Nonlinear electronic circuit with neuron like bursting and spiking dynamics

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ABSTRACT

It is difficult to design electronic nonlinear devices capable of reproducing complex oscillations because of the lack of general constructive rules, and because of stability problems related to the dynamical robustness of the circuits. This is particularly true for current analog electronic circuits that implement mathematical models of bursting and spiking neurons. Here we describe a novel, four-dimensional and dynamically robust nonlinear analog electronic circuit that is intrinsic excitable, and that displays frequency adaptation bursting and spiking oscillations. Despite differences from the classical Hodgkin–Huxley (HH) neuron model, its bifurcation sequences and dynamical properties are preserved, validating the circuit as a neuron model. The circuit's performance is based on a nonlinear interaction of fast–slow circuit blocks that can be clearly dissected, elucidating burst's starting, sustaining and stopping mechanisms, which may also operate in real neurons. Our analog circuit unit is easily linked and may be useful in building networks that perform in real-time.

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1. Modeling of Biological Bursting Phenomena

Oscillatory electrical activity called bursting is a common feature of single excitable cells in the brain and pancreas, and is thought to underlie some of the normal functions of these organs. Bursting is characterized by quiescent or quasi-stationary states interrupted by episodes of fast spiking activity. Bursting has also been observed in models of artificial neural networks called central patterns generators (Wang and Rinzel, 1995; Coombes and Bressloff, 2005). It is still unknown exactly how bursting is generated, or what causes the frequency adaptation that is seen in inter-spike intervals during a burst. There have been two approaches to analysis of bursting behavior. One is mathematical (Izhikevich, 2000, 2007; Guckenheimer et al., 1997), the other has been the development of analog electronic circuits (Maeda and Makino, 2000; Wijekoon et al., 2008). The advantages of analog circuits are real-time action and connectivity, characteristics that allow large scale neural network building and dynamical modeling (Rabinovich et al., 2006).

Electronic circuits that implement two-dimensional neuron models, such as the integrate-and-fire model and the FitzHugh–Nagumo model (Fitzhugh, 1961; Nagumo et al., 1962), are unable to produce bursting behavior because the models have only one fast timescale closed orbit that simulates the neuron's action potential (AP). In spite of this significant limitation, such circuits are used frequently as building blocks in neural networks.

More complex circuits implementing three or higher dimensional models can provide the additional slow timescale variable (Simoni et al., 2004; Le Masson et al., 1999; LaFlaquière et al., 1997) and have been successful in reproducing bursting and frequency adaptation patterns. However, for a long time no one was able to dissect the circuits clearly into their interacting fast and slow parts, and thus understand the transitions between quiescent and oscillatory states through different bifurcation scenarios. The bifurcations are what determine the neuron-computational properties (Izhikevich, 2000). Recently, the bifurcations were geometrically (i.e., mathematically) classified for the Hodgkin–Huxley model (Izhikevich, 2000, 2007). And, we succeeded in reproducing different bifurcation scenarios using Fig. 1 analog circuit (Savino and Formigli, 2007). The Hodgkin and Huxley model (HH) is a multi-dimensional model based on ion channel physiology (Hodgkin and Huxley, 1952).

The goal of this communication is to describe the circuit operation, such as the slow–fast current interaction, voltage-dependence and time-dependence of the intrinsic bursting dynamics, control of its characteristic times, and the effects of external excitations delivered via the input channels. We also present the basic circuit equations for future geometrical analysis and numerical simulation.

2. The Circuit and Its Dynamical Behavior

Our circuit is shown in Fig. 1. The values of the electronic components are given in the legend. The circuit consists of three sections, an input, modulator, and generator. The input section is merely a way to link multiple circuits or to apply external stimuli, and is not necessary for the generation of intrinsic burst dynamics. Details of

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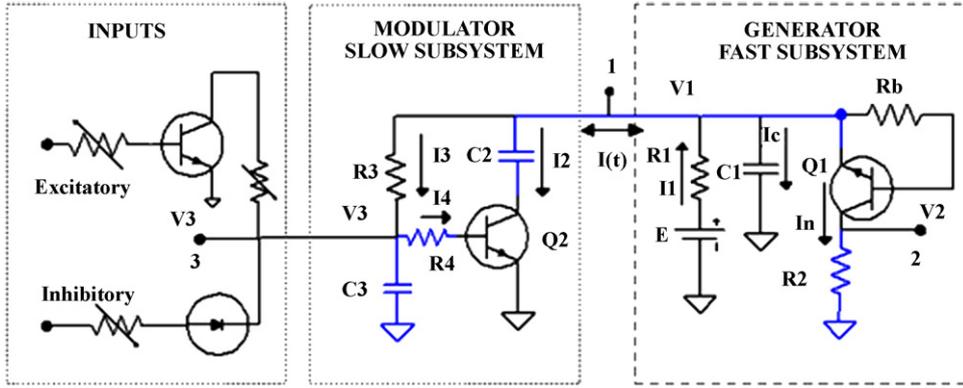
Fig. 1. The bursting and spiking analog circuit. The "frequency adaptation loop" includes $C3$, $R4$, $Q2$ base-collector junction, $C2$, $Q1$ emitter–collector junction and $R2$. Transistors $Q1$ (reverse-biased) and $Q2$ are 2N2222 type, battery $E = 10$ V, resistance value in KΩ and capacitances in μF: $R1 = 3.3$, $R2 = 0.1$, $R3 = 100$, $R4 = 1$, $Rb = 50$, $C1 = 1$, $C2 = 10$ $C3 = 2$.

an example of intrinsic bursting behavior exhibited by the circuit is shown in Fig. 2. Bursting is seen at the $V1$ node, $V2$ node, and the $Q2$ collector. The voltage at the $V3$ node displays bursting superimposed on a fluctuating baseline, resulting in a staircase-like pattern. The entire range of bursting behavior possible with the circuit is shown in Fig. 3 with $V2$ and $Q2$ node voltages omitted for clarity. The different dynamics are all produced by changing the variable resistor $R3$, which changes the intensity of the coupling current $I(t)$ between the *generator* and *modulator*. The range of bursting behaviors possible is also summarized in the bifurcation diagram plotted against $R3$ values in Fig. 4. We emphasize here that the role of the coupling current is remarkably non-trivial. It does not merely segment the fast periodic *generator* oscillation into bursts and pauses, but produces variable inter-spike interval sequences and frequency adaptation patterns (Fig. 5) that are similar to those of real neurons.

3. The Generator Circuit

When isolated, i.e., when $I(t) = 0$, the *generator* is a classical threshold-negative-resistance oscillator. The negative conductance is implemented by the reverse bias transistor $Q1$ collector–emitter

Fig. 3. The range of dynamical behaviors exhibited by the circuit (from top to bottom), as $R3$ is reduced from 400 to 20 KΩ and when $R4 = 10$ KΩ are shown by the voltage $V1$ at node 1 and voltage $V3$ at node 2, range from astable, to bursting (many to two to single spike), to spiking, to quiescent but excitable. IP indicates the $V3$ voltage inflection in each behavior.

characteristic curve $V_{ec} = V_{ec}(In)$ with an *avalanche* threshold Vth of ≈9.5 V. This is a two-dimensional nonlinear dynamical system in the phase-plane $(V1, In)$ with the equations:

$$L \cdot \frac{dIn}{dt} = V1 - V_{ec}(In)$$
$$C1 \cdot \frac{dV1}{dt} = \left(\frac{E - V1}{R1}\right) - In \tag{1}$$

Fig. 2. Typical bursting waveform at nodes 1, 2, 3, and $Q2$ collector. Times T_r and T_d are the durations of the burst and quiescent phases respectively, and T_i is the variable inter-spike interval during a burst. Transistor $Q1$ triggers a pulse or spike each time $V1 > V$th during T_r meanwhile transistor $Q2$ switches between reverse and cutting after the first burst spike and remains saturate $(0.3 < V3 < 0.5$ V) during the pause T_d. The staggered voltage $V3$ remains below 0.5 V having the inflection point IP.

Fig. 4. Codimension-one bifurcation diagram for resistor $R3$ parameter controlling, at the same time, the coupling strength and the burst duration T_r.

The isolated ($I(t) = 0$) *generator* oscillates with fixed period and does not burst. Similarly, when resistor $R3$ is greater than about 350 KΩ, current $I(t)$ is lower than the minimal for bursting, and the weakly coupled *generator–modulator* ensemble oscillates with fixed period and does not burst. This is the astable behavior shown at the top of Fig. 3 and far right of Fig. 4. In this regime, for each oscillation, the capacitor $C1$ is charged exponentially by the battery E through resistor $R1$, with a time constant $\tau_1 = R1C1$ and activation time $t_a \approx 10$ ms, and $C1$ discharges through resistor $R2$ each time $V1$ exceeds Vth, with $\tau_2 = R2C1$ and excursion time $t_e \approx 1$ ms. Times t_a and t_e are named from analogy with the neuron action potential excitable period (t_a) and the refractory period (t_e). For weak coupling, the capacitor $C2$ charge does not change significantly because transistor $Q2$ remains in its cutting (no conduction) state all the time. The period of the oscillations is fixed at $T_o = t_a + t_e \approx 11$ ms.

The triggering condition $V1 > V$th provides the voltage dependent mechanism (VDM) which initiates or ends a burst, and resides in the *generator*. Bursts begin when $V1 > V$th triggers the first spike and end when $V1 < V$th fails to trigger a spike after the last burst spike. Voltage $V1$ can approach threshold Vth in different ways depending on circuit parameters. This gives rise to the different bifurcation scenarios for burst starts and ends as reported in our original paper (Savino and Formigli, 2007). Bifurcations always involve a transition from equilibrium to a limit cycle and vice-versa. Three scenarios are shown in Fig. 7. For the circuit parameter values used for figures in this paper, the bifurcation type was a saddle-node on an invariant circle, because it includes the pause or rest potential (Izhikevich, 2000) (Fig. 7A).

4. The Modulator Circuit

Unlike most previous electronic designs, our *modulator* circuit when isolated, is not self-oscillating. The *modulator* provides a time dependent mechanism (TDM) and a graduated coupling current $I(t)$ intensity for the generation of the dynamics of Fig. 3. This may be best understood by studying Fig. 2. The behavior of voltage $V3$ controls the burst duration T_r as follows. Since $V3$ is the capacitor $C3$ charge level, its duration and inflection point (IP) location result from the balance between the $C3$ charging current $I3 = (V1 - V3)/R3$ and the $C3$ discharging current $I4$. During a burst, $V3$ displays a sawtooth pattern since current $I3$ and $I4$ alternate, driven by transistor $Q1$. At the start of the burst, the $Q2$ saturating voltage $V3$ is 0.5 V, but $V3$ begins to decrease with the first spike. The burst duration T_r is determined by the time it takes $V3$ to saturate $Q2$ again, causing the burst to end. Thus T_r is determined by the $V3$ recovery rate,

Fig. 5. Stable frequency adaptation patterns: (A) increasing, (B) diminishing, (C) constant and (D) parabolic. In the bottom panel, averages of ten consecutive bursts were plotted against interval number.

where Rb is not connected and L is the distributed inductance. The *generator* might be regarded as an electronic implementation of the FitzHugh–Nagumo system (Fitzhugh, 1961; Nagumo et al., 1962) or any other threshold-based two-dimensional excitable system. Although there are differences, it may be helpful to recognize that the reverse-biased transistor $Q1$ collector–emitter current–voltage curve $V_{ec} = V_{ec}(In)$ (the In nullcline from $dIn/dt = 0$ of Eq. (1)) corresponds to the "activation" cubic parabola (flipped N-shape) of the FitzHugh–Nagumo system, and that the straight line $V1 = E - R1 \cdot In$ (the $V1$ nullcline from $dV1/dt = 0$ of Eq. (1)) corresponds to the "restitution function".

Fig. 6. Effects of an external train of pulses of period $T = 0.1$ (s), amplitude 1.5 (V) and variable duty cycle on the burst duration T_r.
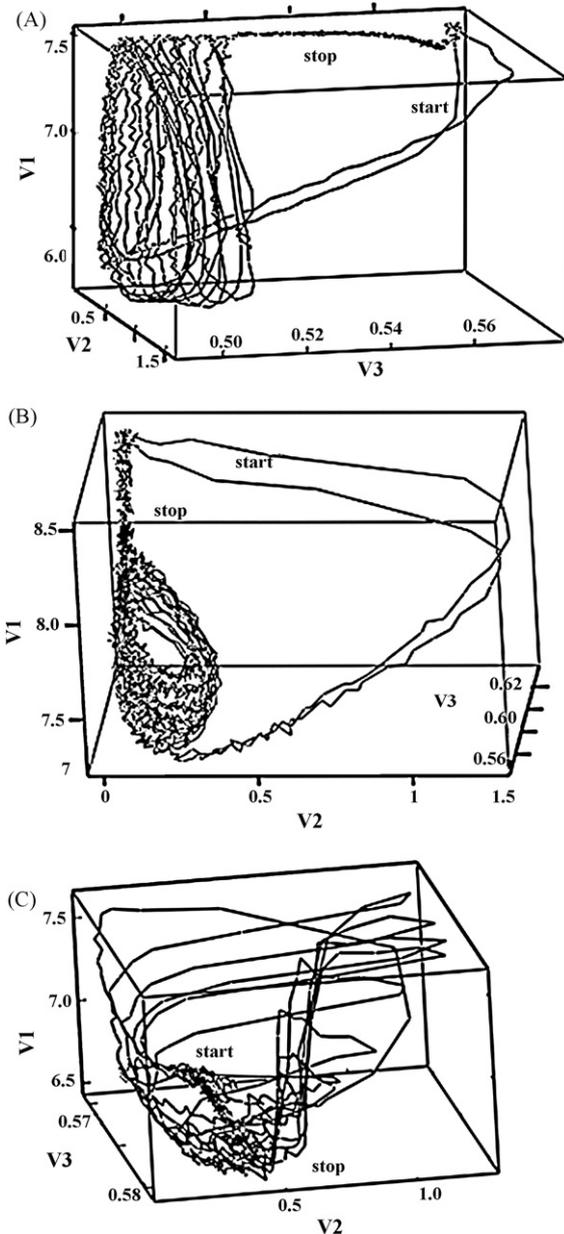
Fig. 7. Burst starting and ending bifurcations: (A) saddle-node on the invariant circle (the same as Figs. 2 and 3), (B) saddle-homoclinic orbit, (C) subcritical and supercritical Andronov–Hopf.

which is a function of the $I3$ and $I4$ current balance. $I3$ and $I4$ are in turn determined by $R3$. Fig. 4 shows the dependence of T_r on $R3$. A smaller $R3$ leads to a larger $I3$, which speeds up the $V3$ recovery rate and shortens T_r.

Resistance $R3$ has simultaneously two functions. It controls the burst duration T_r by the TDM as explained above. It also controls the *generator–modulator* coupling current $I(t)$. This is because $I(t) = I2 + I3$ where $I3 = (V1 - V3)/R3$ while $I2$ has weak dependence on $R3$. We mentioned in Section 3 that high $R3$ (>350 KΩ) inhibited bursting. In contrast, when $R3 \approx 50$ KΩ, coupling strength is strong and the two spike burst changes to a period T_s spiking. We note that the two spike bursts and one spike bursts alternate in the region of $R3 \approx 90$ KΩ. Further $R3$ reductions lead first to an increase in the spiking period T_s, before it becomes non-periodic at $R3 \approx 35$ KΩ. When $R3 < 20$ KΩ, spiking stops, and the circuit becomes excitable (is quiescent in the absence of external stimulation).

5. The Burst Frequency Adaptation Mechanism

Frequency adaptation patterns of T_i intervals are shown in Fig. 5. Experimentally we found each to be determined by the $I3$ and $I4$ current balance. Each T_i is determined by the amount of charge $C2$ lost during the spike. The current $I2$ partially discharges the capacitors $C2$ and $C3$ through the "frequency adaptation loop" (indicated in Fig. 1) when $Q1$ is in the avalanche conduction. But $C2$ does not recover its charge during a burst because $Q2$ remains cutting or reverse bias.

6. Effect of *Excitatory* and *Inhibitory* Inputs

Regardless of whether *excitatory* or *inhibitory* input is used, moderate-amplitude (1 V) and duration (10^{-3} s) pulses modify the voltage $V3$ recovery rate and therefore the TDM. Fig. 6 shows how the burst duration T_r is shortened and lengthened by a train of positive pulses. Also, brief (relative to T_i) and high amplitude (>1 V) pulses applied at the right moment during the burst may shorten or lengthen T_i according to which input is used to modify the free-running frequency adaptation pattern. This suggests that some information can be encoded into the burst instantaneous frequency $f_i = 1/T_i$.

7. The *Generator–Modulator* Ensemble Equations

The essential circuit equations of Fig. 1 are:

$$
\begin{aligned}
L \cdot \frac{dIn}{dt} &= V1 - V_{ec}(In) \\
C1 \cdot \frac{dV1}{dt} &= \left(\frac{(E - V1)}{R1} \right) - In - I(t) \\
C2 \cdot \frac{dV_{C2}}{dt} &= I2 \\
C3 \cdot \frac{dV_{C3}}{dt} &= I3 - I4,
\end{aligned}
\tag{2}
$$

where $I(t) = I2 + I3$, $R4$ is assumed to be zero, Rb to be infinite, and inductance L, the same as in Eq. (1), is the distributed inductance. V_{C2} and V_{C3} are the capacitors $C2$ and $C3$ voltages, respectively. From Eq. (2) it is obvious that the circuit is a four-dimensional nonlinear dynamical system in the dynamical variables $V1$, In, V_{C2} and V_{C3}.

In order to solve Eq. (2) numerically, the transistor $Q1$ avalanche current–voltage characteristic $V_{ec} = V_{ec}(In)$ curve can be obtained by adjusting a mathematical function to the measured experimental data of the particular NPN type transistors 2N2222 and BC547 that we used, whereas for transistor $Q2$ the basic Ebers and Moll model (Ebers and Moll, 1954; Getreu, 1978) may be adopted. Although the numerical results of Eq. (2) have not been included in this paper, they reproduce all of the circuit dynamics of Fig. 3, the frequency adaptation patterns of Fig. 5 and the bifurcations in Fig. 7.

8. Discussion and Conclusions

Our circuit, created from an unusual utilization of the nonlinearity of bipolar transistors, has a wealth of advantageous features compared to previous circuits modeling intrinsic bursting and spiking neurons, although there do exist mathematical and electronic models that reproduce neuronal bursts more faithfully in other respects (Simoni et al., 2004; Le Masson et al., 1999; LaFlaquière et al., 1997; Maeda and Makino, 2000). For one, our circuit is simple, yet dynamically robust. No fine-tuning of its parameters is needed to make it burst. It is easily reproduced for the purpose of studying the dynamics of a single unit, or the dynamics of a network of them in any desired topology. The brain is thought to be composed of individual neurons with dendritic connections to other neurons numbering on the order of 10,000. The outstanding connectivity of our circuit could be useful in

studying the role of bursting in fundamental functions of the brain such as information transmission, encoding and processing.

Secondly, our circuit is the first intrinsic burster in the literature that displays a stable burst with frequency adaptation patterns similar to those reported in real neurons (Connors and Gutnick, 1990; Izhikevich, 2007). For example, a decrease in spiking frequency as a burst progresses, or *spike-frequency adaptation*, is a prominent feature of cortical pyramidal neurons of the regular spiking type (Connors and Gutnick, 1990). Alternatively, some neurons display an increase in spiking frequency as a burst progresses, or *spike-frequency acceleration*, for example, cortical fast spiking interneurons (Gibson et al., 1999). Our circuit is capable of exhibiting both types of adaptation and also more complex ones (Fig. 5). In both the neuron and our circuit, the frequency pattern depends on the strength and nature of the slow current(s), and how the spiking limit cycle of the fast subsystem is affected.

Thirdly, our circuit is the simplest circuit designed to date that allows a study of the dynamics of the classical phenomenological HH equations. The generator replicates the dynamics of two-dimensional mathematical approximations (Izhikevich, 2000) of the HH equations. Namely, it has the same bifurcation types (Savino and Formigli, 2007) as the HH equations, some of which are shown in Fig. 7. Its real-time performance may eliminate the need for current efforts to reduce the HH equation among others, to two-dimensional maps that preserve the dynamics (Channell et al., 2007; De Vries, 2005). Also the circuit Eq. (2) can be used for theoretical studies.

We hypothesize the following correspondences between sections of our circuit and neuronal structure: the generator with the soma, the modulator with the dendrite, the input block with the synapse. In both systems, the fast–slow current interaction operates with strength and characteristics that are modified in some way by the system components and the inputs arriving at the input block. Based on similar work with cardiac cells (Padmanabhan, 1977), we can make detailed analogies for components of the generator block. The reverse-biased transistor $Q1$ with its low-threshold voltage avalanche region corresponds to the transient negative conductance displayed by sodium current when neuronal voltage threshold is reached and triggers cell depolarization. The $Q1$ base lead further provides weak capacitive coupling, which allows synchronization of multiple units. $C1$ and $V1$ can be seen to correspond to cell-membrane capacitance and potential without much effort, as are $R1$ and $R2$ to the extracellular and intracellular resistance, respectively. Currents In and $I1$ correspond to the depolarizing (activation) sodium current, and the polarizing (recovery) potassium current, respectively. The pulse $V2$ that develops across $R2$ corresponds to the neuronal action potential or spike.

Likewise, we hypothesize that components of the modulator block have close correspondences with dendritic components. Currents $I2$ and $I3$ represent the sum of all currents at the soma and dendrite, respectively. Capacitor $C2$ represents the concentration of intracellular ions, mostly Ca^{2+}, and transistor $Q2$ drives current $I2$, which represents Ca^{2+}-gated current. Capacitor $C3$ represents capacitance of the dendritic compartment where many synaptic arriving inputs are integrated, changing the free-running time dependent voltage $V3$ and current $I3$, and therefore burst features.

Whether one accepts these fairly straightforward correspondences between constituent components of our circuit and the neuron or not, we can and do draw analogies between the circuit and neuron in the following respects. The isolated generator has fast intrinsic periodic oscillations. The modulator injects slow (longer characteristic timescale) currents into the fast subsystem similar to the modification of the soma by dendritic slow cur-

rents, and gives rise to bursting, and the frequency adaptation of burst. Our circuit also has in its dynamics, an excitable regime, like that of excitable biological cells. Thirdly, in neuronal physiology, characteristics of bursting such as its timing and frequency are widely attributed to voltage and time dependent mechanisms. Our circuit depends on voltage (VDM) and time (TDM) dependent mechanisms to generate various bursting characteristics.

To summarize, we believe that our circuit provides a valuable tool for answering various biological and mathematical questions. Examples of the latter, enunciated by Izhikevich (2007), for bursting HH neuron models are: *What initiates sustained spiking during the burst? and What terminates sustained spiking temporally and ends the burst?* The answers are immediate for our circuit. Bursts are initiated and terminated by the VDM, and bursts are sustained for duration T_r by the TDM. We also mention that in the past, a spike and burst were considered different dynamic entities. In our circuit dynamics, an isolated spike can be seen to be nothing more than a single spike burst. In other words, single isolated spikes have the same starting and ending bifurcation sequence as bursts, and do not require special scenarios. As for applications to biology, the simplicity and connectivity of our circuit, together with the hypothesized correspondences between circuit components and neuronal components allow the construction of virtual experiments, whether of networked neurons, or of mechanisms underlying pathological dynamics in bursting neurons.

Acknowledgements

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