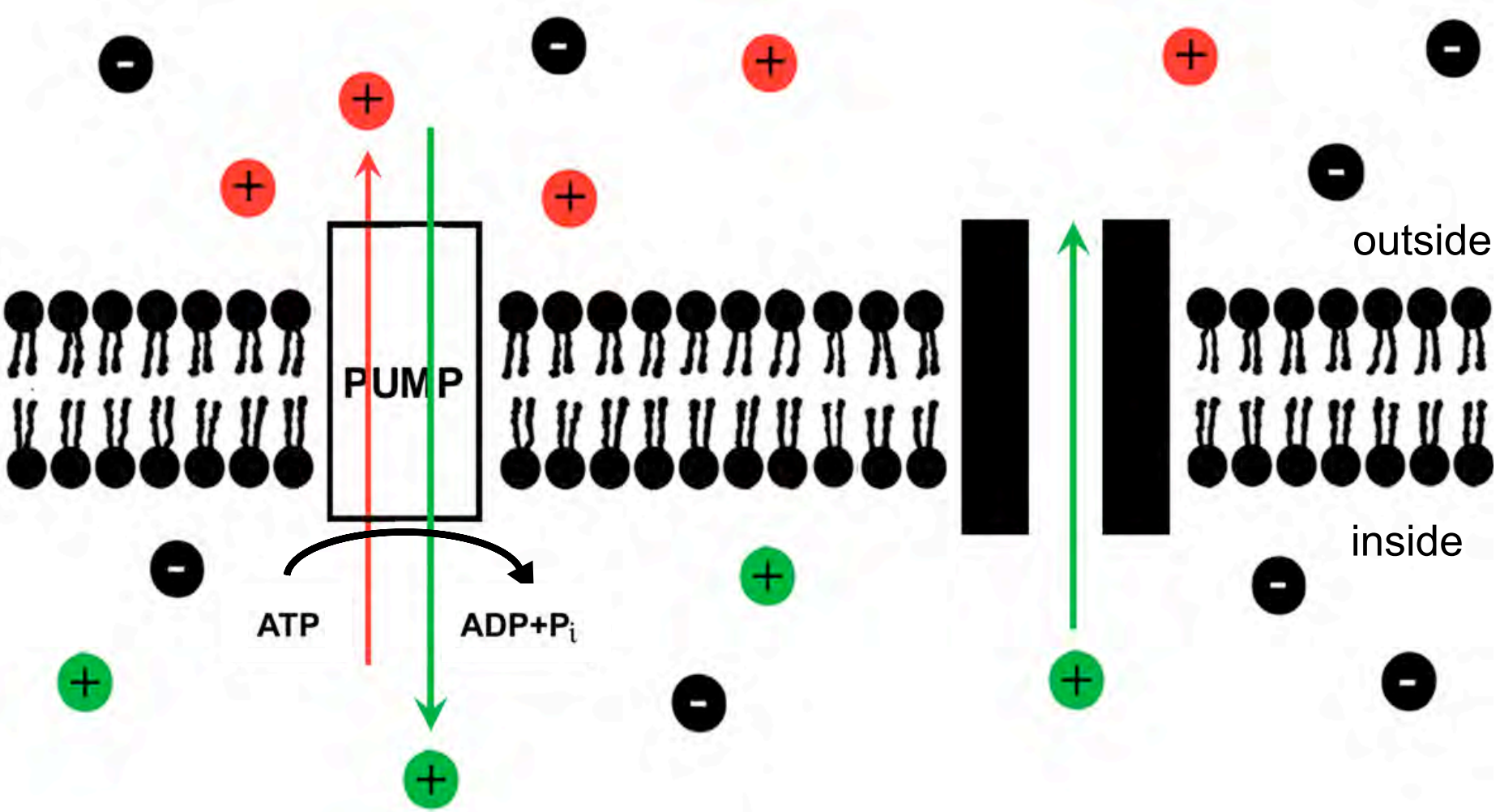
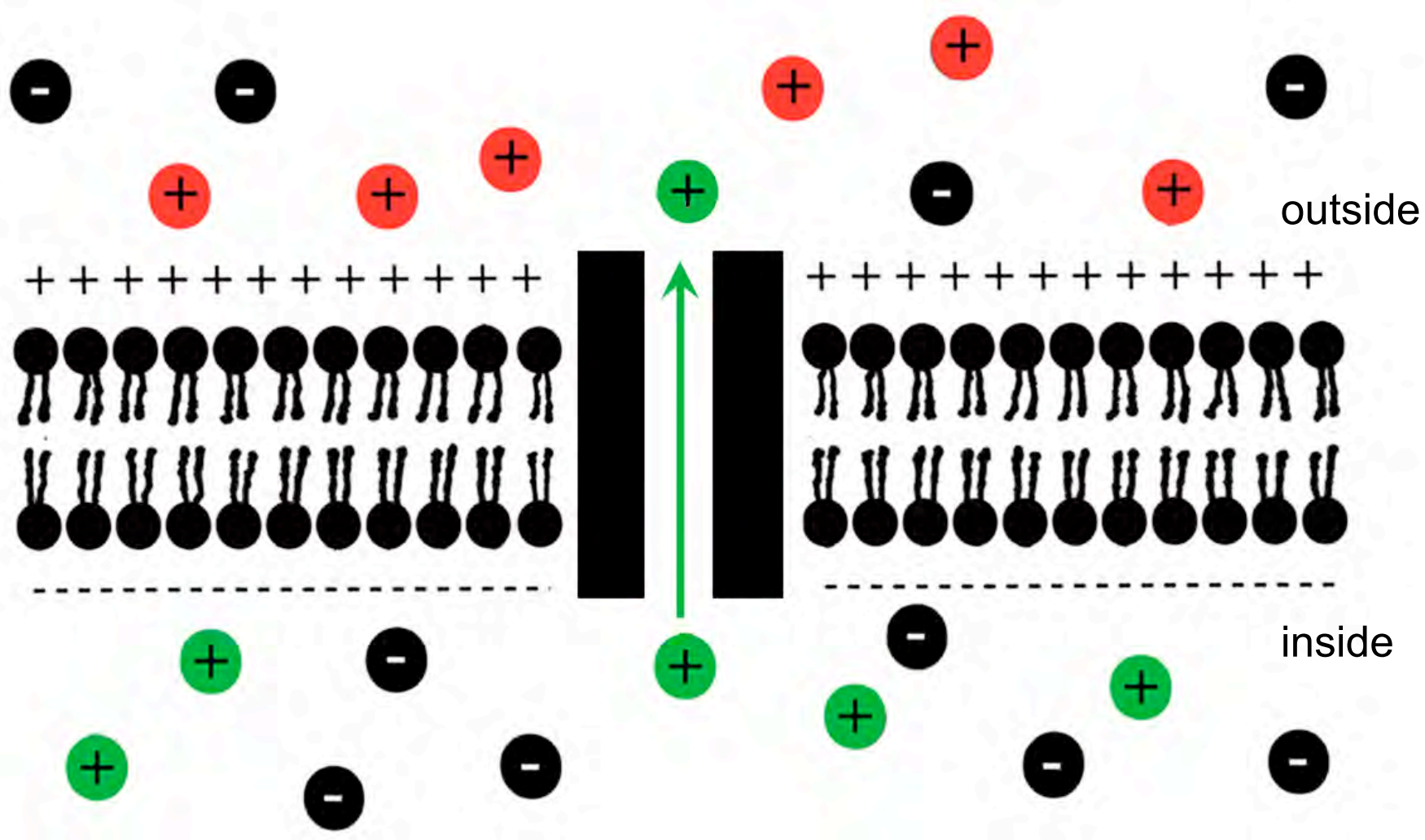
Membrane Channels

June 21, 2005

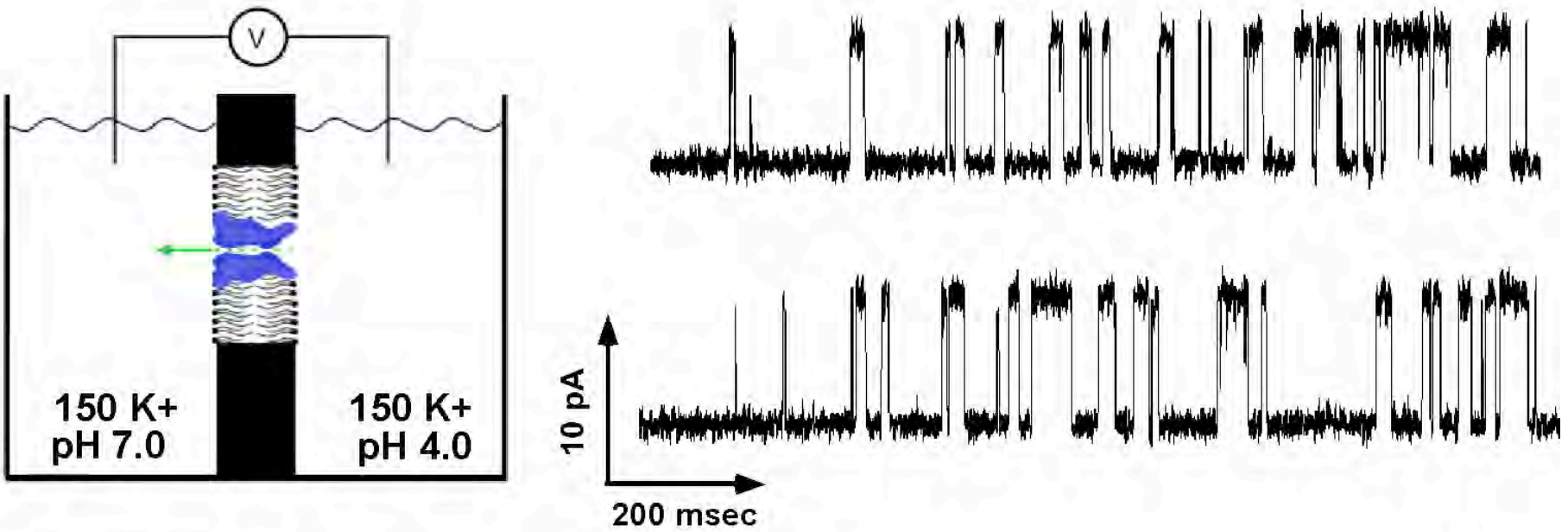
Pumps build ion gradients, ion channels dissipate gradients

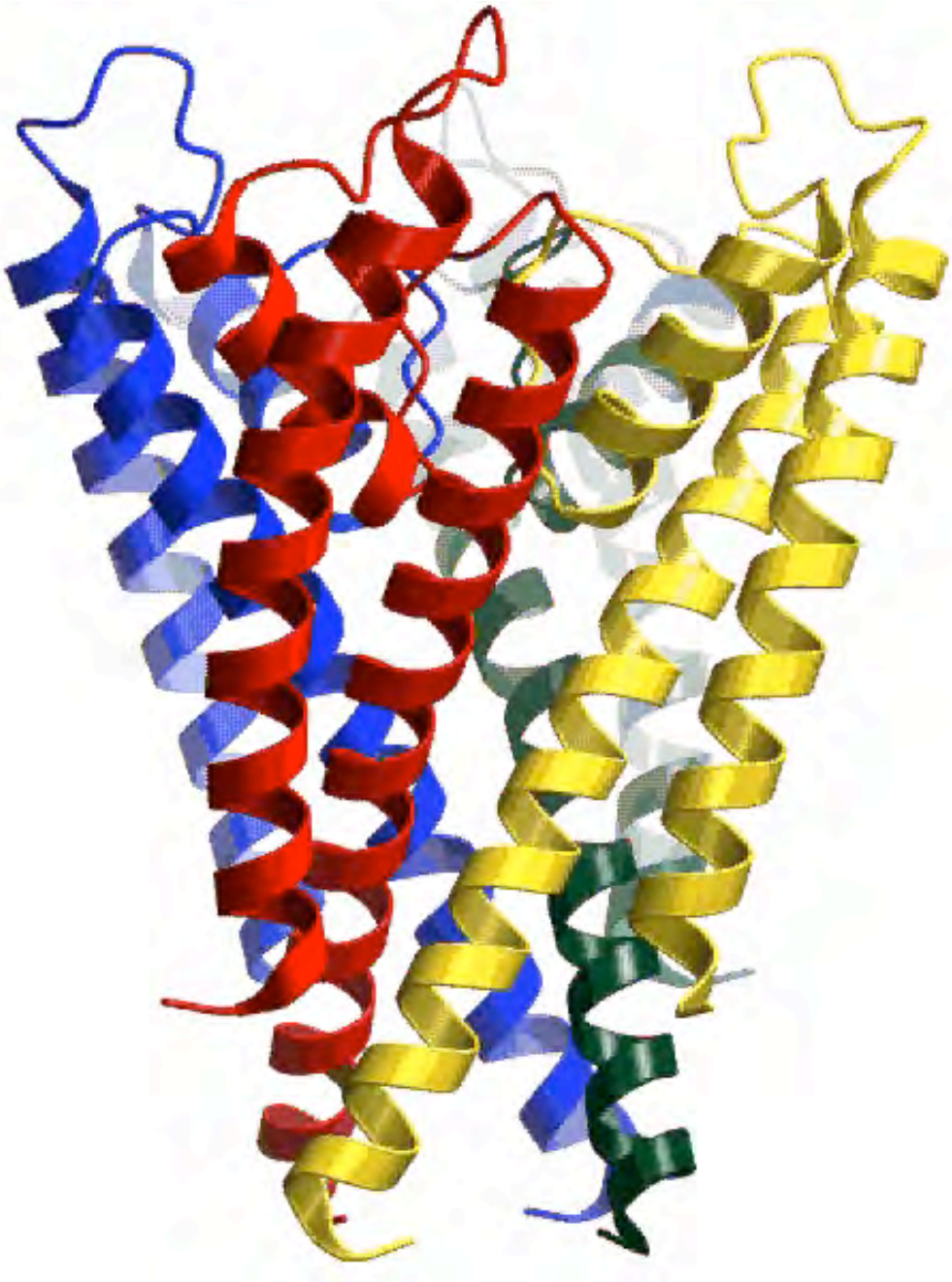


Ion channels electrically polarize the cell membrane

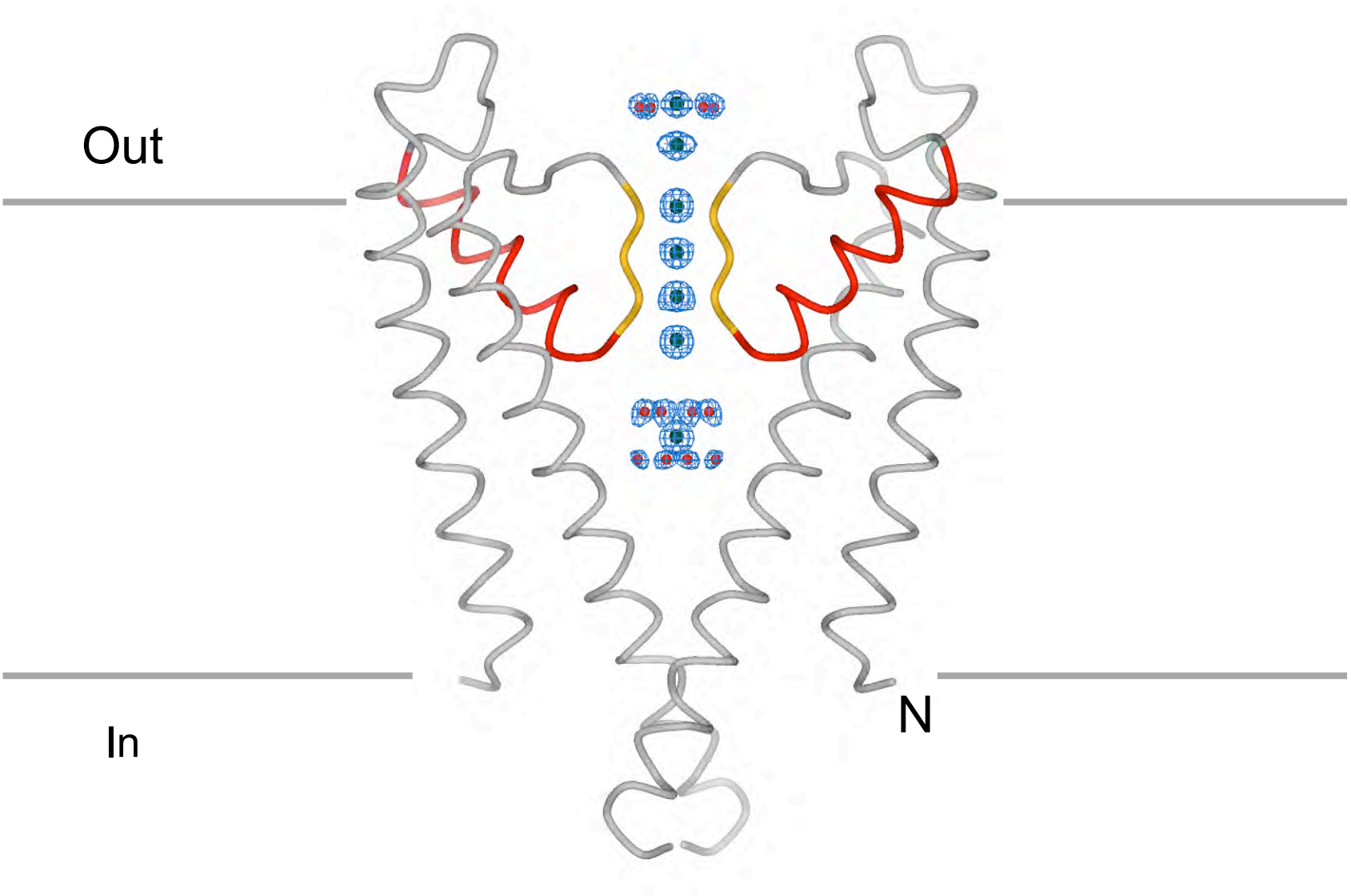


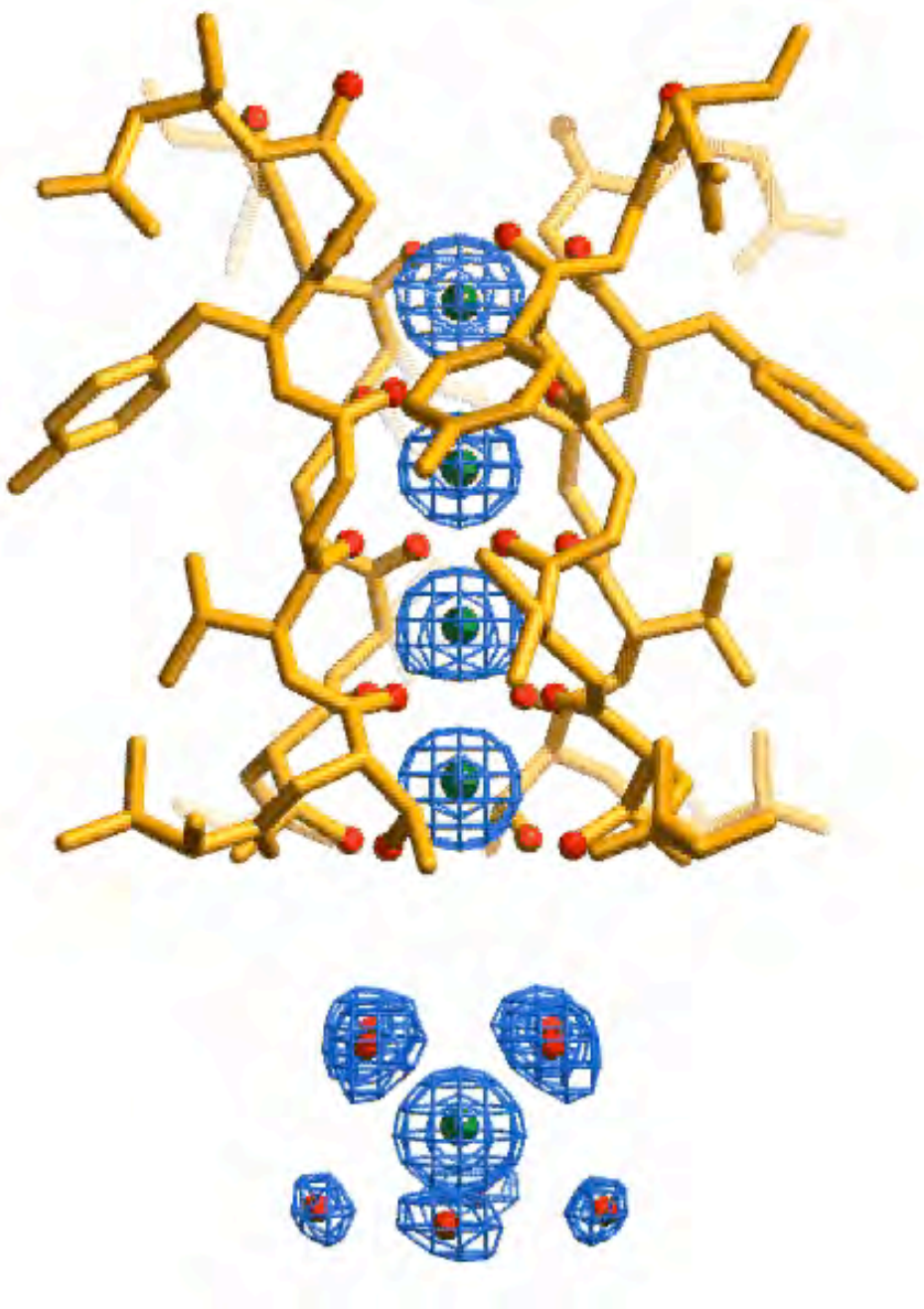
Conduction through a single K^+ channel



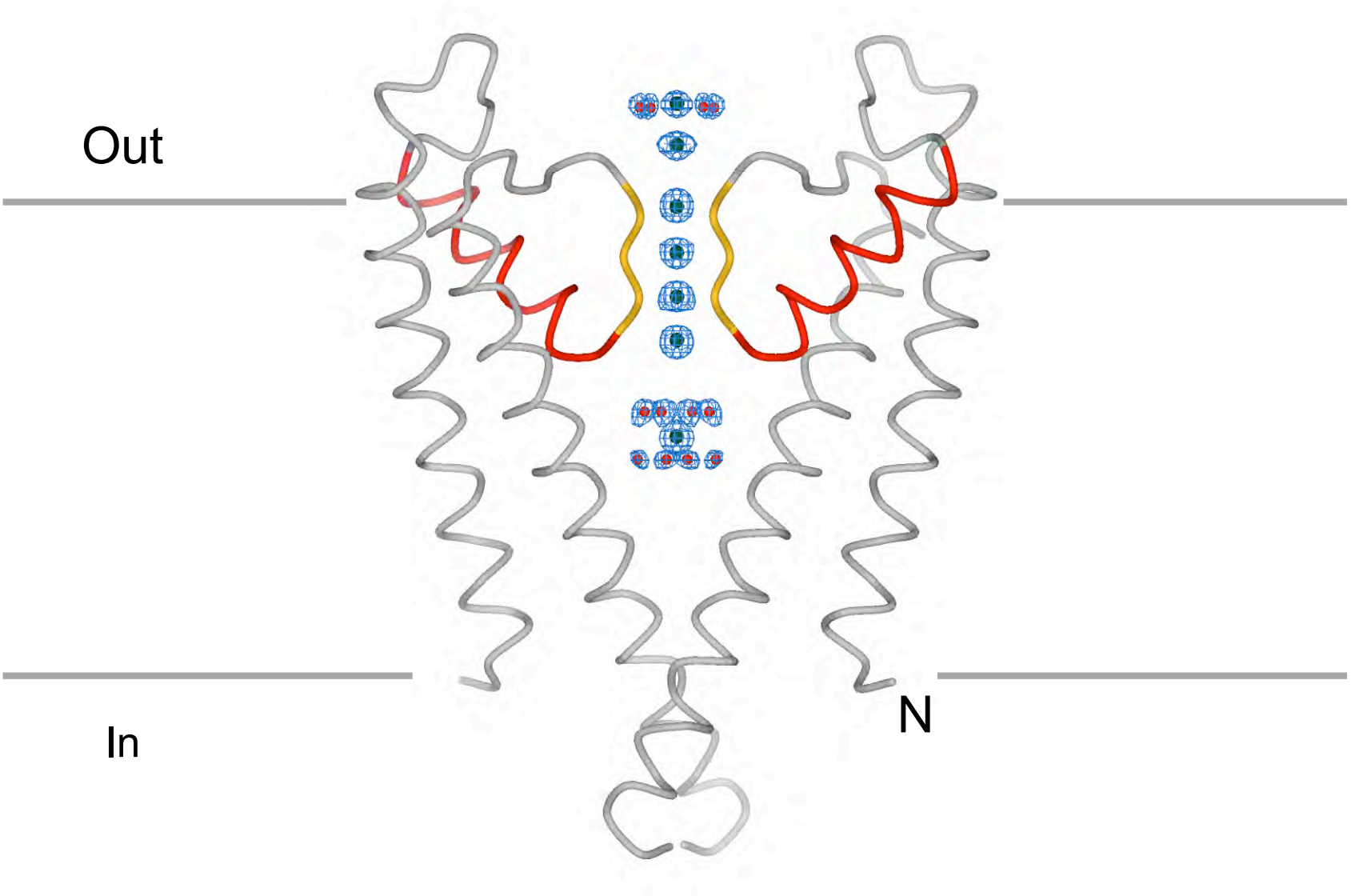


Two subunits of a K^+ channel

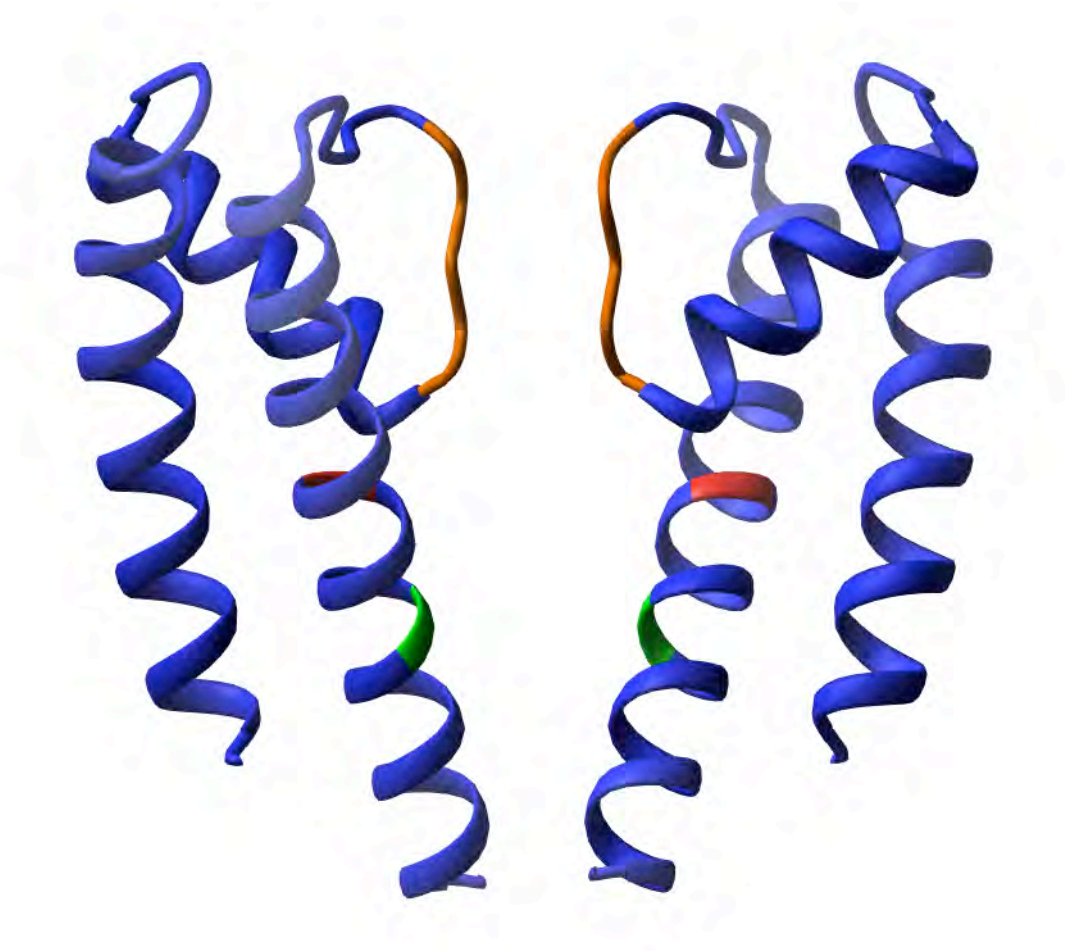




Two subunits of a K^+ channel

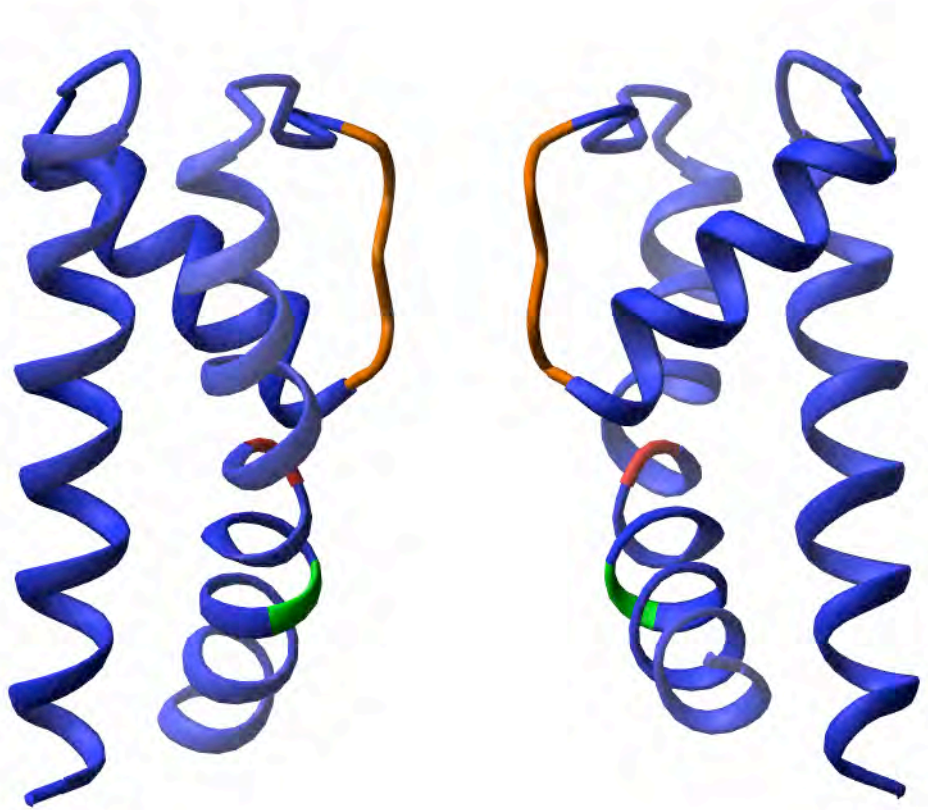


Mechanics of pore gating



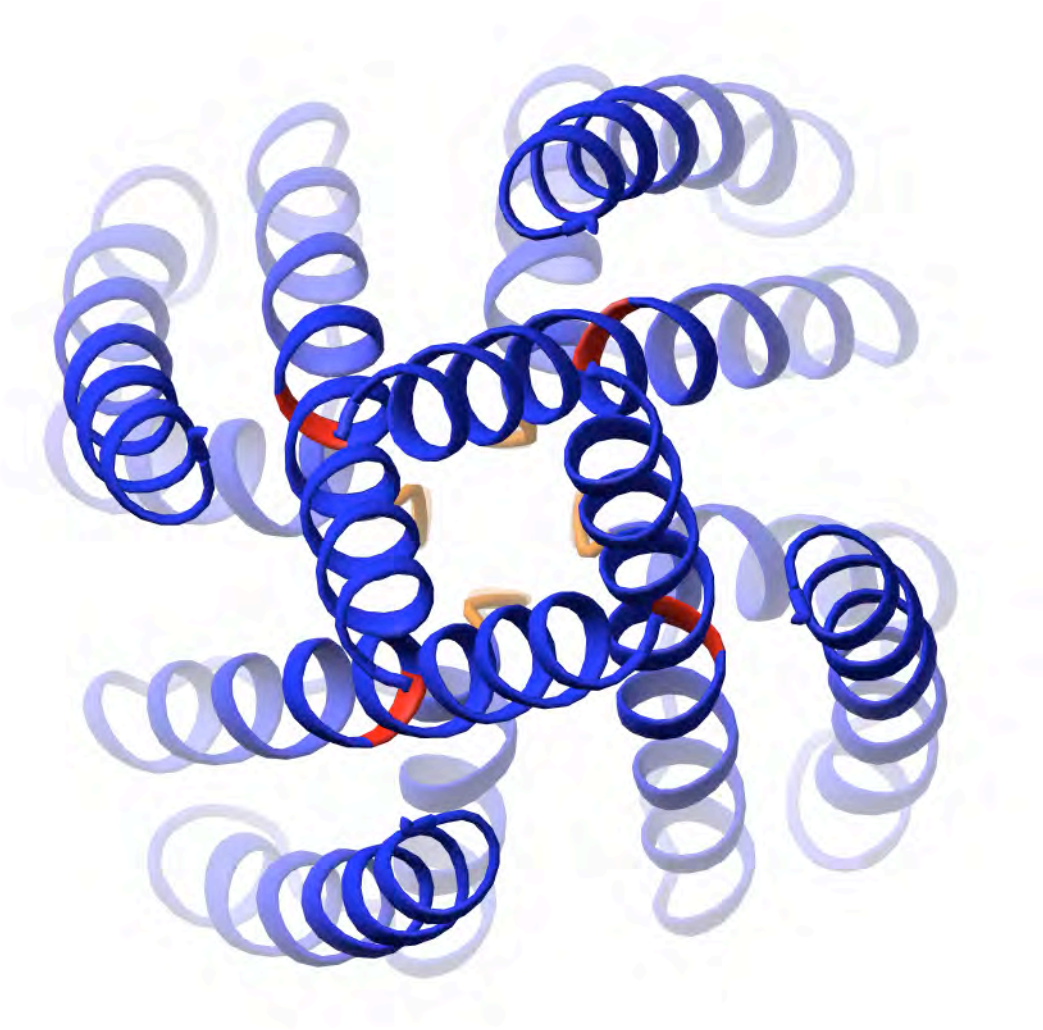
(Closed)

Mechanics of pore gating



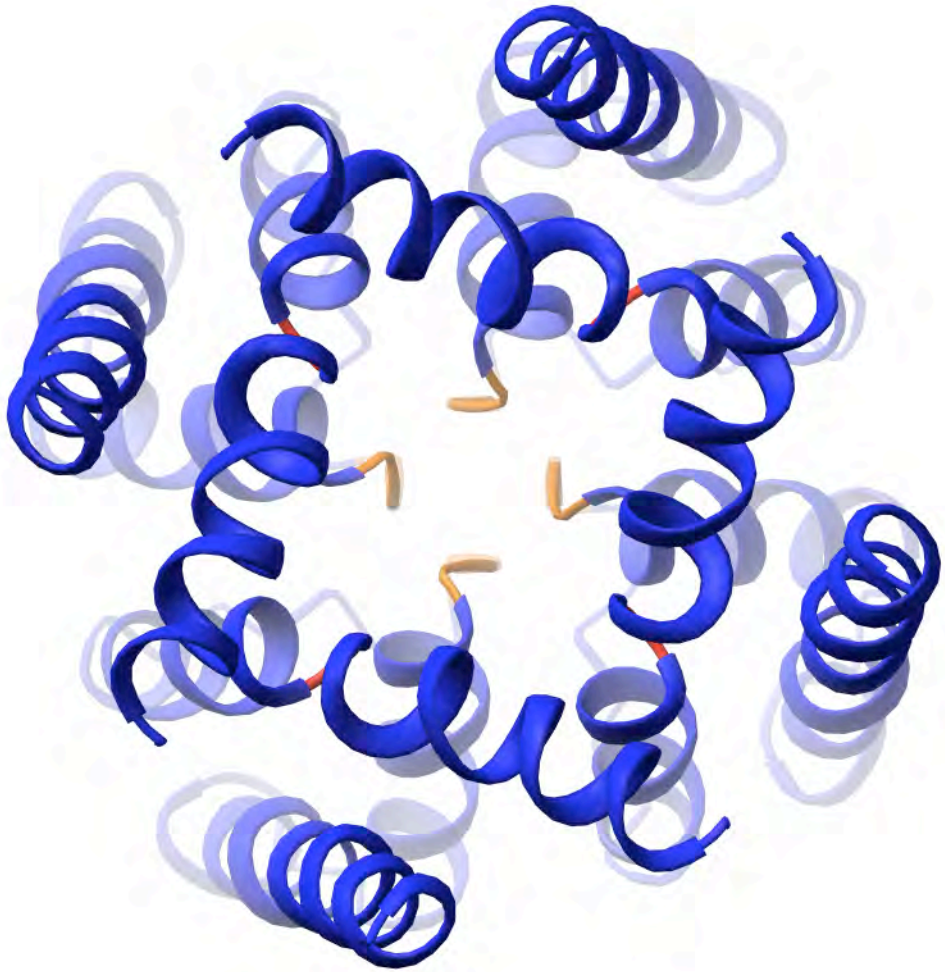
(Opened)

Mechanics of pore gating



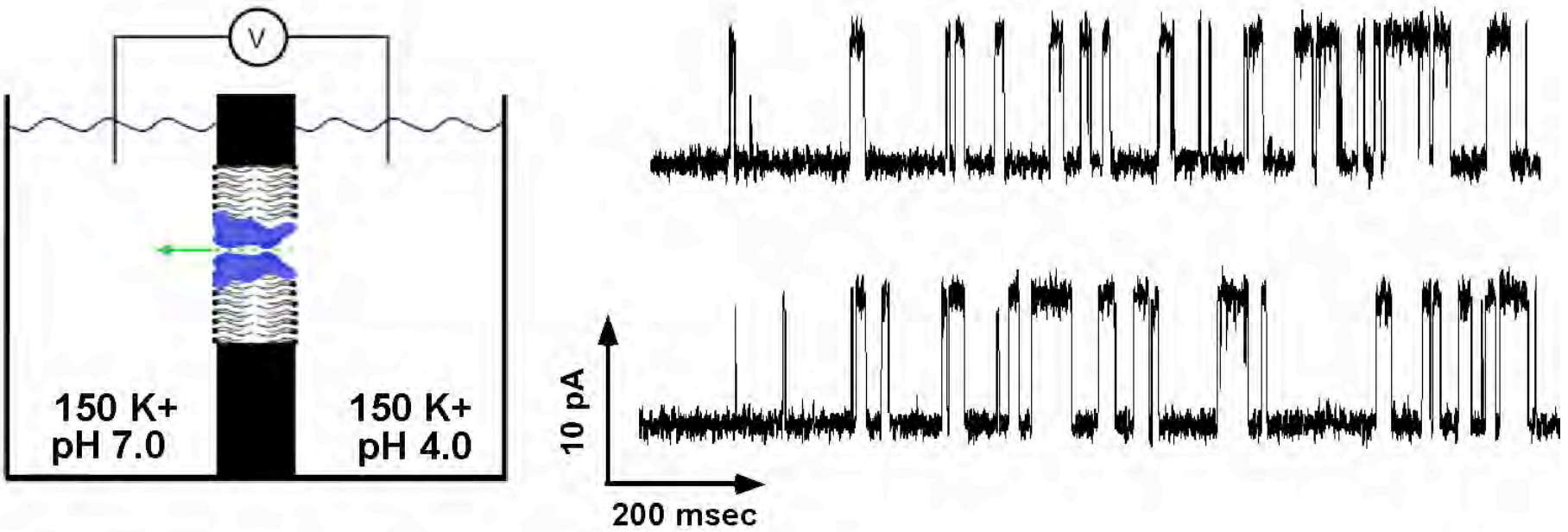
(Closed)

Mechanics of pore gating

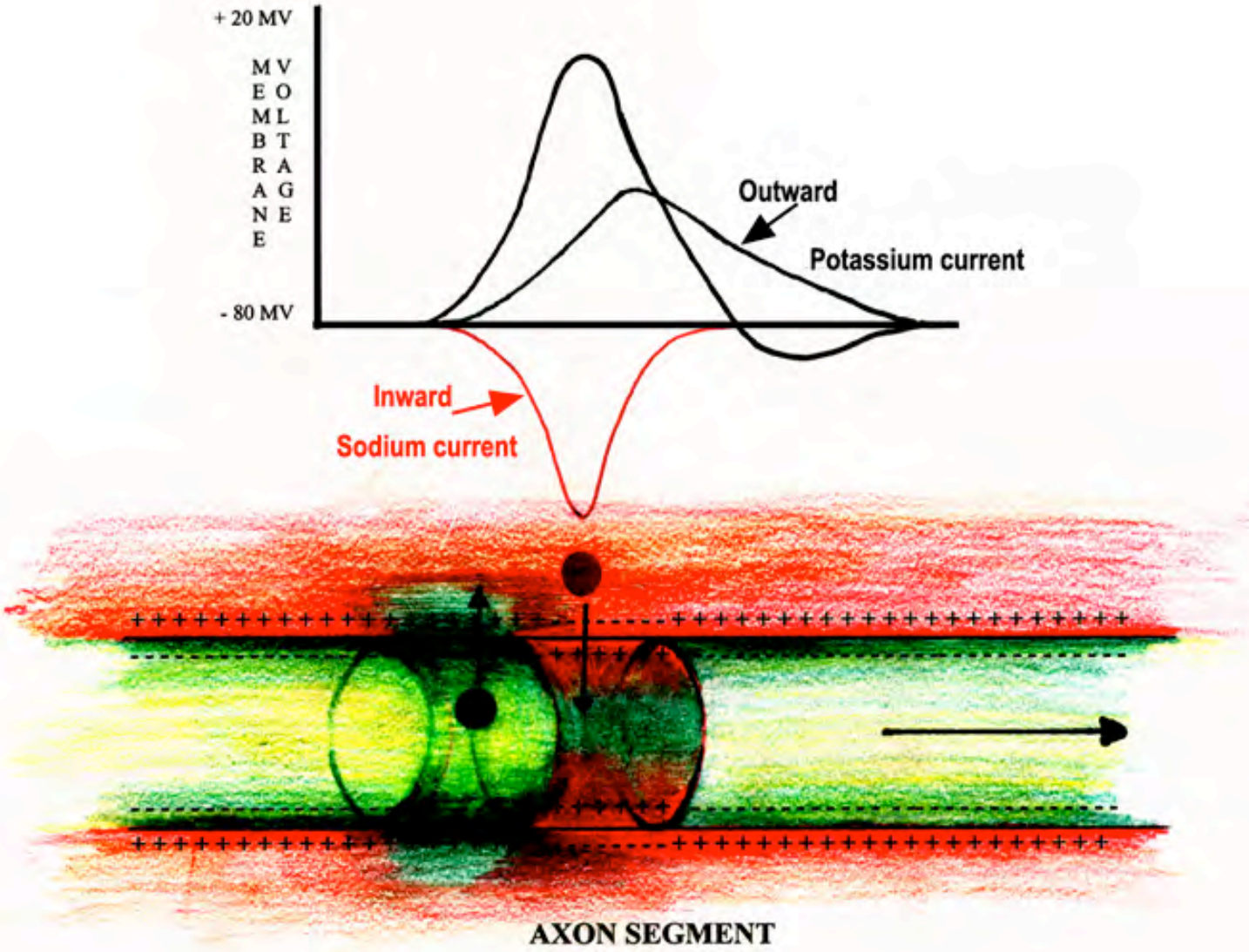


(Opened)

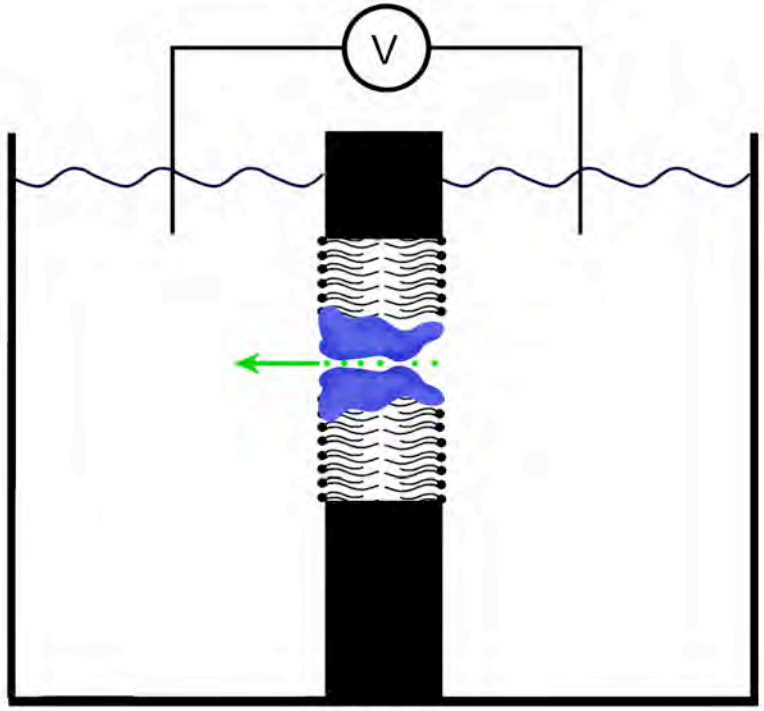
Current from a single K^+ channel

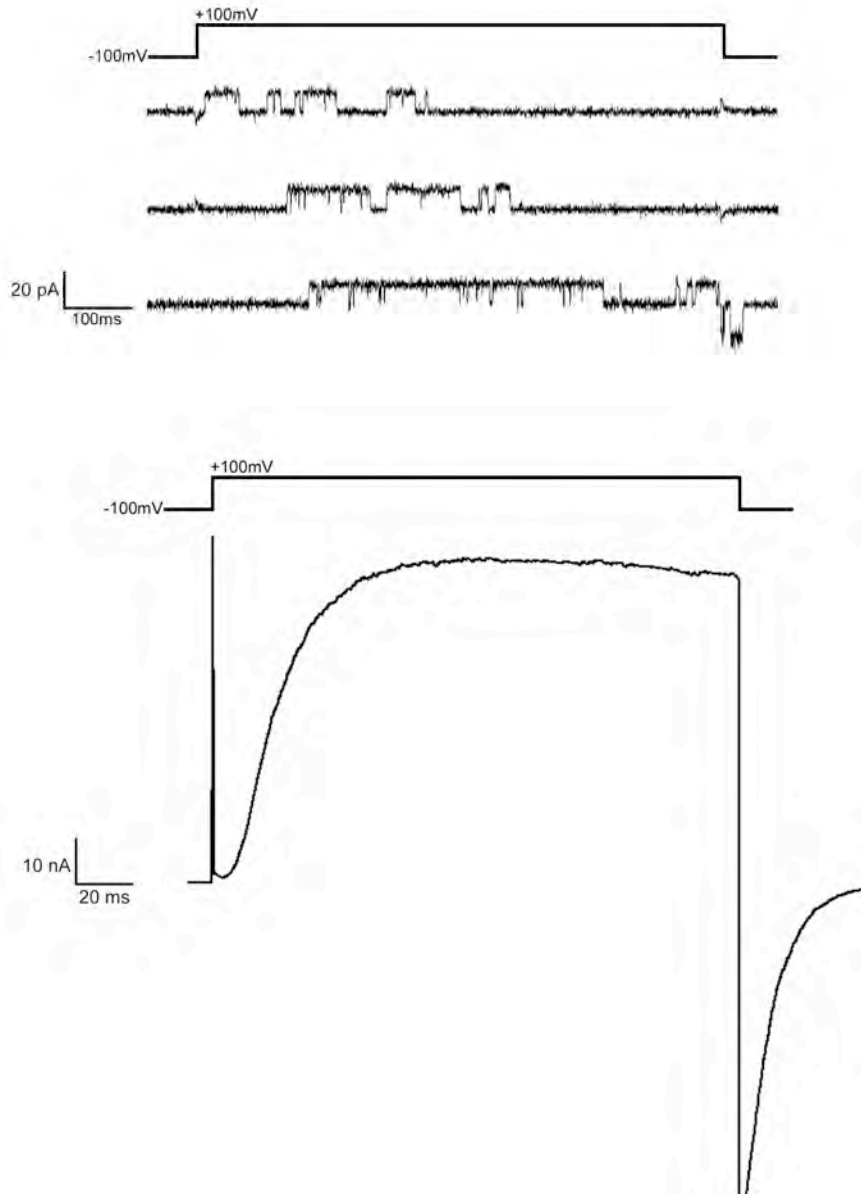


THE ELECTRICAL IMPULSE DEPENDS ON THE FLOW OF IONS ACROSS THE CELL MEMBRANE

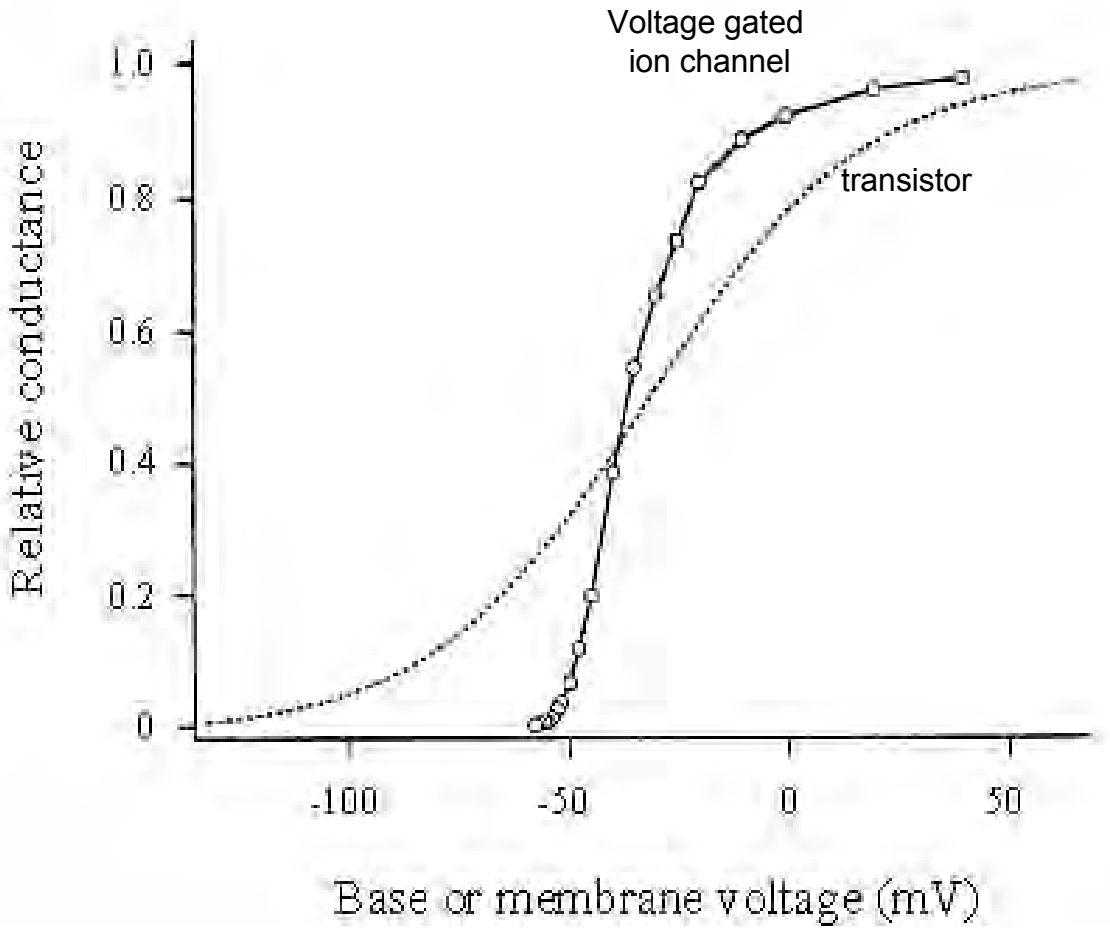


Voltage-dependent K^+ channels



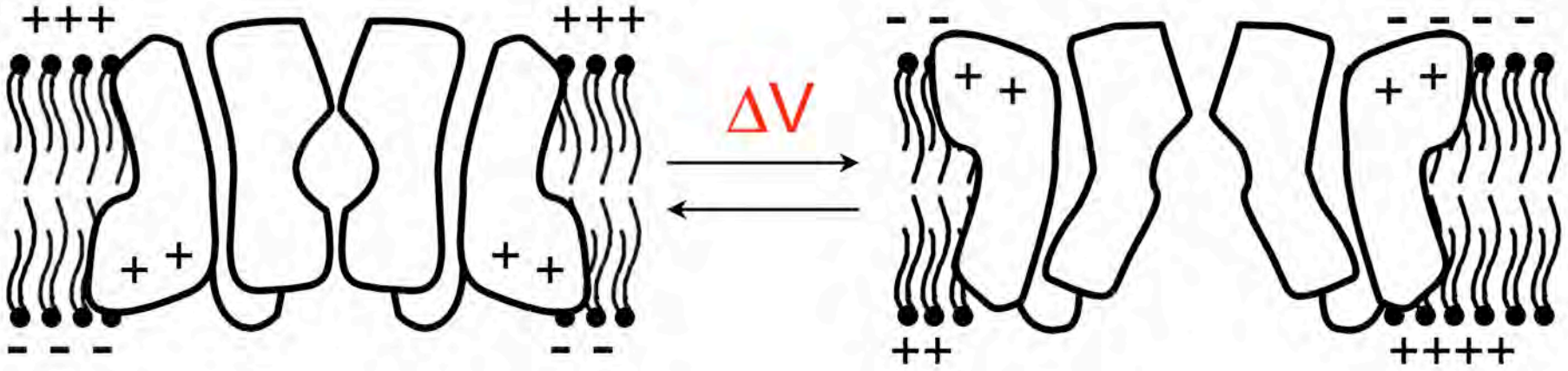


Comparing a voltage-dependent K^+ channel to a bipolar transistor

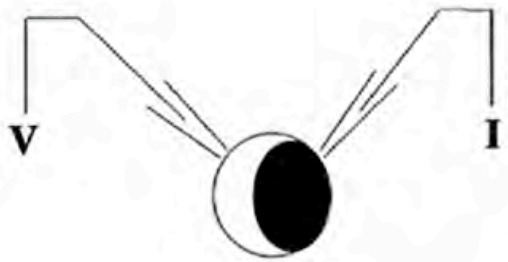


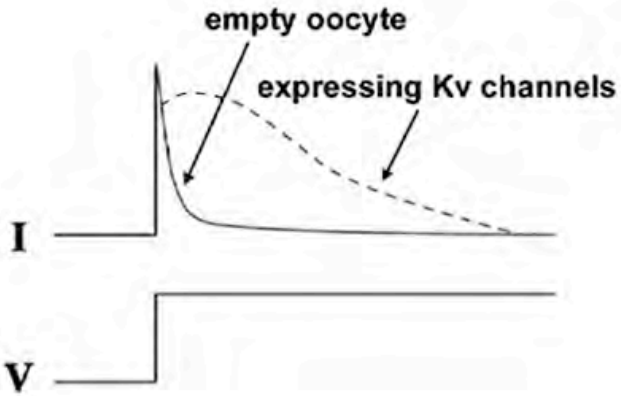
Sigworth, FJ (1994) *Q Rev Biophys* 27:1-40

Such channels need a volt meter

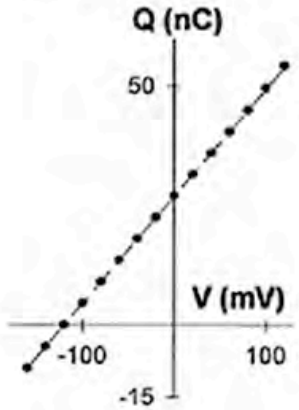


Gating charges

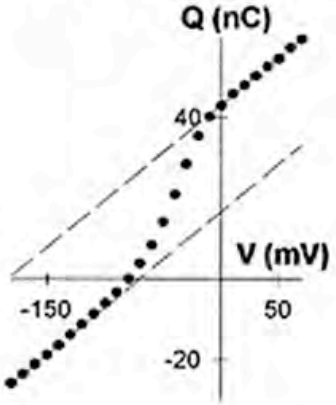


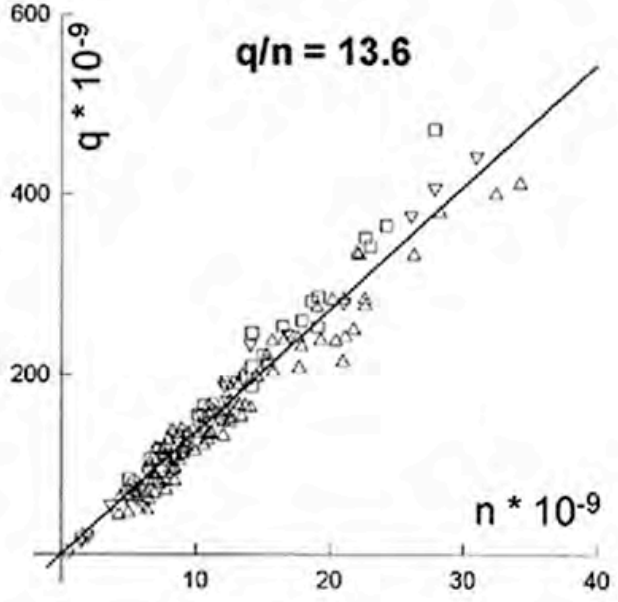


empty oocyte

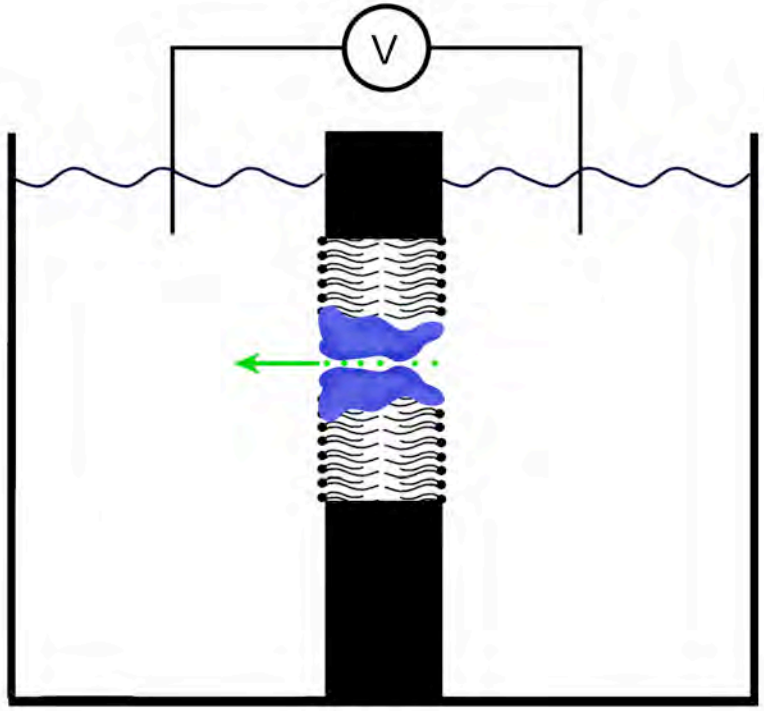


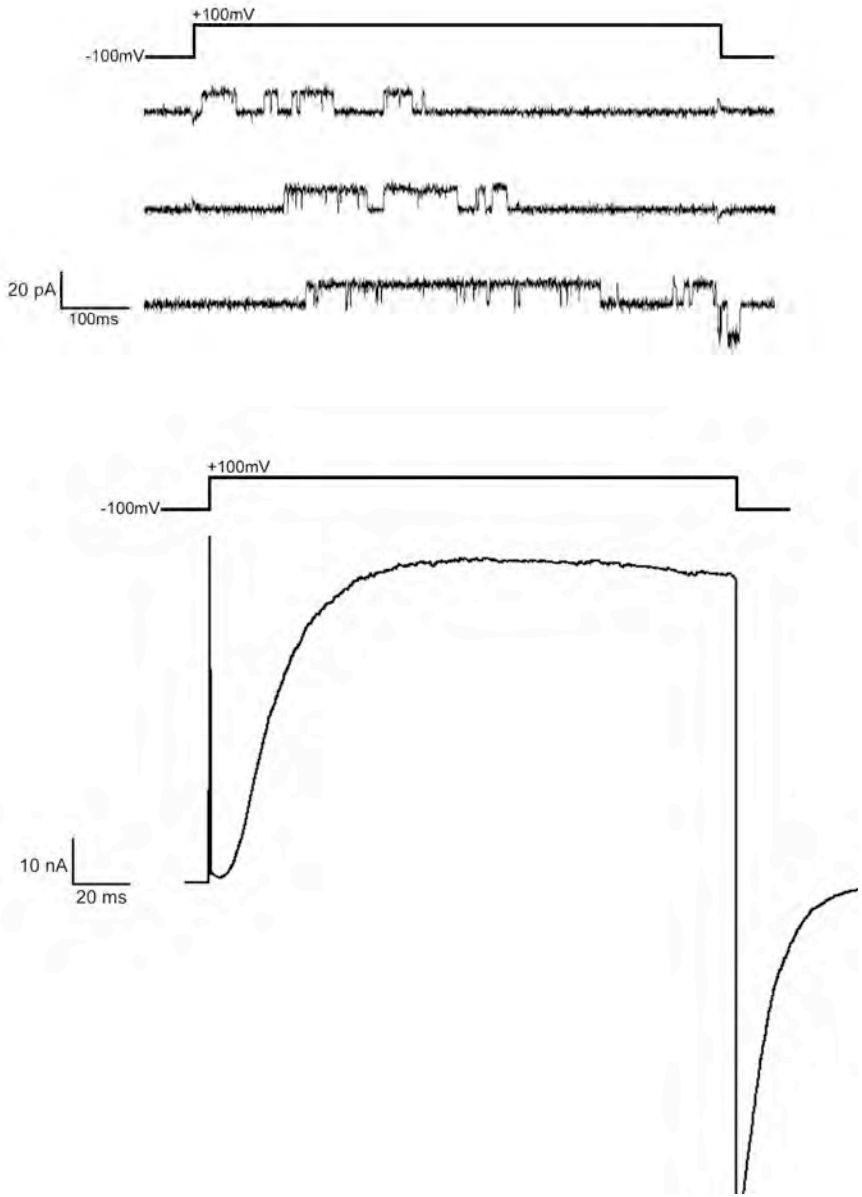
expressing Kv



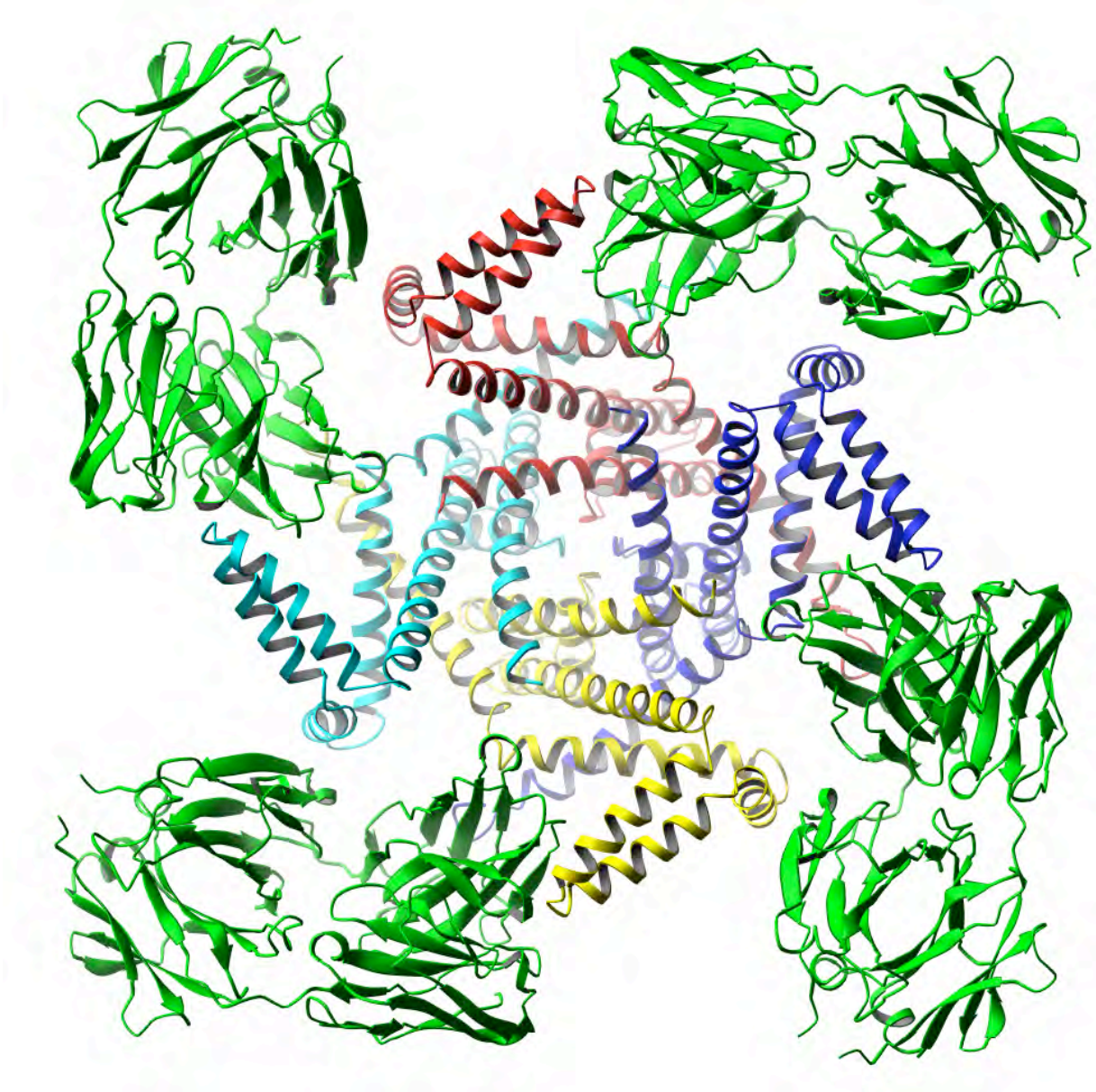


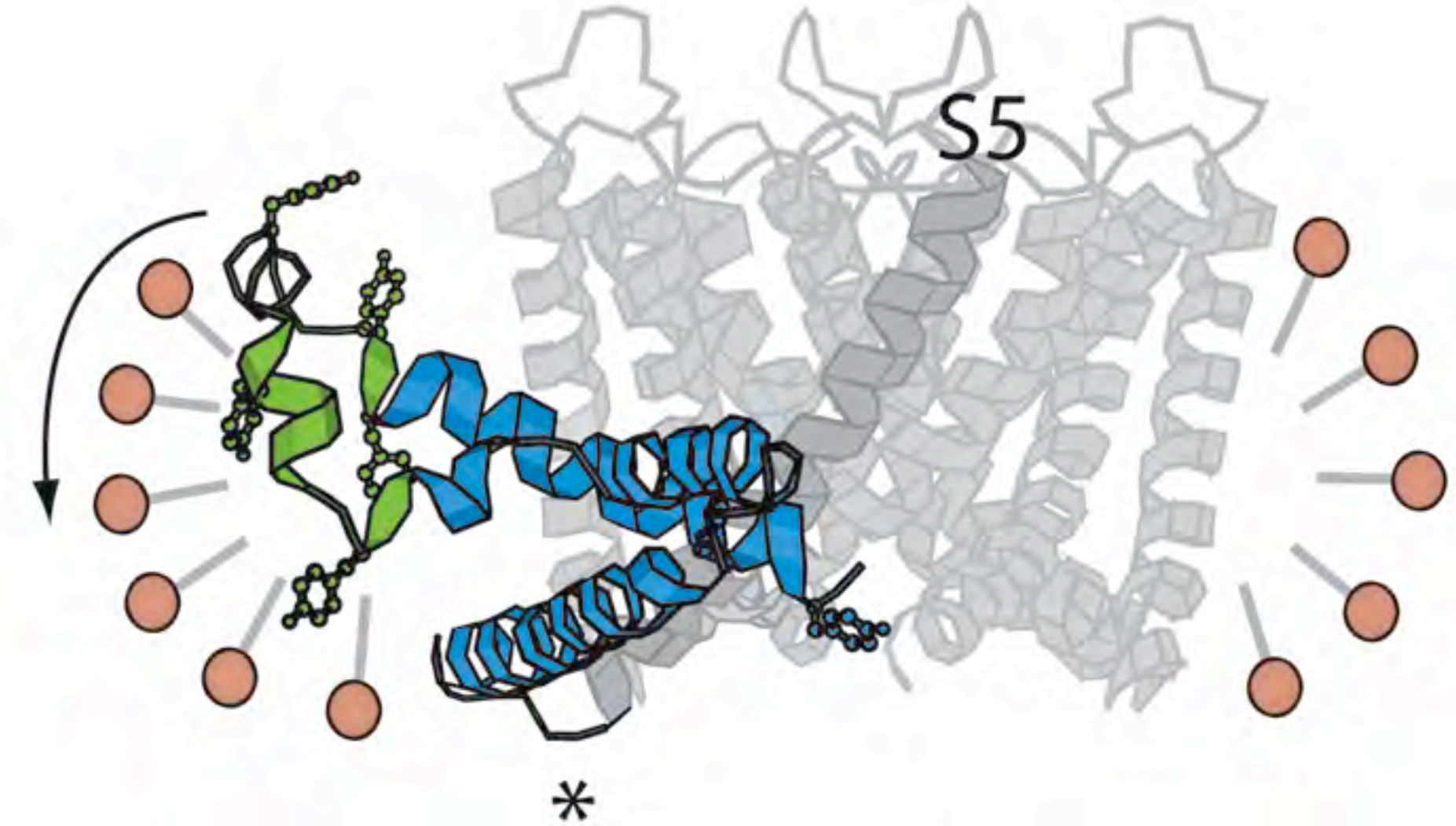
Opening is fairly slow (ms timescale)





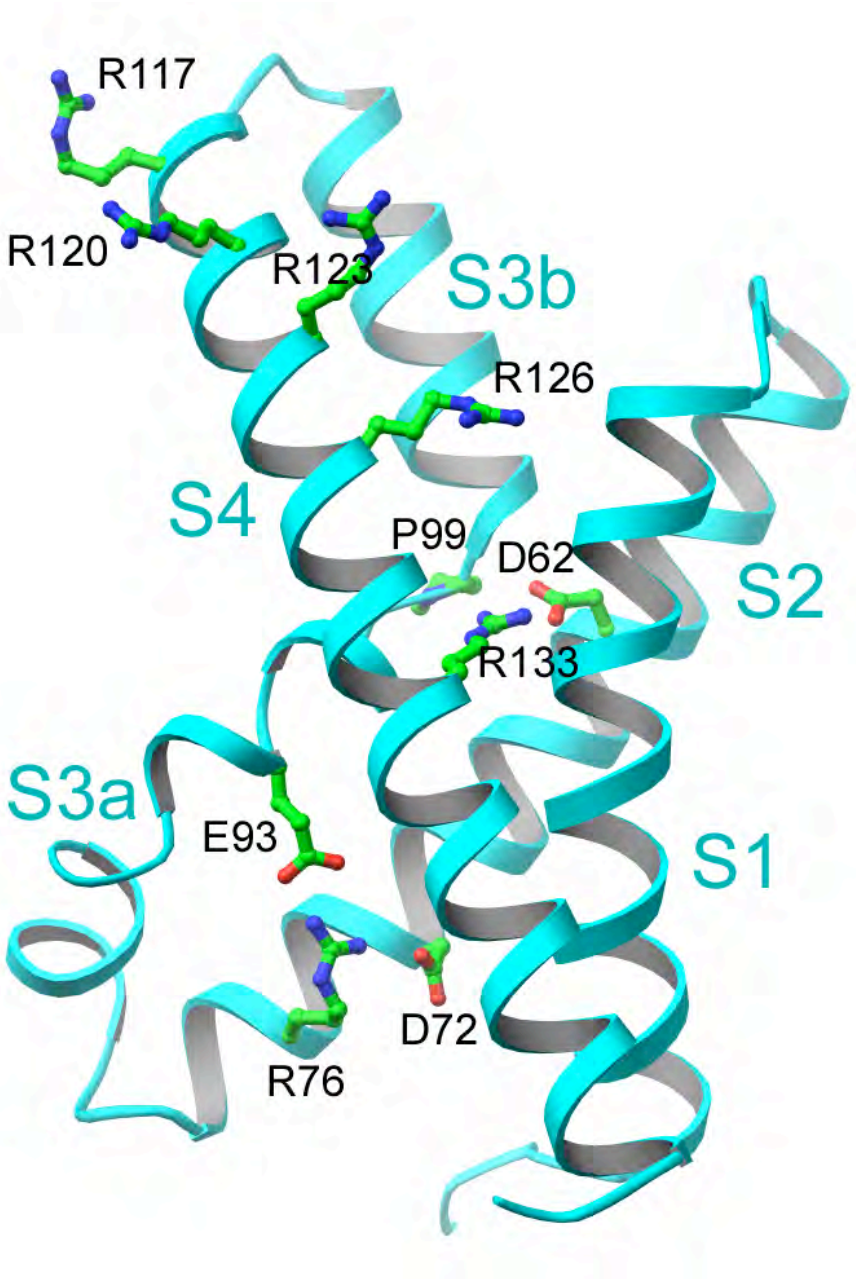
Fab 6E1 KvAP at 3.2 Å



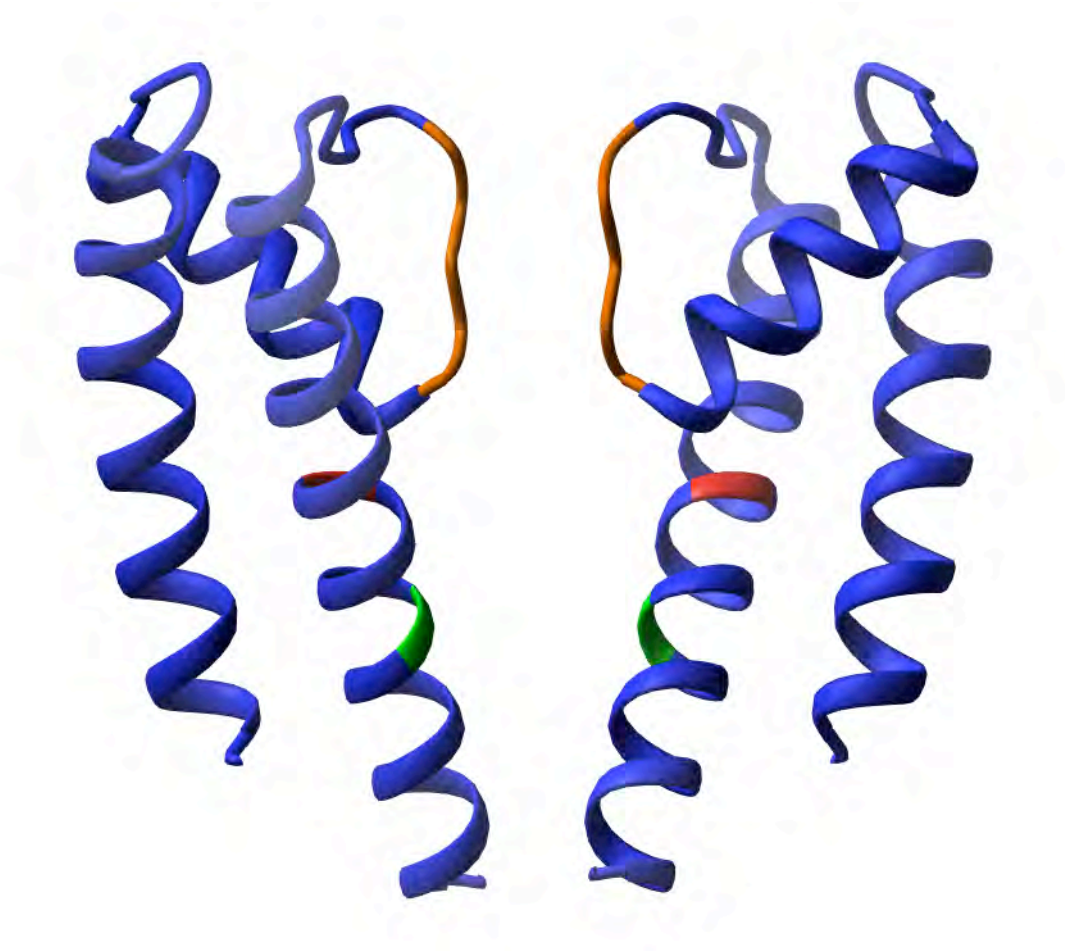

S5
*


S5
*

Isolated voltage sensor at 1.9 Å resolution

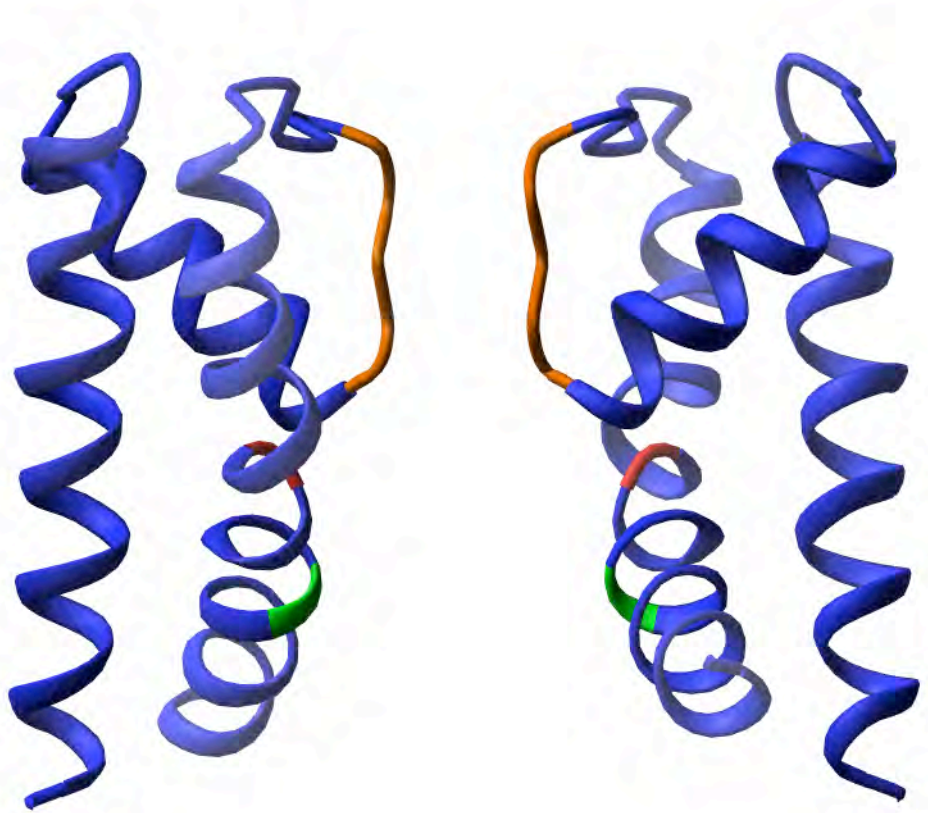


When the pore does this:



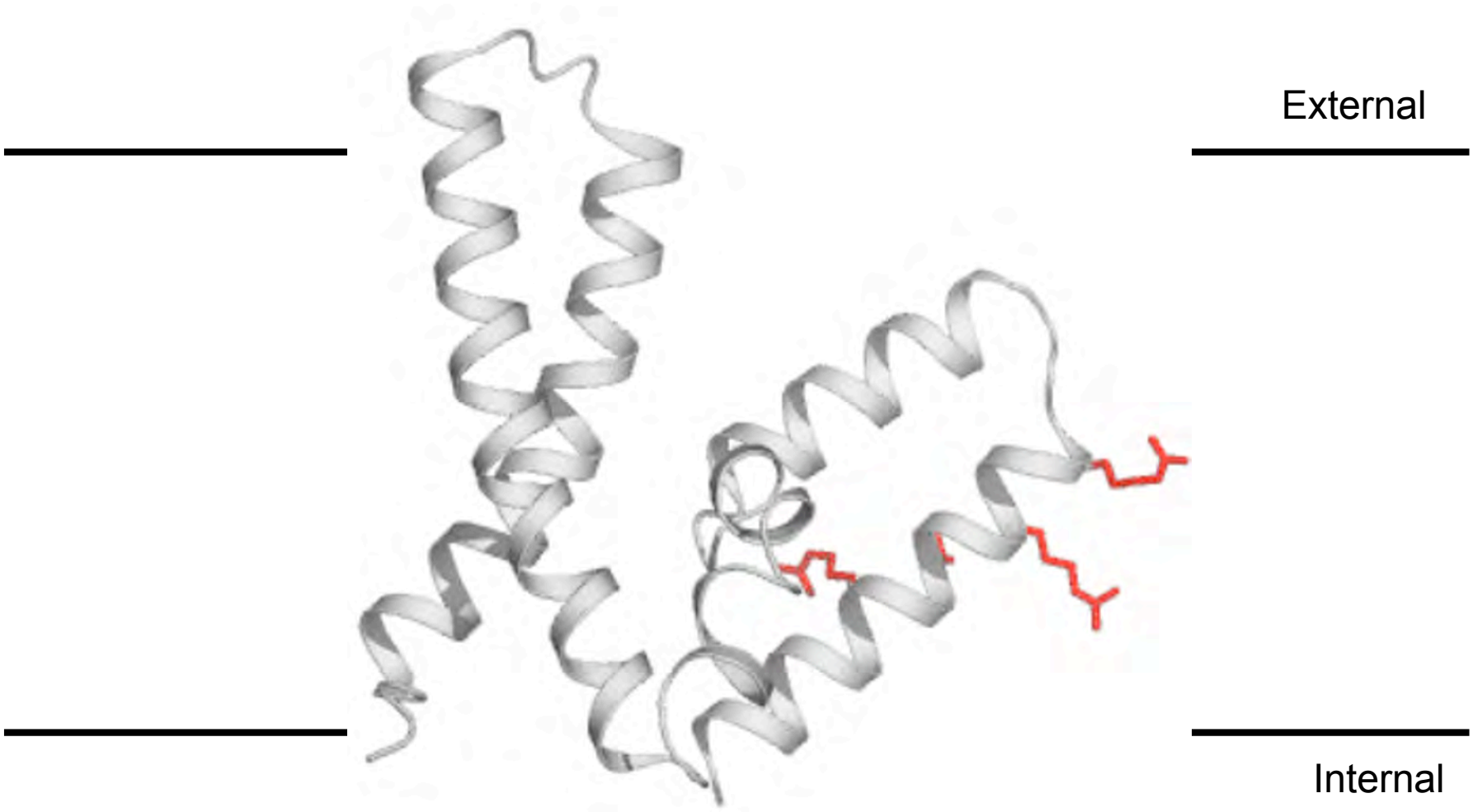
(Closed)

When the pore does this:

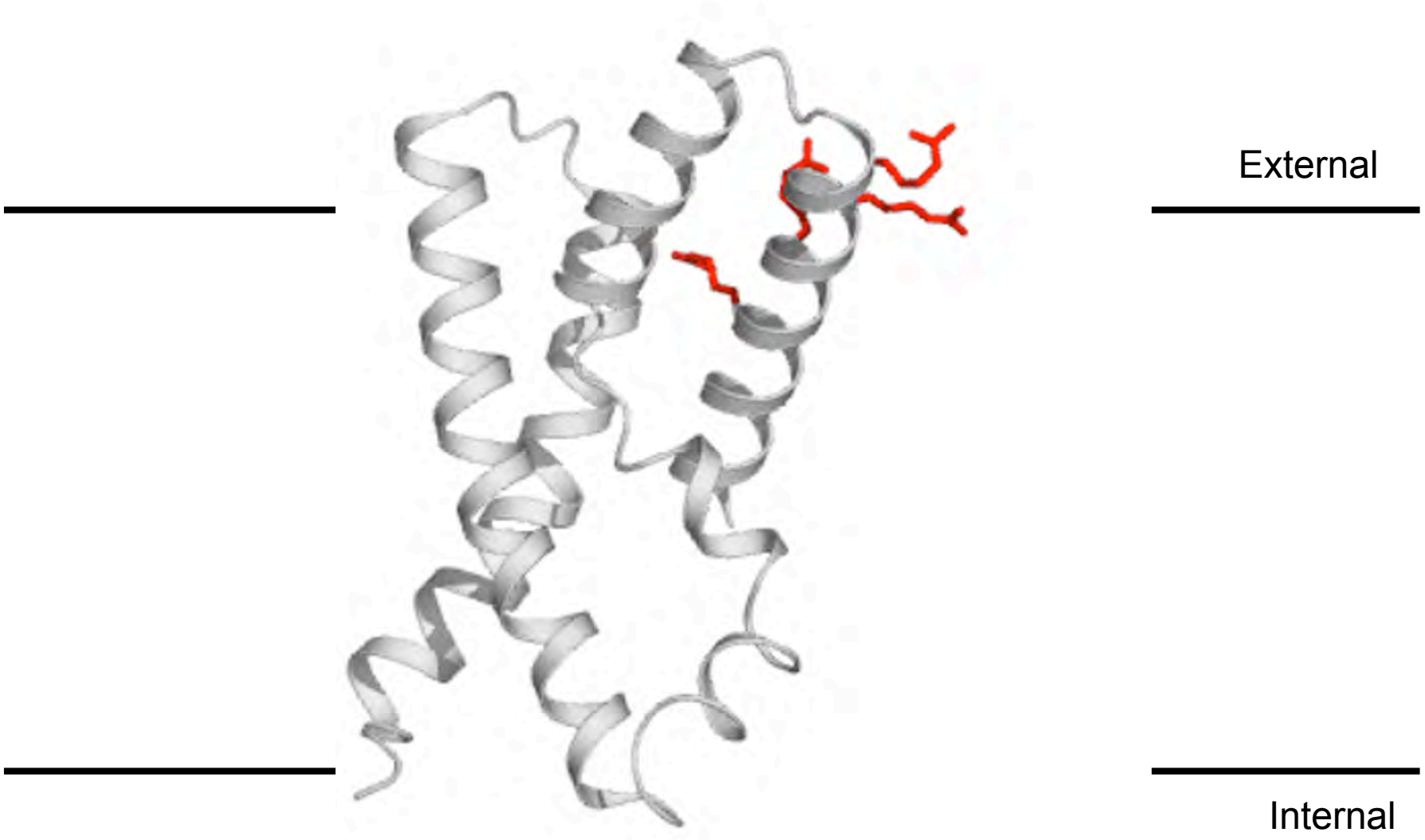


(Opened)

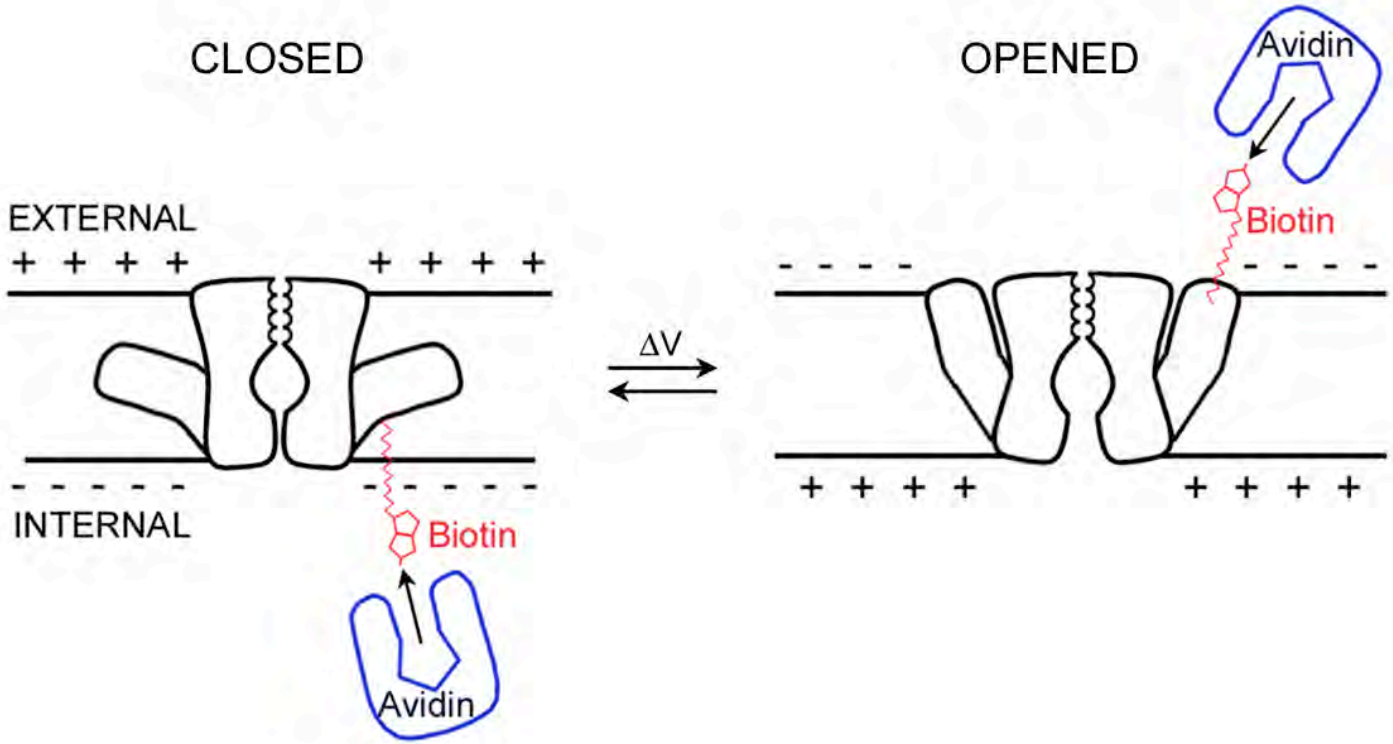
The voltage sensor does this:

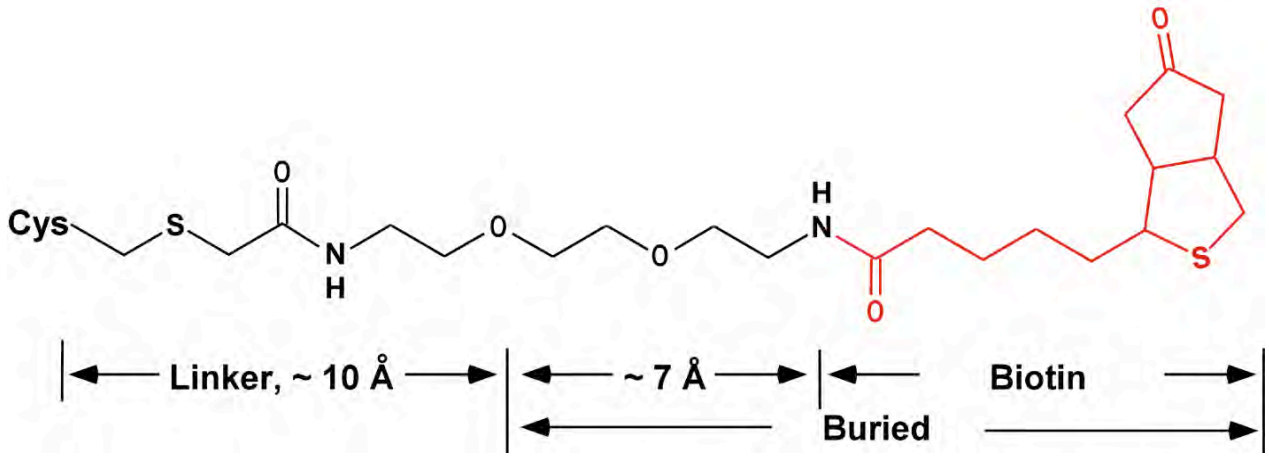


The voltage sensor does this:

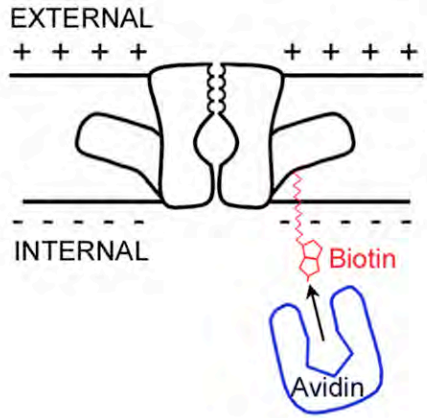


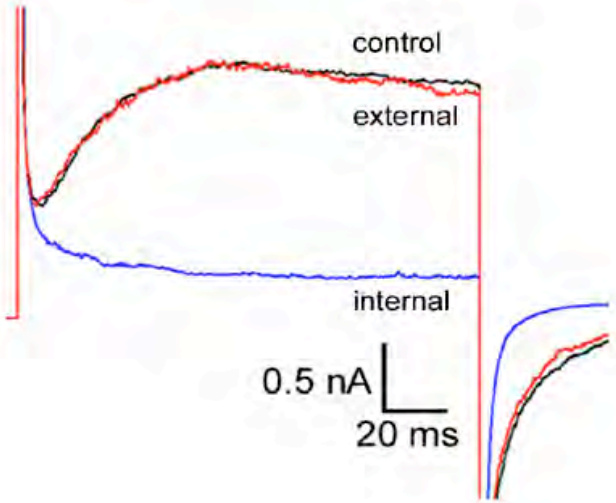
Detecting channel conformational changes with biotin

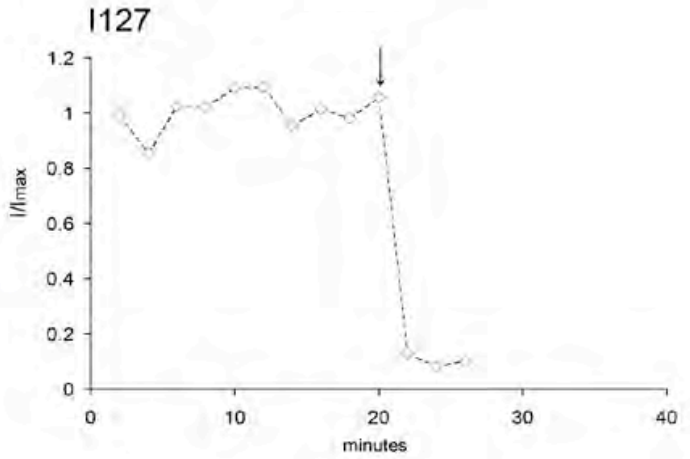




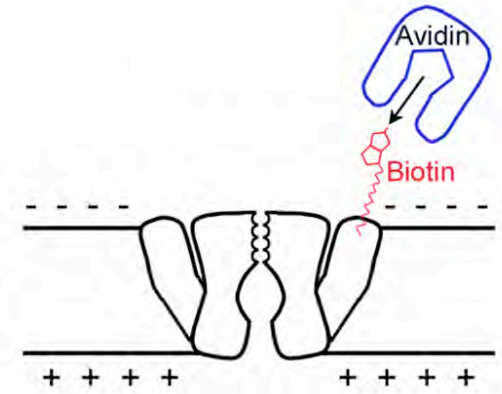
Example of inhibition from internal side

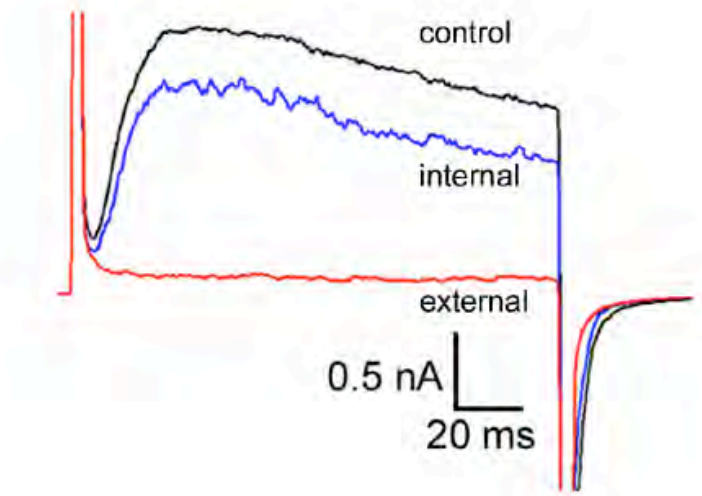


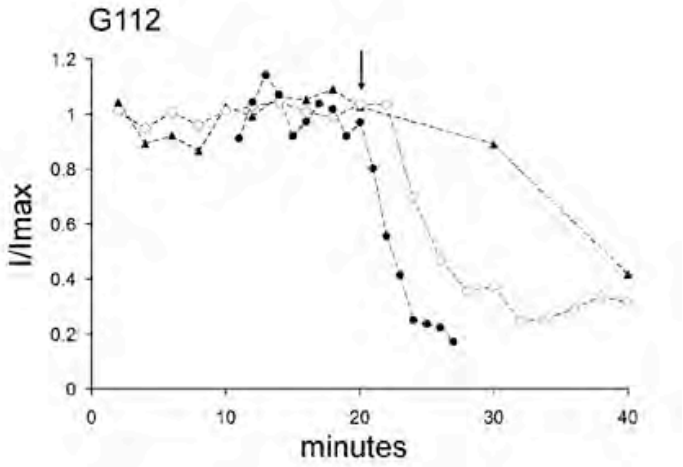




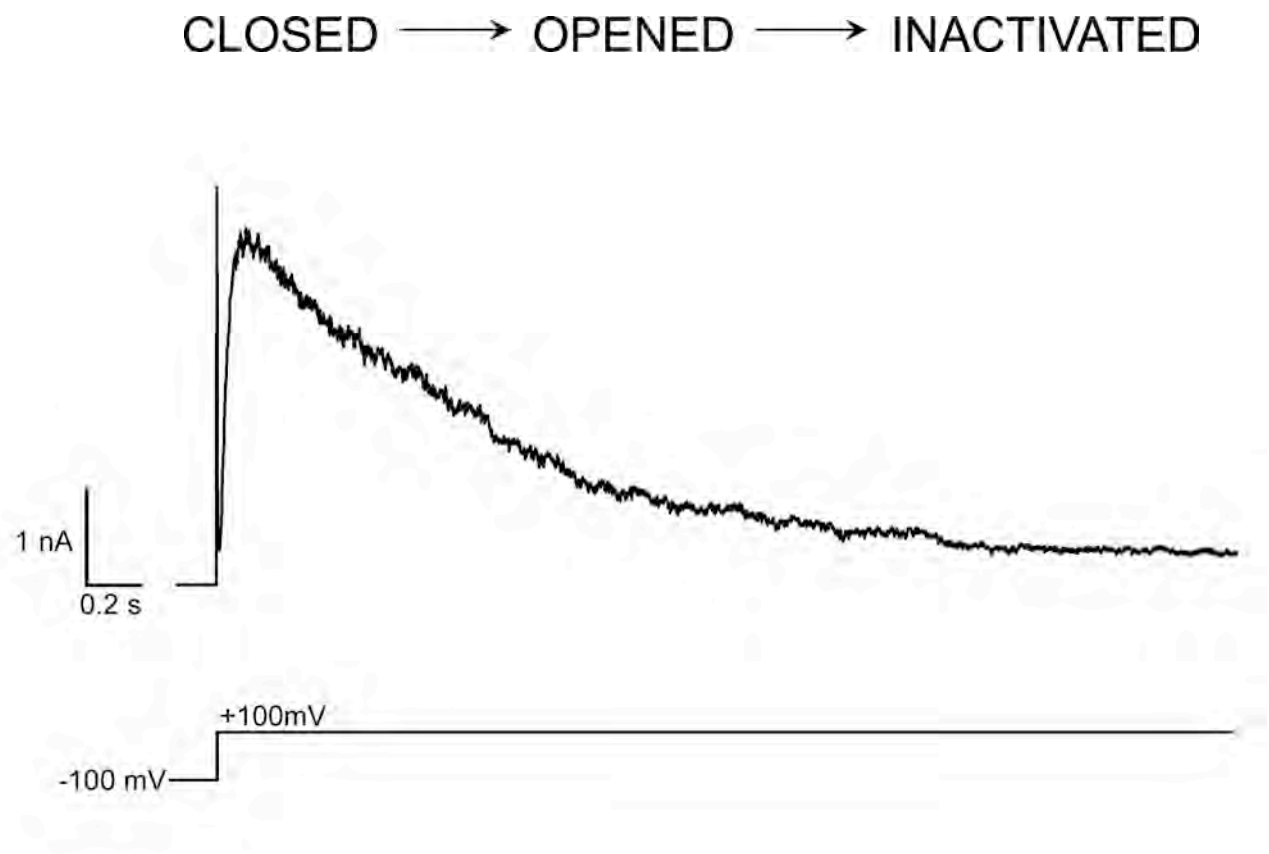
Example of inhibition from external side



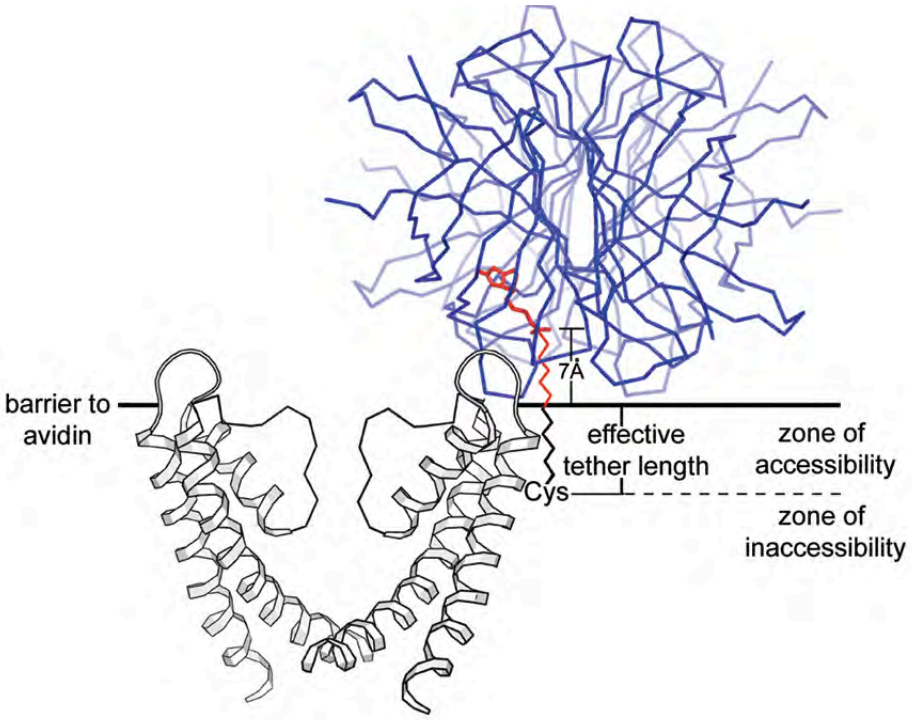


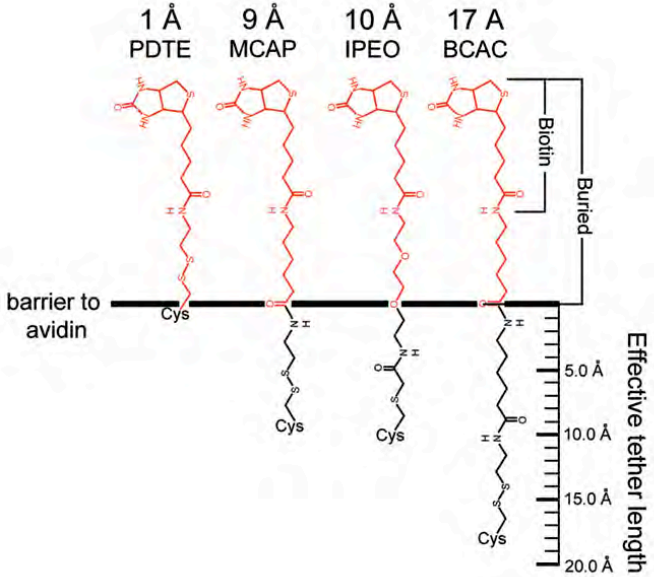


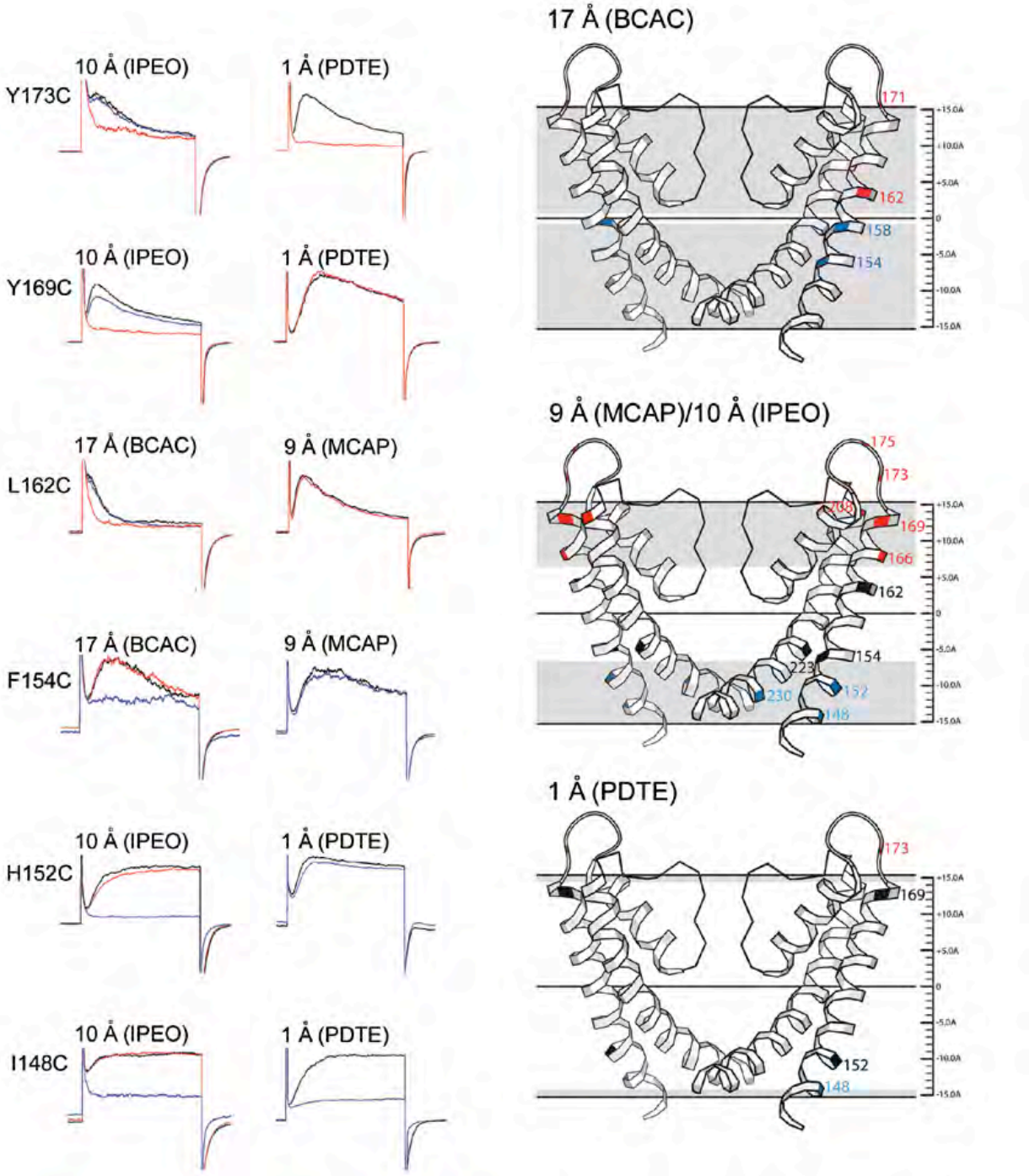
Voltage-dependent channels ‘inactivate’



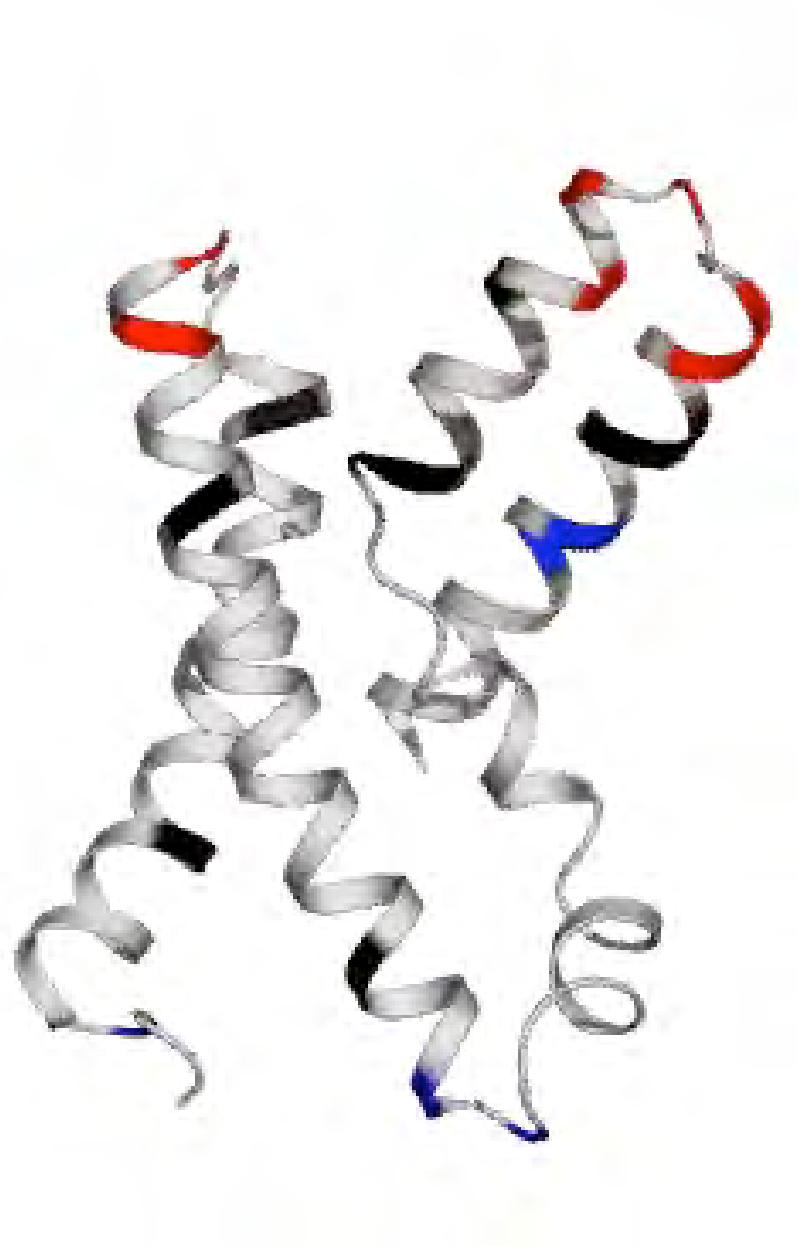
Calibration using the pore: biotin as a molecular ruler for depth of an amino acid in the membrane






10 Å (IPEO)
1 Å (PDTE)
Y173C
10 Å (IPEO)
1 Å (PDTE)
Y169C
17 Å (BCAC)
9 Å (MCAP)
L162C
17 Å (BCAC)
9 Å (MCAP)
F154C
10 Å (IPEO)
1 Å (PDTE)
H152C
10 Å (IPEO)
1 Å (PDTE)
I148C
17 Å (BCAC)
171
162
158
154
9 Å (MCAP)/10 Å (IPEO)
175
173
169
166
162
154
152
148
1 Å (PDTE)
173
169
152
148

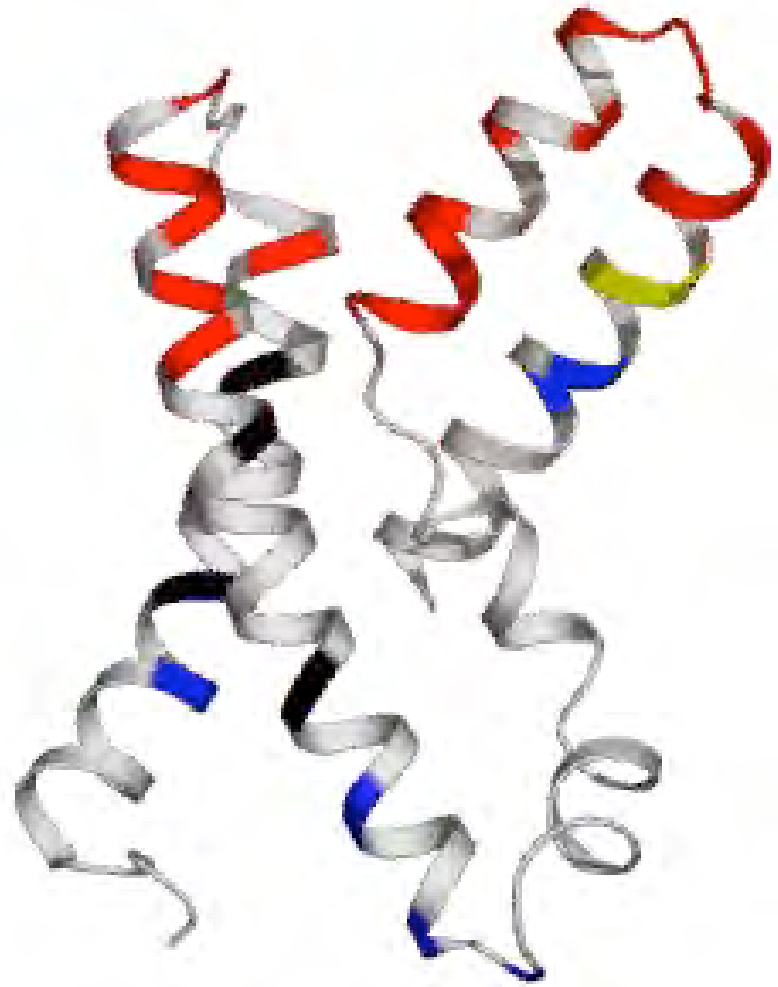
1Å PDTE biotin



External

Internal

9Å-10Å MCAP/IPEO biotin



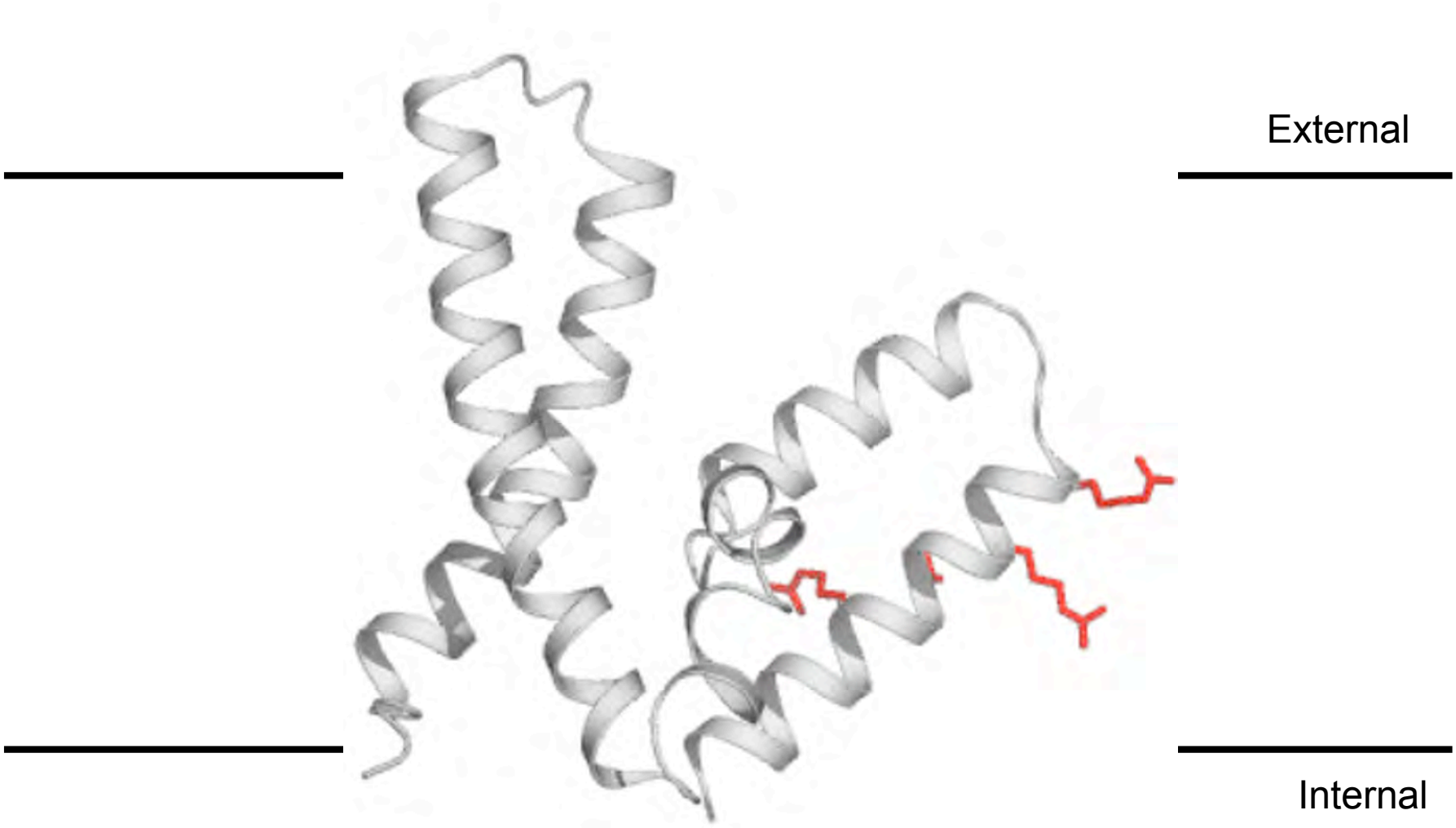
External

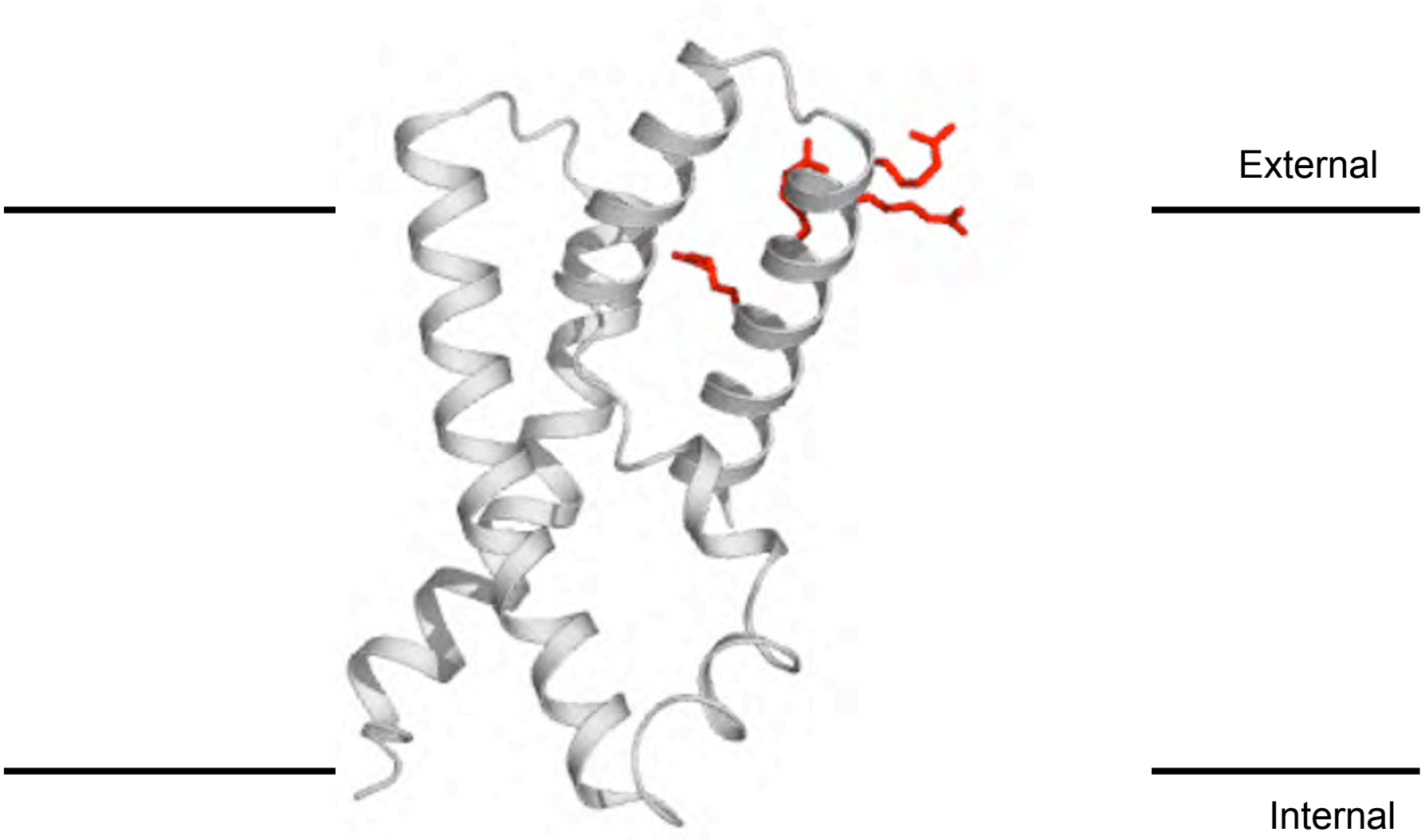
Internal

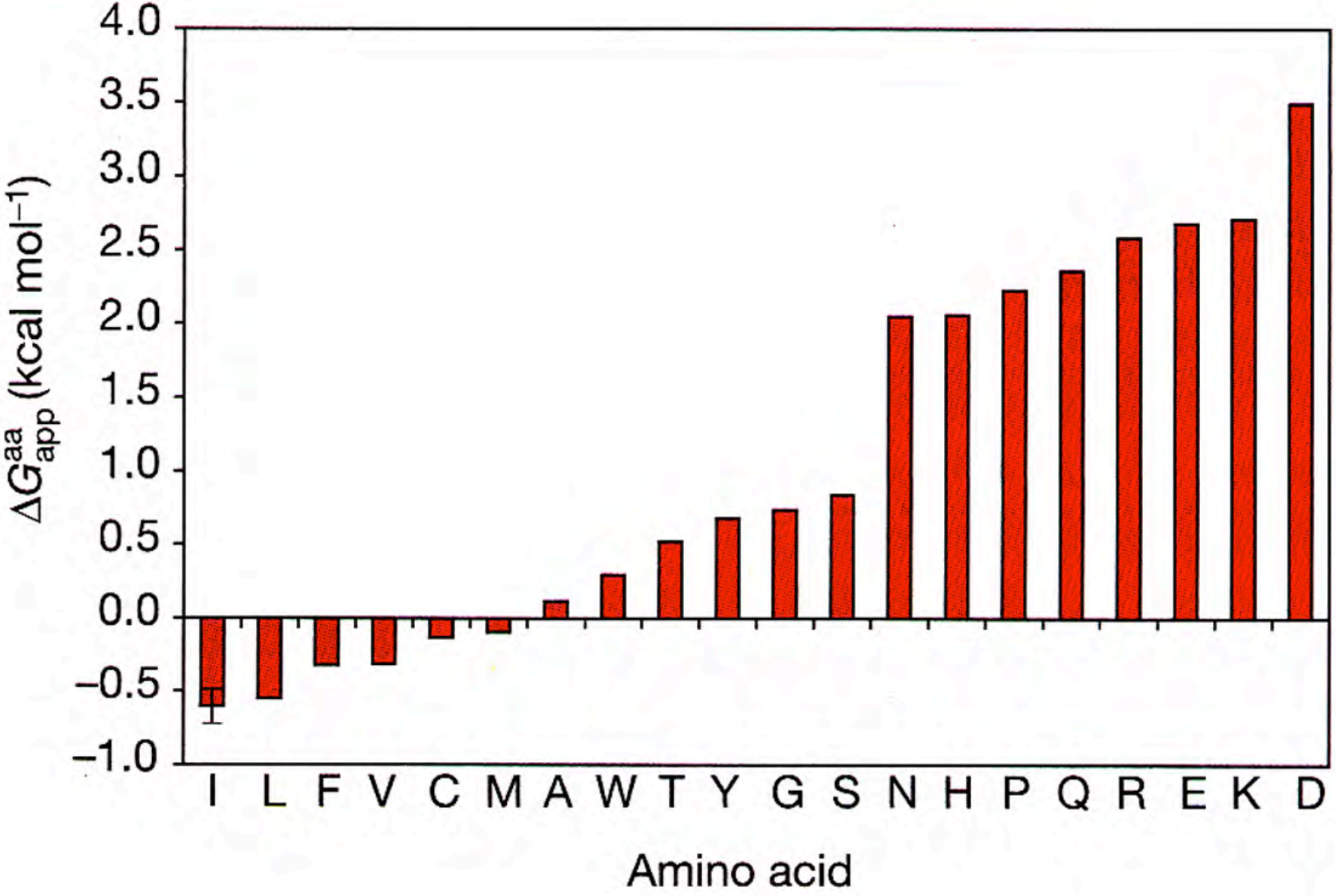
17Å BCAC biotin

External

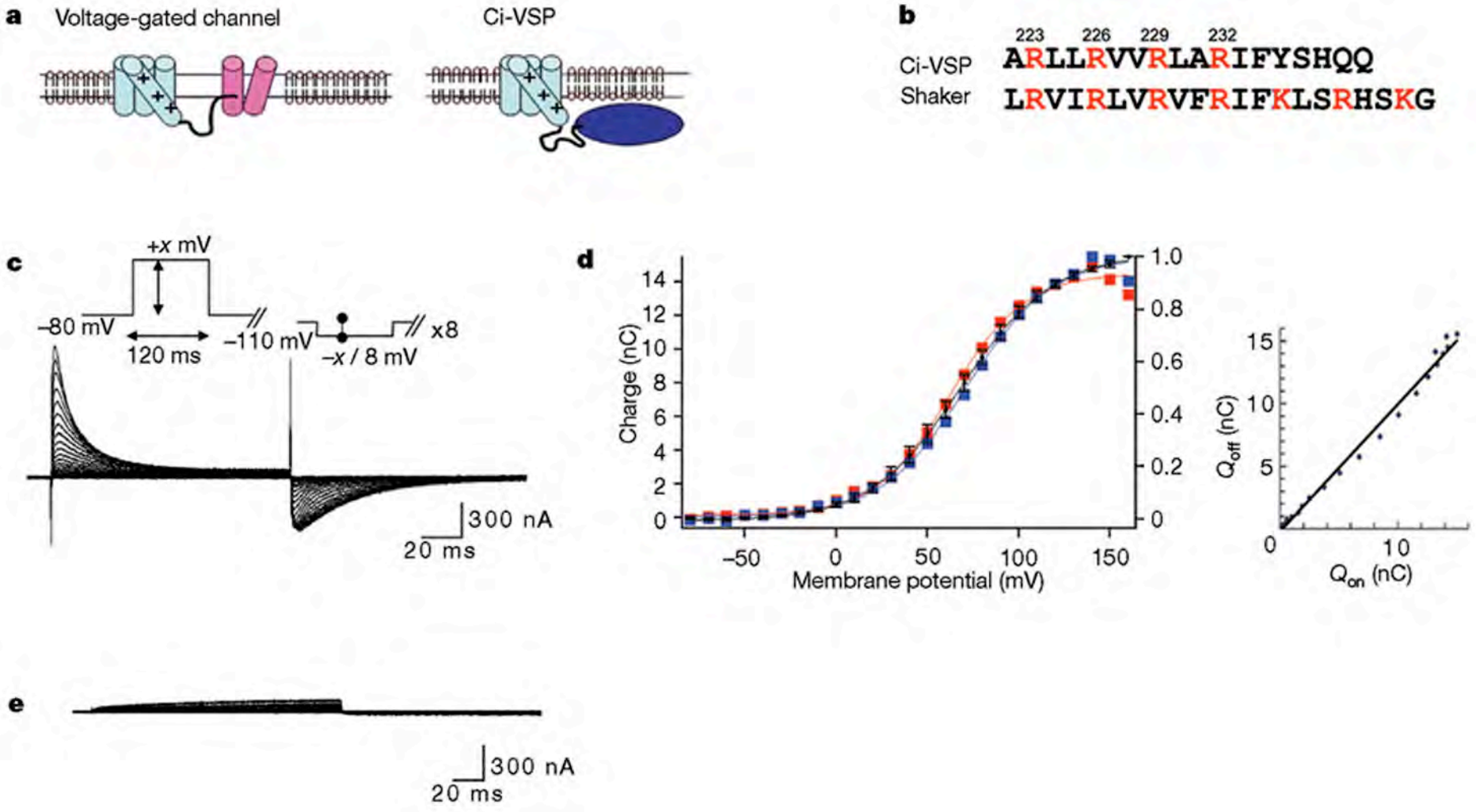
Internal


External
Internal


External
Internal

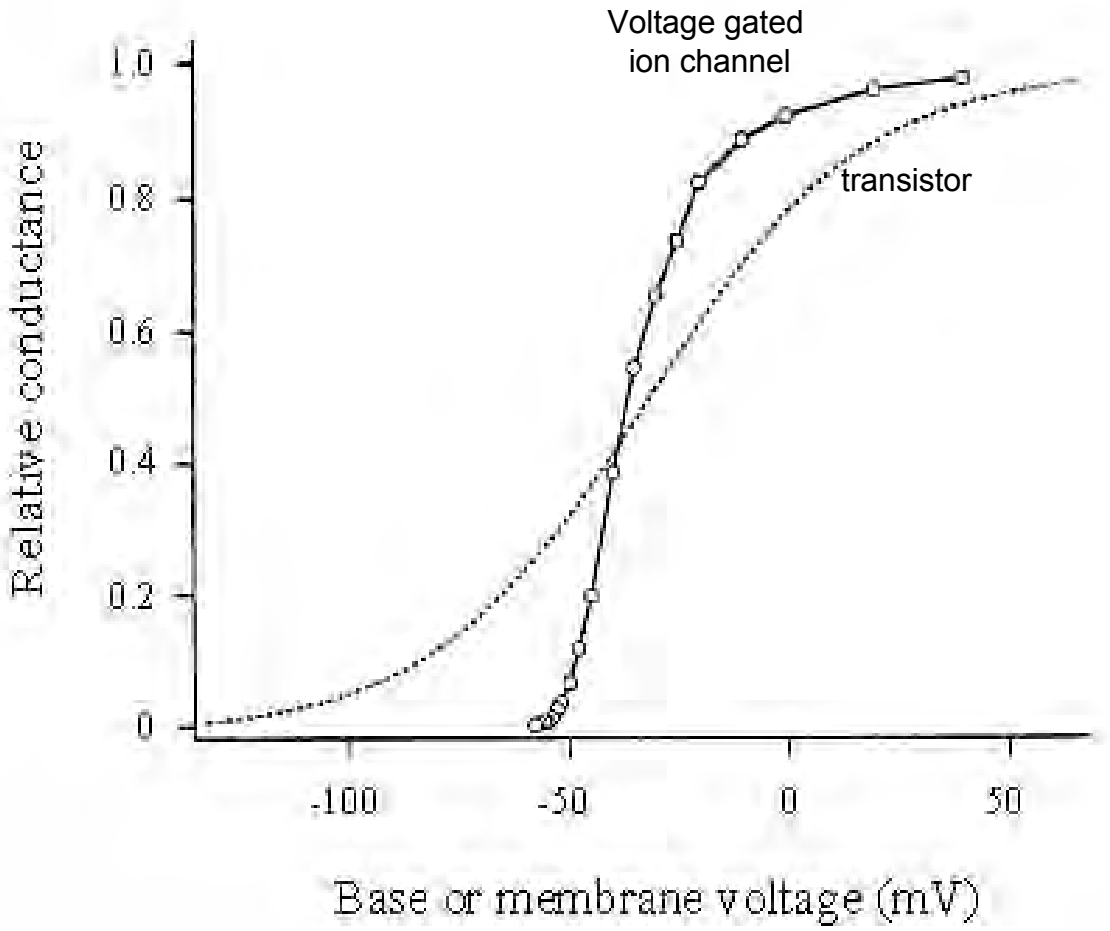


Hessa et al. Nature 433, 2005



Yoshimichi M. et al. Nature advance online publication,; 18 May 2005

Comparing a voltage-dependent K^+ channel to a bipolar transistor



Sigworth, FJ (1994) *Q Rev Biophys* 27:1-40

Acknowledgements

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Youxing Jiang

Alice Lee

Jiayun Chen

Vanessa Ruta

Seok-Yong Lee

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Brian Chait

Martine Cadene

Synchrotron Data Collection:

CHESS: A1, F1, NSLS: X25