Supplemental data

1. Voltage-gated ion channel models

The equation for the voltage-gated ion channel's steady-state and their time constants are stated below. The time constant were converted from room temperature (20 °C) to body temperature (37 °C) by the Q12 factor (see table below). The Q10 values were adopted from the Tigerholm et al study (2012)

	Q10 factor
Sodium channels	2.5
Potassium channel	3.3
HCN	3

G_{Max}: the maximum conductance of for each channel and are presented in table 2 in the paper.
E_{Na}: 70 mV (reversal potential of sodium)
E_K: -82 mV (reversal potential of potassium)
V: membrane potential

Aδ model
All the ion channel models were adopted from the Tigerholm et. al. study (2012).
1. Na_{TTXs}

$$I_{NaTTXs} = G_{Max} m^3 hs(V - E_{Na})$$

$$a_m = \frac{15.5}{1 + e^{\frac{V-15}{-12.08}}}$$

$$b_m = \frac{35.2}{1 + e^{\frac{V+62.7}{16.7}}}$$

$$t_m = \frac{1}{a_m + b_m}$$

$$m_{inf} = \frac{a_m}{a_m + b_m}$$

$$a_h = \frac{0.38685}{1 + e^{\frac{v+132.35}{15.29}}}$$

$$b_h = -0.00283 + \frac{2.00283}{1 + e^{\frac{V-4.4739}{-12.70195}}}$$

$$t_h = \frac{1}{a_h + b_h}$$

$$h_{inf} = \frac{a_h}{a_h + b_h}$$

$$a_s = 0.00003 + \frac{0.00092}{1 + e^{\frac{V+83.9}{16.6}}}$$

$$b_s = 132.05 - \frac{132.05}{1 + e^{\frac{V-394.9}{28.5}}}$$

$$t_s = \frac{1}{a_s + b_s}$$
$$s_{inf} = \frac{a_s}{a_s + b_s}$$

2. Na_{TTXr}:

$$I_{NaTTXr} = G_{Max} m^3 hsu(V - E_{Na})$$
$$a_m = 2.85 - \frac{2.839}{1 + e^{\frac{V-1.159}{13.95}}}$$
$$b_m = \frac{7.6205}{1 + e^{\frac{V+46.463}{8.8289}}}$$
$$t_m = \frac{1}{a_m + b_m}$$
$$m_{inf} = \frac{a_m}{a_m + b_m}$$
$$t_h = (1.218 + 42.043e^{\frac{-(V+38.1)^2}{461.47}})$$
$$h_{inf} = \frac{1}{1 + e^{\frac{V+32.2}{4}}}$$
$$s_{inf} = \frac{1}{1 + e^{\frac{V+45}{8}}}$$
$$a_s = \frac{0.0054203}{1 + e^{\frac{V+79.816}{16.269}}}$$
$$b_s = \frac{0.0050757}{1 + e^{-\frac{V+15.968}{11.542}}}$$
$$t_s = \frac{1}{a_s + b_s}$$
$$u_{inf} = \frac{1}{1 + e^{\frac{V+51}{8}}}$$
$$a_u = \frac{0.00040868}{1 + e^{\frac{V+67.499}{19.51}}}$$
$$b_u = \frac{0.00039904}{1 + e^{-\frac{V+30.963}{14.792}}}$$
$$t_u = \frac{1}{a_u + b_u}$$

3. Na_P:

$$I_{NaP} = G_{Max} mhs(V - E_{Na})$$
$$a_m = \frac{1.032}{1 + e^{\frac{V+6.99}{-14.87155}}}$$
$$b_m = \frac{5.79}{1 + e^{\frac{V+130.4}{22.9}}}$$
$$t_m = \frac{1}{a_m + b_m}$$

$$m_{inf} = \frac{a_m}{a_m + b_m}$$
$$a_h = \frac{0.06435}{1 + e^{\frac{V+73.26415}{3.71928}}}$$
$$b_h = \frac{0.13496}{1 + e^{\frac{V+10.27853}{-9.09334}}}$$
$$t_h = \frac{1}{a_m + b_m}$$
$$h_{inf} = \frac{a_m}{a_m + b_m}$$
$$a_s = 0.00000016e^{-\frac{V}{12}}$$
$$b_s = \frac{0.0005}{1 + e^{-\frac{V+32}{23}}}$$
$$t_s = \frac{1}{a_m + b_m}$$
$$s_{inf} = \frac{a_m}{a_m + b_m}$$

4. HCN:

$$I_{NaHCN} = G_{Max}0.5(0.5ns + 0.5nf)(V - E_{Na})$$
$$I_{KHCN} = G_{Max}0.5(0.5ns + 0.5nf)(V - E_K)$$
$$ns_{inf} = \frac{1}{1 + e^{\frac{V+87.2}{9.7}}}$$
$$nf_{inf} = \frac{1}{1 + e^{\frac{V+87.2}{9.7}}}$$
$$t_{ns} = 300 + 542e^{\frac{V+25}{-20}} \quad if\ V \geq -70$$
$$t_{ns} = 2500 + 100e^{\frac{V+240}{50}} \quad if\ V < -70$$
$$t_{nf} = 140 + 50e^{\frac{V+25}{-20}} \quad if\ V \geq -70$$
$$t_{nf} = 250 + 12e^{\frac{V+240}{50}} \quad if\ V < -70$$

5. K_{Dr}:

$$I_{KDr} = G_{Max}n^4(V - E_K)$$
$$n_{inf} = \frac{1}{1 + e^{\frac{V+40}{-15.4}}}$$
$$t_n = 0.16 + 0.8e^{-0.0267(V+11)} \quad if\ V \geq -31$$
$$t_n = 1000\left(0.000688 + \frac{1}{e^{\frac{V+75.2}{6.5}}} + e^{\frac{V-131.5}{-34.8}}\right) if\ V < -31$$

7. K_M:

$$I_{KM} = G_{Max}(0.25ns + 0.75nf)(V - E_K)$$
$$ns_{inf} = \frac{1}{1 + e^{\frac{-(V+30)}{6}}}$$
$$nf_{inf} = \frac{1}{1 + e^{\frac{-(V+30)}{6}}}$$
$$t_{ns} = 13(V + 1000)\ if\ V \geq -60$$
$$t_{ns} = 219\ if\ V < -60$$
$$a_{nf} = 0.00395e^{\frac{V+30}{40}}$$
$$b_{nf} = 0.00395e^{-\frac{V+30}{20}}$$
$$t_{nf} = \frac{1}{a_{nf} + b_{nf}}$$

Aβ model

1. Na_{TTXs}:

The dynamic properties of Na_{TTXs}: was adopted from Watanabe et. al. study (2002). This current consists of the sodium subunit Nav1.6.

$$I_{NaTTXs} = G_{Max}m^3hs(V - E_{Na})$$
$$m_{inf} = \frac{a_m}{a_m + b_m}$$

$$a_m = \frac{0.4(V+22)}{1-e^{-\frac{V+22}{7.2}}}$$ if abs(v+22) > 1e-6) else a_m=2.88

$$b_m = \frac{0.124(-V-22)}{1-e^{\frac{V+22}{7.2}}}$$ if abs(v-22) > 1e-6) else b_m=0.8928

$$h_{inf} = \frac{1}{1 + e^{\frac{V+50}{4}}}$$
$$s_{inf} = \frac{1}{1 + e^{\frac{V+50}{2}}}$$
$$t_m = \frac{1}{a_m+b_m}$$ if $t_m > 0.02$ else $t_m = 0.02$

$$a_h = \frac{0.03(V+45)}{1-e^{-\frac{V+45}{1.5}}}$$ if abs(v+45) > 1e-6) else a_m= 0.0450
$$b_h = \frac{-0.01(V+45)}{1-e^{\frac{V+45}{1.5}}}$$ if abs(v-45) > 1e-6) else b_m= 0.0150
$$t_h = \frac{1}{a_h+b_h}$$ if $t_h > 0.5$ else $t_h = 0.5$
$$t_s = \frac{e^{0.0996(V+52)}}{0.003(1+e^{\ 0.4982(V+52)})}$$ if $t_s > 10$ else $t_s = 10$

2. Na_P:

The dynamic properties of $Na_{P:}$ was adopted from Jankelowitz, et. al. study (2007

$$I_{NaP} = G_{Max} m^3 (V - E_{Na})$$
$$a_m = 1.741 \frac{V + 36.5}{1 - e^{\frac{-36.5 - V}{10.3}}}$$
$$b_m = 0.0805 \frac{-40.8 - V}{1 - e^{\frac{40.8 + V}{9.16}}}$$
$$t_m = \frac{1}{a_m + b_m}$$
$$m_{inf} = \frac{a_m}{a_m + b_m}$$

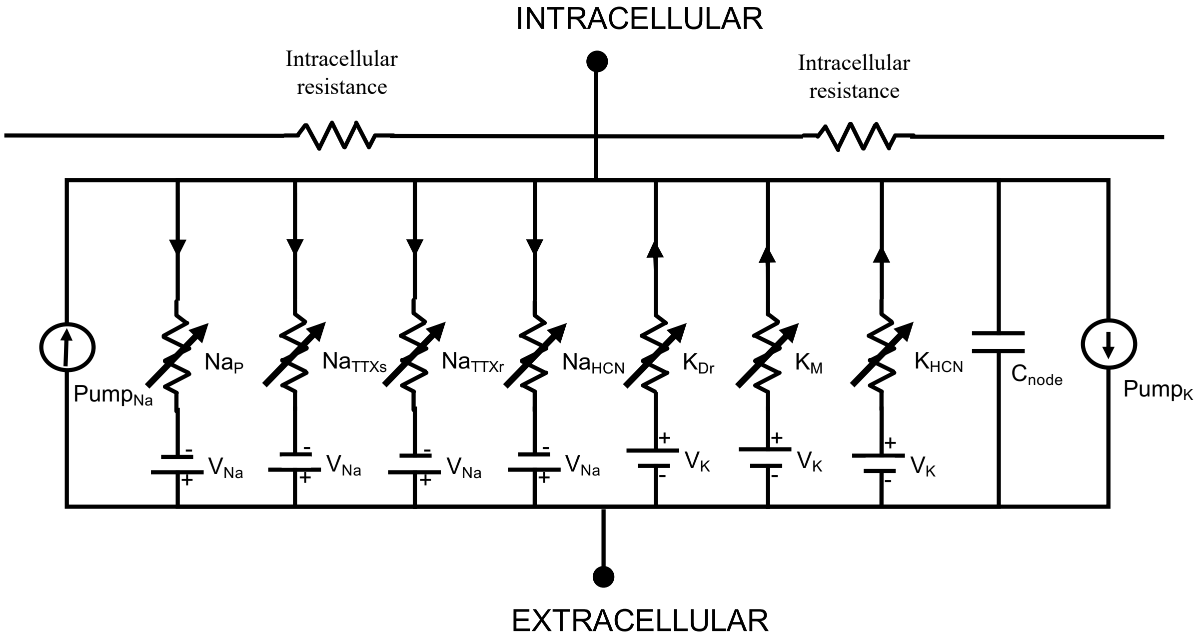
3.HCN: The dynamic equations are the same as for the Aδ model
4.K_{Dr}: The dynamic equations are the same as for the Aδ model
5.K_M: The dynamic equations are the same as for the Aδ model

2. Equivalent electrical circuit

Both of the nerve fiber models are based on the previous published model by Tigerholm et. al. (2014). In the Tigerholm model the two ionic currents, potassium and sodium, are balanced individual to generate a specific resting potential. The sum of all the current when the membrane potential is the resting potential is equal to either a sodium pump or a potassium pump. The HCN current mediate both a sodium and a potassium current and is therefore divided as two resistors in the equivalent circuit scheme.

2.1Aδ model

The Aδ model is an unmyelinated axon model and the equivalent circuit for one compartment are show in the figure below.

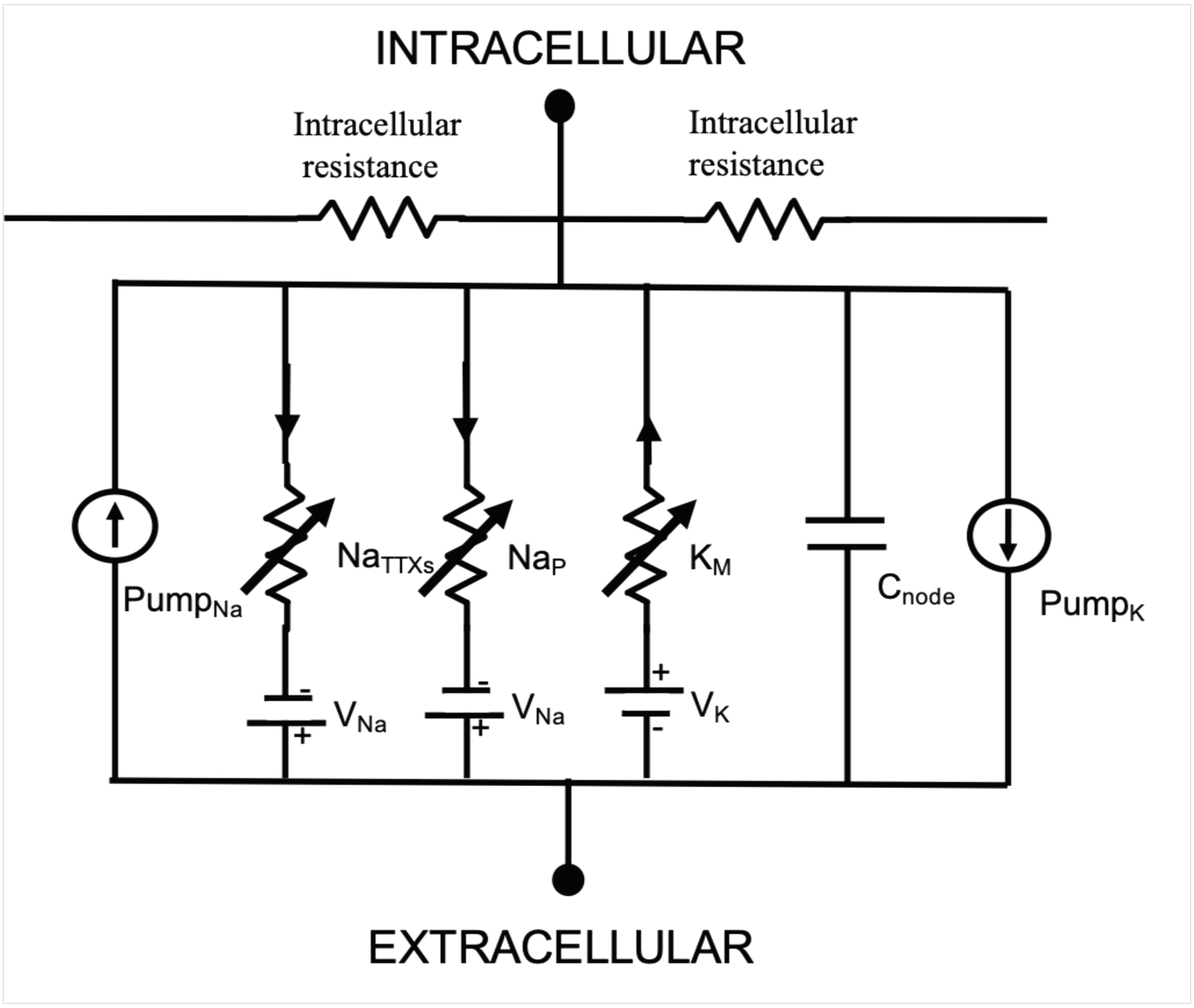


Supplemental data Figure 1. The equivalent circuit for one compartment of the Aδ model. Three sodium channel (Na_P, Na_{TTXs} and Na_{TTXr}) and two potassium channels (K_{Dr} and K_M) was implemented. Also the HCN current was implemented.

V_{Na}=70 mV
V_K=−82 mV
Cnode= *1* µF/cm^2
PumpNa=0.00006672 mA/cm^2
PumpK=-0.00001707 mA/cm^2

2.2 Aβ model

2.2.1 Node of Ranvier



Supplemental data Figure 2. The equivalent circuit for one compartment of the Aδ model Tow sodium channel (Na_p and Na_{TTXs}) and one potassium channels (K_M) was implemented.

V_{Na}=70mV

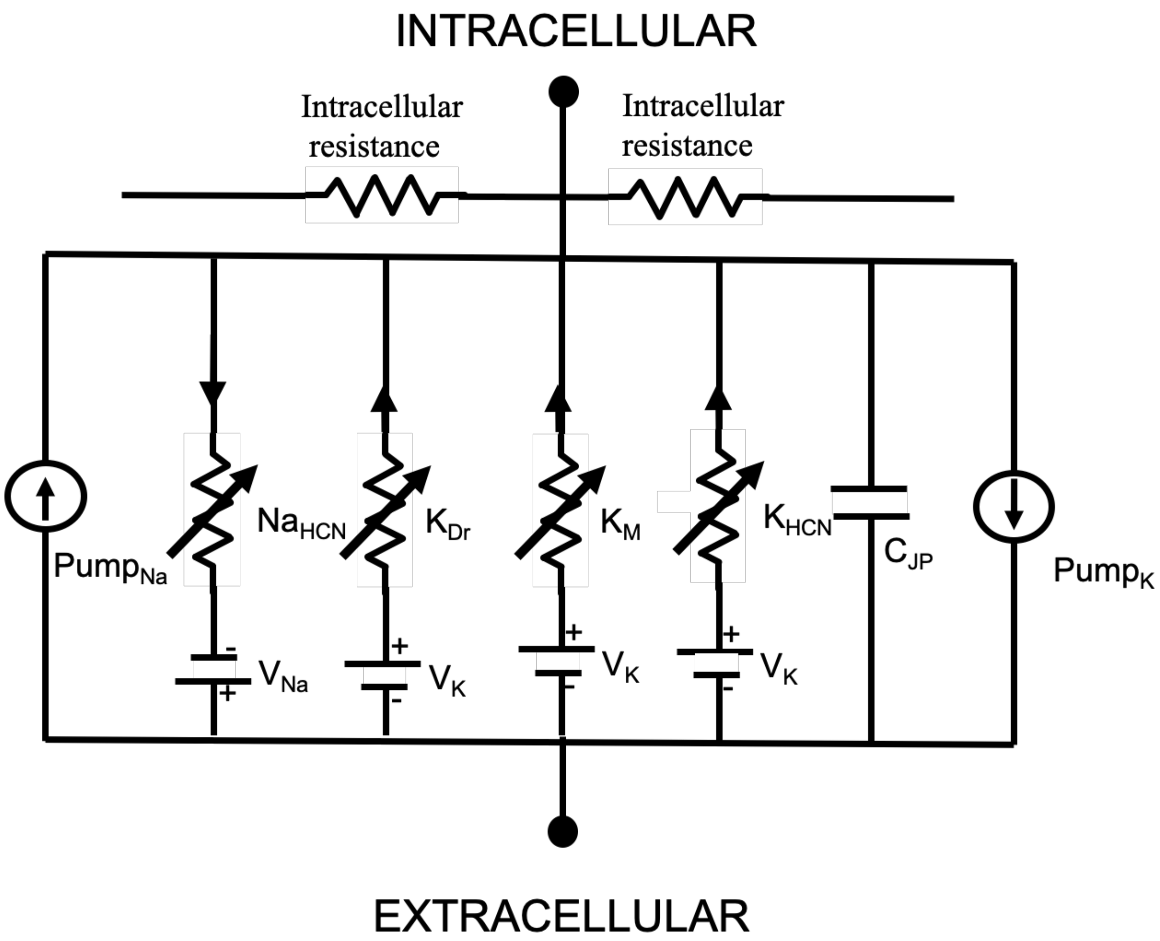
V_K=−82 mV

C_{node}=1μF/cm^2

Pump$_{Na}$= 0.004062 mA/cm^2

Pump$_K$= −0.000309 mA/cm^2

2.2.1 JUXTAPARANODE



Supplemental data Figure 3. The equivalent circuit for one compartment of the Aδ model Two potassium channels (K_{Dr} and K_M) was implemented. Also the HCN current was implemented.

V_{Na}=70mV

V_K=−82 mV

C_{JP}= 0.0141μF/cm^2

$Pump_{Na}$=0.003380 mA/cm^2

$Pump_K$= -0.000886 mA/cm^2

3. Reference

1. Tigerholm J, Petersson M, Obreja O, Lampert A, Carr R, Schmelz M, Fransén E. Modeling activity-dependent changes of axonal spike conduction in primary afferent C-nociceptors. J Neurophysiol. 2014;111:1721–1735. doi: 10.1152/jn.00777.2012. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

2. Watanabe, S., D. A. Hoffman, ., D. Johnston. 2002. Dendritic K+ channels contribute to spike-timing dependent long-term potentiation n hippocampal pyramidal neurons. Proc. Natl. Acad. Sci. USA. 99:8366–8371.
3. Jankelowitz, S. K., J. Howells, and D. Burke. 2007. Plasticity of inwardly rectifying conductances following a corticospinal lesion in human subjects. J. Physiol. 581:927–940.