2. Exercise Sheet – Brain-Inspired Computing (WS 15/16)

Due date 26.10.16.

Name(s): Group: Points: ___/___/___/___

2.1 Passive electrical properties of the cell membrane (15 Points)

Cortical neurons have extremely diverse morphologies (`http://www.nature.com/nrn/journal/v5/n10/full/nrn1519.html`) which lend to correspondingly diverse electrophysiological properties. However, simplified models can still be very helpful by offering instructive order-of-magnitude approximations.

a) Assume that a neuron can be reduced to a spherical soma with a diameter of 20 µm. The thickness of the cell membrane is $d = 5\,\text{nm}$ and its relative permittivity (dielectric constant) $\epsilon_r = 3$. Calculate the specific and the total membrane capacitance.

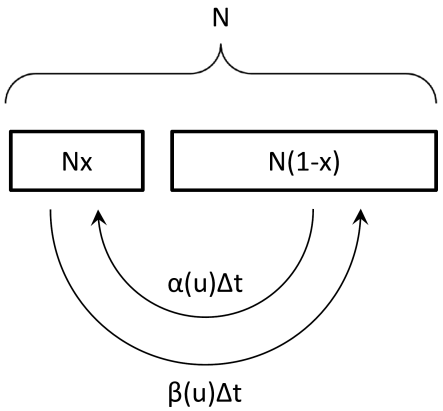
b) The Na^+ ion concentration inside the cell is $[Na^+]_{in} = 3 \cdot 10^7\,\text{ions}/\mu\text{m}^3$. How many Na^+ ions need to be moved across the membrane to shift the membrane potential by 10 mV? Compare that to the total number of Na^+ ions inside the cell.

c) In addition to the Na^+ and K^+, Ca^{2+} also plays a (small) role in determining the equilibrium potential of the membrane. Assuming an extracellular concentration of $[Ca^{2+}]_{out} = 1.5\,\text{mmol}$ and an intracellular one of $[Ca^{2+}]_{out} = 10 \cdot 10^{-4}\,\text{mmol}$, what is the Ca^{2+} reversal potential at room temperature?

2.2 Channel activation functions (25 Points)

Since the variables m, n and h represent probabilities of particular molecular gates being open, some authors prefer describing them with a different set of equations that more intuitively depict their stochastic switching between "open" and "closed" states.

a)



Assume that a protein is "open" with the probability x. Out of N such proteins that are embedded in a membrane, Nx will be open and $N(1-x)$ closed, on average, at any point in time. If, during a very short time interval Δt, the protein may switch from "open" to "closed" with the probability $\beta_x(u)\Delta t$ and from "closed" to "open" with the probability $\alpha_x(u)\Delta t$, then the population of open proteins will lose $Nx \cdot \beta_x(u)\Delta t$ and gain $N(1-x) \cdot \alpha_x(u)\Delta t$ members during this Δt.

Write this down as a differential equation for x (we can replace Δs with "d"s in the limit of $\Delta t \to 0$).

Hint: the total number of channels does not change, so $\Delta(Nx) = N\Delta x$.

b) Transform the ODE in a) to the form

$$\dot{x} = \frac{1}{\tau_x(u)}[x_0(u) - x]$$

(which we used in the lecture to describe the dynamics of the activation variables m, n and h).

What are the required transformations from α_x and β_x to τ_x and x_0?

c) Show that with the switching rates

$$\alpha(u) = \frac{1}{1 + e^{-\frac{u+a}{b}}} \quad \text{and} \quad \beta(u) = \frac{1}{1 + e^{\frac{u+a}{b}}}$$

the stationary value of the activation variables x can be written as

$$x_0(u) = \frac{1}{2}\big[1 + \tanh\left[\beta(u - \Theta_{\text{act}})\right]\big].$$

Determine the activation threshold Θ_{act} and the activation slope β.

2.3 Euler moving forward (60 Points)

The "forward Euler" method is the simplest and most straightforward way of numerically approximating solutions to complex systems of coupled ODEs. In its most general form, such a system can be written as

$$\frac{d\vec{x}}{dt} = \vec{F}(\vec{x}, t),$$

which is shorthand for

$$\begin{aligned} \frac{dx_1(t)}{dt} &= f_1(x_1(t) \dots x_n(t), t) \\ &\vdots \\ \frac{dx_n(t)}{dt} &= f_n(x_n(t) \dots x_n(t), t). \end{aligned}$$

The forward Euler algorithm then simply does the following:

1) Initialize $\vec{x}(t = 0)$ with $\vec{x}_0$.
2) Calculate $\vec{\Delta x}(t) = \Delta t \cdot \vec{F}(\vec{x}, t)$.
3) Increment $\vec{x}$ by $\vec{\Delta x}$, i.e., $\vec{x}(t + \Delta t) = \vec{x}(t) + \vec{\Delta x}(t)$.
4) Set $t \leftarrow t + \Delta t$, go to 2), and repeat until $t \geq t_{\text{sim}}$. (t_{sim} is the desired simulation duration)

In the limit $\Delta t \to 0$, the calculation trajectory $(\vec{x}(0), \vec{x}(\Delta t), \vec{x}(2\Delta t), \dots, \vec{x}(n\Delta t))$ converges towards the true trajectory of the system.

a) **1D case (stable system)**
Assume the single linear ODE $\tau\dot{u} = -u + I(t)$ (to avoid unnecessary complications, use unit-free coordinates) with $\tau = 10$ and $I = 1\Theta(t - 100)$. Simulate the system with $u(t = 0) = 0$ and $t_{\text{sim}} = 200$ using several different $\Delta t = 30, 20, 10, 5$ and 0.1. Compare with the exact solution (sheet 1, ex. 2b).

b) **1D case (unstable system)**
Repeat a), only with a switched sign in front of n: $\tau\dot{u} = u + I(t)$.

c) **2D case**
The harmonic oscillator obeys the 2nd order ODE $\ddot{x} = -x$ (w.l.o.g., all constants are set to 1). Any higher-order ODE can be easily decomposed into a set of lower-order ODEs by introducing additional variables. For the harmonic oscillator, this requires the velocity $y = \dot{x}$ to the picture (in addition to position x and the acceleration $\ddot{x}$:

$$y := \dot{x} \Rightarrow \dot{y} = -x \quad \text{and} \quad \dot{x} = y$$

Simulate this system for $t_{\text{sim}} = 10$ using the forward Euler method for $x(t = 0) = 1$, $y(t = 0) = 0$ and compare it to the exact solution. What happens if the time step Δt is too large? (Hint: try $\Delta t = 1, 0.1$ and 10^{-5}).

d) **4D case**
Simulate a Hodgkin-Huxley neuron with forward Euler. As an external stimulus, use a step current that is strong enough to elicit spikes. Take care to choose an appropriately small Δt. Use the definitions from the tables below.

The values, as originally reported by Hodgkin and Huxley in 1952, are based on a voltage scale where the resting potential is zero. To comply with electrophysiological measurements, the voltage scale had to be subsequently shifted down by 65 mV.

x	E_x	g_x
Na	115 mV	120 mS cm^{-2}
K	−12 mV	36 mS cm^{-2}
l	10.6 mV	0.3 mS cm^{-2}

Reversal potentials and conductances.

x	α_x(u[mV])	β_x(u[mV])
n	$(.1 - .01u)/(\exp(1. - .1u) - 1.)$	$0.125\exp(-u/80.)$
m	$(2.5 - .1u)/(\exp(2.5 - 0.1u) - 1.)$	$4.\exp(-u/18.)$
h	$.07\exp(-u/20.)$	$1./(\exp(3. - .1u) + 1.)$

Gating variables.

2.4 **Hodgkin-Huxley bonus** (50 Points)

Use your forward Euler Hodgkin-Huxley integrator from ex. 3 to reproduce the three interesting effects from the lecture: the lack of a rheobase, the inhibitory rebound and the resonant spiking.