Title (Modeling bursting neurons of the lobster cardiac network)

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Abstract

We develop a biophysical bursting cell model from our previous minimal model (Av-Ron et al 1991). The minimal cell model can exhibit excitability (single action potentials) and oscillatory behavior. By incorporating a new process we construct a minimal bursting model which can show altered durations of oscillations and quiescence but with a fixed firing frequency. An additional process is then incorporated that allows for control of the firing frequency. This basic model is shown to describe different individual cell firing patterns found experimentally in the nine cell lobster cardiac ganglion network.

Introduction

The lobster cardiac ganglion is a neuronal network that stimulates the heart of the lobster. We wish to investigate the behavior of this network in a theoretical manner as a case study for research in neuronal networks. In this paper we present a model that can exhibit different firing patterns seen for the cells of this network. This model is based on a *minimal model* (Av-Ron et al 1991, hereafter denoted as I) that exhibits excitability and oscillatory behavior.

A typical behavior of motorneuron cells in the lobster cardiac ganglion (and of many other neurons in other systems) is periodic intervals of high frequency "bursting", as illustrated in Fig. 1a (Bullock and Terzuolo 1957). As a preparatory step to analyze this observation, we define three types of cells; oscillatory, burster and follower. A cell is oscillatory if it fires indefinitely when subjected to a suitable transient input. If for the same input the cell exhibits alternating intervals of oscillation and quiescence it is a burster. And if it responds with action potentials for the duration of the input, it is a follower.

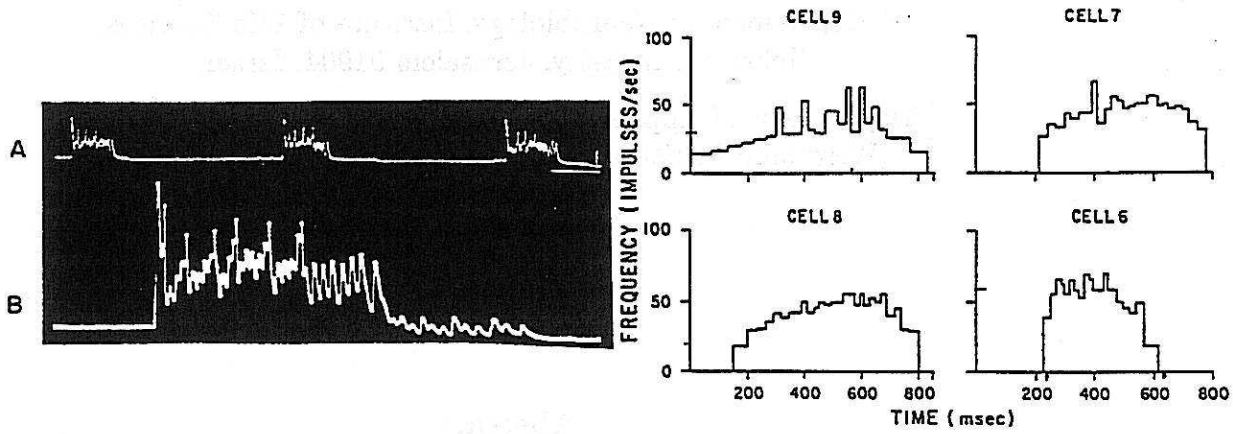

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Fig. 1. (a) Intracellular voltage recording from a motorneuron cell of the cardiac ganglion of the lobster *Panulirus interruptus*. B enlargement of A. Scales in A (right): $10mV$, $500ms$. Taken with permission from Bullock and Terzuolo (1957). (b) Experimental frequency graphs for the interneuron cells 6-9 of the cardiac ganglion of the lobster *Panulirus interruptus* taken with permission from Friesen (1975).

The lobster cardiac ganglion is an autonomous interactive neuronal network composed of nine cells, that stimulates the heart of the lobster. The network is comprised of four interneurons (cells 6-9) and five motorneurons (cells 1-5). The duration of a single burst episode is approximately 850 ms, although the motorneurons are active for less than half of this time. A hierarchy of behavior usually seen, Fig. 1b (Friesen 1975a), is that cell 9 is the first and last to fire, cell 8 is next followed by cell 7 and then cell 6, which has the shortest burst duration. In terms of firing frequencies, the order is reverse, cell 6 has the highest and cell 9 has the lowest, see Fig. 1b. With the first cell 6 pulse, the motorneurons cells 1-4 fire an inital high frequency burst (20 ms duration) and subsequently follow cell 6. Once cell 6 stops firing they halt as well. Cell 5 has a tonic firing pattern for a duration slightly longer than the other motorneurons.

Given that a cell exhibits bursting, one possibility is that the bursting is *endogenous* in that it occurs even in the absence of external stimulation. Since it is generally the first to fire, cell 9 is assumed to be of this "*pacemaker*" type. Another possibility is that a cell is a *conditional burster* whereby an input is required to establish the conditions needed for bursting. Because their frequency is higher than that of cell 9, cells 8-6 are usually regarded as conditional bursters. A final possibility is that the oscillations observed in a cell are principally due to their input. The large cells 1-5 are believed to be of this nature and hence are termed *follower cells.*

A number of people have considered bursting models, for review see Rinzel and Ermentrout (1989) and Rinzel and Lee (1987). The goal of this paper is to present a 'basic' biophysically motivated bursting model that will be sufficient to describe the various firing patterns seen in the lobster cardiac ganglion. To that end we begin by describing the oscillatory properties of the minimal model. We then alter that model into a minimal burster model. Finally our more realistic *basic model* is presented.

A minimal cell model

In I we presented a minimal cell model based on the work of Hodgkin and Huxley (1952) and Rinzel (1984). The model involved three types of currents, an inward sodium current I_{Na}, an outward potassium current I_K and a leak current I_L. An ion current I_i was described by the product of its maximal conductance $\bar{g}_i$, activation and inactivation variables, and driving force $(V - V_i)$. The system was represented by two variables, the voltage variable V and a recovery variable W. Such a model can exhibit excitability, in that a suprathreshold stimulus will cause it to generate an action potential. For other parameter regimes the model yields oscillatory behavior, but does not exhibit bursting.

The minimal model of I is the following:

$$C_m \cdot dV/dt = I - I_{Na} - I_K - I_L, \qquad dW/dt = (W_\infty(V) - W)/\tau_w(V), \qquad (1,2)$$

$$\text{with} \qquad I_{Na} = \bar{g}_{Na} m_\infty^3(V)(1 - W)(V - V_{Na}), \qquad (3a)$$

$$I_K = \bar{g}_K (W/s)^4 (V - V_K), \quad \text{and} \quad I_L = \bar{g}_L (V - V_L). \qquad (3b,c)$$

The following equations give the voltage dependence of the steady state recovery (W_∞), the steady state sodium activation (m_∞) and the relaxation time for recovery (τ_w):

$$W_\infty(V) = 1/(1 + exp[-2a^{(w)}(V - V_{1/2}^{(w)})]), \qquad (4)$$

$$m_\infty(V) = 1/(1 + exp[-2a^{(m)}(V - V_{1/2}^{(m)})]), \qquad (5)$$

$$\text{and} \qquad \tau_w(V) = 1/(\bar{\lambda}\, exp[a^{(w)}(V - V_{1/2}^{(w)})] + \bar{\lambda}\, exp[-a^{(w)}(V - V_{1/2}^{(w)})]). \qquad (6)$$

The steady state functions are modeled as sigmoid curves. The parameter $V_{1/2}$ is the voltage for the half maximal value and the parameter 'a' controls the slope of the curve at this midpoint (inflection point).

An action potential is composed of a relatively brief period of extensive depolarization followed by an interval of repolarization that brings the voltage toward and (generally) below the rest level. The membrane potential may return to rest with ensuing quiescence. Alternatively, for oscillatory cells, the membrane potential increases

until the excitation threshold is crossed and another spike is generated.

Our minimal model exhibited two types of long term qualitative behaviors, oscillation and quiescence. In order to obtain bursting, we must add some process to our minimal model so that the model cell will now pass back and forth between oscillation and quiescence.

A minimal burster model

We would like to alter our minimal model in a simple way so as to achieve a bursting model. We will first note that the minimal model can exist in three dynamic states. A bifurcation diagram for parameter $\bar{g}_K$ is presented in Fig. 2a. For $\bar{g}_K = 10\mu A/cm^2$, for example, we have an oscillatory behavior with an unstable steady state point. With $\bar{g}_K = 17$ the system is bistable, i.e. it has both a stable limit cycle and a stable steady state point. Above $\bar{g}_K = 20$ the steady state is globally stable and the model is excitatory (a short input current will bring about a single action potential). It follows from our conclusions in I that for the unstable case, one can achieve bursting by altering the potassium current, first by increasing I_K, and hence halting the oscillations, followed by a decrease in I_K, thereby allowing oscillations to resume. There is data as to the existence of calcium-dependent potassium channels, for example (Hille 1992; Schwarz and Passow 1983). We have therefore chosen to incorporate a calcium-dependent potassium current that will bring about the quiescent phase during oscillation so as to produce a bursting model.

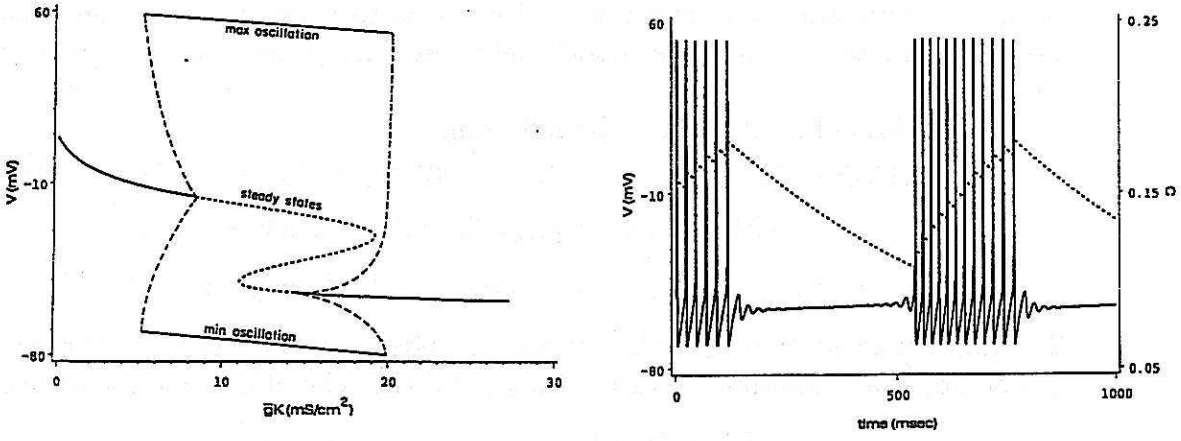

Fig. 2. (a) Bifurcation diagram as a function of $\bar{g}_K$, the maximal potassium conductance per unit area. Depicted are steady states that are stable (heavy solid line) and unstable (heavy dashed line) as well as minimum and maximum voltages for limit cycle solutions, both stable (light solid line) and unstable (light dashed line). Model parameters: $\bar{g}_{Na} = 120mS/cm^2$, $\bar{g}_L = 0.3mS/cm^2$, $V_{Na} = 55mV$, $V_K = -72mV$, $V_L = -49.4mV$, $V_{1/2}^{(m)} = -33mV$, $a^{(m)} = 0.055$, $V_{1/2}^{(w)} = -55mV$, $a^{(w)} = 0.045$, $\bar{\lambda} = 0.2$, $s = 1.3$. (b) Bursting behavior of the minimal bursting model. Depicted is membrane voltage (solid line) and intracellular calcium (dashed line). Model parameters: $\bar{g}_{Na} = 120mS/cm^2$, $\bar{g}_K = 15mS/cm^2$, $\bar{g}_{K(Ca)} = 0.6mS/cm^2$, $\bar{g}_{Ca} = 0.5mS/cm^2$, $\bar{g}_L = 0.3mS/cm^2$, $V_{Na} = 55mV$, $V_K = -72mV$, $V_{Ca} = 110mV$, $V_L = -60mV$, $V_{1/2}^{(m)} = -10mV$, $a^{(m)} = 0.025$, $V_{1/2}^{(w)} = -43mV$, $a^{(w)} = 0.025$, $\bar{\lambda} = 0.11$, $s = 1$,

$K_p = 0.0008$, $R = 0.0015$ and $K_d = 0.5$.

Another possibility to achieve bursting is from the bistable or stable cases with a calcium current that will depolarize the system, leading to oscillations, and will inactivate with increased internal calcium concentration, thereby halting the oscillations. It is not clear that one can achieve this in a simple manner, so that we will not pursue this option. Our goal is not to explore all possible ways to achieve bursting, but to present a simple and biophysically plausible method. We thus introduce a new variable to describe the intracellular calcium concentration that is used to control the calcium-dependent potassium channel. The increase in corresponding current $I_{K(Ca)}$ will halt the oscillations. Upon the removal of calcium, oscillations will resume. The calcium-dependent potassium current $I_{K(Ca)}$ is described, following Plant (1978), as the product of the maximal conductance $\bar{g}_{K(Ca)}$, a saturating function of intracellular calcium $C/(C + K_d)$ and the driving force $(V - V_K)$:

$$I_{K(Ca)} = \bar{g}_{K(Ca)}[C/(K_d + C)](V - V_K). \tag{7}$$

For simplicity, the influx of calcium is modeled as part of the inward sodium current. The calcium enters via the sodium channel, and so the channel properties are those of the sodium channel. The new calcium current is

$$I_{Ca} = \bar{g}_{Ca} m_\infty^3(V)(1 - W)(V - V_{Ca}). \tag{8}$$

The internal calcium concentration (in dimensionless form) is modeled by

$$dC/dt = K_p \cdot (-I_{Ca}) - R \cdot C \tag{9}$$

where R is the removal rate constant and K_p is a conversion factor from current to concentration.

Fig. 2b shows the bursting behavior of the new model together with the corresponding level of internal calcium. Oscillations commence when calcium is at a minimum such that the total potassium current, $I_K + I_{K(Ca)}$, is not sufficient to hold the membrane at its resting potential. In Fig. 2b at time=500 ms, the stability of the system is such that the outward currents are reduced enough such that oscillations begin. It should be pointed out that the model is based on the fact that with $I_{K(Ca)} = 0$, we reduce to our minimal model, with an unstable steady state point, and hence the oscillatory behavior. Bursting begins when the inward current is sufficient to depolarize the membrane, i.e. the outward currents are not sufficient to repolarize. One can picture the dynamics as a competition between these two opposing forces, the inward depolarizing currents and the outward repolarizing currents. Perfect balance between them occurs at the resting potential. But if no balance exists, the system oscillates. The bistable situation can be described as one in which a balance exists but when the inertia of the system as it traverses the refractory phase is sufficient to drive the membrane potential past threshold, the system oscillates. The quiescent period of the burst is during the removal of calcium. See Fig. 2b.

In terms of system dynamics, oscillations begin when the system has shifted such that the steady state point is unstable, the consequence of calcium removal. Once the system oscillates, calcium enters the cell via the sodium channel, activated by the voltage dependent $m_\infty(V)$ function. The increased internal calcium concentration allows more outflow of potassium via the calcium-dependent potassium channel. Eventually

the level of internal calcium becomes such that the total potassium conductance halts the oscillations. The total potassium conductance has brought about a globally stable steady state point.

With the present model one can affect the duration of bursting and the duration of quiescence by altering the rate of inflow and removal of calcium, but there is nearly fixed oscillation frequency during bursting. The cells we want to model exhibit a wide range of firing frequencies. As well, during the lobster cardiac burst there is a noticeable increase and then a decrease of the firing frequency. None of these features are displayed in the present model.

The basic model

The present bursting model must be altered to obtain the observed features just mentioned. The key to what is required is obtained by noting that Tazaki and Cooke (1983) observed the existence of a long lasting depolarizing current which oscillates about a voltage that is not close to the rest value. By contrast, our previous model, based on bursting while in a bistable region, yields oscillations about a value close to rest (see Fig. 2b).

The next question is what type of current can promote the slow wave of depolarization. We recall that Tazaki and Cooke (1990) showed that the driver potential (that is, the part of the slow depolarization wave that is high) resembles the calcium current that flows in the soma. Calcium channels are indeed thought to play an important role in bursting neurons (Hille 1992; Hagiwara and Byerly 1981). It is thus natural to consider the possibility that calcium currents,can promote the slow wave of depolarization. For such depolarization to decline, either (internal) calcium-dependent inactivation of this calcium channel must occur or an (internal) calcium-dependent positive ion outflow must take place. Relevant here is evidence (Connor 1969) for the hypothesis that a prolonged potassium conductance leads to the hyperpolarization seen after bursting.

Our new model is a natural extension of the previous bursting model. We employ the same mechanism to turn off the oscillation. But, as stated above, a slow depolarization is observed to turn on the oscillation. To obtain this we no longer make the simplifying hypothesis that the inward calcium current enters through the same channels as sodium [see (8)]. The reason that the calcium channel must be more precisely and separately modeled is that the "new" depolarizing current must change on a slow time scale. This is accomplished by introducing a new equation for the activation of the calcium channel.

In considering how to represent I_{Ca} we note that voltage clamp experiments monitoring calcium currents show a bell shaped curve (Hille 1992). According to Tazaki and Cooke (1990), the voltage clamp of a large cell from the lobster cardiac ganglion shows such a response. Also, Hagiwara and Byerly (1981) show that the conventional ohmic law is not accurate for modeling calcium currents. Replacing (8), we thus model the calcium current as

$$I_{Ca} = I_{Ca}max \cdot X \cdot Ce/[Ce + Ke(V)], \tag{10}$$

which attains the observed bell shaped steady state I_{Ca} curve. Here $I_{Ca}max$ is the maximal current, X is the voltage dependent fraction of open channels and Ce is the external calcium concentration. The term $Ke(V)$ is the product of a constant, ke_c,

and a sigmoid function, $k_\infty(V) = 1/(1 + exp[-2a^{(k)}(V - V_{1/2}^{(k)})])$. $Ke(V)$ increases with depolarization. This behavior of $Ke(V)$ represents the decrease in permeability of the channel to inward movement of calcium as membrane voltage increases. Since X saturates at high depolarization and $Ke(V)$ continues to rise, the observed bell shaped steady state current is obtained.

Paralleling (2) and (4) we assume

$$dX/dt = [X_\infty(V) - X]/\tau_x \quad \text{with} \quad X_\infty(V) = 1/(1 + exp[-2a^{(x)}(V - V_{1/2}^{(x)})]), \quad (11)$$

where τ_x is taken to be constant. The parameters of the calcium activation variable X will be discussed in the following section.

We are not modeling the calcium buffering that occurs in the cell and therefore simply convert the calcium current into free intracellular calcium ions. Normal resting $[Ca]_i$ ranges from $0.01 - 0.3\mu M$ (Hille 1992). It is found that above an internal calcium concentration of $0.1 - 1\mu M$ calcium channels inactivate (Hille 1992; Hagiwara and Byerly 1981). In our model, the cell is at rest or quiescent with approximately $0.04\mu M$ of free calcium. During bursting, the intracellular calcium concentration builds up to around $1\mu M$.

The intracellular calcium concentration is described by

$$dC/dt = Y_{Ca} \cdot X \cdot Ce/[Ce + Ke(V)] - R \cdot C/(C + K_r). \quad (12)$$

The parameter Y_{Ca} is the maximal concentration change in $\mu M/ms$, R is removal in $\mu M/ms$ and K_r is a dissociation constant. Saturating removal has been assumed, in line with Parnas et al (1990).

Our *basic bursting model* is therefore

$$C_m(dV/dt) = I - I_{Na} - I_{Ca} - I_K - I_{K(Ca)} - I_L, \quad (13)$$

with eqs (2)-(7), and (10)-(12).

Bursting behavior

In an effort to determine parameter values for the basic model, we first note that the resting potential found in cells of the lobster cardiac ganglion range close to $-60mV$ (Bullock and Terzuolo 1957). Tazaki and Cooke (1983; 1990) carried out relevant experiments on somas of large cell from the lobster cardiac ganglion. Comparing model behavior with experimental results lead us to choose steady state function $X_\infty(V)$ parameters $a^{(x)} = 0.18$ and $V_{1/2}^{(x)} = -50mV$ and a relaxation time constant of $50ms$. It is interesting to note that our obtained values for the lobster are remarkably similar to those employed by Plant (1981) in a bursting model for the *Aplysia* R15 cell, namely, $a^{(x)} = 0.15$ and $V_{1/2}^{(x)} = -50mV$. His relaxation time constant was larger than ours, as the *Aplysia* cell has a driver potential that lasts for seconds in contrast to our system that bursts for a few hundred milliseconds.

Fig. 3a shows a simulation of our new model. The burst rides on a slow wave as seen in Fig. 3b. The oscillation frequency alters from low to high and back to low during the burst. One can see slow depolarization that occurs during the quiescent phase. The change in frequency during the burst is the result of the changing calcium and calcium-dependent potassium currents.

The variable X controls the flow of calcium ions. As X increases the calcium current increases and this leads to a higher inward current and hence a faster frequency (see top of Fig. 4a). As the burst continues the internal calcium concentration increases, which in turn increases the outward potassium flow via the calcium-dependent potassium channel. As the effect of the outward currents increases, the frequency decreases and so does the voltage dependent variable X, thereby leading to even further decrease in frequency and eventual cessation of the oscillations. As in the previous model, removal of the internal calcium takes place during the quiescent period, but now we also see a slowly depolarizing membrane potential during this period.

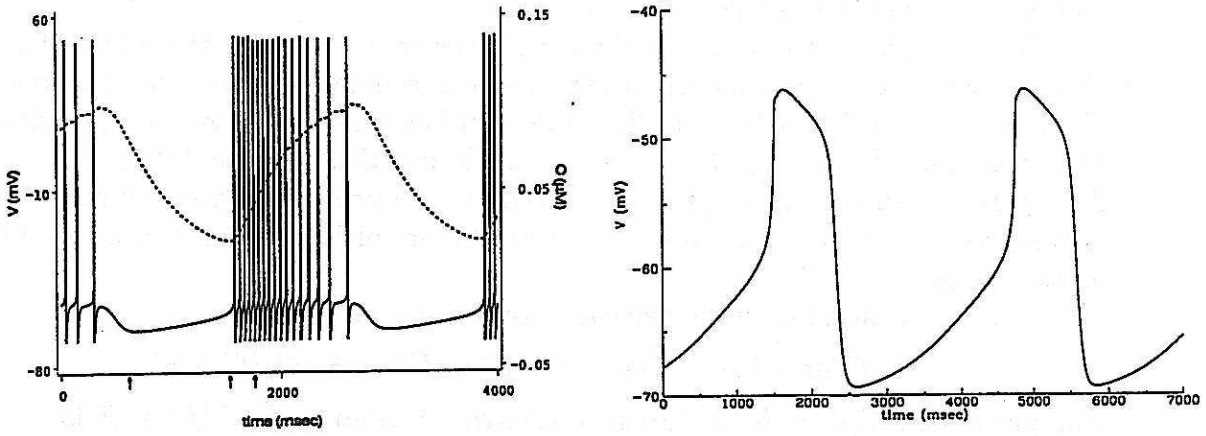

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Fig. 3. (a) Bursting behavior of the basic model. Depicted are membrane voltage (solid line) and intracellular calcium concentration (dashed line). (b) Slow depolarizing wave of basic model is uncovered by turning off the sodium current, $\bar{g}_{Na} = 0mS/cm^2$, to mimic soma currents. Model parameters: $\bar{g}_{Na} = 100mS/cm^2$, $\bar{g}_K = 35mS/cm^2$, $\bar{g}_{K(Ca)} = 3mS/cm^2$, $I_{Ca}max = 110mS/cm^2$, $Y_{Ca} = 0.00125\mu M/ms$, $V_{Na} = 55mV$, $V_K = -72mV$, $V_L = -60mV$, $V_{1/2}^{(m)} = -30mV$, $a^{(m)} = 0.055$, $V_{1/2}^{(w)} = -47mV$, $a^{(w)} = 0.045$, $\bar{\lambda} = 0.02$, $s = 1$, $V_{1/2}^{(x)} = -50mV$, $a^{(x)} = 0.18$, $\tau_x = 50ms$, $Ce = 10\mu M$, $ke_c = 100$, $V_{1/2}^{(k)} = 60mV$, $a^{(k)} = 0.04$, $K_r = 0.5$, $K_d = 0.5$, $R = 0.001\mu M/ms$.

Bursting behavior with the basic model can be seen in Figs. 3a and 3b. Two sets of components that contribute to the resulting behavior are the fast variables, voltage V and recovery W, and the slow variables, intracellular calcium concentration C and the calcium channel activation variable X. The fast components are responsible for the action potentials that are seen during the burst. This is the essence of the minimal model. The time scale of the fast system is on the order of milliseconds. On the other hand, the slow variables oscillate on the order of hundreds of milliseconds (see Fig. 3b). The slow components are responsible for the slow wave and driver potential that underlie the bursting phenomena. *The two types of components probably are physically separate.* The fast system exists mainly in the axon while the slow component is mainly observed in the soma (Hille 1992). A two compartment model would be more accurate, but for simplicity we presently are modeling the system with one compartment.

We can alter the bursting behavior of this model in a number of ways. By having faster removal the duration of the quiescent phase will be shorter. Similarly, by

increasing the inflow of calcium the burster will oscillate for a shorter period. And by increasing the calcium conductance, a stronger calcium current will bring about a higher firing frequency. We will use these parameters to alter our model to describe the behavior of the different cardiac ganglion cells.

An alternative hypothesis was considered by Rinzel and Lee (1987), who showed that bursting could be obtained by hypothesizing a calcium-dependent inactivation of a calcium current. In order to obtain the observed hyperpolarization, Rinzel also introduced a basal potassium conductance. A point in favor of our model is its consonance with the accepted role of calcium-dependent potassium channels in the soma (Schwarz and Passow 1983). But one model does not exclude the other. Both the existence of Ca-dependent potassium channels and long term calcium channel inactivation owing to increased intracellular calcium are in accord with experimental findings, and both processes probably should be incorporated in an accurate model.

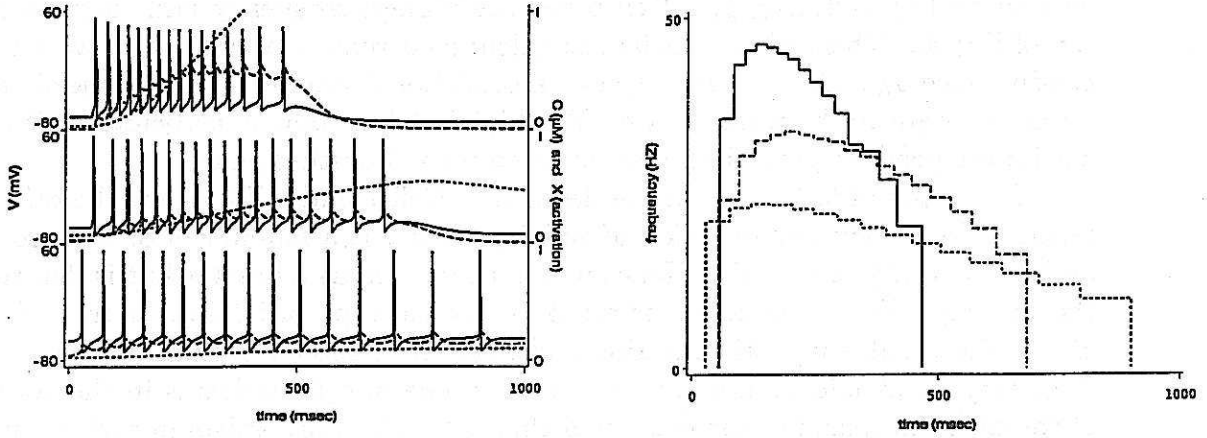

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Fig. 4. (a) Bursting behavior for basic model depicting three types of bursters. Membrane potential (solid line), internal calcium concentration (short dashed line) and calcium activation variable X (long dashed line). Cell 9 (bottom) as in Fig. 3a. Cell 8 (middle) as cell 9 but with $\bar{g}_K = 25mS/cm^2$, $I_{Ca}max = 200mS/cm^2$ and $Y_{Ca} = 0.005\mu M/ms$. Cell 8 was depolarized by an input current $I = 5\mu A/cm^2$ for 5 ms at time = 50 ms. Cell 6 (top) as cell 9 but with $\bar{g}_K = 10mS/cm^2$, $\bar{g}_{K(Ca)} = 6mS/cm^2$, $I_{Ca}max = 250mS/cm^2$ and $Y_{Ca} = 0.009\mu M/ms$. Cell 6 was depolarized by an input current $I = 5\mu A/cm^2$ for 20 ms at time = 50 ms. (b) Frequency graphs for cells of (a), cell 9 (short dashed line), cell 8 (long dashed line) and cell 6 (solid line).

The lobster cardiac ganglion bursting cells

The basic model can describe the bursting cells of the lobster cardiac ganglion. Fig. 4a shows three major types of bursting firing patterns seen in the lobster cardiac network. The corresponding cell firing frequency graphs are shown in Fig. 4b, compare with experimentally found results in Fig. 1b. Fig. 4b shows three major properties– duration of burst, maximal frequency and rate of change of frequency. The simulation and experimental results show a good fit for the first and second properties, but not the third. It should be noted that the experimental results (Fig. 1b) are taken from an intact ganglion and describe the resulting behavior of the network as a whole, while

the simulation results are from individual cell models. Once connected into a network (paper in preparation) the cells should exhibit a similar frequency change to that shown in the experiments. The reason is that the network will drive the cells to a higher frequency towards the middle of the bursting phase; this will increase calcium inflow, which will cause an abrupt cessation of cell firing. A simulation of cell 9 is shown in the bottom of Fig. 4a. This cell is an endogenous burster with the longest burst duration, $900msec$, and the lowest frequency. The low frequency is mostly determined by the low value of X, relating to the calcium current, and the high value of $\bar{g}_K$. Also a low $\bar{g}_{K(Ca)}$ allows for the long burst duration. Cell 8, middle of Fig. 4a, was originally considerded as a conditional burster but in fact was an endogenous burster, but with a quiescence period longer than that of cell 9. This could be an advantage for the system to have multiple pacemakers incase cell 9 fails, cell 8 can initiate the burst. Cell 8 has a higher frequency, caused by the higher value for X, which corresponds to a higher calcium current. This was achieved in our model by increasing the maximal calcium current and by reducing $\bar{g}_K$. Cell 6 has the highest frequency and shortest duration, top of Fig. 4a. This cell has the largest calcium current, as well as the lowest potassium conductance $\bar{g}_K$. Cell 6 is modeled as a conditional burster. The cell needs an initial input to begin its bursting phase. The high calcium flow is associated with a larger calcium-dependent potassium current to stop the bursting phase.

Two types of follower cells are described. Cell 7 and cell 5 follow the other cells in terms of frequency and duration of activity. Cell 7 is a follower of 8, both in duration and frequency, (see Fig. 1b). Hence it is not modeled as a burster but is determined by the network. The same holds for cell 5. A second type of follower is that of cells 1-4. They follow cell 6 in both duration and frequency, though initially firing at a higher frequency. It should be noted that the difference in cell models is in the conductance of the different ions, i.e. the density of channels. The mechanism in each version is the same. The different behaviors were achieved by altering the potassium currents, both $\bar{g}_K$ and $\bar{g}_{K(Ca)}$, as well as the maximal calcium current $I_{Ca}max$, in conjunction with the calcium flow variable Y_{Ca}.

Summary and discussion

To model bursting neurons we incorporated into our minimal model a slow variable, internal calcium concentration, associated with a calcium-dependent potassium channel.

A feature of bursting in the lobster cardiac ganglion, and in other preparations (e.g. *Aplysia*) is that the bursting occurs on a driver potential. To model this observed behavior, we incorporated a fourth variable X, (in addition to the three variables needed for the minimal bursting model) that describes the activation of the calcium channel. By means of X we can shift the membrane potential and exhibit a driver potential. If X is taken to be a constant, no driver potential is obtained in the model. A question to be investigated in the future is the information processing function of the driver potential - which, as we have seen, is not necessary for bursting.

We have argued that bursting is brought about by calcium-dependent components in the soma. These can be readily altered by external stimuli such as hormones and neurotransmitters. Hence the essential bursting behavior of the network would be subject to modulations, yielding behavioral plasticity. Our research suggests a reason for

the observation that there are fewer types of sodium channels but many types of potassium channels. The sodium channels are the action potential generators. Since we have a FM signaling system, the form of a spike is expected to be constant. It is conceivable that various potassium channels will be needed to alter the signaling frequency which is essential for information transduction.

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