Neurosciences

Introduction in Neuroscience Lab 1

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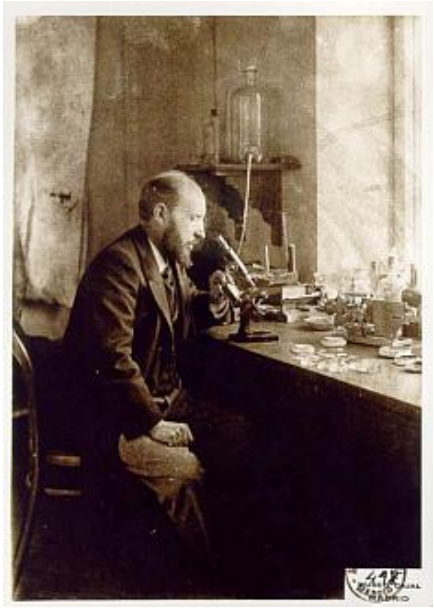
As the father of Neuroscience **Santiago Ramón Cajal** put it:

"As long as our brain is a mystery, the universe - which is a reflection of the structure of the brain - will also be a mystery."



Why is it interesting and important?

From the point of view of basic research:

- Neuroscientist hope to understand how cellular circuits enable us to read and speak, how we bond with other humans, how we learn and retain information, how we experience pain, and how we feel motivation.
- Computer science specialists can also hope to increase the performance of artificial intelligence systems by means of understanding the real neural networks operation.
- The understanding of the biological basis of learning, memory, behavior, perception, and consciousness has been described by Eric Kandel as the "ultimate challenge" of the modern sciences.

Why is it interesting and important?

From the point of view of medicine:

- Neuroscientists hope to find causes for devastating disorders of the brain and body, as well as ways to prevent or cure them:
  - Understanding the best strategies for recovery from brain injury, including stroke
  - Prediction of the development of various diseases, as well as their treatment or suppression of abnormal brain activity, for example, various types of epilepsy
  - The problem of brain aging and the possibility of treating such terrible diseases as dementia, Parkinson's and Alzheimer's diseases

Why is it interesting and important?

From the point of view of neurotechnology:

- controlling the movement of robots and exoskeletons
- revealing and controlling some brain pathologies
- assessing and controlling the person's psychophysiological state
- monitoring human cognitive activity

Project and Rating

Overall Assessment Rating

Points earned	Rating	Grade Point
≥ 81	Excellent	A
≥ 66	Good	B
≥ 51	Mediocre	C

- **Project I** Numerical simulation of a model neuron
- **Project II** Methods for analysis of EEG data

Performance assessment: Neuroscience

	Points	Remarks (tentative time)
1^{st} Test: Fundamentals of Neuroscience, Neurons, and Computational Neuroscience	10	Held at the 5^{th} lecture
2^{nd} Test: Structure and functions of Brain, Functional brain Networks, and Neuroimaging	10	Held at the 8^{th} lecture
3^{rd} Test: Methods of connectivity detection, cognitive abilities	10	Held at the 11^{th} lecture
4^{th} Test: Previous materials, and Brain-Computer Interfaces	20	Held at the last lecture
1^{st} Project: Computational Neuroscience	25	5 points per task
2^{nd} Project: Neuroscience bigdata processing and analysis	25	5 points per task
Additional exam	20	Optional paper test

Point Breakdown

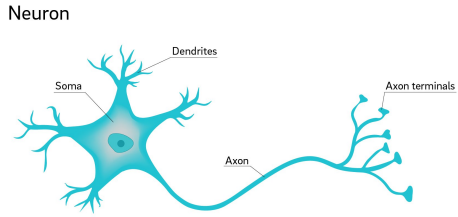
Solving Time	Point
Final Report	3
In Class solving without help (End of the class)	2 or
In Class solving with help (End of the class)	1.75 or
In week solving (Before Monday)	1.5
Total	5

Project I Breakdown

- Description of a neuron, numerical simulation of a model neuron: solving the system of differential equations using the Runge Kutta 4th order method, analyzing the correctness of choosing the time step.
- Analyzing different regimes of a neuron dynamics, plotting time series and phase portraits of the signal, calculation of a regime map.
- Adding Gaussian noise to the system, solving the system of differential equations with noise, analyzing the influence of noise amplitude on the system dynamics.
- Adding the coupling between 2 neurons, analyzing synchronization between neurons for different values of the coupling strength.
- Simulation of a neural network with global topology, analyzing the influence of external stimulus and noise amplitude by calculating characteristic correlation time.

Neurons

Neurons are responsible for carrying information throughout the human body. Using electrical and chemical signals, they help coordinate all of the necessary functions of life. In this article, we explain what neurons are and how they work.



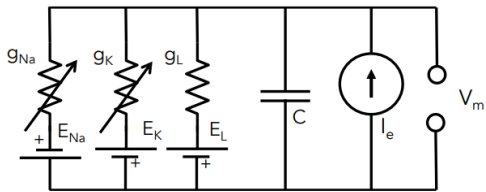
- Soma (cell body) — this portion of the neuron receives information. It contains the cell's nucleus.
- Dendrites — these thin filaments carry information from other neurons to the soma. They are the "input" part of the cell.
- Axon — this long projection carries information from the soma and sends it off to other cells. This is the "output" part of the cell. It normally ends with a number of synapses connecting to the dendrites of other neurons.

What is neural computation?

- Brain and cognitive sciences are no longer primarily descriptive
  - Engineering-level descriptions of brain systems.
- Use mathematical techniques to analyze neural data in a way that allows us to relate it to mathematical models.
- we will apply some of these techniques to understand the circuits and computational principles that underlie behavior.
- Computational and quantitative approaches are also important in cognitive science.
- Importance of computation and quantitation in medical sciences

A mathematical model of a neuron

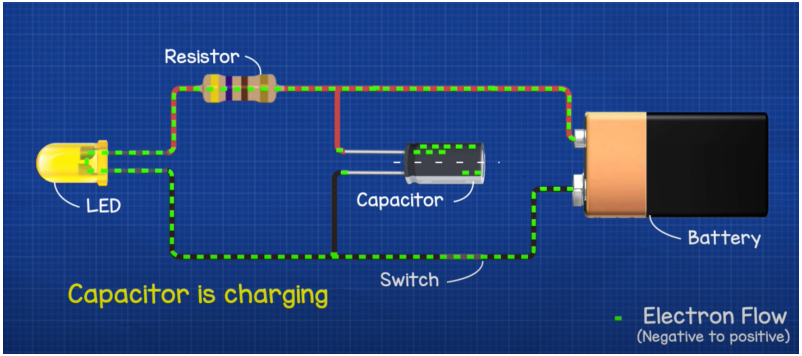
- Equivalent circuit model



- Different parts of this circuit do different interesting things
  - Power supplies
  - Integrator of past inputs
  - Temporal filter to smooth inputs in time
  - Spike generator
  - Oscillator

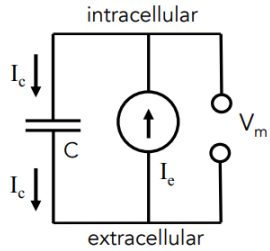
Basic knowledge

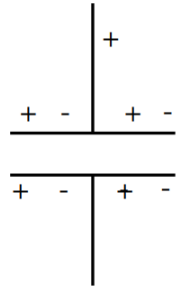
Neurons can perform analog numerical integration over time
Voltage$(t) = \int_0^t$ Current$(t)dt$



Why is this a capacitor? [A capacitor is two conductors separated by an insulator]

A neuron is a capacitor





Charge imbalance: ΔQ

Voltage difference: ΔV

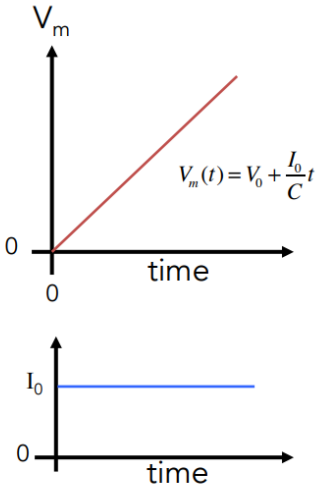
As positive charges build up on the inside of the membrane, they repel positive charges away from the outside of the membrane…

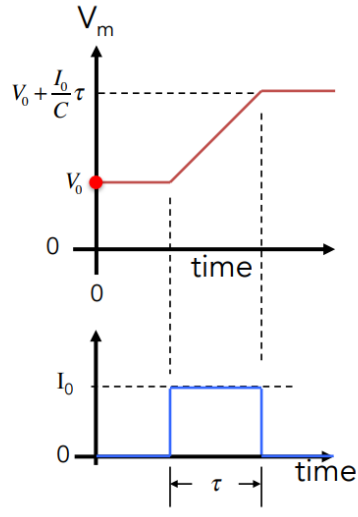
This looks like a current flowing through the capacitor!

$$\Delta Q = C \cdot \Delta V$$

Q: charge (Coulombs, C = 6 x 10^{18} charges)
C: capacitance (Farads, F)
V: voltage difference across capacitor (Volts, V)

Some examples





What is a Spike?

- There can be a potential difference across the membrane, just like a battery.
- During a spike, or action potential as it is called by neuroscientists, a neuron's membrane potential quickly rises from values around -65 mV to about 20 mV and then drops back to -65 mV.
- Small holes in the membrane called channels let sodium and potassium ions pass through the membrane, changing the potential difference across the membrane over the time course of the spike.

Neuron models

- Hodgkin-Huxley model
- FitzHugh-Nagumo model
- Hindmarsh–Rose model
- Morris–Lecar model
- Izhikevich Neuron model
- Leaky integrate-and-fire model

Leaky integrate-and-fire model

- Most spiking nerual network use some kind of differential equation model
- Describe how variable in the model change in time
- Then simulate the network Spikes are quick enough that consider then as discrete events

$C_m \frac{dv}{dt} = I_{leak} + I_{spikes} + I_{Current}$
$I_{leak(t)} = -\frac{C_m}{\tau_m}(v(t) - V_0)$

C_m is the capacitance
I_{leak} is leak current, which pulls the $v(t)$ to the resitting potential
I_{spikes} is the current causes by receiving a spike; we can think of this as being nearly instant (Being a value A when we receive a spike ans 0 otherwise)
$I_{current}$ is an injected or driving current; we might omit it or it might be constant

Leaky integrate-and-fire mode II

Let's do some substitution, and drop the spiking and injected currents :

$$\frac{dv}{dt} = -\frac{1}{\tau}(v(t) - V_0)$$

where τ is a time-constant and V_0 is the resting or equilibrium potential

Morris–Lecar model

Sodium : Na^+ voltace increade Potassium : K^+ voltace discrice
$C_m \frac{dV}{dt} = I_{ion}(V, w) + I_{stim}$
$\frac{dw}{dt} = (w_\infty(V) - w)/\tau(V)$
$I_{ion}(V, w) = gc_a * m_\infty(V) * (V - V_{Ca}) + gk * w * (V - V_k) + gL * (V - V_L)$ I_stim is an external stimulating current, and the constituent functions
$m_\infty(V) = .5[1 + tranh\frac{V - V_1}{v_2}]$
$w_\infty(V) = .5[1 + tranh\frac{V - V_3}{V_4}]$
$\tau(V) = \frac{\tau_{max}}{cosh\frac{V - V_3}{2V_4}}$

Hindmarsh–Rose model I

The Hindmarsh–Rose model has the mathematical form of a system of three nonlinear ordinary differential equations on the dimensionless dynamical variables x(t), y(t), and z(t). They read:

$$\begin{aligned}\frac{dx}{dt} &= y + \phi(x) - z + I \\ \frac{dy}{dt} &= \psi(x) - y \\ \frac{dz}{dt} &= r\left[s\left(x - x_R\right) - z\right]\end{aligned}$$

where

$$\begin{aligned}\phi(x) &= -ax^3 + bx^2 \\ \psi(x) &= c - dx^2\end{aligned}$$

Hindmarsh–Rose model II

The model has eight parameters: a, b, c, d, r, s, x_R and I. It is common to fix some of them and let the others be control parameters. Usually the parameter I, which means the current that enters the neuron, is taken as a control parameter. Other time control parameters used often in the literature are a, b, c, d, or r, the first four modeling the working of the fast ion channels Simulation of Hindmarsh-Rose neuron showing typical neuronal and the last one the slow ion channels, respectively. Frequently, the parameters held fixed are $s = 4$ and $x_R = -8/5$. When a, b, c, d are fixed the values given are $a = 1, b = 3, c = 1$, and $d = 5$. The parameter r governs the time scale of the neural adaptation and is something of the order of 10^{-3}, and / ranges between -10 and 10 . The third state equation: $\frac{dz}{dt} = r\left[s\left(x - x_R\right) - z\right]$ allows a great variety of dynamic behaviors of the membrane potential, described by variable x, including unpredictable behavior, which is referred to as chaotic dynamics. This makes the Hindmarsh-Rose model relatively simple and provides a good qualitative description of the many different patterns that are observed empirically.

FitzHugh-Nagumo model

The dynamical FitzHugh-Nagumo equations modified to account for the global coupling are as follows:

$$\epsilon \dot{x}_i = x_i - \frac{1}{3} x_i^3 - y_i + \frac{K}{N} \sum_{j=1}^{N} (x_j - x_i)$$

$$\dot{y}_i = x_i + a + D\xi_i(t)$$

where independent noises of intensity D have been added to the slow variables y_i. The $\xi_i(t)$ are white noises with Gaussian distribution of zero mean and correlations $\langle \xi_i(t) \xi_j(t') \rangle = \delta_{ij} \delta(t - t')$.

Hodgkin Huxley Models

- In mathematical terms, the membrane potential V_M is defined as $V_M = V_{in} - V_{out}$; where V_in is the potential on the inside of the cell and V_out is the potential on the outside

$$C_m \frac{dv}{dt} = -\bar{g}_{\mathrm{K}} n^4 (v - v_{\mathrm{K}}) - \bar{g}_{\mathrm{Na}} m^3 h (v - v_{\mathrm{Na}}) - \bar{g}_{\mathrm{L}} (v - v_{\mathrm{L}}) + I_{\mathrm{app}}$$

$$\frac{dm}{dt} = \alpha_m(1-m) - \beta_m m, \alpha_m = 0.1\frac{25-v}{\exp\left(\frac{25-v}{10}\right)-1}, \quad \beta_h = \frac{1}{\exp\left(\frac{30-v}{10}\right)+1}$$

$$\frac{dn}{dt} = \alpha_n(1-n) - \beta_n n, \quad \beta_m = 4\exp\left(\frac{-v}{18}\right), \quad \alpha_n \quad \alpha_{n_i},$$

$$\frac{dh}{dt} = \alpha_h(1-h) - \beta_h h. \quad \alpha_h = 0.07\exp\left(\frac{-v}{20}\right), \quad \beta_n = 0.125\exp\left(\frac{-v}{80}\right)$$

$$\frac{dx_i}{dt} = \alpha_{x_i}(V_i)(1-x_i) - \beta_{x_i}(V_i)x_i + \xi_{x_i}(t), \quad x = m, n, h$$

$$\langle \xi_{m_i}(t)\xi_{m_i}(t')\rangle = \frac{2\alpha_{m_i}\beta_{m_i}}{N_{Na}\left(\alpha_{m_i}+\beta_{m_i}\right)}\delta(t-t')$$

$$\langle \xi_{h_i}(t)\xi_{h_i}(t')\rangle = \frac{2\alpha_{h_i}\beta_{h_i}}{N_{Na}\left(\alpha_{h_i}+\beta_{h_i}\right)}\delta(t-t')$$

$$\langle \xi_{n_i}(t)\xi_{n_i}(t')\rangle = \frac{2\alpha_{n_i}\beta_{n_i}}{N_{K}\left(\alpha_{n_i}+\beta_{n_i}\right)}\delta(t-t')$$

HH model to help coding

$$I = C_m \frac{dV}{dt} + \bar{g}_K n^4 (V - V_K) + \bar{g}_{Na} m^3 h (V - V_{Na}) + \bar{g}_l (V - V_l)\}$$

$$\frac{dn}{dt} = \alpha_n(1 - n) - \beta_n n$$

$$\frac{dm}{dt} = \alpha_m(1 - m) - \beta_m m$$

$$\frac{dh}{dt} = \alpha_h(1 - h) - \beta_h h$$

Secondary Equations:
Ion Channel Behavior -
Probability of Open or Closed

Gate States.

$$\alpha_n = \frac{0.01(V+10)}{e^{\left(\frac{V+10}{10}\right)}-1}$$

$$\beta_n = 0.125e^{\left(\frac{V}{80}\right)}$$

$$\alpha_m = \frac{0.1(V+25)}{e^{\left(\frac{V+25}{10}\right)}-1}$$

$$\beta_m = 4e^{\left(\frac{V}{18}\right)}$$

$$\alpha_h = 0.07e^{\left(\frac{V}{20}\right)}$$

$$\beta_h = \frac{1}{e^{\frac{V+30}{10}}+1}$$

Izhikevich Neuron model

Just two variable U is recovery variable

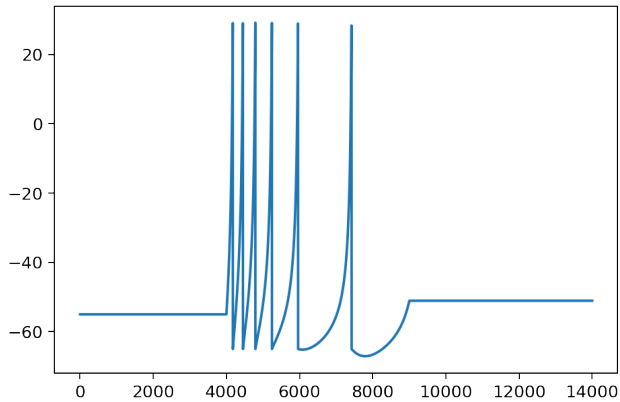
$$\frac{dv}{dt} = .004v^2 + 5v + 140 - u + I$$
$$\frac{du}{dt} = a(bv - u)$$

if V = 30mV : v= c (reset potential); u = U+d
Source : `https://www.izhikevich.org/publications/spikes.pdf`

python code (Izhikevich Neuron mode)

```
import matplotlib.pyplot as plt
t = 0.0
dt = 1.0/200.0
v= -55.0
vth = 30.0
u = 0.0
a = 0.02
b= 0.2
c= -65
d= 8.0
vs = []
spiketimes = []

while t<70.0:
    vs.append(v)
    dv = (0.04*v**2) + (5.0*v) +140.0 -u
    du = a* ((b*v)-u)
    if t>20.0 and t<45.0:
      dv+=50.0
      v +=dv*dt
      u+=du*dt

    if v>=vth:
        spiketimes.append(t) #spike

        v = c # reset
        u = u+d
    t+=dt

fig = plt.figure(dpi = 180)
plt.plot(vs)
plt.show()
```

picture (Izhikevich Neuron mode)



Variation I

Variation 1

Hodgkin-Huxley model

1. Model: https://sci-hub.si/10.1007/978-0-387-75847-3, Pp. 205-206
2. Regime map https://sci-hub.si/10.1007/978-0-387-75847-3, P. 2103
3. Reference to a model with noise: https://journals.plos.org/ploscompbiol/article/file?id=10.1371/journal.pcbi.1005646&type=printable, eq. (4-7)
4. Reference to model with coupling: https://journals.plos.org/ploscompbiol/article/file?id=10.1371/journal.pcbi.1005646&type=printable, eq. (8)
5. Number of neurons $N = 5$, reference to characteristic correlation time: http://www.math.pitt.edu/~cbsg/Materials/PhysRevLett.78.775.pdf, eq. (3-4)

Variation II

Variation 2

FitzHugh-Nagumo model

1. Model: https://ifisc.uib-csic.es/raul/publications/P/P97_tmg03.pdf, eq. (1-2) without the last term
2. Regime map: https://b-ok.cc/book/2104926/560800, fig. 5.1.1a
3. Reference to model with noise: https://ifisc.uib-csic.es/raul/publications/P/P97_tmg03.pdf, eq. (2) - the last term
4. Reference to model with coupling https://ifisc.uib-csic.es/raul/publications/P/P97_tmg03.pdf, eq. (1) - the last term
5. number of neurons N = 25, reference to characteristic correlation time: http://www.math.pitt.edu/~cbsg/Materials/PhysRevLett.78.775.pdf, eq. (3-4)

Variation III

Variation 3

Hindmarsh–Rose model

1. Model: https://sci-hub.si/10.1088/1009-1963/14/6/006, eq. (1)
2. Regime map: https://sci-hub.si/10.1088/1009-1963/14/6/006, Fig. 1
3. Reference to model with noise:
https://sci-hub.si/10.1088/1009-1963/14/6/006, eq. (2)
4. Reference to model with coupling:
https://sci-hub.si/10.1088/1009-1963/14/6/006, eq. (5)
5. number of neurons N = 15, reference to characteristic correlation time:
http://www.math.pitt.edu/~cbsg/Materials/PhysRevLett.78.775.pdf, eq. (3-4)

Variation IV

Variation 4

Morris–Lecar model

1. Model:
https://link.springer.com/content/pdf/10.1007/s00422-013-0580-4.pdf, eq. (1)
2. Regime map:
https://link.springer.com/content/pdf/10.1007/s00422-013-0580-4.pdf, fig. 1
3. Reference to model with noise:
http://users.df.uba.ar/balen/Papers/PhysRevE_72_021901.pdf, eq. (1)
4. reference to model with coupling
http://users.df.uba.ar/balen/Papers/PhysRevE_72_021901.pdf, eq. (1,8)
5. number of neurons $N = 25$, reference to characteristic correlation time:
http://www.math.pitt.edu/~cbsg/Materials/PhysRevLett.78.775.pdf, eq. (3-4)

Variation V

Variation 5

Izhikevich Neuron model

1. Model: https://www.izhikevich.org/publications/spikes.pdf, eq. (1-3)
2. Regime map: https://www.researchgate.net/publication/267480919_Bifurcation_analysis_of_Izhikevich_model, fig. 3
3. Reference to model with noise: http://www.readcube.com/articles/10.3389/fncom.2018.00059, eq. (1-3,5)
4. Reference to model with coupling: https://www.ieice.org/nolta/symposium/archive/2016/articles/1135.pdf, eq. (2)
5. number of neurons $N = 25$, reference to characteristic correlation time: http://www.math.pitt.edu/~cbsg/Materials/PhysRevLett.78.775.pdf, eq. (3-4)

Variation VI

Variation 6

Leaky integrate-and-fire model 1. Model:
https://www.nature.com/articles/s41598-017-07418-y.pdf, eq. (1)
2. Regime map: https://www.nature.com/articles/s41598-017-07418-y.pdf, fig. 5 (b)
3. Reference to model with noise:
https://sci-hub.si/10.1103/PhysRevE.59.3427, eq. (2.3) – the last term
4. Reference to model with coupling:
https://link.springer.com/content/pdf/10.1140/epjb/e2017-80162-0.pdf, 3(a) – the last term
5. number of neurons $N = 50$, reference to characteristic correlation time:
http://www.math.pitt.edu/~cbsg/Materials/PhysRevLett.78.775.pdf, eq. (3-4)

Variation VII

Variation 7
Regenerate those paper
1. https://arxiv.org/pdf/2004.13532v2.pdf
2. https://link.springer.com/article/10.1007/s10827-008-0131-5