Ghostbursting in sensory cells of electric fish

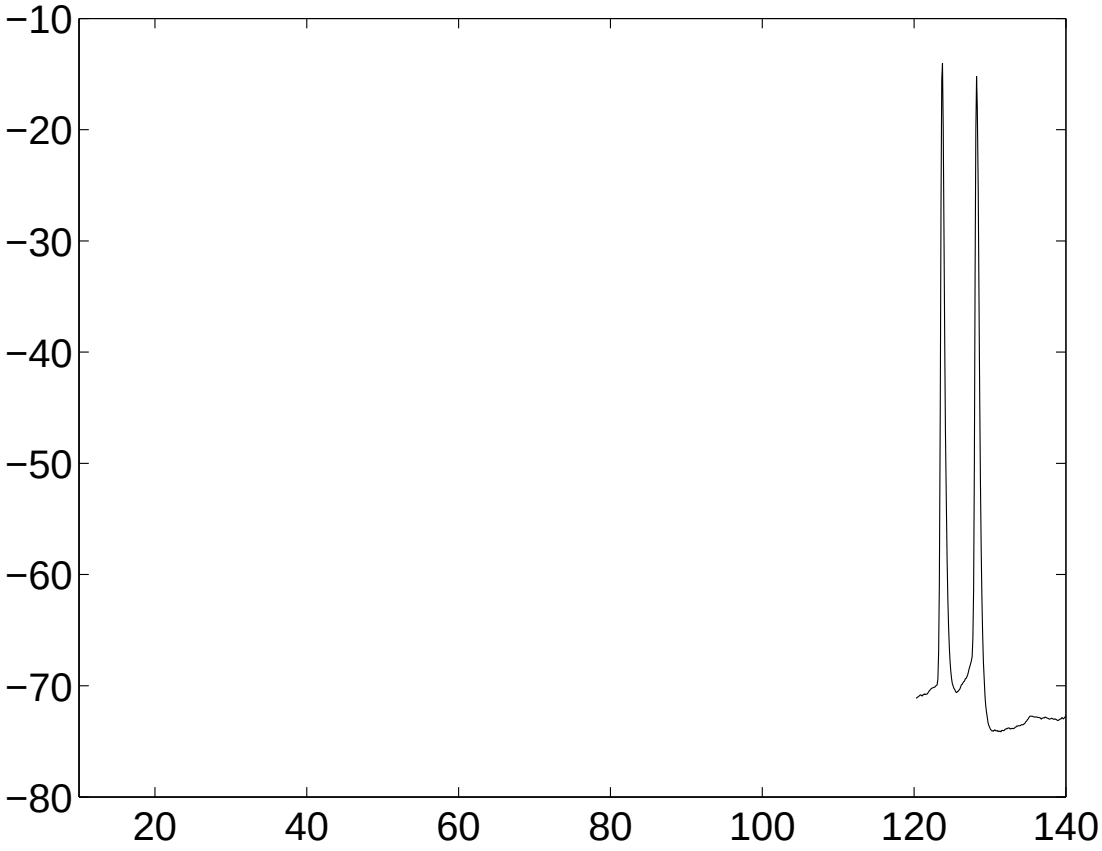
Carlo R. Laing
Institute of Information and Mathematical Sciences, Massey University,
Private Bag 102-904, North Shore Mail Centre, Auckland, New Zealand
November 4, 2003

AMS Subject classification: 92C20, 37N25, 34C15
Key words: Bursting, electric fish, sensory processing, integrate–and–fire.

Abstract: We give an overview of the analysis of a new type of bursting ("ghostbursting") seen in pyramidal cells of weakly electric fish. We start with the experimental observations and characterization of the bursting, describe a compartmental model of a pyramidal cell that undergoes ghostbursting and the development of a simplified yet realistic conductance–based model of this cell. This model then motivates a minimal leaky integrate–and–fire model that also has the qualitative features of ghostbursting.

1 Introduction

Bursting, the slow alternation between spiking behavior and quiescence, is a common cellular phenomenon [7, 8]. It was recognised early on that not all bursting is qualitatively the same, and early classifications of bursting systems reflected their qualitative nature, e.g. parabolic or square–wave bursting [16]. An almost universal assumption in the mathematical analysis of bursting systems was that the system could be decomposed into two subsystems, a "fast" subsystem and a "slow" subsystem, and that when the variables in the slow subsystem were held constant the fast subsystem either oscillated or was quiescent [7, 16]. The slow variables were assumed to be driven by the dynamics of the fast subsystem and thus bursting could be viewed as


−10
−20
−30
−40
−50
−60
−70
−80
20
40
60
80
100
120
140

a necessary component of the bursting. These authors observed that most somatic action potentials were followed by a depolarizing afterpotential (DAP) of similar duration to the dendritic action potential, and that during repetitive ring the DAPs could increase in amplitude, resulting in progressively shorter interspike intervals and an increase in the minimum voltage between spikes in a burst [13]. This process of DAP growth was terminated when a very short ISI (a "doublet") occurred at the soma, which was followed by a long ISI. These long ISIs thus grouped the action potentials into bursts (see Figure 1). The existence of DAPs in Figure 1 is inferred, since without them the voltage after each action potential would drop to a lower value, similar to that seen immediately after each doublet.

Further work [13] determined that the dendritic refractory period was longer than the somatic, and the termination of a burst occurred when a somatic ISI (the doublet) was shorter in duration than the dendritic refractory period and the dendrite could not produce an action potential in response to the second of the two somatic action potentials forming the doublet. It was also determined that the pyramidal cells switched from periodic to burst ring as the injected current was increased (in contrast with many other types of bursting [8, 15]), and that the duration of bursts (once they occurred) decreased as current increased.

2 A Large Compartmental Model

The rst model of a neuron capable of ghostbursting was presented in [5]. This was a "compartmental" model, in which a particular neuron was photographed and the main features of its morphology digitized, so that a "virtual neuron" could be constructed within a computer. The neuron was necessarily represented as a nite number of isopotential compartments (over 300), and appropriate ion channels were distributed over the compartments. The exact nature of these channels was chosen so as to match experimental recordings of individual action potentials as closely as possible, with some parameters being estimated from previous experimental work. Doiron et al. [5] found that to successfully reproduce the experimentally observed burst patterning they had to include a slow cumulative inactivation of the repolarizing potassium current in the dendrite.

While this large compartmental model was very realistic, it was too complex for many such neurons to be simulated at the same time (for example, in a simulation of a network of neurons) and more importantly, it was very dif cult to understand the "essence" of bursting in the model in the same

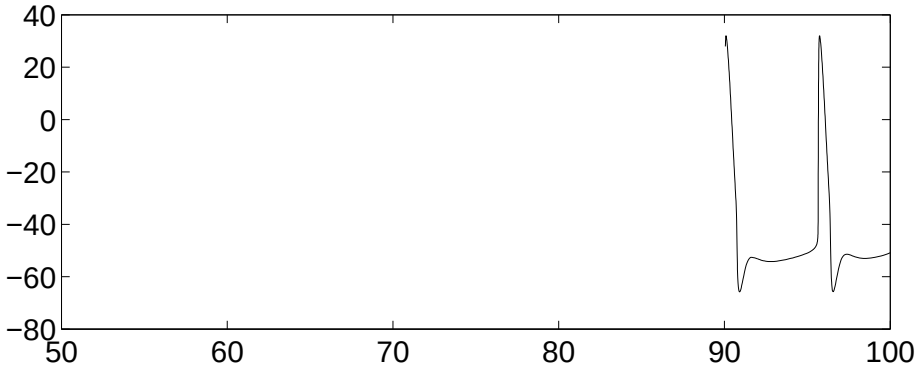
in [15]. Secondly, the ion channels not thought to be necessary for the bursting behavior were eliminated. Crucially, it was important not to eliminate the dendritic potassium current, as it is thought that the presence of this current underlies the bursting discussed here. Thirdly, previously–used simpli cations were used to further reduce the number of variables. (Specifically, it was assumed that the activation of sodium channels is instantaneous. Also, use was made of the observation that $h_s + n_s$ is approximately equal to 1 during an entire action potential [4, 8], where h_s is the somatic sodium inactivation variable and n_s is the somatic potassium activation variable.)

The resulting equations, presented in [4], are

$$\begin{aligned}
C\frac{dV_s}{dt} &= I - g_{Na,s}[m_{\infty,s}(V_s)]^2(1-n_s)(V_s - V_{Na}) - g_{dr,s}n_s^2(V_s - V_K) \\
&\quad -g_L(V_s - V_L) - \frac{g_c}{\kappa}(V_s - V_d) && (1)\\
\frac{dn_s}{dt} &= \frac{n_{\infty,s}(V_s) - n_s}{0.39} && (2)\\
C\frac{dV_d}{dt} &= -g_{Na,d}[m_{\infty,d}(V_d)]^2 h_d(V_d - V_{Na}) - g_{dr,d}n_d^2 p_d(V_d - V_K) \\
&\quad -g_L(V_d - V_L) - \frac{g_c}{1-\kappa}(V_d - V_s) && (3)\\
\frac{dh_d}{dt} &= h_{\infty,d}(V_d) - h_d && (4)\\
\frac{dn_d}{dt} &= \frac{n_{\infty,d}(V_d) - n_d}{0.9} && (5)\\
\frac{dp_d}{dt} &= \frac{p_{\infty,d}(V_d) - p_d}{5} && (6)
\end{aligned}$$

Subscripts s and d refer to somatic and dendritic variables, respectively. Equations (1) and (3) are current balance equations for the soma and dendrite of the neuron, respectively, and the other equations govern the ion channel dynamics. The variables m and h are activation and inactivation of Na^+, respectively, and n and p are activation and inactivation of K^+, respectively. Parameter values are $C = 1$, $g_{Na,s} = 55$, $V_{Na} = 40$, $g_{dr,s} = 20$, $V_K = -88.5$, $g_L = 0.18$, $V_L = -70$, $g_c = 1$, $\kappa = 0.4$, $g_{Na,d} = 5$, $g_{dr,d} = 15$. I is the somatic input current, g_c is the coupling conductance, and κ is the ratio of the somatic area to the total area of the cell. Other functions are $m_{\infty,s}(V) = 1/[1 + \exp(-(V + 40)/3)]$, $n_{\infty,s}(V) = 1/[1 + \exp(-(V + 40)/3)]$, $m_{\infty,d}(V) = 1/[1 + \exp(-(V + 40)/5)]$, $h_{\infty,d}(V) = 1/[1 + \exp((V + 52)/5)]$, $n_{\infty,d}(V) = 1/[1 + \exp(-(V + 40)/5)]$, $p_{\infty,d}(V) = 1/[1 + \exp((V + 65)/6)]$. Note that these functions and parameter values are the same as used in the large model [5].

An example of the behaviour of (1)-(6) is shown in Figure 2 for $I = 10$. Note that the dendritic action potentials are wider than the somatic. During a burst, the dendritic potassium inactivation variable p_d slowly decreases, resulting in the progressive widening of the dendritic action potentials and the decrease in ISIs. There are several differences between the results plotted in Figure 2 and the experimental results in Figure 1 and elsewhere. For example, the minimum somatic voltage between action potentials in the experimental recordings gradually rises during a burst, whereas such a rise is not seen in the model results. Also, experimental recording show a slow decrease in the amplitude of dendritic action potentials during a burst [4, 5], whereas this does not appear in Figure 2. These are minor discrepancies that do not affect the understanding of the mechanisms involved in the bursting, and overall, the model (1)-(6) qualitatively, and to a large extent quantitatively, reproduces the bursting seen both in experiments [13] and in the large compartmental model [5].


40
20
0
−20
−40
−60
−80
50
60
70
80
90
100

As

In the ionic models, the dendritic action potential halfwidth is greater than that of the somatic, and the effect of this is that a short time after each somatic spike (except for the second one in a doublet), a depolarizing current ows from the dendrite to the soma. This "delayed feedback" was implemented in the minimal model with an actual delay. The failure of the dendrite to respond to a somatic action potential was implemented with a simple comparison between the last ISI and the dendritic refractory period, and the effective DAP height was used to instantaneously increment the effective somatic voltage.

The equations chosen for the minimal model were

$$\frac{dV}{dt} = I - V +$$

Assuming that the injected current I is constant, the map (9)-(10) is equivalent to the system (7)-(8), but is much quicker to simulate and is also easier to analyse.

In [11] the periodic forcing of (7)-(8) (by modulating the current I) was investigated. An explicit map similar in form to (9)-(10) was derived for the case of sinusoidal modulation, although it had three variables rather than two. This map made the analytic study of resonance (Arnol'd) tongues possible, and also facilitated the study of stochastic resonance in (9)-(10).

5 Other Work

Other relevant work involving the ghostburster is now described. In Ref. [14] the minimal model (7)-(8) was modified so that the second variable controlled both the width of the dendritic action potential and the dendritic refractory period. This formulation allowed an investigation into the effects of varying both the somatic and dendritic spike widths, as would occur when potassium channels in the soma or dendrite were selectively blocked. The analytical results derived compared favourably with experiments in which this occurred, and provided further insight into the differential effects of such selective blocking.

In Ref. [10] the concept of "burst excitability", first introduced in [11], was investigated. Burst excitability is a generalization of "normal" excitability [8], in which a small perturbation causes a system to return monotonically to rest, but a large perturbation causes the system to make a stereotypical large excursion in phase space before returning to rest. Since the transition from periodic firing to bursting in (1)-(6) is via a saddle–node bifurcation, and a burst involves a large stereotypical excursion through phase space, there is an analogous form of excitability in (1)-(6). The main difference between burst excitability in (1)-(6) and normal excitability is that the large excursion is a burst, and the system returns to periodic firing after the burst, rather than to a steady state.

The effects of time–varying input to a model ghostbursting neuron were further investigated in [12]. Here, the input current to the soma was sinusoidally modulated. It was found that the modulation could switch the model neuron from bursting to periodic firing, or vice versa, depending on the frequency of forcing and the distance from the periodic / burst threshold. This could be explained by mapping resonance tongues in parameter space. Stochastic resonance was also observed in this periodically forced system, assuming that the doublet at the end of a burst was used to form the "signal".

The pyramidal cells that show burst excitability and entrainment to periodic inputs are primary sensory neurons, i.e. they receive input directly from electroreceptors on the fish's skin [2]. It is reasonable to suppose that bursts are somehow involved in signalling information about the environment of the fish to its higher brain centres, and it was discussed in [10] how burst excitability might contribute to this processing and transfer of information. For example, given the unreliability of some neural processes, a burst of action potentials could be a more robust means of signalling an event than a single action potential. Also, it may be the case that a facilitating synapse could be "tuned" to pick out the accelerating action potentials that characterize ghostbursting.

The role of the saddle–node bifurcation of periodic orbits that separates periodic from burst firing was further investigated in [6]. Here, the authors added a persistent sodium current with a slow timescale (on the order of one second) to the compartmental model in [5]. The effect of this is qualitatively the same as slowly increasing the current injected into the cell's soma, and thus results in the cell's firing frequency slowly increasing until burst discharge starts. The lengths of these bursts then slowly decrease over time. The purpose of adding this

[5] B. Doiron, A. Longtin, R. W. Turner and L. Maler, Model of gamma frequency burst discharge generated by conditional backpropagation, J. Neurophysiol. 86 (2001), 1523-1545.

[6] B. Doiron, L. Noonan, N. Lemon, and R. W. Turner, Persistent Na^+ current modi es burst discharge by regulating conditional backpropagation of dendritic spikes, J. Neurophysiol. 89 (2003), 324-337.

[7] E. M. Izhikevich, Neural excitability, spiking, and bursting, Int. J. Bifn. Chaos 10 (2000), 1171-1266.

[8] J. Keener and J. Sneyd. "Mathematical Physiology", Interdisciplinary Applied Mathematics, Vol. 8. Springer–Verlag New York, 1998.

[9] C. R. Laing, B. Doiron, A. Longtin and L. Maler, Ghostbursting: the effects of dendrites on spike patterns, Neurocomputing, 44-46 (2002), 127-132.

[10] C. R. Laing, B. Doiron, A. Longtin, L. Noonan, R. W. Turner and L. Maler, Type I burst excitability, J. Comput. Neurosci. 14(3), (2003) 329-342.

[11] C. R. Laing and A. Longtin, A two–variable model of somatic–dendritic interactions in a bursting neuron, Bull. Math. Biol 64(5), (2002), 829-860.

[12] C. R. Laing and A. Longtin, Periodic forcing of a model sensory neuron, Phys. Rev. E, 67 (2003) 051928.

[13] N. Lemon and R. W. Turner, Conditional spike backpropagation generates burst discharge in a sensory neuron, J. Neurophysiol. 84 (2000) 1519-1530.

[14] L. Noonan, B. Doiron, C. R. Laing, A. Longtin and R. W. Turner, A dynamic dendritic refractory period regulates burst discharge in the electrosensory lobe of weakly electric sh, J. Neurosci. 23(4), (2003), 1524-1534.

[15] P. F. Pinsky and J. Rinzel, Intrinsic and network rhythmogenesis in a reduced Traub model for CA3 neurons, J. Comput. Neurosci. 1 (1994), 39-60.

[16] J. Rinzel and G. B. Ermentrout, Analysis of neural excitability and oscillations, in "Methods in Neuronal Modeling: From Ions to Networks" (ed. C. Koch and I. Segev), MIT Press, 1998.

[17] S. H. Strogatz. "Nonlinear Dynamics and Chaos with Applications to Physics, Biology, Chemistry, and Engineering". Addison-Wesley, Reading, MA., 1994.

[18] R. W. Turner, L. Maler, T. Deerinck, S. R. Levinson, and M. H. Ellisman, TTX-sensitive dendritic sodium channels underlie oscillatory discharge in a vertebrate sensory neuron, J. Neurosci. 14 (1994), 6453-6471.