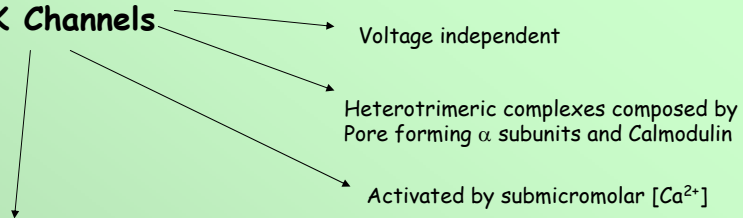


CALMODULIN BINDING DOMAIN OF SMALL CALCIUM ACTIVATED POTASSIUM CHANNEL

AIM

- to investigate the structure of the calmodulin binding domain of the SK potassium channel
- to compare different calcium binding domains

SK Channels



They are high affinity (~ 100 nM) Ca^{2+} sensors: they transduce fluctuation in intracellular $[Ca^{2+}]_i$ into changes in membrane potential.

Calmodulin

Examples of Target molecules:

- calcium/calmodulin-dependent protein kinase IV
- calcineurin
- muscle myosin light chain kinase

Biological roles of Ca

- Protein Translation
- Cell Cycle Progression
- LTP
- Microtubule assembly

Small-conductance Ca²⁺-activated k⁺K channels family

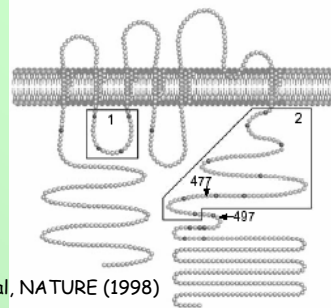
Sequence Homology between the SK K⁺ channels

	SK1	SK2	SK3
SK1	-	74% Identity	63% Identity
SK2	74% Identity	-	69% Identity
SK3	63% Identity	69% Identity	-

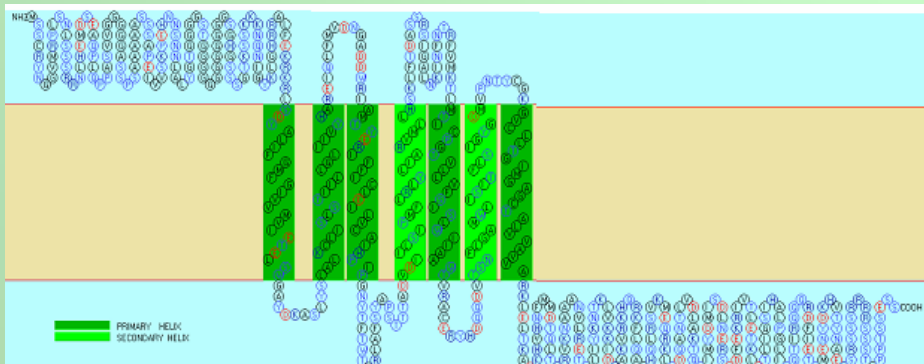
Homology between species

	SK1	SK2	SK3
Mouse	85% Identity	84% Identity	81% Identity
Human	76% Identity	83% Identity	79% Identity

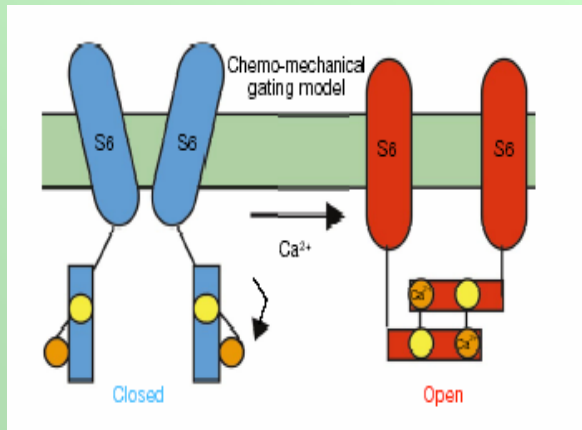
The SK2 subunit. Region two contains the calmodulin binding domain between residues 395-490



X.-M. Xia et al, NATURE (1998)
395,503-507

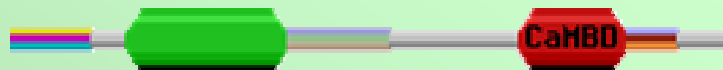


CHEMO-MECHANICAL GATING MODEL



' the CaMBD/CaM complex is monomeric in the absence and dimeric in the presence of Ca^{2+} '

Schumacher et al, NATURE (2001)
410,
1120-1124



MSSRSHNGSV GRPLGSGPGF LGWEPVDPEA GRPRQPTQGP GLQMMAKGQP
AGLSPSGPRG HSQAQEEEE EEDDRPGSG KPPTVSHRLG HRRALFEKRK
RLSDYALIFG MFGIVVMVTE TELSWGVTYK ESLCSFALKC LISLSTVILL
GLVILYHARE IQLFLVDNGA DDWRIAMTWE RVSLISLELA VCAIHPVPGH
YRFTWTARLA FSLVPSAAEA DVDVLLSIPM FLRLYLLARV MLLHSRIFTD
ASSRSIGALN RVTFNTRFVT KTLMTICPGT VLLVFSISSW IVAAWTVRVC
ERYHDKQEV TSNFLGAMWLI SITFLSIGYG DMVPHTYCGK **GVCLLTGIMG**
AGCTALVVAV VARKLELTKA EKHVHNFMMD TQLTKRVKNA AANVLRETWL
IYKHTRLVKK PDQSRVRKHQ RKFLQAIHQ QKLRTVKIEQ GKVNDQANTL
ADLAKAQSIA YEVVSELQAQ QEELEARLAA LESRLDVLGA SLQALPSLIA
QAICPLPPPW GPPSHLTTAA QSPQSHWLPT TASDCG

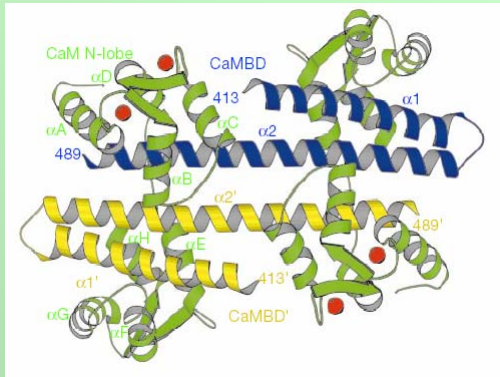
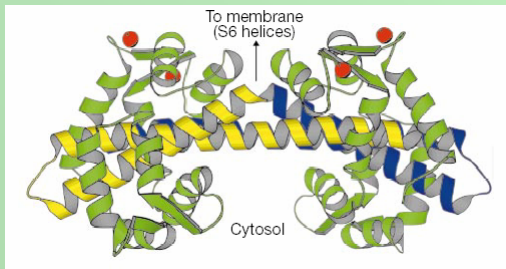


Diagram of the CaMBD/Ca²⁺/CaM dimeric complex. CaM are shown in green.



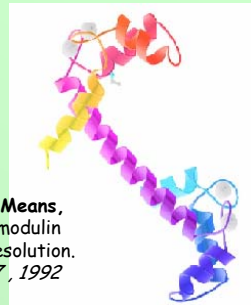
The diagram has been rotated 90°, to show the orientation of the complex relative to the membrane

(Schumacher et al, 2001)



Sutton, R.B., Sprang, S.R.
Structure of the protein kinase C beta phospholipid-binding C2 domain complexed with Ca²⁺.
Structure v6 pp. 1395, 1998

Chatto., Meador, W.E., Means, A.R., Quijcho, F.A. Calmodulin structure refined at 1.7 Å resolution.
J.Mol.Biol. v228 pp. 1177, 1992



Griffith, J.P. et al X-ray structure of calcineurin inhibited by the immunophilin-immunosuppressant FKBP12-FK506 complex. *Cell* 82 pp. 507 (1995)