Analysis of the influence of differences in somatic symmetry and sharpness on the firing rate

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Abstract

The shape and the size of a pyramidal cell depend on hippocampus subregions and even on locations within a same subregion. In this paper, we analyze quantitatively influence of the differences in somatic symmetry and sharpness on the firing rate. The bursting rate (lower frequency) is unchanged by the differences in the symmetry and sharpness. However, the rate of repetitive action potential (higher frequency) is influenced by them. The rate of a swelling cell tends to get larger than that of shrinking one since the swelling cell fires at single spiking mode while the shrinking one at couple of spikes. The rate depends on the firing mode.

Key words: Hippocampus, Pyramidal cell, Somatic shape, Firing mode, Micro-compartmental modeling

1 Introduction

The shape and the size of a pyramidal cell depend on hippocampus subregions such as CA1 and CA3. Each pyramidal cell even on locations within a same subregion has different shape which is regulated by the intracellular osmotic pressure. On the simulation study of neuronal function, in recent years, new neuronal modeling methods which pay attention to this variation in the shape has

been proposed. By using such methods, we can express the electrical characteristics which cannot be explained by using conventional simple cylinder model.

According to the cable theory[1], the propagation velocity of action potential v on cylindrically shaped membrane such as dendrites and axons has a dependence of $v \propto D^{1/2}$ on the effective conductive-layer thickness D. The thickness D is the effective thickness of the intracellular conductive layer that has a direct interaction with the membrane ionic-channel activity when we assume that the membrane is infinite plane. Hirose and Murakami[3] predicted that the action-potential velocity v on a round soma has a dependence of $v \propto D^{0.77}$ through a numerical analysis using a two-dimensional membrane-potential equations. The somatic shape is significantly influential at least when we consider the propagation of action potential in the backward propagation.

We presume that the somatic shape also influences the signal processing dynamics on the neuron. We consider that the influence is attributed to the variation of spreading speed and the property of spatial integration of membrane potential. Because of the strong nonlinearity of the membrane potential dynamics, many parameters are complicatedly tangled and they modulate and modify the neuronal signal processing functions. We[5] previously reported a possible influence of the somatic shape on the firing characteristics. We predicted in a preliminary analysis that the symmetry of somatic shape have influences on the firing rate and firing latency.

In this paper, we evaluate quantitatively influence of the differences in somatic symmetry and sharpness on the firing rate. We need to divide a soma in fractions for the analysis since the membrane potential has a nonlinearity that depends strongly on the potential waveform. For this reason, we propose micro-compartmental modeling to treat the shape effect of the soma.

2 Cell models and analysis conditions

In the conventional compartmental model, a soma is represented as a single cylinder. On the other hand, to analyze the somatic shape effect, we propose the micro-compartmental modeling and construct the models shown in Fig.1A by which we represent each soma as a series of cylinders

of various size. With this micro-compartmental modeling method, we construct variously shaped somatic model instead of a simple cylinder. If we compare the method with the two-dimensional membrane potential equations[3], it has a smaller calculation cost since it is fundamentally based on one-dimensional treatment.

The somas shown in each column in Fig.1A have an equal apical-to-basal direction lengths to each other. Blunter somas are laid in the top row and the sharper ones are in the bottom row, and the middle ones in the center row, respectively. On the other hand, the symmetry is changed in the columns. That is, the highly symmetric somas are located in the right-hand side column, while the lower ones are in the left-hand side.

It can be said that the models in the left column represent CA3 pyramidal cells and those in the middle column correspond CA1 pyramidal cells, while the right-column ones are symmetrical cells for control. They are divided into cylinders whose lengths are 2.5 μm and connected by resistance in series. Each compartment has active ionic channels and the channel densities are uniform. We construct such systematic models, rather than realistic ones, since we intend to investigate what factor of the shape-related electric parameters determine the firing rate.

We index the somatic compartment nos.1–28 from left (axon side) to right (apical dendrite side). Soma no.1 is connected to the initial segment of axon and Soma no.5 is to the basal dendrite, while soma no.28 is to the apical one. We define the sharpness-degree parameter n and radius of each model is proportional to nth power of index and choose at 0.5 (top), 1 (middle), 2 (bottom) respectively.

In a resting state, the membrane electrical potential balances the chemical potential. Once a certain amount of ions are injected at a synapse, the chemical potential is modulated locally and then the membrane potential is also changed. Because of the membrane potential variation, the electric potential far inside the cell is also changed to get almost equal to that just beneath the membrane. However, this deep potential does not affect directly the membrane ionic diffusion. That is to say, the ionic distribution and relevant current that flows far from the membrane have no influence on the membrane potential dynamics, though they do have on other phenomena such as magnetic-field generation. Therefore, in the present analysis, we define the thickness of the intracellular ionic-current

layer D, just under the membrane, as the thickness that has a direct interaction with the chemical potential equilibrium. In other words, only the ions within depth D under the membrane contribute to the propagation of the membrane potential.

The value D is related to the intracellular resistance of the micro-compartmental model where we attribute the ionic diffusion to the conductivity (or resistivity) of the intracellular material. In the micro-compartmental model analysis, the conductivity / resistivity is converted into conductance / resistance through a calculation with membrane width, length, and the depth D. We estimate the value D in Models a_2, b_2 and c_2 as 0.84 μm, 0.90 μm, 0.86 μm, respectively by comparing the intracellular resistance. Then we choose thickness D in both the top and bottom rows as the same as that in the corresponding middle row. In the following calculation, the electrophysiological parameters follow the references[4][5][6].

3 Calculation results

We calculate the firing frequency when the center of the soma (somatic compartment index no.15) is stimulated. The CA3 cells express three different modes of firing in response to steady injection of current into the soma, depending on the magnitude of the injected current[7]. The soma generates rhythmic bursts at low frequency for small injected current 0–0.3 nA[2]. At somewhat higher currents 0.3–0.4 nA, rhythmic bursts with intercalated runs of fast spikes occur. At sufficiently large current more than 0.4 nA, rhythmic action potentials are observed after an initial burst. The action potential rate is calculated during 1000 ms from first spiking time except for initial burst spiking.

We calculated the firing rate versus somatic current injection for three degree of symmetry to analyze the effect of the somatic sharpness to the firing rate.

In Fig.2(A), the curves are almost the same traces. In the bursting mode, the firing rates are the same among the cells which have the difference in sharpness. However, there is the difference in the current where the firing mode is changed from bursting mode to bursting with intercalated runs of first spikes. The turning current gets larger as the somatic shape becomes sharper since the sharper

cells have larger intracellular resistance.

In Fig.2(B), the firing rates are almost the same in the middle figure. However the rates differ in the sharpness degree in other figures. Firing rates of normal sharpness cells in model a (left column) and c (right column) are larger than those of swelling and shrinking ones. The rates of swelling cells are also larger than those of shrinking ones.

To reveal the phenomenon, we show spike interval at each time when injection current is 0.7 nA in Fig.3(A). The spike intervals of normal sharpness cells in each column decrease rapidly at 310 ms (left column), 660 ms (middle column) and 410 ms (right column). In Fig.3(B), we show the potential-time relation at the corresponding time window. The normal sharpness cells (middle rows in Fig.1) change their firing mode from couple of spikes to single one. As the result, the spike intervals change. Therefore, the rapidly decreasing intervals are caused by the change in firing mode.

The spike intervals of swelling cell are larger than those of shrinking ones at every time in Fig.3(A). We can explain this phenomenon by the firing mode. Swelling cells fire at single spiking mode and shrinking cells fire at couple of spikes in Fig.3(B). Therefore, the spike interval depends on their firing mode.

Figure 4 shows relationship current and turning time from couple of spikes to single one among normal sharpness cells (middle rows in Fig.1). The turning time in model a_2 (CA3 cell) is smaller than that in model c_2 (Control) in at every current. The times in model b_2 (CA1 cell) are also larger than those in model c_2 (Control) at all currents. Although capacitance and intracellular resistance are the same among these cells, the turning times are different. Therefore, the turning time of firing mode depends on the degree in symmetry, in other words, capacitance and resistance distribution in soma.

4 Conclusion

The shape and the size of a pyramidal cell depend on hippocampus subregions such as CA1 and CA3. Each pyramidal cell even on locations within a same subregion has different shape which is

regulated by the intracellular osmotic pressure. In this paper, we proposed micro-compartmental modeling method to analyze quantitatively the influence of the difference in somatic symmetry and sharpness on the firing rate. We found that bursting rate (lower frequency) is unchanged by the difference in the symmetry and sharpness. The injection current which changes firing mode from bursting mode to bursting with intercalated runs of first spikes gets larger as the somatic shape becomes sharper since the sharper cells have larger intracellular resistance. We also found that the rate of repetitive action potential frequency (higher frequency) is influenced by them. At repetitive action potential mode, the rates of swelling cells tend to get larger than those of shrinking ones since the swelling cells fire at single spike and the shrinking cells fire at couple of ones. Therefore, the difference in firing rate depends on the firing mode. The firing mode of normal sharpness cells change from couple of spikes to single one. The turning time of firing mode depends on the degree in symmetry, in other words, capacitance and resistance distribution in soma.

Acknowledgements

This work was partly supported by the Ministry of Education, Culture, Sports, Science and Technology, Grant-in-Aid for Scientific Research on Grant-in-Aid for JSPS Fellows 15-11148.

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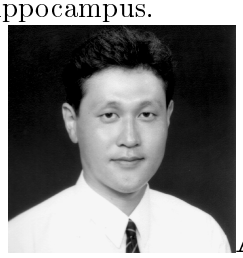
Seiichi Sakatani received the B.S. degree in information and communication engineering from the University of Tokyo, Japan, in 1999. He received the M.S. degree in frontier informatics from the University of Tokyo, Japan, in 2001. Now he is the Ph.D. student at the Department of Frontier Informatics, Graduate School of Frontier Sciences, the University of Tokyo, Japan and Japan Society for the Promotion of Science Fellows. His current research involves cellular magnetism, neuronal membrane potential dynamics, intracellular ionic movement dynamics and memory forming and recalling process in hippocampus.



Akira Hirose received the B.S., M.S. and Ph.D. degrees, all from the University of Tokyo, Tokyo, Japan, in 1985, 1987, 1991, respectively, all in electrical and electronic engineering. In 1987 he joined the Research Center for Advanced Science and Technology(RCAST), University of Tokyo, as a Research Associate at the Optical Devices Laboratory. In 1991 he was appointed an Instructor, and in 1995, became an Associate Professor. From 1999, he has been an Associate Professor at the Department of Frontier Informatics, Graduate School of Frontier Sciences, the University of Tokyo. The main fields of his present interest are neural networks, information processing devices, optical computing and computational neuroscience. Dr. Hirose is a member of the IEEE and the IEICE.

List of Figures

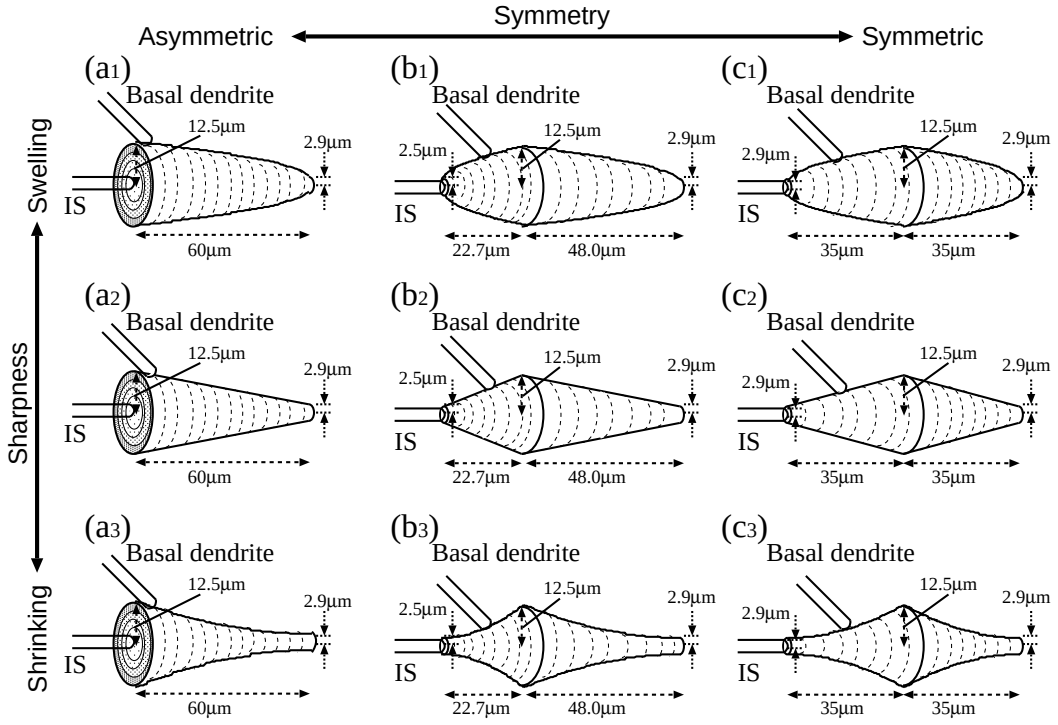

Symmetry
Asymmetric
Symmetric
Swelling
Sharpness
Shrinking
(a1)
(b1)
(c1)
(a2)
(b2)
(c2)
(a3)
(b3)
(c3)
Basal dendrite
12.5µm
2.9µm
2.5µm
IS
60µm
22.7µm
48.0µm
35µm

Fig. 1.

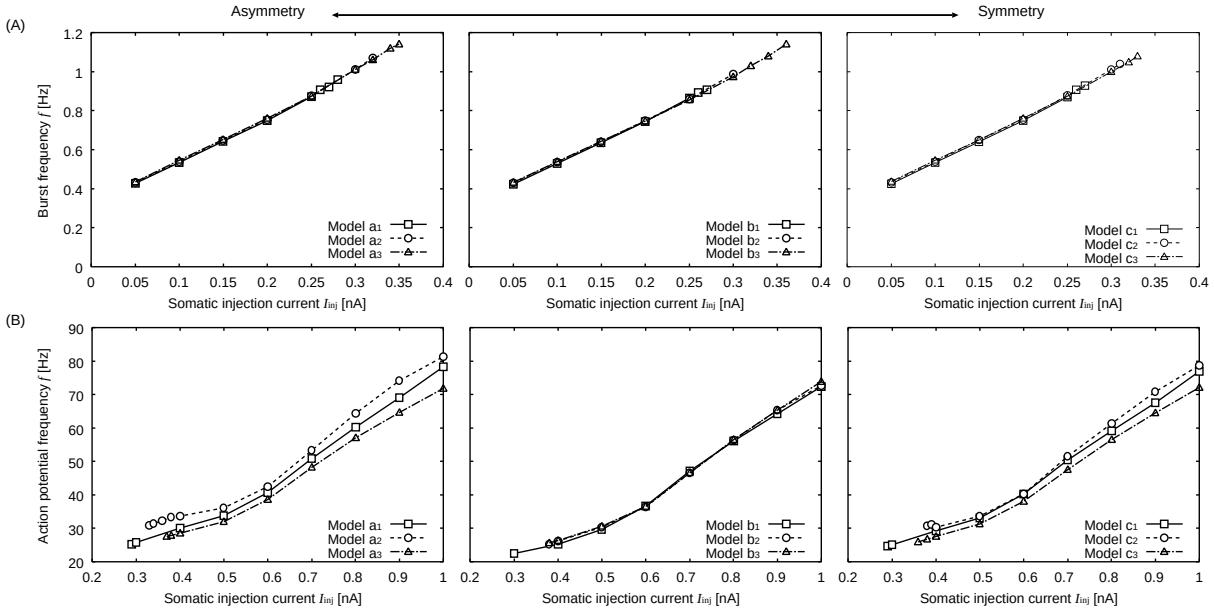

(A)
(B)
Asymmetry
Symmetry
Burst frequency f [Hz]
Action potential frequency f [Hz]
Somatic injection current I_{inj} [nA]
Model a1
Model a2
Model a3
Model b1
Model b2
Model b3
Model c1
Model c2
Model c3

Fig. 2.

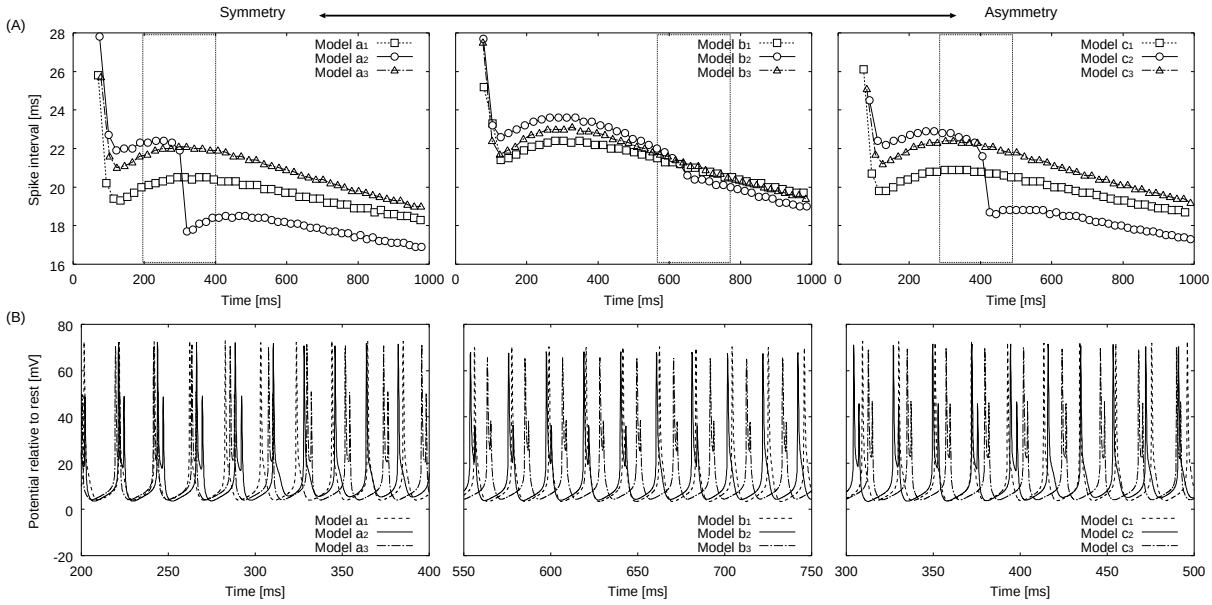

(A)
Symmetry
Asymmetry
Spike interval [ms]
Time [ms]
Model a1
Model a2
Model a3
Model b1
Model b2
Model b3
Model c1
Model c2
Model c3
(B)
Potential relative to rest [mV]
Time [ms]

Fig. 3.

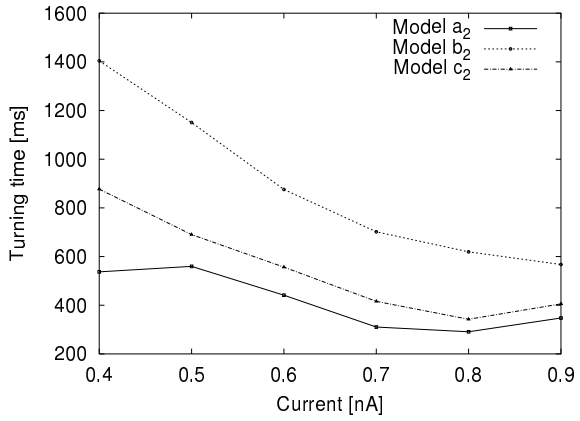

Turning time [ms]
Current [nA]
Model a2
Model b2
Model c2

Fig. 4.