Biological Modeling of Neural Networks

Wulfram Gerstner
EPFL, Lausanne, Switzerland

TA in 2018:
Vasiliki Liakoni
Chiara Gastaldi
Bernd Illing

new Mooc, Inverted classroom

Week 1: A first simple neuron model/neurons and mathematics
Week 2: Hodgkin-Huxley models and biophysical modeling
Week 3: Two-dimensional models and phase plane analysis
Week 4: Two-dimensional models, type I and type II models
Week 5,6: Associative Memory, Hebb rule, Hopfield
Week 7-10: Networks, cognition, learning
Week 11,12: Noise models, noisy neurons and coding
Week 13: Estimating neuron models for coding and decoding: GLM
Week x: Online video: Dendrites/Biophysics
LEARNING OUTCOMES

• Solve linear one-dimensional differential equations
• Analyze two-dimensional models in the phase plane
• Develop a simplified model by separation of time scales
• Analyze connected networks in the mean-field limit
• Formulate stochastic models of biological phenomena
• Formalize biological facts into mathematical models
• Prove stability and convergence
• Apply model concepts in simulations
• Predict outcome of dynamics
• Describe neuronal phenomena

Transversal skills

• Plan and carry out activities in a way which makes optimal use of available time and other resources.
• Collect data.
• Write a scientific or technical report.

Look at samples of past exams

Use a textbook, (Use video lectures) don’t use slides (only)

miniproject
Written Exam (2/3) + miniproject (1/3)

Miniproject consists of three extended computer exercises

Textbook:

Biological Modeling of Neural Networks

Videos (for half the material):

http://neuronaldynamics.epfl.ch/

http://lcn.epfl.ch/~gerstner/NeuronalDynamics-MOOC1.html + new mooc lectures as we go along
Welcome back to EPFL!!
Week 1 – neurons and mathematics: a first simple neuron model

Wulfram Gerstner
EPFL, Lausanne, Switzerland

Reading for week 1: NEURONAL DYNAMICS
- Ch. 1 (without 1.3.6 and 1.4)
- Ch. 5 (without 5.3.1)

Cambridge Univ. Press

1.1 Neurons and Synapses:
  Overview

1.2 The Passive Membrane
  - Linear circuit
  - Dirac delta-function

1.3 Leaky Integrate-and-Fire Model

1.4 Generalized Integrate-and-Fire Model

1.5. Quality of Integrate-and-Fire Models
Biological Modeling of Neural Networks

1.1 Neurons and Synapses: Overview
1.2 The Passive Membrane
   - Linear circuit
   - Dirac delta-function
1.3 Leaky Integrate-and-Fire Model
1.4 Generalized Integrate-and-Fire Model
1.5 Quality of Integrate-and-Fire Models
How do we recognize things?
Models of cognition
Weeks 10-14
Neuronal Dynamics – 1.1. Neurons and Synapses/Overview

10,000 neurons
3 km of wire

motor cortex
frontal cortex
to motor output
Neuronal Dynamics – 1.1. Neurons and Synapses/Overview

- 10,000 neurons
- 3 km of wire

Signal: action potential (spike)

Ramon y Cajal
Hodgkin-Huxley type models: Biophysics, molecules, ions (week 2)

Signal: action potential (spike)
Neuronal Dynamics – 1.1. Neurons and Synapses/Overview

Signal:
action potential (spike)
Integrate-and-fire models: Formal/phenomenological
(week 1 and week 7-9)

- spikes are events
- triggered at threshold
- spike/reset/refractoriness

Spike reception

Spike emission

Postsynaptic potential

Synapse

$u$

$\theta$

$t$
Noise and variability in integrate-and-fire models

Output
- spikes are rare events
- triggered at threshold

Subthreshold regime:
- trajectory of potential shows fluctuations

Spike emission
Random spike arrival

\[ \text{Output} \]

\[ \text{Subthreshold regime:} \]

\[ \vartheta \]

\[ u_i \]
Neuronal Dynamics – membrane potential fluctuations

Spontaneous activity *in vivo*

What is noise?
What is the neural code?

*awake mouse, cortex, freely whisking,*

Lab of Prof. C. Petersen, EPFL  *Crochet et al., 2011*
<table>
<thead>
<tr>
<th>A cortical neuron sends out signals which are called:</th>
</tr>
</thead>
<tbody>
<tr>
<td>[ ] action potentials</td>
</tr>
<tr>
<td>[ ] spikes</td>
</tr>
<tr>
<td>[ ] postsynaptic potential</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>The dendrite is a part of the neuron</th>
</tr>
</thead>
<tbody>
<tr>
<td>[ ] where synapses are located</td>
</tr>
<tr>
<td>[ ] which collects signals from other neurons</td>
</tr>
<tr>
<td>[ ] along which spikes are sent to other neurons</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>In an integrate-and-fire model, when the voltage hits the threshold:</th>
</tr>
</thead>
<tbody>
<tr>
<td>[ ] the neuron fires a spike</td>
</tr>
<tr>
<td>[ ] the neuron can enter a state of refractoriness</td>
</tr>
<tr>
<td>[ ] the voltage is reset</td>
</tr>
<tr>
<td>[ ] the neuron explodes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>In vivo, a typical cortical neuron exhibits</th>
</tr>
</thead>
<tbody>
<tr>
<td>[ ] rare output spikes</td>
</tr>
<tr>
<td>[ ] regular firing activity</td>
</tr>
<tr>
<td>[ ] a fluctuating membrane potential</td>
</tr>
</tbody>
</table>

*Multiple answers possible!*
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Biological modeling of Neural Networks

Course: Monday : 9:15-13:00

A typical Monday:
1st lecture 9:15-9:50
1st exercise 9:50-10:00
2nd lecture 10:15-10:35
2nd exercise 10:35-11:00
3rd lecture 11:15 – 11:40
3rd exercise 11:45-12:40

Course of 4 credits = 6 hours of work per week
4 ‘contact’ + 2 homework

http://lcn.epfl.ch/~gerstner/   moodle.epfl.ch
Biological Modeling of Neural Networks

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1.5. Quality of Integrate-and-Fire Models
Neuronal Dynamics – 1.2. The passive membrane

Integrate-and-fire model

Spike emission

electrode

synapse

potential

Integrate-and-fire model
Neuronal Dynamics – 1.2. The passive membrane

Spike reception

Subthreshold regime
- linear
- passive membrane
- RC circuit
Math development: Derive equation (Blackboard)
Passive Membrane Model

\[ I(t) \]

\[ u \]
Passive Membrane Model

Math Development: Voltage rescaling (blackboard)

\[
\tau \cdot \frac{d}{dt} u = -(u - u_{rest}) + RI(t)
\]

\[
\tau \cdot \frac{d}{dt} V = -V + RI(t); \quad V = (u - u_{rest})
\]
Passive Membrane Model

\[ \tau \cdot \frac{d}{dt} u = -(u - u_{\text{rest}}) + RI(t) \]

\[ \tau \cdot \frac{d}{dt} V = -V + RI(t); \quad V = (u - u_{\text{rest}}) \]
Passive Membrane Model/Linear differential equation

\[ \tau \cdot \frac{d}{dt} V = -V + RI(t); \]

Free solution: exponential decay
Neuronal Dynamics – Exercises NOW

\[ \tau \cdot \frac{d}{dt} u = -(u - u_{\text{rest}}) + RI(t) \]

\[ \tau \cdot \frac{d}{dt} V = -V + RI(t); \quad V = (u - u_{\text{rest}}) \]

Start Exerc. at 9:47. Next lecture at 10:15

Step current input:

Pulse current input:

arbitrary current input:

Calculate the voltage, for the 3 input currents
Passive Membrane Model – exercise 1 now

Step current input:

\[ i(t) \]

\[ u_i \]

Linear equation

\[ \tau \cdot \frac{d}{dt} u = -(u - u_{rest}) + RI(t) \]

impulse reception:

impulse response function

Start Exerc. at 9:47.
Next lecture at 10:15

TA’s:
Marco Lehmann
\[ \tau \cdot \frac{d}{dt} u = -(u - u_{\text{rest}}) + RI(t) \]
Pulse input – charge – delta-function

\[ I(t) = q \cdot \delta(t - t_0) \]

\[ \tau \frac{du}{dt} = -(u - u_{\text{rest}}) + RI(t) \]

\[ u(t) \]

\[ I(t) \]

Pulse current input
Dirac delta-function

\[ I(t) = q \cdot \delta(t - t_0) \]

\[ 1 = \int_{t_0-a}^{t_0+a} \delta(t - t_0) \, dt \]

\[ f(t_0) = \int_{t_0-a}^{t_0+a} f(t) \delta(t - t_0) \, dt \]
Neuronal Dynamics – Solution of Ex. 1 – arbitrary input

\[ \tau \cdot \frac{d}{dt} u = -(u - u_{\text{rest}}) + RI(t) \]

Arbitrary input
\[ u(t) = u_{\text{rest}} + \int_{-\infty}^{t} e^{-\frac{(t-t')}{\tau}} I(t') dt' \]

Single pulse
\[ \Delta u(t) = \frac{q}{c} e^{-\frac{(t-t_0)}{\tau}} \]

you need to know the solutions of linear differential equations!
Passive membrane, linear differential equation

\[ \tau \cdot \frac{d}{dt} u = - (u - u_{\text{rest}}) + RI(t) \]
Passive membrane, linear differential equation

If you have difficulties, watch lecture 1.2detour.

Three prerequisites:
- Analysis 1-3
- Probability/Statistics
- Differential Equations or Physics 1-3 or Electrical Circuits
**LEARNING OUTCOMES**

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**miniproject**
Biological Modeling of Neural Networks

Written Exam (2/3) + miniproject (1/3)

Miniproject consists of three extended computer exercises

Textbook:

Videos (for half the material):

http://lcn.epfl.ch/~gerstner/NeuronalDynamics-MOOC1.html + new mooc lectures as we go along
Biological Modeling of Neural Networks

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Questions?

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Biological Modeling of Neural Networks

Week 1 – neurons and mathematics: a first simple neuron model

Wulfram Gerstner
EPFL, Lausanne, Switzerland

Week 1 – part 3: Leaky Integrate-and-Fire Model

1.1 Neurons and Synapses: Overview

1.2 The Passive Membrane
- Linear circuit
- Dirac delta-function
- Detour: solution of 1-dim linear differential equation

1.3 Leaky Integrate-and-Fire Model

1.4 Generalized Integrate-and-Fire Model

1.5 Quality of Integrate-and-Fire Models
Neuronal Dynamics – 1.3 Leaky Integrate-and-Fire Model

\[ \tau \cdot \frac{d}{dt} u = -(u - u_{\text{rest}}) + RI(t) \]
Neuronal Dynamics – Integrate-and-Fire type Models

Simple Integrate-and-Fire Model:
- passive membrane
- + threshold

Leaky Integrate-and-Fire Model:
- output spikes are events
- generated at threshold
- after spike: reset/refractoriness

Input spike causes an EPSP
= excitatory postsynaptic potential

Spike emission

ϑ

Input

u

Output

\( \vartheta \)

\( u \)

\( \vartheta \)

\( u \)

Output
Neuronal Dynamics – 1.3 Leaky Integrate-and-Fire Model

\[ \tau \cdot \frac{d}{dt} u = -(u - u_{\text{rest}}) + RI(t) \]

\[ u(t) = \mathcal{G} \Rightarrow \text{Fire+reset} \quad u \rightarrow u_r \]

linear

threshold
Neuronal Dynamics – 1.3 Leaky Integrate-and-Fire Model

Math development: Response to step current

- spikes are events
- triggered at threshold
- spike/reset/refractoriness

Time-dependent input

\[ u \]

\[ I(t) \]
Consider the linear differential equation 
\[ \tau \cdot \frac{d}{dt} x = -x + x_c \]
with initial condition 
\[ at \ t = 0 : x = 0 \]
The solution for \( t > 0 \) is

(i) \[ x(t) = x_c \exp(t / \tau) \]
(ii) \[ x(t) = x_c \exp(-t / \tau) \]
(iii) \[ x(t) = x_c[1 - \exp(-t / \tau)] \]
(iv) \[ x(t) = 0.5x_c[1 + \exp(-t / \tau)] \]

You will have to use the constant input/step input again and again
Neuronal Dynamics – 1.3 Leaky Integrate-and-Fire Model

CONSTANT input/step input
Leaky Integrate-and-Fire Model (LIF)

\[ \tau \frac{du}{dt} = -(u - u_{\text{rest}}) + RI_0 \]

If \( u(t) = \mathcal{I} \Rightarrow u \to u_r \)

Repetitive, current \( I_0 \)

Repetitive, current \( I_1 > I_0 \)

'Firing'

frequency-current relation

f-I curve
Neuronal Dynamics – First week, Exercise 2

\[ \tau \cdot \frac{d}{dt} u = - (u - u_{\text{rest}}) + RI(t) \]
EXERCISE 2 NOW: Leaky Integrate-and-fire Model (LIF)

**LIF** \[ \tau \cdot \frac{d}{dt} u = -(u - u_{rest}) + RI_0 \]

If firing: \[ u \rightarrow u_r. \]

**Exercise!**
Calculate the interspike interval $T$ for constant input $I$.
Firing rate is $f=1/T$.
Write $f$ as a function of $I$.
What is the frequency-current curve $f=g(I)$ of the LIF?

**Start Exerc. at 10:53.**
Next lecture at 11:15.
Biological Modeling of Neural Networks

Week 1 – neurons and mathematics: a first simple neuron model

Wulfram Gerstner
EPFL, Lausanne, Switzerland

1.1 Neurons and Synapses:
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1.2 The Passive Membrane
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   - Dirac delta-function

1.3 Leaky Integrate-and-Fire Model

1.4 Generalized Integrate-and-Fire Model

1.5 Quality of Integrate-and-Fire Models
Integrate-and-fire model

LIF: linear + threshold
Neuronal Dynamics – 1.4. Leaky Integrate-and-Fire revisited

LIF

\[ \tau \cdot \frac{du}{dt} = -(u - u_{\text{rest}}) + RI(t) \]

If firing:
\[ u \rightarrow u_r \]

If resting:
\[ u \rightarrow \text{rest} \]

If repetitive firing:
\[ u \rightarrow \text{repetitive} \]
LIF
\[ \tau \cdot \frac{d}{dt} u = -(u - u_{\text{rest}}) + RI(t) \]

NLIF
\[ \tau \cdot \frac{d}{dt} u = F(u) + RI(t) \]

If firing:
\[ u \rightarrow u_{\text{reset}} \]
Nonlinear Integrate-and-Fire (NLIF)

\[ \tau \cdot \frac{d}{dt} u = F(u) + RI(t) \]

firing: \( u(t) = \theta \Rightarrow u \to u_r \)
Nonlinear Integrate-and-fire Model

\[ \tau \frac{d}{dt} u = F(u) + RI(t) \]

\[ u(t) = \mathcal{G}_r \Rightarrow \text{Fire+reset} \]

NONlinear threshold

Spike emission

reset
Nonlinear Integrate-and-fire Model

\[ \tau \cdot \frac{d}{dt} u = F(u) + RI(t) \]

**NONlinear**

\[ u(t) = \vartheta_r \Rightarrow \text{Fire+reset threshold} \]

**Quadratic I&F:**

\[ F(u) = c_2(u - c_1)^2 + c_0 \]
Nonlinear Integrate-and-fire Model

\[ \tau \cdot \frac{d}{dt} u = F(u) + RI(t) \]

\[ u(t) = \theta_r \Rightarrow \text{Fire+reset} \]

**Quadratic I\&F:**
\[ F(u) = c_2(u - c_1)^2 + c_0 \]

**Exponential I\&F:**
\[ F(u) = -(u - u_{\text{rest}}) + c_0 \exp(u - \theta) \]
Nonlinear Integrate-and-fire Model

\[ \tau \cdot \frac{d}{dt} u = -(u-u_{rest}) + RI(t) \]

\[ u(t) = \mathcal{G}_r \Rightarrow \text{Fire+reset threshold} \]

exponential I&F:
\[ F(u) = - (u - u_{rest}) + c_0 \exp(u - \mathcal{G}) \]
Nonlinear Integrate-and-fire Model
Where is the firing threshold?

\[ \tau \frac{d}{dt} u = F(u) + RI(t) \]
Biological Modeling of Neural Networks

Week 1 – neurons and mathematics: a first simple neuron model

Wulfram Gerstner
EPFL, Lausanne, Switzerland

Week 1 – part 5: How good are Integrate-and-Fire Model?

1.1 Neurons and Synapses:
   - Overview

1.2 The Passive Membrane
   - Linear circuit
   - Dirac delta-function

1.3 Leaky Integrate-and-Fire Model

1.4 Generalized Integrate-and-Fire Model
   - where is the firing threshold?

1.5. Quality of Integrate-and-Fire Models
   - Neuron models and experiments
Can we compare neuron models with experimental data?

\[ \tau \cdot \frac{d}{dt} u = F(u) + RI(t) \]

if \( u = \theta_r \) then \( u \rightarrow u_r \)
Neuronal Dynamics – 1.5. How good are integrate-and-fire models?

What is a good neuron model?

Can we compare neuron models with experimental data?
Neuronal Dynamics – 1.5. How good are integrate-and-fire models?
Nonlinear Integrate-and-fire Model

\[ \frac{d}{dt} u = F(u) + RI(t) \]

\[ u(t) = \mathcal{G}_r \Rightarrow \text{Fire+reset} \]

Can we measure the function \( F(u) \)?

**Quadratic I&F:**

\[ F(u) = c_2 (u - c_1)^2 + c_0 \]

**Exponential I&F:**

\[ F(u) = -(u - u_{\text{rest}}) + c_0 \exp(u - \mathcal{G}) \]
Neuronal Dynamics – 1.5. How good are integrate-and-fire models?

\[ \frac{du}{dt} - \frac{1}{C} I(t) = F(u) \frac{1}{\tau} \]

\[ F(u) = -(u - u_{\text{rest}}) + \Delta \exp\left(\frac{u - \vartheta}{\Delta}\right) \]

Badel et al., J. Neurophysiology 2008
Neuronal Dynamics – 1.5. How good are integrate-and-fire models?
Nonlinear integrate-and-fire models are good

Mathematical description $\rightarrow$ prediction

Need to add
- adaptation
- noise
- dendrites/synapses

Computer exercises: Python
Biological Modeling of Neural Networks

http://neuronaldynamics.epfl.ch/

Textbook:

Lecture today:
- Chapter 1
- Chapter 5

Exercises today:
- Install PYTHON for Computer Exercises
- Exercise 3, on sheet

Videos (for today: ‘week 1’):
http://lcn.epfl.ch/~gerstner/NeuronalDynamics-MOOC1.html
\[ \tau \cdot \frac{du}{dt} = F(u) + RI(t) \]
First week – **References and Suggested Reading**


**Selected references to linear and nonlinear integrate-and-fire models**

First week

THE END (of main lecture)

MATH DETOUR SLIDES
(for online VIDEO)
Neuronal Dynamics: Computational Neuroscience of Single Neurons

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EPFL, Lausanne, Switzerland

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Neuronal Dynamics – 1.2 Detour – Linear Differential Eq.

\[ \tau \cdot \frac{d}{dt} u = -(u - u_{rest}) + RI(t) \]
Neuronal Dynamics – 1.2 Detour – Linear Differential Eq.

\[ \tau \frac{du}{dt} = -(u - u_{rest}) + RI(t) \]

Math development: Response to step current

![Diagram of a neuron model showing an input current I(t) over time t with potential u.](image)
Neuronal Dynamics – 1.2 Detour – Step current input

\[ \tau \cdot \frac{du}{dt} = -(u - u_{rest}) + RI(t) \]

\[ u(t) \]

\[ I(t) \]

\[ t \]
Neuronal Dynamics – 1.2 Detour – Short pulse input

\[ u(t) = u_{rest} + RI_0 \left[ 1 - e^{-(t-t_0)/\tau} \right] \]

short pulse: \( (t - t_0) \ll \tau \)

\[ \tau \cdot \frac{d}{dt} u = -(u - u_{rest}) + RI(t) \]

Math development: Response to short current pulse
Neuronal Dynamics – 1.2 Detour – Short pulse input

\[ u(t) = u_{rest} + RI_0 \left[ 1 - e^{-\frac{(t-t_0)}{\tau}} \right] \]

short pulse: \( (t-t_0) \ll \tau \)

\[ \tau \frac{d}{dt} u = -(u - u_{rest}) + RI(t) \]

\[ u(t) = u_{rest} + \frac{q}{C} e^{-\frac{(t-t_0)}{\tau}} \]
Neuronal Dynamics – 1.2 Detour – arbitrary input

Single pulse
\[ u(t) = u_{\text{rest}} + \frac{q}{C} e^{-(t-t_0)/\tau} \]

Multiple pulses:
\[ u(t) = u_{\text{rest}} + \int_{-\infty}^{t} \frac{1}{C} e^{-(t-t')/\tau} I(t') dt' \]

\[ \tau \cdot \frac{du}{dt} = -(u - u_{\text{rest}}) + RI(t) \]
Neuronal Dynamics – 1.2 Detour – Greens function

Single pulse
\[ \Delta u(t) = q \frac{1}{C} e^{-(t-t_0)/\tau} \]

Multiple pulses:
\[ u(t) = u_{rest} + [u(t_0) - u_{rest}] + \int_{t_0}^{t} \frac{1}{C} e^{-(t-t')/\tau} I(t') dt' \]

Impulse response function, Green’s function

\[ u(t) = u_{rest} + \int_{-\infty}^{t} \frac{1}{C} e^{-(t-t')/\tau} I(t') dt' \]
If you don’t feel at ease yet, spend **10 minutes** on these mathematical exercise
And quiz 2 in week 1.

\[ \tau \cdot \frac{d}{dt} u = -(u - u_{\text{rest}}) + RI(t) \]

**Arbitrary input**

\[ u(t) = u_{\text{rest}} + \int_{-\infty}^{t} \frac{1}{c} e^{-\frac{(t-t')}{\tau}} I(t') dt' \]

**Single pulse**

\[ \Delta u(t) = \frac{q}{c} e^{-\frac{(t-t_0)}{\tau}} \]

you need to know the solutions of linear differential equations!