An Introduction to Mathematical Neuroscience

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Computational neuroscience provides quantitative tools and methods for “characterizing what nervous systems do, determining how they function, and understanding why they operate in particular ways” (Dyan and Abbott)
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Interdisciplinary field: mathematics/statistics/computer science/physics.
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Interaction with experiments
What is Mathematical/Computational Neuroscience?

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- **Interdisciplinary field**: mathematics/statistics/computer science/physics.

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  - Fit and interpret existing data
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  - Fit and interpret existing data
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- **Interdisciplinary field**: mathematics/statistics/computer science/physics.

- **Interaction with experiments**
  - Fit and interpret existing data
  - Test hypothesis
  - Make predictions and suggest new experiments
The Human Brain

$\sim 10^{12}$ Neurons

$\sim 10^{15}$ Synapses
<table>
<thead>
<tr>
<th>Spatial Scale</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>≈ 10 cm</td>
<td>Whole brain</td>
</tr>
<tr>
<td>≈ 1 cm</td>
<td>Cortical area; other brain structure</td>
</tr>
<tr>
<td>100 μm - 1 mm</td>
<td>Local network/&quot;column&quot;/&quot;module&quot;</td>
</tr>
<tr>
<td>10 μm - 1 mm</td>
<td>Neuron</td>
</tr>
<tr>
<td>10 nm - 1 μm</td>
<td>Sub-cellular compartments</td>
</tr>
<tr>
<td>1-10 nm</td>
<td>Molecules (channels, receptors, etc)</td>
</tr>
</tbody>
</table>
## Temporal scales of the brain

<table>
<thead>
<tr>
<th>Time Scales</th>
<th>Long-term memory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days-Years</td>
<td></td>
</tr>
<tr>
<td>Seconds-Minutes</td>
<td></td>
</tr>
<tr>
<td>100ms - 1s</td>
<td>Short-term (working) memory</td>
</tr>
<tr>
<td>≈ 10ms</td>
<td>Behavioral time scales/Reaction times</td>
</tr>
<tr>
<td>≈ 1ms</td>
<td>Single neuron/synaptic time scales</td>
</tr>
<tr>
<td>≪ 1ms</td>
<td>Action potential duration; local propagation delays</td>
</tr>
<tr>
<td></td>
<td>Channel opening/closing</td>
</tr>
</tbody>
</table>

*Adapted from slides by N. Brunel*
From molecules to neuronal networks

Fig by Scientific American and Magnus Richardson
• Numerical methods
Numerical methods

Analytical methods
Mathematical Methods

- Numerical methods
- Analytical methods
  - Single neuron/synapse models/firing rate models: systems of coupled differential equations. Tools of dynamical systems (linear stability analysis, bifurcation theory, etc.)

Netw orks: Graph theory, topology, algebra. Large N limit: tools of statistical physics.

Noise: ubiquitous at all levels of the nervous system. Statistics, probability theory, stochastic differential equations.

Coding. Information theory

Gemma Huguet
Numerical methods

Analytical methods

- **Single neuron/synapse models/firing rate models**: systems of coupled differential equations. Tools of *dynamical systems* (linear stability analysis, bifurcation theory, etc.)
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Mathematical Methods

- Numerical methods
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  - Coding. Information theory
A few historical landmarks

- Before mid-1980s: a few isolated pioneers
  - 1907: Louis Lapicque (leaky integrate-and-fire neuron)
  - 1940s-50s: Alan Hodgkin, Andrew Huxley (model for AP generation)
  - 1950s: Wilfrid Rall (cable theory)
  - 1970s: Hugh Wilson, Jack Cowan, Shun-Ishi Amari ('rate models')
  - 1980s: John Hopfield, Daniel Amit, Hanoch Gutfreund, Haim Sompolinsky (associative memory models)
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- From the 1990s: establishment of a field
  - Specialized journals, summerschools, conferences created
  - Birth of major Computational Neuroscience centers in the US and Europe
Contents - Outline

- Introduction to the field
- Single cell Neurophysiology (Neuron biophysics and basic neuron models)
  - The Hodgkin-Huxley model for the generation of an action potential
  - Excitability properties and oscillations
  - Two-dimensional neuron models
  - One-dimensional neuron models: Integrate-and-fire models
  - A zoo of firing behaviors; bursting
- Neuronal networks
  - Synaptic transmission.
  - Network architecture and network dynamics.
  - Mean field models; firing rate models.
  - Applications: decision making, working memory, perceptual multistability, spreading depression.
**The Neuron**

**Electrical signal:** Action potential that propagates along the axon
Membrane Potential

The cell membrane separates two ionic solutions with different concentrations (ions are electrically charged atoms)

- **Membrane potential** due to charge separation across the cell membrane. $V = V_{\text{in}} - V_{\text{out}}$ (by convention $V_{\text{out}} = 0$).
- **Resting state** $V = -60$ to $-70$ mV.
- **Ionic channels** embedded in the cell membrane ($\text{Na}^+$ and $\text{K}^+$ channels)
The action potential

See video
The action potential

See video

Travelling wave

Action potential
The Hodgkin-Huxley model for the generation of an action potential
Hodgkin-Huxley model (1952)

Nobel prize for medicine in 1963
Nernst Potential or Reversal Potential

Nernst Potential. The potential value at which the concentration and the electrical potential gradients exert equal and opposite forces and the net cross-membrane current is zero. It is given by the Nernst equation:

$$E_{ion} = \frac{RT}{zF} \ln \frac{[Ion]_{out}}{[Ion]_{in}}$$

$[Ion]_{in}$ and $[Ion]_{out}$ are concentrations of the ions inside and outside the cell, respectively; $R$ is the universal gas constant (8315 mJ/K$^\circ$·Mol); $T$ is temperature in degrees Kelvin ($K^\circ = 273.16 + C^\circ$); $F$ is Faraday’s constant (96480 Coulombs/Mol); $z$ is the valence of the ion ($z = 1$ for $Na^+$ and $K^+$; $z = -1$ for $Cl^-$; and $z = 2$ for $Ca^{2+}$).
Illustration of different ionic concentrations and the corresponding reversal potentials applying the Nernst equation.
Electrical activity of cells

Electrical parameters

- Membrane Potential $V$ (Volts)
- Current $I$ (Ampere)
- Conductance $g$ (Siemens),
- Resistance $R = 1/g$ (Ohms).
- Capacitance $C$ (Farads)
### Electrical activity of cells

#### Electrical parameters

- **Membrane Potential** $V$ (Volts)
- **Current** $I$ (Ampere)
- **Conductance** $g$ (Siemens),
- **Resistance** $R = 1/g$ (Ohms).
- **Capacitance** $C$ (Farads)
Types of currents:

- **Capacitive current** $I_C$ (Capacitor: Two conducting plates separated by an insulating layer. It stores charge). Faraday’s law: $Q = CV$; derivating $I_C = CdV/dt$.

- **Ionic currents** $I_{ion}$. The net current for each ion is proportional to the difference between the membrane potential $V$ and the reversal potential $E_{ion}$ (Ohm’s law):

  $$I_{ion} = g_{ion}(V - E_{ion}).$$

- **Leak current**: $I_L = g_L(V - E_l)$. In the absence of other currents, the membrane potential tends to $E_L$ (ionic pumps, other ion currents, etc).

- **External current** $I_{app}$.

Current balance equation (Kirchhoff’s current law):

$$I_C + \sum_{ion} I_{ion} + I_L = I_{app}$$

$$C \frac{dV}{dt} = -g_{Na}(V - E_{Na}) - g_K(V - E_K) - g_L(V - E_L) + I_{app}$$
Ionic conductances $g_{ion}$ are functions of $V$ and $t$. Hodgkin and Huxley studied the dynamics of $K^+$ and $Na^+$ conductances and proposed that

$$g_K = \bar{g}_K n^4 \quad \text{and} \quad g_{Na} = \bar{g}_{Na} m^3 h,$$

where $m$, $h$ and $n$ are gating variables (taking values between 0 and 1). They control whether the channels are open or close.

Structure of voltage-gated ion channels.
Voltage-gated channels

When gating particles are sensitive to voltage, channels are voltage-gated. Types of gates:

1. activate or open channels \((m-Na^+, n-K^+);\)
2. inactivate or close channels \((h-Na^+).\)

The proportion of open channels in a large population is

\[ p = m^a h^b \]

where \(a\) is the number of activation gates and \(b\) is the number of inactivation gates per channel. The channels can be partially \((0 < m < 1)\) or completely activated \((m = 1)\); not activated or deactivated \((m = 0)\); inactivated \((h = 0)\); released from inactivation or deinactivated \((h = 1)\).

- \(b = 0 \rightarrow \text{persistent currents}.\) For instance \(K^+\) in the HH-model.
- \(b \neq 0 \rightarrow \text{transient currents}.\) For instance \(Na^+\) in the HH-model.
Activation and time functions

Recall that the dynamics of $K^+$ and $Na^+$ conductances is modeled by:

$$g_K = \bar{g}_K n^4 \quad \text{and} \quad g_{Na} = \bar{g}_{Na} m^3 h,$$

where $m, h$ and $n$ are gating variables (take values between 0 and 1).
Activation and time functions

Recall that the dynamics of $K^+$ and $Na^+$ conductances is modeled by:

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where $m$, $h$ and $n$ are gating variables (take values between 0 and 1). $w =$ fraction of open gates (can be $h$, $m$ or $n$). Law of mass action:

$$\frac{d}{dt} \left( \frac{\alpha(V)}{\beta(V)} \right) = \phi \left( \frac{w_{\infty}(v) - w}{\tau_w(v)} \right), \quad (1)$$
Activation and time functions

Figure 2.20: Boltzmann (2.11) and Gaussian (2.12) functions and geometrical interpretations of their parameters.

\[
\begin{align*}
&w_\infty(v) = \frac{1}{1 + \exp\left((V_{1/2} - V)/k\right)}, \\
&\tau_w(v) = C_{\text{base}} + C_{\text{amp}} \exp\left(\frac{-(V_{\text{max}} - V)^2}{\sigma^2}\right).
\end{align*}
\]
Hodgkin-Huxley model (1952)

Model for electrically compact neurons \( V(x, t) = V(t) \).

\[
\begin{align*}
C \dot{V} &= -I_{Na} - I_{K} - I_{L} + I_{app} \\
&= -g_{Na} m^3 h (V - V_{Na}) - g_{K} n^4 (V - V_{K}) - g_{L} (V - V_{L}) + I_{app} \\
\dot{m} &= \left( m_{\infty}(V) - m \right)/\tau_{m}(V) \\
\dot{h} &= \left( h_{\infty}(V) - h \right)/\tau_{h}(V) \\
\dot{n} &= \left( n_{\infty}(V) - n \right)/\tau_{n}(V)
\end{align*}
\]

- **Membrane Potential**: \( V \)
- **Reversal potential**: \( V_{K} \approx -80 \text{ mV}, \ V_{Na} \approx 50 \text{ mV} \).
- **Channel state variables (associated probability)**: \( h, m, n \)
The Hodgkin-Huxley model (1952)

Models flow of ions across neural membrane as an electrical circuit

\[
\begin{align*}
C \dot{V} &= -I_{Na} - I_{K} - I_{L} + I_{app} \\
&= -g_{Na} m^3 h (V - V_{Na}) - g_{K} n^4 (V - V_{K}) - g_{L} (V - V_{L}) + I_{app} \\
\dot{m} &= \frac{(m_{\infty}(V) - m)}{\tau_{m}(V)} \\
\dot{h} &= \frac{(h_{\infty}(V) - h)}{\tau_{h}(V)} \\
\dot{n} &= \frac{(n_{\infty}(V) - n)}{\tau_{n}(V)}
\end{align*}
\]
Action potential

Mechanisms underlying the action potential

- Sodium (Na+) enters the cell.
- Voltage (V) increases.
- Sodium (Na+) channels activate: m↑.
- Sodium (Na+) channels inactivate: h↓.
- Potassium (K+) channels activate: n↑.
- Sodium (Na+) deactivates: m↓.
- Sodium (Na+) deactivates: h↑.
- Potassium (K+) deactivates: n↓.

E_{Na}, E_{K}:

V_{rest}, V
Action potential (main features of the neurons and the Hodgkin-Huxley model)
The action potential: movies

- Action potential, channels opening (4:01)
- Action potential, channels opening and propagation (5:42)
- Action potential, channels opening (1:02)
- Action potential, channels opening and propagation (4:01)
- Action potential and myelin sheaths (5:07)
Excitability properties & oscillations
Neuronal response to a brief current pulse and steady current (exc)
Excitability & Oscillatory regime

Bifurcation diagram for HH-model

$I_1, I_2$ Hopf bifurcation, $I_\nu$ saddle-node of limit cycles. Bistability between $I_\nu$ and $I_1$
Excitability classes

Hodgkin’s classification, 1948

CLASS I

CLASS II

Cortical pyramidal cells

Cortical interneurons
Excitability classes

Hodgkin’s classification, 1948

Recordings from spinal sensory neurons. Adapted from Prescott et al., 2008
Hodgkin’s classification, 1948

Excitability types:

- **Type I.** Sharp thresholds, excitability with long latency and firing at arbitrarily low frequencies.
- **Type II.** Variable thresholds, excitability with short latency and a positive minimal frequency for firing.
- **Type III.** High threshold, short response time, failed to repeat.

Mathematical formulation: Rinzel and Ermentrout ’89
Excitability types: mathematical formulation

Rinzel and Ermentrout’98

Figure adapted from Prescott et al., 2008
Two-dimensional neuron models
Reductions of the HH-model: an example

- $m$ activates very fast: set $m = m_\infty(V)$
- There is a linear relationship between the gating variable $n(t)$ and $h(t)$, namely
  \[ 1.1n(t) + h(t) \approx 0.89. \]
- We reduce the HH-model to
  \[
  C \dot{V} = -g_{Na} m_\infty^3(V)(0.89 - 1.1n)(V - E_{Na}) - g_K n^4(V - E_K) - g_L (V - E_L) + I_{app} \\
  \dot{n} = (n_\infty(V) - n)/\tau_n(V)
  \]
Excitability classes (Hodgkin, 1948)

Goal: Relate each excitability class to a different bifurcation.
Other 2D-models

- **Morris–Lecar model** (giant muscle fiber of the barnacle)

\[
C \dot{V} = -g_{Ca} m_{\infty}(V)(V - E_{Ca}) - g_K w(V - E_K) - g_L (V - E_L) + I_{app}
\]
\[
\dot{w} = \phi \frac{w_{\infty}(V) - w}{\tau_w(V)}
\]

We consider different sets of parameters, that correspond to different types of bifurcations from steady state to periodic behavior as \(I_{app}\) varies: Hopf, saddle-node on an invariant circle (SNIC) and homoclinic.

- **FitzHugh-Nagumo** (simpler model of excitability)

\[
\dot{V} = V(V - a)(1 - V) - w + I_{app}
\]
\[
\dot{w} = \varepsilon(V - \gamma w)
\]
Phase plane – Nullclines

\[\dot{V} = f(V, w)\]

\[\dot{w} = g(V, w)\]

- **V-nullcline**: \( f(V, w) = 0 \) (cubic function)
- **w-nullcline**: \( g(V, w) = 0 \) (sigmoidal function)

Equilibrium points: intersections of both nullclines
Slow-fast dynamics: \( \dot{V} \gg \dot{w} \)
Consider a fixed point \((\bar{V}, \bar{w})\) of the system

\[
\begin{align*}
\dot{V} &= f(V, w) \\
\dot{w} &= g(V, w)
\end{align*}
\]

Linearize the system around the fixed point \((\bar{V}, \bar{w})\). The linearization matrix is called the Jacobian matrix:

\[
J = \left( \begin{array}{cc}
\frac{\partial f}{\partial V} & \frac{\partial f}{\partial w} \\
\frac{\partial g}{\partial V} & \frac{\partial g}{\partial w}
\end{array} \right) |(\bar{V}, \bar{w})
\]

Fixed point is stable if both eigenvalues have \(Re(\lambda) < 0\).

Bifurcation occurs when \(Re(\lambda) = 0\) when a parameter (such as \(I_{app}\)) is varied.
Classification of equilibria according to the trace $\tau$ and the determinant $\Delta$ of the Jacobian matrix.
Equilibria: Linear stability analysis

Consider a fixed point \((\bar{V}, \bar{w})\) of the system
\[
\begin{align*}
\dot{V} &= (-I_{ion}(V, w) + I_{app})/C \\
\dot{w} &= \phi(w_{\infty}(V) - w)/\tau_w(V)
\end{align*}
\]

The trace and det of the Jacobian matrix evaluated at \((\bar{V}, \bar{w})\) is
\[
\begin{align*}
\Delta &= \det(J) = \frac{\phi}{C\tau_w} \frac{dI_{ss}}{dV} \\
\tau &= \text{tra}(J) = -\frac{1}{C} \frac{\partial I_{ion}}{\partial V} - \frac{\phi}{\tau_w}
\end{align*}
\]
2-D models for spike generation - Class II excitability

- Morris–Lecar model (Class II parameter set)

\[
\dot{V} = -g_{Ca} m_\infty(V)(V - E_{Ca}) - g_K w(V - E_K) - g_L (V - E_L) + I \\
\dot{w} = \phi \frac{w_\infty(V) - w}{\tau_w(V)}
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\dot{w} &= \phi \frac{w_\infty(V) - w}{\tau_w(V)}
\end{align*}
\]
Hopf bifurcation (supercritical)

Normal form in polar coordinates for supercritical Hopf bifurcation:

\[
\begin{align*}
\dot{r} &= (\mu - r^2)r \\
\dot{\theta} &= \omega + br^2
\end{align*}
\]

Eigenvalues at origin: \( \lambda_{\pm} = \mu \pm i\omega \).

- \( \mu < 0 \), the origin is attracting.
- \( \mu = 0 \), the origin is nonlinearly attracting.
- \( \mu > 0 \), the origin is repelling, there exists an attracting periodic orbit.

- The size of the LC increases proportional to \( \sqrt{\mu} \) for \( \mu \) close to 0.
- The frequency of the LC is given approximately by \( \omega = \text{Im}\, \lambda + O(\mu) \).
Hopf bifurcation (subcritical) + Double limit cycle bifurcation

Example of a subcritical Hopf bifurcation:

\[
\begin{align*}
\dot{r} &= (\mu + r^2)r - r^5 \\
\dot{\theta} &= \omega + br^2
\end{align*}
\]

Eigenvalues at origin: \( \lambda_\pm = \mu \pm i\omega \).

- \( \mu < 0 \), the origin is attracting, there exists a repelling periodic orbit.
- \( \mu = 0 \), the origin is nonlinearly repelling.
- \( \mu > 0 \), the origin is repelling.

There exists an attracting limit cycle surrounding the subcritical bifurcation.
Morris–Lecar model (Class I - parameter set)

\[
\begin{align*}
C \dot{V} &= -g_{Ca} m_{\infty}(V)(V - E_{Ca}) - g_{K} w(V - E_{K}) - g_{L}(V - E_{L}) + I \\
\dot{w} &= \phi \frac{w_{\infty}(V) - w}{\tau_{w}(V)}
\end{align*}
\]

Smeal, Ermentrout and White, 2010
Morris–Lecar model (Class I - parameter set)

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\]

Smeal, Ermentrout and White, 2010
SNIC bifurcation

Saddle Node bifurcation. A real eigenvalue of an equilibrium point vanishes.

A saddle-node occurring on a closed curve leads to a global bifurcation:
Saddle Node on an invariant circle bifurcation (SNIC)

Period of one oscillation is $T = O(|\mu|^{-1/2})$, frequency is $O(\sqrt{|\mu|})$
Excitability classes and bifurcations

- **Class I excitability**: Repetitive firing onset through a SNIC bifurcation
- **Class II excitability**: Repetitive firing onset through a Hopf bifurcation
Bifurcations of fixed points

- Node vs Saddle
- Saddle-node bifurcation

- Node vs Saddle vs Invariant Circle
- Saddle-node on Invariant Circle (SNIC) bifurcation

- Supercritical Andronov-Hopf bifurcation

- Subcritical Andronov-Hopf bifurcation
Bifurcations of stable limit cycles

- Saddle-node on invariant circle (SNIC) bifurcation
- Supercritical Andronov-Hopf bifurcation
- Fold limit cycle bifurcation
- Saddle homoclinic orbit bifurcation
One-dimensional neuron models: Integrate-and-fire models
Integrate-and-fire model (Louis Lapicque, 1866–1952)

\[
\begin{aligned}
    C \dot{V} &= -g_L (V - E_L) + I_{\text{app}}, \\
    \text{if } V(t) &> V_{\text{th}}, \text{ then } V \to V_{\text{re}}
\end{aligned}
\]
Integrate-and-fire model in dimensionless form:

\[ v' = -v + I, \quad \text{if} \quad v(t) = 1, \quad \text{then} \quad v(t^+) = 0 \]
Integrate-and-fire model in dimensionless form:

\[ v' = -v + I, \quad \text{if} \quad v(t) = 1, \quad \text{then} \quad v(t^+) = 0 \]

Solution: \[ v(t) = I + (v_0 - I)e^{-t}, \quad \text{with} \quad v(0) = v_0. \]
Integrate-and-fire model in dimensionless form:

\[ \dot{v} = -v + I, \quad \text{if} \quad v(t) = 1, \text{then} \quad v(t^+) = 0 \]

Solution: \( v(t) = I + (v_0 - I)e^{-t} \), with \( v(0) = v_0 \).

Take \( I = 0.5 \) and \( v_0 = 0 \),

![Graph](image)
Integrate-and-fire model in dimensionless form:

\[ v' = -v + I, \quad \text{if} \quad v(t) = 1, \text{then} \quad v(t^+) = 0 \]

Solution: \( v(t) = I + (v_0 - I)e^{-t} \), with \( v(0) = v_0 \).

Take \( I = 0.5 \) and \( v_0 = 0, \quad v_0 = 0.9 \)
Integrate-and-fire model in dimensionless form:

\[ v' = -v + I, \quad \text{if} \quad v(t) = 1, \text{then} \quad v(t^+) = 0 \]

Solution: \( v(t) = l + (v_0 - l)e^{-t} \), with \( v(0) = v_0 \).

Take \( l = 0.5 \) and \( v_0 = 0, \ v_0 = 0.9 \) and \( v_0 = 0.5 \).
Integrate-and-fire model in dimensionless form:

\[ v' = -v + I, \quad \text{if} \quad v(t) = 1, \text{then} \quad v(t^+) = 0 \]

Solution: \( v(t) = I + (v_0 - I)e^{-t}, \) with \( v(0) = v_0. \)

Take \( I = 0.5 \) and \( v_0 = 0, \) \( v_0 = 0.9 \) and \( v_0 = 0.5. \)

\( v = I = 0.5 \) is a stable equilibrium point.
Take $I = 2$ and $\nu_0 = 0$. 
Take $l = 2$ and $v_0 = 0$.

What happens when we add the reset? Recall when $v(t) = 1$ then $v(t) = 0$. 

![Graph showing oscillatory behavior and reset](image)
Take $I = 2$ and $v_0 = 0$.
What happens when we add the reset? Recall when $v(t) = 1$ then $v(t) = 0$.
There is a qualitative change in the behavior of the solutions (stable equilibrium to a periodic solution). The system undergoes a bifurcation.
Take $I = 2$ and $v_0 = 0$.

What happens when we add the reset? Recall when $v(t) = 1$ then $v(t) = 0$.

There is a qualitative change in the behavior of the solutions (stable equilibrium to a periodic solution). The system undergoes a bifurcation.
We have found a periodic solution. Let’s compute the period...
We have found a periodic solution. Let’s compute the period…

$T$ is the time it takes for $v$ to go from $v(0) = v_0 = 0$ to $v(T) = 1$. Then
We have found a periodic solution. Let’s compute the period...

$T$ is the time it takes for $v$ to go from $v(0) = v_0 = 0$ to $v(T) = 1$. Then

$$v(T) = 1 = I + (0 - I)e^{-T}$$
We have found a periodic solution. Let’s compute the period...

$T$ is the time it takes for $v$ to go from $v(0) = v_0 = 0$ to $v(T) = 1$. Then

$$v(T) = 1 = I + (0 - I)e^{-T}$$

$$\frac{1 - I}{-I} = e^{-T}$$
We have found a periodic solution. Let’s compute the period...

$T$ is the time it takes for $v$ to go from $v(0) = v_0 = 0$ to $v(T) = 1$. Then

\[
v(T) = 1 = I + (0 - I)e^{-T}
\]

\[
\frac{1 - I}{-I} = e^{-T}
\]

\[
\ln((I - 1)/I) = -T
\]
We have found a periodic solution. Let's compute the period...

$T$ is the time it takes for $v$ to go from $v(0) = v_0 = 0$ to $v(T) = 1$. Then

$$v(T) = 1 = I + (0 - I)e^{-T}$$

$$\frac{1 - I}{-I} = e^{-T}$$

$$\ln((I - 1)/I) = -T$$

$$\ln(I/(I - 1)) = T$$
We have found a periodic solution. Let’s compute the period...

$T$ is the time it takes for $v$ to go from $v(0) = v_0 = 0$ to $v(T) = 1$. Then

$$v(T) = 1 = I + (0 - I)e^{-T}$$
$$\frac{1 - I}{-I} = e^{-T}$$

$$\ln\left(\frac{(I - 1)}{I}\right) = -T$$
$$\ln\left(\frac{I}{I - 1}\right) = T$$

It can only be computed when $I > 1$, since $I/(I - 1) > 0$. 
We have found a periodic solution. Let’s compute the period... $T$ is the time it takes for $v$ to go from $v(0) = v_0 = 0$ to $v(T) = 1$. Then

$$v(T) = 1 = I + (0 - I)e^{-T}$$

$$\frac{1 - I}{-I} = e^{-T}$$

$$\ln((I - 1)/I) = -T$$

$$\ln(I/(I - 1)) = T$$

It can only be computed when $I > 1$, since $I/(I - 1) > 0$. 

![Graph showing the period as a function of $I$]
We have found a periodic solution. Let’s compute the period…

$T$ is the time it takes for $v$ to go from $v(0) = v_0 = 0$ to $v(T) = 1$. Then

$$
v(T) = 1 = I + (0 - I)e^{-T}$$

$$
\frac{1 - I}{-I} = e^{-T}
$$

$$
\ln((I - 1)/I) = -T
$$

$$
\ln(I/(I - 1)) = T
$$

It can only be computed when $I > 1$, since $I/(I - 1) > 0$. 

![Graphs showing the periodic solution and frequency as a function of $I$.]
Comparison of the model with experimental data

$\text{V (a.u.)}$

Time (a.u.)

$I=0.5$

$I=1.5$

$I=3$
General form of integrate-and-fire models

- Capacitance current $C \frac{dV}{dt}$

- Projection of high-dimensional ionic current onto a current-voltage relation $F(V)$

- Low or high threshold $V_{th}$ and with reset to $V_{re}$.

\[
C \frac{dV}{dt} + I_{ion}(V, m, h, n, t) = 0
\]
\[
C \frac{dV}{dt} + \langle I_{ion}(V) \rangle = 0
\]
\[
\frac{dV}{dt} = F(V) \quad F(V) = -\frac{\langle I_{ion} \rangle}{C}
\]
Leaky-IF model

\[ F(V) = \frac{E_L - V}{\tau} \]

Quadratic-IF model

\[ F(V) = \frac{(E_L - V)(V_T - V)}{\tau(V_T - E_L)} \]

Exponential-IF model

\[ F(V) = \frac{E_L - V + \Delta_T e^{(V - V_T)/\Delta_T}}{\tau} \]
Leaky IF neuron

- Lapicque (1907) - ohmic form for the ionic current.
- Low threshold at spike initiation $V_{th}$ and reset to $V_{re}$.

\[
\frac{dV}{dt} = F(V) \quad F(V) = \frac{E_L - V}{\tau}
\]

\[
\tau \frac{dV}{dt} = E_L - V + RI_{app}
\]
Leaky-IF model

\[ F(V) = \frac{E_L - V}{\tau} \]

Quadratic-IF model

\[ F(V) = \frac{(E_L - V)(V_T - V)}{\tau(V_T - E_L)} \]

Exponential-IF model

\[ F(V) = \frac{E_L - V + \Delta_T e^{(V-V_T)/\Delta_T}}{\tau} \]
Quadratic IF neuron


- Explicit spike above onset $V_T$

- Threshold at high value $V_{th} >> V_T$ and reset to $V_{re}$

\[
\tau \frac{dV}{dt} = \frac{(E_L - V)(V_T - V)}{(V_T - E_L)}
\]

\[
F(V) = \frac{(E_L - V)(V_T - V)}{\tau (V_T - E_L)}
\]

\[
\text{Voltage (mV)}
\]

\[
(V_{th}, V_T, E_L, V_{re})
\]

\[
\text{F(V)}
\]
Quadratic Integrate-and-fire model QIF

\[ C \frac{dV}{dt} = g_L \frac{(V - E_L)(V - V_T)}{V_T - E_L} + I \]

Introduce the dimensionless voltage

\[ v(t) = \left[ V(t) - (E_L + V_T)/2 \right]/\left[ V_T - E_L \right] \]

and replace \( t \) by \( \tau = t/\tau_v \)

where \( \tau_v = C/g_L \), then the QIF model becomes:

\[ \frac{dv}{d\tau} = v^2 + b \quad \text{with firing/reset: } v(\tau_f) = v_{\text{peak}}, \text{ then } v(\tau_f^+) = v_{\text{reset}}. \]

Here, \( b = I/(g_L(V_T - E_L)) - 1/4 \) and

\[ v_{\text{peak}} = \left[ V_{\text{th}} - (E_L + V_T)/2 \right]/\left[ V_T - E_L \right] \]

and

\[ v_{\text{reset}} = \left[ V_{\text{reset}} - (E_L + V_T)/2 \right]/\left[ V_T - E_L \right]. \]
Quadratic Integrate-and-fire model QIF

\[ V' \]
\[ V_{\text{reset}} \quad V_{\text{peak}} \]

\[ v(t) \]
\[ t \]

Fixed Points
- \( V_{\text{reset}} \)
- \( V_{\text{peak}} \)

Trajectories:
1. \( \text{Trajectory 1} \)
2. \( \text{Trajectory 2} \)
3. \( \text{Trajectory 3} \)
Quadratic Integrate-and-fire model QIF
Quadratic Integrate-and-fire model QIF
The theta neuron model

- Consider the change $v = \tan(\theta/2)$, $\theta \in [-\pi, \pi]$.

\[ \dot{\theta} = 1 - \cos \theta + (1 + \cos \theta) b \, \text{ (mod2}\pi) \]

- Convention: When $\theta = \pi$, the neuron produces an action potential.

- Normal form for the saddle-node on a limit cycle bifurcation (SNIC).

\[
T_{\text{per}} = \frac{1}{\sqrt{b}} \arctan \left( \frac{x}{\sqrt{b}} \right) \bigg|_{x(0)}^{x(T)} = \frac{\pi}{\sqrt{b}} \quad f = 1/T = \sqrt{b}/\pi
\]
Leaky-IF model

\[ F(V) = \frac{E_L - V}{\tau} \]

Quadratic-IF model

\[ F(V) = \frac{(E_L - V)(V_T - V)}{\tau(V_T - E_L)} \]

Exponential-IF model

\[ F(V) = \frac{E_L - V + \Delta_T e^{(V - V_T)/\Delta_T}}{\tau} \]
Exponential IF model

• Developed by fitting a non-linear IF model to the Wang-Buszaki H-H type model

• Comprises an ohmic subthreshold and fast spike

\[
\tau \frac{dV}{dt} = E_L - V + \Delta_T e^{(V - V_T) / \Delta_T}
\]

\[F(V) = \frac{E_L - V + \Delta_T e^{(V - V_T) / \Delta_T}}{\tau}\]
EIF model
Comparison IF models

Linear Integrate and Fire

Quadratic Integrate and Fire

Exponential Integrate and Fire
A zoo of firing behaviors; bursting
A zoo of firing behaviors

- Large diversity of electrophysiological behaviors of single neurons (not present in the original HH):
  - Firing rate adaptation
  - Bursting
  - Delayed firing
  - Stuttering
  - Irregular firing
- What are the mechanisms of each behavior?
Bursting

Brief bursts of oscillatory activity interspersed with quiescent periods
Bursting

Brief bursts of oscillatory activity interspersed with quiescent periods

Figure 9.5: Basic characteristics of bursting dynamics.
Bursting dynamics

The first bursting models are related to the physiological function of pancreatic beta-cells (Rinzel 1985, 1987).

- **Fast dynamics** (Spike generator, like ML or HH)
- **Slow dynamics** (for example, Ca activated K current that activates at a slower rate than the others)
\[ \begin{align*}
C \dot{V} &= -g_{Na} m_{\infty}(V)(V - E_{Na}) - g_K n(V - E_K) - g_L(V - E_L) + I \\
&\quad - g_w w(V - E_K) \\
\tau_n \dot{n} &= n_{\infty}(V) - n \\
\tau_w \dot{w} &= w_{\infty}(V) - w \quad \tau_w \gg \tau_n
\end{align*} \]
Vector $X$ denotes the fast variables associated to spike generation and vector $Y$ denotes the slow variables:

\[
\begin{align*}
\dot{X} &= F(X, Y) \quad (1) \\
\dot{Y} &= \varepsilon G(X, Y) \quad (2)
\end{align*}
\]

Analysis in two steps:

- **Step 1.** *Description of the fast subsystem.* We consider the slow variables $Y$ as parameters and describe the spike-generating fast subsystem (1) for $X$ as a function of the now “parameter” $Y$.

- **Step 2.** *Overlay with the slow dynamics.* We overlay the slow dynamics (2) on the fast subsystem (1) behavior.
Square-wave bursting

BIFURCATION DIAGRAM

- Fixed Points
- Limit Cycle (min & max values)

V

HB

HC

max Vosc

min Vosc

SN

Vss

w > 0

w < 0

w > 0

w < 0

w hb

w hc

w hb

w hc
Square-wave bursting
Square-Wave Bursting

http://www.scholarpedia.org/article/Bursting
Effects of resetting and noise
Effects of resetting and noise

A

Model

stim

stim

interval before episode

stim

B

episode duration

25 50 75 100 125 150 175

interval before episode

200 400 600 800 1000

C

Experiment

stim

d

stim

e

stim

f

50 sec

D

episode duration (sec)

10 20 30 40 50

interval before episode (sec)

50 100 150 200 250 300 350

spontaneous

evoked
### Other types of bursting

<table>
<thead>
<tr>
<th></th>
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<th>Saddle homoclinic orbit</th>
<th>Supercritical Andronov-Hopf</th>
<th>Fold limit cycle</th>
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</thead>
<tbody>
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<td>Saddle-node (fold)</td>
<td>fold/circle</td>
<td>fold/homoclinic</td>
<td>fold/Hopf</td>
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<tr>
<td>Saddle-node on invariant circle</td>
<td>circle/circle</td>
<td>circle/homoclinic</td>
<td>circle/Hopf</td>
<td>circle/fold cycle</td>
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<td>Supercritical Andronov-Hopf</td>
<td>Hopf/circle</td>
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<td>subHopf/Hopf</td>
<td>subHopf/fold cycle</td>
</tr>
</tbody>
</table>

- **Square-wave bursting**
- **Elliptic bursting**
- **Parabolic bursting**
Elliptic & parabolic bursting

(a) Elliptic burster (subthreshold oscillations; the amplitude profile of the burst sometimes looks like an ellipse)

(b) Parabolic bursting (freq of spiking first increases and then decreases during the active phase; the frequency profile within a burst looks like a parabola)
Elliptic bursting

(a) Stable Periodic Orbits
Unstable Fixed Points
Stable Fixed Points
Hopf Point

(b) 

\[ V \] vs. \[ Ca \]

(time)
Elliptic bursting
Parabolic bursting

Two slow variables/no hysteresis


