Frequency and burst duration in oscillating neurons and two-cell networks

Frances K. Skinner, Gina G. Turrigiano, Eve Marder
Biology Department and Center for Complex Systems, Brandeis University, Waltham, MA 02254-9110, USA

Received: 18 January 1993/Accepted in revised form: 28 April 1993

Abstract. We study the relationship of injected current to oscillator period in single neurons and two-cell model networks formed by reciprocal inhibitory synapses. Using a Morris-Lecar-like model, we identify two qualitative types of oscillatory behavior for single model neurons. The "classical" oscillator behavior is defined as type A. Here the burst duration is relatively constant and the frequency increases with depolarization. For oscillator type B, the frequency increases and then decreases as the membrane potential is depolarized, due to the variable burst duration. Our simulations show that relativelty modest changes in the maximal inward and outward conductances can move the oscillator from one type to another. Cultured stomatogastric ganglion neurons exhibit both A and B type behaviors and can switch between the two types with pharmacological manipulation. Our simulations indicate that the stability of a two-cell network with injected current can be extended with inhibitory coupling. In addition, two-cell networks formed from type A or type B oscillators behave differently from each other at lower synaptic strengths.

1 Introduction

Neurons with oscillatory properties play important roles in the nervous system (Jackett 1989; Llinas 1988). Central pattern-generating networks that produce rhythmic movements commonly contain pacemaking neurons and/or neurons with conditional plateau properties that are crucial to the generation of these rhythmic movements (Harris-Warrick and Marder 1991; Marder 1991). Additionally, oscillatory processes are likely to play important roles in sensory processing as well as other cortical functions (Başar and Bullock 1992). Therefore, understanding which properties of neural oscillators are general features of all oscillators and which are specific properties of a particular neuron, or neural model, is critical both for understanding how the nervous system operates and for choosing oscillator models with which to describe real neurons and neural circuits. It is of particular significance to experimentalists to understand how the intrinsic properties of neurons depend on membrane potential and are modified by synaptic interactions. In this paper we focus on several features of neuronal oscillators that are particularly important to experimentalists. These include the relationship of imposed current to oscillator frequency and burst duration, in both single neurons and two-cell networks.

A useful oscillator model is that originally described by Morris and Lecar (1981). This model has only two voltage-dependent conductances, an inward Ca$^{2+}$ current, and an outward K$^+$ current. This model is simple enough for mathematical analyses (Rinzel and Ermentrout 1989), and because it contains currents with some biophysical realism, it is possible to relate the properties of this model directly to biophysical properties of biological neurons. Rinzel and Ermentrout (1989) analyzed the properties of the Morris-Lecar equations in different parameter regimes and described oscillators on the basis of their behavior at the onset of oscillation. Zero-frequency oscillations originated at a saddle-node bifurcation, whereas non-zero oscillations originated at a Hopf bifurcation.

In this paper we examine the relationship between injected current and burst duration and period, as a function of the parameters controlling the Ca$^{2+}$ and K$^+$ currents. We find that in some parameter regimes, Morris-Lecar oscillators show relatively constant burst durations and increase in frequency when depolarized. We call this oscillator type A. In other parameter regimes, Morris-Lecar oscillators show variable burst durations as a function of injected current. These oscillators first increase and then decrease in frequency when depolarized. We call this oscillator type B. Our simulations illustrate that relatively small changes in the maximal conductances underlying bursting may move the oscillator from one to the other state. Electrophysiological recordings from isolated neurons in dissociated cell culture also show both behaviors; pharmacological manipulations can move biological neurons between these two forms of behavior. Finally, we study reciprocal inhibitory networks formed from these model oscillators of the two types and describe their behavior.

Correspondence to: F. Skinner
The Morris–Lecar model

\[ C \frac{dV}{dt} = I_{\text{ext}} - \left[ g_L (V - V_L) + g_{Ca} M_a (V - V_Ca) \right] + \frac{g_K N (V - V_K)}{2} \]  
\[ \frac{dN}{dt} = \lambda_N (N_{\infty} - N) \]

and

\[ M_a(V) = \frac{1}{2} \left[ 1 + \tanh \left( \frac{V - V_1}{V_2} \right) \right] \]

\[ N_a(V) = \frac{1}{2} \left[ 1 + \tanh \left( \frac{V - V_3}{V_4} \right) \right] \]

\[ \lambda_N(V) = \phi_N \cosh \left( \frac{V - V_2}{2V_4} \right) \]

where \( C \) is the capacitance; \( V \) is the membrane voltage; \( I_{\text{ext}} \) is the external or imposed current; \( g_L, g_{Ca}, g_K \) are the leak, \( Ca^{2+} \) and \( K^+ \) maximal conductances respectively; \( V_L, V_{Ca}, V_K \) are the reversal potentials for the leak, \( Ca^{2+} \) and \( K^+ \) conductances respectively; \( M_a, N_a \) are the fraction of open \( Ca^{2+} \) and \( K^+ \) channels at steady state respectively; \( N \) is the fraction of open \( K^+ \) channels with a rate constant of opening given by \( \lambda_N \); \( \phi_N \) is the minimum rate constant for \( K^+ \) channel opening; \( V_1 \) is the voltage at which half of the \( Ca^{2+} \) channels are open at steady state; \( V_2 \) is the voltage whose reciprocal is the slope of voltage dependence of the fraction of open \( Ca^{2+} \) channels at steady state; \( V_3 \) is the voltage at which half of the \( K^+ \) channels are open at steady state; \( V_4 \) is the voltage whose reciprocal is the slope of voltage dependence of the fraction of open \( K^+ \) channels at steady state.

Note that the activation of \( g_{Ca} \) is assumed to be instantaneous, or significantly faster than the activation of \( g_K \).

For the case of two-cell networks, we consider the case of reciprocal inhibition. Equation (1) is adjusted to include the inhibitory synaptic current, and the fraction of open synaptic channels at steady state is included. Therefore, cell 1 would be given by:

\[ C \frac{dV^1}{dt} = I_{\text{ext}} - \left[ g_L (V^1 - V_L) + g_{Ca} M_a^1 (V^1 - V_Ca) \right] + g_K N_1 (V^1 - V_K) + g_{syn} S_1^1 (V^1 - V_{syn}) \]

\[ \frac{dN^1}{dt} = \lambda_N^1 (N^1_{\infty} - N^1) \]

and

\[ M_a^1(V^1) = \frac{1}{2} \left[ 1 + \tanh \left( \frac{V^1 - V_1}{V_2} \right) \right] \]

\[ N_a^1(V^1) = \frac{1}{2} \left[ 1 + \tanh \left( \frac{V^1 - V_3}{V_4} \right) \right] \]

where \( g_{syn} \) is the maximal synaptic conductance; \( V_{syn} \) is the reversal potential of the synaptic current; \( S_1 \) is the fraction of open synaptic channels at steady state; \( V_1 \) is the voltage at which half of the synaptic channels are open at steady state; \( V_2 \) is the voltage whose reciprocal is the slope of voltage dependence of the open synaptic channels at steady state. The superscripts refer to cell 1 or 2 in the network. For the reciprocal inhibitory coupling, the fraction of open synaptic channels of cell 1 is dependent on the voltage of cell 2, and vice versa. Note that the synaptic activation is assumed to be instantaneous. The equations for cell 2 would be similar.

Due to the simplicity of the Morris–Lecar model, there are no action potentials on top of the oscillation. In particular, this is due to fast sodium channels responsible for spiking not being included in the model. In the model simulations, the burst is approximately the phase of the oscillation where the membrane potential is above 0 mV. In biological neurons, the burst would be the phase of the oscillation above threshold for action potentials, approximately \(-40 \text{ mV} \) for neurons.

Numerical integrations are performed using LSODE a double-precision subroutine capable of handling stiff systems of first-order ordinary differential equations which is based on the Gear method (Gear 1971). The AUTO program (Doedel 1981) is used to generate the bifurcation diagrams, which give the range of external current for which oscillations occur in a single cell and in two-cell networks. AUTO is also used to determine the period versus external current figures.

3 Oscillator types

3.1 Single cell

Figure 1 shows plots of voltage as a function of time for the two oscillator types, for increased amounts of depolarizing current injection. For \( g_{Ca} = 0.01 \text{ mS/cm}^2 \), the oscillator exhibits behavior type A, with the frequency increasing with depolarization and the burst duration remaining fairly constant (Fig. 1, left). For \( g_{Ca} = 0.015 \text{ mS/cm}^2 \), the oscillator exhibits behavior type B, with the frequency increasing and then decreasing with depolarization. In this case, the burst duration increases significantly with depolarization (Fig. 1, right). Figure 2 shows a plot of period as a function of external current for four values of \( g_{Ca} \). As \( g_{Ca} \) increases, the oscillator changes behavior from type A to type B. These figures illustrate that relatively modest changes in \( g_{Ca} \) can transform the oscillator from one showing type A behavior to one showing type B behavior. Figure 2 also illustrates that small modifications of the maximal conductances influence the range over which the model is in its oscillatory mode. Figure 2 also indicates the range of injected current over which the model oscillates. At lower levels of
Fig. 1. Voltage waveforms for five values of injected current (µA/cm²), and two values of maximal calcium conductance. Oscillator type A is given with \( g_K = 0.01 \text{ mS/cm}^2 \), oscillator type B with \( g_K = 0.015 \text{ mS/cm}^2 \). The dotted line represents the 0 mV line, and the scale bars are 0.5 s and 50 mV. The other parameter values are: \( g_L = 0.005 \text{ mS/cm}^2 \), \( V_C = 100 \text{ mV} \), \( V_I = -80 \text{ mV} \), \( V_o = -50 \text{ mV} \), \( \phi_v = 0.002 \text{ ms}^{-1} \), \( C = 1 \mu\text{F/cm}^2 \), \( V_1 = 0 \text{ mV} \), \( V_2 = 15 \text{ mV} \), \( V_3 = 0 \text{ mV} \), \( V_4 = 15 \text{ mV} \).

Fig. 2. Period versus external current for changes in the maximal calcium conductance. As \( g_K \) increases, the oscillator behavior changes from type A to type B. The other parameter values are: \( g_L = 0.02 \), \( g_K = 0.005 \text{ mS/cm}^2 \), \( V_C = 100 \text{ mV} \), \( V_I = -80 \text{ mV} \), \( V_o = -50 \text{ mV} \), \( \phi_v = 0.002 \text{ ms}^{-1} \), \( C = 1 \mu\text{F/cm}^2 \), \( V_1 = 0 \text{ mV} \), \( V_2 = 15 \text{ mV} \), \( V_3 = 0 \text{ mV} \), \( V_4 = 15 \text{ mV} \).

injected current the model neuron is silent; at higher levels it becomes locked up at a depolarized membrane potential (see Fig. 1 for illustrations). For the examples shown in Fig. 2, there is an approximately twofold increase in period with increasing current, regardless of whether it is exhibiting type A or B behavior. However, the range of injected current over which the model is in its oscillatory mode is somewhat greater for oscillator type A than oscillator type B.

In Fig. 3 we show that modest changes in \( g_K \) can also influence whether an oscillator shows type A or type B behavior. Figure 3 shows plots of voltage as a function of time for the two oscillator types, for increased amounts of depolarizing current injection. Behavior type A is obtained with \( g_K = 0.02 \text{ mS/cm}^2 \). Here the frequency increases with depolarization and the burst duration remains fairly constant (Fig. 3, left). Behavior type B, with the frequency increasing and then decreasing with depolarization, is obtained with \( g_K = 0.01 \text{ mS/cm}^2 \). In this situation, the burst duration increases significantly with depolarization (Fig. 3, right). Figure 4 shows the period versus external current for four values of \( g_K \). As \( g_K \) increases, the oscillator changes behavior from type B to type A. These figures show how behavior transformations can occur with changes in \( g_K \). Again, there is an approximately twofold increase in period for the examples shown in Fig. 4, regardless of whether it is exhibiting type A or type B behavior. Also, in this figure, it is very obvious that the range of injected current over which the model is in its oscillatory mode is greater for oscillator type A than for oscillator type B. Similar changes in behavior can be obtained by varying other parameters, such as \( V_C \) and \( \phi_v \) that govern oscillator behavior. The parameter values used are shown in the figures and figure legends.

Biological neurons can display both type A and type B behaviors. Stomatogastric ganglion (STG) neurons from the spiny lobster, Panulirus interruptus, were removed from the STG and placed into primary cell culture.
Fig. 4. Period versus external current for changes in the maximal potassium conductance. As \( g_K \) increases, the oscillator behavior changes from type B to type A. The other parameter values are: \( g_K = 0.01 \), \( g_L = 0.005 \) mS/cm², \( V_K = 100 \) mV, \( V_L = -80 \) mV, \( \phi = 0 \) mV, \( \phi_L = 0 \) mV, \( \phi = 0.002 \) ms⁻¹, \( C = 1 \) μF/cm², \( V_L = 0 \) mV, \( V_K = 15 \) mV, \( V_L = 0 \) mV, \( V_L = 15 \) mV as previously described (Turrigiano and Marder 1993). Neurons were plated onto individual culture dishes in defined medium and were thus completely isolated from all synaptic and modulatory inputs. Cultures were maintained at room temperature, and microelectrodes were used to make intracellular recordings from each neuron after 3 days in culture (Turrigiano and Marder 1993).

Under these conditions, many stomatogastric neurons burst either spontaneously or as a result of current injection. Figure 5 shows the membrane potential as a function of time for increasing amounts of depolarizing current injection for one such neuron. This neuron behaves as a "classical" oscillator, in that the frequency of the oscillations increases with increasing current injection, as it does for the simulated oscillator type A. Figure 6 shows the voltage as a function of time for increasing current injection for another cultured STG neuron. In contrast to the behavior of the neuron in Fig. 5, in this neuron the oscillations first increase in frequency, and then decrease again with higher levels of depolarizing current.

Fig. 5. Intracellular recording from a stomatogastric neuron isolated in culture for 3 days. Traces show the intracellular voltage as a function of time for increasing amounts of DC current injection. The dashed line indicates −40 mV in each panel. The plot of period versus injected current illustrates that this neuron is behaving like a type A oscillator. Data are the mean ± SEM for six to ten periods.

Fig. 6. Intracellular recording from a stomatogastric neuron isolated in culture for 3 days. Traces show the intracellular voltage as a function of time for increasing amounts of DC current injection. The dashed line indicates −40 mV in each panel. The plot of period versus injected current illustrates that this neuron is behaving like a type B oscillator. Data are the mean ± SEM for six to ten periods.
Altering the balance of inward and outward currents can convert a neuron of type B to a neuron of type A, as shown in Fig. 7. The depolarizing phase of the burst in these neurons is driven by two conductances, a calcium conductance and a persistent, tetrodotoxin (TTX)-sensitive sodium conductance (Turrigiano and Marder 1992). The control activity in Fig. 7 shows a biological neuron of type B, for which the frequency first increases and then decreases with increasing current injection. Reducing the inward current by placing the neuron into TTX converts it from a type B oscillator into a type A oscillator.

Since the model simulations are a simplistic representation of a neuron, there are some differences in the behavior of the simulations and the biological neurons. For the type A biological neurons, the burst duration either remains relatively constant (Fig. 7) or decreases (Fig. 5) with increasing current injection, whereas the burst duration in the model type A oscillator either increases slightly (Fig. 1) or remains relatively constant (Fig. 3) with increasing injected current. For the type B biological neurons, the burst duration either increases steadily (Fig. 7) or first decreases and then increases steadily (Fig. 6) with increasing current injection, whereas the burst duration in the model type B oscillator always increases with increasing injected current (Figs. 1, 3). These differences probably reflect the complex interactions of the large number of voltage and time dependent conductances in the biological neurons.

3.2 Two-cell networks

The fact that oscillators can respond qualitatively differently to injected current suggests that this will influence the properties of networks in which they are found. Therefore, we compared the properties of isolated type A and type B oscillators to two-cell networks in which the two cells were connected by reciprocally inhibitory chemical synapses. In the next set of model simulations, the networks consisted of two identical neurons, and the synapses were symmetrical (identical in strength and voltage dependence). In the network simulations, current was injected identically into both neurons of the network.

In Fig. 8 we show plots of voltage as a function of time for type A oscillators, as a function of increased amounts of depolarizing current injection. The left panel shows a single type A oscillator (the uncoupled case, for comparison), and the right panel shows one of the pair of oscillators in the coupled case. In this simulation, \( g_{syn} = 0.0025 \text{ mS/cm}^2 \). The most striking difference between the behavior of the isolated type A oscillator (left) and that of the coupled oscillators (right) is the amplitude of the oscillations. The baseline membrane potential of the isolated oscillator is depolarized by the injected current. However, the inhibitory synapse from the second oscillator brings the membrane potential of the coupled oscillator down to a more hyperpolarized range, thus increasing the total range of membrane potentials through which it can travel. Therefore, this might suggest that the two cell network can function over a larger range of current before "locking up." The plots shown in Fig. 9 illustrate that this is the case for lower values of \( g_{syn} \).

Figure 9 shows that, as the strength of the inhibitory synapse is increased from \( g_{syn} = 0 \) to \( g_{syn} = 0.01 \text{ mS/cm}^2 \), the range of injected current over which the network operates is increased. When \( g_{syn} \) is raised to 0.03 mS/cm², another behavior is revealed. This behavior is illustrated in the voltage and synaptic current plots of Fig. 10. In this figure the voltage and synaptic current of both cells are plotted as a function of time, for each value of injected current. At lower values of injected current (\( i = 0.3 \) and \( i = 0.8 \mu A/cm^2 \)) the two cells are in the range in which
they are able to oscillate in isolation. As the injected current is increased (i = 1.8 μA/cm²), the cells are out of the range in which they are intrinsically oscillatory in isolation, and one of the pair "locks up," thus inhibiting the second permanently. However, if the amount of injected current is still greater, a network oscillation is produced. In this case, neither cell is capable of sustaining an oscillation in isolation, but a true "half-center oscillation" that depends on the inhibitory synapses for its existence is seen. This behavior gives the broken plot of period as a function of injected current in Fig. 9 for g_m = 0.03 mS/cm².

Figure 11 shows plots of voltages as a function of time for type B oscillators as a function of increased amounts of depolarizing current injection. Again, the two cases shown correspond to runs without and with reciprocal inhibition where g_m = 0.0025 mS/cm². As with type A oscillators, the amplitude of the oscillations is less affected as the cells are depolarized. It is interesting to note that networks formed from type B oscillators can operate faster than those without the reciprocal inhibition. For example, this is shown in Fig. 11 at an injected current value of 0.58 μA/cm², where the reciprocal inhibitory network has a higher frequency than the uncoupled case. This occurs because of the variable burst duration of the type B oscillator. The inhibition terminates the burst sooner than it would have done when uncoupled, thus increasing the frequency. This does not occur for the type A oscillator because the burst duration is relatively constant.

Figure 12 illustrates the family of curves for oscillator type B, where each curve represents the period of the network oscillation versus the external current for a given strength of the inhibitory synapses. Again, these plots indicate that the two-cell circuits oscillate over a much larger range of injected current than the single cells, and that, as g_m increases, the range of injected current over which the network oscillates also increases. Note again that, at higher g_m values (i.e., 0.03 mS/cm²), there is a break in the plot. Figure 13 shows the emergence of network oscillations again for values of injected
Fig. 11. Oscillator type B. Voltage waveforms for four values of injected current (μA/cm²), with and without reciprocal inhibition. The other parameters are: \( g_L = 0.005 \text{ mS/cm}^2 \), \( V_m = \text{-80 mV} \), \( V_C = 100 \text{ mV} \), \( V_E = \text{-80 mV} \), \( V_I = \text{-50 mV} \), \( \phi_E = 0.002 \text{ ms}^{-1} \), \( C = 1 \mu\text{F/cm}^2 \), \( P_1 = 0 \text{ mV} \), \( P_2 = 15 \text{ mV} \), \( P_3 = 0 \text{ mV} \), \( P_4 = 15 \text{ mV} \). The dotted line represents 0 mV, and the scale bars are 0.5 s and 50 mV. Note that for the waveforms with reciprocal inhibition, only one cell in the network is shown; the other is antiphase.

Fig. 12. Oscillator type B. Period versus external current for maximal synaptic conductances of 0.00025, 0.0005, 0.001, 0.003 mS/cm². The other parameters are: \( g_L = 0.015 \), \( g_E = 0.02 \), \( g_I = 0.005 \text{ mS/cm}^2 \), \( V_m = \text{-80 mV} \), \( V_C = 100 \text{ mV} \), \( V_E = \text{-80 mV} \), \( V_I = \text{-50 mV} \), \( \phi_E = 0.002 \text{ ms}^{-1} \), \( C = 1 \mu\text{F/cm}^2 \), \( P_1 = 0 \text{ mV} \), \( P_2 = 15 \text{ mV} \), \( P_3 = 0 \text{ mV} \), \( P_4 = 15 \text{ mV} \). Extended considerably over that shown by the uncoupled case. In other words, the stability of the oscillatory behavior is increased. Second, in networks of type A oscillators, the period is not as sensitive to injected current as those formed from type B oscillators (compare Figs. 9 and 12). Third, for these parameter ranges, the strength of the synaptic interaction is more critical for oscillators of the B form than for the A form (compare Figs. 9 and 12). Figures B (oscillator type A) and 11 (oscillator type B) show the extension of stability of oscillatory behavior where at depolarized values, the network continues to oscillate stably but the uncoupled system has stopped oscillating fully.

At lower synaptic conductances (0.00025 - 0.0005 mS/cm²), the frequency profile of the network is similar to the single oscillator in that it increases when depolarized (type A) or increases and decreases when depolarized (type B). As in the uncoupled case, the burst duration of the type A network is relatively constant, whereas the burst duration of the type B network is variable. However, at higher synaptic conductances (0.01 mS/cm² and higher), the strong synaptic current causes both network types to show similar behaviors. The frequency first increases, then decreases and then increases again with depolarization. If the synaptic conductance is high enough, the network will increase and decrease in frequency, then stop oscillating, and then increase in frequency with depolarization.

4 Discussion

In this paper we have explored the relationship of imposed current to oscillator period in single model
neurons and two-cell networks formed by reciprocal inhibitory connections. By varying parameters in the simple, semi-realistic Morris–Lecar model (1981) we have defined two qualitatively different types of oscillators. This classification is not meant to imply that these two types are mechanistically different, but is intended to focus attention on the fact that their behaviors are qualitatively different. Type A oscillators increase in frequency as the amount of depolarizing current is increased, through their entire range of activity. Type B oscillators show large variations in the interburst interval and relatively little change in their burst duration as they change period. In contrast, type B oscillators show highly variable burst durations, and therefore display U-shaped plots of period versus external current as they are depolarized. A simple consequence of this is that a type B oscillator may display the same frequency with different waveforms (e.g., Fig. 1) produced by different levels of depolarization.

The simulations in this paper demonstrate that relatively modest changes in the ratio of the inward and outward conductances in the Morris–Lecar model can switch the model neuron between type A and type B behavior. Most real neurons have not just two voltage-dependent conductances, but many (Golowasch and Marder 1992; Linás 1988), that determine their characteristic behavior. Cultured STG neurons exhibit both types of oscillator behavior and are able to switch between the two types with pharmacological manipulation. In addition, modulatory influences that change the balance of inward and outward currents may be capable of switching a neuron’s behavior between type A and type B. The pacemaker for the pyloric rhythm of the STG; the AB neuron, shows type A behavior (Abbott et al. 1991; Bal et al. 1988), while other STG neurons show type B behavior (Bal et al. 1988).

From the literature it is often difficult to determine whether neurons exhibit type A or type B behavior or both, because the response of a neuron to a large enough range of injected currents is not often reported. The original Hodgkin–Huxley equations (Hodgkin and Huxley 1952) have been shown to exhibit oscillator behavior type A (Fitzhugh 1961). The parabolic burster R15 in Aplysia shows oscillatory behavior type A (Wilson 1982) for the injected current levels shown. This activity has been simulated by several authors (Adams and Benson 1985; Both et al. 1976; Canavier et al. 1991; Plant and Kim 1976). In their examples, for the range of injected current levels shown, the model neuron always exhibited behavior type A. In a simplified cortical pyramidal neuron model, oscillator type A behavior was demonstrated (Lytton and Sejnowski 1991).

In the simulations performed, it was possible to obtain both type A and type B behaviors when the oscillations originated at either a Hopf or a saddle-node bifurcation. At a saddle-node bifurcation, oscillations emerge with zero frequency, whereas at a Hopf bifurcation, the oscillations emerge with a frequency at a well-defined non-zero minimum (Rinzel and Ermentrout 1989). This indicates that a saddle-node or Hopf bifurcation is not the determining factor for the two types of behavior. However, it was more likely that the type A behavior would be obtained if the oscillations originated at a saddle-node bifurcation. In addition, the transition between Hopf and saddle-node bifurcations is not abrupt, making it difficult to predict what type of behavior would be obtained with a particular choice of parameters. Therefore, to determine the types of behavior, it was necessary to do a parametric study as we have done.

It is important to know what types of behavior a neuron can exhibit. The importance of the U-shaped relation of period to injected current in the type B oscillator is apparent when one considers the effect of synaptic input on the cell. If the cell is close to the "tough" region, its frequency can be increased by either excitatory or inhibitory synaptic input, which injects depolarizing and hyperpolarizing currents respectively. Thus the cell's characteristic behavior, as determined by its underlying currents, can cause the cell to respond similarly to different synaptic input.

In this paper we controlled the amount of injected current. In previous work the influence of electrical coupling between a neural oscillator and a passive cell or two oscillators was studied (Kepler et al. 1990; Sharp et al. 1992). In some parameter ranges, as the strength of electrical coupling between a neural oscillator and a passive hyperpolarized cell was increased, the frequency first increased and then decreased. This behavior was dependent on the balance of inward and outward currents (Kepler et al. 1990).

Some oscillatory networks control behaviors in which stability over a wide range of frequencies is important, despite small perturbations to the system. For the parameters investigated, our simulations suggest that the stability of a two-cell network to inputs may be extended by reciprocal inhibitory coupling between the oscillators. Therefore, reciprocal inhibition may be considered as a mechanism to increase the stability of a network.

It matters whether two-cell networks are formed from type A or type B oscillators. For low coupling strengths and for the parameters investigated, our simulations suggest that the qualitative differences in oscillator behavior (types A and B) are maintained in two-cell reciprocal inhibitory networks formed from oscillators of each type. Due to the variable burst duration of oscillator type B, it is possible for the frequency of the two-cell network of type B oscillators to increase beyond the frequency for a single cell with reciprocal inhibition. This is not possible with oscillators of type A. In the parameter regimes that we have considered, the type A network's period is not as sensitive to injected current as that of the type B network. It also appears that the strength of the synaptic inhibition is more critical for type B oscillators.

Wang and Rinzel (1992) studied pacemaker rhythms generated by two non-oscillatory model cells coupled by inhibitory synapses. They identified two mechanisms for oscillations, namely release (the inhibition is turned off, allowing the inhibited cell to fire) and escape (the inhibited cell "escapes" from the maintained inhibition). For the release mechanism to occur, it is necessary for the synaptic threshold voltage to be greater than the
steady-state voltage when uninhibited. The system is bistable and the period depends critically on the synaptic threshold. In the escape mechanism, the synaptic threshold voltage must be less than the steady-state voltage of the cell when it is not receiving any inhibition, and the period is insensitive to the synaptic threshold voltage. In our simulations, we found that large depolarizing currents in networks with high synaptic inhibition gave rise to oscillations which were an emergent property of the network. In this case, the mechanism of alternating oscillations can be identified as an escape mechanism, since the synaptic threshold is less than the steady-state voltage of the cell when it is not inhibited (Wang and Rinzel 1992). As suggested by Wang and Rinzel (1992), it is possible that this condition could be met in leech heart beat interneurons, which exhibit a very slowly decaying plateau potential. This potential may contribute to maintaining a quasi-stationary potential level in a free cell that is higher than the synaptic threshold. The mechanisms which result in oscillatory behavior in two-cell reciprocal inhibitory networks have been mathematically analyzed (F. Skinner et al., in preparation). The network behavior has been found to depend not only on release and escape mechanisms, but also on intrinsic and synaptic mechanisms.

One of our major interests lies in determining the relative importance of individual neural properties and their interactions in generating network behavior. As a first step, we have investigated the relationship between frequency and injected current in single and reciprocally inhibited cells. Even two-cell networks show rich and complex patterns of behavior that depend on whether the neurons are type A or type B. It will be instructive to determine how larger networks of these oscillators behave.

Acknowledgements. This work was supported by the National Science Foundation grant BNS 9009251 to L.R. Epstein and E. Marder and the National Institute of Mental Health grant MH-46742.

References