Gamma frequency synchronization in a local cortical network model

Masaki Nomura [a,c] Toshio Aoyagi [a,c] Tomoki Fukai [b,c]

[a]*Department of Applied Analysis and Complex Dynamical Systems, Graduate School of Informatics, Kyoto University, Kyoto 606-8501 JAPAN*

[b]*Department of Information-Communication Engineering, Tamagawa University, Tokyo 194-8610, JAPAN*

[c]*CREST, Japan Science and Technology Corporation, Kawaguchi, Saitama 332-0012, JAPAN*

Abstract

In this modeling study, we show the combined effects of gap junctions and GABAergic synapses on the synchronous firing in networks of FS interneurons. We found analytically that two identical electrically coupled FS interneurons fire synchronously at arbitrary firing frequencies, whereas an FS neuron pair coupled through GABAergic synapses show asynchronous firing. Accordingly, an FS neuron pair connected simultaneously by electrical and chemical synapses achieves both synchronous and anti-synchronous firing state in a physiologically plausible range of the conductance ratio between electrical and chemical synapses. We also investigate how two identical oscillator units composed of a regular-spiking (RS) pyramidal neuron and an FS interneuron may cooperatively fire at several phase-locked states.

Key words: Fast-Spiking Interneuron; Regular-Spiking neuron; Gamma-band Synchronization; Phase Analysis

1 Introduction

Synchronous firing phenomena in local cortical circuitries are considered to play important functional roles [1,2]. Although the neural mechanism of such synchronous oscillations has not been fully clarified, it appears likely that networks of inhibitory interneurons play a role of promoting synchrony in local cortical circuitries [3–6]. Recently, inhibitory interneurons have been classified into a great diversity of structural and functional types [7], but whether this diversity reflects different functions has yet remained unknown. Among these cell types, fast-spiking (FS) interneuron is considered to be one of major
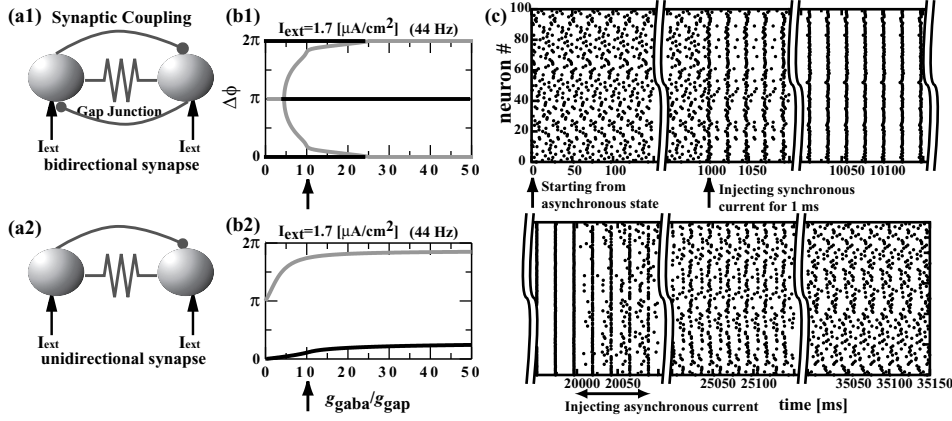
Fig. 1. (a.1,a.2) Two-neuron networks interconnected simultaneously by a gap junction and bidirectional (a.1) or unidirectional (a.2) GABAergic synapses (For details, see [10]). (b.1,b.2) Phase diagrams obtained by the phase-reduction method as functions of the conductance ratio $g_{\mathrm{gaba}}/g_{\mathrm{gap}}$ (firing frequencies are 44 Hz.) (c) Raster plots representing the activity of 100 FS interneurons (Here, $I_{\mathrm{ext}} = 1.7\ \mu\mathrm{A/cm}^2$ and $g_{\mathrm{gaba}}/g_{\mathrm{gap}} = 10$. see Figures 1b.1-1b.2.)

categories of GABAergic interneurons in the neocortex [8]. It is well known that nearby pairs of FS interneurons are often interconnected simultaneously by electrical and chemical synapses, the latter of which are sometimes bidirectional [9,8]. To obtain a better understanding of the coherence of cortical activity, the different functional roles of electrical and chemical synapses in an inhibitory network must be clarified. In this paper, we model a network of FS cells by incorporating the characteristic electronic properties of the K^+ channels expressed on the interneurons and explore the combined effects of electrical and chemical synapses on the synchronous firing of interneurons. One of the modulatory excitatory input to FS interneurons is an ensemble of pyramidal neurons projecting to the FS interneurons in the local cortical circuitry. Furthermore, in the local cortical circuitry, pyramidal neurons and interneurons may cooperatively modulate their firing states such as firing frequency and coherence level. Therefore, we also investigate how regular-spiking (RS) pyramidal neurons and FS interneurons synchronize at the gamma frequency.

2 Model

A characteristic feature of FS interneuron is the appearance of sustained high-frequency trains of brief action potentials with little spike frequency adaptation [11]. It was recently revealed that Kv3.1 and Kv3.2 voltage-gated K^+ channels play significant roles in the creation of this feature [12,13]. In this study, we adopt the FS neuron model proposed by Erisir et al. [12].

In our FS-neuron network, any FS neuron pair is interconnected by a gap junction as well as by a bidirectional (Figure 1a.1) or a unidirectional (Figure 1a.2) GABAergic synapse. Here, the GABAergic chemical couplings are described by a kinetic model of receptor binding [14]. As the gap junction, we use the ordinary form, that is, the current mediated by the gap junction is proportional to the difference of the membrane potentials of the postsynaptic and presynaptic neurons.

Applying the phase reduction method, in Figures 1b.1-1b.2, we show the steady state phase differences as a function of the conductance ratio $g_{\mathrm{gaba}}/g_{\mathrm{gap}}$ (g_{gaba} and g_{gap} are the maximum conductances of chemical and electrical synapses, respectively). In these figures, stable phase differences and unstable phase differences are represented by the black solid lines and the gray solid lines, respectively. We can summarize the characteristics of synchronization in the coupled two-neuron network as follows. i) The spike timing of two weakly coupled neurons depends strongly on the amplitude of the external current (data not shown) and on the conductance ratio between the gap junction and the chemical synapse. ii)For sufficiently small values of $g_{\mathrm{gaba}}/g_{\mathrm{gap}}$, only synchrony is realized asymptotically. iii) When $g_{\mathrm{gaba}}/g_{\mathrm{gap}}$ is sufficiently large, only anti-synchrony is realized in symmetric network. In asymmetric network, a phase-locked state with a nonzero phase difference or a non-phase-locked state is realized. iv) In an intermediate range of $g_{\mathrm{gaba}}/g_{\mathrm{gap}}$, phase-locked state with several phase differences coexist. In particular, in this range of $g_{\mathrm{gaba}}/g_{\mathrm{gap}}$, synchrony and anti-synchrony are simultaneously stable over almost the entire range of the gamma oscillation. v) With $g_{\mathrm{gaba}}/g_{\mathrm{gap}}$ fixed, the relative spike timing in the stable state changes with the amplitude of the external current (data not shown).

3   Large-Scale Networks

In the local cortical circuitry, nearby pairs of FS interneurons are often connected either bidirectionally or unidirectionally by GABAergic synapses [9]. Here, we study a large-scale network such that 70% of FS neuron pairs have unidirectional GABAergic synapses and the rest have bidirectional ones. The directions of the unidirectional connections were determined randomly. Gap junctions are presented between all the neuron pairs. In Figure 1c, we show how the synchronous spiking behavior of this network can be rapidly modulated by injecting either synchronous or random input current. In this figure, the network was initially in the non-phase-locked state. At $1,000$ ms, all the neurons simultaneously received a brief depolarizing current ($I_{\mathrm{ext}} = 20\ \mu\mathrm{A/cm^2}$) for 1 ms (synchronous current). This input caused a rapid increase of the coherence of the network activity to achieve a near-synchronous state. Conversely, established synchronous firing could be desynchronized by an asynchronous input.
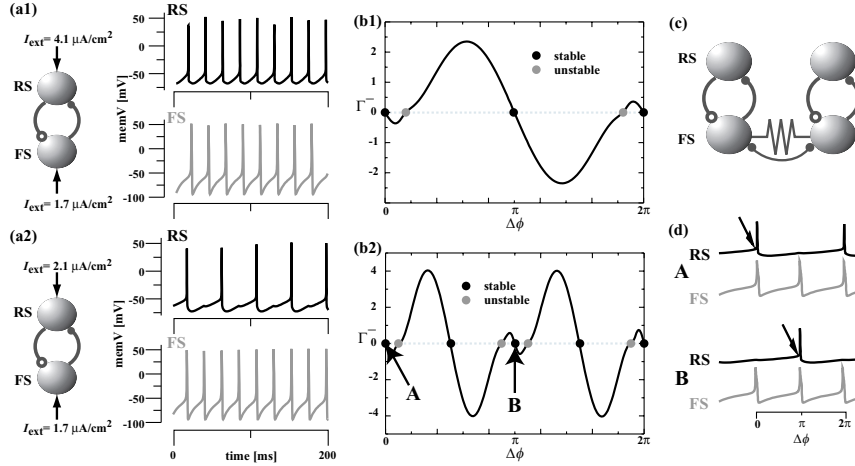
3

Fig. 2. (a.1,a.2) The *oscillator unit* is composed of a RS and an FS neuron strongly interconnected by AMPA and GABA synapses. These neurons can fire in several phase-locked states. (b.1,b.2) Gamma functions for the two oscillator units network (see Figure 2c) whose firing behaviors are corresponding to those of Figures 2a.1 and 2a.2, respectively. (c) Two identical oscillator units network. Here, $g_{gaba}/g_{gap} = 10$. (d) Time course of membrane potentials of RS and FS neurons corresponding to stable solutions **A** (top) and **B** (bottom), respectively.

In the simulation, a neuron was randomly selected every 1 ms and innervated by the previous brief depolarizing current (random current). The random input, which lasted for 100 ms, from $20,000$ ms to $20,100$ ms, resettled the network in the non-phase-locked state. This simulation demonstrates that the degree of synchrony in an FS interneuron network can change between the two levels, high and low, depending on the coherence level of excitatory inputs to FS interneurons.

4 RS and FS neuron network

One of the modulatory excitatory input to FS interneurons is an ensemble of pyramidal neurons projecting to the FS interneurons in the local cortical circuitry, and pyramidal neurons and interneurons may cooperatively modulate their firing states such as firing frequency and coherence level. In this section, we investigate how regular-spiking (RS) pyramidal neurons and FS interneurons synchronize at the gamma frequency.

As for RS neuron, we adopt the same model as the pyramidal neuron model proposed by Aoyagi et al. [15] except that the cationic current is absent from their model. Conducting numerical simulations, we found that strongly interconnected RS and FS neurons, which we call *oscillator unit*, can phase-lock even at different firing frequencies (for example, at 1 : 2 firing frequencies. see Figures 2a.1-2a.2.) To investigate how RS and FS neurons network syn-

chronize, we analytically study a network of two identical oscillator units as shown in Figure 2c. Here, we found that when RS and FS neuron fire at same firing frequency, their firing behavior shows bistability similar to that of FS neuron network as shown in Figure 2b.1. In the case that the firing frequency of RS neuron is half of the former case, the shape of the gamma function result in being similar to two period of that in the former case, and thus, stable solutions are increased (see Figure 2b.2). Stable solutions **A** and **B** can be distinguished by firing timing of RS neuron, although FS neurons have the same firing timings (see Figure 2d). We also found that these spiking behaviors can be modulated by incorporating another synaptic connections between the two oscillator units (data not shown).

5   Conclusions

We have shown that the synchrony observed in a network of FS interneurons depends strongly on the magnitude of the external current and the conductance ratio between electrical and chemical synapses. These results suggest that coherence activity in a network of FS interneurons may vary through synaptic learning and that the state of synchrony can be changed by an excitatory input to the FS interneurons. We demonstrated that an excitatory input can switch the state of the FS interneuron network between synchronous firing and non-phase-locked firing. We have also found that two identical RS-FS units interconnected by weak electrical and bidirectional GABAergic synapses can show multi stability (synchrony and so on) even if the firing frequencies of RS and FS neurons are different.

References

[1] G. Buzsáki, R. Llinás, W. Singer, A. Berthoz, Y. Christen, Temporal Coding in the Brain, Berlin:Springer, 1994.

[2] W. Singer, C. M. Gray, Visual feature integration and the temporal correlation hypothesis, Annu. Rev. Neurosci. 18 (1995) 555–586.

[3] W. W. Lytton, T. J. Sejnowski, Simulations of cortical pyramidal neurons synchronized by inhibitory interneurons, J. Neurophysiol. 66 (1991) 1059–1079.

[4] S. R. Cobb, E. H. Huhl, K. Halasy, O. Paulsen, P. Somogyi, Synchronization of neuronal activity in hippocampus by individual gabaergic interneurons, Nature 378 (1995) 75–78.

[5] M. A. Whittington, R. D. Traub, J. G. R. Jefferys, Synchronized oscillations in interneuron networks driven by metabotropic glutamate receptor activation, Nature 373 (1995) 612–615.

[6] M. Beierlein, J. R. Gibson, B. W. Connors, A network of electrically coupled interneurons drives synchronized inhibition in neocortex, Nat. Neurosci. 3 (2000) 904–910.

[7] Y. Kawaguchi, Y. Kubota, GABAergic cell subtypes and their synaptic connections in rat frontal cortex, Cerebral Cortex 7 (1997) 476–486.

[8] J. R. Gibson, M. Beierlein, B. W. Connors, Two networks of electrically coupled inhibitory neurons in neocortex, Nature 402 (1999) 75–79.

[9] M. Galarreta, S. Hestrin, Electrical and chemical synapses among parvalbumin fast-spiking gabaergic interneurons in adult mouse neocortex, Proc. Natl. Acad. Sci.USA 99 (2002) 12438–12443.

[10] M. Nomura, T. Fukai, T. Aoyagi, Synchrony of fast-spiking interneurons interconnected by gabaergic and electrical synapses, Neural Comput. 15 (2003) 2179–2198.

[11] B. W. Connors, M. J. Gutnick, Intrinsic firing patterns of diverse neocortical neurons, Trends Neurosci. 13 (1990) 99–104.

[12] A. Erisir, D. Lau, B. Rudy, C. S. Leonard, Function of specific k^+ channels in sustained high-frequency firing of fast-spiking neocortical interneurons, J. Neurophysiol. 82 (1999) 2476–2489.

[13] B. Rudy, C. J. McBain, Kv3 channels: voltage-gated k^+ channels designed for high-frequency repetitive firing, Trends Neurosci. 24 (2001) 517–526.

[14] A. Destexhe, Z. F. Mainen, T. J. Sejnowski, An efficient method for computing synaptic conductances based on a kinetic model of receptor binding, Neural Comput. 6 (1994) 14–18.

[15] T. Aoyagi, Y. Kang, N. Terada, T. Kaneko, T. Fukai, The role of ca^{2+}-dependent cationic current in generating gamma frequency rhythmic bursts: modeling study, Neuroscience 115 (2002) 1127–1138.

Masaki Nomura received the Ph.D. degree in informatics from Kyoto University, Kyoto, Japan, in 2001. At present, he is a postdoctoral researcher in Core Research for the Evolutional Science and Technology Program (CREST), JST.

Toshio Aoyagi is the lecturer in the Department of Applied Analysis and Complex Dynamical Systems, Kyoto University. He is also serving as a researcher for a project by CREST, Japan Science and Technology. His present research focuses on the mechanisms of synchronization in neuronal systems and its functional roles in information processing.

Tomoki Fukai received a Ph.D. degree in physics from Waseda University, Tokyo, Japan. His research project supported by Japan Science and Technology focuses on modeling cortical neurons and their local circuits, coincident neural activities and its functional implications, and the interplay between the cortical and basal-ganglia neural networks in organizing behavior.