Bursting Electrical Activity

MATH 550

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Overview

A number of mathematical models have been proposed to describe the electrical bursting activity of biological excitable membrane systems.
My **goal** in this project is to understand the basic underlying qualitative structure of these models and to distinguish the classes of models for bursting.
Content of the Slides:

- Introduction
- Bursting in Pancreatic β-cell
- Parabolic Bursting
- Polynomial Model
- Classifications of Bursting Models

Introduction

Calcium ion is crucial in a number of physiological processes in the human body including muscle contraction, secretion, metabolism, fertility, phagocytes, bursting oscillations and many others.

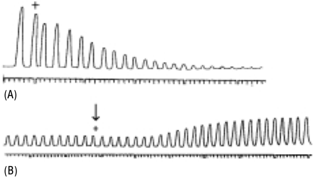
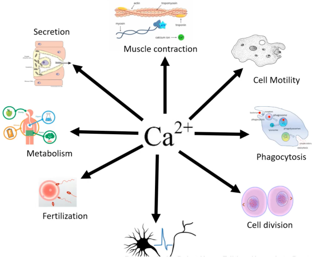


FIG. 2 Original recording of Ringer's frog heart (from left to right) perfused with blood mixture. At the point indicated, saline was substituted for the blood mixture, and the amplitude of contractions declined (A). When calcium chloride (3.5 cc) was added to the saline solution (at arrow), contractions recovered to almost normal amplitude (B). Original Figure VIII of Ref. No. 4.



Bursting

Bursting is a dynamic state where a neuron repeatedly fires bursts of spikes. Each such burst is followed by a period of quiescence before the next burst occurs. Neuronal bursting can play important roles in communication between neurons.

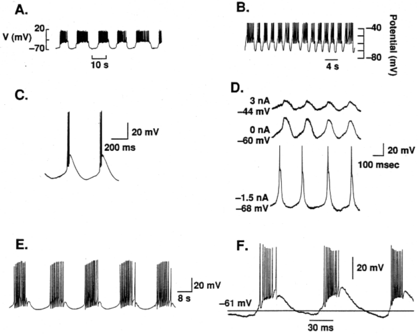


Figure: Electrical bursting in different cell types. A: Pancreatic β-cell. B: Dopamine-containing neurons in the rat midbrain. C: Cat thalamocortical relay neuron. D: Guinea pig inferior olivary neuron. E: Aplysia R15 neuron. F: Cat thalamic reticular neuron.

Bursting in Pancreatic β-cell

- Pancreatic β-cells are a type of cells found in the pancreatic islets of our pancreas, whose primary function is to store and release insulin.
- Pancreatic β-cells respond to periodic bursting in the presence of glucose and this activity is correlated with their release of insulin.
- The interruption of insulin secretion system may result in health conditions such as diabetes, heart diseases, kidney failure and death. It is believed that electrical bursting plays a crucial role in the release of insulin from the cell.

Mathematical Model

The Chay-Keizer β-cell model was modified by removing the time dependence (m and h) of the Ca^{2+} current by (Rinzel and Lee, 1986). The simplified three-variable model equations:

Rinzel-Lee's Model

$$c_m \frac{dV}{dt} = -I_{Ca}(V) - (\bar{g}_k n^4 + \frac{\bar{g}_{K,Ca} c}{K_d + c})(V - V_K) - g_L(V - V_L) \tag{1}$$

$$\tau_n(V) \frac{dn}{dt} = n_\infty(V) - n \tag{2}$$

$$\frac{dc}{dt} = f(-k_1 I_{Ca}(V) - k_c c) \tag{3}$$

where $I_{Ca} = \bar{g}_{Ca} m_\infty^3 h_\infty(V)(V - V_{Ca})$

Phase Plane Analysis

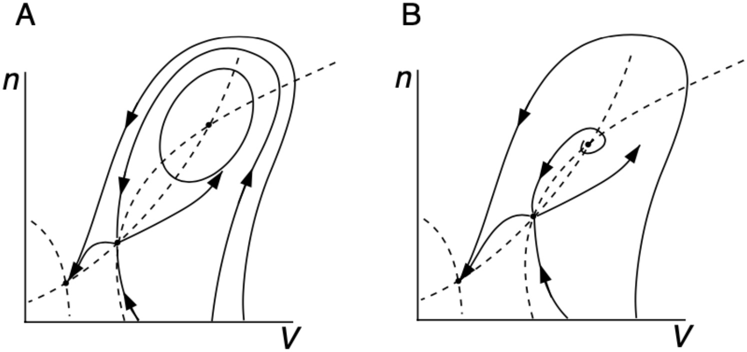


Figure: Phase-planes of the fast subsystem of the β-cell model, for two different values of c in A and B. For both values of c there are three fixed points, of which the middle one is a saddle point.

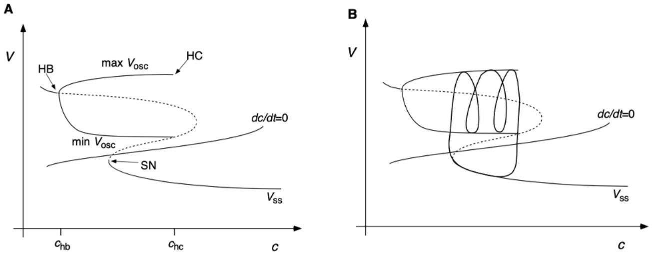


Figure: A: Sketch of bifurcation diagram for the simplified β-cell model, with c as the bifurcation parameter. B: Illustrates the bursting pattern in A.

We assume k_c is related to glucose concentration.

- Low k_c concentration, β-cell rest state.
- high glucose, leads to continuous spiking.
- Intermediate glucose, leads to bursting.

Parabolic Bursting

This form of bursting is found in the Aplysia R-15 neuron. A model by Plant (1981) explained the mechanism underlying parabolic bursting oscillations. In this model, bursting arises from the presence of two slow variables with their own oscillation.

Plant's parabolic bursting model is similar in some respects to the β-cell model. However, it also includes a voltage-dependent Na^+ channel that activates and inactivates in typical Hodgkin–Huxley fashion and a slowly activating Ca^{2+} current.

Mathematical Model

Plant's Model

$$c_m \frac{dV}{dt} = -\bar{g}_{Na} m_\infty^3(V) h (V - V_{Na}) - \bar{g}_{Ca} x (V - V_{Ca}) - (\bar{g}_k n^4 + \frac{\bar{g}_{K,Ca} c}{0.5 + c})(V - V_K) - \bar{g}_L (V - V_L) \quad (4)$$

$$\tau_h(V) \frac{dh}{dt} = h_\infty(V) - h \quad (5)$$

$$\tau_n(V) \frac{dn}{dt} = n_\infty(V) - n \quad (6)$$

while the Ca^{2+} current and its activation x form the slow subsystem.

$$\tau_x \frac{dx}{dt} = x_\infty(V) - x \quad (7)$$

$$\frac{dc}{dt} = f(k_1 x (V_{Ca} - V) - c) \quad (8)$$

- V is the membrane potential (mV) and t is time (ms)
- c_m is the membrane capacitance (μ/cm^2)
- $\bar{g}_c$ is maximal ion conductances $(mmho/cm^2)$
- V_{Na} nerst potential(mV)
- $m_\infty(V)$ is the instantaneous activation function for the fast inward current
- x and n are dimensionless activation variables
- h is a dimensionless inactivation variable
- Ca represents the dimensionless intracellular calcium ion concentration

Bifurcation Diagram

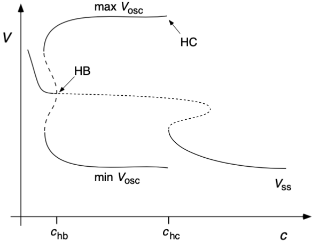


Figure: Sketch of the bifurcation diagram of the fast subsystem of the parabolic bursting model, with $x = 0.7$.

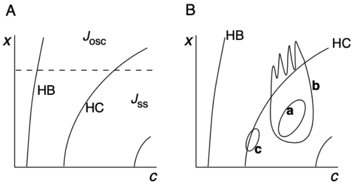


Figure: A: The Hopf and homoclinic bifurcations in the (x,c) plane. B: Three typical slow oscillations in x and c.

Qualitative Bursting Models

Mathematical properties of bursting models can be incorporated into simpler polynomial models, in much the same way that the FitzHugh–Nagumo model provides a simplification of the Hodgkin–Huxley model.

A Polynomial Model

A modified version of FitzHugh-Nagumo model by Hindmarsh and Rose(1982 & 1984) with some more modifications is used as a model for bursting. The new model equations are:

$$\frac{dv}{dt} = \alpha(\beta w - f(v) + I) \tag{9}$$

$$\frac{dw}{dt} = \lambda(g(v) + h(v) - \delta w) \tag{10}$$

$\alpha, \beta, \delta \text{and} \lambda$ are constants. $f(v)$ is cubic and $g(v)$ is non-linear.

Nondimensionalization

Introduce new variables: $T = \lambda\delta t, \quad x = v, \quad y = \frac{\alpha\beta w}{\lambda\delta}$

Nondimensional Model

$$\frac{dx}{dT} = y - \tilde{f}(x) \tag{11}$$

$$\frac{dy}{dT} = \tilde{g}(x) - y \tag{12}$$

$\tilde{f}(x) = \frac{\alpha f(x)}{\lambda\delta}$ and $\tilde{g}(x) = \frac{\alpha\beta[g(x)+h(x)]}{\lambda\delta^2}$
$\tilde{f}(x)$ and $\tilde{g}(x)$ are chosen so that the model can exhibit bistability.

A Polynomial Model

To generate bursting, it is necessary to have a slow variable.

Our final model

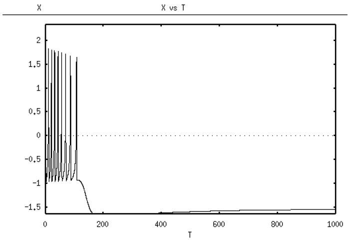
$$\frac{dx}{dT} = y - (x^3 - 3x^2 - I) - z \tag{13}$$

$$\frac{dy}{dT} = (1 - 5x^2) - y \tag{14}$$

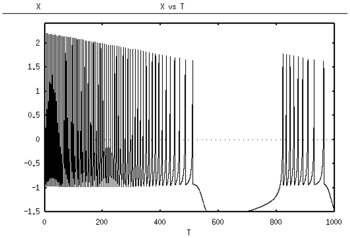
$$\frac{dz}{dT} = r[s(x - x_1) - z] \tag{15}$$

where $x_1 = -\frac{1}{2}(1 + \sqrt{5})$, $r = 0.001$ and $s = 4$.
This model exhibits type one bursting like the Rinzel-Lee simplification of the Chay-Keizer model.

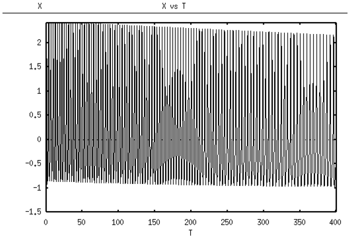
Numerical Simulations of the Polynomial Model



(a) $I = 0.4$



(b) $I = 2$



(c) $I = 4$

Figure: Bursting in the polynomial model

Numerical Simulations of the Polynomial Model

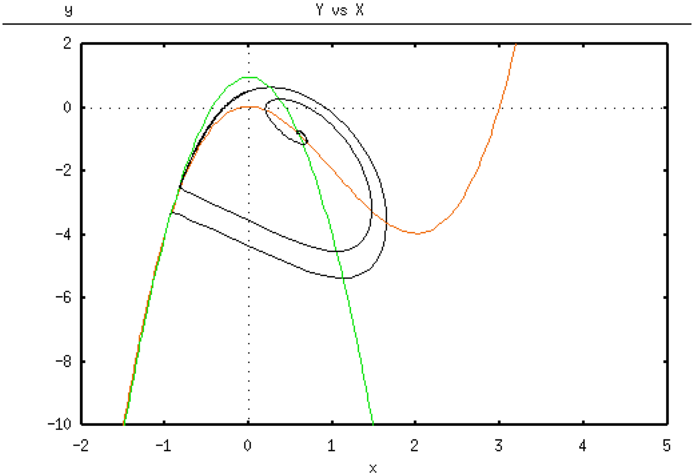


Figure: Phase-plane of polynomial bursting model

Classification scheme for bursting oscillations

A classification scheme for the different mechanisms was proposed by Rinzel (1987) and extended by Bertram et al. (1995). Burst oscillations were grouped into three classes: type I, with bursts arising from hysteresis and bistability as in the B-cells; type II, with bursts arising from an underlying slow oscillation, as in parabolic bursting model; and type III, which arises from subcritical Hopf bifurcation.

Classification scheme for bursting oscillations

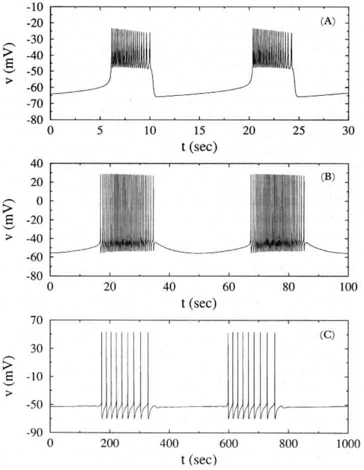


Figure: A: Type I bursting, B: Type II bursting, C: Type III bursting

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