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

Neural Networks and Biological Modeling Exam
23 June 2011

- Write your name in legible letters on top of this page.
- 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. .... / 12 pts
2. .... / 15 pts
3. .... / 5 pts
4. .... / 11 pts
5. .... / 10 pts
6. .... / 9 pts

Total: .... / xx pts

1 Model of an Ion Channel (12 points)

Alan and Andrew think that they have discovered a new type of ion channel. They describe the current I_{ion} through the channel by the equation:

$$I_{\text{ion}} = \bar{g}_{\text{ion}} n(t)^p \left(u(t) - E_{\text{ion}}\right), \tag{1}$$

where $u(t)$ is the membrane potential and $\bar{g}_{\text{ion}}$, p and E_{ion} are constants. $n(t)$ is a dimensionless variable that obeys a first-order differential equation:

$$\frac{dn}{dt} = \alpha(1 - n(t)) - \beta n(t), \tag{2}$$

with two constants α and β. $n(t)$ takes values in the interval $(0, 1)$.

a) [1.5 pts] What is the biological interpretation of the following parameters and variables:

$\bar{g}_{\text{ion}}$: ....

E_{ion} : ....

n : ....

b) [0.5 pts] What is the physical unit of $\bar{g}_{\text{ion}}$?

$[\bar{g}_{\text{ion}}]$: ....

c) [1 pt] Rewrite equation (2) in the form $\frac{dn}{dt} = -\frac{n(t) - n_\infty}{\tau_n}$. Identify n_∞ and τ_n as functions of α and β. Note that in general, these parameters are voltage-dependent. Here, we assume that only n_∞ is a function of u, but not τ_n.

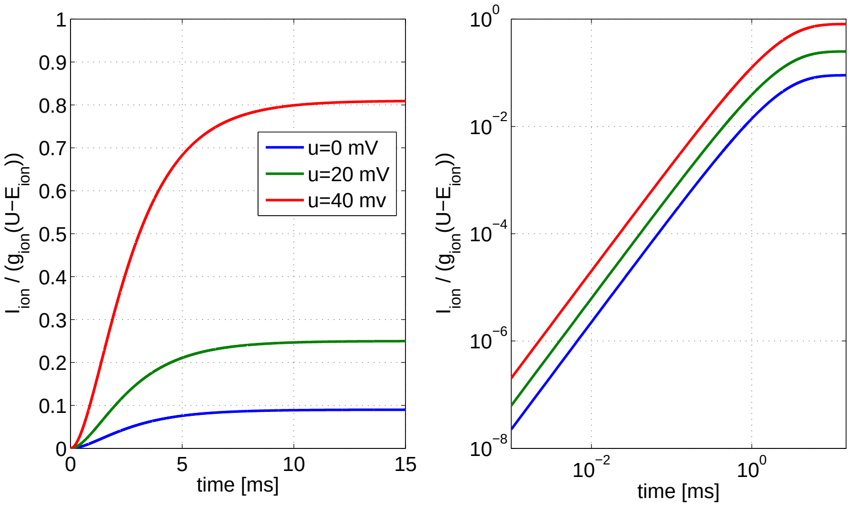
$n_\infty =$ ....

$\tau_n =$ ....

d) [1 pt] Alan works in voltage-clamp mode, i. e. the voltage is kept constant. What is the general solution of $n(t)$ for all $t > 0$ with arbitrary initial condition $n(t = 0) = n_0$?

$n(t) =$ ....

e) [3 pts] To determine the voltage-dependence of n_∞, Alan and Andrew pharmacologically block all other ion channels except the one considered here. They measure the current across the membrane as a response to voltage jumps of various amplitudes. For $t < 0$, the voltage $u(t)$ is at $u(t) = E_{\text{ion}}$. For $t \geq 0$, they clamp the voltage at $u(t) = u_i$ with three different amplitudes: $u_i = \{0, 20, 40\}$ mV. The left figure shows the normalized current $I_{\text{ion}}(t)/(\bar{g}_{\text{ion}}(u_i - E_{\text{ion}}))$ as a function of time. The right figure uses logarithmic scales.



From the plots, how can you determine the (integer) exponent p that appears in equation (1)? To do this, first find a linear approximation to the solution of $n(t)$ for $t \ll \tau_n$ and plug the result into equation (1) (Hint: Use $\exp(-x) \approx 1 - x$ for $x \ll 1$ and assume that $n_0 \approx 0$). Then, take the logarithm on both sides.

$n(t) \approx$ ....

$I_{\text{ion}}(t) \approx$ ....

$\log I_{\text{ion}}(t) \approx$ ....

From the graphs, you can now read off p:

$p =$ ....

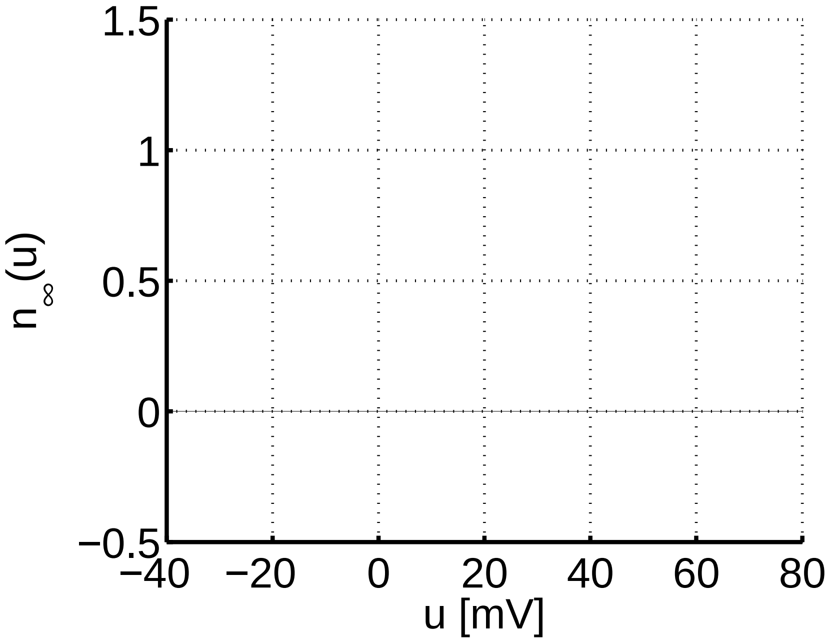
f) [2 pts] After you determined p, obtain n_∞ from the plots:

$n_\infty(u = 0 \text{ mV}) \approx$ ....

$n_\infty(u = 20 \text{ mV}) \approx$ ....

$n_\infty(u = 40 \text{ mV}) \approx$ ....

Plot the values into the diagram and sketch the shape of $n_\infty(u)$.



g) [1 pt] After waiting for a long time T (i.e. $T \gg \tau_n$), Alan and Andrew release the voltage clamp and the voltage is allowed to follow its dynamics, i. e. apart from the ion current (1), the membrane can be considered as passive. What is the direction of the current directly after the release of the clamp? In other words, will the current de- or increase the membrane potential (for your information: $E_{\text{ion}} \approx -80$ mV)?

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h) [2 pts] Our two experimenters are debating about the asymptotic value of the membrane potential a long time after the release of the voltage-clamp. Alan argues that $\lim_{t\to\infty} u(t) = E_{\text{ion}}$ because in that case $I_{\text{ion}} \equiv 0$ and the voltage has reached a stationary value. Andrew claims that as the ion channel is never absolutely closed ($n(t) \neq 0$), the ionic concentrations inside and outside the membrane will ultimately align and any potential difference will vanish, i. e. $\lim_{t\to\infty} u(t) = 0$. Help to settle the debate. (Hint: Consider the role of ion pumps.)

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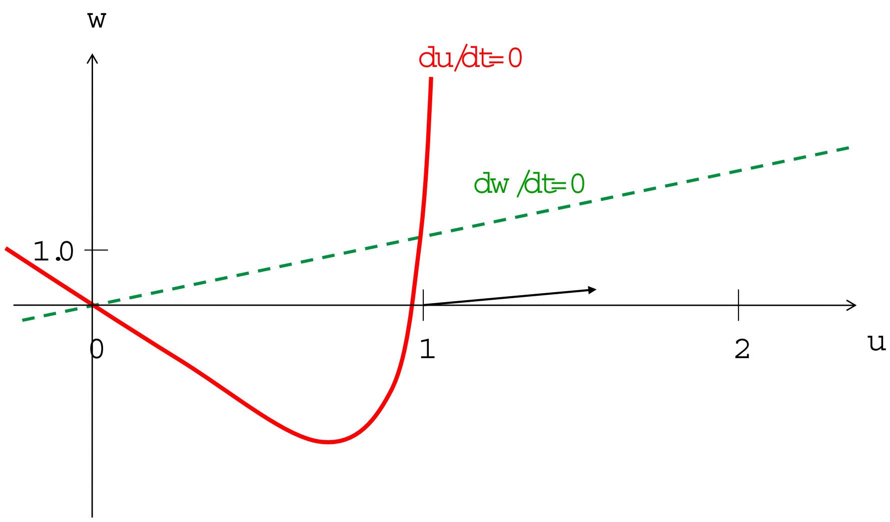
2 Adaptive Nonlinear Integrate-and-Fire Model (15 points)

A nonlinear integrate-and-fire neuron model with adaptation is described by the two differential equations:

$$\frac{du}{dt} = \gamma\,(F(u) - w) + I \tag{3}$$
$$\frac{dw}{dt} = \epsilon(-w + u) \tag{4}$$

If $u > 2.5$ the variable u is reset to $u = -0.2$. The variable w is increased by an amount of 0.5 during reset. The constants γ and ϵ have appropriate units (you may assume, $\gamma = 0.5$ and $0 < \epsilon < 1$). You may assume that the point (0,0) is a stable fixed point. The nullclines for a standard set of parameters are shown in the figure here ($I = 0$).



a) [2 pts] In the above graph, add representative arrows indicating qualitatively the flow on the nullclines *and* in different regions of the phase plane. One flow arrow at the point $(1.0, 0.0)$ is already indicated in the graph.

b) [2 pts] In the same graph, indicate a trajectory in the phase plane, after a stimulus $I(t) = 0.5\delta(t)$ has been applied [δ denotes the Dirac delta function]. Note, if necessary, that there is a the reset condition.

c) [1 pts] In the same graph, indicate a trajectory in the phase plane, after a stimulus $I(t) = 1\delta(t)$ has been applied [δ denotes the Dirac delta function]. Note, if necessary, that there is a the reset condition.

d) [2 pts] Draw qualitatively (by hand) the voltage trajectory $u(t)$ for the two cases in b and c here:

e) [1 pt] Without calculation, what can you say about the stability of the fixed point at $u = 1, w = 1$? Give an argument.

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f) [1 pt] What kind of stimulus could have caused a shift in the nullclines to the following picture?

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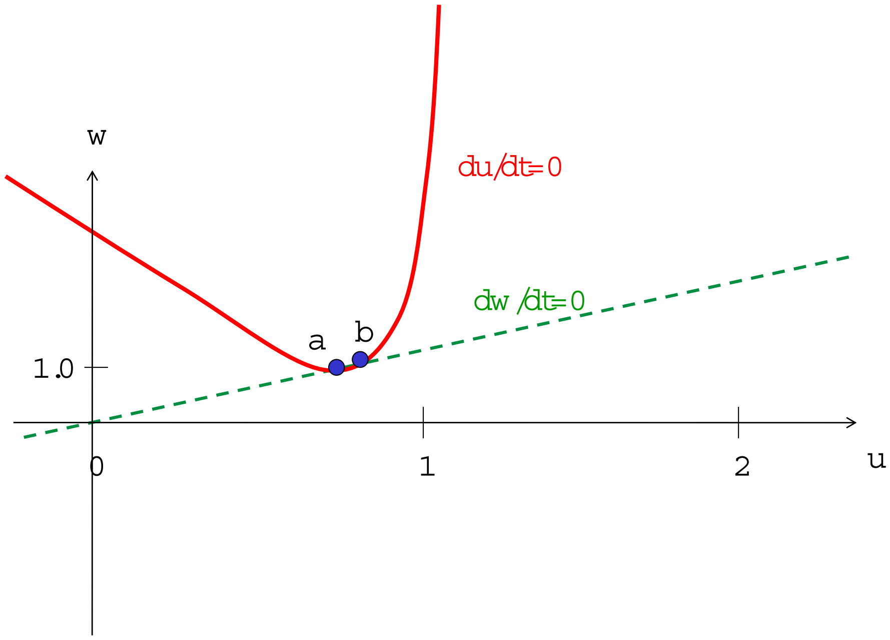

g) [1 pt] Without calculation, and without adding new arrows, what can you say about the fixed point marked b? Give an argument.

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h) [3 pts] With explicit calculation, what can you say about the stability of the fixed point marked a? You can denote the derivative of $F(u)$ by F'.

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i) [1 pt] Assume that $\epsilon \ll \gamma$ and approximate the system of two equations by a single equation. Give this equation:

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j) [1 pt] What follows in this limit for the stability of the fixed point marked by a?

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3 Stochastic ion channel opening (5 points)

Consider a passive membrane with N ion channels of the same type, i. e. the ionic current is given by:

$$I_{\text{ion}}(t) = (u(t) - E_0)g(t). \tag{5}$$

with membrane potential $u_(t)$ and constant E_0. The total conductance $g(t) = \sum_j^N \sum_f g_j(t - t_j^f)$ is created by the openings at times t_j^f of the N individual channels. The opening of a single ion channel can be modeled by a transient increase in conductance $g_j(s)$ where s is the time since channel opening. The time course of $g_j(s)$ is rectangular: When a channel is open, it contributes to the total conductance by g_0. After opening, the channel closes again after time τ_c and its conductance is 0. Assume that $\tau_c^{-1} \gg \nu$ and that the N ion channels open stochastically with rate ν each.

a) [1 pt] Determine an expression for $g_j(s)$ when s is the time since channel opening (Hint: Make use of the Heaviside function $\theta(x)$, defined as $\theta(x) = 0$ for $x \leq 0$ and $\theta(x) = 1$ for $x > 0$).

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b) [2 pts] Show that the mean conductance $\bar{g} = \langle g \rangle_t$ is given by $\bar{g} = N g_0 \nu \tau_c$.

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c) [2 pts] Calculate the variance of the ionic current.

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4 Passive membrane with stoachastic channel opening (11 points)

A passive membrane,

$$\frac{du}{dt} = -\frac{u(t) - u_r}{\tau_m} + \frac{RI(t)}{\tau_m}, \tag{6}$$

(equilibrium potential u_r, membrane time constant τ_m and constant R) is driven by an input current of the form

$$I(t) = g(t)(u(t) - E_0). \tag{7}$$

The mean conductance is given by $\bar{g}$.

a) [2 pts] Show that the linearized current around the mean conductance $\bar{g}$ and the (unknown) mean membrane potential $\langle u \rangle$ is given by

$$I(t) \approx \bar{g}\,(u(t) - \langle u \rangle) + \sum_{i,j} g(t - t_i^{(j)})(\langle u \rangle - E_0). \tag{8}$$

(Hint: Write $g(t) = \bar{g} + \delta g(t)$ and $u(t) = \langle u \rangle + \delta u(t)$ and neglect higher-order terms to obtain a linearized version of Eq. (7).)

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b) [6 pts] Plug the result into eq. 6 to get a model of a passive membrane with effective time constant τ_m^* and effective equilibrium potential u_r^* such that the input current is now *voltage-independent*:

$$\frac{du}{dt} = -\frac{u(t) - u_r^*}{\tau_m^*} + \frac{R^*}{\tau_m^*} g(t). \tag{9}$$

$\tau_m^* =$ ....

$u_r^* =$ ....

$R^* =$ ....

c) [3 pts] Calculate the mean membrane potential $\langle u \rangle$ self-consistently.

$\langle u \rangle =$ ....

Room for additional calculations:

5 Associative Memory (9 points)

Consider the Hopfield network defined by the following equations

$$S_i(t+1) = \text{sign}\left(\sum_j^N w_{ij} S_j(t)\right) \tag{10}$$

and

$$w_{ij} = \frac{1}{N}\sum_\mu \xi_i^\mu \xi_j^\mu \quad (i \neq j)$$

where N is the number of units and $\xi \in \{-1, +1\}$. **a)** [1.5 pts] What is the interpretation of:

S : ....

w : ....

ξ : ....

b) [0.5 pts] What does Eq. (10) describe?

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c) [2 pts] Suppose you store a single pattern ξ, show that the pattern is a fixed point of the dynamics.

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d) [5 pts] The dynamics of the system can be seen as an evolution according to the potential energy landscape

$$H = -\sum_{i=1}^{N} \sum_{j=i+1}^{N} w_{ij} S_i S_j. \tag{11}$$

The central property of this idea is that the dynamics never increases the potential energy. Show that $H(t+1) \leq H(t)$. (Hints: For simplicity consider the asynchronous update, where only one bit is flipped at a time (or none). Assume without loss of generality that at time t, unit 1 was updated. Write $H(t+1) = H(t) + X$ and determine the sign of the expression X.)

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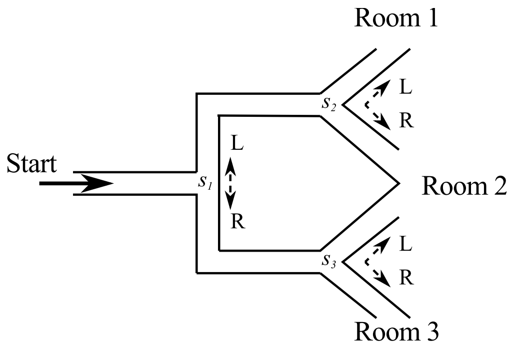
6 Reinforcement Learning (10 points)

One of your friends is working on the following experiment: a rat is released at the entrance of a small maze, as shown on Figure 1a. At each branch, the rat has to decide whether to go left or right (it never turns back) and eventually reaches one of three rooms, after exactly two decisions. When it arrives in a room, the rat is given food pellets according to Table 1b: always one pellet in room 1, always no food in room 3 and 0 or 3 pellets with $p = 0.5$ in room 2. Then the trial is stopped and the rat is put back to the entrance of the maze. Your friend tells you that his rats get on average 1.47 pellets per trial, but doesn't know what he can deduce about the rat behavior. Using your knowledge of reinforcement learning, you decide to help him.

a) [3 pts] During an initial learning phase, the rat updates its belief about the expected reward $Q(s, a)$ in the future when action a is chosen in state s. Consider the following update rule for the Q-value:

$$\Delta Q(s, a) = \eta[r - (Q(s, a) - Q(s', a^*))] \tag{12}$$



(a) Maze layout

Room	Probability	Reward
Room 1	1	1
Room 2	0.5	3
	0.5	0
Room 3	1	0

(b) Reward table

Figure 1: Setup of the reinforcement learning experiment.

with $a^* = \arg\max_a Q(s', a)$. Here, s' is the state following the state-action pair (s, a). If an action at state s led to the end of a trial, set $Q(s', a^*) \equiv 0$. What are the Q-values at the end of the learning phase? Fill the values in the table below.

$\mathbf{Q(s,a)}$	$s = s_1$	$s = s_2$	$s = s_3$
$a = L$			
$a = R$			

b) [2 pts] Assume that the rat chooses its next action according to an ε-greedy policy, i. e. with probability ε, it chooses a random action and with probability $1-\varepsilon$, it chooses the best action according to $a^* = \arg\max_a Q(s, a)$. If the maximal Q-value is shared by several actions, a random action a among this set is chosen. What is the expected reward per trial for:

$\epsilon = 0 : \langle R \rangle =$ ....

$\epsilon = 1 : \langle R \rangle =$ ....

c) [2 pts] For what choice of ε does Eq. (12) correspond to the SARSA algorithm? Why?

$\epsilon =$ ....

because : ....

d) [3 pts] Calculate the expected reward per trial for arbitrary choice of $\varepsilon \in (0, 1)$. Which ε gives the highest expected reward, i. e. $\varepsilon^* = \arg\max_\varepsilon \langle R \rangle(\varepsilon)$? Interpret your result. Can you think about a modification of the experimental setup for which a $\varepsilon \neq \varepsilon^*$ would be more advantageous?

$\langle R \rangle(\varepsilon) =$ ....

$\varepsilon^* =$ ....

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