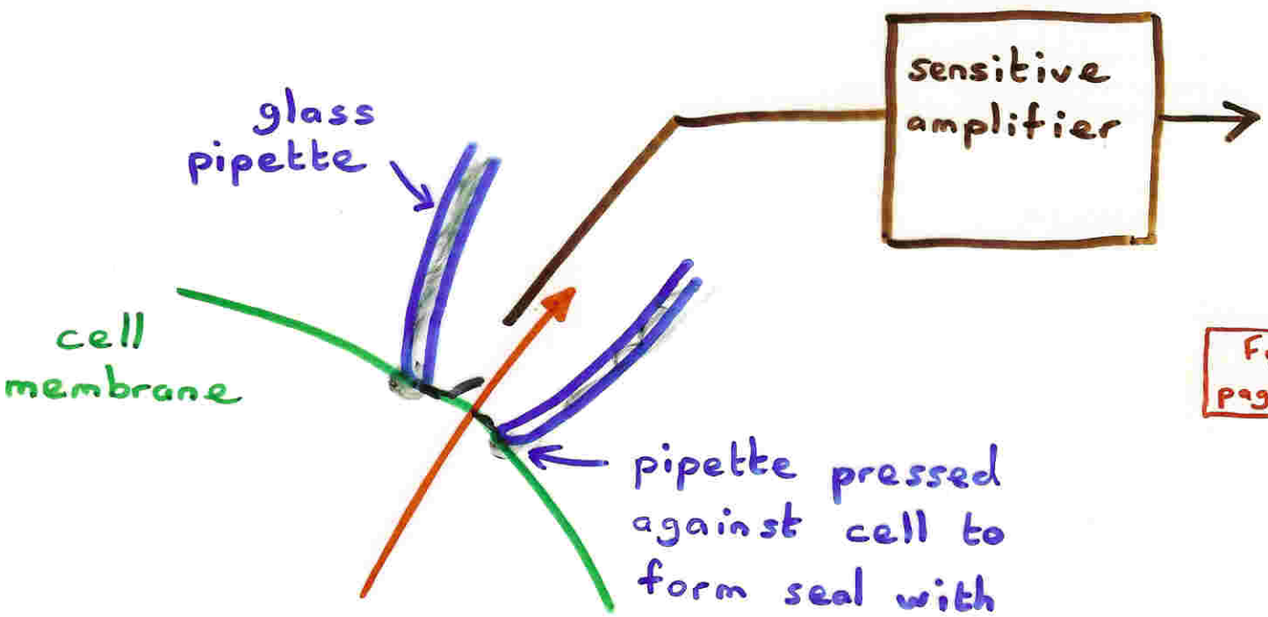
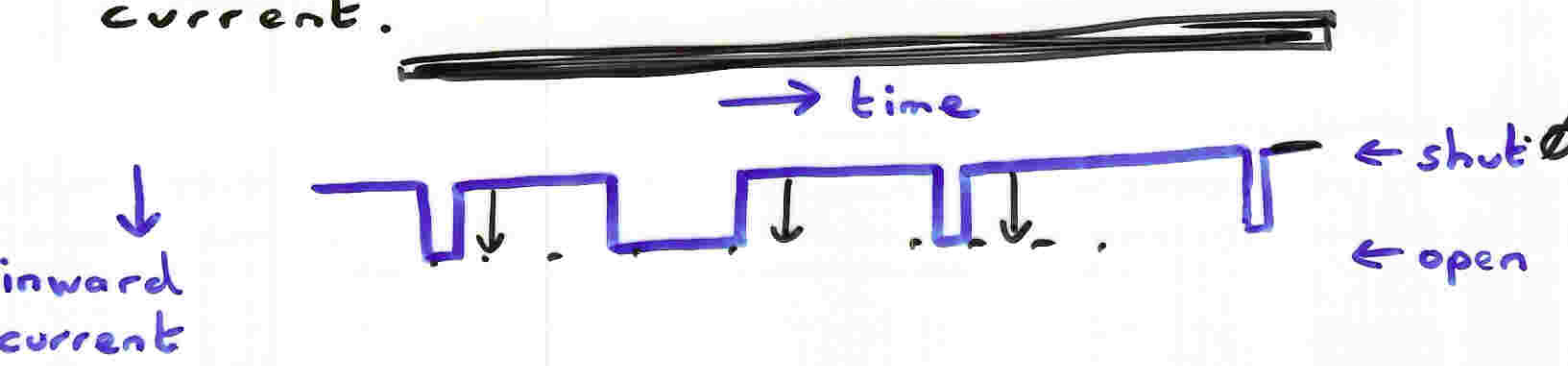


Fig. page 70

Single channel currents

Channels switch between open and closed states, producing rectangular pulses of current.



Durations of each opening and closing are random, but current is the same for each opening.

Total current in a cell is summation of activity of many channels : e.g. Na^+ current in axon

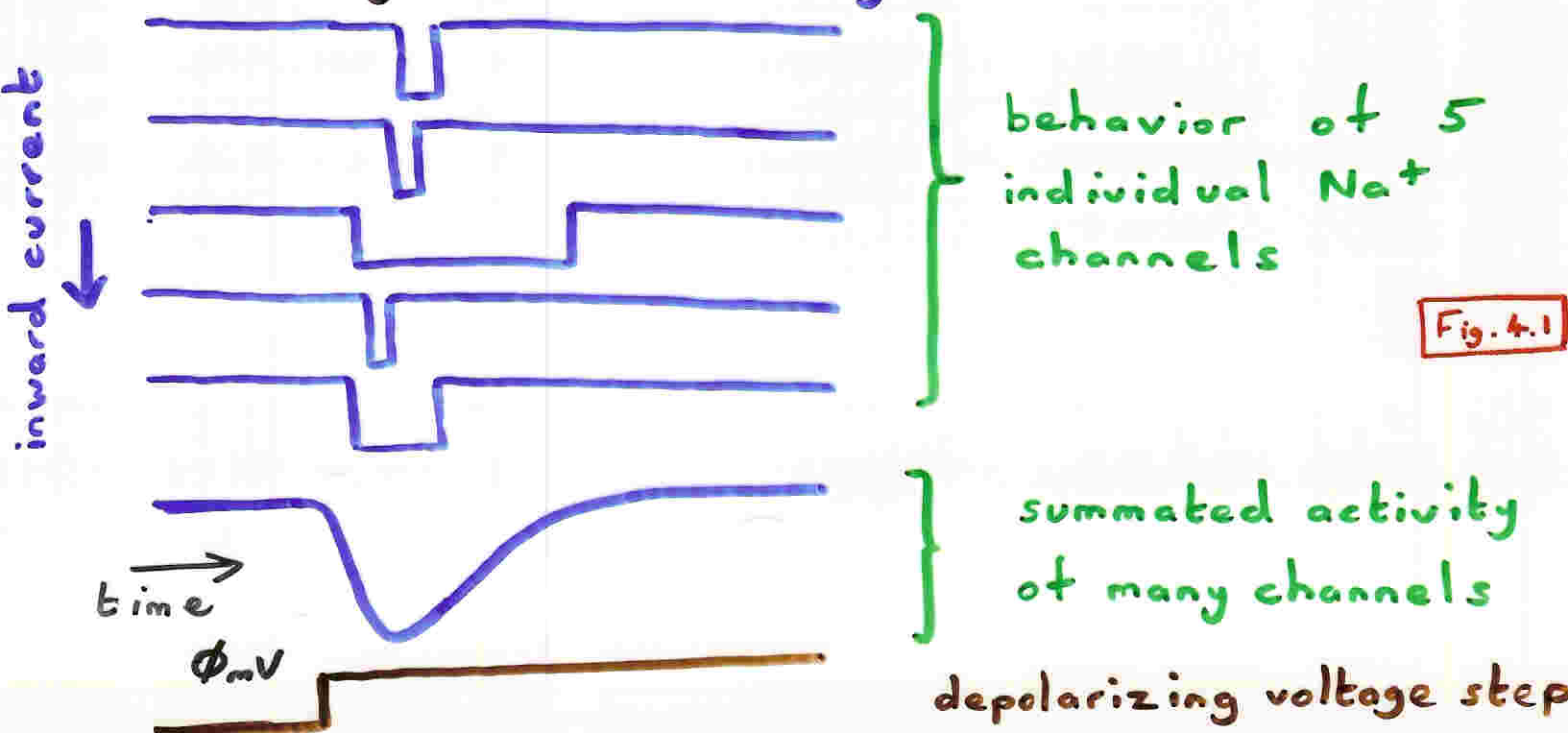


Fig. 4.1

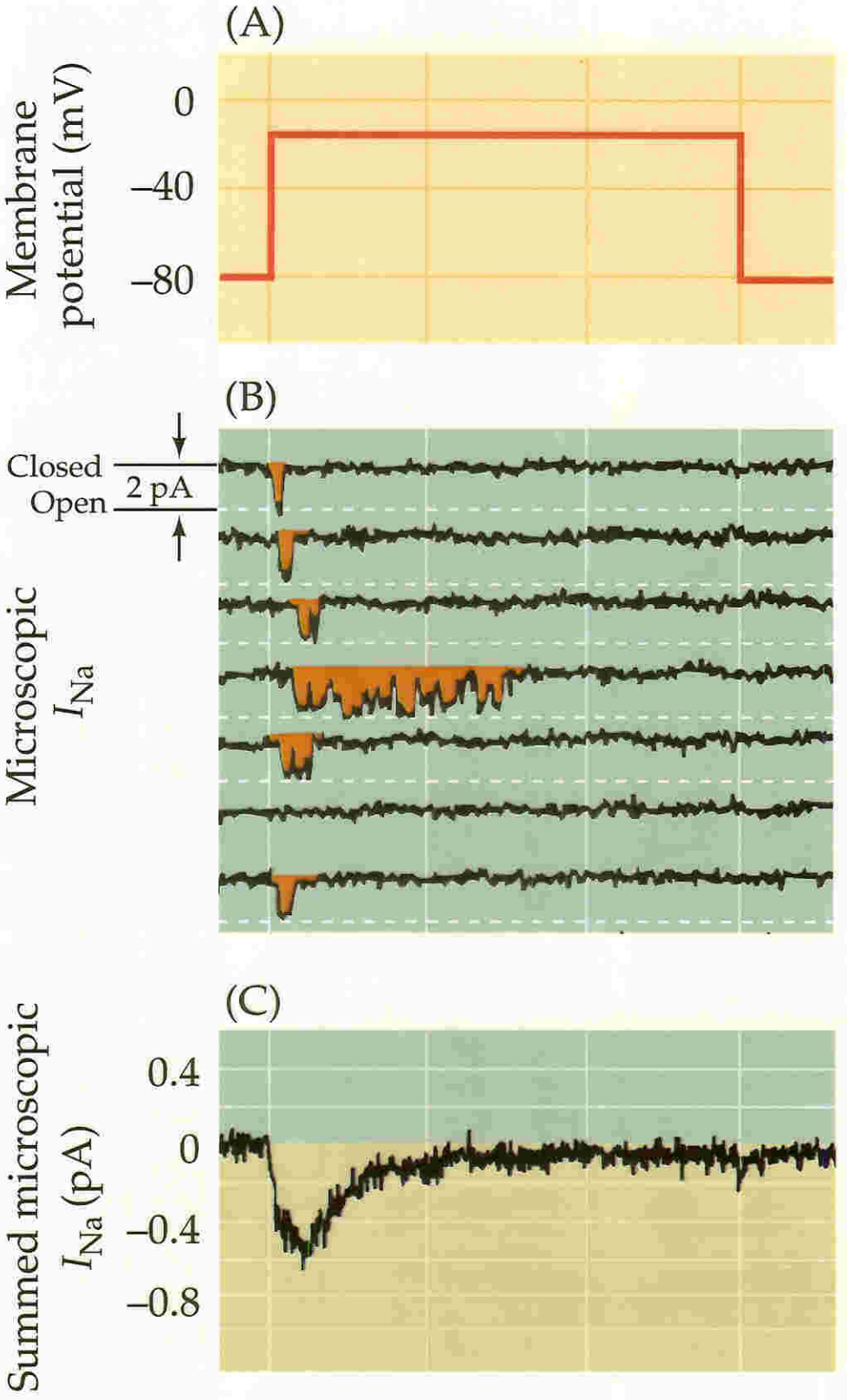


Figure 4.1 (Part 1) Patch Clamp Measurements of Ionic Currents Flowing Through Single Na^+ Channels

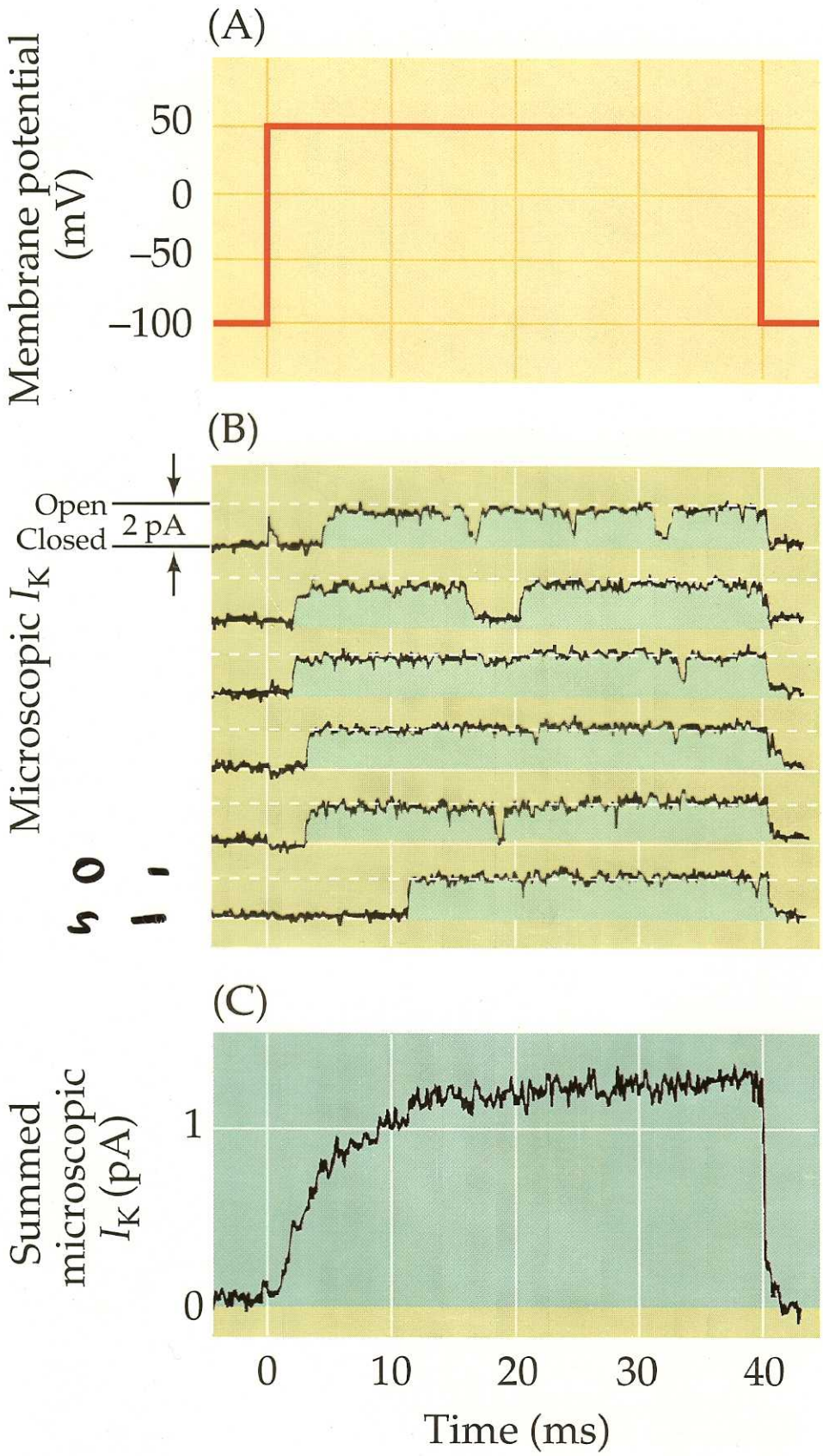
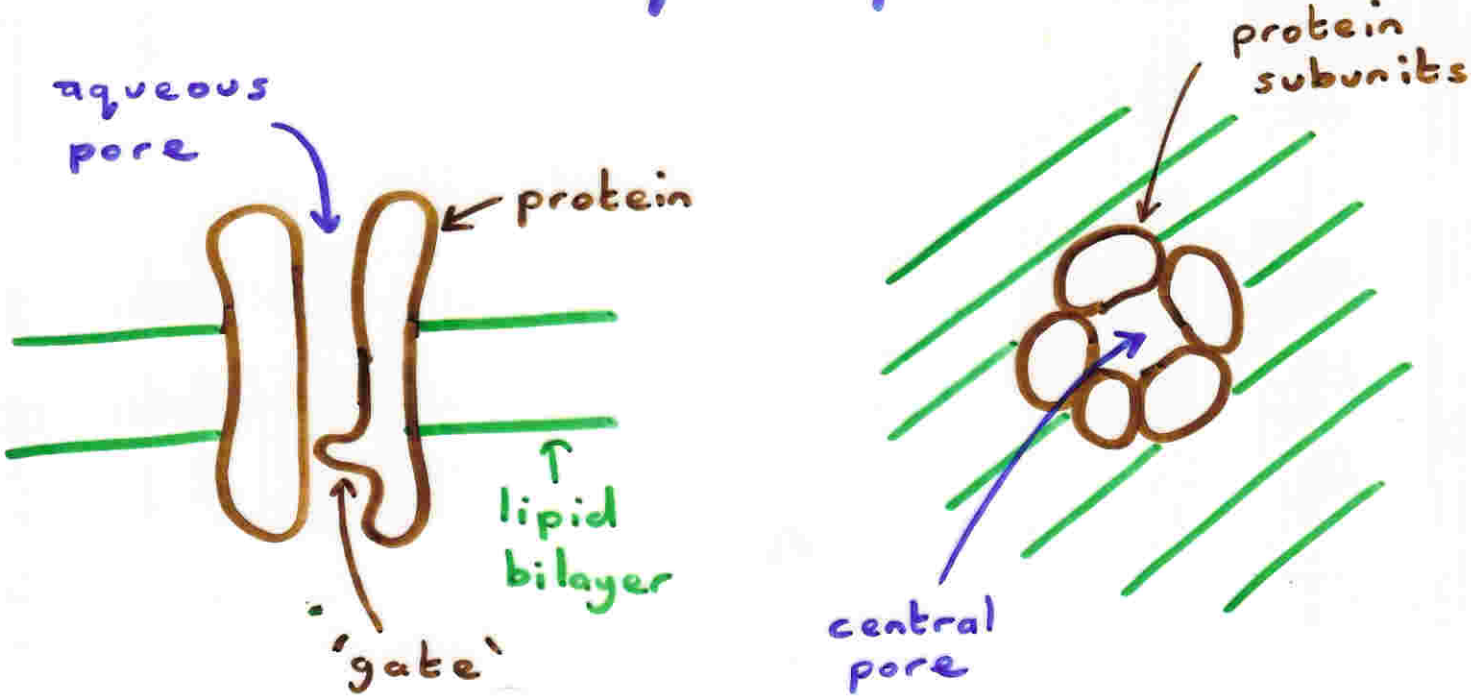


Figure 4.2 (Part 1) Patch Clamp Measurements of Ionic Currents Flowing Through Single K^+ Channels

② Molecular structure. — Genes for many ion channels have been cloned and sequenced. Thus we know primary structure of channel protein (amino acid composition) and can predict secondary structure (protein folding).

Ion channels formed from several 'building blocks' — either separate protein subunits or homologous repeats within a single giant protein. These associate so that hydrophyllic regions in each unit form aqueous pore.



Cross section

Looking down on membrane

5.7

Channels may be made from:

A single, very big protein molecule with several repeating units

OR

By the association of several smaller protein subunits

(A)

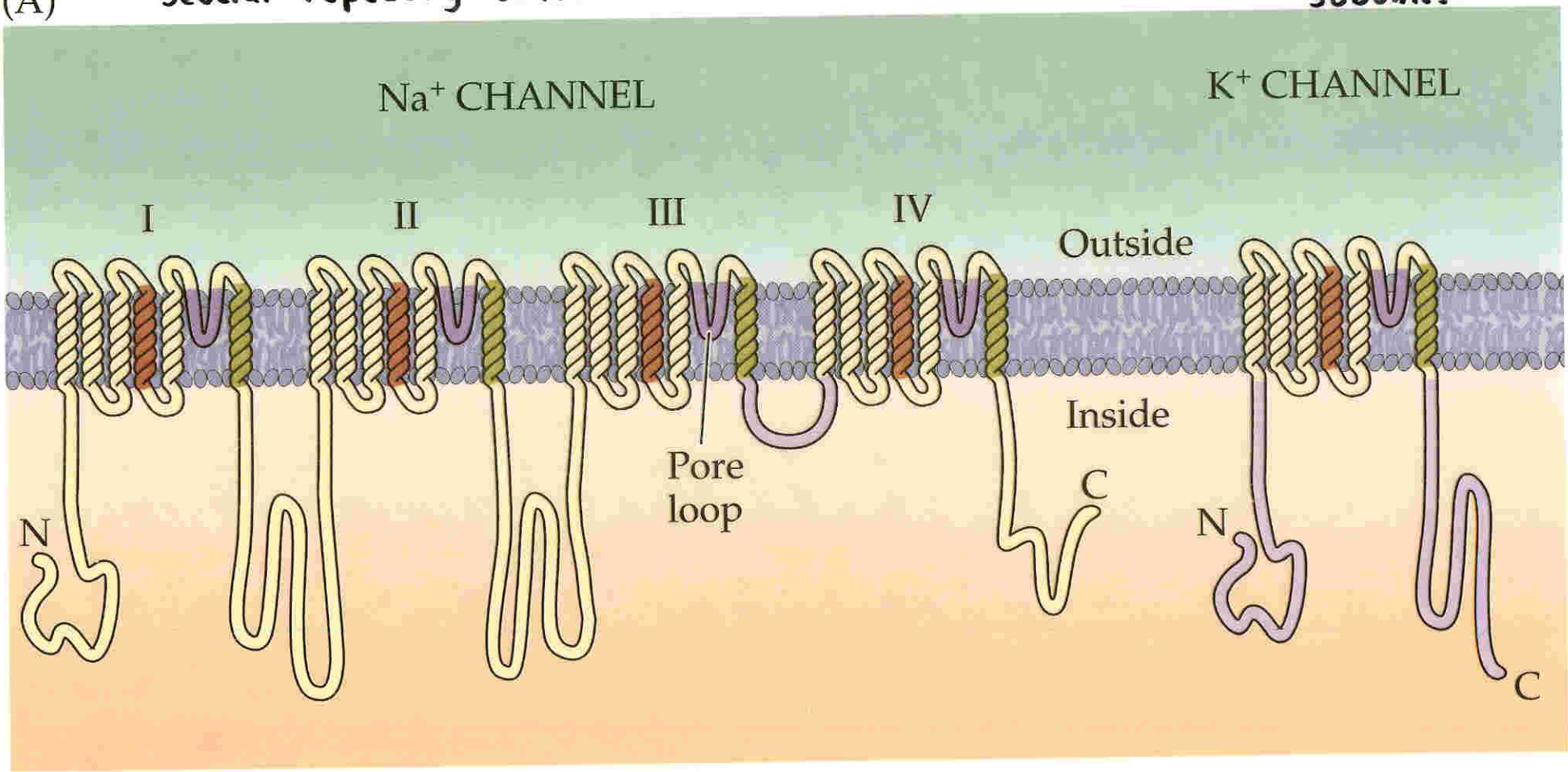
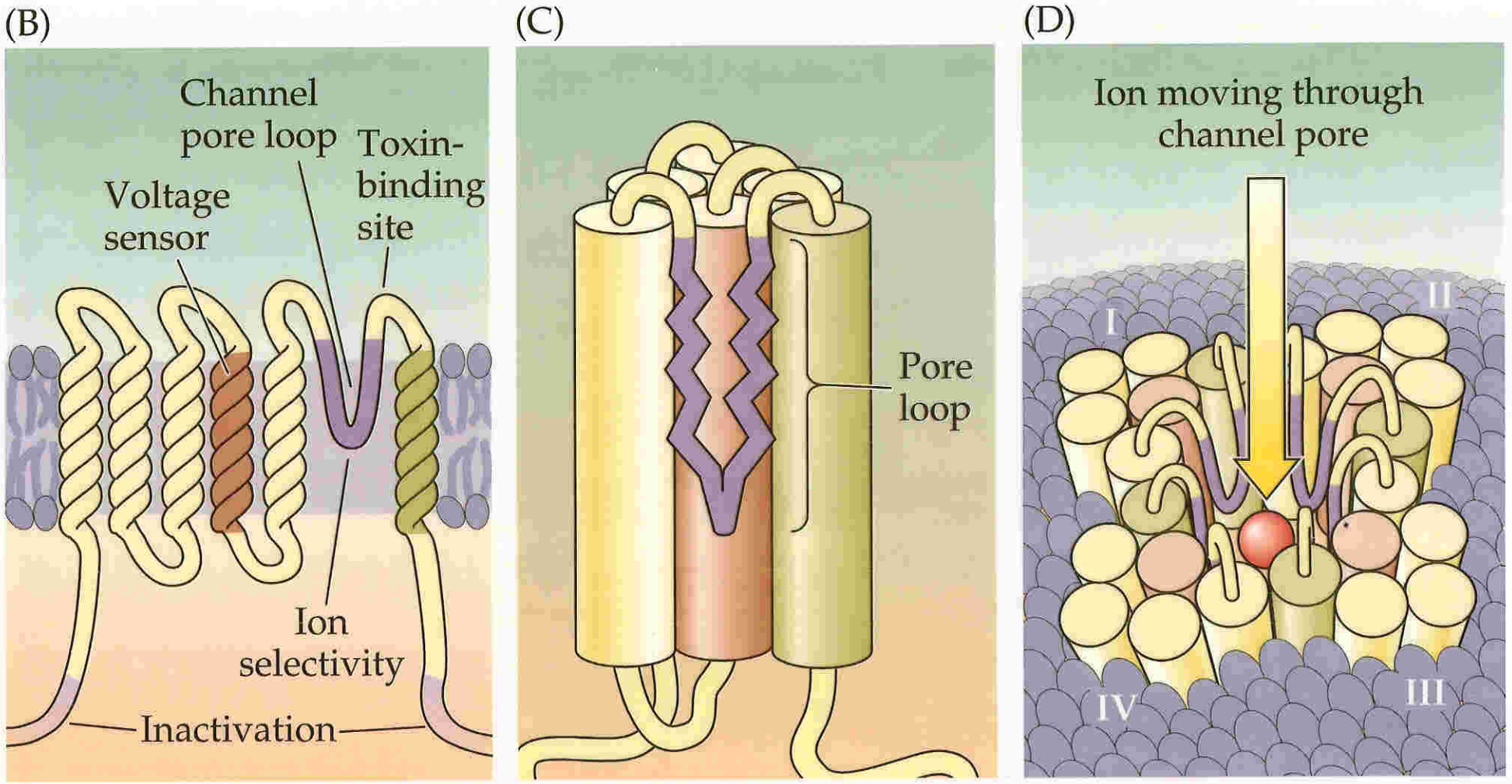


Fig 4.6

5.8


(B)
Channel pore loop
Toxin-binding site
Voltage sensor
Ion selectivity
Inactivation
(C)
Pore loop
(D)
Ion moving through channel pore
I
II
III
IV

Channel gating –

Channel activity (opening of 'gate') may be controlled by;

Membrane potential – e.g. Na^+ and K^+ chann of axon

Binding of agonist molecule to receptor site on channel protein.

e.g. acetylcholine receptor at musel endplate

Gating currents

Special regions within each domain of the Na^+ channel have strong electrical charge. They act as voltage sensors ('gating particles') by moving across membrane in response to electric field

Movement of voltage sensors is coupled to opening of the ion pore.

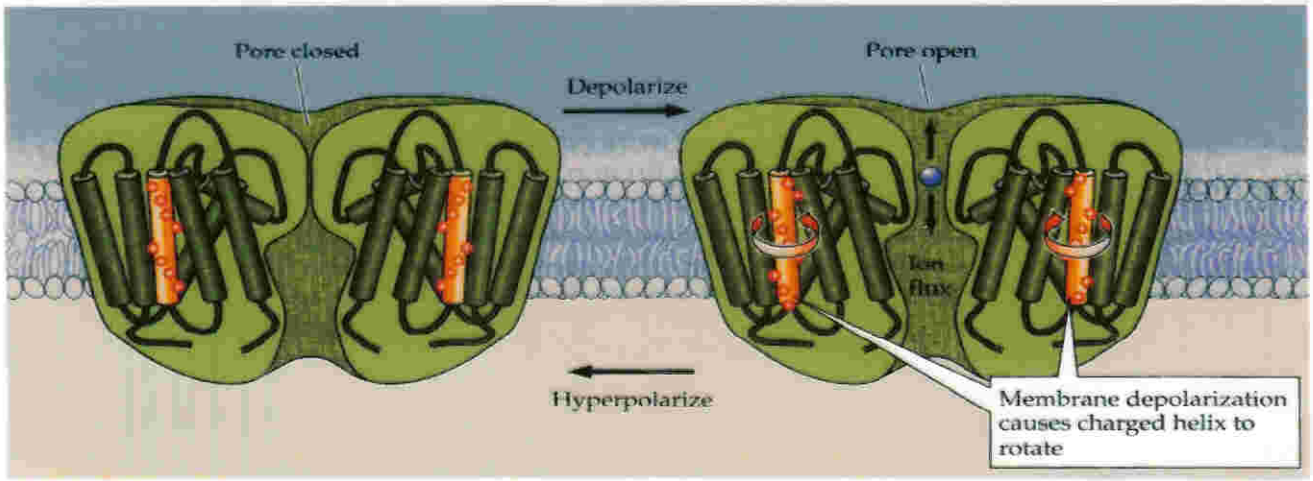


Fig. 4.7

The sodium pump

Establishing concentration gradients across the cell membrane requires energy —

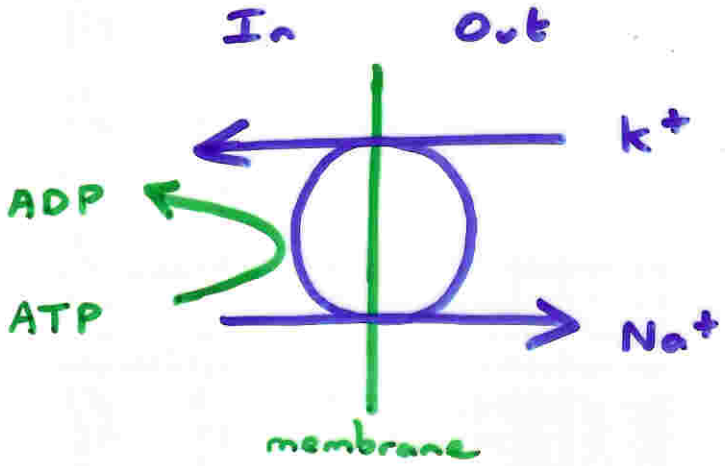
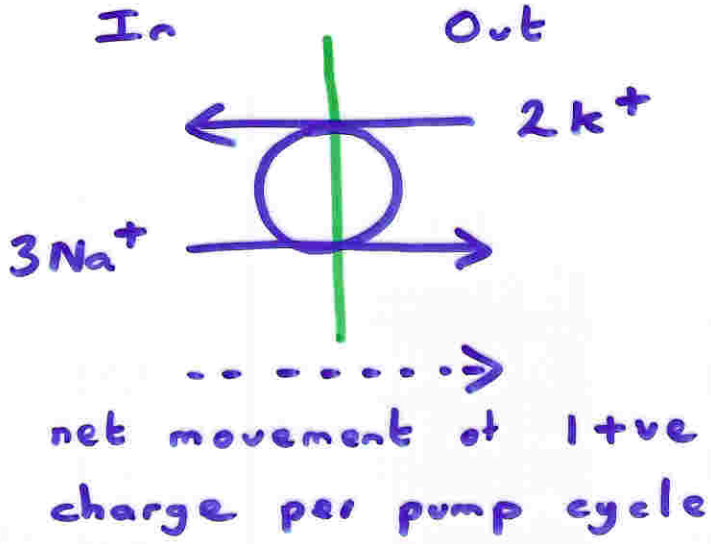


Fig. 4.7B

This is done by the Na^+/K^+ ATPase (Na pump) which actively extrudes Na^+ from the cell using metabolic energy provided by ATP. Pump is a protein (enzyme) in the cell membrane which functions as an antiporter.

Pump accounts for 1/3 total energy requirement in resting neuron, rising to 2/3 after electrical activity.

Na pump is electrogenic. 3 Na^+ ions extruded for every 2 K^+ going in



Thus, pump activity tends to hyperpolarize the cell (make its potential more negative)

But - this effect is slight. The resting potential arises because of the concentration gradient established by the pump, not because the pump directly generates a voltage.