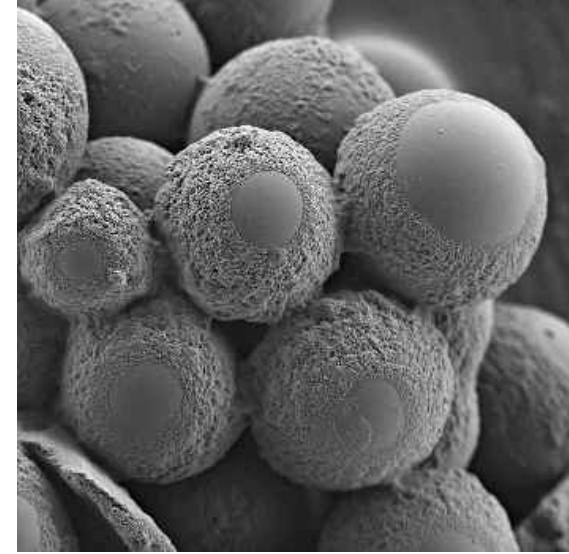


*Potassium channel*

# Potassium 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



KUNGL.  
VETENSKAPSAKADEMIEN  
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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.

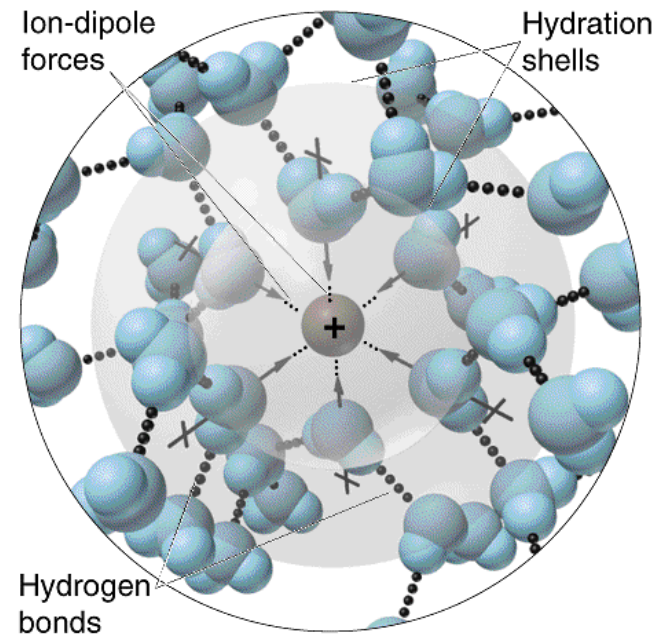
# Hydrophobic barrier

## Born-Formula

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

Each water molecule stabilizes the ion by approximately 24 kT.

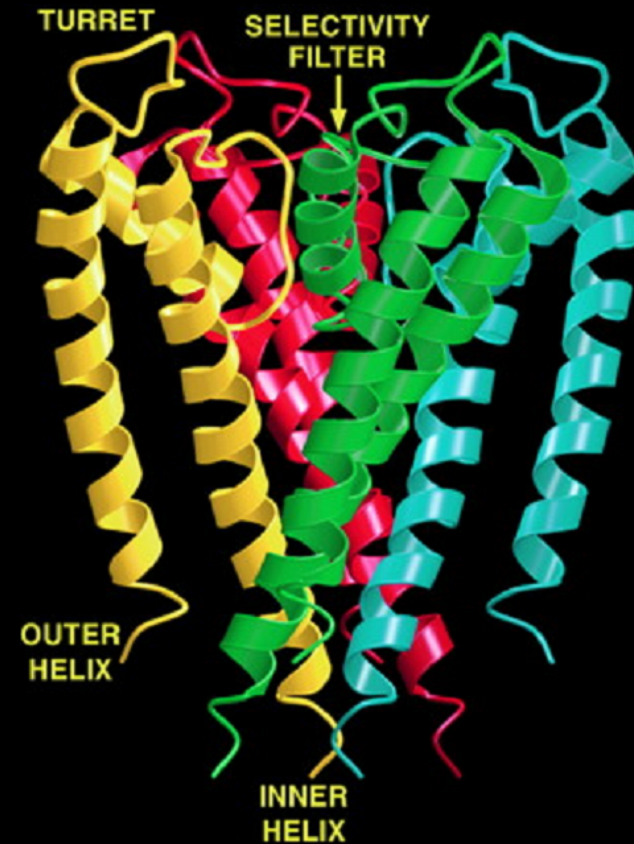
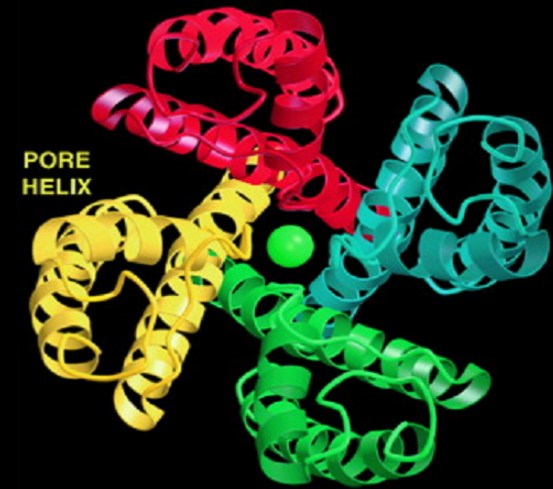
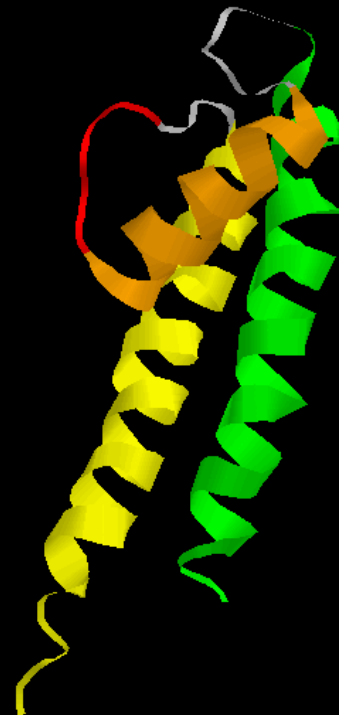
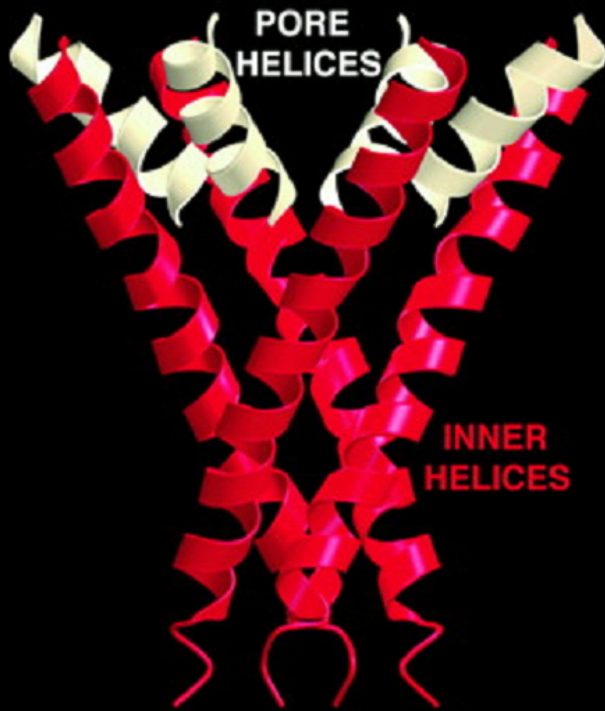
$$\Delta E = \frac{1}{2} \frac{Q^2}{r} \left( \frac{1}{\epsilon_m} - \frac{1}{\epsilon_w} \right)$$

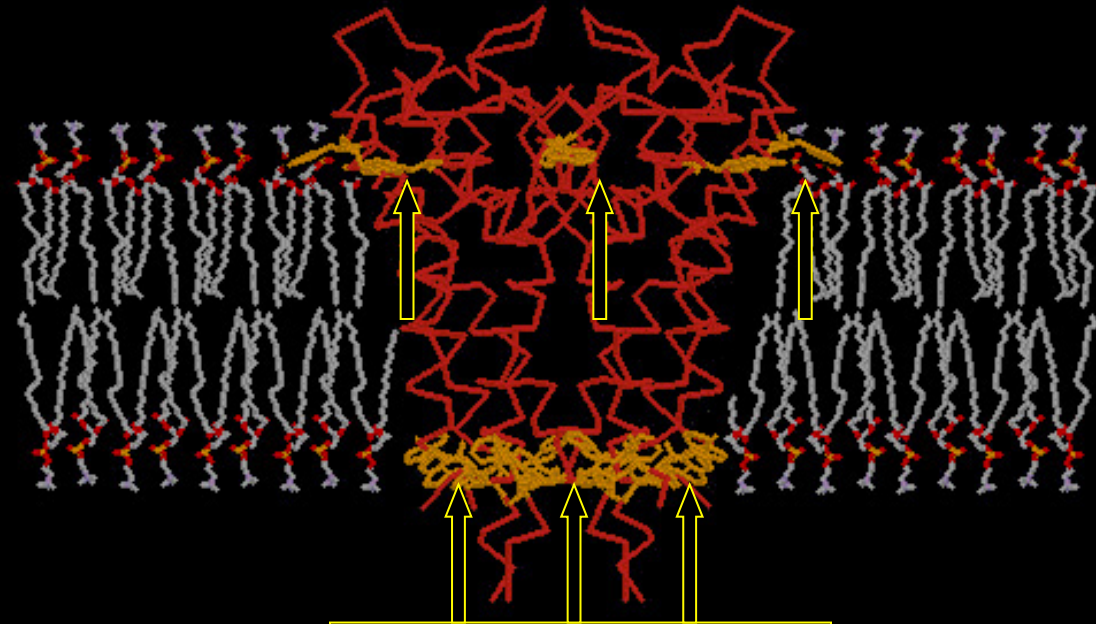
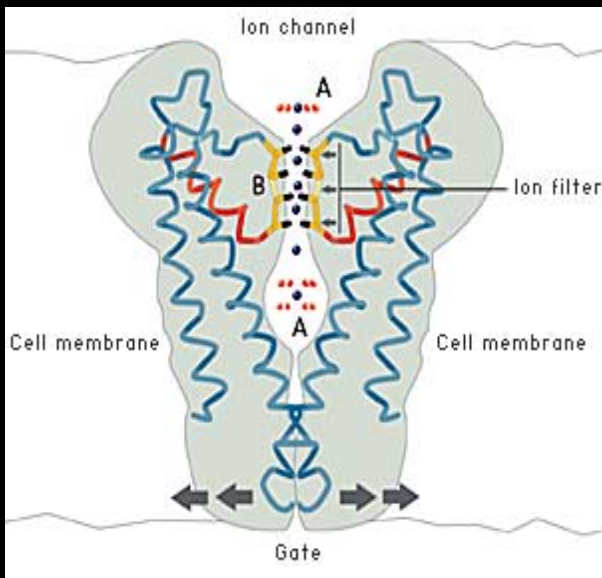


# *The Potassium Channel (KcsA)*

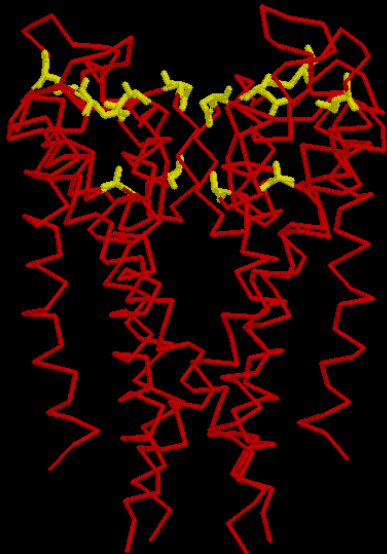
It is a **tetramer**.

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

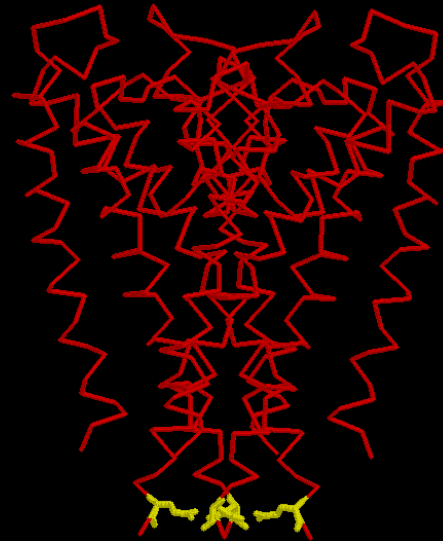




*The aromatic residues*



*Negatively charged acidic residues are on top attract  $K^+$*



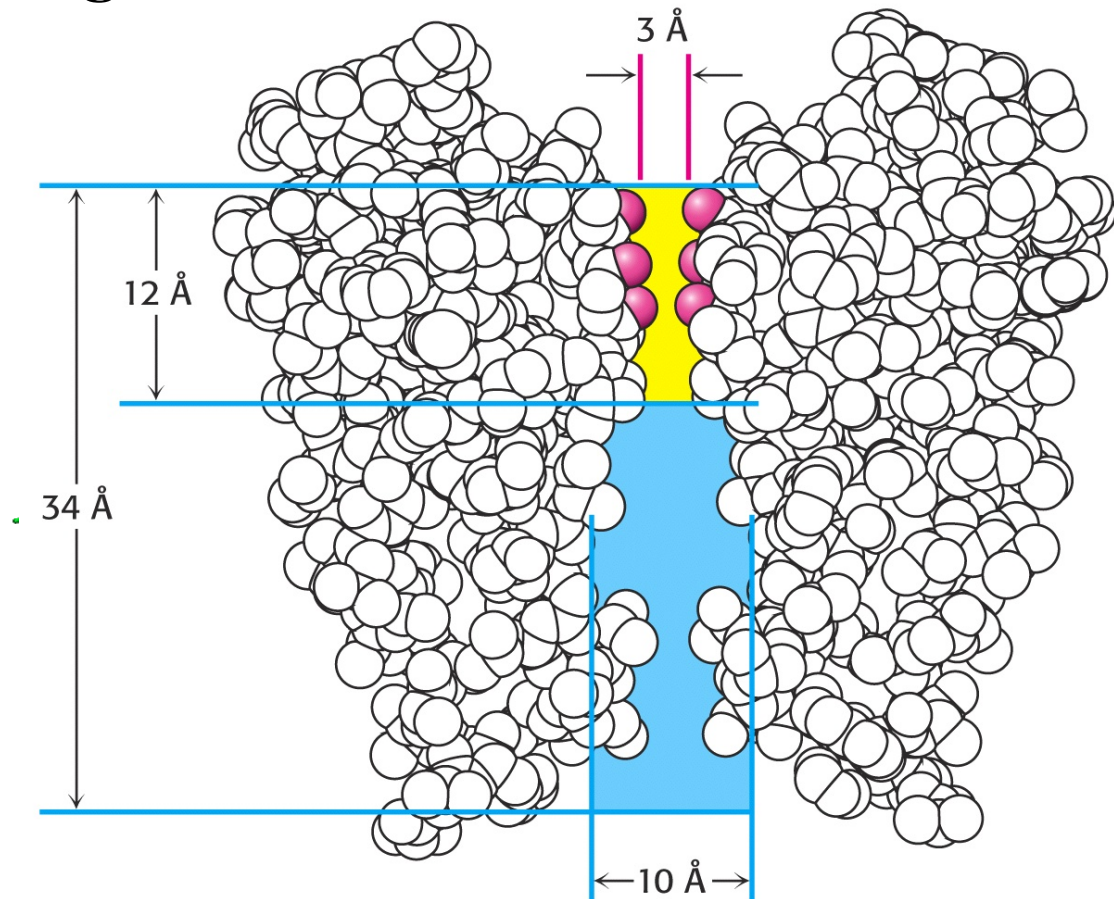
*The negative charges on the bottom help to pull the  $K^+$  ion through the pore.*

# *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, transferred, and rehydrated every 10 ns.*

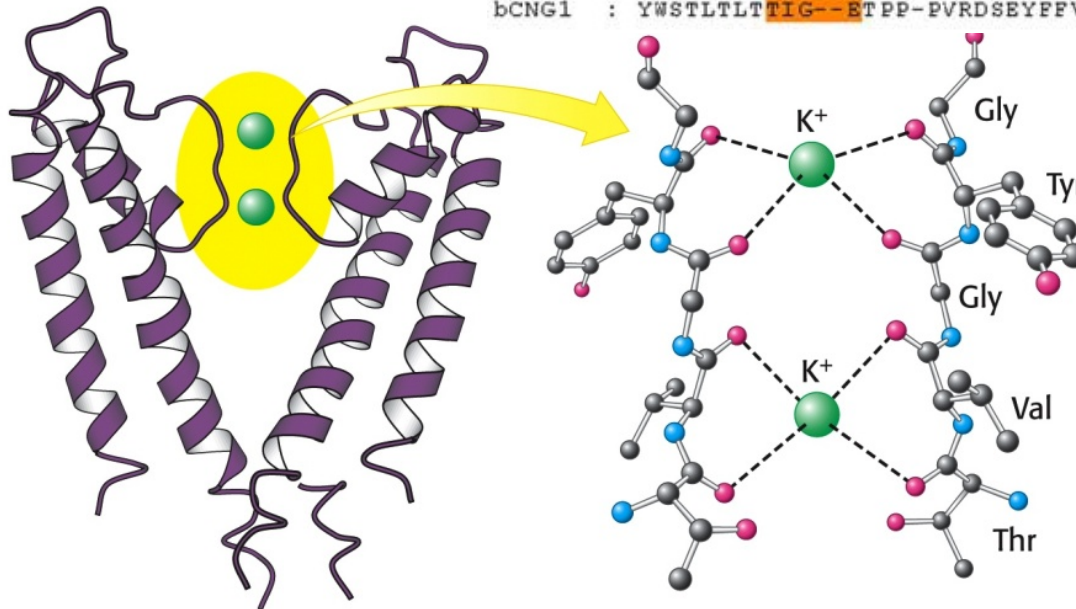


# Selectivity filter

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

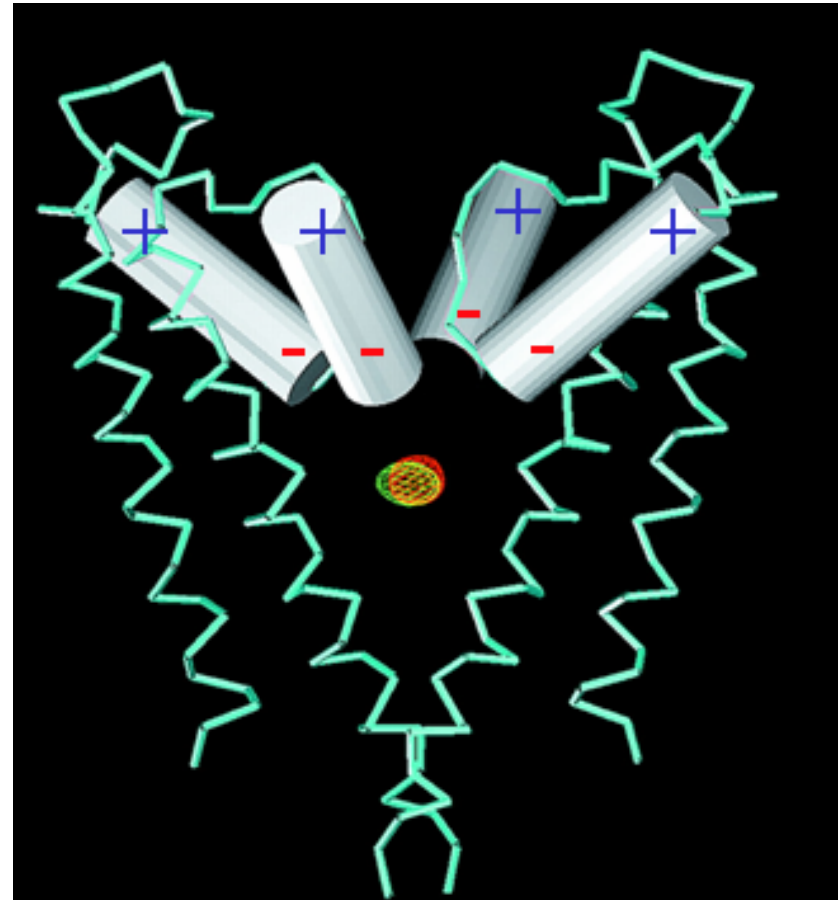
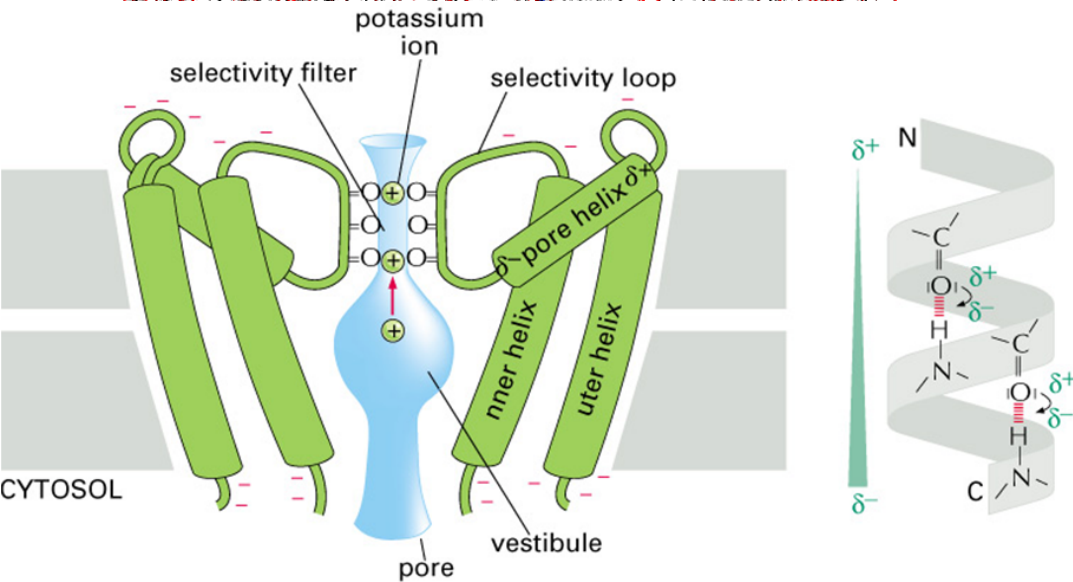
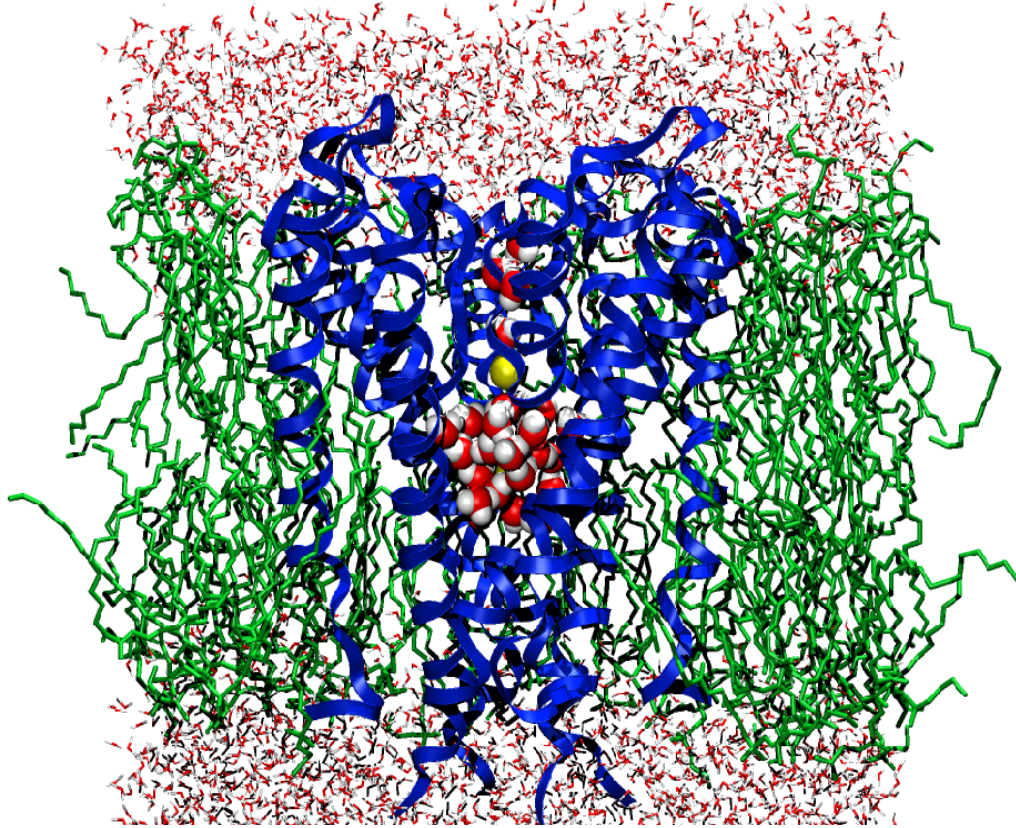
The sequence is **conserved** in all  $K^+$ -channels.

	Filter	Inner Helix	.....
MthK	: YWTFVTTIATVGYGDYS--PSTPLGMYFTVTLIVL	IGTFAVAVERLLEFLINRE	
KCSA	: WWSVETATTVGYGDLY--PVTLWGRIVAVVMVA	ITSEGLVTAALATWFGRE	
Dradio	: YWAVVTVTTVGYGDYS--PKTGLGKFIATLAML	SYAIIAVPTGIVTVGLQQAQ	
Ecoli	: YFSIETMSTVGYGDIV--PVSEARLEPISVVIS	ITVFEATSMTSIFGPLIRGG	
Shaker	: WWAVVTMTTVGYGDMT--PVGFNGKIVGSLCVVA	VLTIALPVPVIVSNFNFY	
hDRK1	: WWATITMTTVGYGDIY--PKTLGKIVGGLCCIA	VLVIALPIPIVNNFSEFY	
hBK	: YLLMVTMSTVGYGDVY--AKTLGRLEMFVFI	GLAMEASYVPEIIEIIGNRK	
hSK3	: WLSITFLSISIGYDMV--PHTYCGKGVCLLTGIM	AGCTALVVAVVARKLELTK	
hERG2	: YTFSSLTSVGFGNVS--PNTNSEKIFSI	CVMLISLMYASIFGNVS	SAIIQRLY
hGIRK2	: LPSIETETTVIGYGYRVI	TDKCPGIIILLIQSVL	SIVNAFMVGCMPVKISQPK
hIRK1	: LPSIETQTTVIGYGERCVT	DECPVAVMVFQSI	VCIIIDAFIIGAVMAKMAKPK
bCNG1	: YWSTLTLTIVIG--ETPP--PVRDSEY	PFVVAADFLLI	VLIFATIVGNIGSMISNMN

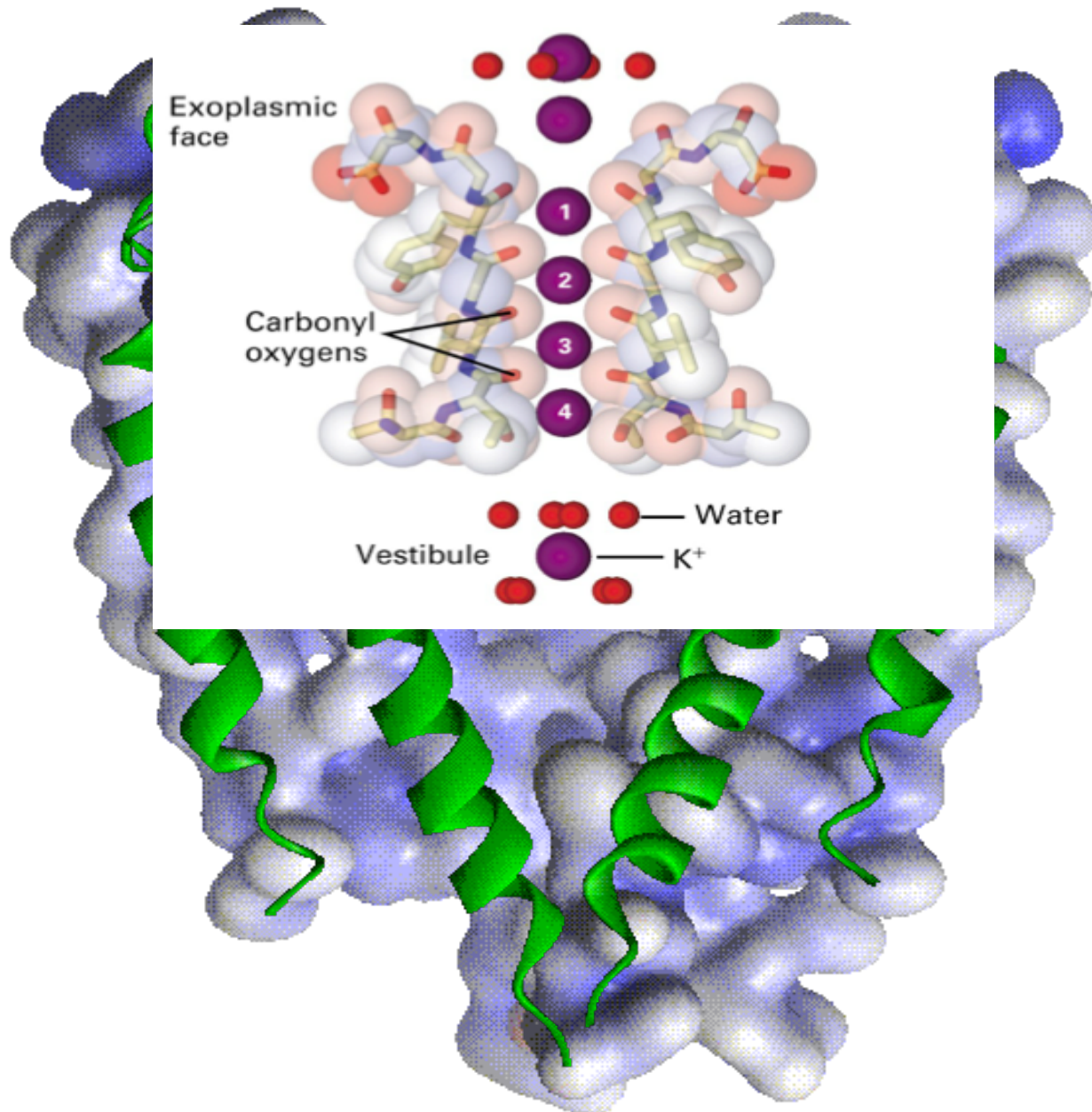


- $K^+$  is surrounded by eight oxygen atoms from the protein
  - four 'above' and four 'below'.
  - very similar to water molecules around hydrated  $K^+$ .

*The central cavity is lined with hydrophobic residues.*

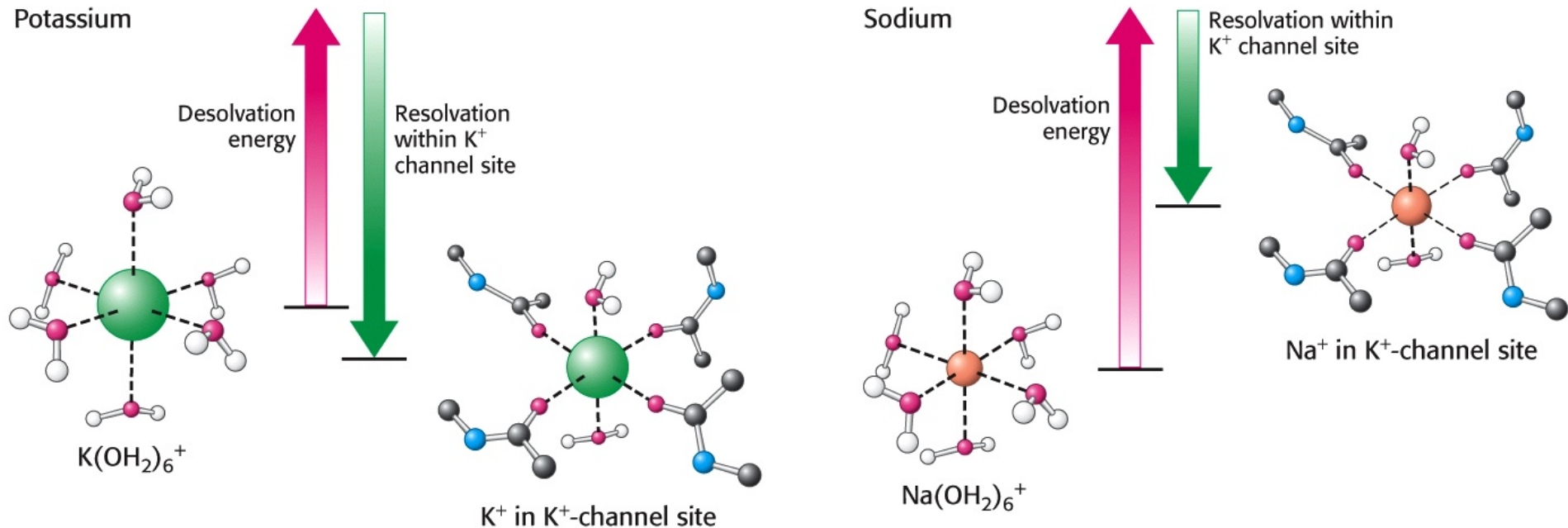






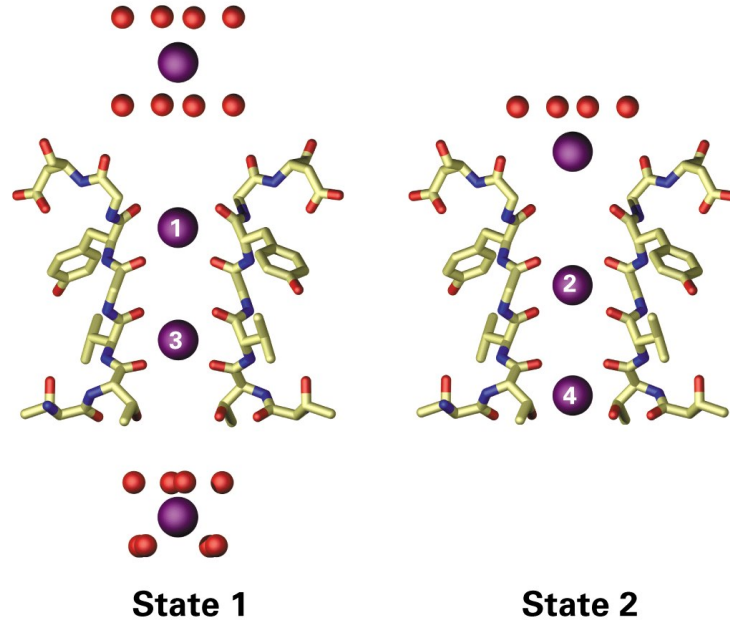
# *The selectivity is based on the size difference between $K^+$ and $Na^+$*

Ion	Atomic weight	Crystal radius [ $\text{\AA}$ ]	Hydrated radius [ $\text{\AA}$ ]	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

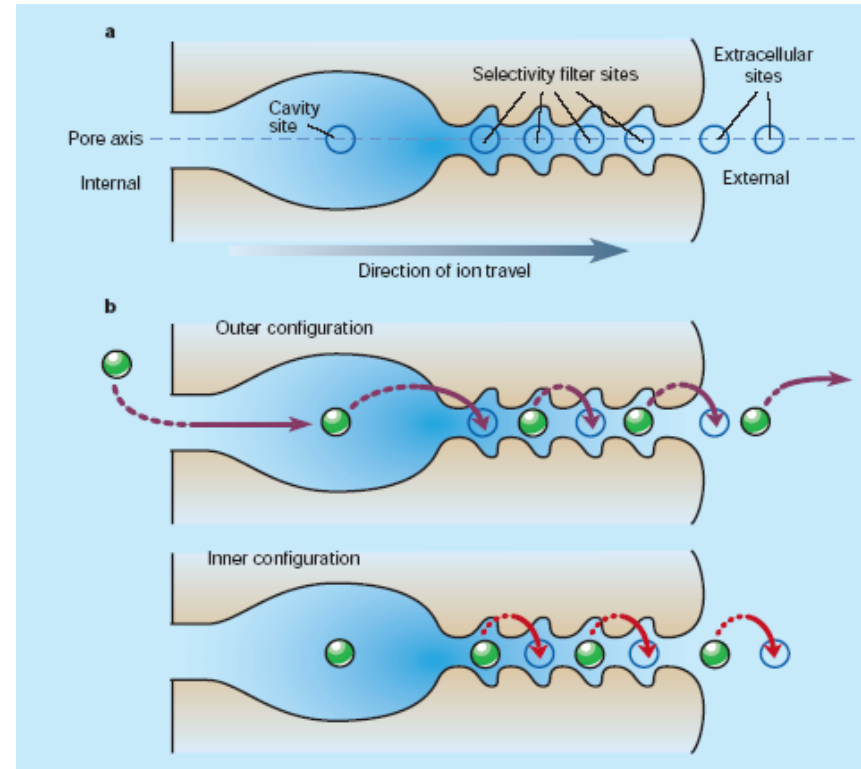


# *Why does the ion coordination required for high selectivity not cause the ions to bind too tightly & prevent rapid diffusion through the pore?*

(c) Ion movement through selectivity filter



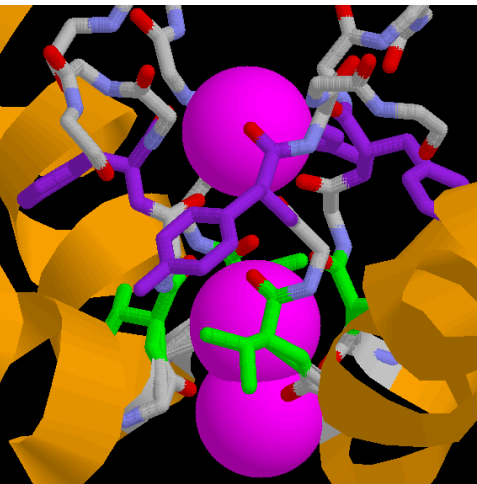
*Selectivity filter contains more than one ion – repulsion between closely spaced ions will help overcome the intrinsic binding site affinity.*



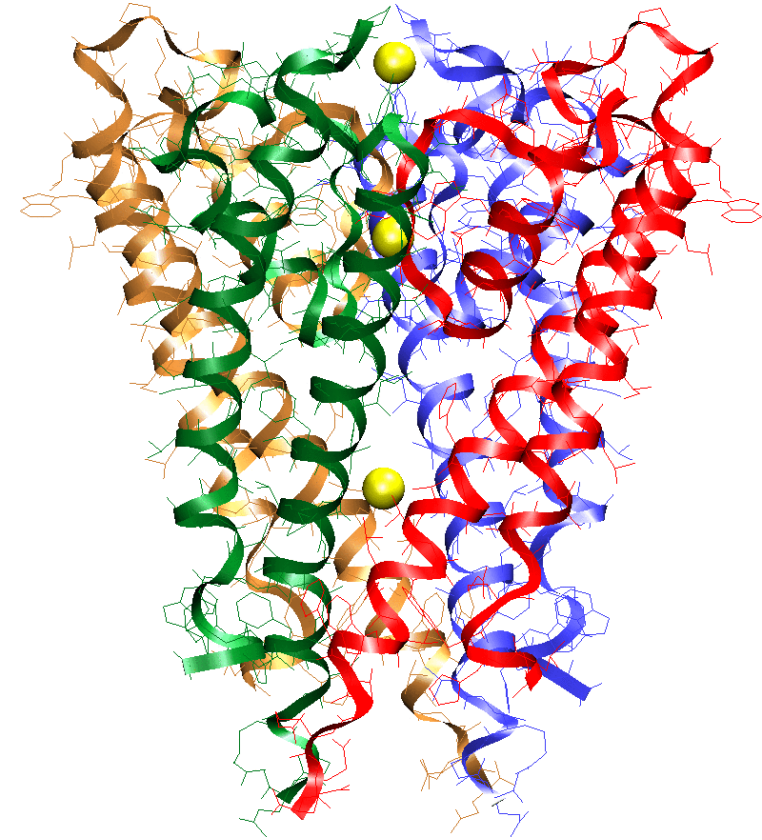
*Transfer is isoenergetic → conductivity close to diffusion limit.*

# *The selectivity filter needs to be rigid*

- ❑ 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.

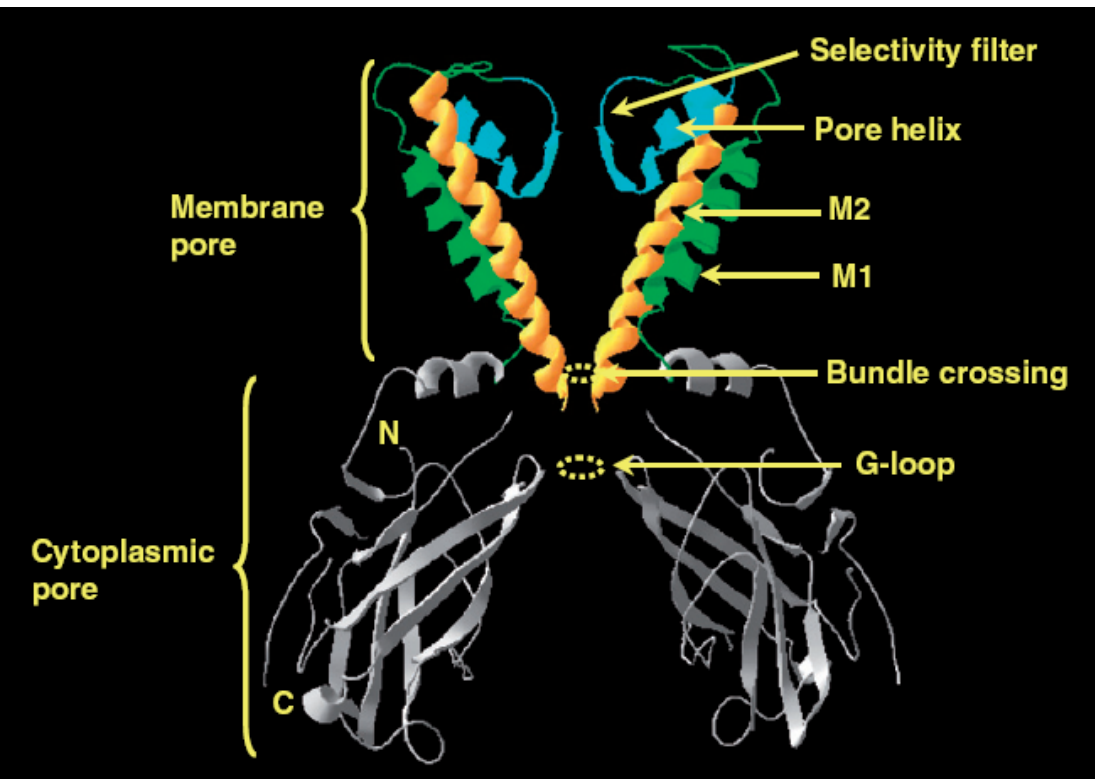


## **KcsA Potassium Channel from *Streptomyces lividans***

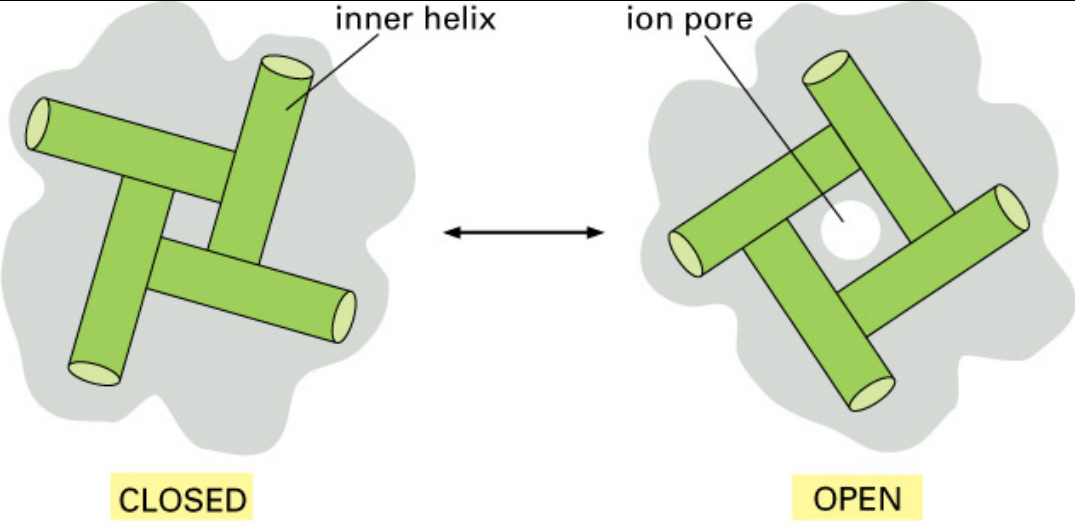
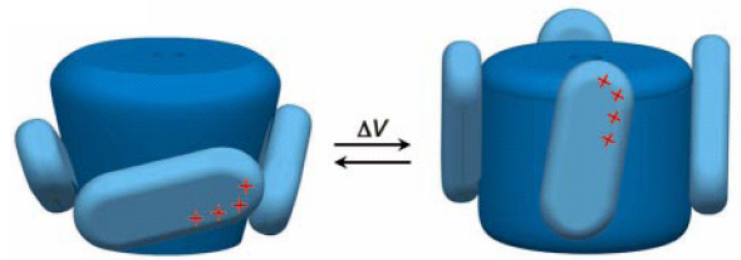


- ❑ The "springs" prevent the selectivity filter from interacting with cations smaller than  $K^+$ .

# Topology of a Kir subunit.



# The bacterial voltage-gated $K^+$ channel *KvAP*



# The gate

