

CSE2330 Introduction to Computational Neuroscience

From soap to volts — hardware of the brain

Tutorial 5 **Duration:** two weeks

5.1 About this tutorial

The objective of this tutorial is to study a low level electrical activities of a neuron, in particular the way the train of spikes arriving at a synapse is aggregated into a post-synaptic potential (PSP) at the membrane of the neuron, and the way a neuron generates a train of spikes known as action potentials.

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getting started ...

The amount of information and the number of technical terms, computational methods and concepts that you are expected to master increase quickly, therefore, you are strongly advised to come well prepared to the practical classes.

Read at least the previous prac manuals, but you cannot go wrong if you also read related lecture notes and book chapters.

I also encourage you to execute MATLAB scripts line-by-line in order to build-up your understanding of computational methods involved.

5.1.1 Biological neurons and their connections

Recall that a biological nerve cell known as a neuron consists of the following major parts illustrated in Figure 1.

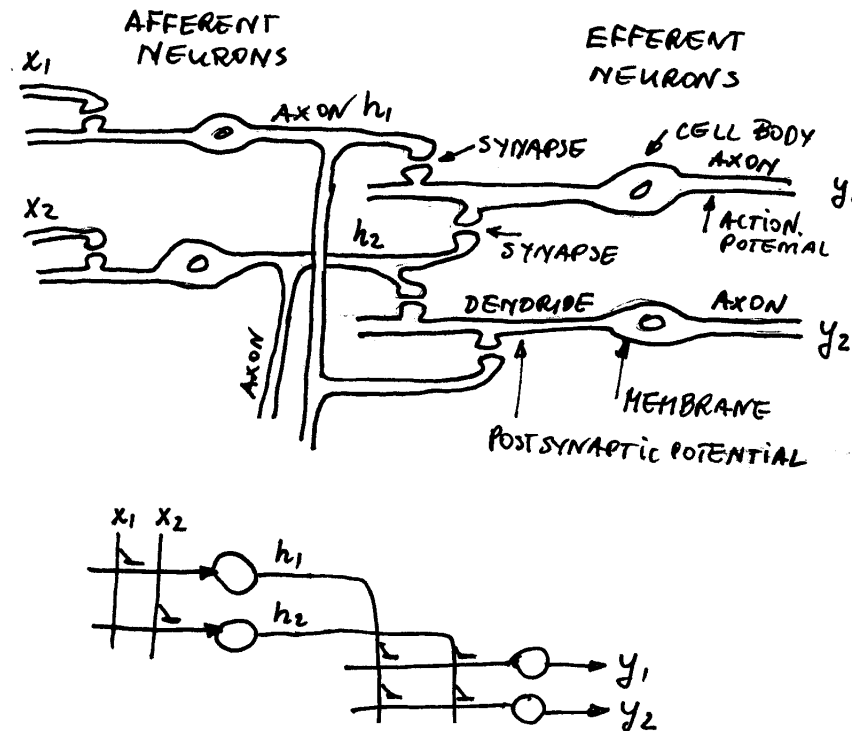


Figure 1: Major components of biological neurons and their networks

Identify the **cell body**, **membrane**, **axon**, **dendrite** and **synapses**.

We will study the low level neuronal activities that can be described in the following simplified way:

- An efferent neuron generates a train of spikes known as **action potentials**.
- The spikes arrive at the synapse of an afferent neuron and generate a **post-synaptic potential (PSP)** at the membrane of the neuron.

Other facts to remember are:

- Working of neurons is described by the movements of chemicals and associated ions which are electric carriers (charges)
- Movement of electric charges creates an electric current which flows under the influence of related voltages, or potentials.

The best analogy for the above electrical quantities is a water flowing (current) under pressure (potential/voltage) through small pipes (resistors) and big containers (capacitors).

5.2 Cell membrane as an RC electrical circuit

The biological membrane surrounding the cell can be first approximated as an electrical circuit consisting of a conductor (resistor) and a capacitor.

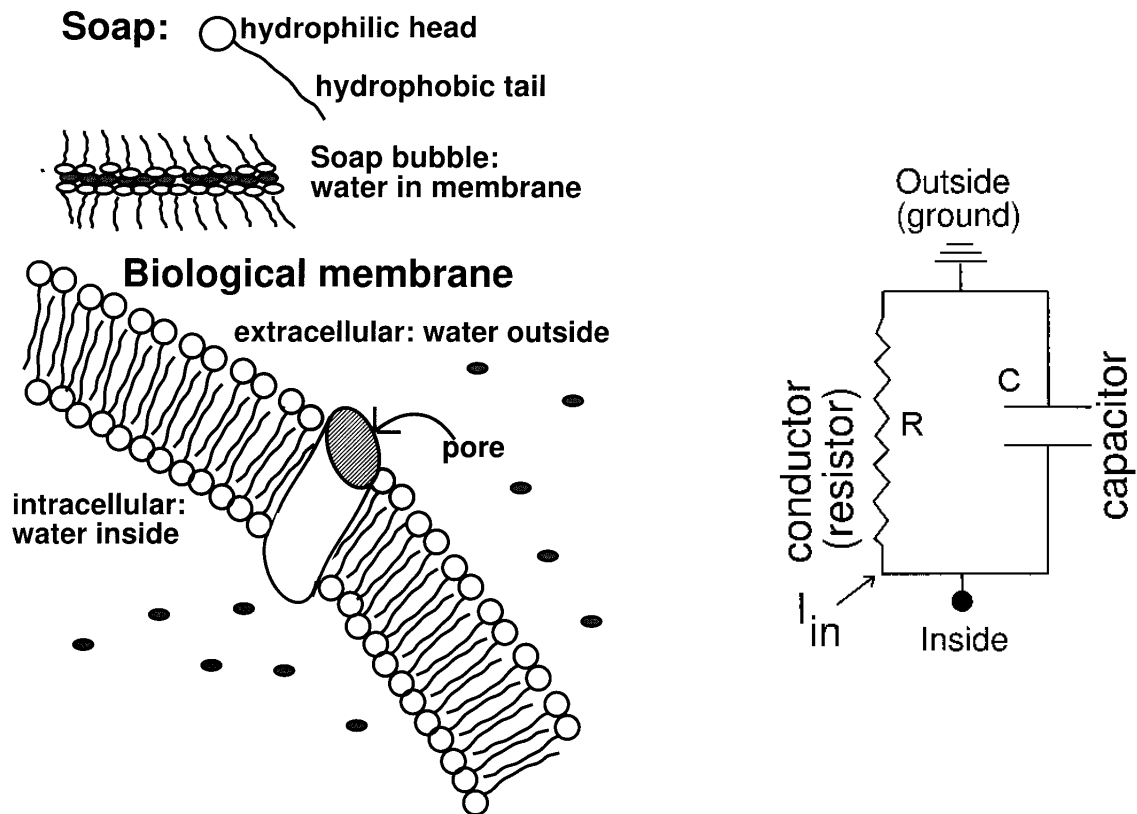
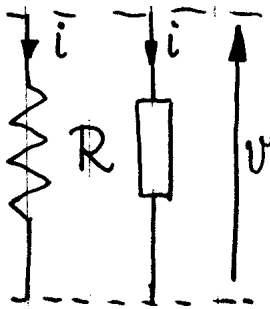


Figure 2: The cell membrane and its RC model

- Modeling the neuron as an electrical circuit involves predicting **voltage changes based on current flow**.
- In the case of neurons we typically are injecting currents, or thinking about the effects of extra pores that cause extra current to flow into the cells.
- Electric current is a rate of change of charge.
- Typical charges are: electrons, ions and charged proteins

5.2.1 Resistors

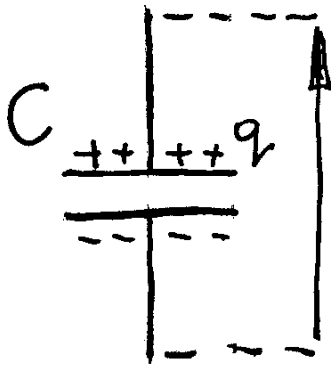


- Voltage across a resistor is proportional to the current flowing through the resistor.

$$v = R \cdot i = \frac{1}{g} i$$

- Resistance (or its inverse, conductance) is a property of material through which the current flows.
- If we inject current into the resistor a voltage across the resistor appears.
- If we apply voltage then the current flows.

5.2.2 Capacitors

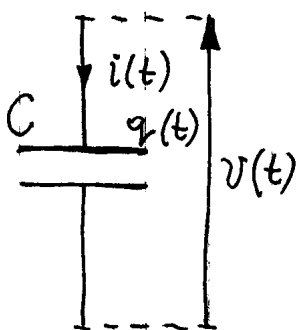


- Charge on a capacitor is proportional to the voltage applied to the capacitor.

$$q = C \cdot v$$

- Conversely, voltage across the capacitor is proportional to the amount of charge stored on the capacitor
- Capacitance is a property of the geometry of the charge storing plates, the membrane, in our case.

Current through a capacitor

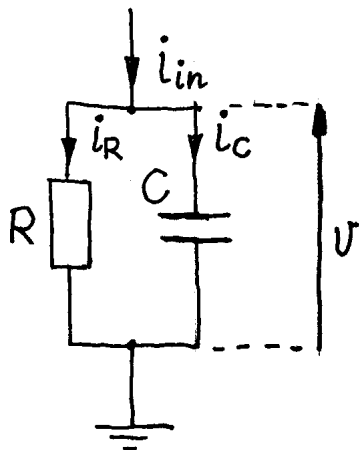


- If the charge stored in the capacitor varies, then the current (derivative of charge) flows and can be calculated as

$$q = C \cdot v ; \quad i = \frac{dq}{dt} = C \frac{dv}{dt}$$

- Current flowing through the capacitor is proportional to the gradient (time derivative) of the voltage on the capacitor

5.2.3 Summing currents — Kirchoff's law



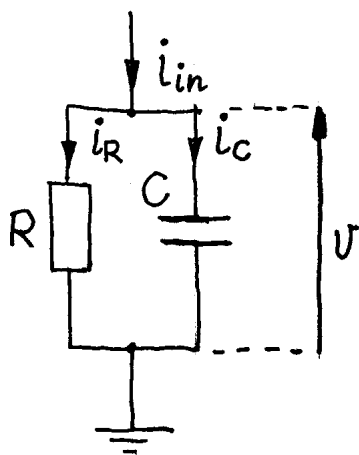
- Kirchoff's law on conservation of charge says that the sum of currents incoming into an electric node and outgoing from the node is equal.

Hence

$$i_{in} = i_R + i_C$$

It means that the injected current, i_{in} flows into the resistor i_R and capacitor i_C

5.2.4 Equation of the RC circuit



- Substituting expressions related currents and voltages in resistors and capacitors, we can write the following equation:

$$i_{in} = \frac{1}{R}v + C \frac{dv}{dt}$$

- For a given injected current, the unknown quantity is a time varying voltage across the membrane $v = v(t)$. Therefore the equation, after multiplication by R is usually re-written in the form with swapped left and right-hand sides:

$$RC \frac{dv}{dt} + v = R i_{in}$$

Let us denote

$$\tau_m = R \cdot C \text{ — a **time constant** of the membrane, and } V_{in} = R \cdot i_{in}$$

The equation for the voltage across the membrane can now be written as:

$$\tau_m \frac{dv}{dt} + v = V_{in}$$

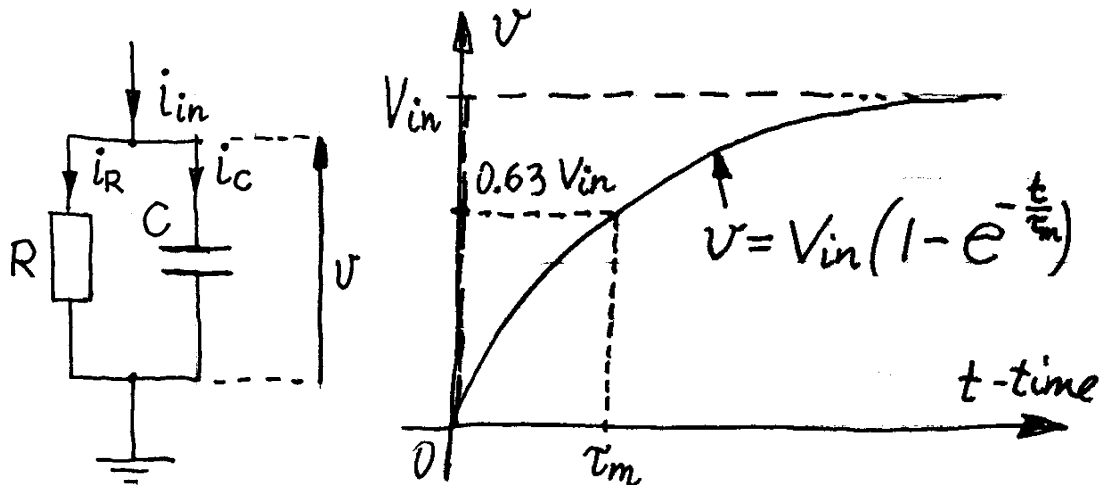
It is a **first order, linear differential equation** for $v(t)$ that can be easily analytically solved if you know the trick. Let us guess that the solution for a constant i_{in} is:

$$v(t) = V_{in}(1 - e^{-\frac{t}{\tau_m}})$$

we can verify this solution substituting it back into the equation and confirming that LHS = RHS.

The solution described the way the voltage across the membrane, $v(t)$, evolves with time.

5.2.5 Time constant of the RC circuit



- If a constant current is injected, the voltage across the membrane (RC circuit) grows exponentially, until it saturates at the value $V_{in} = R i_{in}$
($e \approx 2.7183$ is the base of the natural logarithm)
- If analytical solution is known (which is hardly ever the case) it is simple to use your favourite MATLAB to get the plot of the voltage.

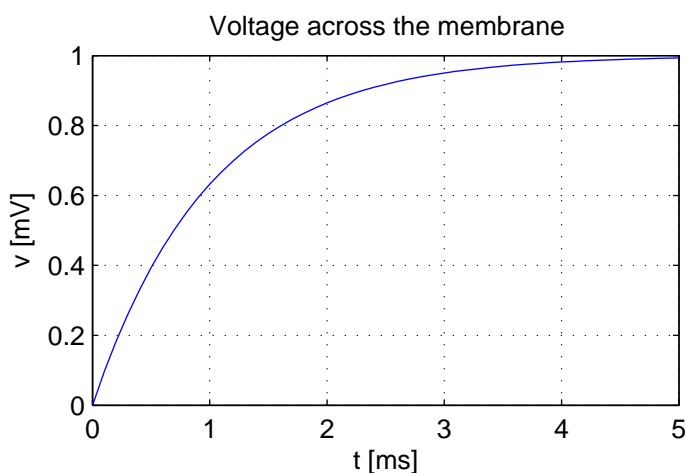
```

g = 1 ;           % mS/cm^2
% R = 1/g ;      % kOhm x cm^2
C = 1 ;          % uF/cm^2
taum = C/g ;    % ms
Iin = 1 ;        % uA/cm^2
Vin = Iin/g ;   % mV
t = 0:0.1:5 ;   % time in ms
v = Vin*(1-exp(-t/taum));
plot(t, v), grid on

```

Note the typical values of parameters:

- conductance : $g = 1 \text{ mS/cm}^2$
- capacitance : $C = 1 \mu\text{F/cm}^2$
- time constant : $\tau_m = \frac{C}{g} = 1 \text{ ms}$
- injected current : $i_{in} = 1 \mu\text{A/cm}^2$
- max voltage : $V_{in} = \frac{i_{in}}{g} = 1 \text{ mV}$



Exercise 5.1

Calculate and plot on a single figure voltage across the membrane for three different time constants to demonstrate how the time constant influences the change of the voltage

□

2 marks

If analytical solution cannot be found, differential equations can be solved recursively using approximation of derivatives.

$$\tau_m \frac{dv}{dt} + v = V_{in} \quad \text{use:} \quad \frac{dv}{dt} \approx \frac{\Delta v}{\Delta t} = \frac{v(t + \Delta t) - v(t)}{\Delta t}$$

Substitution yields:

$$\frac{\tau_m}{\Delta t} (v(t + \Delta t) - v(t)) + v(t) = V_{in}$$

Dividing by $\frac{\tau_m}{\Delta t}$ and grouping the like terms we obtain

$$v(t + \Delta t) = \left(1 - \frac{\Delta t}{\tau_m}\right) v(t) + \frac{\Delta t}{\tau_m} V_{in}$$

This can be written in the following simple form:

$$v(k + 1) = r \cdot v(k) + (1 - r) \cdot V_{in} \quad \text{where} \quad r = 1 - \frac{\Delta t}{\tau_m} \quad \text{and} \quad t = k \cdot \Delta t$$

This equation is a simple geometric progression with the ratio r and can be easily solved recursively with a simple program, starting with zero initial value.

```
v(1) = 0;
for k = 1:K
    v(k+1) = r*v(k) + (1-r)*Vin;
end
```

5.3 Temporal integration

- Consider a **current pulse** of duration t_p ms **injected through the membrane**,
- Results depends on the relative ratio of the current pulse duration t_p and the membrane's time constant τ_m

Consider the following MATLAB script:

```
% TempInteg.m
% Voltage across membrane after
% injection of m current pulses
% fixed frequency
clear
```

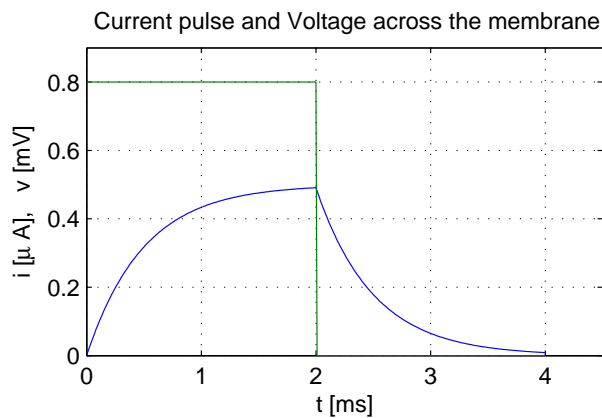
```

% membrane parameters
g = 0.8 ; % mS/cm^2 conductance
C = 2 ; % uF/cm^2 capacitance
taum = C/g; % ms membrane time constant
Iin = 0.8; % uA/cm^2 current pulse amplitude
Vm = Iin/g; % mV equivalent voltage amplitude
tp = 4 ; % ms Current pulse period
tp1 = 1; % ms Current pulse duration
kk = 40 ; % number of time steps per period tp
dt = tp/kk; % ms Time step
kk1 = round(tp1/dt) ; % steps per pulse
r = 1-dt/taum; % progression ratio
np = 1 ; % number of pulses
% simulation time
v = zeros(1, np*kk+1) ;
% during the pulse
for n = 1:np
    for k = (1:kk1)+(n-1)*kk
        v(k+1) = r*v(k) + (1-r)*Vm;
    end
    % after the pulse
    for k = ((kk1+1):kk)+(n-1)*kk
        v(k+1) = r*v(k) ;
    end
end
t = (0:(np*kk))*dt; % ms
% current pulse
ip = [0 kron(ones(1,np), [Iin*ones(1, kk1) zeros(1, kk-kk1)])];
figure(1)
plot(t, v, t, ip), grid on
title('Current pulses and voltage across the membrane')
xlabel('t [ms]'), ylabel('i [\mu A], v [mV]')
text(1.1*tp1, 0.95*Iin, ['\tau = ', sprintf('%1.2f ms', taum)])
axs = axis; axis([axs(1:3) 1.1*Iin]);
% print -f1 -depsc2 pulses

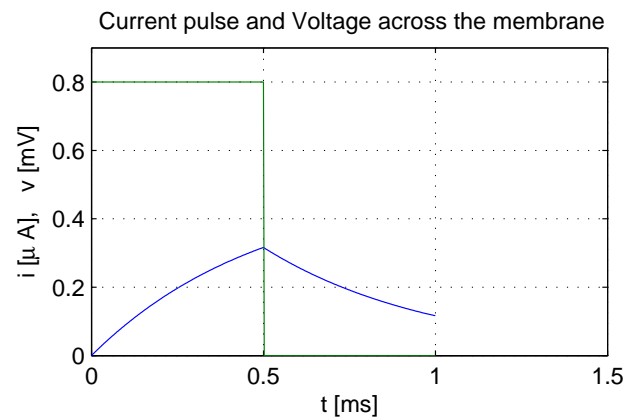
```

The script has been executed with two different membrane parameters and the following results have been obtained:

$\tau_m = 0.25 t_p$ “fast”/high conductance membrane



$\tau_m = t_p$ “slow”/low conductance membrane



If the membrane time constant is long comparing with the pulse duration (“slow” or low conductance membrane),

- the voltage across the membrane does not reach its maximum value during the pulse, and
- does not go back to zero in the period equal to the current pulse duration.

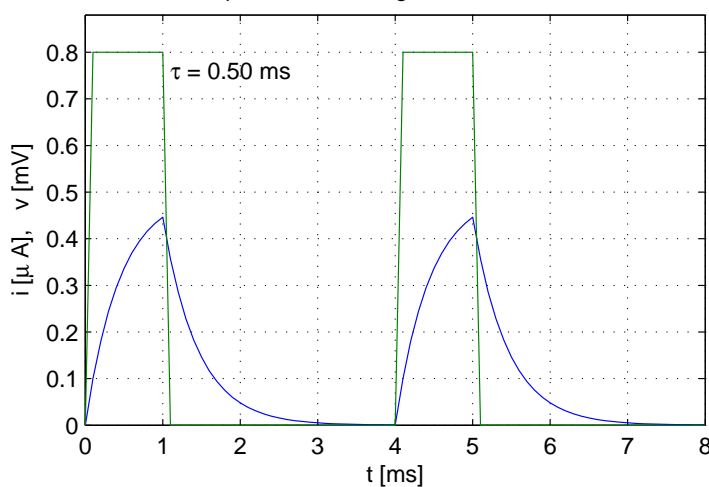
5.3.1 Temporal integration of two current pulses

- We will show first that temporal integration is achieved when the membrane time constant is sufficiently long comparing with the current pulse duration.
- Integration depends on the relative value of the membrane time constant τ_m
- In the example, pulses are $t_p = 1$ ms duration and repeated every 5 ms.

Short membrane time constant

$$\tau_m = 0.5 \text{ms} = 0.5 t_p$$

Current pulses and voltage across the membrane

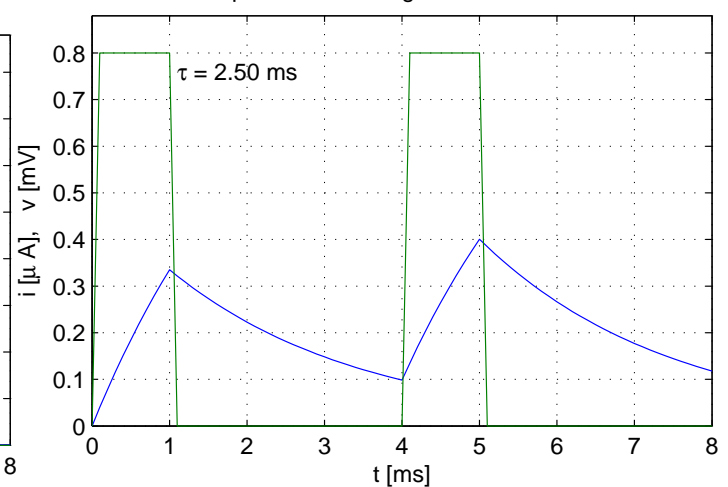


The membrane voltage is NOT integrated.

Long membrane time constant

$$\tau_m = 2.5 \text{ms} = 2.5 t_p$$

Current pulses and voltage across the membrane



The membrane voltage is integrated (summed up).

Exercise 5.2

Modify the `TempInteg.m` script to produce the plots as in sec. 5.3.1

□

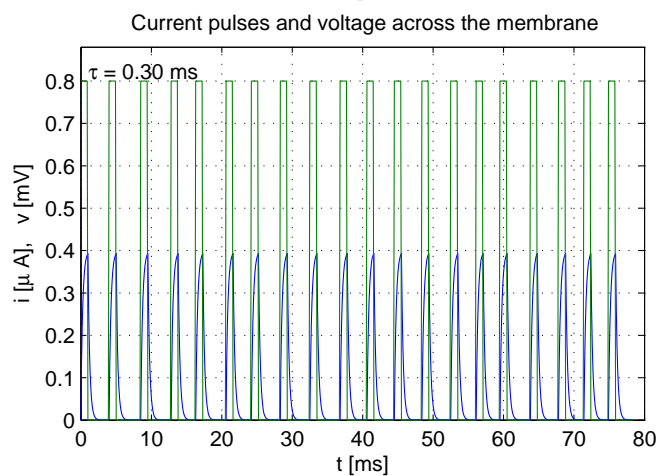
5 marks

5.3.2 Temporal integration of many current pulses

- To investigate further the problem of temporal integration let us observe the membrane voltage after injection of 20 pulses of duration $t_p = 1\text{ms}$.
- The time intervals between pulses randomly vary by 20% from its average value of 3ms.

Short membrane time constant

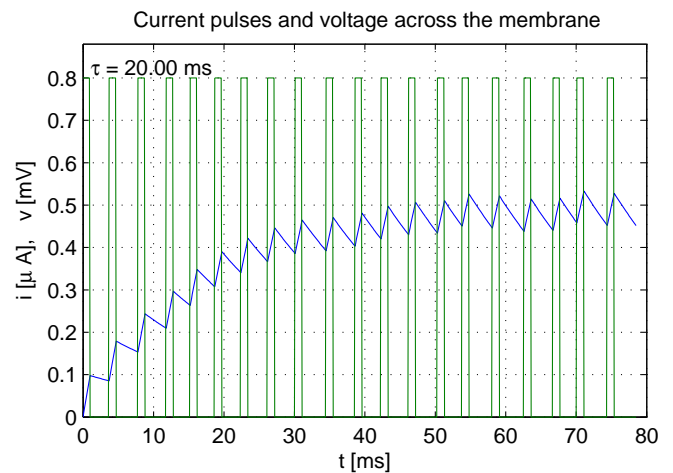
$$\tau_m = 0.3\text{ms} = 0.3 t_p$$



- Nothing interesting happens.
The voltage resembles the current pulses.
The membrane is too quick to respond.
- This is **temporal integration**.

Long membrane time constant

$$\tau_m = 20\text{ms} = 20 t_p$$



- Here the membrane reacts slower to the pulses — the voltages caused by each current pulse are “stretched out” in time and therefore add up.

Exercise 5.3

Modify the `TempInteg.m` script to produce the plots as in sec. 5.3.2.

Change:

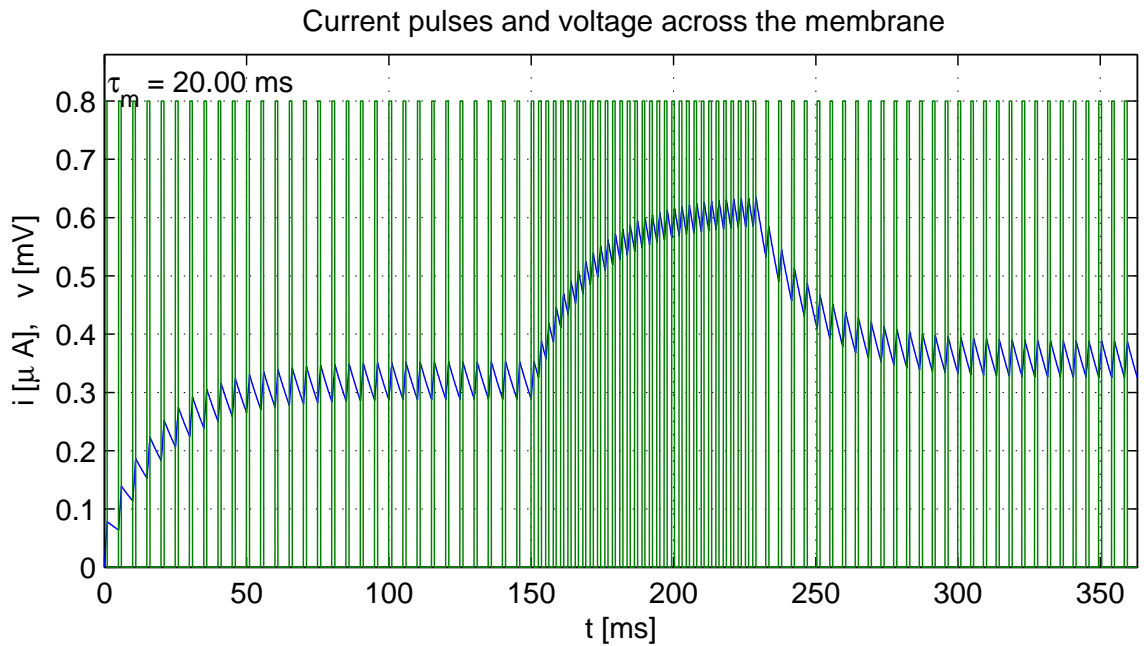
- the pulse duration to $t_p = 1.5\text{ms}$,
- the average interval between pulses to $t_0 = 4.5\text{ms}$, so that the pulse repetition period is $t_r = 6\text{ms}$,
- random variations of the distance between pulses to $rv=30\%$.

□

5 marks

5.3.3 Membrane as a frequency detector

- In this example the pulses have been generated with three different frequencies.
- We can observe that with a membrane with a long time constant act as frequency detector.



- You can clearly see when the frequency changes.
- The membrane voltage replicates the frequency changes after a not settle down period.
- The voltages induced by current spikes are called **Post-Synaptic Potentials (PSPs)**

Exercise 5.4

Modify the `TempInteg.m` script to produce the plot as in sec. 5.3.3. Use the pulse parameters as in the previous exercise.

□

5 marks

5.4 Model of Post-Synaptic Potentials

The postsynaptic potential (PSP) is typically modeled by means of the alpha functions:

$$y = t \cdot e^{-\frac{t}{\tau_\alpha}} \quad (1)$$

Note that y attains maximum for time: $t = \tau_\alpha$. The maximum is equal to $y_m = \tau_\alpha \cdot e^{-1}$. Dividing y by y_m we get the alpha function with the maximum equal to one. Renaming y to current I_{in} we get

$$I_{in} = I_m \cdot \frac{t}{\tau_\alpha} \cdot e^{1-\frac{t}{\tau_\alpha}} \quad (2)$$

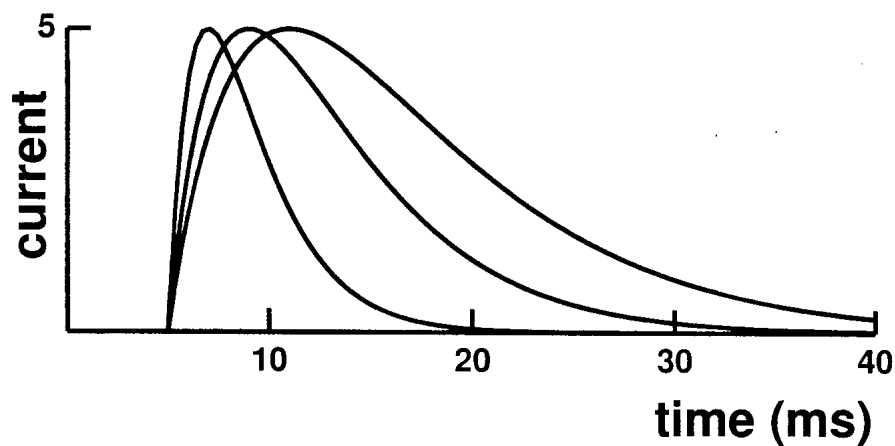


Figure 3: Alpha functions with onset at 5 ms and amplitude of $5 \mu\text{A}/\text{cm}^2$. Three curves with $\tau_\alpha = 2, 4, 6$ ms. Note that τ_α equals the time from onset to peak. τ_α also determines decay time.

The alpha function rises quickly for τ_α time and then falls slowly over about $5\tau_\alpha$ (a little slower than exponentially).

It can be shown that the function as in eqn (1) can be generated recursively by the following equation:

$$y(k) = 2ry(k-1) - r^2y(k-2) + t_s r \delta(k) \quad (3)$$

where $r = e^{-\frac{t_s}{\tau_\alpha}}$ is the decaying factor

t_s is the sampling time

τ_α is the time constant

$$\delta(k) = \begin{cases} 1 & \text{for } k = 0 \\ 0 & \text{for } k \neq 0 \end{cases}$$

Exercise 5.5

Use the recursion (3) and develop a MATLAB script that produces the plots as in Figure 3.

□

10 marks

5.5 Hodgkin-Huxley model

Please read Lecture Notes for full explanation. Here we present equations that are used in the simulation script.

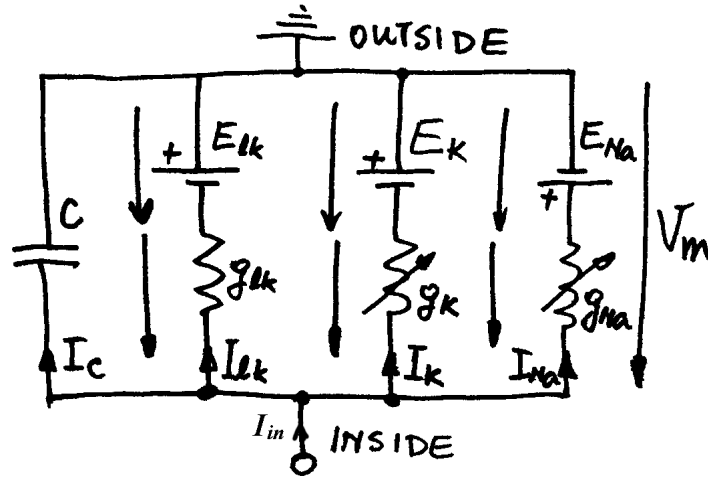


Figure 4: The Hodgkin-Huxley parallel conductance model

The membrane voltage equation:

$$C \cdot \frac{dV_m}{dt} = g_{lk} \cdot (E_{lk} - V_m) + g_K \cdot (E_K - V_m) + g_{Na} \cdot (E_{Na} - V_m) + I_{in} \quad (4)$$

Membrane capacitance: $C = 1 \mu\text{F}/\text{cm}^2$

5.5.1 Potassium Channel

Potassium battery: $E_K = -12 \text{ mV}$ relative to the resting potential of the axon.

Potassium conductance:

$$g_K = G_K \cdot n^4 \quad (5)$$

Maximum Potassium conductance: $G_K = 36 \text{ mS}/\text{cm}^2$

Activation particle n :

$$\tau_n \frac{dn}{dt} = n_\infty - n \quad (6)$$

A time constant and a steady-state value:

$$\tau_n = \frac{1}{\alpha_n + \beta_n}, \quad n_\infty = \alpha_n \cdot \tau_n = \frac{\alpha_n}{\alpha_n + \beta_n} \quad (7)$$

The voltage-dependant rate constants:

$$\alpha_n(V) = \frac{10 - V}{100(e^{(10-V)/10} - 1)}, \quad \beta_n(V) = 0.125e^{-V/80} \quad (8)$$

where V is the membrane potential relative to to the axon's resting potential in millivolts.

5.5.2 Sodium Channel

Sodium battery: $E_{Na} = 115$ mV sodium reversal potential relative to the resting potential of the axon.

Sodium conductance:

$$g_{Na} = G_{Na} \cdot m^3 \cdot h \quad (9)$$

Maximum Sodium conductance: $G_{Na} = 120$ mS/cm²

$$\tau_m \frac{dm}{dt} = m_\infty - m \quad \tau_h \frac{dh}{dt} = h_\infty - h \quad (10)$$

The time constants and steady state values are defined in terms of the rate constants:

$$\tau_m = \frac{1}{\alpha_m + \beta_m} \quad \tau_h = \frac{1}{\alpha_h + \beta_h} \quad (11)$$

$$m_\infty = \alpha_m \cdot \tau_m = \frac{\alpha_m}{\alpha_m + \beta_m} \quad h_\infty = \alpha_h \cdot \tau_h = \frac{\alpha_h}{\alpha_h + \beta_h} \quad (12)$$

The voltage-dependant rate constants are experimentally derived to be equal to

$$\alpha_m(V) = \frac{25 - V}{10(e^{(25-V)/10} - 1)} \quad \alpha_h(V) = 0.07e^{-V/20} \quad (13)$$

$$\beta_m(V) = 4e^{-V/18} \quad \beta_h(V) = \frac{1}{e^{(30-V)/10} + 1}$$

5.5.3 Membrane Leakage

Leakage conductance: $g_{lk} = 0.3$ mS/cm² is voltage-independent.

Leakage battery is calculate from the equilibrium condition:

$$g_K(V_m) \cdot (E_K - V_m) + g_{Na}(V_m) \cdot (E_{Na} - V_m) + g_{lk} \cdot (E_{lk} - V_m) = 0 \quad (14)$$

where V_m is the membrane relative resting potential. Assuming for simplicity $V_m = 0$ we have

$$E_{lk} = -\frac{g_K(0) \cdot E_K + g_{Na}(0) \cdot E_{Na}}{g_{lk}} = 10.613 \text{ mV} \quad (15)$$

The above set of equations have been implemented in the MATLAB script

... \prac5 \HodgHux.m

Exercise 5.6

Run the script for different values of the current pulse $I_{in} = 8 : 0.2 : 9$.

Plot each group of results/curves on the common plots and annotate the curves with the value of the current pulse.

□

6 marks

Written Submission

Your written submission should include results of all exercises you have performed (relevant MATLAB scripts, **plots**, **numerical results**, etc) with brief comments and explanations. It should be in a form ready for electronic submission when requested.