**Sodium channels**

**Nav1.1**

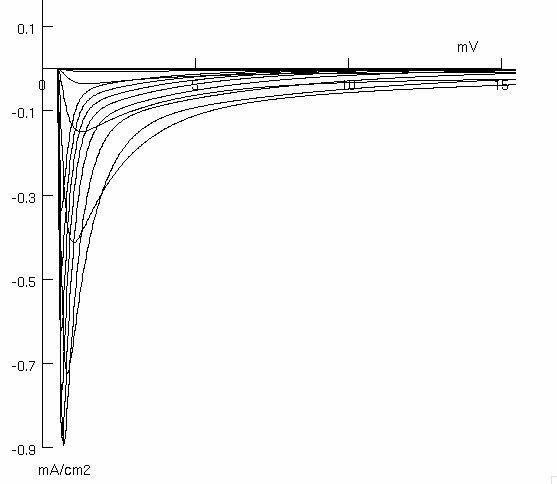
Rhodes et al, 2004

|  |  |  |  |
| --- | --- | --- | --- |
| Parameters | Experimental values | Reference | Simulation values |
| Temperature | not available |  | 22°C (preset value) |
| Sodium reversal potential | ~64 mV | Rhodes et al, 2004 (fig 3a) | 64 mV (preset value) |
| TC HMA of normalized conductance | -23.6 ± 1.2 mV | Rhodes et al, 2004 (Table 1) | -23.0 mV |
| Slope of normalized conductance | 7.4 ± 0.3 | Rhodes et al, 2004 (Table 1) | 7.7 |
| SS HMI of normalised current of fast inactivation | -64.2 ± 1.1 mV | Rhodes et al, 2004 (Table 1) | -63.8 mV |
| Slope of normalized current of fast inactivation | -5.8 ± 0.1 | Rhodes et al, 2004 (Table 1) | -6.0 |
| First time constant of the recovery from fast inactivation | 3.8 ± 0.5 ms | Rhodes et al, 2004 (Table 1) | 3.9 ms |
| Fraction of first recovery from fast inactivation | 83 ± 2 % | Rhodes et al, 2004 (Table 1) | 81 % |
| Second time constant of the recovery from fast inactivation | 96 ± 16 ms | Rhodes et al, 2004 (Table 1) | 102 ms |
| Fraction of second recovery from fast inactivation | 17 ± 2 % | Rhodes et al, 2004 (Table 1) | 18 % |

TC: transient current; SS: steady-state; HMA: half maximal activation; HMI: half maximal inactivation

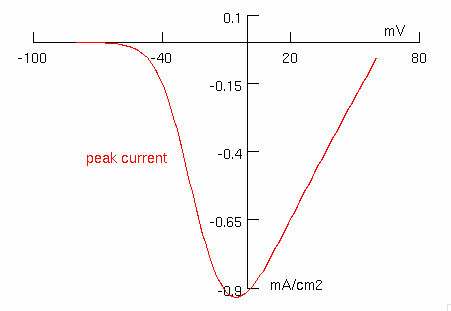
Voltage-clamp: -80 mV to 40 mV in step of 10 mV

see Rhodes et al, 2004, fig 1a



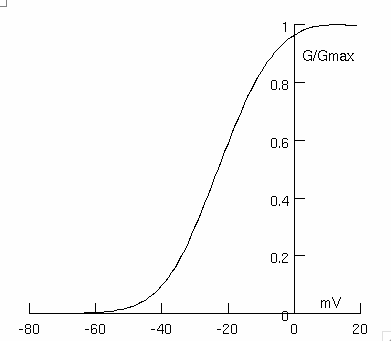
Voltage-current relationship

see Rhodes et al, 2004, fig 3a



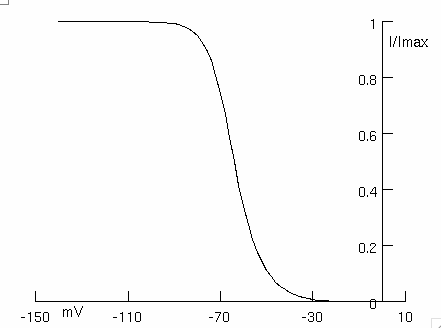
Voltage dependence of the normalised conductance

see Rhodes et al, 2004, fig 3b



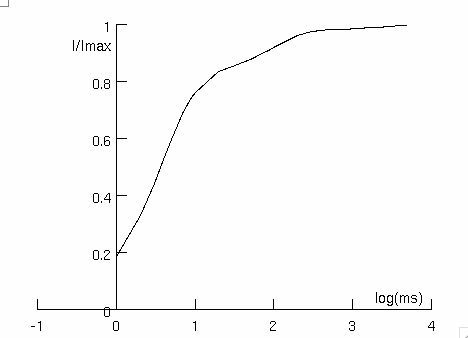
Voltage dependence of normalized current during fast inactivation

see Rhodes et al, 2004, fig 3c



Recovery from fast inactivation

see Rhodes et al, 2004, fig 3d



**Nav1.2**

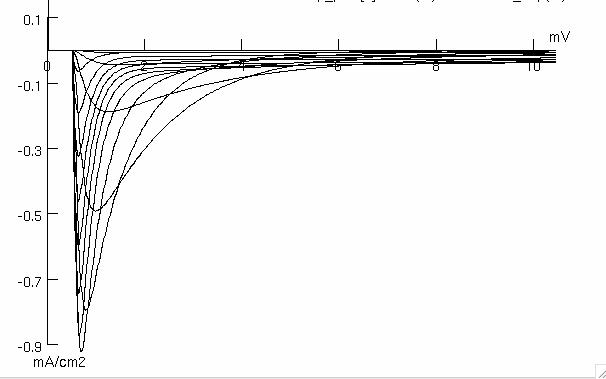
Misra et al, 2008

|  |  |  |  |
| --- | --- | --- | --- |
| Parameters | Experimental values | Reference | Simulation values |
| Temperature | 21-23°C | Misra et al, 2008 (pg 3) | 22°C |
| Sodium reversal potential | 65 mV ? | Misra et al, 2008 (fig 2A) | 65 mV |
| TC HMA (normalized conductance) | -25.3 ± 1.4 mV | Misra et al, 2008 (table 1) | -25.6 mV |
| TC Slope (normalized conductance) | 7.5 ± 0.4 | Misra et al, 2008 (table 1) | 7.4 |
| TC HMI for fast inactivation (normalized current) | -67.4 ± 1.7 mV | Misra et al, 2008 (table 1) | -67.5 mV |
| TC Slope for fast inactivation (normalized current) | 9.1 ± 0.8 | Misra et al, 2008 (table 1) | -8.9 |
| First time constant of the recovery from inactivation | 1.4 ± 0.1 ms | Misra et al, 2008 (table 1) | 1.5 ms |
| Fractional recovery with first time constant | 75 ± 2 % | Misra et al, 2008 (table 1) | 76 % |
| Second time constant of the recovery from inactivation | 53.6 ± 6.9 ms | Misra et al, 2008 (table 1) | 53.6 ms |
| Fractional recovery with second time constant | 24 ± 2 % | Misra et al, 2008 (table 1) | 24 % |

TC: transient current; HMA: half maximal activation; HMI: half maximal inactivation

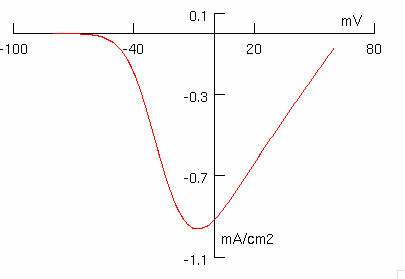
Voltage-clamp: -120 mV to 60 mV in step of 10 mV

see Misra et al, 2008, fig 1B



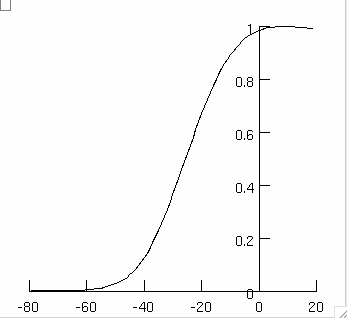
Voltage-current relationship

see Misra et al, 2008, fig 2A



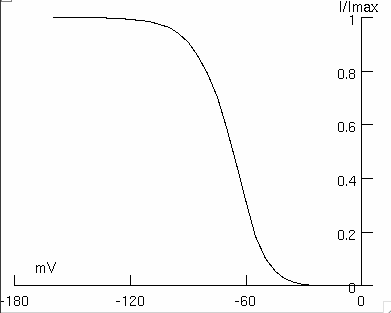
Voltage dependence of the normalised conductance

see Misra et al, 2008, fig 2B



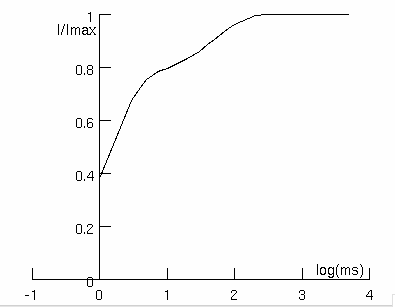
Voltage dependence of normalized current during fast inactivation

see Misra et al, 2008, fig 2C



Recovery from fast inactivation

see Misra et al, 2008, fig 3d



**Nav1.3**

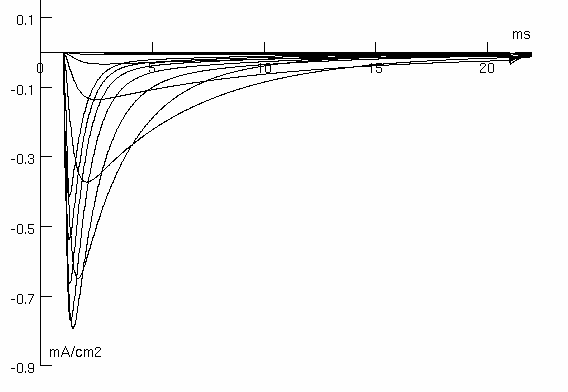
Clare et al, 2000; Cusdin et al, 2010

|  |  |  |  |
| --- | --- | --- | --- |
| Parameters | Experimental values | Reference | Simulation values  (nav13\_p.mod) |
| Temperature | 19°C | Cusdin et al, 2010 (pg 33405) | 19°C (preset value) |
| Sodium reversal potential | not available |  | 64 mV (preset value) |
| TC HMA (normalized conductance) | -24.1 ± 0.9 mV | Cusdin et al, 2010 (table 2) | -24.0 mV |
| TC activation slope (normalized conductance) | 7.8 ± 0.1 | Cusdin et al, 2010 (table 2) | 7.4 |
| SS HMI (normalised current) | -71.9 ± 1 mV | Cusdin et al, 2010 (table 3) | -72.3 mV |
| SS inactivation slope (normalised current) | 7.4 ± 0.3 | Cusdin et al, 2010 (table 3) | -7.7 |
| Time constant of the recovery from inactivation | 13 ± 2 ms | Clare et al, 2000 (fig 2) | 13.5 ms |

TC: transient current; HMA: half maximal activation; HMI: half maximal inactivation

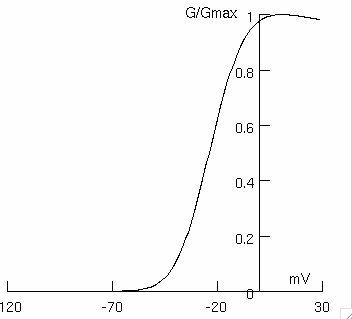
Voltage-clamp: -90 mV to +30 mV in step of 10 mV

see Cusdin et al, 2010, fig 1A



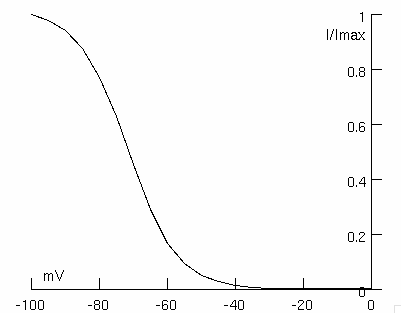
Voltage dependence of the normalised conductance

see Cusdin et al, 2010, fig 1B



Voltage dependence of normalized current after steady-state fast inactivation

see Cusdin et al, 2010, fig 2B



**Nav1.4**

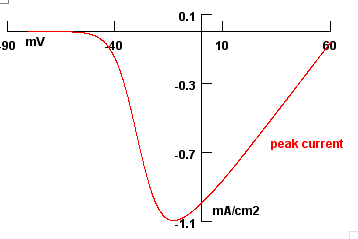
Arnold et al, 2015

|  |  |  |  |
| --- | --- | --- | --- |
| Parameters | Experimental values | Reference | Simulation values |
| Temperature | not available |  | 22°C (preset value) |
| Sodium reversal potential | not available |  | 64 mV (preset value) |
| TC HMA (normalized conductance) | -23.7 ± 1.2 mV | Arnold et al, 2015 (Table 1) | -23.5 mV |
| TC Slope (normalized conductance) | 7.7 ± 0.2 | Arnold et al, 2015 (Table 1) | 7.2 |
| SS HMI for fast inactivation (normalised current) | -75.9 ± 1.6 mV | Arnold et al, 2015 (Table 1) | -76.0 mV |
| SS Slope for fast inactivation (normalized current) | 7.2 ± 0.4 | Arnold et al, 2015 (Table 1) | 6.9 |
| First time constant of the recovery from fast inactivation | 2.3 ± 0.2 ms | Arnold et al, 2015 (Table 1) | 2.5 |
| Percentage of 'fast' recovery | 84 ± 4 % | Arnold et al, 2015 (Table 1) | 82 |
| Second time constant of the recovery from fast inactivation | 113 ± 43 ms | Arnold et al, 2015 (Table 1) | 113 |
| Percentage of 'slow' recovery | 16 ± 4 % | Arnold et al, 2015 (Table 1) | 18 |

TC: transient current; SS: steady-state; HMA: half maximal activation; HMI: half maximal inactivation

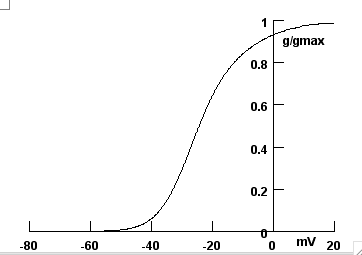
Voltage-current relationship

see Arnold et al, 2015, fig 4A



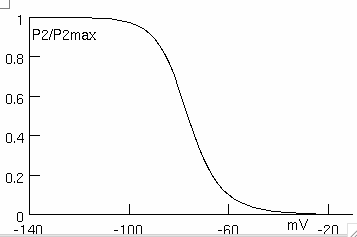
Voltage dependence of the normalised conductance

see Arnold et al, 2015, fig 4B



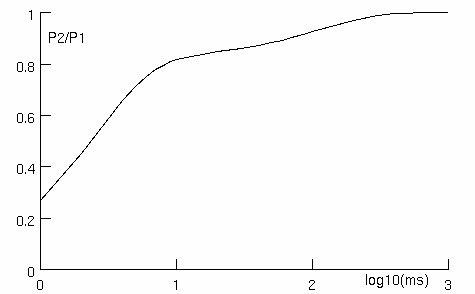
Steady-state availability during fast inactivation

see Arnold et al, 2015, fig 4C



Recovery from fast inactivation

see Arnold et al, 2015, fig 4D



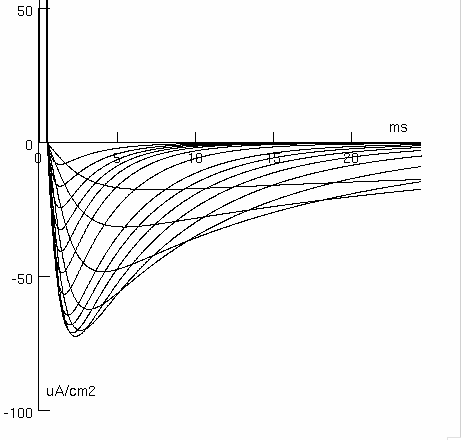
**Nav1.5**

Sheets and Hanck, 1999

|  |  |  |  |
| --- | --- | --- | --- |
| Parameters | Experimental values | Reference | Simulation values |
| Temperature | 12°C | Sheets and Hanck, 1999 (pg 428) | 12°C |
| Sodium reversal potential | not available |  | 60 mV |
| TC HMA (normalized conductance) | -56 ± 5 mV | Sheets and Hanck, 1999 (fig 1) | -50.8 mV |
| TC Slope (normalized conductance) | -6.6 ± 0.7 | Sheets and Hanck, 1999 (fig 1) | -6.0 |
| TC start of activation | ~ 80 mV | Sheets and Hanck, 1999 (Fig 1C) | ~ 80 mV |
| TC peak of activation | -40 mV | Sheets and Hanck, 1999 (pg 428) | -35 mV |
| TC time of peak activation | ~ 3 ms | Sheets and Hanck, 1999 (Fig 1B) | 1.9 ms |

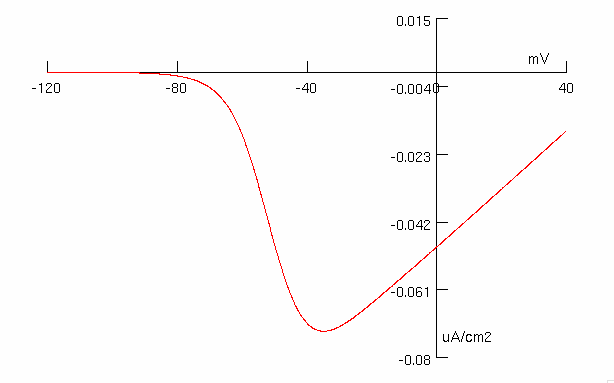
Voltage-clamp: -70 mV to 30 mV in mixed steps

see Sheets and Hanck,1999, fig 1A



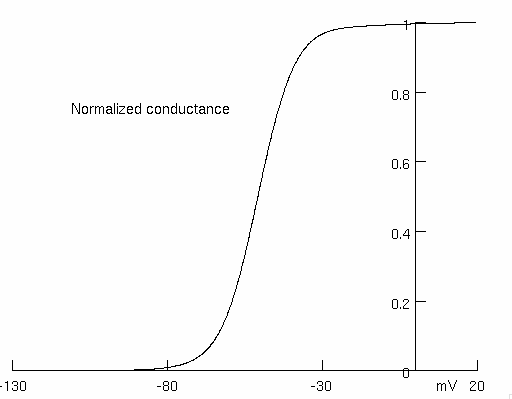
Voltage-current relationship

see Sheets and Hanck,1999, fig 1C



Voltage dependence of the normalised conductance

see Sheets and Hanck,1999, fig 1D



**Nav1.6**

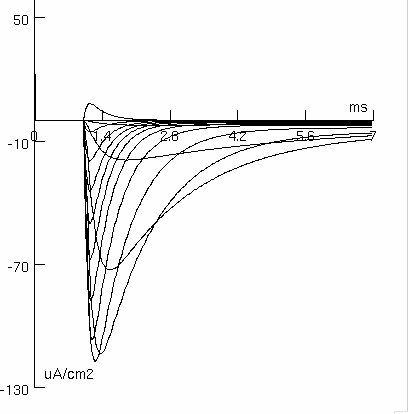
Clare et al, 2000; Burbidge et al, 2002

|  |  |  |  |
| --- | --- | --- | --- |
| Parameters | Experimental values | Reference | Simulation values |
| Temperature | 21-23°C | Burbidge et al, 2002 (pg 82) | 22°C |
| Sodium reversal potential | +64 mV | Burbidge et al, 2002 (pg 85) | +64 mV |
| TC HMA (normalized conductance) | -29.2 ± 1.8 mV | Burbidge et al, 2002 (fig 2D) | -28.9 mV |
| TC Slope (normalized conductance) | 6.0 ± 0.2 | Burbidge et al, 2002 (fig 2D) | -6.51 |
| TC time of peak | < 1 ms | Burbidge et al, 2002 (page 83, fig 2A) | 0.29 ms |
| TC time of (full) inactivation | ~ 10 ms | Burbidge et al, 2002 (pg 83, fig 2A) | ~ 10 ms |
| TC start of activation | ~ -50 mV | Burbidge et al, 2002 (pg 85, fig 2A) | ~ -50 mV |
| TC peak of activation | -10 mV | Burbidge et al, 2002 (pg 85, fig 2A) | -14 mV |
| TC HMI for fast inactivation (normalized current) | -53 ± 2 mV | Burbidge et al, 2002 (fig 3B) | -48.5 mV |
| TC Slope for fast inactivation (normalized current) | 11.6 ± 0.6 | Burbidge et al, 2002 (fig 3B) | 16.8 |
| TC HMI for slow inactivation (normalized current) | -71.6 ± 2 mV | Burbidge et al, 2002 (fig 3B) | -68.8 mV |
| TC Slope for slow inactivation (normalized current) | 6.5 ± 0.3 | Burbidge et al, 2002 (fig 3B) | 8.56 |
| TC time constant of inactivation | 1.08 ± 0.06 ms | Burbidge et al, 2002 (fig 3C) | 1.01 ms  (tau at the peak current of -14 mV) |
| TC time constant of the recovery from inactivation | 12.6 ± 2 ms | Burbidge et al, 2002 (fig 3D) | 11.8 ms |
| Recovery curve asymptote | not available |  | 90.6 % |
| PC duration | > 100 ms | Burbidge et al, 2002 (fig 4A) | > 100 ms |
| PC proportion compared to the peak current | 26 ± 4 % | Burbidge et al, 2002 (pg 85, fig 4C) | 27.4 % |

TC: transient current; HMA: half maximal activation; HMI: half maximal inactivation; PC: persistent current

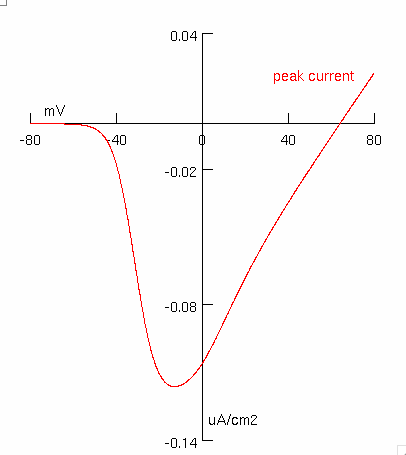
Voltage-clamp: -70 mV to 70 mV in step of 10 mV

see Burbidge et al, 2002, fig 2A



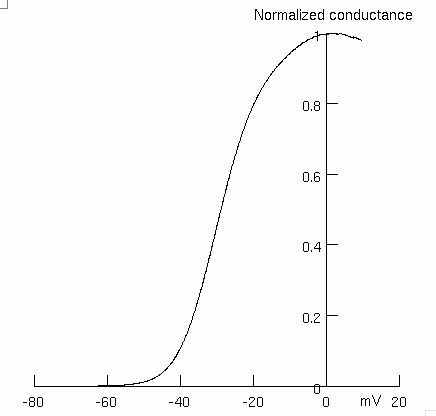
Voltage-current relationship

see Burbidge et al, 2002, fig 2C



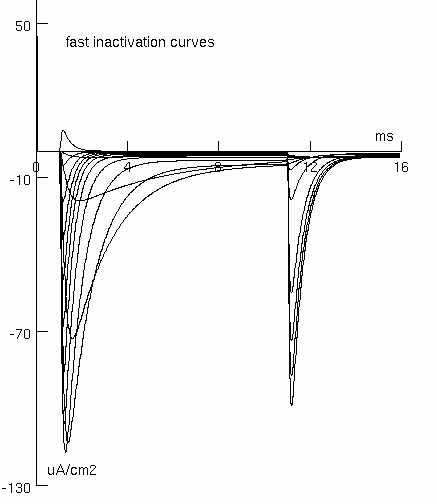
Voltage dependence of the normalised conductance

see Burbidge et al, 2002, fig 2D



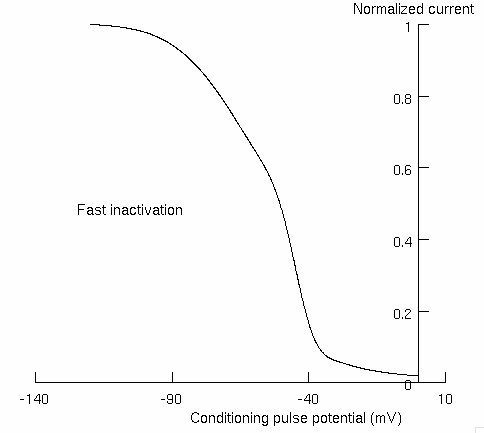
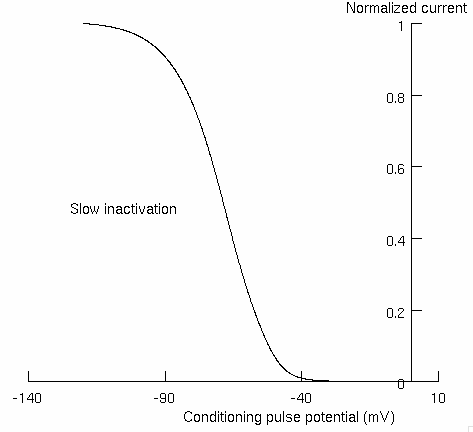
Fast inactivation protocol

see Burbidge et al, 2002, fig 3A



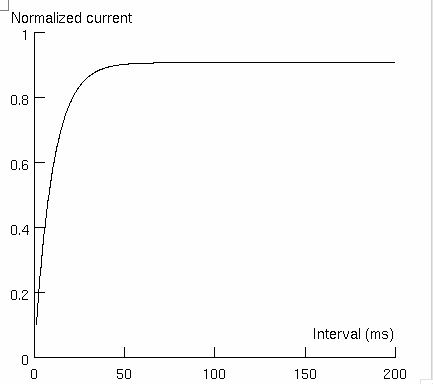
Voltage dependence of normalized current during both fast and slow inactivation

see Burbidge et al, 2002, fig 3B



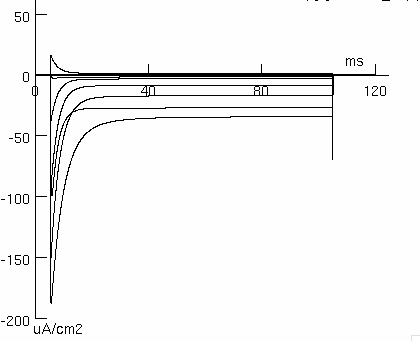
Recovery from inactivation

see Burbidge et al, 2002, fig 3D



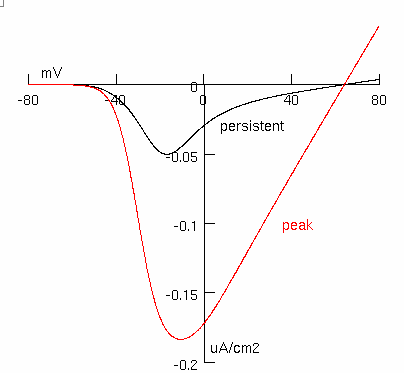
Transient and persistent currents evoked by 100-ms voltage pulses at 20-mV increments

see Burbidge et al, 2002, fig 4A



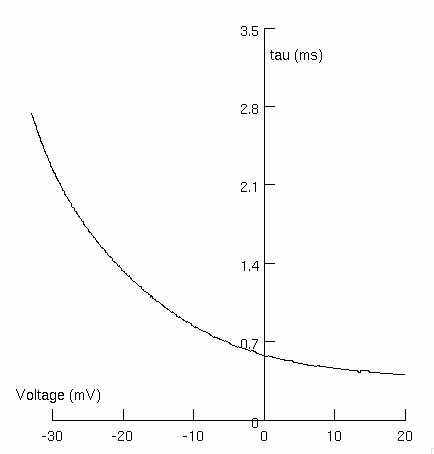
Voltage-current relationships for both transient and persistent currents

see Burbidge et al, 2002, fig 4C



Time constant of inactivation as a function of test pulse potential

see Burbidge et al, 2002, fig 3C



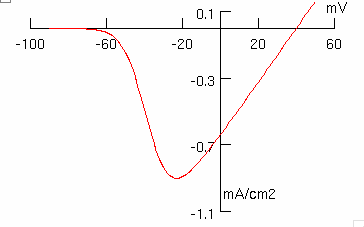
**Nav1.7**

Chatelier et al, 2008

|  |  |  |  |
| --- | --- | --- | --- |
| Parameters | Experimental values [[1]](#footnote-1) | Reference | Simulation values |
| Temperature | ~ 22°C | Chatelier et al, 2008, pg 2243 | 22°C |
| Sodium reversal potential | ~ +40 mV | Chatelier et al, 2008, fig 2A | +40 mV |
| TC HMA (normalized conductance) | -36.15 ± 1.23 mV | Chatelier et al, 2008, table 1 | -36.51 mV |
| TC Slope (normalized conductance) | -6.66 ± 0.34 | Chatelier et al, 2008, table 1 | -6.67 |
| TC HMI for fast inactivation (normalized current) | -93.60 ± 1.26 mV | Chatelier et al, 2008, table 1 | -93.34 mV |
| TC Slope for fast inactivation (normalized current) | 4.94 ± 0.24 | Chatelier et al, 2008, table 1 | 4.54 |
| TC time constant of the recovery from inactivation | 9.54 ± 2.00 ms | Chatelier et al, 2008, table 1 | 9.82 |

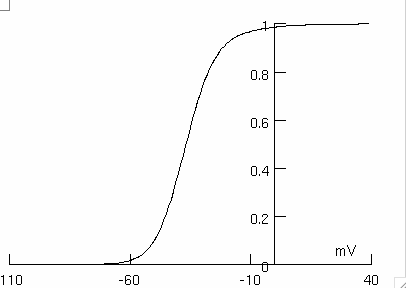
Voltage-current relationship

see Chatelier et al, 2008, fig. 2A



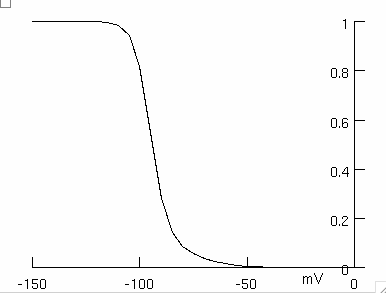
Voltage dependence of the normalised conductance

see Chatelier et al, 2008, fig. 2B



Voltage dependence of normalized current during fast inactivation

see Chatelier et al, 2008, fig. 2C



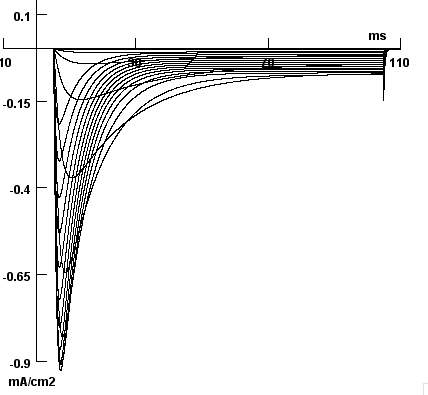
**Nav1.8**

Huang et al, 2013

|  |  |  |  |
| --- | --- | --- | --- |
| Parameters | Experimental values | Reference | Simulation values |
| Temperature | ~ 22°C | Huang et al, 2013 (pg 14088) | 22°C |
| Sodium reversal potential | +65.3 ± 1.1 mV | Huang et al, 2013 (table 1) | +65 mV |
| HMA (normalized conductance) | -1.11 ± 1.6 mV | Huang et al, 2013 (table 1) | 0.98 mV |
| Slope (normalized conductance) | -8.77 ± 0.45 | Huang et al, 2013 (table 1) | -7.80 |
| SS HMI for fast inactivation (normalized current) | -29.9 ± 1.2 mV | Huang et al, 2013 (table 1) | -30.8 mV |
| SS Slope for fast inactivation (normalized current) | 6.33 ± 0.30 | Huang et al, 2013 (table 1) | -6.4 |
| Percentage of non-inactivating channels | 6.58 ± 0.43 % | Huang et al, 2013 (table 1) | 7.62 % |
| TC time constant of the recovery from inactivation (-70 mV) | ~ 4 ms | Huang et al, 2013 (fig. 3E) | 4.08 ms |
| TC time constant of the recovery from inactivation (-50 mV) | ~ 11 ms | Huang et al, 2013 (fig. 3D) | 10.36 ms |

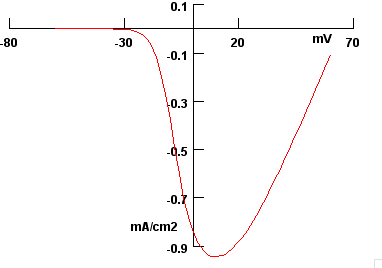
Voltage-clamp: -60 mV to 60 mV in step of 10 mV

see Huang et al, 2013, fig 2A



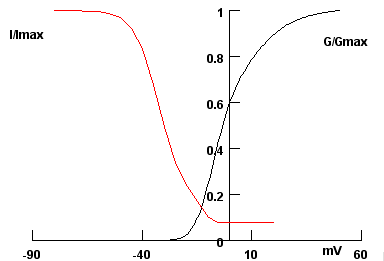
Voltage-current relationship

see Huang et al, 2013, fig 2C



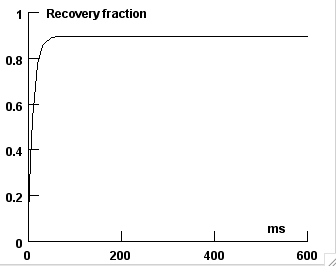
Voltage dependence of normalized conductance and normalized current during activation and inactivation, respectively

see Huang et al, 2013, fig 2D



Recovery from inactivation

see Huang et al, 2013, fig 2E



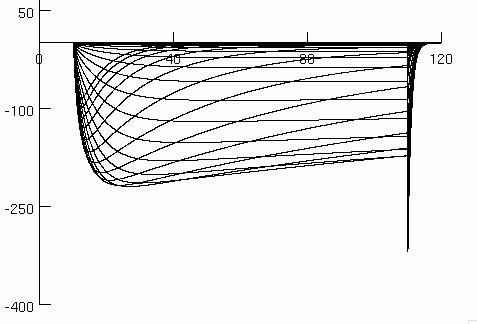
**Nav1.9**

Han et al, 2015

|  |  |  |  |
| --- | --- | --- | --- |
| Parameters | Experimental values | Reference | Simulation values |
| Temperature | 22°C | Han et al, 2015 (pg 160) | 22°C |
| Sodium reversal potential | not available |  | 60 mV |
| TC HMA (normalized conductance) | -50.0 ± 1.5 mV | Han et al, 2015 (pg 162) | -50.9 mV |
| TC Slope (normalized conductance) | -8.4 ± 0.3 | Han et al, 2015 (pg 162) | -9.6  x0=-45 |
| TC HMI for fast inactivation (normalized current) | -42 ± 1.1 mV | Han et al, 2015 (pg 162) | -45.1 mV |
| TC Slope for fast inactivation (normalized current) | 10.3 ± 0.3 | Han et al, 2015 (pg 162) | 10.9  (x0=-55 mV) |

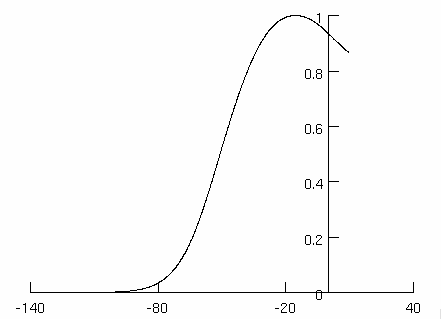
Current-voltage curves during voltage-clamp

see Han et al, 2015, fig 2A



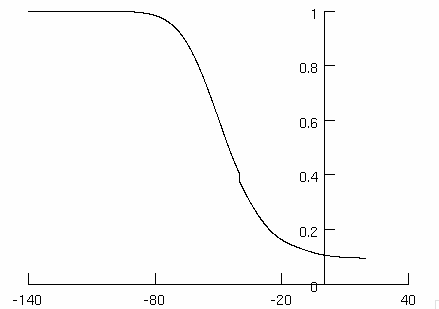
Voltage dependence of the normalised conductance

see Han et al, 2015, fig 2C



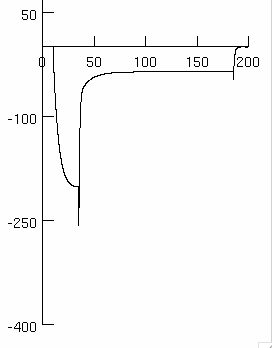
Voltage dependence of normalized current during fast inactivation

see Han et al, 2015, fig 2C



Tail current following repolarization at -70 mV

see Han et al, 2015, fig 3A inset



**Potassium channels**

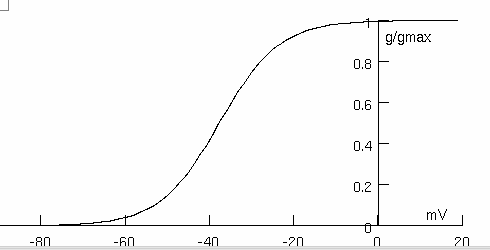
**mKv1.1**

Hopkins et al, 1994

|  |  |  |  |
| --- | --- | --- | --- |
| Parameters | Experimental values | Reference | Simulation values |
| Temperature | 22°C | Hopkins et al. 1994 (pg 383) | 22°C |
| Potassium reversal potential | not available |  | -77 mV |
| TC HMA (normalized conductance) | -37 ± 2 mV | Hopkins et al. 1994 (Table 1) | -37.6 mV |
| TC Slope (normalized conductance) | 6.1 ± 0.3 | Hopkins et al. 1994 (Table 1) | -7.1 |
| Prepulse inactivation V1/2 | -49 ± 1 mV | Hopkins et al. 1994 (Table 1) | -48.8 mV |
| Prepulse inactivation slope | 4.0 ± 0.3 | Hopkins et al. 1994 (Table 1) | 5.6 |
| Prepulse inactivation fraction | 0.64 ± 0.03 | Hopkins et al. 1994 (Table 1) | 0.64 |
| Time constant of inactivation onset | 2484 ± 300 ms | Hopkins et al. 1994 (Table 1) | not performed |
| Time constant of the recovery from inactivation | 3304 ± 10 ms | Hopkins et al. 1994 (Table 1) | 3350 ms |

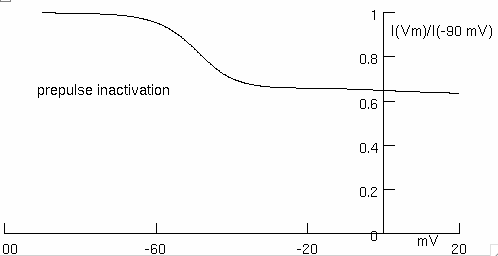
Voltage dependence of the normalised conductance

see Hopkins et al, 1994, fig 1B



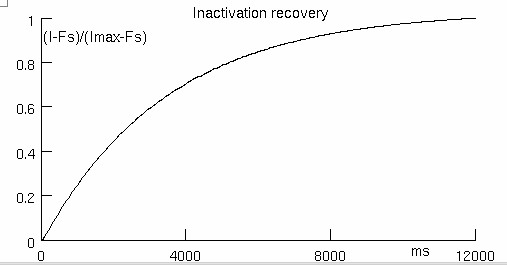
Voltage dependence of normalized current during inactivation

see Hopkins et al, 1994, fig 2B



Recovery from inactivation

see Hopkins et al, 1994, fig 3B



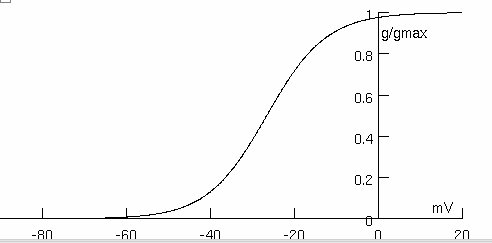
**mKv1.2**

Hopkins et al, 1994

|  |  |  |  |
| --- | --- | --- | --- |
| Parameters | Experimental values | Reference | Simulation values |
| Temperature | 22°C | Hopkins et al. 1994 (pg 383) | 22°C |
| Potassium reversal potential | not available |  | -77 mV |
| TC HMA (normalized conductance) | -27 ± 1 mV | Hopkins et al. 1994 (Table 1) | -26.6 mV |
| TC Slope (normalized conductance) | 5.9 ± 0.2 | Hopkins et al. 1994 (Table 1) | -7.1 |
| Prepulse inactivation V1/2 | -37 ± 1 mV | Hopkins et al. 1994 (Table 1) | -36.8 mV |
| Prepulse inactivation slope | 4.5 ± 0.2 | Hopkins et al. 1994 (Table 1) | 5.8 |
| Prepulse inactivation fraction | 0.55 ± 0.03 | Hopkins et al. 1994 (Table 1) | 0.55 |
| Time constant of inactivation onset | 3559 ± 272 ms  131 ± 10 ms | Hopkins et al. 1994 (Table 1) | not performed |
| Time constant of the recovery from inactivation | 2400 ± 272 ms  314 ± 222 ms | Hopkins et al. 1994 (Table 1) | 2250 ms |

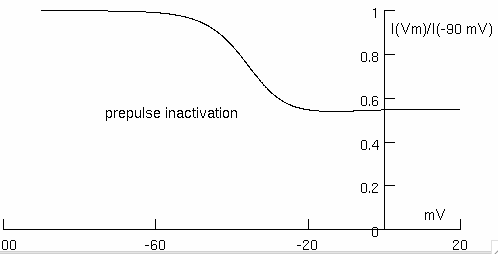
Voltage dependence of the normalised conductance

see Hopkins et al, 1994, fig 1B



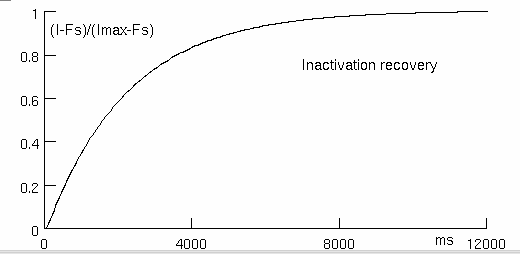
Voltage dependence of normalized current during inactivation

see Hopkins et al, 1994, fig 2B



Recovery from inactivation

see Hopkins et al, 1994, fig 3B



References

Arnold WD, Feldman DH, Ramirez S, He L, Kassar D, Quick A, Klassen TL, Lara M, Nguyen J, Kissel JT, Lossin C, Maselli RA. Defective fast inactivation recovery of Nav 1.4 in congenital myasthenic syndrome. Ann Neurol. 2015 May;77(5):840-50.

Burbidge SA, Daleb TJ, Powell AJ, Whitaker WRJ, Xie XM, Romanos MA, Clare JJ. Molecular cloning, distribution and functional analysis of the Nav 1.6 voltage-gated sodium channel from human brain. Molecular Brain Research 103 (2002) 80–90

Chatelier A, Dahllund L, Eriksson A, Krupp J, Chahine M. Biophysical properties of human Nav1.7 splice variante and their regulation by protein kinase A. J Neurophysiol 2008, 99: 2241-2250.

Clare JJ, Tate SN, Nobbs M, Romanos MA. Voltage-gated sodium channels as therapeutic targets. Drug Discov Today 2000 Nov 1; 5(11): 506-520.

Cusdin FS, Nietlispach D, Maman J, Dale TJ, Powell AJ, Clare JJ, Jackson AP. The sodium channel β3-subunit induces multiphasic gating in Nav1.3 and affects fast inactivation via distinct intracellular regions. J Biol Chem. 2010 Oct 22;285(43):33404-12.

Han C, Yang Y, de Greef BT, Hoeijmakers JG, Gerrits MM, Verhamme C, Qu J, Lauria G, Merkies IS, Faber CG, Dib-Hajj SD, Waxman SG. The Domain II S4-S5 Linker in Nav1.9: A Missense Mutation Enhances Activation, Impairs Fast Inactivation, and Produces Human Painful Neuropathy. Neuromolecular Med. 2015 Jun;17(2):158-69.

Hopkins WF, Allen ML, Houamed KM, Tempel BL. Properties of voltage-gated K+ currents expressed in Xenopus oocytes by mKv1.1, mKv1.2 and their heteromultimers as revealed by mutagenesis of the dendrotoxin-binding site in mKv1.1. Pflügers Arch (1994) 428: 382-390.

Huang J, Yang Y, Zhao P, Gerrits MM, Hoeijmakers JG, Bekelaar K, Merkies IS, Faber CG, Dib-Hajj SD, Waxman SG. Small-fiber neuropathy Nav1.8 mutation shifts activation to hyperpolarized potentials and increases excitability of dorsal root ganglion neurons. J Neurosci. 2013 Aug 28;33(35):14087-97.

Misra SN, Kahlig KM, George AL. Impaired Nav1.2 Function and reduced cell surface expression in benign familial neonatal-infantile seizures. Epilepsia 2008 Sep, 49 (9): 1535-1545.

Rhodes TH, Lossin C, Vanoye CG, Wang DW, George AL. Noninactivating voltage-gated sodium channels in severe myoclonic epilepsy of infancy. Proc Natl Acad Sci U S A. 2004 Jul 27; 101(30): 11147-52.

Sheets MF, Hanck DA. Gating of skeletal and cardiac muscle sodium channels in mammalian cells. J Physiol (1999) 514.2: 425-436.

Xie X, Dale TJ, John VH, Cater HL, Peakman TC, Clare JJ. Electrophysiological and pharmacological properties of the human brain type IIA Na+ channel expressed in a stable mammalian cell line. Pflügers Arch - Eur J Physiol (2001) 441: 425-433

Balbi P et al, Aprile 2016

1. Data from the 5N11S splice variant. [↑](#footnote-ref-1)