

Fig. 10H. Sodium channel S4 alignments with S6 gating cavities U1, U2.

Domain I						Domain III					
-5	-1	01234	11	18	22	-5	-1	01234	11	18	22
Pore loop		U1		U2	Pore loop	Pore loop		U1		U2	Pore loop
LCLFRLMLQ	•	DYWENLYQ	MTLRAAGKSY	MVF	IFIGSFY	LSSLQVSTF	•	KGWMDIMY	AAVDSREVED	QPIYEIN	VYMYLYF
•	FIDL	RNV	SALRTFRVLR	RALKTITIF	PGLKTI	•	YEEL	GAIKNLRT	TIRALRPLR	ALS	RFEQMKVV
LCAFRMLTQ	•	DYWENLYQ	LVIIRAEGPV	HALFF	IFLGSFY	LALFQVATF	•	KGWINIM	S DATDIRD	IGDQPI	KENS
•	VVDL	GNLS	SALRTFRVLR	RALKTVAVI	PGLKTI	•	MGNL	TAFRSMR	TLRALRPL	RAVSR	SEGMRVV
LSAFRLMTQ	•	DFWEDLYQ	LVLR AAGPWH	MLFF	IFLGSFY	LCLFQVATF	•	KGWIQIM	NDAIDSRE	VDKQPI	IRETN
•	GIDL	GNL	AALRTFRVLR	RALKTVAI	PGLKTI	•	AGGI	GAFKTM	R TLRALRPL	RAMSRM	QGMRVV
LSLFRMLTQ	•	DFWENLYQ	TLRAAGKTY	MIF	IFIGSFY	LSSLQVATF	•	KGWMDIMY	AAVDSRN	VELGPKY	EES
•	FVDL	GNVS	SALRTFRVLR	RALKTIS	VI PGLKTI	•	YSEL	GAIKSLR	TLRALRPL	RALS	RFEGMRVV
LSLFRMLTQ	•	DFWENLYQ	TLRAAGKTY	MIF	IFIGSFY	LSSLQVATF	•	KGWMDIMY	AAVDSRN	VELQPKY	EDN
•	FVDL	GNVS	SALRTFRVLR	RALKTIS	VI PGLKTI	•	YSEL	GAIKSLR	TLRALRPL	RALS	RFEGMRVV
LALFRMLTQ	•	DYWENLYQ	TLRAAGKTY	MIF	IFLGSFY	LSSLQVATF	•	KGWMDIMY	AAVDSRE	KEEQPY	EVN
•	FVDL	GNIS	SALRTFRVLR	RALKTIT	VI PGLKTI	•	YSEL	GPIKSLR	TLRALRPL	RALS	RFEGMRVV
LALFRMLTQ	•	DCWERLYQ	QTLRSAGKI	YMI	IFIGSFY	LALLQVATF	•	KGWMDIMY	AAVDSRG	YEEQ	PQWEYN
•	FVDL	GNVS	SALRTFRVLR	RALKTIS	VI SGLKTI	•	FAEM	GPIKSLR	TLRALRPL	RALS	RFEGMRVV
LALFRMLTQ	•	DYWENLYG	TLRAAGKTY	MIF	IFVGSFY	LALLQVATF	•	KGWMDIMY	AAVDSRK	PDEGPKY	EDN
•	FVN	LGNS	SALRTFRVLR	RALKTIS	VI PGLKTI	•	YSEL	GAIKSLR	TLRALRPL	RALS	RFEGMRVV
LALFRMLTQ	•	DYWENLYG	QTLRAAGKTY	MIF	IFLGSFY	LSSLQVATF	•	KGWTIIMY	AAVDSVN	VDKQPKY	EYS
•	FVN	LGNS	SALRTFRVLR	RALKTIS	VI PGLKTI	•	YSDL	GPIKSLR	TLRALRPL	RALS	RFEGMRVV
LSLFRMLTQ	•	DSWERLYQ	TLRTSGKI	YMI	IFLGSFY	LALLQVATF	•	KGWMDIMY	AAVDSRE	VNMQPK	WEDN
•	AIDL	RGIS	GLRTRFRVLR	RALKTIV	SVI PGLKVI	•	YSEV	APIKALR	TLRALRPL	RALS	RFEGMRVV
LAMFRMLTQ	•	DSWEKLYQ	TLRTTGLYS	VFF	IFIGSFY	LALLQVATF	•	KGWMDII	YAAVDSTE	KEEQPE	FESN
•	PGIT	IKLL	PLRTRFRV	FRALKAI	SVSRLKVI	•	LINL	MELKSF	R TLRALRPL	RALS	QFEGMKVV

Domain II						Domain IV						
LIVFRALCG	•	EWIETM	WDCMEV	GGVPM	CLAVYMMY	IIIGNLV	ICLFEITTS	•	AGWDG	LLLLPTL	NTGPP	DCDPDENP
•	LSNQ	MGMS	VLRSLR	LLRIF	KLAKSWPT	LNIL	•	EKYF	VSP	TLFRVIR	LARIAR	VRLRIRA
MIVFRVLCG	•	EWIESM	WTCMEV	AGYACV	PFFLLTM	IIGNLVV	ILLFQ MSTS	•	AGWDG	VLAAIM	REPPAC	QPD
•	LGGI	QGLS	VLR SFRL	LRVFKL	AKSWPT	LNML	•	KQYF	VSP	TLRVRV	FRVGR	VLRLVKS
MIVFRVLCG	•	EWIESM	WDCMYV	GDVSCI	PFFLATV	VIGNLVV	ILLFQ MSTS	•	AGWDG	VLD AI	INEEAC	PPDND
•	LEGV	QGLS	VLR SFRL	LRVFKI	AKSWPT	LNLL	•	EKYF	VSP	TLRVRV	VAKVGR	VLRLVKG
LIVFRVLCG	•	EWIETM	WDCMEV	AGGAM	CLTVFMMV	MVIGNLV	ICLFQITTS	•	AGWDG	L LAPIL	NSKPP	DCDP
•	LANV	QGLA	VLR SFRL	LRVFKL	AKSWPT	LNML	•	QKYF	VSP	TLFRVIR	LARIGR	VLRLIRG
LIVFRVLCG	•	EWIETM	WDCMEV	AGQAM	CLTVFMMV	MVIGNLV	ICLFQITTS	•	AGWDG	L LAPIL	NSGPP	DCDP
•	LANV	EGLS	VLR SFRL	LRVFKL	AKSWPT	LNML	•	EKYF	VSP	TLFRVIR	LARIGR	ILRLIKG
LIIFRILCG	•	EWIETM	WDCMEV	SGQAM	CLTVFLMV	MVIGNLV	ICLFEITTS	•	AGWDG	L LNPI	LNSGPP	DCDP
•	LANV	QGLS	VLR SFRL	LRVFKL	AKSWPT	LNML	•	EKYF	VSP	TLFRVIR	LARIGR	ILRLIKG
LIVFRILCG	•	EWIETM	WDCMEV	AGSLC	L LVFLV	MVIGNLV	LCLFQITTS	•	AGWDG	L LSPIL	NTGPP	YCDP
•	LSR	MSNL	SVLR SFRL	LRVFKL	AKSWPT	LNML	•	QKYF	VSP	TLFRVIR	LARIGR	ILRLIRG
LIVFRVICG	•	EWIETM	WDCMEV	AGQAM	CLIVFMMV	MVIGNLV	ICLFQITTS	•	AGWDG	L LLLPIL	NRPP	DCSLD
•	LAD	VEGL	SVLR SFRL	LRVFKL	AKSWPT	LNML	•	EKYF	VSP	TLFRVIR	LARIGR	ILRLIKG
LIVFRVLCG	•	EWIETM	WDCMEV	AGQAM	CLIVYMMV	MVIGNLV	ICLFQITTS	•	AGWDG	L LAPIL	NSKPP	DCDP
•	LAD	VEGL	SVLR SFRL	LRVFKL	AKSWPT	LNML	•	ETYF	VSP	TLFRVIR	LARIGR	ILRLVKG
LIVFRILCG	•	EWIENM	WACMEV	GQKSI	CLILFLTV	MVLGNLV	LCLFQITTS	•	AGWDG	L LSPIL	NTGPP	YCDP
•	VAKK	GSL	SVLR SFRL	LRVFKL	AKSWPT	LNML	•	LQSY	FSP	TLFRVIR	LARIGR	ILRLIRA
LVVFRILCG	•	EWIENM	WECMQE	ANASS	LCVIVFI	LITVIGK	LCLFQIST	•	AGWDS	L LSPML	RLRS	ESCNS
•	VQKR	SWP	FLRSFR	VLRFVFKL	AKSWPT	LNML	•	EHIP	FSP	TLFRVIR	LARIGR	ILRLVRA

Amino acid sequences Accession (NCBI)

- (1) Electric eel [Electrophorus electricus] AAA79960.1; Noda, M & Numa, S. 1987
- (2) Squid [Doryteuthis opalescens] AAA16202.1; Rosenthal & Gilly. 1993
- (3) Fruit fly [Drosophila melanogaster] AAB59195.1; Lounney, Kreber, Ganetzky. 1989
- (4) Human Nav 1.1 SCN1A P35498.2; Escayg, A. et al. 2000
- (5) Human Nav 1.2 SCN2A [Brain] Q99250.3; Ahmed, C.M. et al. 1992
- (6) Human Nav 1.4 SCN4A [Skeletal muscle] P35499.4; George, A.L. et al. 1992
- (7) Human Nav 1.5 SCN5A [Cardiac muscle] Q14524.2; Gallens, M.E. et al. 1992
- (8) Human Nav 1.6 SCN8A NP_055006.1. Ver. 21-FEB-2021
- (9) Human Nav 1.7 SCN9A Q15858.3. Ver. 10-FEB-2021
- (10) Human Nav 1.8 SCN10A NP_006505.4. Ver. 15-DEC-2020
- (11) Human Nav 1.9 SCN11A NP_054858.2. Ver. 20-FEB-2021

Reference for U1 0 position

Bertil Hille. Ion Channels of Excitable Membranes. 2001. Fig. 17.12.
Sodium channel homology
 Position 0 is for the first residue on the U1 cavity. Position 2 is the third residue at cavity center (180°). The third residue of the U2 cavity is also at 180°. All the listed sodium channel sequences have this homology for U1 and U2 gating cavities.