Multistability in inhibitory networks with depressing synapses

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Introduction

The majority of synapses in the central nervous system display short-term changes in their strength or efficacy in response to repeated activation. Short-term synaptic plasticity have also been identified in many different excitatory and inhibitory synapses in cortical (see review of references in [3]) and hippocampal (see review of references in [10]) circuits. It has been suggested to play a role in automatic gain control [1], network stabilization [12], population rhythm generation [7, 8, 11], and in temporal coding in cortical processing such as novelty detection [6] and coincidence detection [10].

In [4], Manor and Nadim experimentally considered a network of two inhibitory (I) cells, reciprocally coupled by two depressing synapses through a dynamic clamp. They showed that this network robustly displayed bistability of a cell-controlled and a synapse-controlled firing pattern. In the cell (synapse)-controlled case both depressing synapses were weak (strong). The experiments leave open the possibility that a third type of solution could exist in which one of the depressing synapses is strong, while the other is weak.

Here, we are interested in investigating how short-term synaptic depression can generate multistability in neuronal networks. By multistability, we mean the ability of a neuronal network to display different stable firing patterns, for the same set of parameters, obtained from different initial conditions. We investigate how synaptic depression can induce multistability in a model network consisting of two oscillating neurons connected reciprocally with inhibitory, depressing synapses.

Model

Our model neurons are described by the Morris-Lecar equations [5]. We consider the case when both neurons are identical, intrinsic oscillators with identical synapses. Equations for each neuron can generically be written as

$$
\begin{aligned}
v_i' &= f(v_i, w_i) + I_{syn,j} \\
w_i' &= h(v_i, w_i) \\
d_i' &= [1 - d_i][1 - d_\infty(v_i)]/\tau_\alpha - d_i d_\infty(v_i)/\tau_\beta \\
s_i' &= [d_i - s_i]s_\infty(v_i)/\tau_\gamma - s_i[1 - s_\infty(v_i)]/\tau_\kappa
\end{aligned}
$$

where $f(v, w)$ incorporates ionic currents intrinsic to each cell, $h(v, w)$ models the effect of potassium gating and $I_{syn,j} = g_{ji}s_j[v_i - E_{inh}]$ is the synaptic current from neuron j to neuron i. The parameters g_{ji} and E_{inh} are the maximal conductance and reversal potential of the synapse. The functions $d_\infty(v) = 0.5[1 + \tanh(v - v_1)/v_2]$ and $s_\infty(v) = 0.5[1 + \tanh(v - v_3)/v_4]$. The variable d_i is a depression variable which keeps track of the extent of depression and recovery of the synapses [2]. This information is transmitted to the post-synaptic cell through the variable s_i. Whenever neuron i goes above the synaptic threshold v_3, s_i approaches d_i with a time constant $\tau_\gamma = 1$. Since this time constant is so small, it means that s_i is effectively equal to d_i whenever the pre-synaptic neuron is above threshold. There the synapse depresses with time constant τ_β. When the presynaptic neuron is below threshold, then d_i and s_i are decoupled. The former grows with time

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constant τ_α, while the latter decays with time constant τ_κ.

Results

When the synapses in the two cell network are not depressing, several different anti-phase firing patterns are obtained as the maximum synaptic conductance is varied. For weak synaptic conductances ($g_{12} = g_{21} \leq 0.17mS/cm^2$), the two neurons alternately fire single spikes in a classic anti-phase pattern that we will call one-to-one anti-phase firing. As the maximum synaptic conductances are increased identically ($0.18 \leq g_{12} = g_{21} < 0.2mS/cm^2$), the one-to-one anti-phase pattern changes to a two-to-two anti-phase pattern where the neurons alternately fire two spikes each. For larger values of g_{12} and g_{21} ($g_{12} = g_{21} \geq 0.2mS/cm^2$), one cell is able to completely suppress the firing of the other cell. Either cell is capable of being suppressed by the other, hence these modes are bistable for large values of the maximum synaptic conductance.

When the synapses in the network are depressing (using the same synaptic decay rate $\tau_\kappa = 100msec^{-1}$), more anti-phase firing patterns can be obtained over different ranges of maximum synaptic conductance values. As in the non-depressing case, for smaller values of g_{12} and g_{21}, one-to-one anti-phase firing is obtained ($g_{12} = g_{21} \leq 0.4mS/cm^2$). As g_{12} and g_{21} are increased, one-to-one anti-phase gives over to two-to-two anti-phase ($0.4 \leq g_{12} = g_{21} \leq 0.65mS/cm^2$) but now there is a small range of values where either mode can be obtained and bistability has been introduced. Specifically, as shown in Fig 1, for $g_{12} = g_{21} = 0.4mS/cm^2$ the network can be switched between the one-to-one anti-phase mode and the two-to-two anti-phase mode. The switch is induced by briefly reducing the applied current to each cell, indicated by the heavy black bar beneath Figs 1A and B. In the case shown, during this reduction of applied current, the firing frequency of cell 1 decreases allowing its synapse to recover such that inhibition to cell 2 is increased (Fig 1C). With increased inhibition, cell 2 is unable to fire before cell 1 fires again, thus leading to a two-to-two anti-phase pattern. Note in Fig 1C that the maximum values of d_1 and s_1 increases when the pattern switches from the one-to-one to two-to-two pattern.

For larger values of g_{12} and g_{21}, more anti-phase patterns are obtained with small regions of bistability near the synaptic conductance values where the modes transition. For $0.65 \leq g_{12} = g_{21} \leq 0.8$, three-to-three anti-phase firing is obtained and at $g_{12} = g_{21} = 0.65mS/cm^2$ there is bistability between two-to-two firing and three-to-three firing as shown in Fig 2. The switch between modes is induced in the same way as in Fig 1 with the same brief decrease in firing frequency that allows one of the synapses to recover more fully. Again note that the maximum values of d_1 and s_1 are larger in the three-to-three solution than for the two-to-two pattern.

Four-to-four anti-phase firing is obtained for $0.8 \leq g_{12} = g_{21} \leq 0.85$ and five-to-five anti-phase firing occurs near $g_{12} = g_{21} = 0.9$. For $g_{12} = g_{21} \geq 1.0mS/cm^2$, one cell can completely suppress firing in the other cell and, as in the non-depressing synapse case, there is bistability of these suppressed-cell modes.

The above results illustrate that the network of two cells is capable of producing a variety of bistable rhythms. In fact, more is possible. In [9], it was shown that if there exists a synaptic delay between mutually inhibitory neurons, then the synchronous solutions is also stable. Including a delay in our study would not qualitatively affect the bistability found above. Such a delay would allow our network to display tristability between synchronous and (two different) anti-phase solutions.

Implications and Current Work

Viewed from the context of temporal coding, multistability provides a cheap way for a network to expand the number of codes it can convey. Synchronous, one-to-one anti-phase and two-to-two anti-phase patterns

each have the potential to carry different information to downstream neurons. A given network could chose to, or be forced by a neuromodulator, to operate in only one of these states, thereby not utilizing the multistability. Alternatively, at no greater cost, the same network could be tuned to be capable of operating in any of the three states. Switches between states could be induced by transient hyperpolarization or depolarizations which respectively strengthen or weaken the depressing synapses. An interesting point of our analysis is that the difference in the stable states is seen not only directly as different firing patterns, but also indirectly by differences in the maximum strengths of the synaptic currents of each type of solution. An open question that we are addressing is what is the upper bound on the number of stable states that the network can have as a function of the number of depressing synapses.

The current work focuses on two identical neurons. It lays the ground work to study networks where the neurons are heterogeneous either in their synaptic or intrinsic properties such as the network consider by Manor and Nadim [4].

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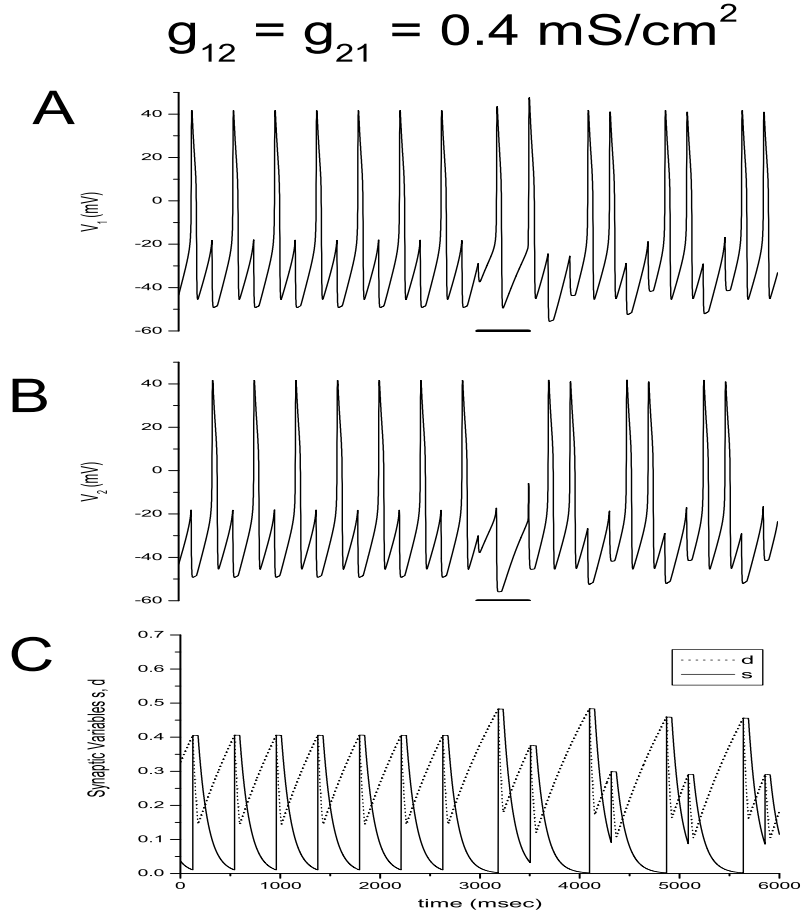
Fig 1

Figure 1: Bistability between one-to-one and two-to-two anti-phase solutions. **A.** and **B.** Voltage traces of both cells are shown. Applied current, transiently lowered to both cells near $t = 3000$, switches the cells between two different bistable rhythms. **C.** The depression and synaptic variables d_1 and s_1 from neuron 1 to neuron 2 are shown. The maximum value of d_1 is larger in the second part of trace indicating a greater recover from depression on each cycle and thus a stronger synapse.

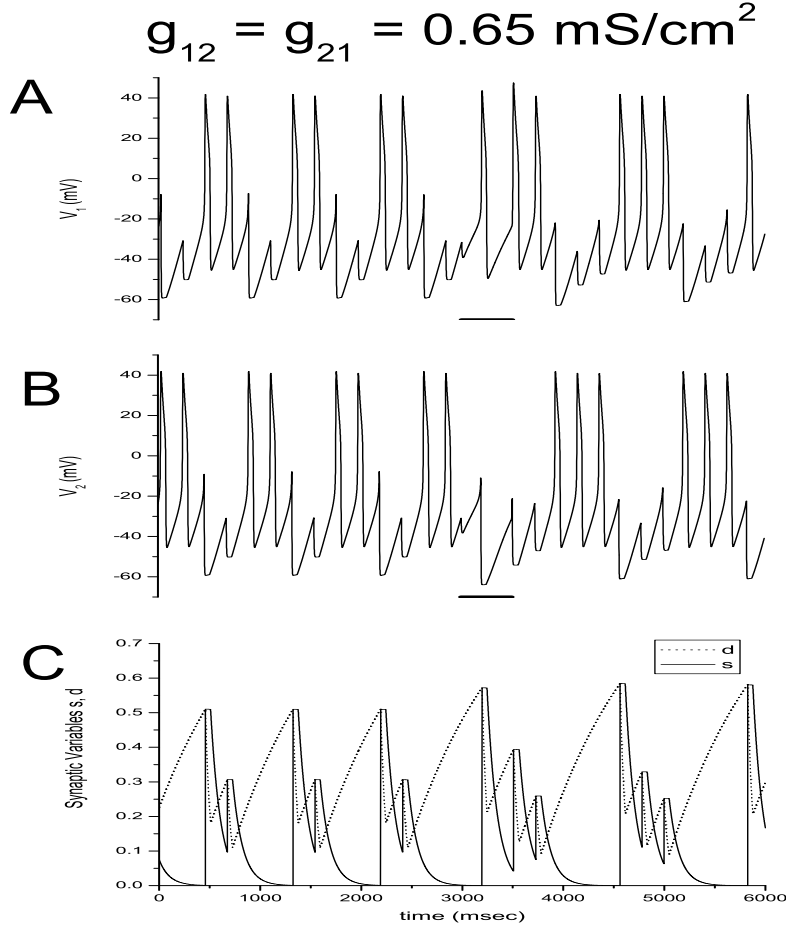$$g_{12} = g_{21} = 0.65 \text{ mS/cm}^2$$

Fig 2

Figure 2: Bistability between a two-to-two and three-to-three anti-phase solutions. **A.** and **B.** Voltage traces of both cells are shown. Applied current, transiently lowered to both cells near $t = 3000$, switches the cells between two different bistable rhythms. **C.** The depression and synaptic variables d_1 and s_1 from neuron 1 to neuron 2 are shown. The maximum value of d_1 is larger in the second part of trace indicating a greater recover from depression on each cycle and thus a stronger synapse.