Neural Models

When the system theorists joins the neuroscience team!

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In modeling neurons, we must deal with two types of complexity: the intricate interplay of active conductances that makes neuronal dynamics so rich and interesting, and the elaborate morphology that allows neurons to receive and integrate inputs from so many other neurons.[1]

The concept of complexity in neuron models can be considered by making a two-dimensional chart. One dimension would be membrane complexity, ranging from the simple case of a passive linear membrane, to that of postsynaptic membrane models with time-varying ion permeability (or conductance), and then to excitable membrane models, possibly with many different species of ion channels. The other dimension would be geometric complexity, ranging from the simple case of an isopotential region of membrane (a soma or a space-clamped section of a cylinder) to complex dendritic trees attached to a soma.[2]

Keywords: neural modeling, dynamic systems, hodgkin-huxley, morris-lecar, hindmarsh-rose, wilson-cowan, LIF, neuroscience

1. Dynamic Models of Single Units

1.1. The Hodgkin–Huxley model (conductance-based model, 1950) Bonus(15 points)

The Hodgkin–Huxley model [3] is one of the most recognized models in computational neuroscience. Describing the propagation of an action potential along the squid's giant axon, the HH model states that the axon carries three ionic currents (Figure 1):

1. Voltage-gated persistent K^+ current with four activation gates (resulting in the term n^4 in the equation below, where n is the activation variable for K^+)
2. Voltage-gated transient Na^+ current with three activation gates and one inactivation gate (the term m^4h below)
3. Ohmic leak current, I_L, mainly carried by Cl^- ions.

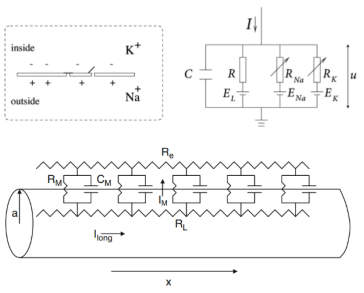


Figure 1: The Hodgkin-Huxley Model: The axon is considered as a cylinder with fixed radius.

The complete set of space-clamped Hodgkin-Huxley equations are given in equation 13:

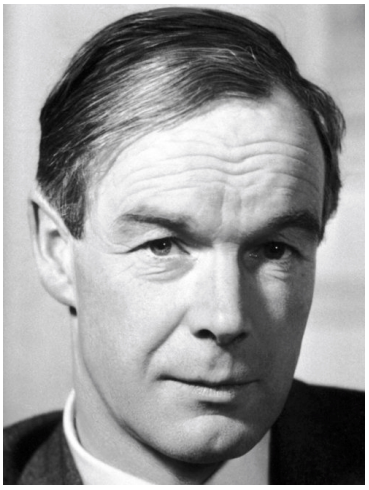
$$\begin{cases} C\dot{V} &= I - \underbrace{\bar{g}_K n^4 (V - E_K)}_{I_K} - \underbrace{\bar{g}_{Na} m^3 h (V - E_{Na})}_{I_{Na}} - \underbrace{g_L (V - E_L)}_{I_L} \\ \dot{n} &= \alpha_n(V)(1-n) - \beta_n(V) n \\ \dot{m} &= \alpha_m(V)(1-m) - \beta_m(V) m \\ \dot{h} &= \alpha_h(V)(1-h) - \beta_h(V) h \end{cases} \tag{1}$$

in which:

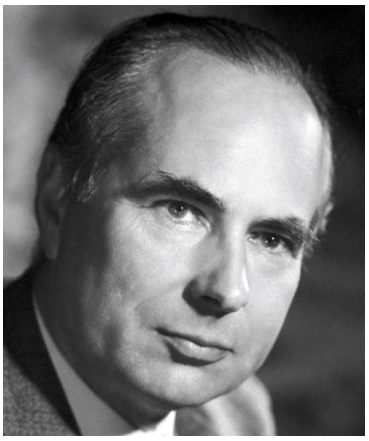
$$\alpha_n(V) = 0.02 \frac{V - 25}{1 - \exp(\frac{-(V-25)}{9})}, \beta_n(V) = -0.002 \frac{V - 25}{1 - \exp(\frac{V-25}{9})}$$

$$\alpha_m(V) = 0.182 \frac{V + 35}{1 - \exp(\frac{-(V+35)}{9})}, \beta_m(V) = -0.124 \frac{V + 35}{1 - \exp(\frac{V+35}{9})}$$

$$\alpha_h(V) = 0.25 \exp(\frac{-(V + 90)}{12}), \beta_h(V) = 0.25 \frac{\exp(\frac{V+62}{6})}{\exp(\frac{V+90}{12})}$$



Alan Hodgkin



Andrew F. Huxley

Analytical Questions

1. What is the minimal current leading to repetitive spiking?
2. If you increase the sodium conductance further, you can observe repetitive firing even in the absence of input, why? Is this phenomenon naturally plausible?

Simulations Questions

1. Using the formula of model, draw the action potential over time. Consider the amplitude of the excitation equal to $20 \frac{\mu A}{cm^2}$ lasting $0.2ms$. Compute the minimum amplitude of excitation for this model to spike for fixed excitation time width.
   After it, compute the minimum excitation current for at least 5 different excitation width.
2. Draw the time change of m, n and h and interpret them comparing to previous plots.
3. Draw the current for Na and K channels.
4. In single excitation state, what is the effect of increasing the capacitance of membrane on the shape of action potential.
5. Now change the program. After 15 ms, apply the second excitation with amplitude $40 \frac{\mu A}{cm^2}$.

Table 1: The Hodgkin–Huxley Constants

Variable	Value
V_0	-65 mv
n_0	0.3
h_0	0.6
m_0	0.05
E_{Na}	55 mv
E_k	-77 mv
E_L	-65 mv
g_{Na}	40 $\frac{mS}{cm^2}$
g_L	0.3 $\frac{mS}{cm^2}$
g_K	35 $\frac{mS}{cm^2}$
C	1 μF

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1.2. The Morris-Lecar Model (The Reduced Hodgkin-Huxley Model, 1981)

60 Points

The Morris-Lecar, a.k.a. $I_{Ca} + I_L$ model [4] is a two-dimensional "reduced" excitation model applicable to systems having two non-inactivating voltage-sensitive conductances (one voltage variable and one gating variable). The original form of the model employed an instantaneously responding voltage-sensitive Ca^{2+} conductance for excitation and a delayed voltage-dependent K^+ conductance for recovery. The model has three channels: a potassium channel, a leak, and a calcium channel. In the simplest version of the model, the calcium current depends instantaneously on the voltage. Thus, the Morris–Lecar equations have the form of formula 2.

Harold Lecar (back), Richard FitzHugh (front), and Cathy Morris at NIH Biophysics Lab, summer of 1983

$$\begin{cases} C_m \frac{dV}{dt} & = I - g_L (V - E_L) - g_K n (V - E_K) - g_{Na} m_\infty (V) (V - E_{Na}) \\ & \equiv I - I_{ion} (V, n) \\ \frac{dn}{dt} & = \frac{1}{\tau_n (V)} (n_\infty (V) - n) \end{cases} \tag{2}$$

Where:

$$\begin{aligned} m_\infty (V) &= \frac{1}{2}[1 + \tanh((V - V_1)/V_2)] \\ \tau_n (V) &= 1/\cosh((V - V_3)/(2V_4)) \\ n_\infty (V) &= \frac{1}{2}[1 + \tanh((V - V_3)/V_4)] \end{aligned}$$

Here, V is the membrane potential, W is the recovery variable, almost invariably the normalized K^*-ion conductance, and I is the applied current stimulus. The variable normalized conductance, $W(t)$, is equal to the instantaneous value of the probability that a K^+-ion channel is in its open (conducting) state. The second equation thus describes the relaxation process by which protein channels undergo conformational transitions between ion-conducting and non-conducting states. The voltage-dependency of energy transition rates for this channel-gating process causes the electrical excitability of the model.

For this part, consider the simple form of Morris-Lecar Model with this formula:

$$\begin{cases} C_m \frac{dV}{dt} & = I - g_L (V - E_L) - g_K n (V - E_K) - g_{Na} m_\infty (V) (V - E_{Na}) \\ \frac{dn}{dt} & = \frac{1}{\tau (V)} (n_\infty (V) - n) \end{cases} \tag{3}$$

Table 2: The Morris-Lecar Constants for simple form

Constant	Value
g_L	8 $\frac{ms}{cm^2}$
E_L	-80 mV
g_{Na}	20 $\frac{ms}{cm^2}$
E_{Na}	60 mV
g_K	10 $\frac{ms}{cm^2}$
E_K	-90 mV
$V_{1/2n}$	-25
$V_{1/2m}$	-20
k_n	5
k_m	15
C_m	1 $\frac{\mu F}{cm^2}$
$\tau(V)$	1

Where:

$$m_\infty(V) = \frac{1}{1 + e^{(\frac{V_{1/2m} - v}{k_m})}}$$

$$n_\infty(V) = \frac{1}{1 + e^{(\frac{V_{1/2n} - v}{k_n})}}$$

Consider the initial value for state-variables at V = -66 mV and n = 0.

Simulation Questions

1. For input current = 0, draw phase plane and nullclines of system and find the equilibrium points and their types.

2. For step input, find the minimum amplitude for current leading the system to spike.

   Draw the voltage for a current below this threshold (I_b) and a current more than this (I_a), for 100 ms and interpret the result.

3. Draw nullclines and phase plane for (I_a) and (I_b) (from previous part), find the equilibrium points and type of them. Compare the results.

4. For impulse input, find the minimum amplitude for current leading the system to spike. Compare this amount to the one for step input. (consider the impulse signal as a pulse signal, starting at zero and end at 0.4 ms)
   Draw the voltage for a current below this threshold (I_b) and a current more than this (I_a), for 100 ms and interpret the result.

1.3. The FitzHugh-Nagumo Model (Bonhoeffer–Van der Pol oscillator, 1961)Bonus(10 points)

BVP model [5] serves as a simple representative of a class of excitable-oscillatory systems, including the Hodgkin-Huxley (HH) model of the squid giant axon. [1]

The BVP phase plane is divided into regions corresponding to the physiological states of a nerve fiber (resting, active, refractory, enhanced, depressed, ...) to form a physiological state diagram. One or more of the Hodgkin-Huxley (HH) state variables (V, m, h, n) are held constant in this model to isolate the behavior of the remaining variables; thus, representing excitability, refractoriness, and qualitatively resembling Bonhoeffer's theoretical model for the iron wire model of nerve.

One may evaluate the stability of this oscillator by setting $\dot{x}$ and $\dot{y}$ equal to zero, and by solving the system of equations for the x and y, form the algebraic description of the nullclines curves. The point of intersection of the two nullclines is the singular point P, which is a stable node.

The x phase line through the resting point P has three singular points where it intersects the three branches of the x nuilcine. The middle one is unstable and represents a threshold phenomenon. y has a slower dynamic than x, except near the y nullcline. Decreasing x increases y gradually, causing the phase line to move upward until the excited and threshold singular points meet and vanish. Then, with x still dropping, the phase point rapidly approaches the only remaining singular point, the quiescent one on the right branch. Finally, y slowly decreases, and the phase trajectory approaches the resting point P.

The dotted line represents the locus of initial conditions following instantaneous z shocks at rest. The displacement of the phase trajectory from P to some point to the left of the unstable threshold singular point produces excitation in the reduced system, and the phase point approaches the exciting singular point. Excitation occurs whenever the phase point is displaced across the separatrix from right to left; abolition occurs for displacement from the resting point to the right.

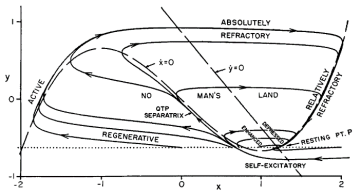


Figure 2: The state point or phase point representing the state of the system moves spontaneously in this plane along the paths (also called trajectories), which are the curves with arrowheads.

1: Mathematical equations of the BVP model:

$$\begin{cases} \dot{x} &= c(y + x - x3/3 + z) \\ \dot{y} &= -\frac{x-a+by}{c} \end{cases}$$

$$\begin{cases} 1 - 2b/3 < a < 1 \\ 0 < b < 1 \\ b < C^2 \end{cases}$$

Both a and b are constants. z is stimulus intensity, a variable corresponding to membrane current I in the HH equations.

Jin-ichi Nagumo

Analytical Question

1. What happens to the state trajectory by applying an instantaneous shock stimulus? Elaborate.

Simulation Questions

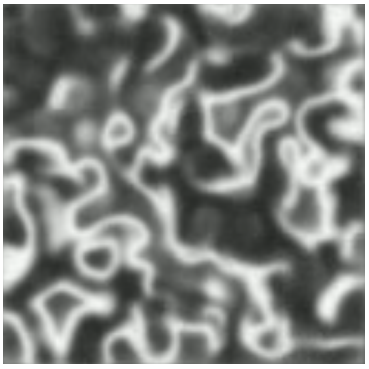
1. Plot the nullclines in the $u - w$ plane, for voltages in the region $u \in [-2.5, 2.5]$.
2. Choosing different initial points, simulate the state trajectory of system.

1.4. The Hindmarsh–Rose model (1984) Bonus(10 points)

The Hindmarsh-Rose model [6] of neuronal bursting uses three coupled first-order differential equations that aim to study the spiking behavior of the membrane potential observed in experiments made with single neurons. This model is a modification of Fitzhugh's B.v.P. that has the mathematical form of a system of three nonlinear ordinary differential equations on the dimensionless dynamical variables $x(t)$, $y(t)$, and $z(t)$. In the phase plane this property results from the close proximity of the nullclines in the subthreshold region of the oscillation. This model is closer to Fitzhugh's model in that the $\dot{x}, \dot{y}, \dot{z}$ equations have cubic, quadratic, and linear terms in x respectively. The equations for the three equilibrium point model with adaptation are listed in Noise is added via stochastic integration of the variable x

[2] The third variable of the Hindmarsh-Rose model implements slow inactivation dynamics of the membrane potential and allows to model neuronal bursting. Spatial coupling is introduced by the voltage variable diffusion ($D\Delta x$): $\dot{x} = y - ax^3 + bx^2 + I - z + D\Delta x$

Here x is the membrane voltage, y is the fast ion exchange (spiking variable), z is the slow ion exchange (bursting variable), b is the switch between spiking to bursting and controls spike frequency, c is the base fast ion exchange rate, d is the scale membrane feedback, I_θ is stimulation current amplitude, r is the control variation of slow ion exchange, s is the adaptation, determines spiking without accommodation and sub-threshold adaptation, x_1 is the resting membrane potential, σ is noise intensity, D is the diffusion constant, N is the lattice size, T is the number of simulation time steps, t_θ is the number of 'warm-up' iterations, d_t is the integration time step



A frame of 2D lattice simulation of the Hindmarsh rose model

2: Mathematical equations of the Hindmarsh–Rose model:

$$\begin{cases} \dot{x} &= y - ax^3 + bx^2 + I - z \\ \dot{y} &= c - dx^2 - y \\ \dot{z} &= r(s\,(x - x_1) - z) \end{cases}$$

$$\begin{cases} d_x = \dot{x}d_t + \sigma dW_t \\ d_y = \dot{y}d_t \\ d_z = \dot{z}d_t \end{cases}$$

Table 3: The Hindmarsh–Rose Constants

Constant	Value
N	128
T	15000
t_θ	2500
d_t	0.05
σ	0.05
D	2.5
a	1.0
b	3.0
c	1.0
d	5.0
s	4.0
r	0.001
x_1	-1.6
I_0	3.5

Analytical Questions

1. Name an Extra property of the Hindmarsh rose model against FitzHugh's BVP model?
2. What is the difference between the equations of the Hindmarsh rose model and the Fitzhugh B.v.P. model?
3. Name five regions on the Hindmarsh rose model according to the Equilibrium points?

Simulation Questions

1. Implement the Hindmarsh-Rose model of neuronal excitability on a 2D lattice via below settings.
   a) Plot number of simulation time steps
   b) Animate 3D array as .mp4 showing the dynamic of system.

1.5. The leaky integrate-and-fire (LIF) model (1907)

40 Points

The leaky integrate and fire model [7] which can be traced back to Louis Lapicque, is an idealization of a neuron having ohmic leakage current and a number of voltage-gated currents that are completely deactivated at rest. Subthreshold behavior of such a neuron can be described by a linear differential equation described in formula 4

$$C\dot{V} = I - \overbrace{g_{\text{leak}}(V)\,(V - E_{\text{leak}})}^{\text{ohmic leakage}} \tag{4}$$

When the membrane potential V reaches the threshold value E_{thresh} , the voltage-sensitive currents instantaneously activate, the neuron is said to fire an action potential, and V is reset to E_K. After appropriate rescaling, the leaky integrate-and-fire model can be formulated as in 5

$$\dot{v} = b - v, \quad \text{if } v = 1, \text{ then } v \leftarrow 0 \tag{5}$$

Where the resting state is $v = b$, the threshold value is $v = 1$, and the reset value is $v = 0$. Apparently the neuron is excitable when $b < 1$ and fires a periodic spike train when $b > 1$ with period $T = -\ln(1 - 1/b)$. The integrate-and-fire neuron illustrates a number of important neuro-computational properties:

- All-or-none spikes. Since the shape of the spike is not simulated, all spikes are implicitly assumed to be identical in size and duration.
- Well-defined threshold. A stereotypical spike is fired as soon as $V = E_{thresh}$, leaving no room for any ambiguity.
- Relative refractory period. When $E_K < E_{\text{leak}}$, the neuron is less excitable immediately after the spike.
- Distinction between excitation and inhibition. Excitatory inputs ($I > 0$) bring the membrane potential closer to the threshold, and hence facilitate firing, while inhibitory inputs ($I < 0$) do the opposite.
- The neuron can continuously encode the strength of an input into the frequency of spiking.

The subthreshold membrane potential dynamics of a LIF neuron is described by

$$C_m \frac{dV}{dt} = -g_L(V - E_L) + I \tag{6}$$

Where C_m is the membrane capacitance, V is the membrane potential, $g_L = 1/R$ is the leak conductance, E_L is the resting potential, and I is the external input current.

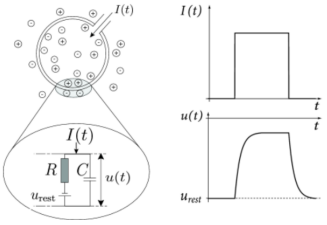


Figure 3: Leaky integrate-and-fire neuron

Louis Lapicque

Dividing both sides of the above equation by g_L gives:

$$\tau_m \frac{dV}{dt} = -(V - E_L) + \frac{I}{g_L} \tag{7}$$

where the τ_m is membrane time constant and is defined as $\tau_m = \frac{C_m}{g_L}$. If I is sufficiently strong such that V reaches a certain threshold value V_{th}, V is reset to a reset potential $V_{reset} < V_{th}$, and voltage is clamped to V_{reset} for τ_{ref} ms, mimicking the refractoriness of the neuron during an action potential:

$$\text{if } V\left(t_{sp}\right) \geq V_{th} : V\left(t\right) = V_{reset} \forall t \in \left(t_{sp}, t_{sp} + \tau_{ref}\right] \tag{8}$$

where t_{sp} is the spike time when $V(t)$ just exceeded V_{th}.

Analytical Question

1. A leaky integrate-and-fire model has the same asymptotic firing rate (1/ln) as a system near saddle homoclinic orbit bifurcation. Explore the possibility that integrate-and-fire models describe neurons near such a bifurcation.
2. List Limitations of the Leaky Integrate-and-Fire Model.

Simulation Questions

1. For input frequencies between 10Hz and 1 kHz, plot the resulting amplitude of subthreshold oscillations of the membrane potential vs. input frequency.
2. The subthreshold regime (no spike), the LIF neuron is a linear system and the membrane voltage is a filtered version of the input current, To what type of filter (High-Pass, Low-Pass) does this correspond to?
3. Simulate the LIF dynamics and plot membrane potential over time with threshold line.
4. We now study the f-I curve for a neuron with a refractory period of 3ms to learn how to set a refractory period what is the maximum rate at which this neuron can fire?

Table 4: The leaky integrate-and-fire Constants

Constant	Value
V_{th} (mV)	-55.0
V_{reset} (mV)	-75.0
τ_m	(ms) 10.0
g_L (ns)	10.0
V_{init} (mV)	-75.0
E_L (mV)	-75.0
t_{ref} (ms)	2.0
T (ms)	400.0
d_t (ms)	0.1

2. Dynamic Models of Population of Units

2.1. The Wilson-Cowan Model (1972-1973)

Bonus(25 points)

The Wilson-Cowan model [8] is a powerful yet simple model that describes the interactions between two populations of excitatory and inhibitory neurons. This model is capable of analyzing neural hysteresis phenomena related to binocular vision and is used as a canonical model of visual cortical activity.

Wilson and Cowan derived effective equations for the proportion of cells in a population that are active per unit of time, as given in formula 9

Hugh R. Wilson

Jack D. Cowan

$$\begin{cases} \tau_e \frac{da_e}{dt} & = -a_e(t) + [1 - r_e a_e(t)] F_e(w_{ee} a_e(t) - w_{ie} a_i(t) + I_e(t)) \\ \tau_i \frac{da_i}{dt} & = -a_i(t) + [1 - r_i a_i(t)] F_i(w_{ie} a_e(t) - w_{ii} a_i(t) + I_i(t)) \end{cases} \quad (9)$$

Crucially, the effective behavior of the population relies on interactions between excitatory and inhibitory cells where $a_e(t)$ and $a_i(t)$ are the proportion of excitatory and inhibitory cells firing per unit time at instant t. Thus, $a_{e,i}(t)$ corresponds to a low-activity resting state. Excitatory (inhibitory) neurons make their neighbors more (less) likely to become active, and activation is a nonlinear function $F_e(F_i)$ of the presently active proportion of cells. These assumptions form the backbone of this model. Thus, the activity variables obey first-order kinetics with timescales, tracking the response of each subpopulation. The nonlinearities are typically sigmoidal [1]. In equation 10 the gain γ_j and threshold θ_j can depend on the population type $j = e, i$. The argument x is a weighted sum of the proportion of active excitatory and inhibitory cells, where $w_{jk} \geq 0$ describes the strength of connection from cell type k to j. the term $1 - r_j a_j(t)$ has often neglected in subsequent considerations of the model.

1: Sigmoidal function:

$$F_j(x) = \frac{1}{1 + \exp(-a_j(x - \theta_j))} \quad (10)$$

Analytical Question

1. Is there any correlation between "the cell sensitive probability (a_*)" and its "excitation level(F_*)"? If positive, describe how this relationship reduces the value of the expression just obtained?
2. Assume "the cell sensitive probability" are independence from "the probability that the cell is currently excited above its threshold" and describe simplicity of the excitation sub-population formula.

Simulation Questions

Assuming the constants of table 5, answer the simulation questions.

1. Simulate the excitatory and inhibitory population activity with similar initial point.
2. Plot the nullcline of previous setup and initial points (similar to the attached plot)
3. Simulate working memory using the Wilson-Cowan model.

Discuss the results based on the mathematical formulation of the system. The discussion is important during grading and the unexplained code and results might not get any scores from this part.

Table 5: The Wilson-Cowan Model Constants

Constant	Value
τ_e (ms)	1
a_e	1.2
θ_e	2.8
τ_i (ms)	2
a_i	1
θ_i	4
W_{EE}	9
W_{IE}	4
W_{EI}	13
W_{II}	11
I_e	0
I_i	0
sim. duration (ms)	50
sim. step (ms)	0.1
E_{i0}	0.2
I_{e0}	0.2

3. Submission

Each of students shall submit a typed `pdf` report by which the gist of their analysis is explained. The figures described in the problem description should be included and discussed within the report. For each parts, a separate script should be included, in either MATLAB (`.m`), python3 (`.py`, `.py3`), R (`.r`) or Julia (`.jl`). Do not submit your scripts in MATLAB live script, python notebook or r markdown. The submitted codes should run on the grader's system as well. Don't forget to attach all of your functions and non-standard libraries.

The report is considered to be an academic writing, rather than a technical one, so it should not include any codes, neither it should explain the coding logic. It should contain the author's insights about the results and reflect their dominance over the reference article. Academic writings usually are compact and use extremely formal tone.

Each section briefly explains the hypothesis that is going to be tested. The design of test and its implementation is considered as the students duty, as well as the explanations of each of the results. Interpretations shall be comprehensive, while avoiding unnecessary prolixity.

The language in which the report is written in should be either Persian or English, with no preference towards any of them. But if the report is written in Persian, it should use B Nazanin with size 14 as text body font and B Titr 18 for titles. English reports shall use Times New Roman 12 for body and Time New Roman 16 for titles. Sentences should be in passive tense. In persian reports, correct use of zero-width non-joiner is mandatory. In all reports, all equations, figures and tables should be labeled with unique numbers and referenced accordingly. Referencing to a figure with sentences like "the following figure", "the figure above" and etc. is incorrect. All Figures should have descriptive captions below them, while tables have the caption above them. Feel free to use footnotes and citations as needed.

You just have to answer the questions for **Morris-Lecar** and **LIF** parts. The other parts have Bonus points, witch their points considered for another homeworks. You have 14 days (two weeks) for answering the questions.

A. Dynamical System Concepts

Dynamical systems theory provides a powerful tool for analyzing nonlinear systems of differential equations, including those used in neuroscience. They can be discrete or continuous in time. Continuous one-dimensional dynamical systems are usually written in the form: $\dot{V} = F(V)$, $V(0) = V_0 \in R$ This theory allows us to interpret solutions geometrically as curves in phase space. By studying the geometric structure of phase space, we may classify the types of solutions that a model may exhibit and determine how solutions depend on the model's parameters. For example, we can often predict if a model neuron will generate an action potential, determine for which values of the parameters the model will produce oscillations, and compute how the frequency of these oscillations depends on the parameters. [9][10][11][12]

Equilibrium points

An equilibrium of a dynamical system is a value of the state variables where the state variables do not change. In other words, an equilibrium is a solution that does not change with time. This means if the systems starts at an equilibrium, the state will remain at the equilibrium forever. Equilibria can be classified by looking at the signs of the eigenvalues of the linearization of the equations about the equilibria. That is to say, by evaluating the Jacobian matrix at each of the equilibrium points of the system, and then finding the resulting eigenvalues, the equilibria can be categorized. Then the behavior of the system in the neighborhood of each equilibrium point can be qualitatively determined, (or even quantitatively determined, in some instances), by finding the eigenvector(s) associated with each eigenvalue. An equilibrium point is hyperbolic if none of the eigenvalues have zero real part. If all eigenvalues have negative real parts, the point is stable. If at least one has a positive real part, the point is unstable. If at least one eigenvalue has negative real part and at least one has positive real part, the equilibrium is a saddle point and it is unstable. If all the eigenvalues are real and have the same sign the point is called a node.

Bifurcations

One of the important concepts in analyzing dynamical systems is bifurcation. Bifurcation theory is concerned with how solutions change as parameters in a model are varied. Equations may exhibit different types of solutions for different values of the applied current. Sometimes there is a stable fixed point and no oscillations, sometimes the fixed point is unstable and a stable limit cycle exists. Using bifurcation theory, we can classify the types of transitions that take place as we change parameters. In particular, we can predict for which value of I the fixed point loses its stability and oscillations emerge. There are, in fact, several different types of bifurcations; that is, there are different mechanisms by which stable oscillations emerge.

The Hopf Bifurcation

In the mathematical theory of bifurcations, a Hopf bifurcation is a critical point where a system's stability switches and a periodic solution arises.

Saddle-Node (Fold) Bifurcation

In the mathematical area of bifurcation theory, a saddle-node bifurcation, tangential bifurcation or fold bifurcation is a local bifurcation in which two fixed points (or equilibria) of a dynamical system collide and annihilate each other.

Nullclines

In mathematical analysis, nullclines, sometimes called zero-growth isoclines, are encountered in a system of ordinary differential equations

$$\begin{cases} x_1' &= f_1(x_1, \ldots, x_n) \\ x_2' &= f_2(x_1, \ldots, x_n) \\ \vdots &= \vdots \\ x_n' &= f_n(x_1, \ldots, x_n) \end{cases}$$

where x' here represents a derivative of x with respect to another parameter, such as time t. The j'th nullcline is the geometric shape for which $x_j' = 0$. The equilibrium points of the system are located where all of the nullclines intersect. In a two-dimensional linear system, the nullclines can be represented by two lines on a two-dimensional plot; in a general two-dimensional system they are arbitrary curves.

Trajectories

In dynamical systems, a trajectory is the set of points in state space that are the future states resulting from a given initial state. In a discrete dynamical system, a trajectory is a set of isolated points in state space. In a continuous dynamical system, a trajectory is a curve in state space.

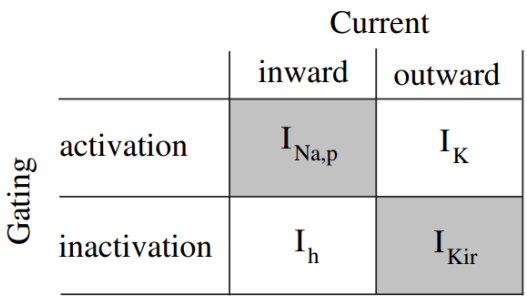
Phase Plane

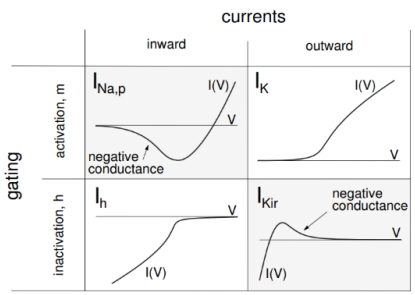
In applied mathematics, in particular the context of nonlinear system analysis, a phase plane is a visual display of certain characteristics of certain kinds of differential equations; a coordinate plane with axes being the values of the two state variables

B. Neural Models

One Dimensional Systems ($I_{Na,p}$ Model, I_K Model, and I_{Kir} Model)

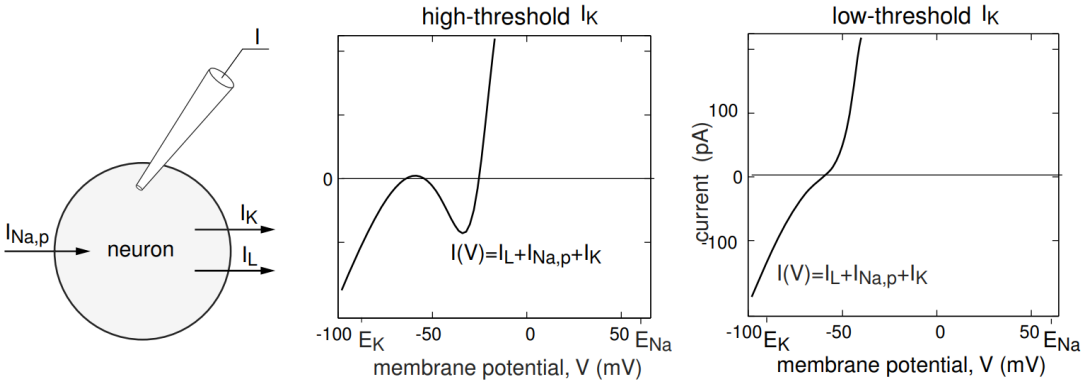
Systems having only one variable, four fundamental examples of voltage-gated currents with one gating variable. we treat *hyperpolarization-activated* currents I_h and I_{Kir} as inactivating currents, which are turned off (inactivated via h) by depolarization and turned on (deinactivated) by hyperpolarization.





Two Dimensional Systems

Also called planar systems and often written in the form: $\dot{x} = f(x, y), \dot{y} = g(x, y)$ where the functions f and g describe the evolution of the two-dimensional state variable (x(t), y(t)) For any point (x_0, y_0) on the phase plane, the vector $(f(x_0,\ y_0), g(x_0,\ y_0))$ indicates the direction of change of the state variable.



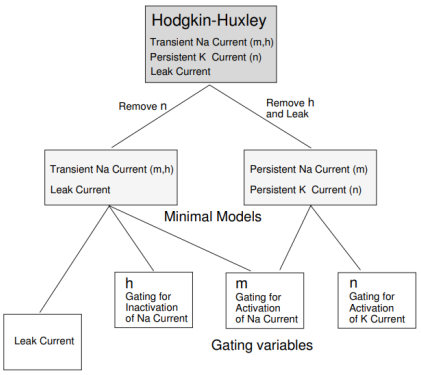
Conductance-Based Models

Minimal models or irreducible for spiking having minimal sets of currents that enable the models to generate action potentials, they can be reduced to planar systems having N-shaped V-nullclines. The Models behavior is not so much depending on the relationship between the time constants and (in)activation curves (The ionic currents) (Que) Does the reduced model have a limit cycle attractor, at least for some values of parameters? (Ans) If it does, we remove one more gating variable or current, and proceed until we arrive at a model that satisfies the following two properties:

1. It has a limit cycle attractor, at least for some values of parameters.
2. If one removes any current or gating variable, the model has only equilibrium attractors for any values of parameters.

Thus, minimal models can exhibit periodic activity, even if it is of small amplitude, but their reductions cannot. For example, the Hodgkin-Huxley model consists of three currents Which of these currents are responsible for excitability and spiking? We can remove the leakage current and the gating variable, h, for the inactivation of the sodium current: The resulting $I_{Na,p} + I_K$ model:

$$
\begin{aligned}
C\dot{V} &= I - \overbrace{g_K n^4 (V - E_K)}^{I_K} - \overbrace{g_{Na} m^3 (V - E_{Na})}^{I_{Na,p}} \\
\dot{n} &= (n_\infty(V) - n)/\tau_n(V) \\
\dot{m} &= (m_\infty(V) - m)/\tau_m(V)
\end{aligned}
$$



Thinking in terms of minimal models, we can understand what is essential for spiking and bursting and what is not. In addition, we can clearly see that some well-known conductance-based models form a partially ordered set. For example, the chain of neuronal models Morris-Lecar

($I_{Ca} + I_K$) < Hodgkin-Huxley ($I_{Na,t} + I_K$) < ButeraRinzel-Smith ($I_{Na,t} + I_K + I_{K,slow}$) is obtained by adding a conductance or gating variable to one model to get the next one. Here, A < B means A is a subsystem of B.

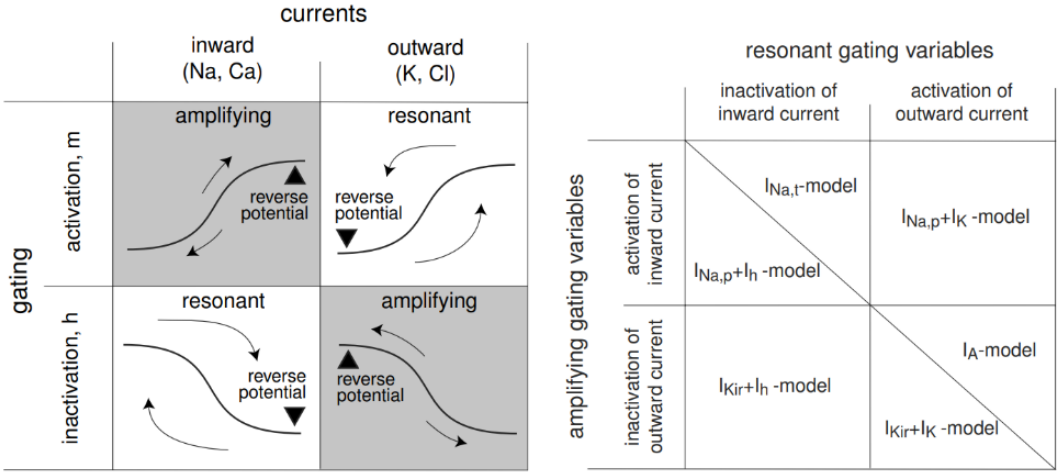
Reduction of the Hodgkin–Huxley Model

The Hodgkin-Huxley description of dynamics of membrane potential and voltage-gated conductances can be reduced to a one-dimensional system when all transmembrane conductances have fast kinetics. For the sake of illustration, let us consider a space-clamped membrane having leak current and a fast voltage-gated current I_{fast} with only one gating variable p:

$$C\dot{V} = -g_L \overbrace{(V - E_L)}^{\text{Leak } I_L} - g_p \overbrace{(V - E)}^{I_{fast}}$$

$$\dot{p} = (p_\infty(V) - p)/\tau(V)$$

Any combination of one amplifying variable and one resonant gating variable results in a spiking model. Gating variables may be amplifying or resonant depending on whether they represent activation/inactivation of inward/outward currents.



$I_{Na,p} + I_K$ Model

This model is in many respects equivalent to the $I_Ca + I_K$ model proposed by Morris-Lecar to describe voltage oscillations in the barnacle giant muscle fiber.

$$\begin{cases} C\dot{V} &= I - \underbrace{g_L(V - E_L)}_{Leak I_L} - \underbrace{g_{Na} m(V - E_{Na})}_{I_{Na,p}} - \underbrace{g_K n(V - E_K)}_{I_K} \\ \dot{n} &= (n_\infty(V) - n)/\tau_n(V) \\ \dot{m} &= (m_\infty(V) - m)/\tau_m(V) \end{cases} \tag{11}$$

$I_{Na,t}$ Model

An interesting example of a spiking mechanism, implicitly present in practically every biological neuron

$$\begin{cases} C\dot{V} & = I - \underbrace{g_L(V - E_L)}_{LeakI_L} - \underbrace{g_{Na}m^3h(V - E_{Na})}_{I_{Na,p}} \\ \dot{m} & = (m_\infty(V) - m)/\tau_m(V) \\ \dot{h} & = (h_\infty(V) - h)/\tau_h(V) \end{cases} \tag{12}$$

$I_{Na,p} + I_h$ **Model**

It believes this system describe the essence of the mechanism of slow subthreshold voltage oscillations in some cortical, thalamic, and hippocampal neurons.

$$\begin{cases} C\dot{V} & = I - \underbrace{g_L(V - E_L)}_{LeakI_L} - \underbrace{g_{Na}m(V - E_{Na})}_{I_{Na,p}} - \underbrace{g_h h(V - E_h)}_{I_h} \\ \dot{m} & = (m_\infty(V) - m)/\tau_m(V) \\ \dot{h} & = (h_\infty(V) - h)/\tau_h(V) \end{cases} \tag{13}$$

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