Last Name .... First Name..................

Biological Modelling of Neural Networks Exam
June 2022

- Write your name in legible letters on top of this page.
- Check that your exam has 10 pages (numbered 1-10).
- The exam lasts 180 min.
- Write **all** your answers in a legible way on the exam (no extra sheets).
- No documentation is allowed apart from 1 sheet A5 of **handwritten** notes.
- No calculator is allowed.
- Have your student card displayed before you on your desk.

Evaluation:

1. .... / 9 pts (phase plane)
2. .... / 8 pts (separation of time scales)
3. .... / 8 pts (mean-field)
4. .... / 9 pts (+3 bonus points) (interval distribution)

Total: .... / 34 pts

1 Phase Plane Analysis (9 points)

In a paper published in 2007, Barak and Tsodyks consider a system of two differential equations that describes a fully connected population of excitatory rectified-linear rate neurons. Neurons are coupled with synapses undergoing short-term plasticity.

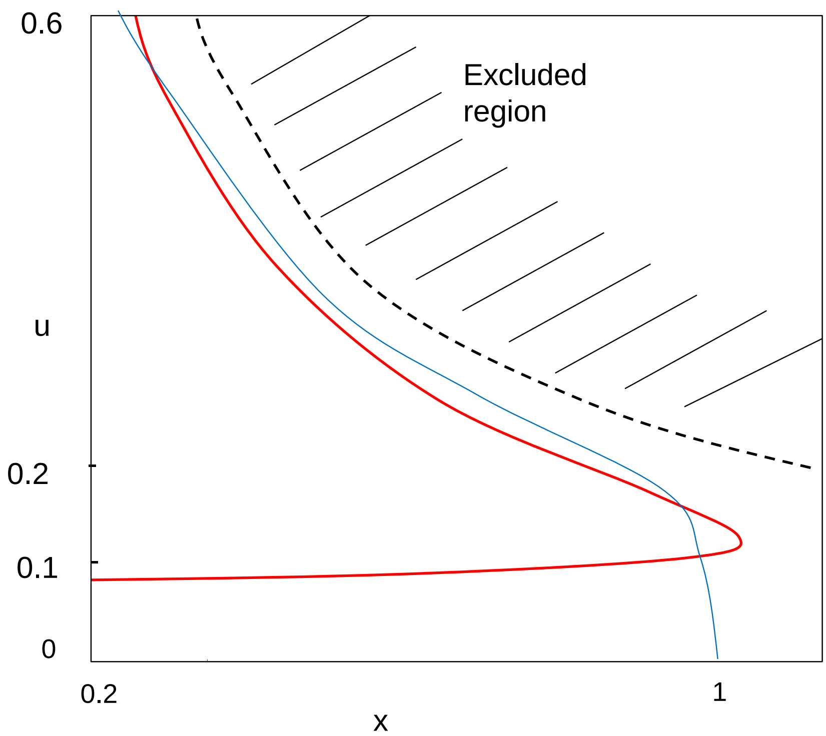
If the population is stimulated with a constant stimulus I_0 (interpreted as spike arrival rate), the two synaptic plasticity variables develop according to

$$\frac{dx}{dt} = -\frac{x-1}{\tau_r} - I_0 \frac{ux}{1-Jux} - a_{\text{pulse}}\delta(t-t_{\text{pulse}}) \quad (1)$$

$$\frac{du}{dt} = -\frac{u-U}{\tau_f} + U\, I_0 \frac{1-u}{1-Jux} + a_{\text{pulse}}\delta(t-t_{\text{pulse}}) \quad (2)$$

$\tau_f = 0.7$**s and** $\tau_r = 0.1$**s are time constants.** For the moment there is no pulse stimulus $a_{\text{pulse}} = 0$. $J = 5$ and $U = 0.05$ are further parameters.

If the constant stimulus is $I_0 = 0.85Hz$, then the nullclines look qualitatively like this. The dynamics cannot enter the excluded region.



a) Evaluate at the point $(x, u) = (1, 0)$ the derivatives (1 digit after the comma is sufficient).

$dx/dt =$ ....

$du/dt =$ ....

number of points: ....../[1]

b) Label the two nullclines

red line = ...

blue line = ...

number of points: ....../[1]

c) Evaluate at the point $(x, u) = (0.9, 0)$ the x-derivative (1 digit after the comma is sufficient).

$dx/dt =$ ....

number of points: ....../[1]

d) Add in your graph flow arrows on the nullclines (at least four on each nullcline).

number of points: ....../[2]

e) Mark all saddle points by a cross and all other fixed points by a circle.

number of points: ....../[1]

f) Construct two trajectories, the first one starts at $(0.2, 0.1)$ and the second one at $(0.2, 0.3)$. Hint: Since $\tau_f = 0.7$s and $\tau_r = 0.1$s you can assume a separation of time scales.

number of points: ....../[2]

g) Assume that the dynamical system is exactly at the fixed point with the largest x-value. At time t_{pulse} you apply a pulse stimulus of amplitude $a_{\text{pulse}} = 0.1$.

Plot qualitatively the trajectory for $t > t_{\text{pulse}}$ in the phase plane

number of points: ....../[1]

space for calculations

2 Separation of time scales (8 points)

In a paper published in 2007, Barak and Tsodyks consider a fully connected population of excitatory rectified-linear rate neurons. Neurons are coupled with synapses undergoing short-term plasticity. They start with a system of three equations, and reduce then to two equations.

The firing rate of the neurons is $R = A \max(h, 0)$ where h is the input potential of the neurons and A a parameter the converts the units from voltage to rate. The system of three equations reads

$$\tau_h \frac{dh}{dt} = -h + J\,x\,y\,R/A + (I_0/A) \tag{3}$$

$$\frac{dy}{dt} = -\frac{y - B}{\tau_y} + B\,(1 - y)\,R \tag{4}$$

$$\frac{dx}{dt} = -\frac{x - 1}{\tau_x} - xyR \tag{5}$$

The time constants are $\tau_h = 0.005$**s and** $\tau_y = 0.7$**s and** $\tau_x = 0.1$**s**

$J > 0$ and $0 < B < 1$ are further parameters. The stimulus I_0 is fixed but arbitrary.

(a) **Assume** $Jxy < 1$ **and** $h > 0$**.** Exploit the separation of time scale and reduce the above system to two differential equations.

first differential equation:

....

second differential equation:

....

number of points: ....../[2]

(b) Can you translate variables and parameters so as to map your result in (a) to equations (1) and (2) in the first exercise.

....

....

number of points: ....../[1]

(d) Has the system of three equations a fixed-point solution for $h \leq 0$? If so, what are the values of h, y, x as a function of I_0?

....

....

....

....

number of points: ....../[2]

(e) We now assume that the external input I_0 switches at time $t = 0$ from a (strongly) negative value to a weakly positive value. Follow **qualitatively the time course** of h, y, x with the aim to give **an interpretation of the variables** x **and** y of short-term plasticity (you should take into account the value of the three time constants)

You should make statements like this: First the variable Z increases. The effect of this is that it increases/decreases the firing rate. Therefore I interpret Z as a variable describing ... (where Z is one of the three variable)

First the variable ....

Second the variable ....

Third, the variable ....

Since this increases/decreases the rate, I interpret the variables x and y as

$x =$ ....

$y=$ ....

number of points: ....../[2]

(f) Based on your results in (e) **sketch qualitatively** the time course of the input potential h over a time interval of $-0.1s < t < 1.5s$ in the space below. [Hints: (i) as in part (a) you can assume $Jxy < 1$; (ii) a temporal resolution at a scale of 0.05s is appropriate for $t < 0.4s$; (iii) $0.2 < B < 0.5$ are good parameter choices.]

number of points: ....../[1]

3 Mean-field and population activity (8 points)

Consider a population of N identical neurons. If driven by an input $I(t)$, each neuron fires independently and stochastically with a Poisson firing rate $\nu(t) = g(I(t))$.

The input $I = I^{\text{ext}} + I^{\text{syn}}$ has a fixed external component I^{ext} as well as a synaptic component I^{syn}. The synaptic weights are all identical and set to $w_0 = J_0/N$.

(a) Suppose that each neuron receives spike input from all other neurons $1 \leq j \leq N$. A single spike arriving at time $t = 0$ evokes a response current $\gamma(t) = w_0[\exp(-t/\tau_2) - \exp(-t/\tau_1)]$ for $t > 0$ with parameters $0 < \tau_1 < \tau_2$.

Write down the total input $I(t_0)$ to a specific neuron i assuming that you know the spike times of all input spikes for $t < t_0$.

....

number of points: ....../[1]

Rewrite your results in terms of the (time-dependent) population activity

....

number of points: ....../[1]

(b) Assume that the gain function $g(I)$ is given by $g(I)$=0 for $I \leq 1$, $g(I) = (I-1)^2$ for $1 < I \leq 2$, and $g(I) = 1$ for $I > 2$.

We now **set** $\tau_2 = 2$ **and** $\tau_1 = 0.5$ **and** $J_0 = 2$ **and** $I^{\text{ext}} = 0$ and $w_0 = J_0/N$. Consider the limit $N \to \infty$ and determine graphically the fixed points of the population activity $A(t)$. Make a graph in the space here:

number of points: ....../[2]

(c) What is the number of fixed points in the above graph?

....

Does the number of fixed points change if you apply an external current of $I^{\text{ext}} = 0.5$? What happens if the external current is even stronger? Comment please!

....

....

number of points: ....../[2]

(d) What happens in the setting of (b) if we increase J_0 from 2 to 10?

....

What happens in the setting of (b) if we decrease J_0 from 2 to 1?

....

number of points: ....../[2]

Space for calculations

4 Linear differential equations and interval distributions (9 points + 3 bonus points)

In class we have studied a Poisson neuron with absolute refractoriness and looked at survivor function, interval distribution, and firing rate. Let us apply this type of mathematics to the problem of a stochastic ion channel. We study the following model of an ion channel.

The current through a single ion channel is

$$I(t) = g(t - t_{\text{open}})\,(u - E) \tag{6}$$

where E is the reversal potential of the channel, u is the voltage, and t_{open} is the moment when the ion channel opens stochastically. After opening, the channel stays open for a duration t_d so that the time course of the ion channel has a 'box-like' shape given by

$$g(s) = g_0 \quad \text{for} \quad \mathbf{0 < s < t_d} \tag{7}$$

with conductance parameter g_0 and zero otherwise (as before).

The Poisson rate of opening of a single channel (starting from a closed state) is given by

$$\frac{d\nu}{dt} = -\frac{\nu - \nu_0(u)}{\tau} \tag{8}$$

with a voltage dependent function $\nu_0(u) = (u - E)^2\,a$ for $u > E$ where a is a constant with units $[Hz/V^2]$. Note that **while the ion channel is open, it cannot open 'again' or open 'even more'**. The ion channel therefore has to close before it can open again.

(a) We **first keep the voltage at** $u = E$ **for a long time**, and then, at time $t_0 = 20\tau$, we switch the voltage to a **new value** $u > E$. What is the time course of the variable $\nu(t)$ for $t > t_0$?

$\nu(t) =$

....

....

number of points: ....../[2]

(b) We observe the switching behavior of the single channel for a time $T = 1000t_d$. We assume that $T \gg \tau$.

Given a certain fixed voltage $u > E$, what is the expected **distribution of waiting times** between a closing event of the channel and its next opening event?

....

Given a certain fixed voltage $u > E$, what is the **interval distribution between two subsequent opening events of the channel?**

....

....

number of points: ....../[3]

(c) Now we observe the switching behavior for a time $T = 1000t_\mathrm{d}$ and choose a voltage such that $\nu = 1/t_d$. What fraction of time is the channel expected to be open? Why?

....

....

....

number of points: ....../[2]

Space for calculations

(d) Assume a large number of independent identical channels and express the fraction $m_0(u)$ of open channels as a function of $\nu_0(u)$ and t_d for fixed but arbitrary voltage.

$m_0(u)$=..

Suppose $u > E$. What happens in the limit of $u \to E$ and $u \to \infty$? Is this what you expect? Interpret your result.

....

....

....

number of points: ....../[2]

(e) **Bonus question - difficult. Start only when you are done with the rest**. Let us introduce a variable $x_0(u) = \nu_0(u)t_d$ and a variable $x(t) = \nu(t)t_d$. Express $m_0(u)$ as a function of $x_0(u)$, using (d).

....

Write down a differential equation for $x(t)$ and transform this into a differentional equation for the fraction $m(t)$ of open channels which should be valid for arbitrary **time-dependent** voltage.

$\frac{dx}{dt}$ = ...

$\frac{dm}{dt}$ = ...

Compare the mathematical expression of your final equation with that of the gating variables in the Hodgkin and Huxley formalism.

Have you made any assumptions for your equation, so far? If so, which ones:

....

....

Now you assume that $m(t)$ is close to $m_0(u(t))$ and approximate $m(t) = m_0(u(t)) + \delta m(t)$. Derive an expression of the **voltage-dependent time constant** of the gating variable m.

Gating equation: ....

with $\tau_m(u)$ = ...

number of points: ....../[3]