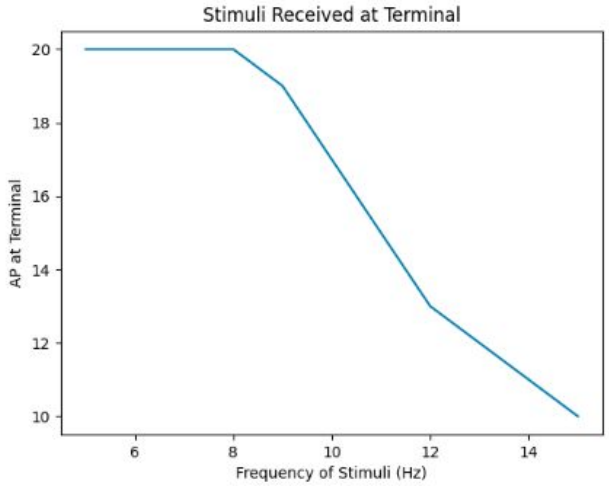
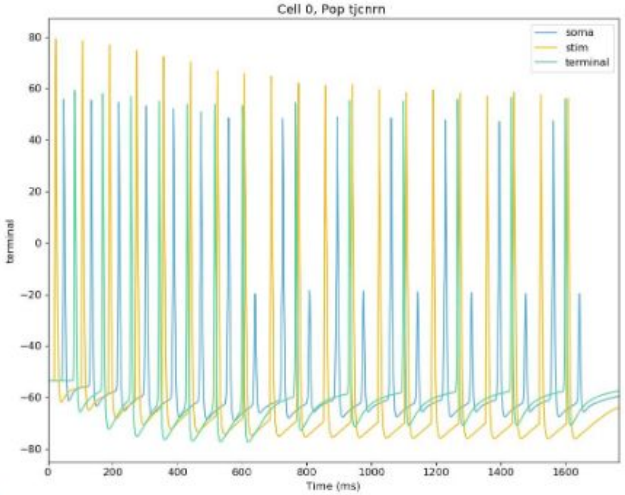
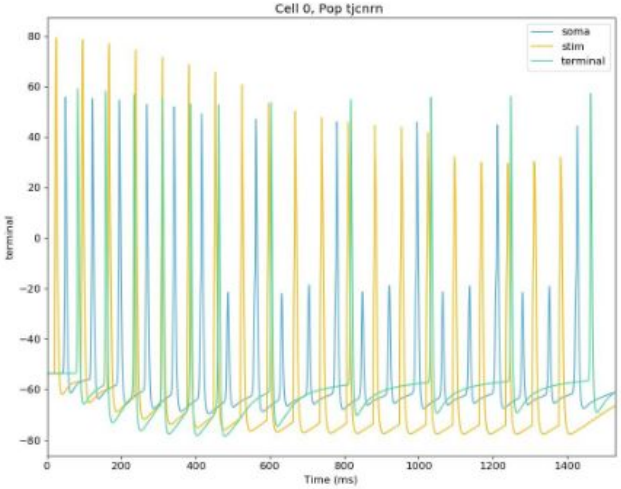
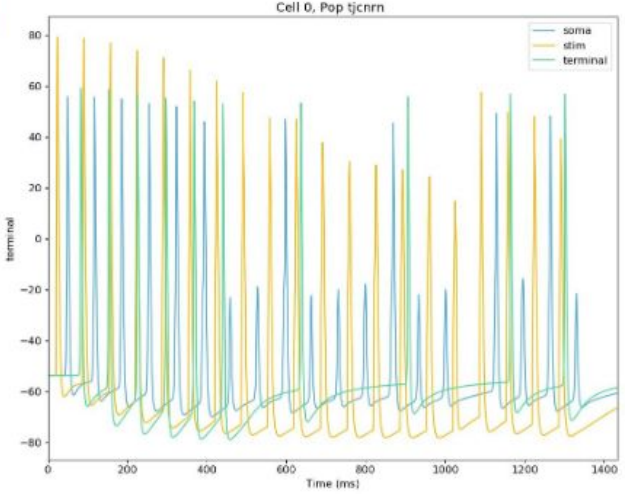




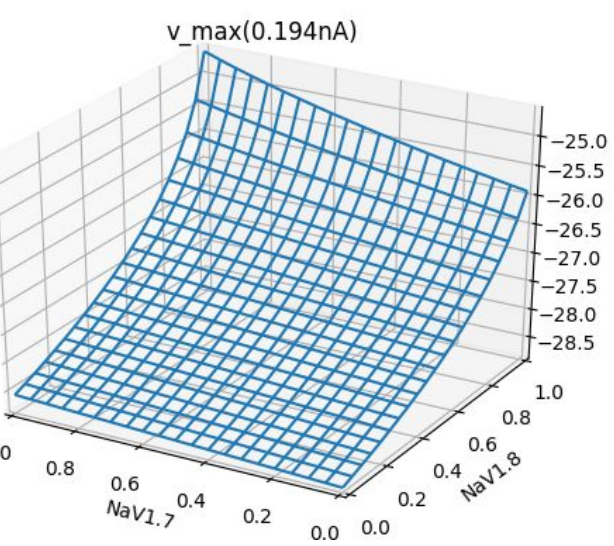


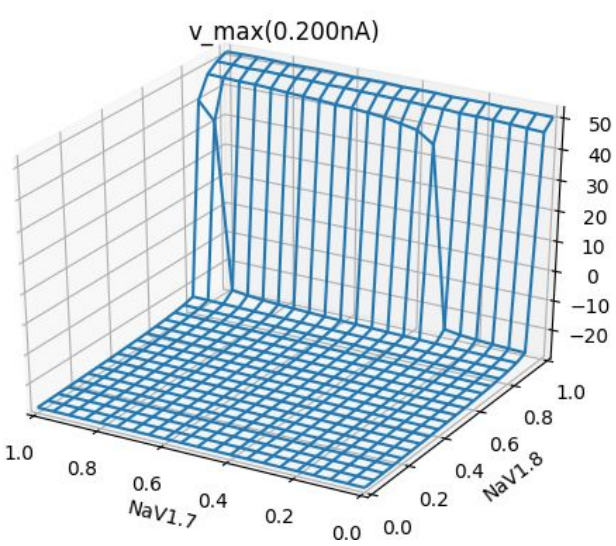


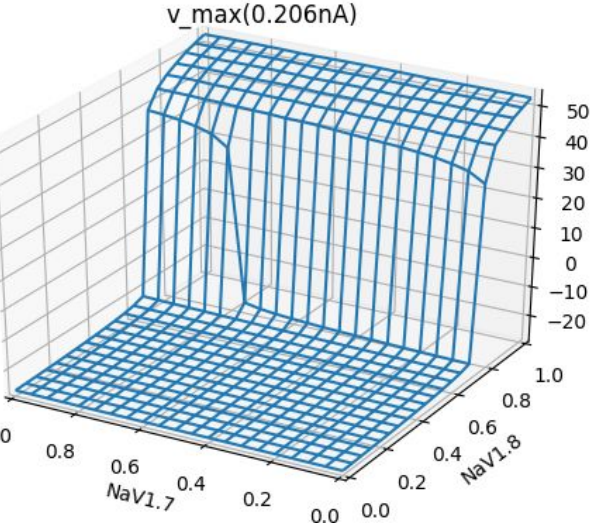
Firing attenuation using an expanded t-junctional model.

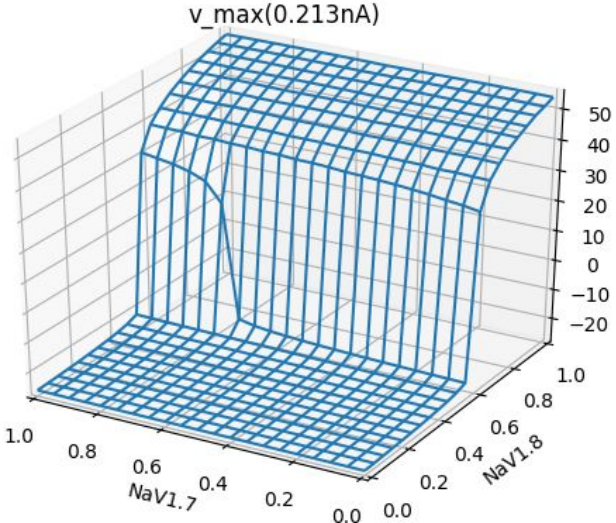
Failure of AP propagation occurred at the soma at higher firing frequencies.

Firing stimuli used in Tigerholm et al. 2014.





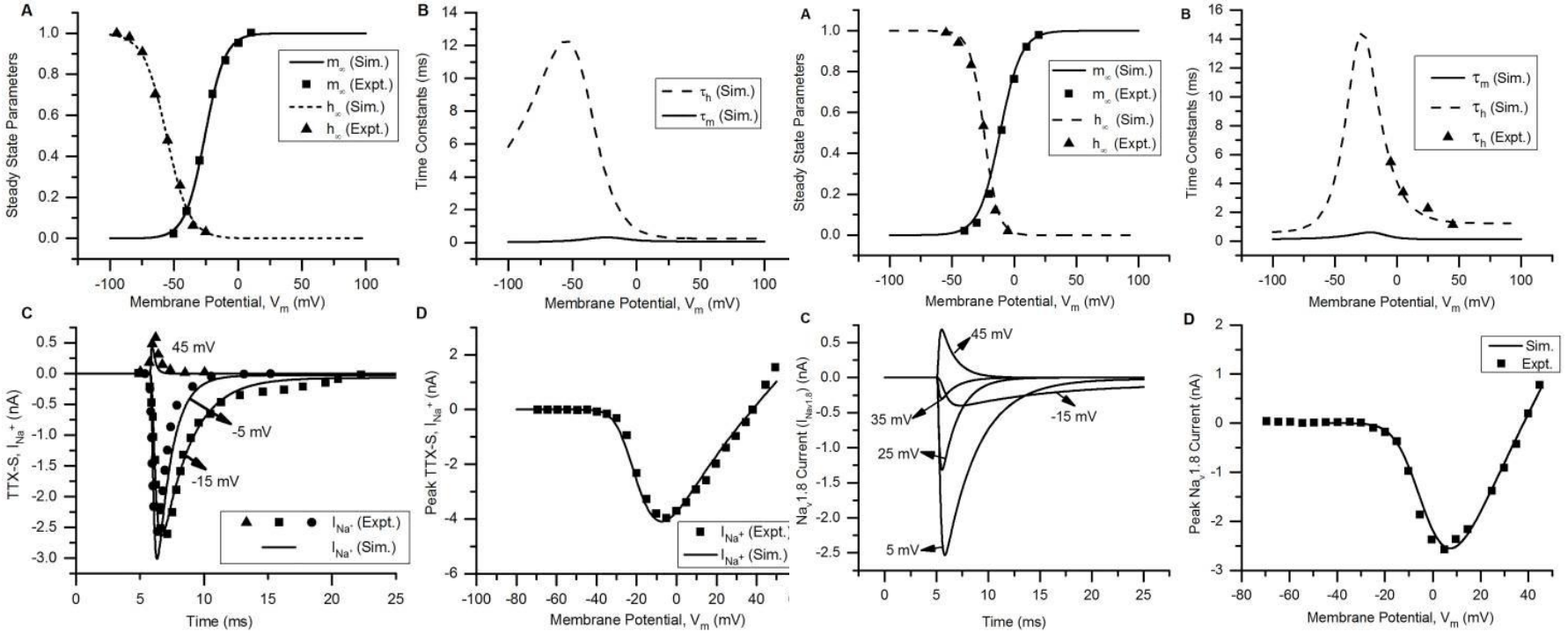




Firing Threshold:
With RMP at -53.5 mV
peak voltage of the soma when stimulated with a rapid narrow square pulse (5 ms)

	NaV 1.7 Increased TTX-S current: Inherited Erythromelalgia ERK1/2 mitogen-activated protein kinase p38 mitogen-activated protein kinase NGF	NaV 1.8 or NaV 1.9 Increase TTX-R current: PGE2 exposure PKA, PKC activation TNF-alpha
Sheets et al. 2007 (Inherited Erythromelalgia)	Human WT transfected into HEK293 cells	Elliott and Elliott 1993 -> Dissected ganglia of female WIstar rats Cummins and Waxman 1997 -> L4-L5 18-25 um DRG of Sprague Dawley rats
Choi et al. 2011 (TTX-S v. TTX-R)	The kinetic characterization of the Nav1.7 channel described by Sheets et al. (2007) has been used	The Nav1.8 sodium current (INav1.8) was best fit with a HH model that employed only one activation gate: INav1.8 = gNav1.8 * m * h * (V − ENa) ... Based on previous reports (Herzog et al. 2001 ; Sheets et al. 2007) *The equations are from Sheets et al. with the exception that Sheets uses m * m * m for activation, and models NaV 1.8. The single activation gate is taken from Herzog et al. 2001 and models TTX-RP*
Mandge et al. 2018 (Bladder DRG, inflammatory pain)	The data for modelling the TTX-S channels of bladder small DRG neurons were obtained by fitting the data from Yoshimura et al. 1996, Baker et al. 2005, Sheets et al. 2007	The data for modelling the channel was derived from Yoshimura et al. 1996, Yoshimura et al. 1997, Yoshimura et al. 1999, Han et al. 2015 for bladder small DRG neurons.
Pelot et al. 2020 (C-fiber modelling, review of several models)	The Tigerholm et al. 2014 model best reproduced the experimental data... Nav1.7 code is consistent with (Sheets et al., 2007), while the manuscript is not. *Experimental data is Schild et al. 1994, Schild et al. 1997*	The Tigerholm et al. 2014 model best reproduced the experimental data... Nav1.8 equations match (Sheets et al., 2007) with the addition of Q10 for the m and h gates. *Experimental data is Schild et al. 1994, Schild et al. 1997*

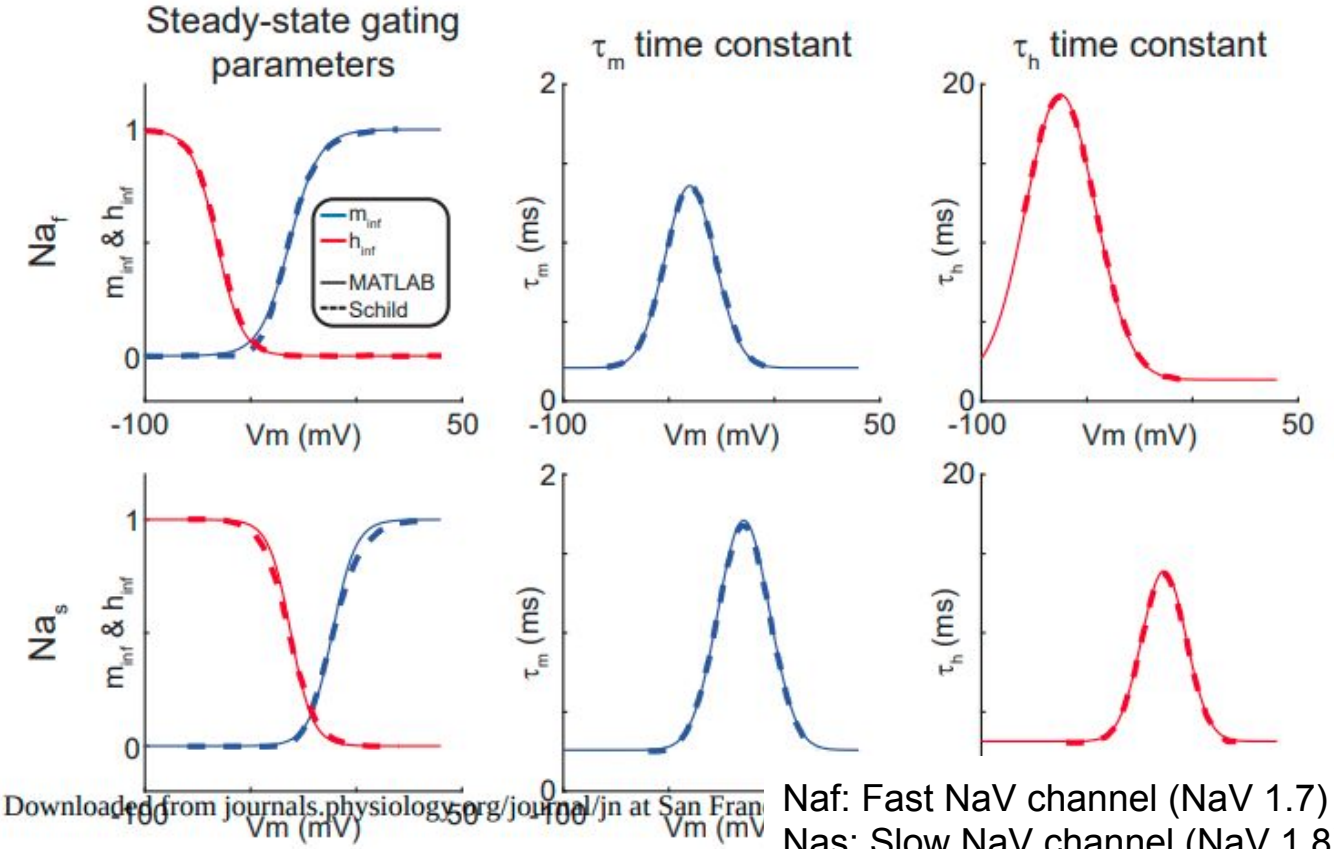
Validation: Mandge et al. 2018



NaV 1.7

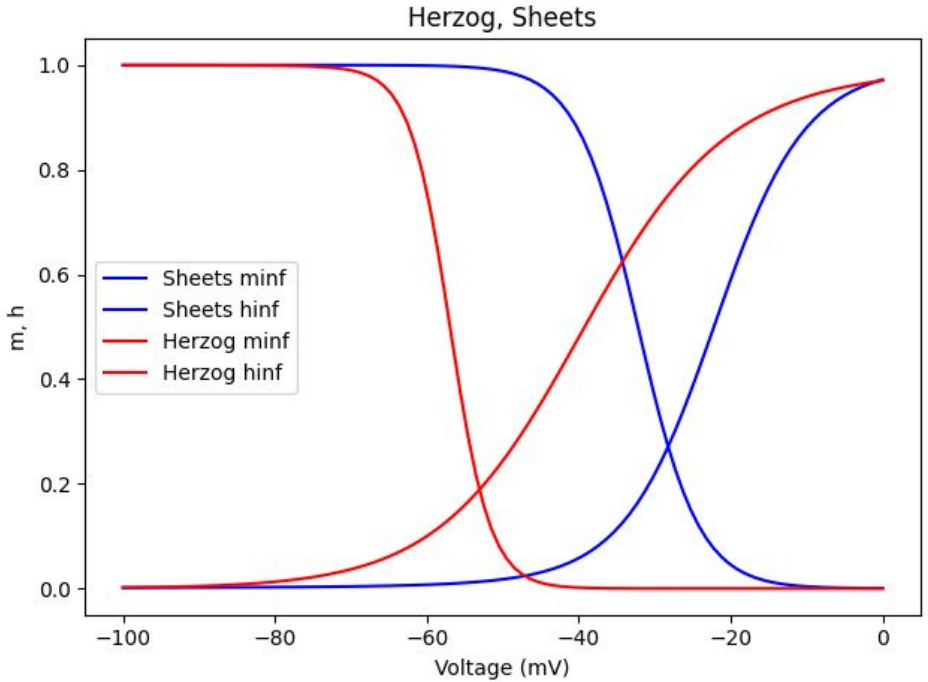
NaV 1.8

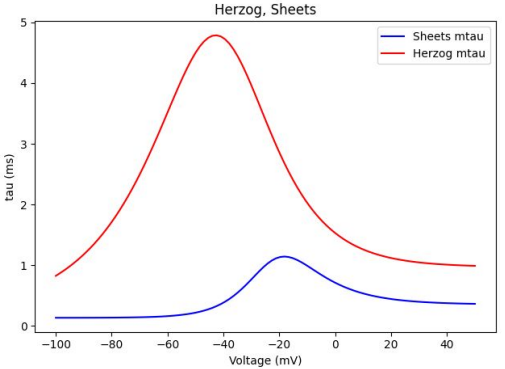
Validation: Pelot et al. 2020

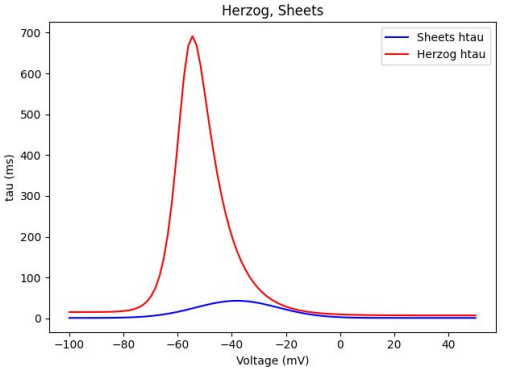


Naf: Fast NaV channel (NaV 1.7)
Nas: Slow NaV channel (NaV 1.8)

Comparison of Herzog, Sheets Na TTX-R Equations

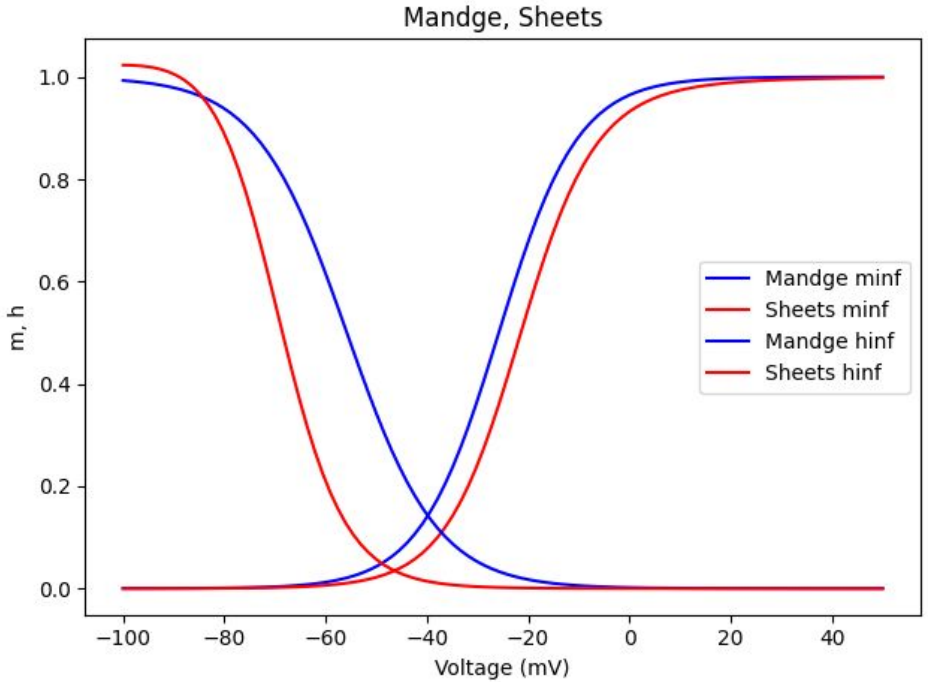


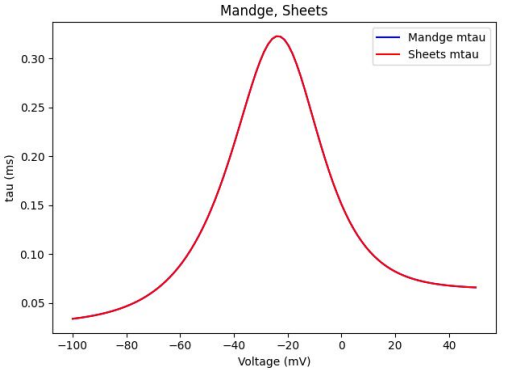


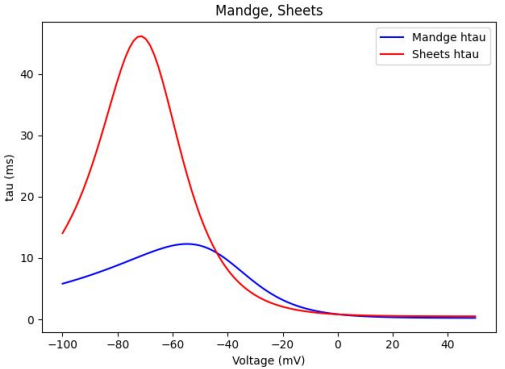


Herzog (R) models Na TTX-R channel with a single activation gate
Sheets (B) models Na TTX-R channel with three activation gates
tau curves for room temperature

Comparison of Mandge, Sheets NaV 1.7 Equations

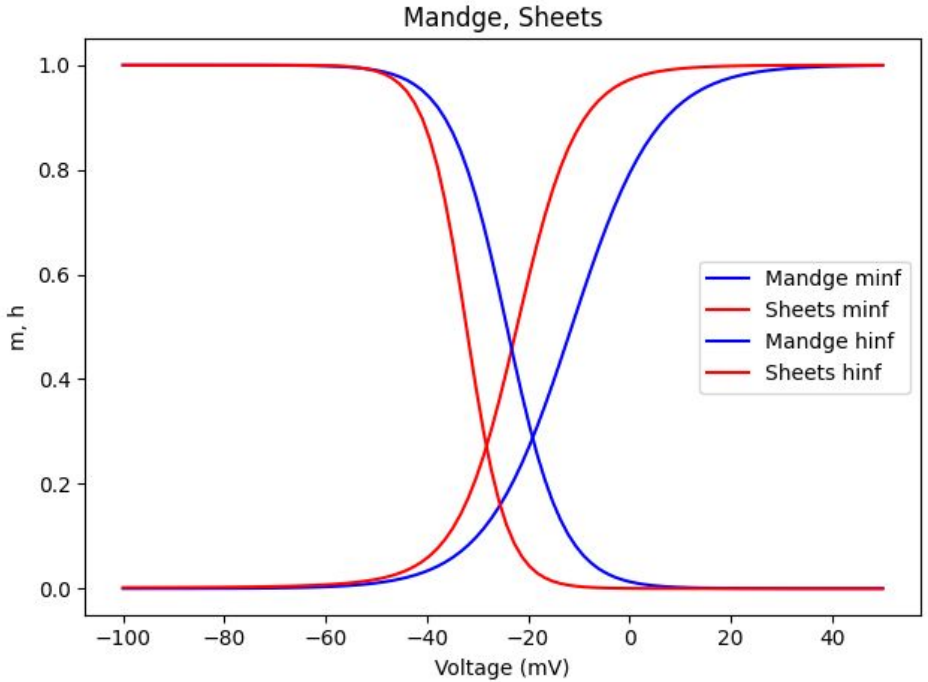


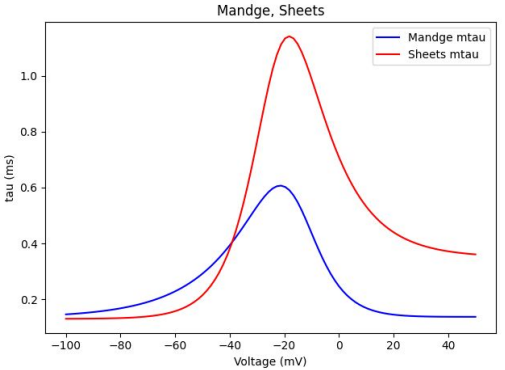


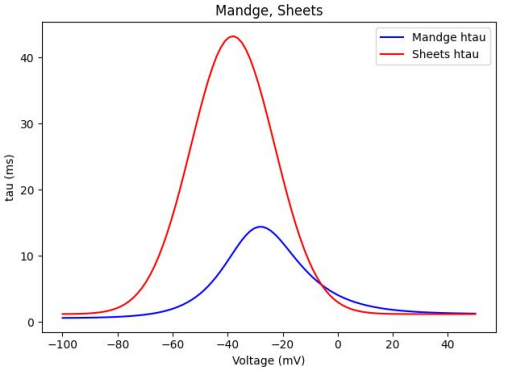


Mandge (B) and Sheets (R) comparison of NaV 1.7

Comparison of Mandge, Sheets NaV 1.8 Equations

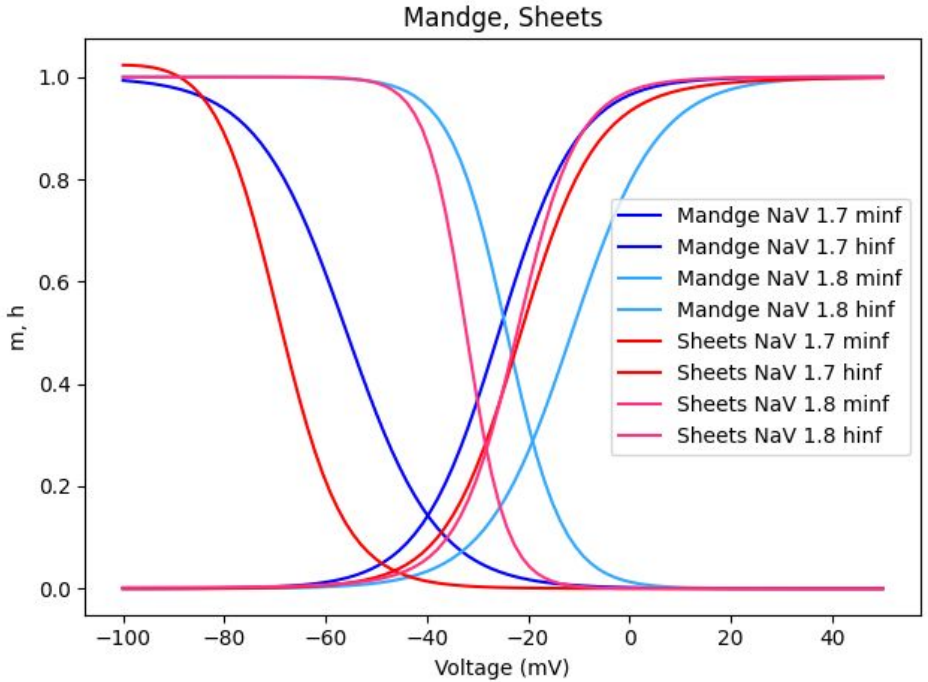


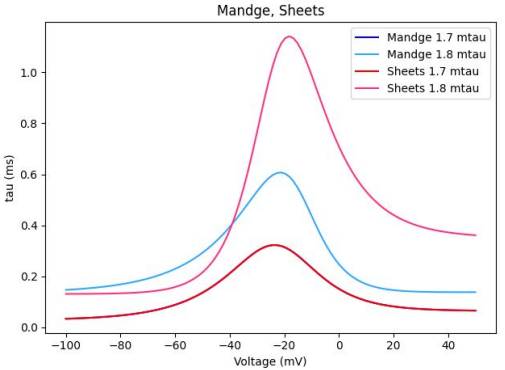


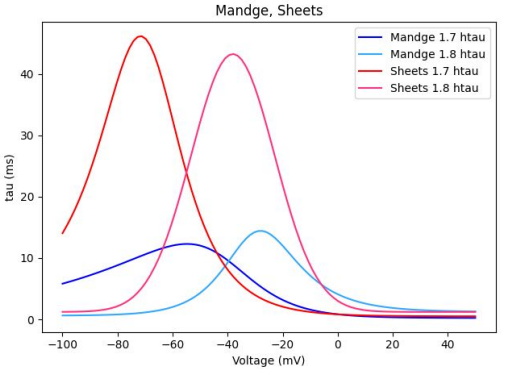


Mandge (B) and Sheets (R) comparison of NaV 1.8

Comparison of Mandge, Sheets NaV 1.8 Equations

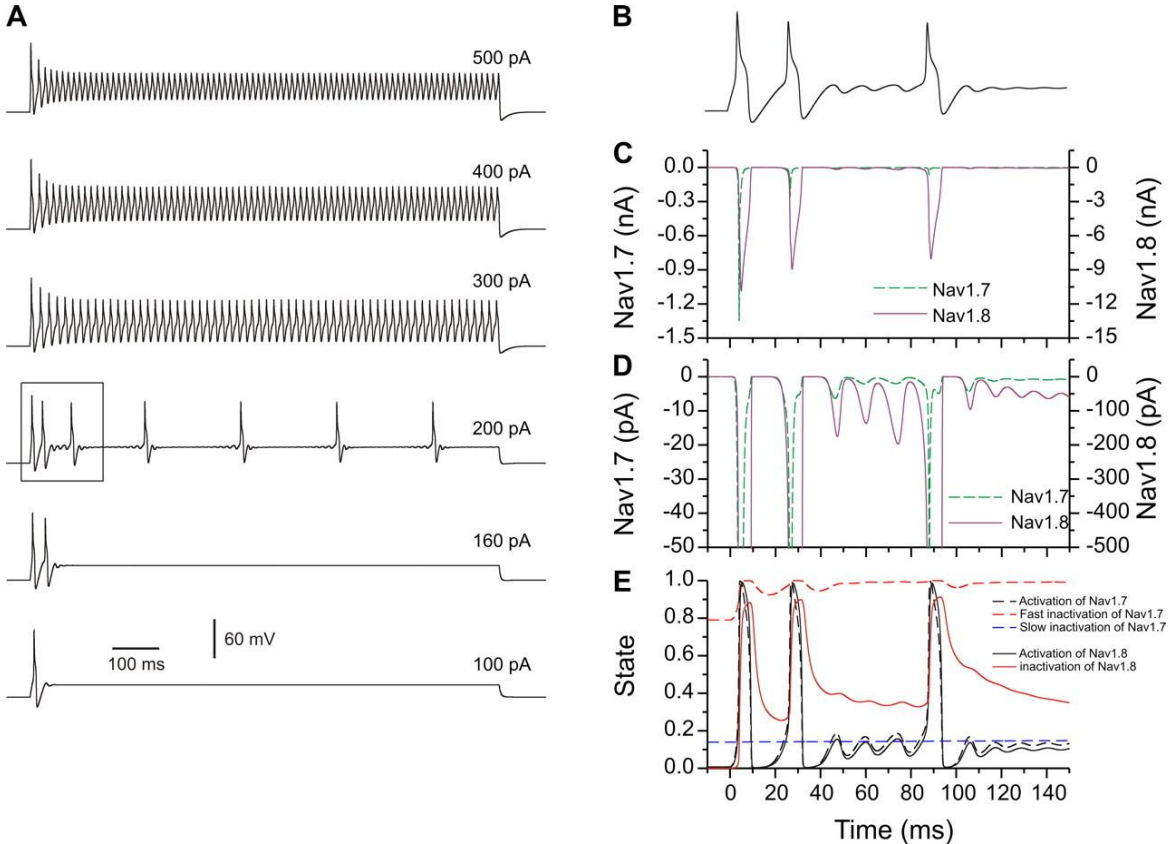




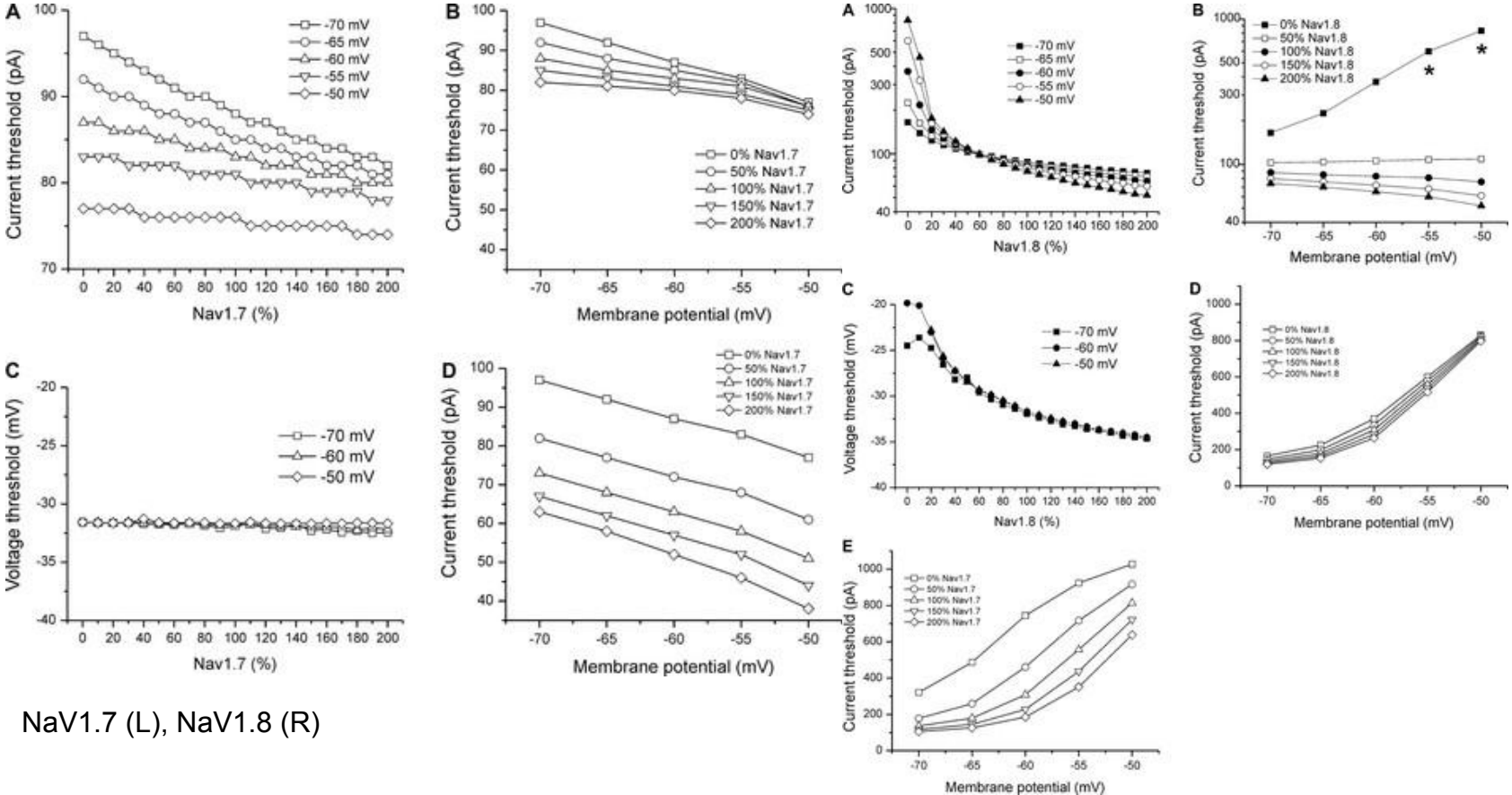


Mandge (B, LB) and Sheets (R, LR) comparison of NaV, combined

NaV 1.7 vs. NaV 1.8 role in repetitive AP



Current Threshold at -50 mV to -60 mV (RMP @ 53.5?)?



NaV1.7 (L), NaV1.8 (R)