The Role of Excitatory and Inhibitory Synaptic Connectivity in the Pattern of Bursting Behavior in a Pyramidal Neuron Model

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Abstract The connections between excitatory and inhibitory synapses are significant for generation of bursting activity in a pyramidal neuron model. We have suggested in previous studies that a reduced neuronal model of synaptically connected neurons could produce repetitive bursting activity. We have also suggested that the modification of the balance between inhibition and excitation by synaptic weight could alter the excitability of neuronal networks. In this computational study, we have investigated the role of the relative locations of excitatory and inhibitory synapses on the dendritic tree and soma in the generation of bursting activity. We have built a reduced pyramidal neuron model of synaptically connected neurons using the simulation software GENESIS. Our model consists of three reduced pyramidal neurons and an inhibitory interneuron. Simulations show that a reduced pyramidal neuron model can accurately replicate bursting behavior. This bursting activity depends upon the synaptic parameters represented by synaptic weight and delay as well as the locations of synaptic inputs. Simulations with an interneuron show that the inhibitory interneuron regulates neuronal bursting activity. The inhibitory effect is stronger when the inhibitory synapse is close to the soma.

Keywords Pyramidal neuron model; Inhibitory interneuron; Epileptiform activity

1. Introduction

Various forms of synaptic reorganization in brain tissue have appeared in evolution of epileptic foci using clinical and experimental data. Kudela et al. (1999) demonstrated the spread of synchronous repetitive firing in locally connected neurons. They suggested that the synaptic weight range for which the velocity of propagation is consistent with measurements of the propagation of epileptiform activity in neocortex [4].

Recent studies have suggested that a relatively simple neuron model can produce firing behavior when the modeled neurons are connected to other similar neurons [5][6]. Kudela at al. (1997) suggested that a simple neuron model can generate different firing patterns: a range of bursting behavior and the firing frequency. Franaszczuk et al. (2000) also suggested that reduced single compartment neuronal models can reproduce a wide range of bursting activity.

Several laboratories have studied that firing patterns in biophysical neuron models can be described by model parameters [1][2][8]. Av-Ron et al. (1993) and Av-Ron (1994) suggested that changing certain parameters in a biophysical model may explain bursting activity as well as the firing frequency. Kudela et al. (2000) suggested that increasing the number of excitatory connections, represented by the synaptic weight, increases the bursting activity in their network model.

The aim of this computational study is to investigate the role of parameters of connectivity in the pattern of burst activity in pyramidal neurons. We have also investigated the influences of excitatory and inhibitory synaptic connections on the patterns of bursting in a pyramidal neuron model.

2. Methodology

We have built a simple pyramidal model of synaptically connected neurons and an interneuron
using the simulation software GENESIS. Three simplified pyramidal neurons and an interneuron are modeled in this study: two neurons connected with excitatory synapses, a neuron where random input is applied to generate action potentials, and an inhibitory interneuron in a negative feedback loop with one of the modeled pyramidal neurons. The generated action potentials spread to one of the other neurons which is excitatory synaptically connected to the other one as a loop.

Each neuron has 15 compartments with soma and a main dendrite which has two branch dendrites. Soma has excitatory synaptic channel (I_{syn}), fast sodium (I_{Na}), delayed potassium (K_{DR}), high-threshold calcium (I_{Ca}), and calcium-activated (C-current) potassium (K_{AHP}) channels, and a slow potassium channel (K_{C}) which depends only on the Ca^{2+} concentration. The equations for these channels are the same as in the Traub et al. (1991) multicompartmental CA3 pyramidal cell model. The synaptic connection between neurons is modeled by a synaptic channel, I_{syn}. The synaptic conductance is modeled as an alpha function with the maximum value of 0.5 nS. The synaptic weight represents the overall strength of a connection and the synaptic delay represents all delays between neurons. The simulation time step was 0.05 ms and simulations were run for 10 sec using Genesis version 2.1 on a UNIX operating system.

3. Previous work

Simulations show that a reduced pyramidal neuron model can produce repetitive burst activity which depends upon synaptic parameters represented as the synaptic weight and delay in several synaptic connections between neurons. When the synaptic inputs are on each soma of the two neurons connected with excitatory synapses, the bursting activity occurs at values of the synaptic weight, >100, and a range of values of the synaptic delay, 0 - 10 msec. When the synaptic weight is decreased to 100 there is no bursting activity in these neurons. When the synaptic delay is above 10 msec there is no bursting activity with any values of the synaptic weight but prolonged depolarization occurs.

In order for the generation of burst of action potentials in the synaptic inputs on each main dendrite of the two neurons connected with excitatory synapses, the synaptic weight needs to increase. When the synaptic weight is > 800 the bursting activity occurs in the synaptic inputs on each main dendrite of the two neurons connected with excitatory synapses. A range of values of the synaptic delay, 0 - 50 msec, is required to generate repetitive bursting activity. When the synaptic inputs on each branch dendrite of the two neurons connected with excitatory synapses the bursting activity occurs if the synaptic weight is > 8200. A range of values of the synaptic delay, 0 - 50 msec, is required to generate repetitive bursting activity.

<table>
<thead>
<tr>
<th>Synaptic input (neuron1)</th>
<th>Synaptic input (neuron2)</th>
<th>values of weight</th>
<th>range of delay (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>soma</td>
<td>soma</td>
<td>&gt; 100</td>
<td>0 - 10</td>
</tr>
<tr>
<td>main dendrite</td>
<td>main dendrite</td>
<td>&gt; 800</td>
<td>0 - 50</td>
</tr>
<tr>
<td>branch dendrite</td>
<td>branch dendrite</td>
<td>&gt; 8200</td>
<td>0 - 50</td>
</tr>
</tbody>
</table>

Simulations with an interneuron show that the inhibitory interneuron regulates neuronal bursting activity. When the excitatory synaptic inputs on each of main dendrites of two connected neurons, the inhibitory effect is stronger if the inhibitory synapse is close to soma; when the synaptic weight is 1200 and synaptic delay is 3 msec in neurons connected with excitatory synapses, which generate the bursting activity without an interneuron, bursting activity is disappeared in values of the synaptic weight of an interneuron, > 500, if the inhibitory synapse is on the main dendrite, which is close to the soma. When the inhibitory synapse is on the branch dendrite, which is far from the soma, there is still bursting activity in values of the synaptic weight preventing bursting activity in the inhibitory synapse on the main dendrite. In order to produce the same inhibitory effect on the branch dendrite the synaptic weight of an interneuron needs to increase.

4. Summary and conclusion

Our simulations show that a reduced pyramidal neuron model can accurately replicate bursting behavior. The pattern of bursting activity is
dependent upon the synaptic weight and delay in several locations of excitable synaptical connections in a reduced pyramidal neuron model. Simulations with an inhibitory interneuron show that the pattern of bursting behavior depends upon the synaptic weight and delay of the inhibitory connection as well as the location of the synapse. The inhibitory effect is stronger when the inhibitory synapse is close to the soma.

References