Passive Soma Facilitates Submillisecond Coincidence Detection in the Owl’s Auditory System

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Ashida G, Abe K, Funabiki K, Konishi M. Passive soma facilitates submillisecond coincidence detection in the owl’s auditory system. J Neurophysiol 97: 2267–2282, 2007. First published October 25, 2006; doi:10.1152/jn.00399.2006. Neurons of the avian nucleus laminaris (NL) compute the interaural time difference (ITD) by detecting coincident arrivals of binaural signals with submillisecond accuracy. The cellular mechanisms for this temporal precision have long been studied theoretically and experimentally. The myelinated axon initial segment in the owl’s NL neuron and small somatic spikes observed in auditory coincidence detector neurons of various animals suggest that spikes in the NL neuron are generated at the first node of Ranvier and that the soma passively receives back-propagating spikes. To investigate the significance of the “passive soma” structure, we constructed a two-compartment NL neuron model, consisting of a cell body and a first node, and systematically changed the excitability of each compartment. Here, we show that a neuron with a less active soma achieves higher ITD sensitivity and higher noise tolerance with lower energy costs. We also investigate the biophysical mechanism of the computational advantage of the “passive soma” structure by performing sub- and suprathreshold analyses. Setting a spike initiation site with high sodium conductance, not in the large soma but in the small node, serves to amplify high-frequency input signals and to reduce the impact and the energy cost of spike generation. Our results indicate that the owl’s NL neuron uses a “passive soma” design for computational and metabolic reasons.

INTRODUCTION

Barn owls can locate prey in total darkness by hearing (Konishi 1993). The acoustic cue for localization in the horizontal plane is the interaural time difference (ITD) (Konishi 1993), which is processed by neural circuits that consist of 1 axons from the cochlear nucleus magnocellularis (NM) serving as delay lines and 2 neurons of the nucleus laminaris (NL) serving as coincidence detectors (Carr and Konishi 1990; Jeffress 1943; Konishi 1993). The NL neuron detects time disparities of less than a few tens of microseconds (Peña et al. 1996). The cellular mechanisms of this temporal precision have long been the subject of both theoretical and experimental studies (Agmon-Snir et al. 1998; Brand et al. 2002; Cook et al. 2003; Dasika et al. 2005; Funabiki et al. 1998; Gerstner et al. 1996; Grau-Serrat et al. 2003; Grothe 2003; Kuba et al. 2005; Reyes et al. 1996; Rothman and Manis 2003; Trussell 1997; Yang et al. 1999). The axon initial segment, which usually has a high density of Na channels to generate spikes, is myelinated in the owl’s NL neuron (Carr and Boudreau 1993a). This characteristic suggests that the soma is likely to constitute a passive component and that spikes should be initiated in the first node of Ranvier. Small somatic spikes observed in NL cells of the chick (Kuba et al. 2005) and in other auditory coincidence detector neurons (Golding and Oertel 1995; Oertel 2000; Scott et al. 2005) also lend support to this suggestion. The location of the spike initiation site and its functional significance have been discussed for over a decade (Carras 1992; Clark et al. 2005; Colbert et al. 1996, 2002; Khalilq and Ramon 2006; Stuart et al. 1994, 1997a,b). However, how a “passive soma” works in a cell performing submillisecond coincidence detection remains to be investigated. We constructed a two-compartment NL neuron model consisting of a cell body and a first node to examine the computational and metabolic reasons for the passive soma structure of NL neurons.

METHODS

Modeling synaptic input (Fig. 1)

1) Input simulation: Phase-locked inputs from the NM fibers into NL neurons were calculated from known physiological data. The input sequence is modeled as an inhomogeneous Poisson process (Grau-Serrat et al. 2003) with the vector strength of 0.7 for 2-kHz, 0.6 for 4-kHz, 0.4 for 6-kHz sound stimulus (Carr and Konishi 1990; Köppl 1997). The shape of a single excitatory postsynaptic current (EPSC) is the so-called alpha-function with a time constant of 0.15 ms and a peak height of 1 nS recorded from chick NL neurons (Kuba et al. 2005). The firing rate of a single NM fiber is set at 400 spikes/s (Carr and Konishi 1990; Köppl 1997) and 100 NM fibers from each ear are assumed to converge to an NL neuron (Carr and Boudreau 1993b).

2) DC and AC conductance inputs: Based on the results obtained in 1) (see text), we made a simple model of the synaptic input: \( g_{\text{synaptic}} = g_{\text{DC}} + g_{\text{AC}} \sin(2\pi f t + \phi) \), where \( g_{\text{DC}} \) is the amplitude of DC input, \( g_{\text{AC}} \) is the amplitude of monaural AC input, \( f \) is the sound frequency, and \( \phi \) is the interaural sound phase difference. The DC component is independent of the ITD; changes in the ITD only shift the phases of the AC signal from the two ears (Fig. 2A).

Two-compartment model

The model consists of two compartments: the soma and the first node of Ranvier, connected electrically by a cylindrical axon (Fig. 2B). For simplicity, we incorporated the axonal initial segment into the soma. The model equations and the parameters are below (C = soma or node, \( x = m, h, n \)): \( C_e \cdot \frac{dV_e}{dt} = I_{\text{ion}}^{\text{m}} + I_{\text{ion}}^{\text{h}} + I_{\text{ion}}^{\text{n}} + I_{\text{synaptic}}^{\text{m,n}} \)

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Simulation procedures

To investigate the relationship between somatic excitability and ITD discrimination, we systematically varied the sodium conductance of the soma \( g_{\text{soma}} \) and of the node \( g_{\text{node}} \) (0 ≤ \( g_{\text{soma}} \) ≤ 11 \( \mu \)S, 0 ≤ \( g_{\text{node}} \) ≤ 18 \( \mu \)S) while keeping potassium and leak conductances fixed. We prepared 2,464 (44 × 56) combinations of \( (g_{\text{soma}}, g_{\text{node}}) \) to make a two-dimensional cell array of model cells. Each pixel in the color figures (Fig. 2, C–E, Fig. 4, G–I, etc.) corresponds to one particular combination of \( (g_{\text{soma}}, g_{\text{node}}) \).

1) Threshold measurement: We first determined the threshold of repetitive firing for DC conductance input. The threshold is a function of the somatic and nodal sodium conductances. A spike was counted when the sodium activation variable of the node \( n_{\text{node}} \) reached 0.5. Neurons with very large excitabilities (DC threshold < 0 nS: the top right purple zone in Fig. 2C) were regarded as useless and excluded from the following simulations because they fire without any input. Neurons with very small excitabilities that do not fire repetitively or have very large DC thresholds of repetitive firing (DC threshold > 50 nS: the bottom left red zone in Fig. 2C) could not or hardly respond to high-frequency AC signals (> 2 kHz) considered in this study and thus were not used in the following simulations (also see DISCUSSION).

2) ITD-rate modulation (Fig. 3, A–F): We reduced the number of variables to clarify the relationship between somatic/nodal excitabilities and ITD discrimination by fixing the synaptic DC inputs close to threshold \( (g_{\text{DC}} = 0.99 × \text{DC threshold}}; \text{this DC input level is fixed in a series of simulations unless indicated otherwise). Monaural AC synaptic conductance is fixed to 6 nS to obtain the curves in Fig. 3, A–D. In calculating the membrane potential AC component (Fig. 3B), spikes were initiated for large AC inputs (good ITDs). In these cases, we set the input DC level below 99% of the threshold to avoid firing and calculate membrane potential AC amplitude at DC = 0.99 × threshold by linear extrapolation. AC synaptic conductance and the interaural phase difference were varied together to compare ITD-rate curves (Fig. 3, E and F). In the noisy case (Fig. 3, D, F, and H), we added Gaussian white noise \( \sigma(t) \) to the input conductance. The noise intensity \( \sigma \) was set at 1% of the DC threshold.

3) AC-rate curve (Figs. 3, G and H and 4, A and D): DC input was fixed below the threshold \( (g_{\text{DC}} = 0.99 × \text{DC threshold}}; \text{and AC input was changed to obtain an AC-rate curve. In the AC-rate figures, the phase difference of the two monaural inputs was always fixed to zero (best ITD). Note that the binaural AC amplitudes change from zero (phase difference = ± 180°) to the doubled monaural AC inputs (phase difference = 0°) as a function of ITD.

4) ITD sensitivity (Figs. 4 and 5): With the DC synaptic input fixed, we calculated “the AC threshold,” defined as “the minimum amplitude of the monaural AC input necessary for ITD modulation.” This value indicates the ITD sensitivity of the model neuron. To compare neurons with different excitabilities, we used the ratio of (AC threshold)/(DC threshold) to measure ITD sensitivity, instead of the AC threshold itself. In the case with noise, AC threshold is defined as the minimum AC amplitude for the firing rate modulation of 200 Hz (the best and worst ITDs). In the case without noise, the criterion of 200-Hz modulation has the same meaning as the criterion introduced above because the firing rate of the model neurons without noise is always over 300 Hz if they fire.

5) Voltage responses to sinusoidal AC input (Fig. 6): AC conductance inputs were applied to the soma and the amplitudes of the subthreshold voltage oscillations were calculated. \( g_{\text{DC}} \) was set at 50% of DC threshold; \( g_{\text{AC}} \) was set at 1% of DC threshold.

Threshold impedance analysis

1) Single-compartment model (Fig. 7): The basic equations are the same as those for the two-compartment model described above except that the number of compartments is just one (axonal current is zero). The equations for the TEA-sensitive (high-voltage-activated) potassium conductance \( K_{\text{HVA}} \) in the DTX-sensitive (low-voltage-activated) potassium conductance \( K_{\text{LVA}} \) (Fig. 7F) are taken from data on the NM neuron of the chick (Rathouz and Trussell 1998): \( I_{\text{K}} = g_{\text{K}}(t) \cdot n(\alpha_{y}(V) - \beta_{y}(V) \cdot V) \), \( n(t) = Q_{10}^{-\Delta \tau_{y}(V)/10} \), \( \alpha_{y}(V) = 0.1 \exp[-(V + 45)/10] \), and \( \beta_{y}(V) = 0.07 \exp[-(V + 70)/10] \). All conductances \( g_{\text{K}} \), \( g_{\text{L}} \), and \( g_{\text{N}} \) are assumed to be applied only to the soma and not to the node; thus, \( \Delta \tau_{y}(V) \) is fixed to 0 throughout the simulation of ITD computation. Numerical integration was performed by using the Runge–Kutta scheme (for deterministic cases) and the Milstein scheme (for stochastic cases) with a time increment of 0.5 \( \mu \)s (results are not affected by the time increment, if its length is sufficiently small).

Roles of low-voltage–activated potassium current (Fig. 10)

To clarify the role of DTX-sensitive (low-voltage-activated) K conductance \( K_{\text{LVA}} \), we replaced part of the leak conductance \( g_{\text{L}} \) with \( K_{\text{LVA}} \) conductance \( g_{\text{LVA}} \): i.e., \( g_{\text{L}} = g_{\text{L}}(t) \cdot n(\alpha_{y}(V) - \beta_{y}(V) \cdot V) \), \( n(t) = Q_{10}^{-\Delta \tau_{y}(V)/10} \), \( \alpha_{y}(V) = 0.103 \exp[-(V + 19)/20] \), \( \beta_{y}(V) = 0.011 \exp(-V + 19)/20 \), and \( \Delta \tau_{y}(V) = 0.1 \exp(V + 60)/21.8 \). All conductances \( g_{\text{K}} \), \( g_{\text{L}} \), and \( g_{\text{N}} \) are set at zero unless indicated.

2) Two-compartment NL model (Figs. 8 and 9): The method for calculating impedance is similar to (1). The size of the input AC current is 10 pA for the soma and 0.05 pA for the node. Axonal length \( L_{\text{axon}} \) is changed to measure the effect of the connection strength between the two compartments.
1) Response to stepped DC inputs (Fig. 10, A–D): Rectangular-shaped pulse inputs (duration: 7 ms, size: −10 to +10 nS, Fig. 9A) were injected into the model neurons held at −65 mV.

2) ITD sensitivity (Fig. 10F): The same calculation as in Simulation procedures (4) was performed to obtain the value of (DC threshold)/(DC threshold).

3) Eff ect of the DC input level (Fig. 10, G and H): The same calculation as in Simulation procedures (3) was performed to draw AC-rate curves, but the DC input level was varied (\( g_{\text{DC}} = Z \times \text{DC threshold} \), \( Z = 0.99, 0.94, 0.89 \)).

Impact of spike generation (suprathreshold analysis) (Fig. 11)

1) Oscillating potential traces and spike initiation: We injected AC conductance input into the soma of the two-compartment model (\( g_{\text{AC}} = 5\% \) of DC threshold, \( g_{\text{DC}} = 90\% \) of DC threshold). At time zero, we set the variables \( m_{\text{soma}} \) and \( m_{\text{node}} \) to 1 to artificially generate an action potential. By changing the phase of the AC input, we obtained traces of oscillating membrane potentials (Fig. 11A). By averaging the potential traces to eliminate the AC signal, we then obtained a spike template (Fig. 11B).

2) Extracting AC component: We subtracted the spike template from the potential traces to obtain a set of traces of the membrane AC component (Fig. 11C). By taking the envelope of the oscillating traces, we finally had a single trace of the membrane AC amplitude. This trace shows the temporal variation of the membrane AC component before, during, and after the spike generation (Fig. 11D).

Estimation of energy consumption (Fig. 12)

1) Ionic flux (Fig. 12): The amount of ionic flux was measured as an estimate of energy costs for repetitive firing. \( Q_{\text{Na}} = \int f I_{\text{Na}} \, dt \), \( Q_{\text{K}} = \int f I_{\text{K}} \, dt \) and \( Q_{\text{total}} = Q_{\text{Na}} + Q_{\text{K}} + Q_{\text{L}} \). This value is a rough index of neuronal energy consumption through active ion transport (Na/K-pumps etc.; Amos III 2000; Clausen et al. 1991; Laughlin 2001).

2) Comparison with normal leak neuron (Fig. 12F): Somatic leak conductance was set to a value in common neurons (Hille 2001) (\( g_{\text{L}}^{\text{soma}} = g_{\text{L}}^{\text{node}} = 0.4 \text{ mS/cm}^2 \), \( g_{\text{L}}^{\text{node}} = 9.6 \text{ nS, } g_{\text{L}}^{\text{soma}} = 0.048 \text{ nS} \) and the same type of calculation was carried out with the procedures listed above.

RESULTS

Simulation of synaptic inputs to the owl’s NL cells

Physiological and morphological data obtained from the barn owl’s NL neuron (Carr and Boudreau 1993a; Funabiki and Konishi 2005) and additional data from other neurons (Hille 2001) were used to construct the NL neuron model. NL neurons receive phase-locked spikes from NM fibers of both sides (Carr and Boudreau 1993b; Carr and Konishi 1990; Konishi 1993; Köppl 1997). We first simulated the synaptic input to the NL neuron. Phase-locked spikes from NM neurons form a sinusoidal AC component of the synaptic conductance, whose frequency is identical to that of the stimulus tones (Fig. 1A; see METHODS). Two monaural inputs from both ears converge to the NL neuron with temporal disparity (or phase difference \( \delta \)) (Fig. 1B). Depending on the phase difference, the binaural synaptic input is changed (Fig. 1, C–E). The size of binaural AC signal is roughly twice the monaural AC amplitude at the best ITD (\( \delta = 0^\circ \), Fig. 1C) and is zero at the worst ITD (\( \delta = 180^\circ \), Fig. 1E).

FIG. 1. Input to an nucleus laminaris (NL) neuron. A: monaural input to an NL neuron. Phase-locked activity of nucleus magnocellularis (NM) neurons forms a sound-analogue monaural synaptic input to NL. B: sample traces of monaural synaptic conductance input. Two monaural inputs (from left and right) assemble in an NL neuron with phase difference \( \delta \). C–E: binaural synaptic conductance input as a sum of two monaural inputs. Phase difference \( \delta \) changes the size of the signal frequency component (same frequency as the stimulus sound) of the binaural input. F: power spectrum of the simulated binaural synaptic inputs. Signal frequency component changes with the interaural phase difference (ITD), whereas the other components are independent of the ITD. G: sample trace of membrane potential. Binaural input shown in C is injected into an RC membrane (\( R = 5.2 \text{ M}\Omega, C = 24 \text{ pF, } E_{\text{rest}} = -68 \text{ mV} \)). In B–G, the input signal frequency is 4 kHz. H–I: sample traces of binaural synaptic conductance input. Phase difference \( \delta \) is zero (best ITD). Input signal frequencies are: (H) 2 kHz, (I) 6 kHz.
ITD ($\delta = +180^\circ$, Fig. 1E). A power spectrum of the simulated synaptic inputs is shown in Fig. 1F. The signal frequency component (4 kHz) of the synaptic input varies with the phase difference of the two input signals from the two ears; the other frequency components (including DC) are independent of ITD.

Figure 1, B–E indicates that the AC component of the synaptic input varies with ITD. However, its amplitude is very small; AC amplitude is 5 nS even for the best ITD, whereas the size of the DC shift is 30 nS (Fig. 1C). This small AC signal becomes further attenuated by the postsynaptic membrane (Fig. 1G). Even using extraordinary parameters for the calculation (see Methods), the AC amplitude in the simulated membrane potential is about 1 mV. Although it is possible, of course, to increase this AC amplitude by making the unit synaptic input larger, this procedure will also boost DC and other frequency components that are independent of the ITD and could be regarded as noise (Fig. 1F). By changing other parameters (vector strength of NM activity, decay time constant of synaptic input, etc.) the AC amplitude can be raised, but the parameters used in the simulation already have exceptional values (see Methods) and thus the room for improvement would be limited.

Because we cannot expect the AC signal in the NL neuron’s synaptic potential to be more than a few millivolts, we assume that the NL neuron should be capable of using a limited amount of AC signals for sensing ITDs. The degree of this difficulty for the NL neuron depends on the input frequency. When the input frequency is low (2 kHz, Fig. 1H), relatively large AC signals are available, but when the input frequency is high (6 kHz, Fig. 1J), the situation becomes much more difficult. Owls can sense ITDs of extremely high frequency sounds (up to 8 kHz; Peña et al. 1996). Thus the sensitivity for small AC signals is the most crucial factor for the detection of ITD by the owl’s NL neurons.

Constructing the NL neuron model

Based on the input simulation (Fig. 1), we made a simple model of the synaptic input to the NL neuron. Monaural synaptic conductance is modeled as a sum of DC and AC components and the binaural input is a superposition of the signals from two sides (Fig. 2A; see Methods).

The NL neuron model consists of two compartments: the soma and the first node of Ranvier (Fig. 2B). The ionic

![Diagram of the NL neuron model](http://jn.physiology.org/)

**FIG. 2.** Two-compartment model of an NL neuron. A: input to the NL neuron model. Monaural synaptic conductance input is modeled as a sum of DC and AC components. Binaural input to NL is a sum of monaural inputs from two sides with a phase difference. Phase difference (or ITD) changes only the AC component and the binaural input is a superposition of the signals from two sides (Fig. 2A; see Methods).

The NL neuron model consists of two compartments: the soma and the first node of Ranvier (Fig. 2B). The ionic
dynamics of each compartment is described by Hodgkin–Huxley-type equations (Gerstner and Kistler 2003; Hodgkin and Huxley 1952) where fast sodium, delayed rectifier potassium, and leak currents are involved. Although previous models studied the effects of various potassium currents on neuronal coincidence detection (Grau-Serrat et al. 2003; Svirskis et al. 2003, 2004), our model incorporates them into the large leak term (small input resistance ≈ 5 MΩ) for simplicity. This value is similar to values obtained in the barn owl’s NL (Funabiki and Konishi 2005) and post hatch chick’s NL (Kuba et al. 2005). The significance of dendrites was discussed in a theoretical study on the chick’s coincidence detector neuron (Agmon-Snir et al. 1998). Our model, however, does not consider dendrites because the dendrites in the owl’s NL are very short and irregularly distributed in high-frequency neurons (>4 kHz; Carr and Boudreau 1993a; Carr and Konishi 1990). The primary aim of this study is to examine the significance of the “passive soma” and “nodal spike initiation” in ITD detection.

We changed the maximum sodium conductances of the soma and the node ($g_{Na\text{soma}}$ and $g_{Na\text{node}}$) to control the excitability of the compartments (see METHODS). Changes in sodium conductance affect the firing properties of the cell, such as the threshold of repetitive firing for DC input (Fig. 2C) and spike height (Fig. 2, D and E). When the somatic sodium conductance is sufficiently large, steep spikes are observed in the soma; we refer to this as an “active soma” (green to red zone in Fig. 2D; a typical trace is shown in Fig. 2F). When the sodium conductance of the soma is small and that of the first node is sufficiently large, the node becomes the site of spike initiation; we refer to this as a “passive soma” (purple to blue zone in Fig. 2D; a typical trace is shown in Fig. 2G).

![Graphs showing the effect of ITD on firing rate](image)

**ITD detection**

A typical response of the model neuron to ITD changes is shown in Fig. 3, A–D. DC input is set subthreshold and the monaural AC input is fixed, after which the phase difference of binaural inputs is varied (see METHODS). The amplitude of the binaural AC input changes according to the phase difference of the two AC inputs (Fig. 3A) and thus the amplitude of the AC component of the membrane potential changes similarly (Fig. 3B). When the two monaural inputs arrive perfectly in phase (phase difference = 0°, best ITD), the binaural sum becomes maximum. When they arrive totally out of phase (phase difference = ±180°, worst ITD), the sum becomes zero. The sum of two sinusoidal inputs with the same amplitude A and with a phase difference $\theta$ is: $A \sin(2\pi t + \theta)$. Thus the amplitude of the summed sinusoidal wave (Fig. 3, A and B) is $2A \cos(\theta/2)$. The ITD curve, showing the firing rate against the ITD (or the phase difference of the two monaural inputs), is in Fig. 3C. The neuron, converting the degree of coincidence into the spiking rate, fires most frequently when the phase difference between the two AC signals is zero and less frequently when the two AC inputs arrive out of phase. The timescale of this coincidence is set by 10.220.33.1 on October 28, 2016 http://jn.physiology.org/ Downloaded from

**FIG. 3.** ITD detection of a model neuron. A: input AC conductance changing with the time difference of the 2 monaural inputs (or ITD). B: AC amplitude of the somatic and nodal membrane potentials changing with ITD. C: firing rate changing with input phase difference (noiseless case). D: firing rate changing with input phase difference (noisy case: intensity = 0.12 nS). AC input used in A–D is $g_{AC\text{left}}$ = $g_{AC\text{right}}$ = 6 nS. E and F: firing rate changing with input phase difference and AC amplitude (E: with noise, F: without noise). Without noise (E), if AC amplitude is small (3.6 nS; dotted thick line), the firing rate does not change with input phase difference. Modulation depths of the firing rate between the minimum (worst ITD) and the maximum (best ITD) increase with the input AC amplitude in both noisy and noiseless cases. G and H: firing rate changing with input AC amplitude (AC-rate curve, G: without noise, H: with noise). Without noise (G), the AC threshold defined by the point where the firing rate jumps from zero is 3.9 nS. With noise (H), the firing rate monotonically increases with AC amplitude when noise is added to the input. Line styles in E and F correspond to those of the vertical lines in G and H, respectively. A “passive soma” neuron was used in A–H: $g_{Na\text{soma}}$ = 0 $\mu$S, $g_{Na\text{node}}$ = 0.869 $\mu$S, $g_{Leak}$ = 11.88 nS, DC threshold = 12 nS.
dence detection is of the order within a cycle of the input frequency and is less than a millisecond if the signal frequency is over 1 kHz. Simple modification of the model, such as adding noise, makes a smoother ITD curve (Fig. 3D), similar to that obtained in physiological experiments (Carr and Konishi 1990; Peña et al. 1996).

We have already indicated in Fig. 3B that the input AC amplitude changes from zero to maximum with the input phase difference. The maximum value is twice that of the monaural AC amplitude. Thus instead of changing the phase difference (or ITD), we can control the binaural AC amplitude by changing only the monaural AC amplitude while fixing the phase difference at 0°. ITD curves for different monaural AC amplitudes are shown in Fig. 3E. For a small AC amplitude, the curve is flat. This means that the neuron cannot sense the ITD because the signal is too small. When the AC amplitude is over a certain value (i.e., the AC threshold), modulation of the firing rate—indicating that the neuron detects ITD—is observed. ITD curves become broader with increased AC amplitude. The relationship between the AC amplitude and ITD sensing is also shown in Fig. 3G. The jump in the firing rate at 3.9 nS indicates the AC threshold of the neuron (see METHODS for the definition of the AC threshold). The flat dotted thick line in Fig. 3E corresponds to the subthreshold flat zone from zero to the vertical line of the same style in Fig. 3G (3.6 nS). Similarly, each ITD curve in Fig. 3E corresponds to the AC-rate curve (Fig. 3G) of the zone between zero and the vertical line of the same style. In this way, the AC-rate curve (Fig. 3G) has almost all the information of the ITD curves (Fig. 3E). Therefore we use, from here, AC-rate curves instead of ITD-rate curves. Addition of noise smooths the ITD curves (Fig. 3F) and the AC-rate curve (Fig. 3H). Exactly the same as in the noisless case, we can also make ITD curves correspond to the AC-rate curve in the noisy case.

To compare neurons with different somatic excitabilities in ITD computation, we first sampled seven model neurons with different somatic and nodal sodium conductances but with the same DC threshold of 12 nS (Fig. 2C, dotted line; Fig. 4A, inset). Spike rates of the model neurons against monaural input AC amplitude are plotted in Fig. 4A. Each neuron begins to fire if the AC input exceeds its AC threshold. As the excitability of the soma changes from active (A) to passive (P), the curve goes to the left (Fig. 4A). This means that a soma with no sodium channels achieved the smallest AC threshold. The maximum firing rate tends to be higher in less-active somata. ITD curves of the neurons are shown in Fig. 4B (monaural AC input is 4.0 nS) and Fig. 4C (monaural AC input is 8.0 nS). In Fig. 4B, only two model cells with small sodium conductance in the soma show ITD modulation. Because the models with more somatic sodium conductances have AC thresholds over 4.0 nS, these model neurons show no ITD modulation. When the input AC amplitude is sufficiently large, both active and passive soma models show ITD-rate modulation (Fig. 4C). As we demonstrated earlier in Fig. 1, the expected AC signal in an owl’s high-frequency NL neuron is very small. Therefore we adopt the AC threshold for measuring ITD sensitivity for high-frequency AC signals, instead of using the width or depth of the ITD-rate curve, which may be suitable for measuring ITD tuning for large AC inputs (Fig. 4C). Figure 4D shows the spiking rate change of the same neurons as in Fig. 4A but with white noise (see METHODS). Adding noise appreciably raises the AC threshold in neurons with active somata, but only slightly affects the threshold in those with passive somata. Also in this noisy case, only the two model cells with small sodium conductance show ITD-rate modulation for a monaural AC input of 4.0 nS (Fig. 4E). Even when the monaural input AC amplitude is large, neurons with active somata do not show ITD-rate modulation (Fig. 4F).

We calculated AC thresholds in the whole parameter range of somatic and nodal sodium conductances (Fig. 4G). The AC threshold of each model neuron is strongly affected by the DC threshold of the neuron (Fig. 2C). Therefore to compare neurons with different levels of excitability (i.e., different DC thresholds), some kind of normalization for eliminating the effect of DC threshold is required. For this reason, we adopt the ratio (AC threshold)/DC threshold to measure the performance in sensing ITDs instead of the AC threshold itself. We call this value the “normalized AC threshold” or, simply, the “AC/DC-ratio.” A small AC/DC-ratio means a high sensitivity in discriminating ITDs. The minimum AC/DC-ratio was achieved in the passive soma area (Fig. 4H). This means that a neuron with a passive cell body requires a smaller AC input in changing spike rates and thus is more suitable than an active soma for ITD detection. The advantage of the passive soma in ITD sensing is further clarified by adding noise (Fig. 4I; see legends). This trend is consistent for all the frequencies tested (2, 3, 5, and 6 kHz; Fig. 5).

In spite of this simple clear conclusion, the underlying mechanism for the advantage of the passive soma has not yet been elucidated. To clarify which characteristics of the neuron are crucial for determining ITD sensitivity, we next examine the property of the neuron in both sub- and suprathreshold regions.

Subthreshold response and impedance

We calculate the membrane potential responses to AC inputs (Fig. 6A; see METHODS). Results from four model neurons with different somatic and nodal sodium conductances but with the same DC threshold of 12 nS (dotted line in Fig. 2C) are shown in Fig. 6, B–E. The somatic membrane response to a low-frequency signal (<1.5 kHz) is larger in an active soma neuron than in a passive soma neuron, whereas that to a high-frequency signal (>1.5 kHz) is almost the same in both types of neurons (Fig. 6B). The nodal response to a low-frequency signal has a complex dependency on somatic excitability, whereas that to a high-frequency signal is larger in a passive than in an active soma neuron (Fig. 6, C and D). This means that when the neuron has a passive soma (i.e., when spikes are initiated in the node), the ITD-dependent AC signal (>2 kHz) is enhanced at the spike initiation site (node in this case) without much altering lower-frequency components (which are regarded as noise) (Fig. 6C). In contrast, when the neuron has an active soma (i.e., when spikes are initiated in the soma), enhancement at the spike initiation site (soma in this case) is limited to only the low-frequency range (Fig. 6B). In other words, the active soma amplifies only the ITD-independent low-frequency noise component without enhancing the ITD-dependent high-frequency signal component at the spike initiation site. This frequency profile can be tied closely to the low
AC threshold and high noise tolerance of the passive soma design.

High-frequency signals (>2 kHz) are enhanced at the first node in passive soma models. To elucidate this nodal enhancement, we calculate signal amplification ratios from the soma to the node by dividing the nodal responses by the somatic responses. At all the frequencies (0–10 kHz), signal amplification is larger in a passive soma neuron than that in an active soma neuron (Fig. 6E). In other words, nodal filtering serves to amplify high-frequency signals. Signal amplification for a 4-kHz input in a whole parameter area is shown in Fig. 6F. Contours parallel to the horizontal axis indicate that this nodal AC signal enhancement depends mainly on the nodal sodium conductance.

We next investigate the biophysical mechanism of the signal amplification shown above. First, we review the roles of neuronal parameters in the membrane response by examining the impedance of a single-compartment neural model (Hutchison and Yarom 2000) (Fig. 7A). In each case (Fig. 7, B–H), only a single parameter is modified or added to the RC circuit (e.g., in Fig. 7D, a delayed rectifier potassium channel is added to the RC circuit and no other channels are included). Raising the capacitance of the membrane increases the membrane time constant and thus lowers the corner frequency of the RC circuit.
Increasing the leak conductance (or decreasing the resistance) of the membrane pushes down the impedance curve to make the corner frequency high (Fig. 7). Asterisks in Fig. 7 and Fig. 8 indicate the parameter values used in our NL neuron model. When these parameters are taken from an appropriate range (e.g., $C_{\text{soma}} \approx 20$ pF, $g_{\text{Na}}^{\text{soma}} \approx 5$ MΩ), the corner frequency of the membrane is about 1 kHz. Increasing the potassium conductance suppresses lower-frequency components, although the strength of this high-pass filtering depends on the voltage dependency of channel kinetics (Fig. 7).
FIG. 7. Effects of biophysical elements on membrane impedance. A: circuit of the single-compartment model used in this figure. B–F: impedance functions of a single-compartment model. RC circuit of $C_m = 24 \text{ pF}$ and $g_L = 192 \text{ nS}$ ($R_L = 5.21 \text{ M} \Omega$) is used as a reference (red line in each panel). Parameter values used in our NL model are indicated by asterisks. B: effects of membrane capacitance. Changing membrane capacitance shifts the corner frequency of the impedance function. C: effects of leak conductance (or membrane resistance). An increase in leak conductance lowers membrane impedance and thus raises the corner frequency. D: effects of delayed rectifier potassium conductance. An increase in delayed rectifier potassium conductance suppresses frequency components of membrane impedance below the corner frequency. E: effects of the TEA-sensitive (high-threshold) potassium conductance. An increase in the TEA-sensitive potassium conductance suppresses low-frequency components, but the effect is much smaller than that of the delayed rectifier (D) and DTX-sensitive (F) potassium conductances. F: effects of DTX sensitive (low-voltage–activated) potassium conductance ($K_{LVA}$). An increase in DTX-sensitive potassium conductance suppresses low frequency components more effectively than the delayed rectifier potassium conductance (D). G: effects of the fast sodium conductance. An increase in fast sodium conductance amplifies the frequency components below the corner frequency. H: effects of fast sodium conductance (extremely large leak case). Corner frequency is elevated by adding leak conductance. In this case, the range of signal amplification by the fast sodium conductance covers the owl's signal frequency (2–8 kHz).

D–F). The DTX-sensitive (low-voltage–activated) potassium conductance ($K_{LVA}$), considered to be important in ITD detection (Rathouz and Trussell 1998; Svirskis et al. 2003, 2004), effectively reduces the low-frequency components and slightly raises the corner frequency (Fig. 7F). Thus the effect of the DTX-sensitive conductance on the membrane impedance is similar to that of the leak conductance. In contrast, adding sodium conductance to the membrane increases the impedance below the corner frequency (Fig. 7G). This effect is brought about by the regenerative dynamics of the inward current. Because the model of Fig. 7G has a corner frequency $= 1 \text{ kHz}$, the signal enhancement is restricted to this range. However, if the corner frequency becomes sufficiently high, sodium conductance can amplify signals of up to 10 kHz (Fig. 7H, corner frequency $= 38.2 \text{ kHz}$). The resonant bumps of the curves in Fig. 7, G and H diminish when the inactivation of sodium conductance is removed (data not shown), indicating that the bumps are from the reduction of low-frequency components derived from the inactivation process of sodium channels. For detailed impedance analyses of ion channels, see, for example, Hutchison and Yarom (2000), Mauro et al. (1970), Rinzel and Ermentrout (1998), and references therein.

Figure 6, E and F implies that the sodium conductance in the node plays a key role in enhancing AC signals. Therefore we focus on the effect of sodium conductance in the two-compartment model. Connecting the soma to the node (Fig. 8A) does not change the somatic impedance (Fig. 8B, black to blue) because the axonal conductance (31.4 nS in this model) is smaller than the somatic leak conductance (192 nS in this model) and thus the impact on the large soma is limited. Adding sodium conductance to the soma increases impedance only below the corner frequency (Fig. 8B, blue to red). Potassium conductance serves to reduce low-frequency components (Fig. 8B, red to green). Linear–linear plots of the somatic impedance curves shown in Fig. 8C have a similar shape to the somatic membrane response curve of an active soma model shown in Fig. 6B, indicating that the somatic membrane response closely corresponds to the somatic impedance.

Connecting the node to the soma (Fig. 8D), in contrast, dramatically reduces the nodal impedance to dramatically raise the corner frequency (Fig. 8E, black to blue). This is because the axonal conductance dominates the nodal leak conductance and, together with the small nodal capacitance, makes the
The conductance of an axon is proportional to its length and inversely proportional to its cross section. To see the effect of axonal conductance on the property of the model neuron, we changed the length of the axon (Fig. 9A) and calculated the impedance (the diameter of the axon was fixed to 2 \( \mu \text{m} \)). If the axonal distance between the soma and the node is too long, the signal is significantly attenuated, especially at high frequencies (Fig. 9B). The curves in Fig. 9B correspond to the dotted “leak only” curve in Fig. 6E showing the response of the membrane without sodium conductance. The dependency of nodal impedance on the soma–node distance is shown in Fig. 9C (nodal Na\(^+\) conductance fixed) and in Fig. 9D (nodal sodium conductance changed in proportion to axonal conductance). When the distance is too short, nodal impedance is profoundly affected by somatic impedance and the amplification by sodium conductance appears only below the somatic corner frequency. When the soma–node distance is in a certain range (25–200 \( \mu \text{m} \)), the impedance curve below 10 kHz is almost flat and the signal in this frequency range can be amplified by sodium conductance. The longer the distance between the soma and the node becomes, the larger is the signal amplification by the same sodium conductance (Fig. 9B). The curves in Fig. 9B correspond to the dotted “leak only” curve in Fig. 6E showing the response of the membrane without sodium conductance. The dependency of nodal impedance on the soma–node distance is shown in Fig. 9C (nodal Na\(^+\) conductance fixed) and in Fig. 9D (nodal sodium conductance changed in proportion to axonal conductance). When the distance is too short, nodal impedance is profoundly affected by somatic impedance and the amplification by sodium conductance appears only below the somatic corner frequency. When the soma–node distance is in a certain range (25–200 \( \mu \text{m} \)), the impedance curve below 10 kHz is almost flat and the signal in this frequency range can be amplified by sodium conductance. The longer the distance between the soma and the node becomes, the larger is the signal amplification by the same amount of sodium conductance contributing to the nodal impedance (Fig. 9C). These results indicate that the distance between the soma and the node has an appropriate range for the nodal AC signal enhancement.

Relevance of DTX-sensitive potassium conductance to the advantage of passive soma

Low-voltage–activated (DTX-sensitive) potassium channels (\( \text{K}_{\text{LVA}} \)) are reported to be expressed abundantly in auditory coincidence detector neurons and is thought to be important in ITD detection (Grau-Serrat et al. 2003; Rathouz and Trussell 1998; Rothman and Manis 2003; Svirskis et al. 2003, 2004). However, in a series of simulations, we merged \( \text{K}_{\text{LVA}} \) conductance into a large leak term to simplify the model and to clarify
the relationship between the distribution of sodium channels and ITD sensitivity. Here, we note the role of $K_{LVA}$ conductance in sensing high-frequency AC signals. When a certain amount of leak conductance is replaced by the DTX-sensitive potassium conductance (see METHODS), the model neuron generates only a single onset spike with a wider range of DC inputs (Fig. 10, A–D) and shows outward rectification (Fig. 10E). We calculated normalized AC thresholds of neurons with $K_{LVA}$ conductance at 4-kHz input (Fig. 10F; compare with Fig. 4H). The existence of $K_{LVA}$ current is irrelevant to the fact that a neuron with a passive soma has higher AC sensitivity. The AC-rate curves are shifted by changing the DC input level (Fig. 10, G and H). Although altering DC input does not affect the advantage of the passive soma structure, the elevation in AC thresholds by reducing DC inputs is much smaller in models with $K_{LVA}$. This means that $K_{LVA}$ serves to render models more tolerant to changes in DC amplitude. Thus we speculate that the role of $K_{LVA}$ conductance is to broaden the appropriate signal range for ITD discrimination in the NL neuron by reducing the effect of DC input (Fig. 10F) with strong rectification (Fig. 10E) and the suppression of low-frequency noise (Fig. 7F).

Impact of spike generation

Because the NL neurons in owls have to handle frequency signals faster than spikes, small impacts of spike generation on high-frequency signals will be preferable. We next investigate the impact of spike initiation on the membrane AC response. Under continuous injection of AC current (4 kHz in Fig. 11) with different phases into the soma of the model neuron, a spike is artificially initiated by forcing all Na channels to activate (Fig. 11A; see METHODS). Averaging the potential traces gives a spike template (Fig. 11B). By subtracting the template from the traces, we obtain spike-subtracted potential traces (Fig. 11C), whose envelope shows temporal variation of the AC component of the membrane potential (Fig. 11D). Results of two model neurons with the same DC threshold of 12 nS (active soma neuron and passive soma neuron; see legends) are shown. The baseline difference before time 0 indicates the difference in the subthreshold membrane impedance of each compartment. As previously discussed (Fig. 6), AC potential becomes largest at the node with passive soma. In both active and passive soma models, spike initiation generates a short transient disturbance and a subsequent slow oscillatory variation in the membrane AC response of the spike initiation sites. This oscillation is damped down more quickly in the passive soma neuron than in the active soma neuron, presumably because the large soma in the passive soma neuron acts as a current sink to stabilize the nodal activity. This result provides theoretical support to the significance of segregating the synaptic integration site from the spike-initiation site in coincidence detection, which was also discussed previously (Golding and Oertel 1995; Oertel 2000; Scott et al. 2005).
Metabolic costs

A short membrane time constant is thought to be necessary for precise ITD computation (Golding et al. 1995; Kempster et al. 1998). This idea is consistent with the extra large leak conductance (low membrane resistance) observed in avian NL (Funabiki and Konishi 2005; Kuba et al. 2005) and mammalian MSO neurons (Scott et al. 2005). However, initiating an action potential against a large leak would require a large amount of ionic influx, which should be pumped out to maintain the cellular homeostasis. Because about one half of the energy in the brain is estimated to be consumed in the activity of Na/K pumps (Ames III 2000; Clausen et al. 1991; Laughlin 2001), too much pumping load would be a critical problem for leaky cells. We calculated the ionic flux in the model neuron. The total ionic flux in firing neurons depends mainly on the somatic excitability (Fig. 12A). Because the surface area of the soma is several hundred times larger than that of the node, most of the ionic flux is associated with the soma (Fig. 12B) but not with the node (Fig. 12C). An active soma requires large sodium current to overcome the large somatic leak to initiate an action potential and, as a result, a large influx (mainly arising from sodium current) and efflux (mainly arising from potassium and leak current) are observed (Fig. 12, D and E). Ionic flux with a normal leak neuron was also calculated for comparison (Fig. 12F). In our simulation, a normal leak cell could not process 6-kHz signals even with a passive soma. Making the soma active slightly increases ionic flux in a normal leak neuron was also calculated for comparison (Fig. 12). It was shown that the somatic sodium conductance (passive soma) achieved higher AC-rate sensitivity than those without K_LVA.

Discussion

In this paper, we have demonstrated the advantage of the passive soma design in the NL neuron model and investigated the biophysical basis for this advantage. A neuron with less somatic sodium conductance (passive soma) achieved higher ITD sensitivity (lower AC threshold) and higher noise toler-
PASSIVE SOMA FACILITATES COINCIDENCE DETECTION IN OWLS

Fig. 11. Effect of spike generation on the membrane AC response. A–C: simulation procedure. A: potential traces. Under continuous injection of an AC input (4 kHz) with different phases, a spike is initiated by forcing all the Na channels to activate at time 0. B: spike template obtained by averaging the potential traces (shown in A). C: traces of the membrane AC component obtained by subtracting the spike template (B) from the traces (A). Envelope of these traces indicates the temporal change of the membrane AC component. D: temporal change of the AC components (width of the envelopes). Baseline level of each line (before time 0) reflects the subthreshold impedance level of each component. Somatic membrane AC component is affected only slightly when a spike is initiated in the node (solid red line). Nodal membrane AC component is transiently disturbed by spike initiation in both passive and active soma neurons, but it recovers more quickly in a passive soma neuron. Parameters used in A–D are: $g_{Na node} = 10.8 \, \mu S$, $g_{Na soma} = 0.6 \, \mu S$, input frequency 4 kHz; (active soma) $g_{Na soma} = 7 \, \mu S$, $g_{Na node} = 0.038 \, \mu S$; (passive soma) $g_{Na soma} = 0.869 \, \mu S$. In A–C, somatic potential traces of the passive soma neuron are shown.

Two-compartment NL model

The model we used had two compartments: the soma and the first node. Previous works with two-compartment models, which consisted of dendrites and the soma, focused on the mechanisms of synaptic integration and spike generation (Booth et al. 1995, 1997; Kepecs et al. 2002). By analogy, the soma of an NL neuron acting as a synaptic integrator is comparable to the dendrites of a common neuron and the node of an NL neuron acting as a spike generator is comparable to the soma of a common neuron. This structure of a small node with high sodium channel density connected to a large cell body without sodium channels seems peculiar but the structure itself contributes to high-frequency AC signal detection.

There are many studies concerning the relationship between the spike initiation site and neuronal function (Carras 1992;...
Clark et al. 2005; Colbert et al. 1996, 2002; Khaliq and Raman 2006; Stuart et al. 1994, 1997a,b). A simulation study on the dorsal root ganglion neuron, in which the soma is attached to the “pseudounipolar” axon in a T-shaped bifurcation, showed that somatic excitability is important for spike invasion to the soma, but not for signal conduction (Amir and Devor 2003). The authors discussed that the somatic excitability with significant metabolic costs would confer some unknown functional benefits such as the regulation of protein synthesis. These unknown benefits, on the other hand, might be detrimental to NL neurons with a passive cell body. We suppose that after comparing the advantages in accurate ITD detection and in metabolic costs with possible disadvantages, the NL neuron adopted the passive soma.

The principal aim of our model study was to examine the rationality of using the passive soma structure in ITD computation. We used generic components (fast Na, delayed rectifying K, leak conductance, large soma, and small node) to show that the enhancement of high-frequency signals can be achieved without any specialized conductances. Our model using the original Hodgkin–Huxley equations sufficed for this purpose but was too simplified to reproduce all the characteristics reported in NL neurons (Carr and Konishi 1990; Funabiki et al. 1998; Kuba et al. 2005; Pen˜a et al. 1995; Reyes et al. 1996). For example, the model neuron does not generate spikes at the worst ITD in the absence of noise (Fig. 3C). Replacing the simplified DC + AC input with a more realistic one (Gerstner et al. 1996; Grau-Serrat et al. 2003), introducing inhibitory synaptic inputs (Dasika et al. 2005; Grothe 2003; Peña et al. 1996), and replacing the leak conductance with a proper amount of K_{LVA} conductance (Grau-Serrat et al. 2003; Svirskis et al. 2003, 2004) are possible modifications of the model to bring its properties closer to those of the real neuron. The spectral profile of the real synaptic noise may be different from the Gaussian white noise used in this study. We also confirmed the effect of adding simulated synaptic noises, but the advantage of having large sodium conductance in the node did not change (data not shown). However, more detailed analyses and simulations of synaptic noise will be necessary when we consider the optimal distribution of potassium and other channels that have various impedance profiles.

Difference in strategies between low- and high-frequency NL cells

Barn owls compute ITDs in higher frequencies than other animals studied so far (Knudsen and Konishi 1979). According to the results on membrane response (Fig. 6) and impedance (Figs. 7 and 8), signals around or below 1 kHz will be enhanced by combining somatic sodium conductances, whereas signals over 2 kHz are not enhanced but attenuated in the cell body. Impedance analysis of the two-compartment model showed that the nodal sodium conductance serves to amplify high-frequency signals (Fig. 8). Thus with respect to the signal amplification at the spike initiation site, somatic spike generation might be appropriate for cells handling low-frequency signals, whereas less somatic sodium conductance and nodal spike generation will be appropriate for cells handling high-frequency signals.

We used AC threshold as a measure for ITD sensitivity. For NL or MSO cells handling low-frequency signals (e.g., <2 kHz), large AC signal inputs above the AC threshold would be expected (Fig. 1H). In those cases, different parameters, such as the width or depth of ITD curves might be more appropriate for estimating ITD sensitivity. For large AC inputs (much above the AC thresholds), ITD curves of active soma models are narrower than those of passive soma models (Fig. 4C). Therefore the merit of a passive soma design in low-frequency cells might be less than that in high-frequency cells. Thus the strategy of high-frequency NL cells such as those in owls may differ from that of other coincidence detector neurons handling lower-frequency signals.

Na channel density, firing property, and AC threshold

One of the remarkable characteristics of auditory temporal coding neurons (avian NM and NL cells, mammalian VCN bushy cells, octopus cells, MNTB cells, MSO cells, etc.) is “phasic” firing (Kuba et al. 2005; Oertel et al. 2000; Rathouz and Trussell 1998; Reyes et al. 1996; Rothman and Manis 2003; Scott et al. 2005; Svirskis et al. 2003, 2004); i.e., the neuron shows only an onset spike against DC step inputs. However, the model neurons we used show “tonic” firing; i.e., the neuron generates repetitive spikes for constant inputs. In our model cell array, there are also parameter combinations with which model neurons show only onset spikes (inside the red zone in Fig. 2C) because of low sodium conductances insufficient to evoke repetitive firing. In this parameter area, however, neurons could not or hardly respond to high-frequency AC inputs (e.g., >4 kHz) even when the amplitude was set exceptionally large (creating over 20-mV oscillation; Fig. 2H). This is why we excluded this area from further analyses.

The AC threshold of a neuron strongly depends on the sodium channel densities and the DC threshold (Figs. 2C and 4G). We also demonstrated that the DC input level should be close to the DC threshold to sense small AC signals and that the AC threshold is elevated when the applied DC level is reduced (Fig. 10G). These results can explain why the model neurons showing only onset spikes were not appropriate for high-frequency signal processing. These neurons cannot afford a sufficient amount of basal DC input to lower the AC threshold to a realistic level. This difficulty does not change when part of the leak conductance is replaced by the K_{LVA} conductance (Fig. 10H). The difference in the firing properties between our models and other reports on auditory coincidence detector neurons may be attributed to the frequency ranges of the neurons because model cells showing only onset spikes can generate multiple spikes in response to low-frequency AC inputs (up to 1 kHz). Repetitive firing for DC current inputs observed in owls’ NL cells in vivo (Funabiki and Konishi 2005) lends support to this interpretation.

Low membrane resistance (Funabiki and Konishi 2005; Kuba et al. 2005; Scott et al. 2005) is believed to be important in temporal coding neurons because it makes the membrane time constant small (Golding et al. 1995; Kempter et al. 1998). A strong outward current by the K_{LVA} conductance makes the membrane resistance low (Grau-Serrat et al. 2003; Rathouz and Trussell 1998; Rothman and Manis 2003; Scott et al. 2005; Svirskis et al. 2003, 2004) and plays a key role in inducing onset firing. In general, the firing property of a neuron is determined by the balance between inward and outward cur-
Consequently, the CF of the soma $f_{soma} \approx h/2\pi = 1.27 \text{ kHz}$ and the CF of the node $f_{node} \approx (h + a + b)/2\pi = 43 \text{ kHz} \gg f_{isolate}$. We can summarize this impedance property in two principles:

1. Similar to that the CF of the RC circuit is determined by $g_L$ and $C_m$, the elevated CF of the RC–RC circuit is determined by $g_L + g_{axon}$ and $C_node$.

2. The ratio of $C_{soma}$ and $C_{node}$ (i.e., the size of the soma and the node) determines which CF (original or elevated) is dominant.

Thus the change in the shape of the impedance curve can be explained:

SOMA. Because $g_L > g_{axon}$ in the soma, $g_L + g_{axon}$ is similar to $g_L$. Therefore the elevated CF is almost the same as the CF of the isolated soma. In addition, the soma is several hundred times larger than the node and thus the original CF appears dominantly in the impedance curve.

NODE. Because $g_L < g_{axon}$ in the node, $g_L + g_{axon}$ is almost the same as $g_{axon}$. Therefore the elevated CF determined effectively by $g_{axon}$ and $C_{node}$, is much larger than the CF of the isolated node. Because the soma is several hundred times larger than the node, the elevated CF appears dominantly in the impedance curve.

We have demonstrated an impedance analysis for a simple RC–RC circuit. One of the earliest analyses of membrane cylinders was performed by Rall (1969). The RC–RC circuit has two system time constants: a time constant of the isolated compartment $1/h$ and a very short “equalization time constant” $1/(h + a + b)$ in Rall’s language. In the asymmetric soma–node circuit, the slower time constant is dominant in the soma and the faster one is dominant in the node. For a complete mathematical analysis of the two-compartment model to investigate the effect of various ion channels, the linearization method will serve as a powerful tool (Brunel et al. 2003; Gutfrank et al. 1995; Mauro et al. 1970; Richardson et al. 2003; Rinzel and Ermentrout 1998; White et al. 1995), although it has to deal with twice as many parameters and variables as the single-compartment model.

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**R E F E R E N C E S**


