Cortical Action Potential Back-Propagation Explains Spike Threshold Variability and Rapid Onset Kinetics

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Figure 1. Action potentials in the axonal initial segment can exhibit a high peak rate of change. Two examples of action potentials from different dual recordings of the soma and axon. The axon of cell 1 was recorded at approximately 44 µm from the soma, while the axon of cell 2 was recorded at approximately 45 µm, and therefore near the site of action potential initiation. Both axons exhibited action potentials that had a peak dV/dt of approximately 1500-1600 mV/msec, while the simultaneous somatic recordings revealed peak dV/dt rates of 450-600 mV/msec. In recordings from 10 different axon initial segments at a high (80 kHz) digitization rate, the average peak dV/dt of the action potential was 1532 V/sec (+/- 573, SD), indicating that the illustrated results are typical. Note the presence of two components in the dV/dt of somatic action potentials (labeled 1, 2; expanded in time for clarity). During these recordings, no filtering was applied and the digitization rate was 83 kHz. Action potentials recorded with the increased digitization rate of 166 kHz exhibited similar peak dV/dt (not shown).
Figure 2. Sealing the end of an axon can artificially increase the peak rate of dV/dt during action potential generation. Model of a uniform axon in which an action potential that was initiated at the left end propagated to the right end. Note that the peak rate of rise of dV/dt is approximately 20% higher at the sealed ends of the axon in comparison to the middle. Similar results have been obtained with patch clamp recordings from either the sealed end of the cut axon in comparison to the nonsealed portions of the axon in layer 5 pyramidal cells (Kole et al., 2007).
Figure 3. Raw phase plots of dV/dt versus Vm showing the biphasic nature of spike generation in 16 out of 32 of our layer 5 pyramidal cells in vitro at 35-36°C. The red line is the average of several action potentials from the recorded neuron.
Figure 4. Raw phase plots of dV/dt versus Vm for the second 16 out of 32 layer 5 pyramidal cells. Note that all cells exhibit a clear biphasic rise to the action potential.

Figure 5. Slope of the phase plot of dV/dt versus Vm at spike onset versus distance along the uniform axon under various conditions of membrane capacitance and axial resistance. When membrane capacitance and axial resistance are low, action potentials propagate very rapidly and phase slope varies little along the axon. With more realistic values of membrane capacitance and axial resistance, spikes propagate more slowly down the axon. These action potentials exhibit a rapid increase in spike phase slope at onset in the first 250-400 μm of the axon, followed by a plateau at further distances.

Basis of Increased Rate of Rise of Propagating Action Potentials Based upon Hodgkin-Huxley Equations

Non-propagating Action Potential For clarity, we first start with the Hodgkin-Huxley equations for a non-propagating action potential (Hodgkin and Huxley, 1952). For non-propagating action potentials, the current across the membrane (I_m) is the sum of the capacity current (I_c or \( C_m \frac{dV}{dt} \)), the ionic current (I_ion), and any externally injected current (I_inj):
\[ I_m = C_m \frac{dV}{dt} + I_{ion} + I_{inj} \]

\[ => \text{In a uniform compartment, such as a "point" model, in which the action potential does not propagate, the total membrane current, } I_m \text{ is zero, since the circuit is closed. Therefore,} \]

\[ \frac{dV}{dt} = \frac{-(I_{inj} + I_{ion})}{C_m} \quad (1) \]

**Propagating Action Potential** In real axons and neuronal processes, action potentials propagate along these elements. This propagation occurs through the flow of current down the axon (axial current; \( i_a(t,x) \)) leading to changes in the membrane potential of neighboring portions of the axon and therefore propagation of the action potential. Consider a simple compartmental model of current flow in a uniform axon:

**Figure 6.** Illustration of the axial flow of ionic current in a model axon. See text for details.

An axial (longitudinal) current \( i_a(t,x) \) passing through the axon causes a voltage change across the axial resistor \( r_a \) according to Ohm’s law,

\[ V(t,x) - V(t,x + \Delta x) = r_a * \Delta x * i_a(t,x) \quad (2) \]

where \( V(t, x + \Delta x) \) is the membrane potential at the neighboring point \( x + \Delta x \).

From (2) we have

\[ -(V(t, x + \Delta x) - V(t, x)) = r_a * \Delta x * i_a(t,x) \quad (3) \]

\[ => -\frac{\partial V(t, x)}{\partial x} = r_a i_a(t, x) \quad (4) \]
According to Kirchhoff's law the current change along the axis, \( \Delta i_a \), while traversing a length of axon, \( \Delta x \), is equal to the current lost across the membrane in that compartment \( i_m \) (\( i_m = i_{ion} + i_c \)) such that:

\[-\Delta i_a(t, x) = i_a(t, x) - i_a(t, x + 1) = -(i_a(t, x + 1) - i_a(t, x)) \text{ in the range of } \Delta x:\]

\[-\Delta i_a = i_a(t, x) - i_a(t, x + \Delta x) = i_m \Delta x \]

\[=> i_m = -\frac{(i_a(t, x) - i_a(t, x + \Delta x))}{\Delta x} \]

i.e., \( i_m = -\frac{\partial i_a(t, x)}{\partial x} \)  \hspace{1cm} (6)

Now, differentiating equation 5 with respect to distance yields:

\[-\frac{\partial i_a(t, x)}{\partial x} = \frac{1}{r_a} \frac{\partial^2 V(t, x)}{\partial x^2} \]  \hspace{1cm} (7)

and combining equations 5 and 6:

\[i_m = \frac{1}{r_a} \frac{\partial^2 V(t, x)}{\partial x^2} \]

Since \( i_m = i_{ion} + i_c \):

\[(i_{ion} + i_c) = \frac{1}{r_a} \frac{\partial^2 V(t, x)}{\partial x^2} \]  \hspace{1cm} (8)

Here \( i_c \) is the membrane capacitance current per unit length; \( i_{ion} \) is the total membrane ionic current per unit length; \( i_m \) is the membrane current per unit length, \( r_a \) is the internal resistance per unit length, and \( x \) is distance along the axon. To convert to specific membrane current, \( I_m \), we use the following relations:

\[I_m = i_m / 2\pi a\]

\[R_2 = \pi a^2 r_a\]

Where \( R_2 \) is the specific membrane resistance and \( a \) is radius.

Therefore, we have:

\[\frac{\pi a^2}{R_2} \frac{\partial^2 V(t, x)}{\partial x^2} = 2\pi a I_m \]

\[=> \frac{a}{2R_2} \frac{\partial^2 V(t, x)}{\partial x^2} = I_m \]

Therefore, we have the propagation Hodgkin-Huxley equation:
Rearranging for $\frac{\partial V(t,x)}{\partial t}$, the Hodgkin-Huxley equation for propagating spikes is

$$\frac{a \cdot \partial^2 V(t,x)}{2R_2} = I_m = (I_c + I_{ion} + I_{inj}) \text{ or}$$

$$\frac{a \cdot \partial^2 V(t,x)}{2R_2} = \frac{\partial V(t,x)}{\partial t} \cdot C_m + (I_{ion} + I_{vbg})$$

Comparing this equation for propagating spikes to that for non-propagating spikes (equation 1 above) reveals that they are the same except for the additional term which corresponds to the propagating current (see also eq.7):

$$I_{prop} = \frac{a \cdot \partial^2 V(t,x)}{2R_2}$$

Substituting in equation 9, we get:

$$\frac{\partial V(t,x)}{\partial t} = \frac{I_{prop} - (I_{ion} + I_{inj})}{C_m} \text{ or}$$

$$I_c = I_{prop} - (I_{ion} + I_{vbg}) \text{ or}$$

$$I_{prop} = I_c + I_{ion} + I_{inj}$$

The properties of $I_{prop}$ are illustrated in Figures 7, 8, and 13 below.

It should be noted that these equations are for calculation of the currents associated with spike initiation and propagation (i.e. non-steady state propagation). It is not appropriate to use the equations as formulated by Hodgkin and Huxley, which are for steady state propagation (e.g. equation 30 on page 522 in Hodgkin and Huxley, 1952).
Units:

$I_m: mA/cm^2$ (specific membrane ionic current density)
$R_s: \Omega \cdot cm$ (specific axial intracellular resistivity)
$C_m: \mu F/cm^2$ (specific membrane capacitance density)
$R_m: \Omega \cdot cm^2$ (specific membrane resistance for a unit area)
$I_{prop}: mA/cm^2$ (leak of axial propagation current to the local compartment)

$r_a: \Omega/cm$ (axial resistance per unit length of axon in axial direction)
$r_a = R_s/(\pi a^2)$

$r_m: \Omega \cdot cm$ (membrane resistance times unit length of axon in radial direction)
$r_m = R_m/(2\pi a)$

$c_m: \mu F/cm$ (membrane capacitance per unit length of axon in radial direction)
$c_m = 2\pi a C_m$

$i_m: mA/cm$ (membrane current per unit length of axon in radial direction)
$i_m = 2\pi a I_m$

$i_a: mA \cdot cm$ (axial current times unit length of axon in axial direction)
Figure 7. Properties of ionic currents including the propagation current, $I_{\text{prop}}$, during the initiation and propagation of an action potential in a uniform axon. a-c. Action potentials and the various currents at the initiation site in a 2 mm long uniform axon. $I_{\text{prop}}$ is negative at the beginning of the spike, owing to the flow of current away from the initiation site.  

d-f. Properties of the action potential and currents after it has propagated 500 µm down the model axon. Note that $I_{\text{prop}}$ is now positive at the beginning of the spike and arrives earlier than local ionic currents. Thus, $I_{\text{prop}}$ depolarizes the local membrane and results in local action potential initiation. Vertical lines are for reference.

Properties of the Propagation Current in a Uniform Axon The key difference between propagating and stationary action potentials is the addition of the propagation current in the case of travelling spikes. Therefore we sought to illustrate the properties of this current in order to better understand the mechanisms by which action potential shape changes with propagation along an axon or neuronal process (Figure 8).

A key feature of propagation current flow is that it changes with distance from the point of spike initiation. At the sight of spike initiation, $I_{\text{prop}}$ occurs only after the initiation of an action potential and represents the flow of current inside the axon away from the site of spike initiation (Figure 8b). However, at more distal portions of the
axon, $I_{\text{prop}}$ contains a positive going component prior to local spike generation. This positive component represents the flow of current from other portions of the axon (Figure 8e). Once the spike generation occurs locally, $I_{\text{prop}}$ flips to a negative going current, as the ionic current in this compartment is greater than neighboring compartments, and therefore ionic current flows away from the compartment under consideration. $I_{\text{prop}}$, particularly the leading edge of $I_{\text{prop}}$, increases in amplitude along the axon until a plateau is reached (see Figure 3e in main text). Comparing the amplitude-time course of the axial (propagation) current and the local ionic currents versus the membrane potential deviation for that axonal compartment reveals that the propagation current is responsible for the initial rise of the action potential (and therefore the “kinkiness” of the spike) (main text, Figure 3f). Interestingly, it is also evident that $I_{\text{Na}}$ exhibits a significantly more rapid rise in the middle portions of the axon, in comparison to the site of spike initiation, owing to the rapidly rising membrane potential induced by $I_{\text{prop}}$ (main text, Figure 3f). Therefore, the increase in rapid rate of rise of action potentials at spike onset is due entirely to increases in the amplitude-time course of the axial current during spike propagation (Figures 7; main text Figure 3f; see also Figure 13 below).
Figure 8. Simultaneous somatic and axonal recordings from real layer 5 pyramidal cells reveal significant variations in membrane potential between the two compartments, particularly prior to spike initiation. a, b. Action potentials initiated in the soma (a) and axon (b) in response to noisy current injection in the soma. c-d. Example raw voltage trace illustrating somatic and axonal membrane potential response to noise injection. e. Comparison of the membrane potential at the soma (blue) and axon (red). Note several periods in which the two membrane potentials do not track each other exactly (arrows). f. Subtraction of the membrane potential in the soma from the membrane potential in the axon illustrating the difference between the two as a function of time. Note that there is a
2-4 mV difference between the two sites and that variations become particularly large just prior to action potential initiation.  

**g.** Axonal membrane potential plotted as a function of somatic membrane potential. Note that there is a substantial variation in this relationship, and this variation increases closer to spike threshold.

**h.** Plot of axonal membrane potential versus somatic membrane potential in a model neuron (Figure 8 of main manuscript), illustrating the same property as observed in real neurons (g).

**Figure 9.** Spike threshold variance increases and then decreases for action potentials propagating away from a source of noise. In this model of a 2 mm long uniform axon, noise was injected into the $X_0$ end of the axon, resulting in the local initiation of action potentials that then propagate down the axon.  

**a-c.** Prespike membrane potentials at points $X_0$ (segment 1), $X_1$ (segment 8) and $X_2$ (segment 51) illustrating the increased followed by decreased apparent spike threshold variance. The axon consists of 51 segments, each of which is 40 µm long.  

**d-f.** Difference in membrane potential prior to spike initiation between segments 1 and 2, 1 and 8, and 1 and 51. Note that the difference in prespike membrane potential (between the point of action potential initiation and the point under consideration) increases towards segment 8 and then decreases towards the end of the axon, segment 51.  

**g.** Plot of the average prespike membrane potential difference between the beginning of the axon and the local point, as
a function of distance. Note that the difference gradually increases and then asymptotes. h. Standard deviation of prespike membrane potential difference between the point of spike initiation and the local point of spike generation versus distance along the axon. Note that the variation in the prespike membrane potential difference increases to a peak and then gradually decreases. i. Linear and strong correlation between variation in spike threshold and variation in prespike membrane potential difference. Each point represents a different compartment along the axon. Note that as there is an increase in the variation in membrane potential difference between the recorded compartment and the point of spike initiation, there is also a proportional increase in the apparent spike threshold variance in that compartment.

Figure 10. Spike threshold variance increases as action potentials propagate towards a noise source. In this simple model of an unmyelinated axon, DC was injected into one end of the axon, resulting in the initiation of action potentials, while colored noise was injected in the opposite end, causing membrane variance. a. Action potential initiation at point $X_0$ shows very little variance. b. Spike threshold variance is increased as the spike propagates towards the noise source. c. Spike threshold variance increases substantially at the axonal end where a noisy current was injected. d-f. Phase plots of the action
potentials in a-c, illustrating the increased in spike threshold variance. g. Variation in spike threshold from the point of spike initiation (0 µm) to the end of the axon where the noise is injected (1000 µm) with different amplitudes of noise injection. h. Variation in the prespike membrane potential difference (difference in membrane potential from the point of initiation of the spike ($X_0$) and the point along the axon), versus distance, in the different conditions shown in g. i. Linear relationship between the prespike membrane potential variation and the variation in spike threshold under the conditions shown in g.

Figure 11. A model of a pyramidal neuron based upon a more negative voltage sensitivity of Na$^+$ current in the axon versus the soma as the basis of spike initiation in the axon gives qualitatively similar results to our models. a-c. Action potential (a) and dV/dt vs. V phase plot (b) as well as spike threshold variance (c) of the model of a CA1
pyramidal cell. Action potential (d), phase plot (e) and spike threshold variance (f) at the axonal point of spike initiation are also shown for comparison. In this model, the density of $g_{\text{Na}^+}$ in the axon initial segment is only 3X that of the soma. Note that this model exhibits a kink in the onset of the somatic vs. axonal spike, a biphasic phase plot in the soma, but not the axon, as well as significantly greater spike threshold variance in the soma. Parameters are derived from models by Johnston, Colbert and Migliore (Hoffman et al., 1997; Migliore et al., 1999; Poolos et al., 2002). Here, we injected noisy current into the soma of this model pyramidal cell. This result reveals that even HH models based upon a relatively low density of Na$^+$ channel in the axon exhibit qualitative features similar to those detailed in our manuscript.

**Figure 12.** Full dendritic model of a layer 5 cortical pyramidal cell with Na$^+$ current density according to Kole, Stuart, et al. (Kole et al., 2008) also exhibits rapidly rising spikes and increased somatic spike threshold variability owing to axonal spike initiation. a. Action potentials in the soma exhibit a “kink” and larger threshold variance (dashed horizontal lines). b. Phase plot of dV/dt vs. V of an action potential as it occurs in the soma. Note the biphasic nature of the spike. c. Expansion of the dV/dt vs. V phase plot for somatic spikes illustrating spike threshold variance. d. In contrast to the soma, action potentials at the site of spike generation show a smooth onset and low threshold variance. e. Phase plot of dV/dt vs. V for axonal spikes. f. Illustration of the lower variance in...
spike threshold in the axon initial segment (vertical dashed lines). In this model, we modified our full layer 5 pyramidal cell model (Figure 8 in manuscript) to contain Na\(^+\) channel concentrations according to the recent study of Kole, Stuart et al. (Kole et al., 2008). (Somatic and dendritic gNa = 50, axon hillock transitions from 50 to 4000, axon initial segment 4000 pS/\(\mu\)m\(^2\); Somatic gK = 120, dendritic gK 10, axon hillock and axon gK 900 pS/\(\mu\)m\(^2\)). The voltage dependence of activation and inactivation of gNa in the axon was shifted by 7 mV more negative. Similar results are obtained using 2500 pS/\(\mu\)m\(^2\) for gNa in the axon, although the peak dV/dt for the action potentials are lower than normally seen in our recordings.
Figure 13. Comparison of the different currents during the generation of an action potential in the full neuron model (Figure 8 in main text). a-c. Comparison of different currents flowing during the action potential in the axon. d. Phase plot of the capacity current vs. membrane potential. e-g. Comparison of the amplitude-time course of the different currents during the action potential in the soma. Note the beginning of the action potential is caused by the positive going “bump” in $I_{\text{prop}}$ (asterisk; expanded for detail) and that this corresponds to the time of spike generation in the axon. h. Phase
Figure 14. Plot of standard deviation of spike threshold versus phase slope of dV/dt vs. V phase plots at a criteria level of 15 mV/msec for real layer 5 pyramidal cells (solid dots) versus a variety of simple and full models of spike initiation. Note that the results from the models are within the range of data recorded from real neurons (although on average the models exhibit slightly lower phase slopes).
Detailed Methods for Computational Model of Action Potential Generation in Cortical Neurons

Cortical neurons initiate action potentials in their axon initial segments in response to current pulses or local stimulation of synaptic inputs (Stuart et al., 1997; Palmer and Stuart, 2006; Shu et al., 2007). These action potentials then propagate antidromically (back propagate) through the soma and to variable degrees into the dendritic arbor (Stuart et al., 1997; Palmer and Stuart, 2006; Shu et al., 2007). There are two different hypothesis concerning spike initiation in the axon initial segment: one based upon a high density of Na\(^+\) channels in the axon initial segment (Mainen et al., 1995; Mainen and Sejnowski, 1996; Komada and Soriano, 2002; Inda et al., 2006) and another based upon a modest density of Na\(^+\) channels which have a more negative threshold than those in the soma (Colbert and Johnston, 1996; Colbert and Pan, 2002). The first model is supported by immunocytochemical studies which demonstrate a high density of Na\(^+\) channels in the axon initial segment and a low density over the cell body (Komada and Soriano, 2002; Inda et al., 2006). The density of Na\(^+\) channels in the axon initial segment, as revealed by anti-Nav1.6 antibodies, appears to be high, perhaps even as high as in nodes of Ranvier of the cerebral cortex (Matthew Rasband, unpublished observations). At nodes of Ranvier, Na\(^+\) conductances are on the order of 20-30 nS/µm\(^2\) (Black et al., 1990; Waxman and Ritchie, 1993; Waxman, 1995), a value similar to that used by models of axonal spike initiation by Mainen et al. (Mainen et al., 1995; Mainen and Sejnowski, 1996). Here we used an empirical approach to approximate the density of Na\(^+\) channels for our first model (see below). We measured the dV/dt of the membrane potential in the axon initial segment in real neurons and adjusting the concentration of Na\(^+\) and K\(^+\) currents in the axon initial segment of our model in order to match these empirically determined values. Using this method, we formed a model that initiates action potentials at approximately 50 µm from the cell body (as we have observed in real neurons; unpublished observations), and which gave rise to dV/dt plots for spike initiation that were similar to those recorded in real neurons (e.g. peak dV/dt of approximately 1200 mV/msec at the axon initial segment was used as a conservative value).

**Detailed Methods of Full Cortical Cell Model: Higher Na\(^+\) Conductance in Axon Initial Segment Model**

**Model Methods:** Our computational model was implemented using NEURON 5.8 (Hines and Carnevale, 1997) and was based upon the published multi-compartmental model of the full dendritic and somatic structure of a layer 5 cortical pyramidal cell (Figure 1D in Mainen and Sejnowski (Mainen and Sejnowski, 1996)). The temperature of the modeled cell was 37°C.

**Dendrites and soma** The soma and dendrites contain 480 segments. The somatic surface area is 2,748 µm\(^2\), while its diameter is 25 µm, and its length is 35 µm. There are 11 primary neurites, 87 branches, totaling 17,668 µm in length and 78,858 µm\(^2\) in surface area.

**Axon** Our model of the axon was based on that of Mainen et al. (Mainen et al., 1995), and was modified in order to match the spike initiation properties of our layer 5 pyramidal cells. The soma connects to the axon hillock, which tapers from 5 µm to 1.4 µm and has a length of 10 µm. The hillock is followed by a 40 µm initial segment of 1.4 µm diameter. Following the initial segment, there is a myelinated axon 500 µm in length,
with internode distances of 100 µm. The diameter of the internode axon is 1.4 µm and the
node diameter 1.1 µm with a length of 1 µm.

**Electrical properties**  The membrane capacitance Cm for the soma, dendrites, unmyelinated axon, and axon collaterals is modeled as 0.75 µF /cm² while for myelinated axon is 0.04 µF /cm². The axial resistance for dendrite and axon is 150 Ω·cm(Mainen and Sejnowski, 1996). The membrane time constant of the soma, dendrite, hillock and initial segment is around 28 msec, while 1.5 msec for the myelinated axon and 0.5 msec for nodes.

**Channel distributions:** The transient Na⁺ current is present in all parts of the modeled cell and its density is moderately high in the initial segment and hillock (8000 pS/µm²), but low in the soma (750 pS/µm²) and dendrites (100 pS/µm²). Myelinated model axon has a low Na⁺ conductance value of 20 pS/µm² and 5000 pS/µm² for the node. The reversal potential of Na⁺ in this model is 60 mV.

The fast, voltage activated K⁺ current, Iᵥ, is present only in the model hillock, initial segment (800 pS/µm²) and soma (80 pS/µm²). The reversal potential of K⁺ is -90 mV.

Background leak current is distributed throughout the cell. In the soma, dendrites, hillock, initial segments and myelinated axon, gleak = 0.33 pS/µm². In the nodes, gleak = 0.2 nS/µm². The reversal potential of the leak current is -70 mV. The slow non-inactivating potassium current (M-current; Iₘ), high-voltage activated Ca²⁺ current, Iᵥ, and one Ca²⁺ dependent K⁺ current, Iᵥ, are distributed throughout the soma and dendrites (Km conductance 0.1, Ca conductance 0.3, and Kca conductance is 3 pS/µm²) as per Mainen et al (Mainen and Sejnowski, 1996). The reversal potential of Ca is 140 mV. For the specific rate functions for the different ionic channels please see Mainen et al.(Mainen and Sejnowski, 1996).

**Detailed Methods of Cortical Cell Model: Spike Initiation Based upon Lower Threshold for Na⁺ current in Axon Initial Segment**

**Model Methods:** The second full neuron model was based upon the published multi-compartmental model of the full dendritic and somatic structure of a hippocampal CA1 layer 5 pyramidal cell(Migliore et al., 1999; Colbert and Pan, 2002) and was implemented using NEURON 5.8(Hines and Carnevale, 1997). The temperature of the modeled cell was 34°C.

**Morphology** The cell contain 203 compartments (13 for soma, 127 for apical dendrites, 60 for basal dendrites and 2 for axon). The maximal somatic diameter is 9 µm, and its length is 17 µm. For details, please consult Migliore et al.(Migliore et al., 1999). The axon’s diameter is 1 µm, and has two parts. The first part represents the axon hillock which connects to the soma and has a length of 10 µm. The second part represents the axon initial segment, which follows the hillock and has a length of 40 µm.

**Electrical properties**  The membrane capacitance Cm for the soma, dendrites and axon is modeled as 1 µF /cm². The axial resistance for dendrite, soma and axon hillock is 150 Ω·cm, while for the initial segment it is 50 Ω·cm(Migliore et al., 1999). Background leak current is distributed throughout the cell. The leak conductance is same for all the compartments: gleak = 0.36 pS/µm².

**Channel distributions:** The transient Na⁺ current is present in all parts of the modeled cell and its density is 1680 pS/µm² for the dendrites and soma, and is 1.5 times higher in the hillock and first 30 µm of axon initial segment, while 3 times higher in the last 10 µm
of axon initial segment accounting for spike initiation. As described in Colbert and Pan (Colbert and Pan, 2002), the half activation and inactivation ($V_{1/2}$) of Na$^+$ channel are set 7 mV lower in the hillock and first 30 µm of axon initial segment, and 10 mV lower in the last 10 µm of axon initial segment than the soma ($V_{1/2} = -40$ mV for activation and -55 mV for inactivation). These distributions of the Na$^+$ channel lead to the lowest spike threshold and spike initiation point being about 50 µm from the soma. The reversal potential of Na$^+$ in this model is 55 mV. A transient ($I_{K(A)}$, A-type) and a sustained ($I_{K(DR)}$, delayed rectifier) potassium channels are present in the soma, dendrites and axon. The density of $g_{K(A)}$ is 180 pS/µm$^2$ for both the soma and dendrites. The $g_{K(DR)}$ is 80 pS/µm$^2$ for both the soma and dendrites. For the axon, the first 40 µm, $g_{K(A)}$ is 120 pS/µm$^2$, and $g_{K(DR)}$ is 40 pS/µm$^2$, while for the last 10 µm, $g_{K(A)}$ is 230 pS/µm$^2$, and $g_{K(DR)}$ is 40 pS/µm$^2$. The reversal potential of K$^+$ is -90 mV.

For the specific rate functions for the different ionic channels please see Migliore et al. (Migliore et al., 1999).
References


