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

Biological Modelling of Neural Networks Exam
21 June 2017

- Write your name in legible letters on top of this page.
- Check that your exam has 12 pages (numbered 1-12). Page 2 is empty.
- The exam lasts 160 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. .... / 15 pts
2. .... / 8 pts
3. .... / 8 pts
4. .... / 7 pts (PLUS ..../ 5 bonus)

Total: .... / 38 pts

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1 Phase Plane Analysis (15 points)

We study a network of coupled rate neurons with all-to-all coupling in the mean-field limit. Thus all neurons have the same input potential h and the same firing rate $g(h)$. However, we assume that the interaction weights w are subject to fatigue (also called synaptic depression) when they are used intensively. We write the total interaction weight as $w = J_0\, s$ with some synaptic depression variable s and a fixed parameter J_0.

The system of equations is:

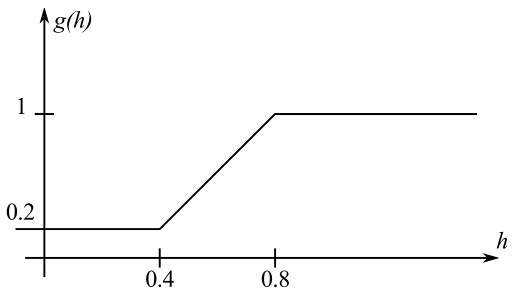
$$\tau \frac{dh}{dt} = -h + J_0\, s\, g(h) \tag{1}$$

$$\tau_s \frac{ds}{dt} = 2.8 - s - 9.0\, s\, g(h) \tag{2}$$

$\tau = 5$ and $\tau_s = 50$ are time constants (arbitrary units).

J_0 is a parameter (but later we will always consider $J_0 = 3$).

The gain function is:
$g(h) = 0.2$ for $h < 0.4$
$g(h) = 2h - 0.6$ for $0.4 \leq h \leq 0.8$
$g(h) = 1$ for $h > 0.8$
(as shown on the right)



space for calculations

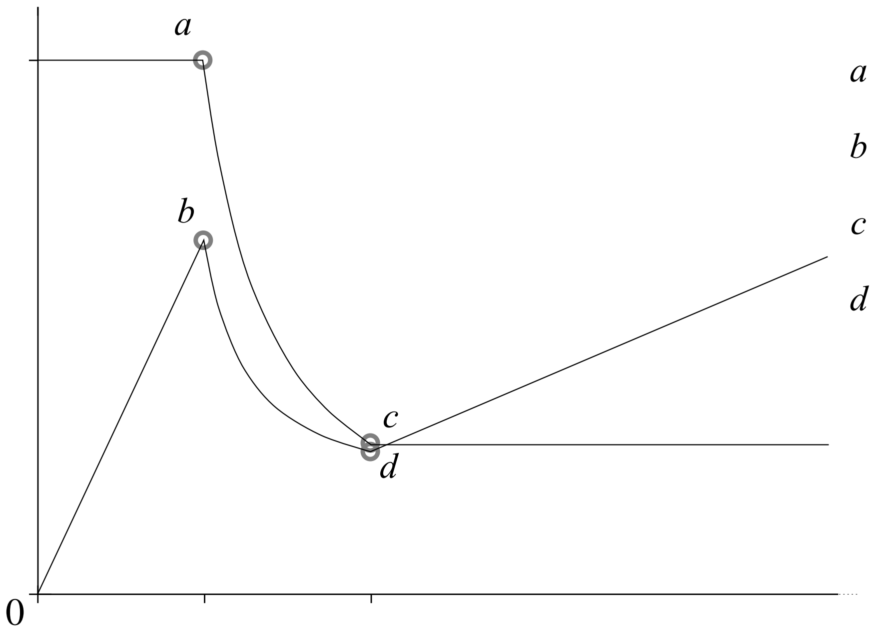
a) Assume $J_0 = 3$ here and for all the following questions. The nullclines are shown below, without axis labels or scale.

- Add the axis labels.
- Label the 2 nullclines.

number of points: [1]

b) Give the numerical values for the 4 circled points a, b, c and d.

number of points: [2]



$a = ($; $)$

$b = ($; $)$

$c = ($; $)$

$d = ($; $)$

c) Evaluate the differential equations at the point $h = 0.5$ and $s = 0$ and draw an arrow in the above graph. (The direction of the arrow should qualitatively point in the 'correct' direction.)

number of points: [1]

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

number of points: [2]

e) Evaluate the differential equations at the point $h = 1.0$ and $s = 1.0$ and draw an arrow in the above graph. (The direction of the arrow should qualitatively point in the 'correct' direction.)

number of points: [1]

f) Draw two trajectories in the graph on the previous page. One starting at $h = 0.5$ and $s = 0$ and another one starting at $h = 0.0$ and $s = 0.8$. *Remark: If you prefer you can do part g) before you finish part f) – it's your choice!*

number of points: [2]

g) Determine analytically the location and stability of the fixed point for arbitrary $\tau_s > \tau$, using Equations 1 and 2 repeated here for convenience:

$$\tau \frac{dh}{dt} = -h + J_0\, s\, g(h) \qquad (3)$$

$$\tau_s \frac{ds}{dt} = 2.8 - s - 9.0\, s\, g(h) \qquad (4)$$

[Hint: you may assume that the fixed point lies in the regime where $h > 0.8$ so that $g(h) = 1$.]

(g1) The fixed point is located at ....

number of points: [1]

(g2) The two eigenvalues (for arbitrary τ and τ_s) are

....

number of points: [2]

(g3) For $\tau = 5$, $\tau_s = 50$, the fixed point is (stable/unstable) because

....

number of points: [1]

(g4) Do the stability properties of the fixed point change, if we change τ_s in the range $0 < \tau_s < 1000$? (keep $\tau = 5$ fixed).

[yes/no] because ....

number of points: [1]

(h) Do the *stability* properties of the fixed point change, if we change J_0 from 3 to 30?

[yes/no] because ....

number of points: [1]

2 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** $\tau_2 = 1$ **and** $\tau_1 = 0.5$ **and** $J_0 = 3$ **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 3 to 10?

....

What happens in the setting of (b) if we decrease J_0 from 3 to 1?

....

number of points: 2

Space for calculations

3 Stochastic processes and ion channels (8 points)

An experimental biologist measures the electrical properties of a single ion channel and finds

$$I(t) = g(t - t_{\text{open}})\,(u - E) \tag{5}$$

where E is the reversal potential of the channel and t_{open} is the moment when the ion channel opens stochastically. She finds by careful observations that, 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

$$g(s) = g_0 \quad \text{for} \quad 0 < s < t_d \tag{6}$$

and zero otherwise. Here g_0 denotes the conductance in the open state.

(a) She now runs an experiment in voltage clamp with constant voltage $u_0 \neq E$ in a patch that contains many ion channels ($N \gg 1$) and finds that the moments of opening can be described by a Poisson process with constant rate $\nu \ll 1/t_d$. Note that ν is the total rate (stochastic intensity) of all the observed ion channels together.

Calculate the mean input current passing through the patch of membrane caused by these stochastic ion channels.

$\langle I(t) \rangle =$

....

number of points: 2

space for calculations

(b) As in (a), but calculate the variance

$\langle I(t)I(t)\rangle - \langle I(t)\rangle^2 =$

....

....

....

number of points: 2

(c) As in (a) but calculate the autocorrelation defined (for $\tau > 0$) as

$\langle I(t)I(t+\tau)\rangle - \langle I(t)\rangle^2 =$

....

....

....

number of points: 2

(d) Make a graph of the autocorrelation as a function of τ in the space here (consider positive and negative τ).

number of points: 2

space for calculations

4 Linear differential equations and interval distributions (7 points plus 5 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. The following questions are completely independent from those of the previous exercise and do not need any solutions from the previous one. We study the following model of an ion channel.

The current through a single ion channel is

$$I(t) = g(t - t_{\text{open}})\,(u - E) \tag{7}$$

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

$$g(s) = g_0 \quad \text{for} \quad 0 < s < t_d \tag{8}$$

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

$$\frac{d\nu}{dt} = -\frac{\nu - \nu_0(u)}{\tau} \tag{9}$$

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 for a time $T = 1000t_d$. We assume that $T \gg \tau$.

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

....

Given a certain fixed voltage $u > E$, what is the **interval distribution between one opening and the next opening??**

....

....

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 will the channel be open? Why?

....

....

....

number of points: 2

Space for calculations

(d)**Bonus question 1** 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.

....

....

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 2 - 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 the fraction $m(t)$ of open channels for arbitrary **time-dependent** voltage.

....

....

Did you have to make additional assumptions for your equation? If so, which ones:

....

....

Compare the mathematical expression of your final equation with that of the gating variables in the Hodgkin and Huxley formalism. To do so, assume that $m(t)$ is close to $m_0(u(t))$ and approximate $m(t) = m_0(u(t)) + \delta m(t)$. Derive the expression of the voltage-dependent time constant of the gating variable m.

....

....

number of points: 3