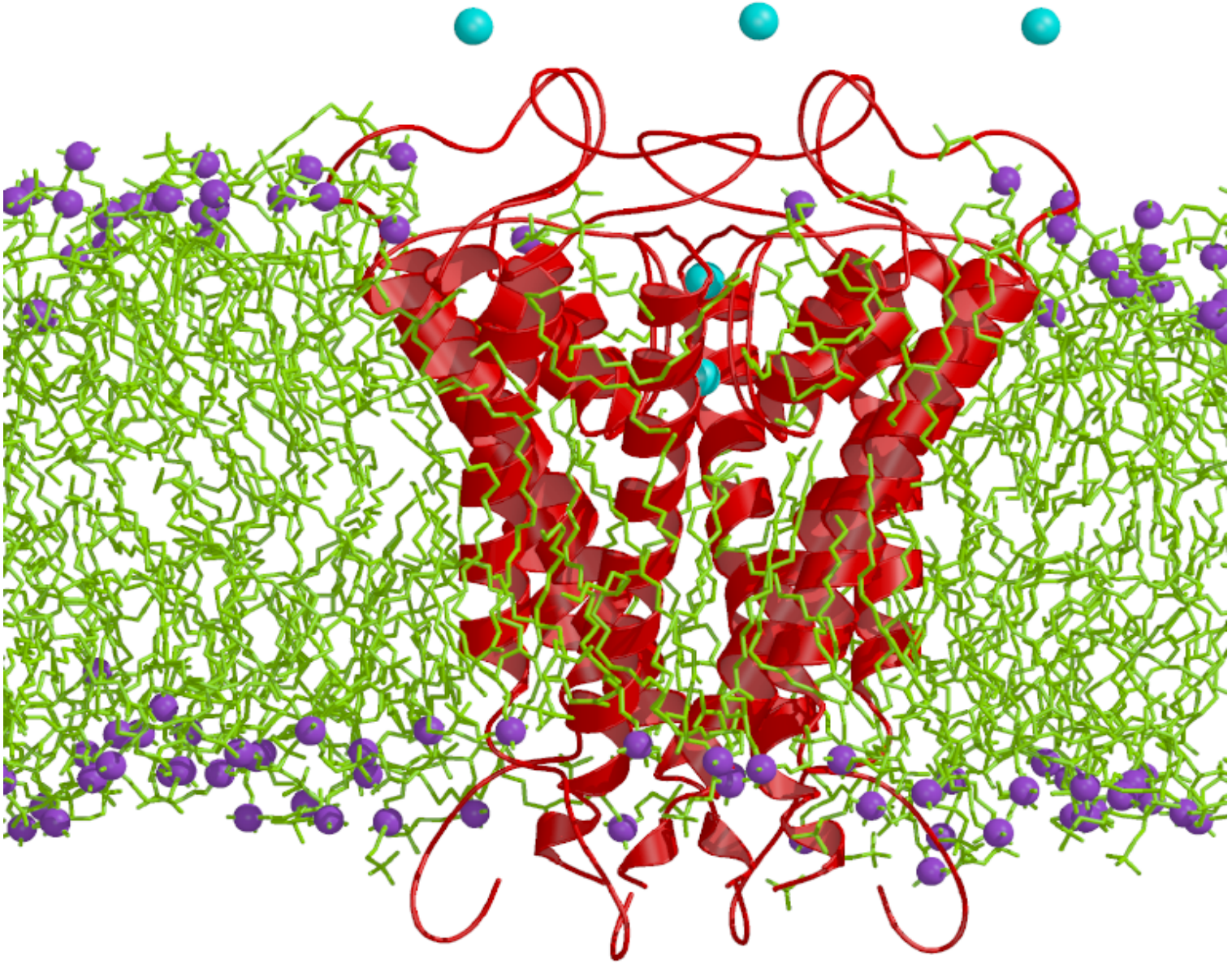
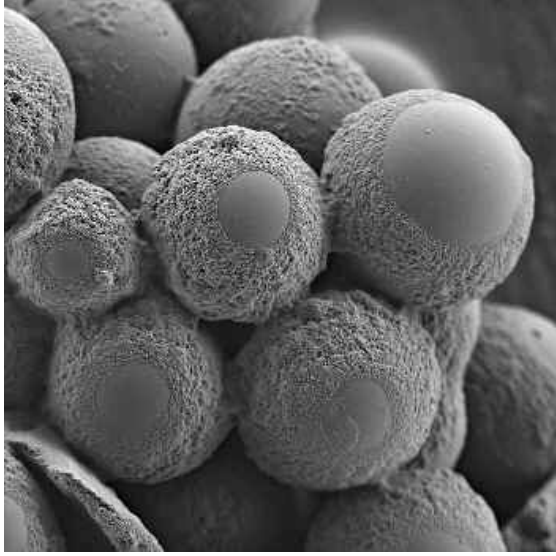


Potasium channel

Potasium channel KcsA

The 3D-structure of KcsA from Streptomyces lividans was the first X-ray structure of an ion channel.

For the Atomic Basis of Selective Ion Conduction in Potassium Channels



Streptomyces lividans

Advanced information on the Nobel Prize in Chemistry, 8 October 2003

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Membrane channels

Introduction

The Nobel Prize in Chemistry for 2003 is shared between two scientists who have made fundamental discoveries concerning how water and ions move through cell membranes. Peter Agre discovered and characterized the first water channel protein and Roderick MacKinnon has elucidated the structural and mechanistic basis for ion channel function.

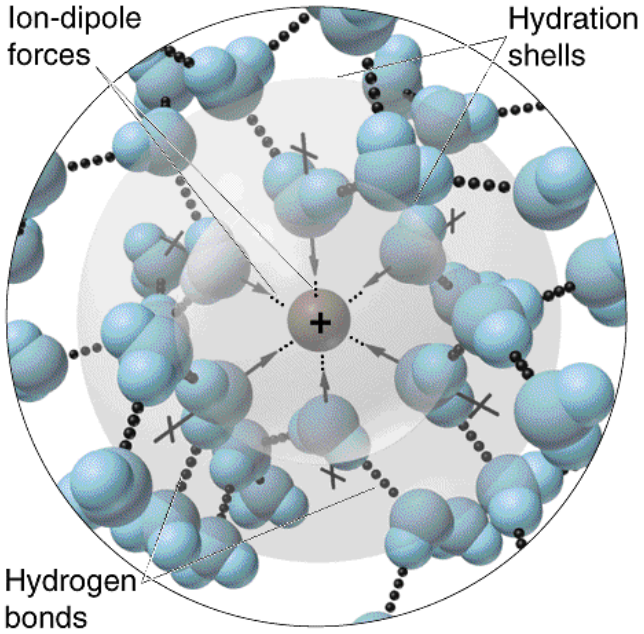
Hydrophobic barrier

Born-Formula

$$\Delta E = \frac{1}{2}\frac{Q^2}{r}\left(\frac{1}{\varepsilon_m} - \frac{1}{\varepsilon_w}\right)$$

- There are about 7 water molecules in the first hydration shell of potassium ion.

- Each water molecule stabilizes the ion by approximately 24 kT.

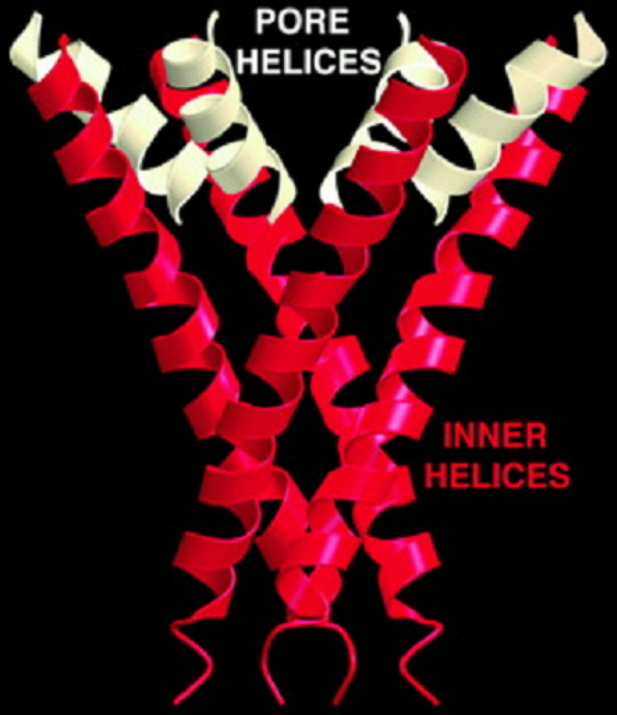


Roux & McKinnon, Science (1999)

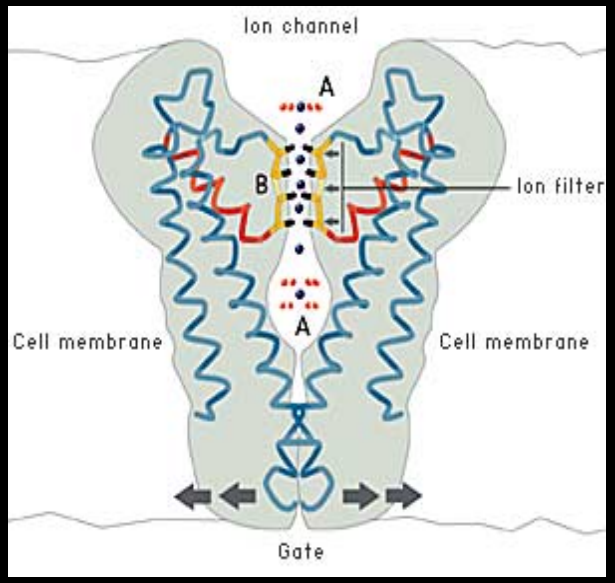
The Potassium Channel (KcsA)

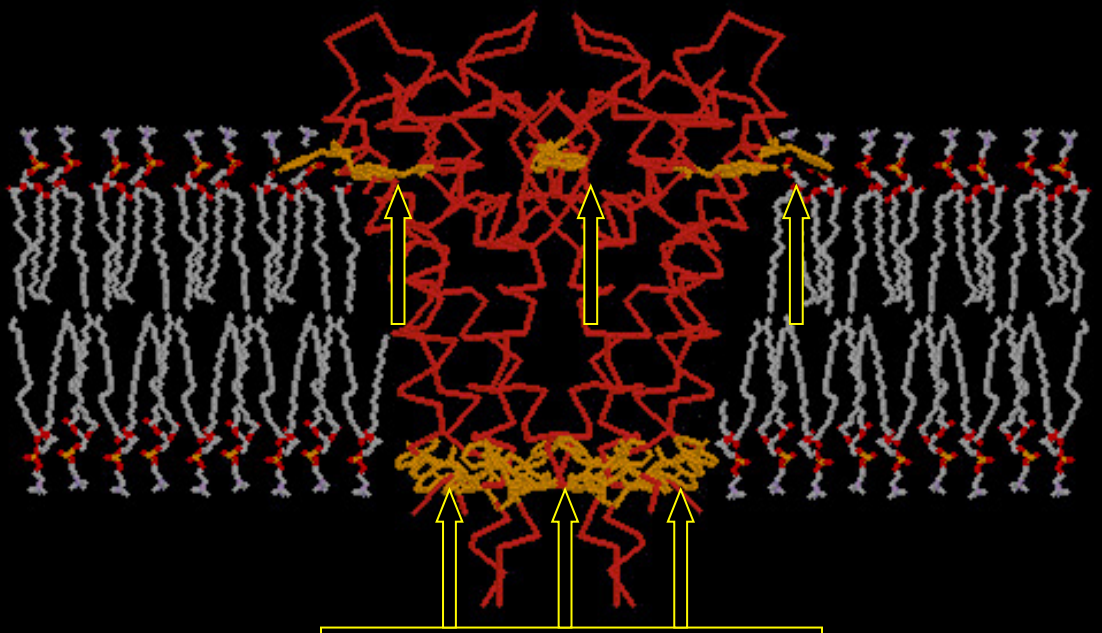
It is a **tetramer**.

Each monomer is 96 amino acids long and consist of 3 helices.

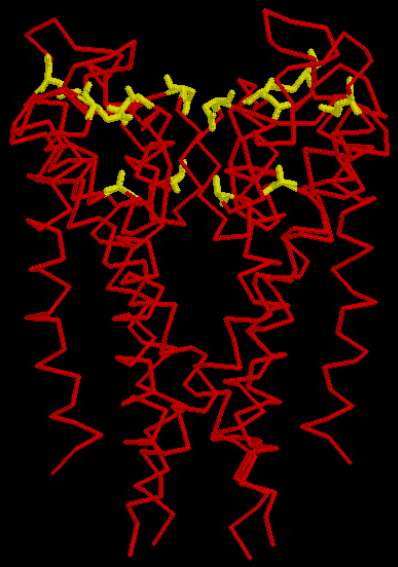


Doyle *et al.* Science (1998)

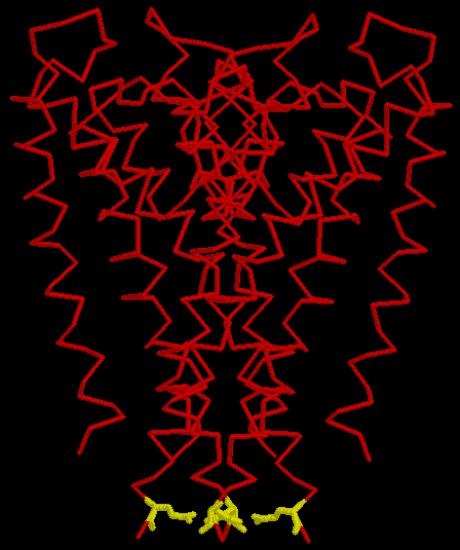




The aromatic residues



Negatively charged acidic residues are on top attract K^+



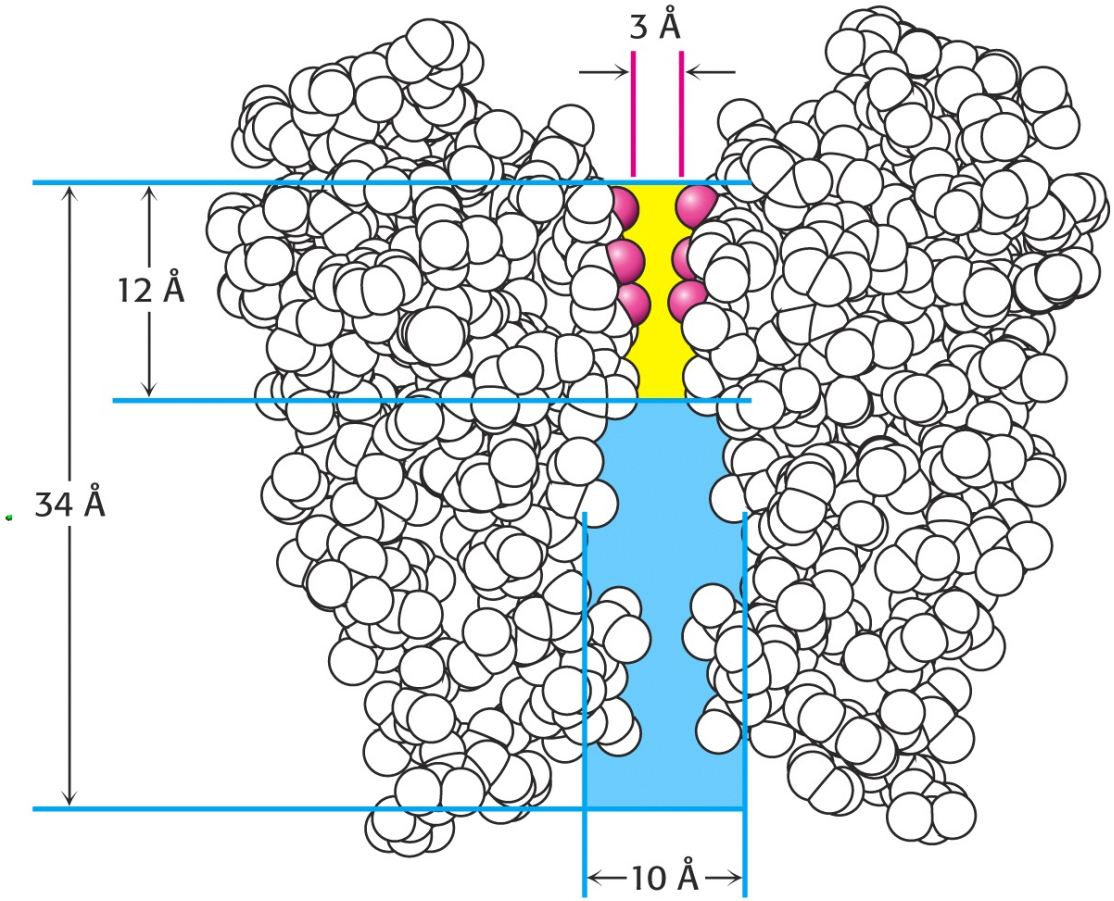
The negative charges on the bottom help to pull the K^+ ion through the pore.

Potassium channel

Potassium channels are a class of ion channels, managing to distinguish between K^+ and Na^+ ions while maintaining a very high throughput of K^+ ions when gated.

It has a diffusion rate of 10^8 ions per second.

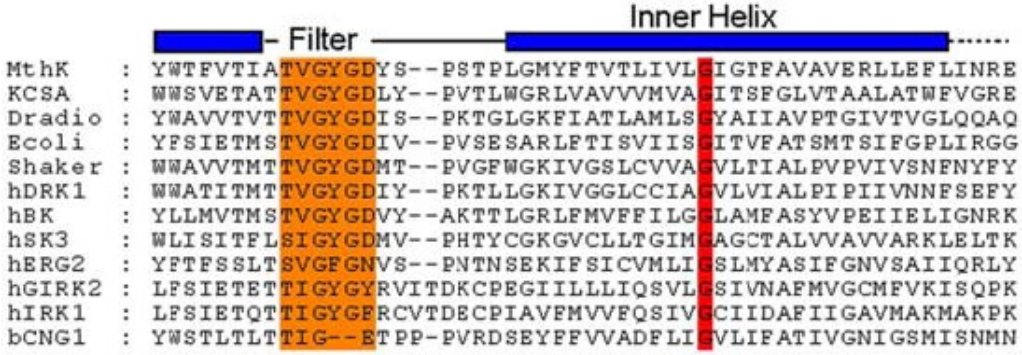
One K^+ ion is dehydrated, transfered, and rehydrated every 10 ns.

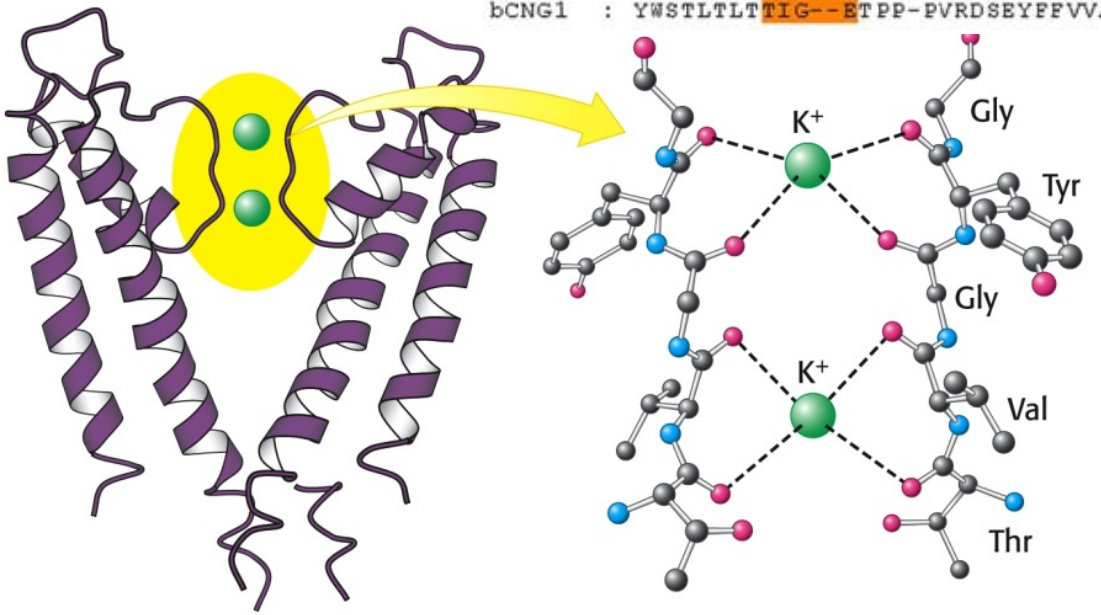


Selectivity filter

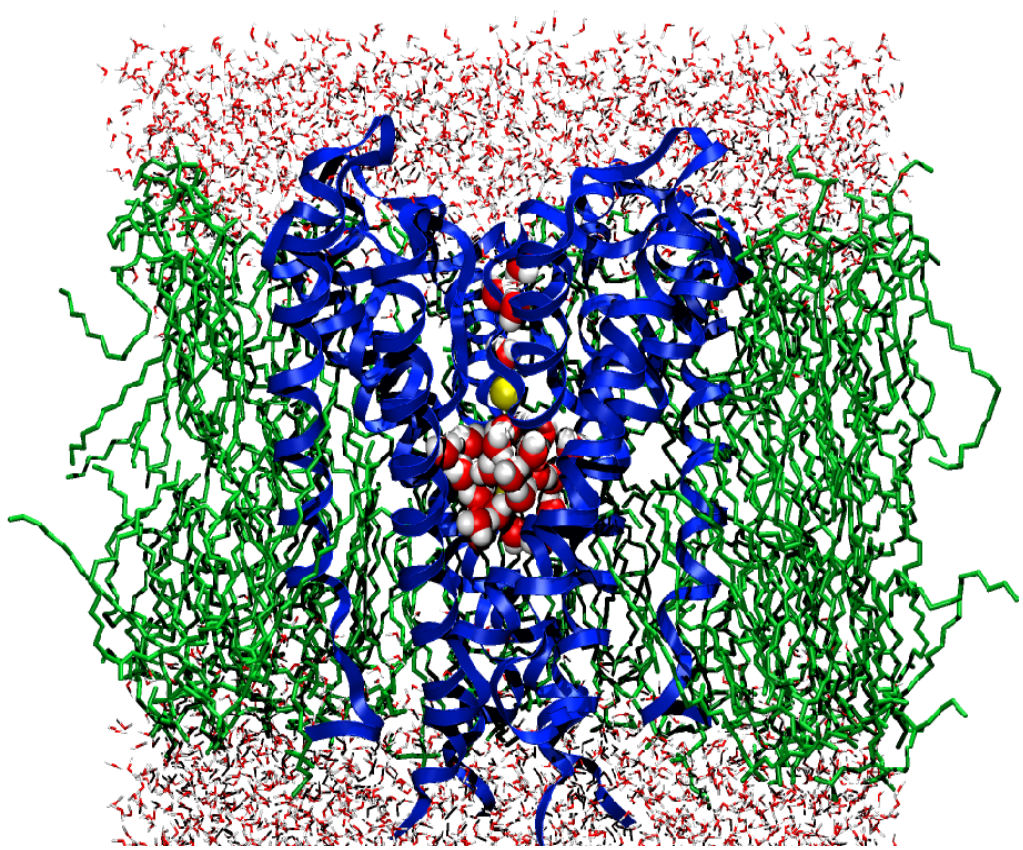
C=O *atoms of the protein backbone form selectivity filter (4 × Tyr-Val-Gly-Tyr-Gly).*

The sequence is **conserved** in all K^+-channels.

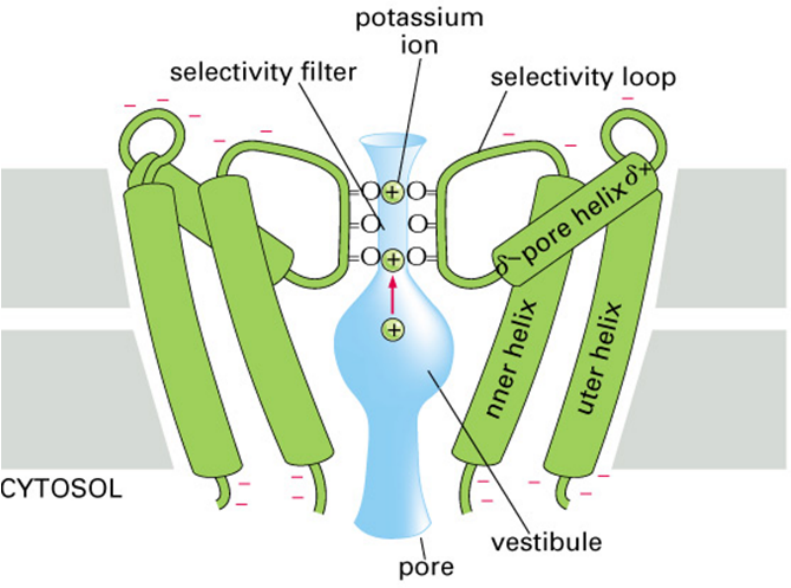


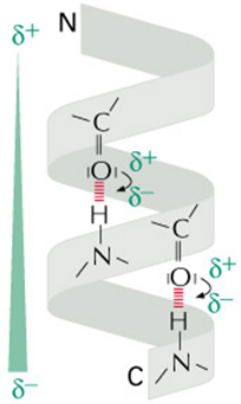


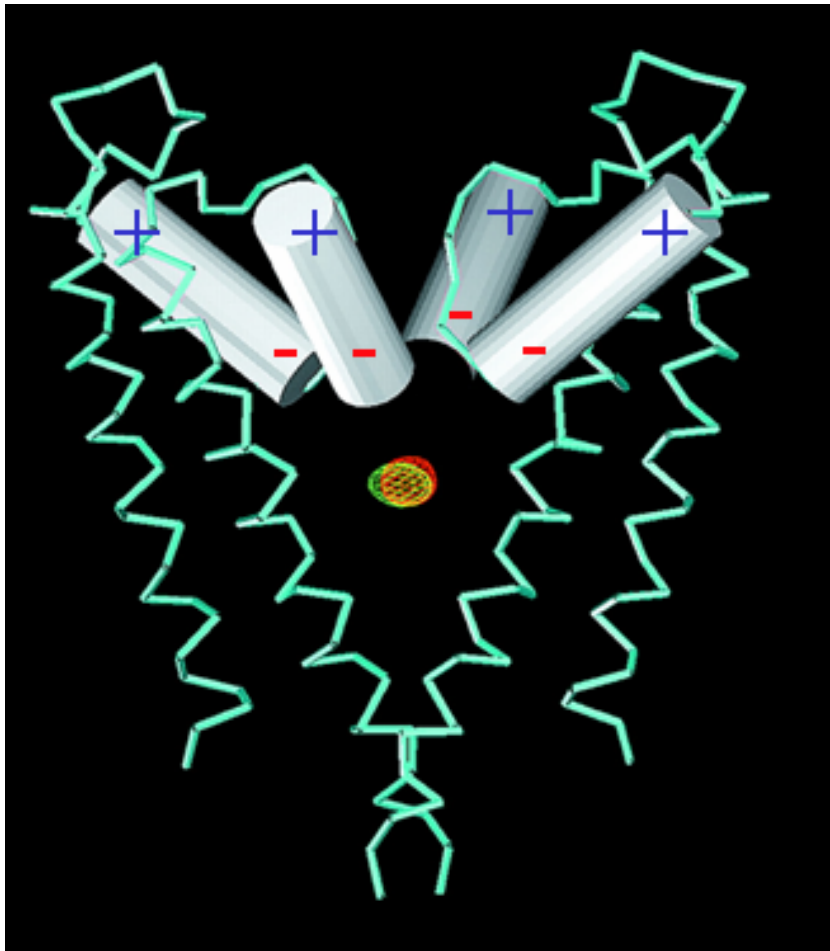
- *K^+ is surrounded by eight oxygen atoms from the protein*
  - *four 'above' and four 'below'.*
  - *very similar to water molecules around hydrated K^+.*

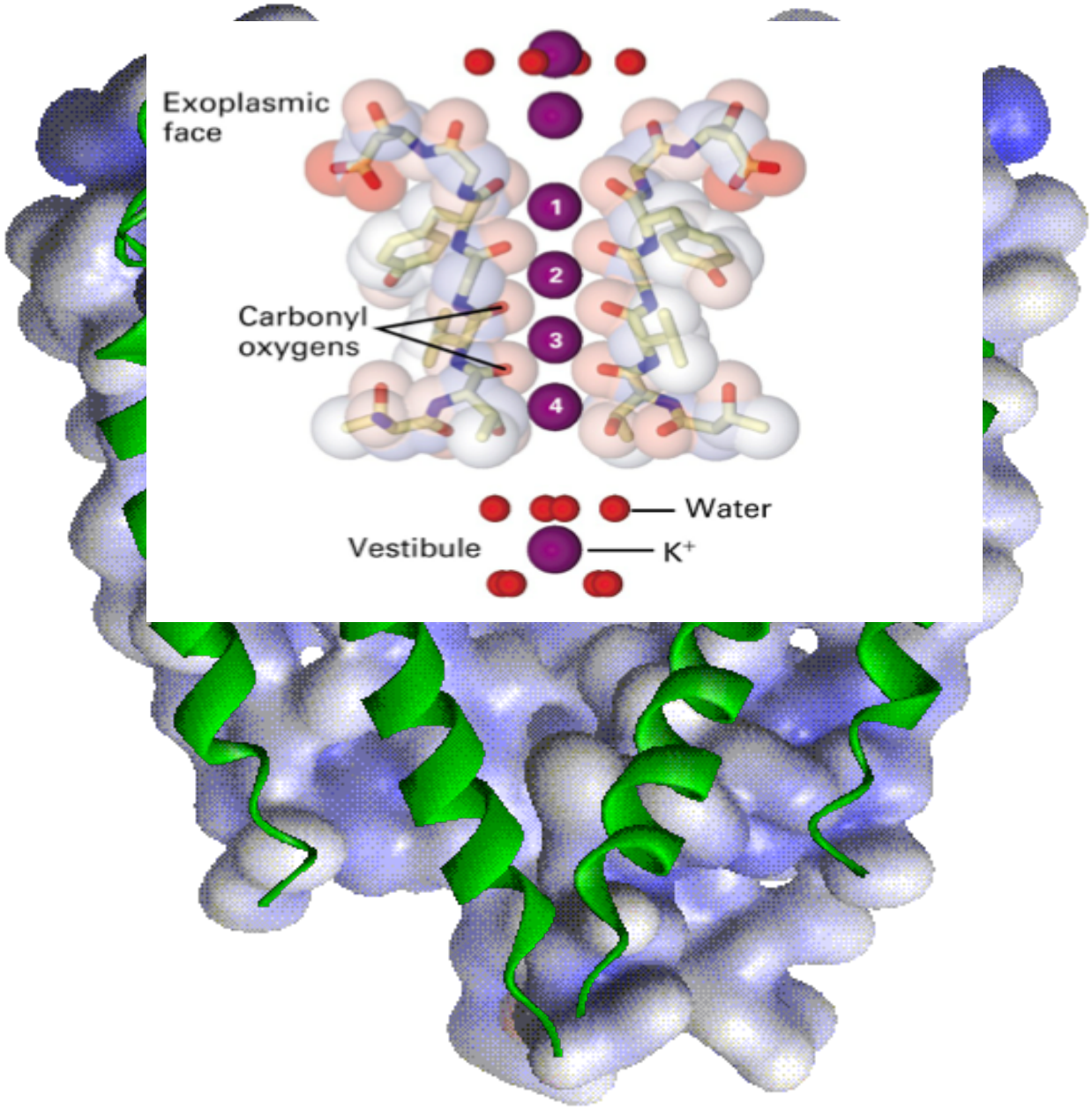


The central cavity is lined with hydrophobic residues.



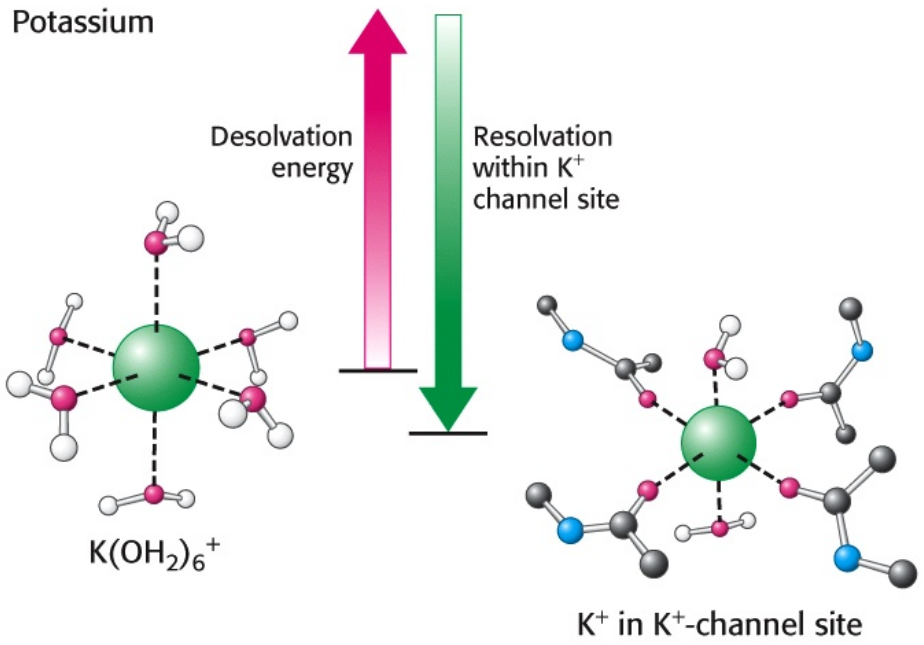


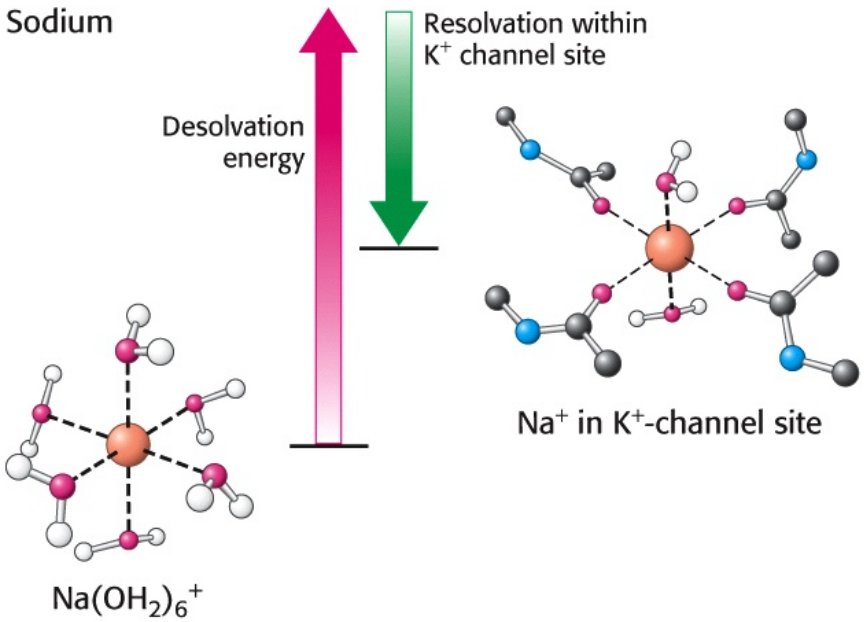



Exoplasmic face
1
2
Carbonyl oxygens
3
4
Water
Vestibule
K+

The selectivity is based on the size difference between K^+ and Na^+

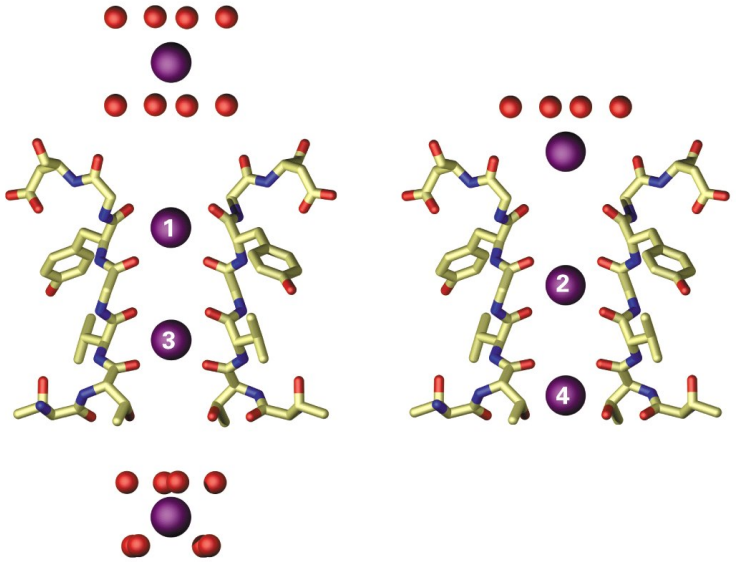
Ion	Atomic weight	Crystal radius [Å]	Hydrated radius [Å]	Mobility in electric field	Hydration free energy [kJ/mol]
Na^+	23	0.95	3.4	5.2	- 301
K^+	39	1.33	2.2	7.6	- 230

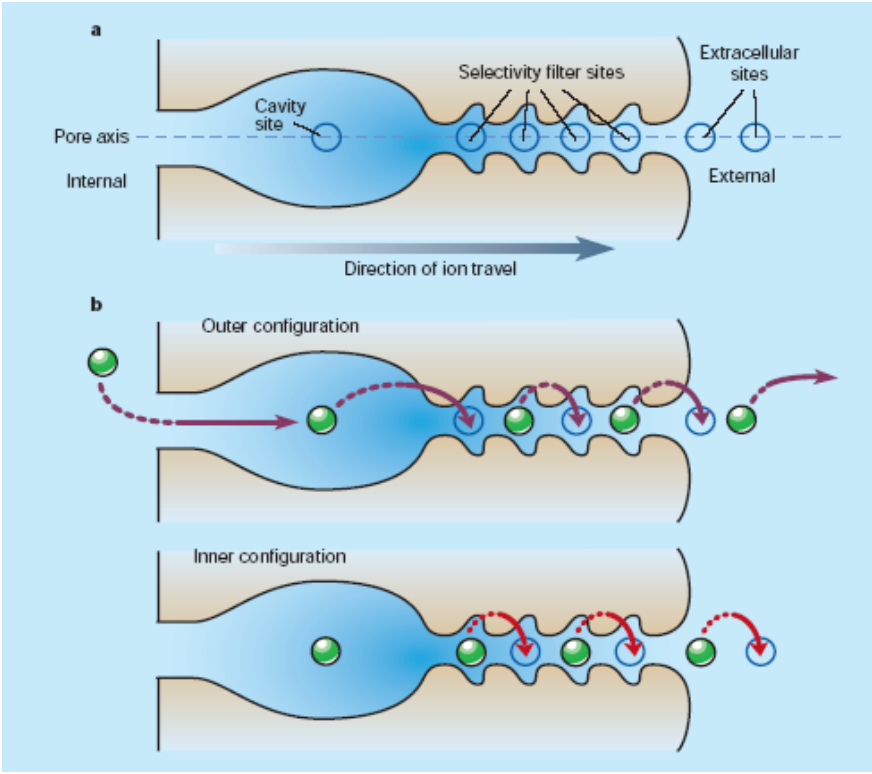




Why does the ion coordination required for high selectivity not cause the ions to bind too tightly & prevent rapid diffusion through the pore?

(c) Ion movement through selectivity filter



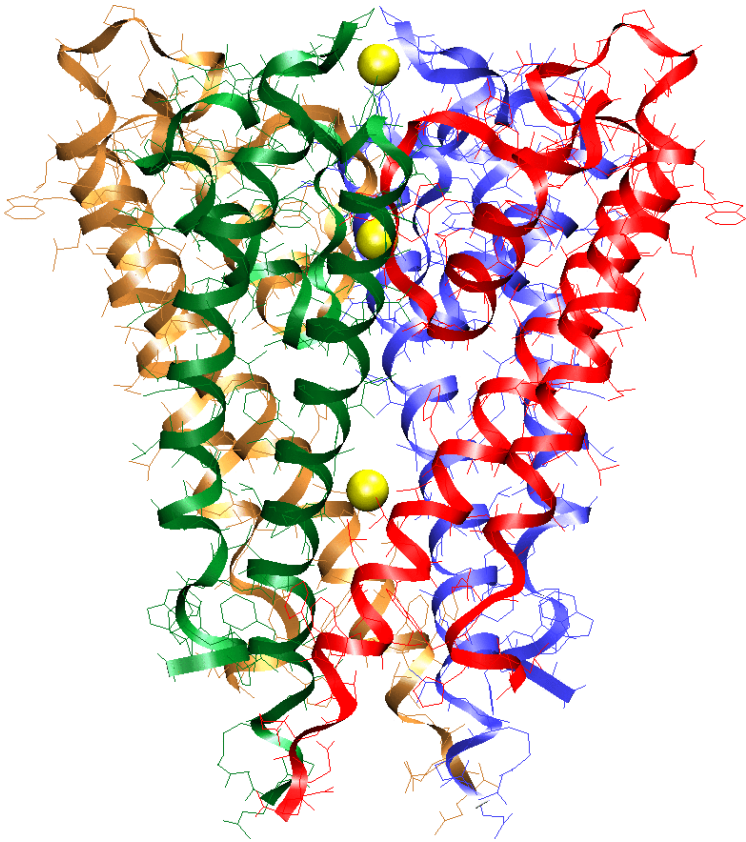


Selectivity filter contains more than one ion – repulsion between closely spaced ions will helps overcome the intrinsic binding site affnity.

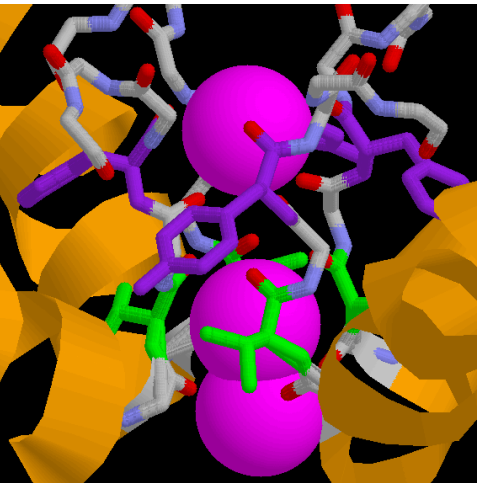
Transfer is isoenergetic → conductivity close to ***diffusion limit.***

The selectivity filter needs to be rigid

KcsA Potassium Channel from *Streptomyces lividans*

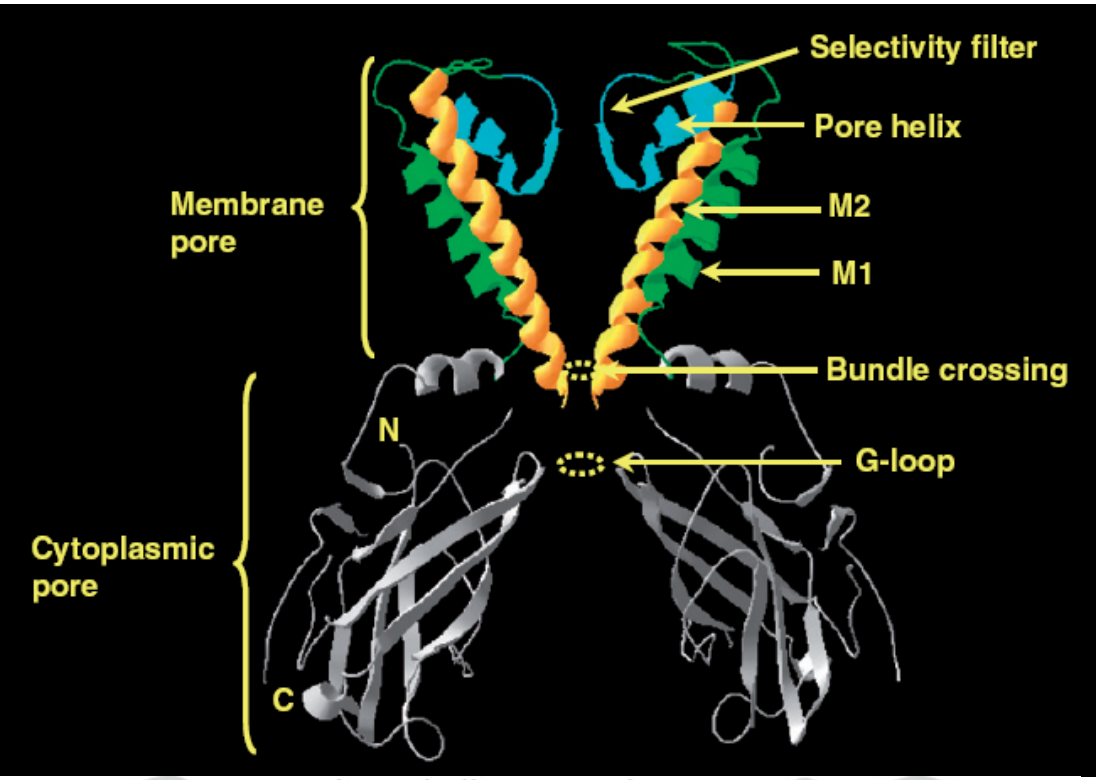


- The Val and Tyr hold the selectivity filter at a certain diameter by hydrogen bonding with the inner helix.
- They form hydrogen bonds which acts as tight springs that will not allow the pore to collapse.

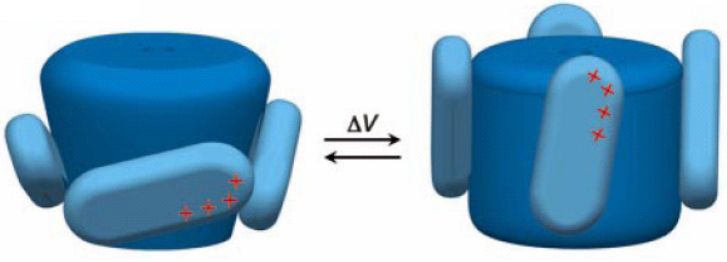


- The "springs" prevent the selectivity filter from interacting with cations smaller than K^+.

Topology of a Kir subunit.



The bacterial voltage-gated K^+ channel KvAP



The gate