Groome and Winston, http://www.jgp.org/cgi/content/full/jgp.201210935/DC1

Template and domain specific VSM models are available for download in a ZIP file.

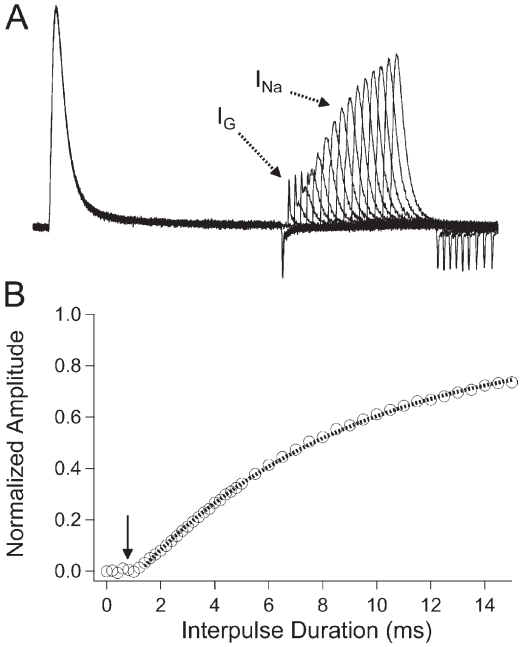
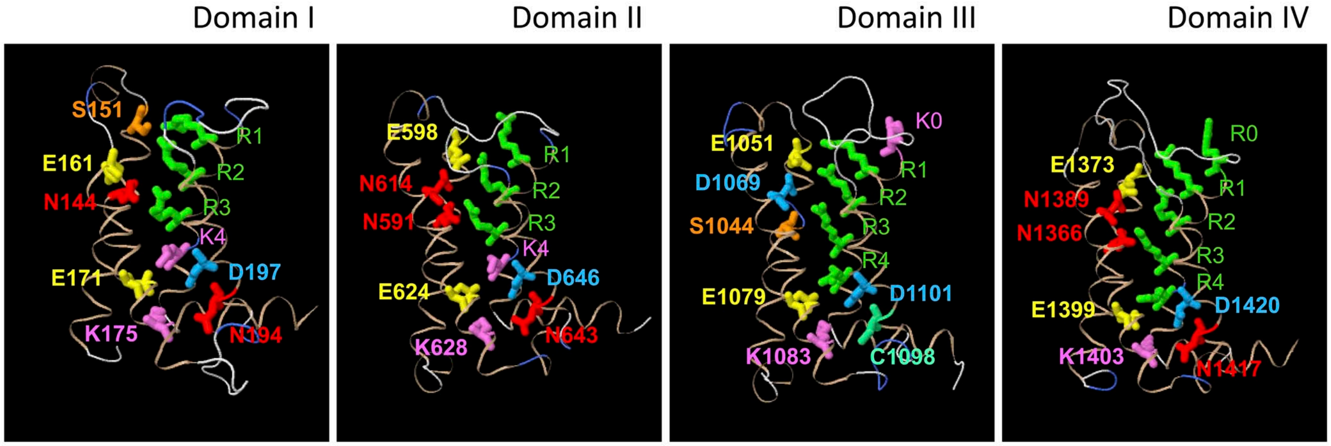


Figure S1. Double pulse protocol. (A) Traces of the initial 15 ms of recovery in hNa$_V$1.4. Channels were inactivated with 30 ms, 30 mV commands from a holding potential of −120 mV. After a variable duration −90 mV interpulse, a second depolarizing (test) pulse was delivered to elicit gating (I_g) and ionic (I_{Na}) currents shown by the arrows. (B) Normalized recovery plotted as peak$_2$/peak$_1$. An exponential fit (broken line) was used to determine recovery time constant and delay (x intercept, arrow).

A $Na_V Ab(2)$ model



B $Na_V Rh$ model

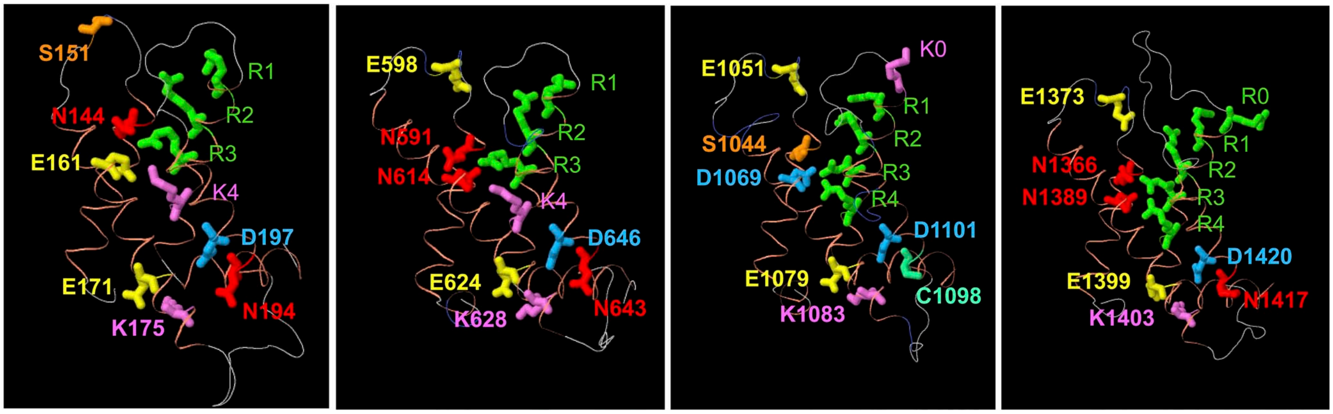


Figure S2. Additional homology models of VSM in domains I–IV. Shown are models based on crystal structures $Na_V Ab(2)$ (A) and $Na_V Rh$ (B). For each domain, locations of putative countercharges in S1-S3 segments are shown, as well as the outer four positive charges in S4.

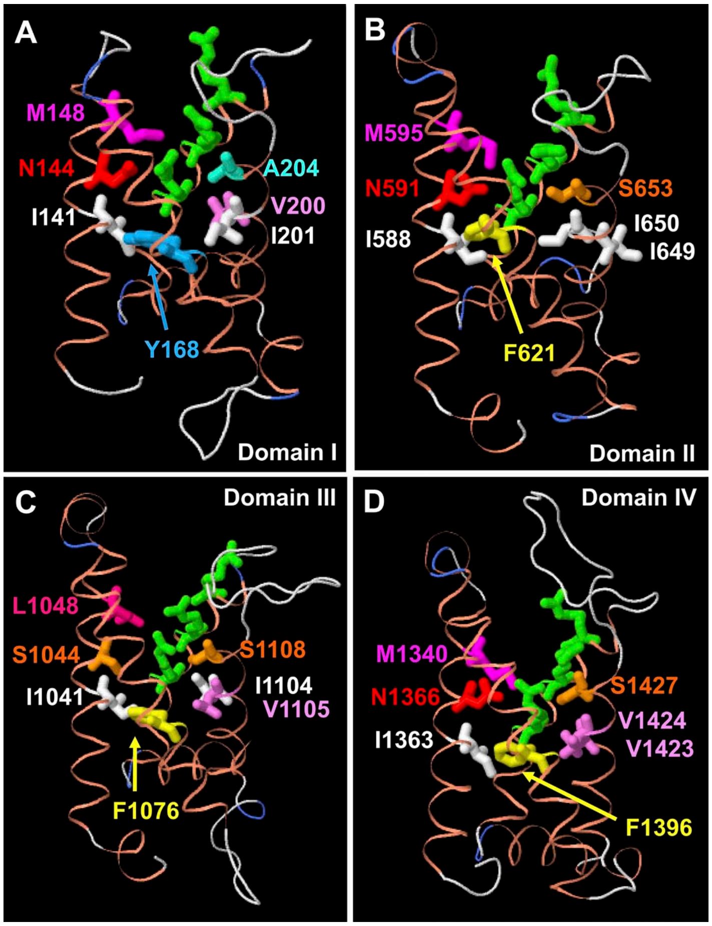


Figure S3. Additional residues in homology models of VSM based on NaVAb. Shown are models of VSM in hNa$_V$1.4 for domains I (A), II (B), III (C), and IV (D). In each panel, R1–R3 of S4 are shown in green, above the HCS, consisting of isoleucine in S1, aromatic tyrosine or phenylalanine in S2, and isoleucine /valine residues in S3. Residues homologous to those in Na$_V$Ab that form a network of hydrogen bond interactions around R3 are shown for domain I (N144, M148, S1; A204, S3), domain II (N591, M595, S1; S653, S3), domain III (S1044, L1048, S1; S1048, S3), and domain IV (N1366, M1340; S1427, S3).

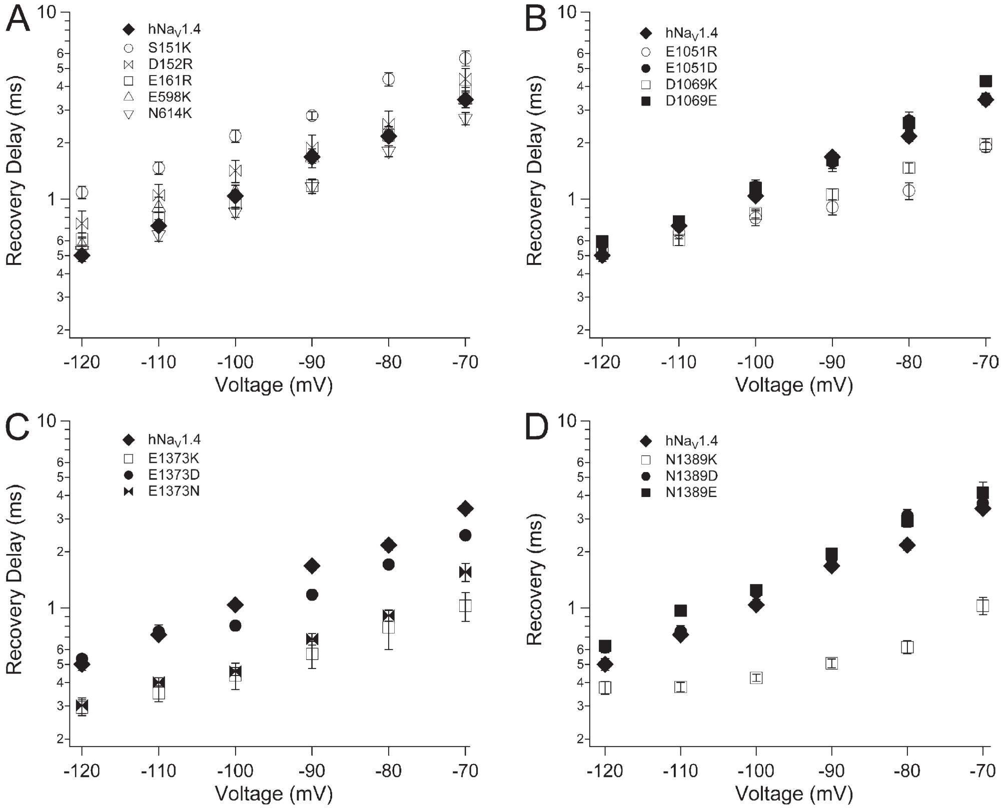


Figure S4. Voltage dependence of recovery delay for hNa$_V$1.4 and ENC mutations. Values represent mean delay ± SEM (error bars) for mutations in domains I and II (A), domain III (B), domain IV S1 (C), and domain IV S2 (D) from 10–18 experiments.

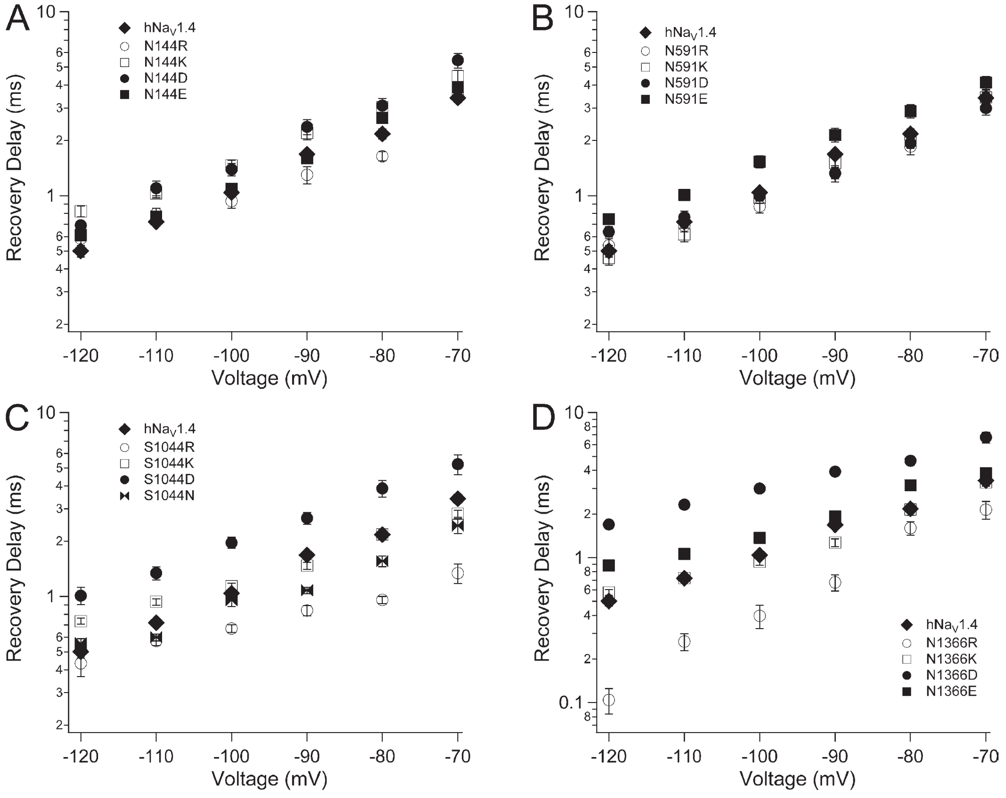


Figure S5. Voltage dependence of recovery delay for hNa$_V$1.4 and HCR mutations. Values represent mean delay ± SEM (error bars) in domain I (N144, A), domain II (N591, B), domain III (S1044, C), and domain IV (N1366, D) from 10–22 experiments.

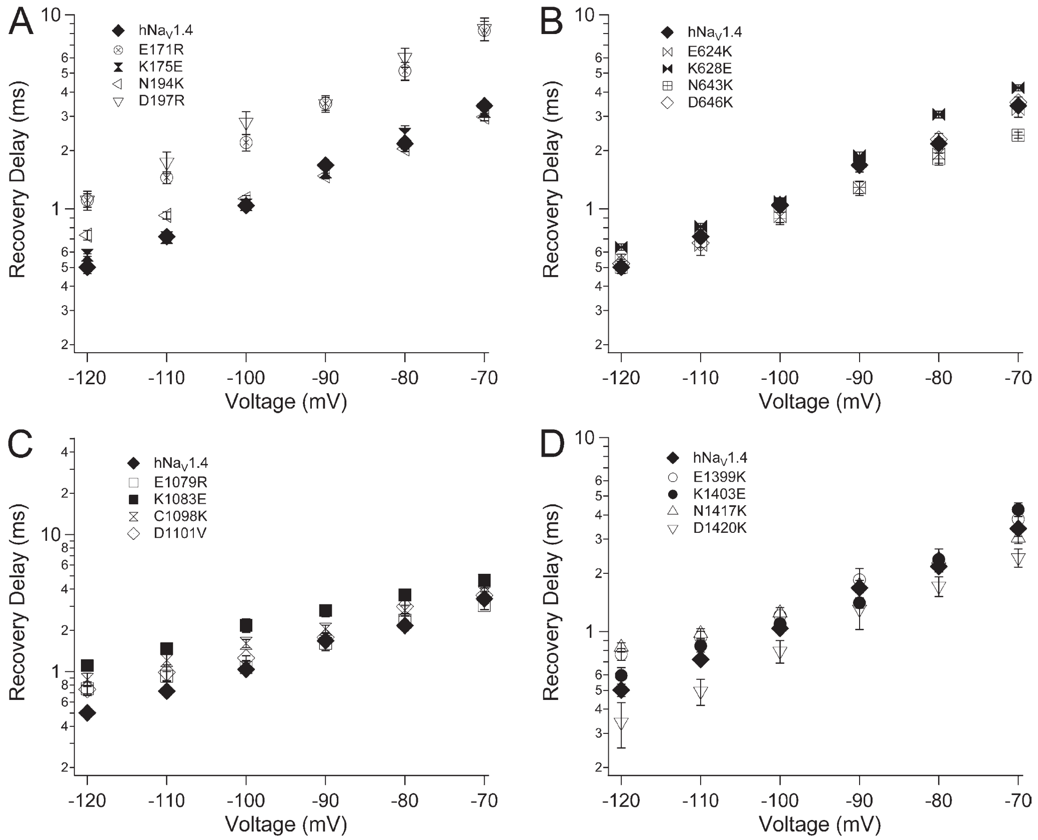


Figure S6. Voltage dependence of recovery delay for hNa$_V$1.4 and INC mutations. Values represent mean delay ± SEM (error bars) in domain I (A), domain II (B), domain III (C), and domain IV (D) from 10–17 experiments.