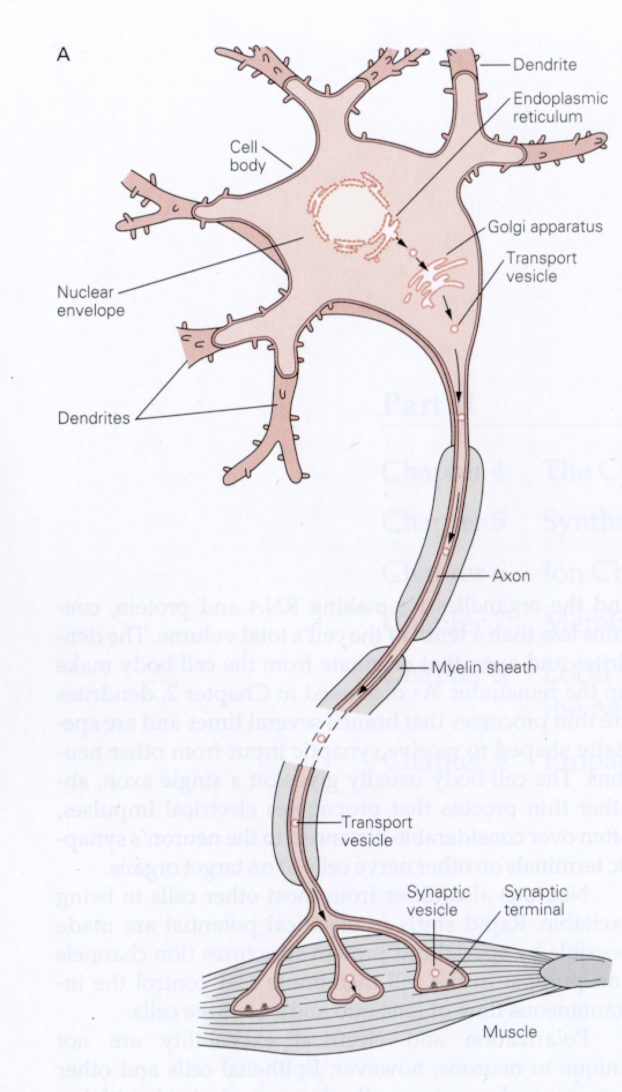
8 From Soap to Volts — Hardware of the brain

(based on chapter 11, W.W. Lytton, *From Computer to Brain*)

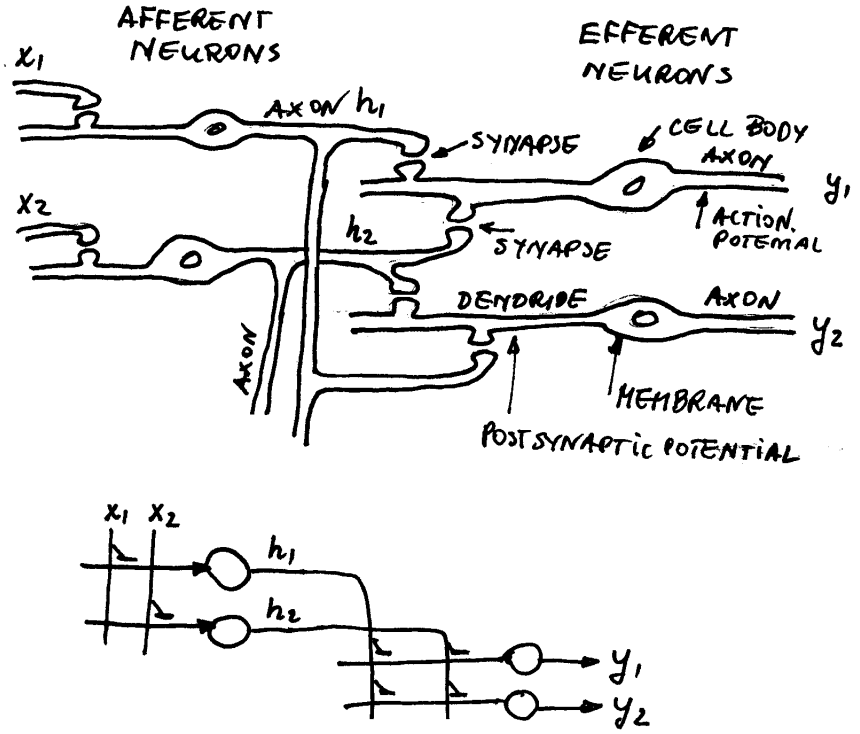
8.1 The cell



from Kandel et.al, *Principles of Neural Science*

- Neurons are biological cells
- Working of a cell, that is, its dynamics is described by the movement of chemicals and associated ions.
- Ions are electric carriers (or charges).
- Movements of electric charges creates an electric current which flows under the influence of related voltages.
- Therefore, a data-based model of a neuronal cell is formulated in terms of electrical quantities.
- Previously considered concept-based models of the nervous system based on artificial neurons and their networks are useful because they help to understand some of the complicated phenomena related to learning and perception.

8.1.1 Neurons and their connections



Recall that a biological neuron consists of the following major parts:

- The cell body,
- membrane,
- axon, dendride 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.

8.1.2 Cell Bio-Chemistry

- A cell is a complex piece of bio-chemical machinery.
- Before a neuron can do any signaling and thinking it must take care of itself through complicated mechanisms for
  - energy metabolism,
  - protection against toxins, and
  - intracellular and intercellular communication
- Chemicals passed around the cell to obtain energy during metabolism are reused in neuronal information processing
- Three of the basic food groups for cells:
  - glucose,
  - adenosine triphosphate (ATP)
  - acetyl-coenzyme A (acetyl-CoA),

  are either used directly, or have close congeners that are used for information processing.

- The major **neurotransmitters**:
  - glutamate
  - GABA (gamma-aminobutric acid)

  are spin-offs from the tricarboxylic acid cycle (Krebs cycle), the main sugar digestion route.

  (Edwin G. Krebs was awarded (with E. Fisher) 1992 Nobel prize for psychology or medicine for demonstrating basic biochemical mechanisms)
- Similarly, acetylcholine (ACh) is related to acetyl-coenzyme A (acetyl-CoA), which is the main product of the Krebs cycle.
- Glucose is processed in order to produce adenosine triphosphate (ATP), the main energy storage medium. ATP is also a neurotransmitter.
- Various ATP by-products
  - adenosine diphosphate (ADP),
  - adenosine monophosphate (AMP),
  - cyclic adenosine monophosphate (CAMP)

  are also used in neuronal signaling.
- Are you thinking about food or is your food thinking about you?

- This sharing of resources is not confined to information processing.

  The same compounds or their close relatives are also amino acids, the construction materials of the cell and the body.

- Both glutamate and GABA are close relatives of amino acids.

- Glycine, another neurotransmitter, is an amino acid.

  Glycine is the major constituent of collagen, making it the building block for skin and bones.

- Similarly, the nucleotides of DNA, the blueprint of the cell whose code is used to construct proteins, is also shared with neurotransmission and metabolism

- Cell maintenance also requires additional intracellular communication between and among various organelles (subcellular organs), as well as extracellular communication with various supporting cells.

- This type of communication cannot always be cleanly separated from classic neurotransmission.

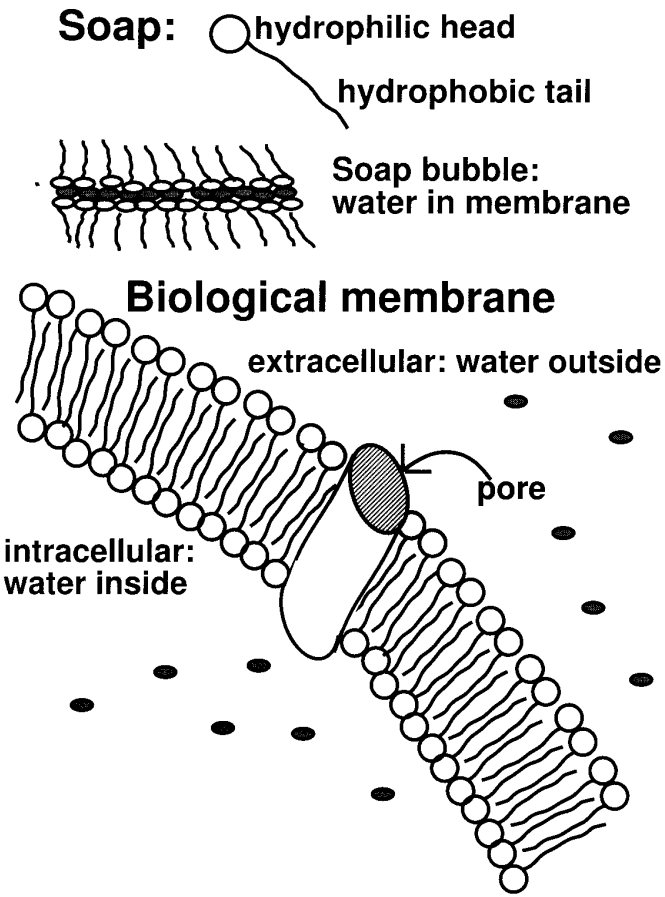
- During development neurotransmitters and second messengers are being used to grow neurons and coordinate their wiring and relations with various supporting cells.

- While a child is using his transmitters to grow a brain, he also has to think using the same transmitters.

- Because of this close enmeshment of functions, it may never be possible to cleanly separate fancy neural information processing from the boring information processing of housekeeping chores.
- Even the electrical charge at the cell membrane, the key attribute that permits action potential signaling between cells, has generic cell maintenance tasks as well.
- Similar electrical potentials are present in all body cells and in yeast and bacteria as well.
- Information transmission (and related encoding and decoding) has to be done in every organ.
- Bone cells communicate in order to adapt to changes in stress patterns when you learn to rollerblade.
- The liver and endocrine systems all have complex non-neural communication protocols in place.
- The immune system has a remarkable interplay of cell types that chat with one another and with other cells in the body, all of which have to continually remind white blood cells that they belong there and should not be eaten.

8.2 Basic cell design

- We can say that cells are build from water, salt, fat and soap.
- Most of the body is salt water. Water and salt can't pass through fat since oil and water don't mix.
- Soap is the compound that connects oil and water, thereby allowing showers to wash oily stuff off your skin.
- Soap works by having a fatty part that connects with the dirt and a hydrophilic (water loving) part.
- Fat is hydrophobic (water fearing).
- Soap thus provides a link that allows water to drag oil away.
- Cell design is based on the separating of inside from outside by means of **membranes**.
- Soap bubbles form with the fatty part of soap pointing inside and outside, away from the water that stays on the interior of the bubble membrane.



- Cell membranes are called lipid bilayers. They are configured in the opposite way: the fatty part is in the interior of the membrane, and hydrophilic heads point both in toward the cytoplasm and out toward extracellular space.

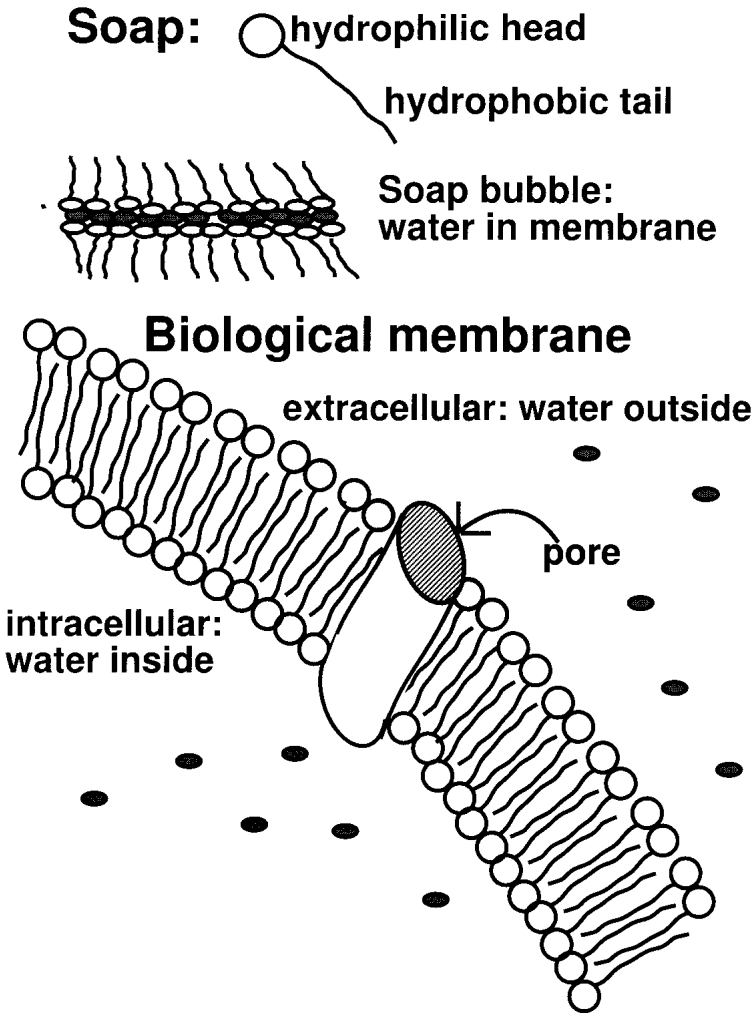
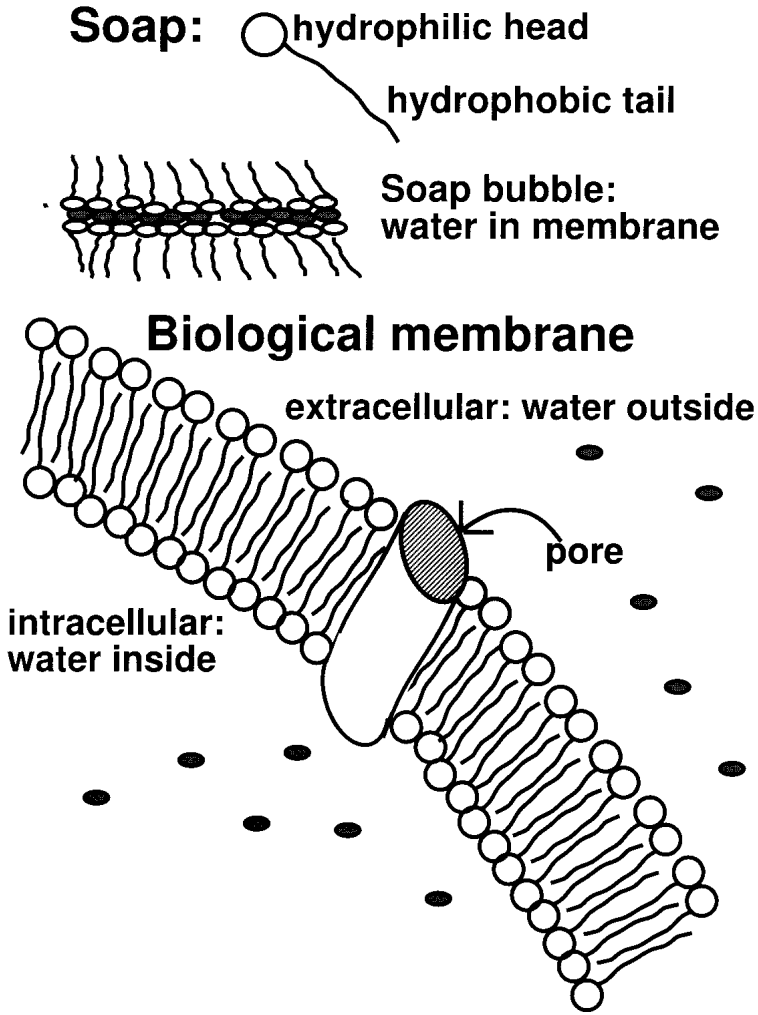


Fig. 11.3: Soap bubbles have fatty tails pointing in and out and water (shaded) interior.
Biological membranes keep the fatty tails interior with hydrophilic heads sticking in and out.

- Just as soap bubbles form spontaneously on the surface of soapy water, lipid bilayers form spontaneously from a mixture of phospholipids (biological soap) and water.
- The cell is filled with a volume of intracellular solution (cytoplasm) that the membrane separates from the extracellular solution outside of the cell.
- Although the membrane is only a thin layer at the surface of the cell, there is enough room in the interior of the membrane for chemicals to float around and react with one another.
- Only hydrophobic compounds can exist in the interior of the membrane.
- Proteins orient themselves using both hydrophilic and hydrophobic amino acids.

  They can form pores that allow ions to move between intracellular and extracellular space.



- Ions and many proteins are hydrophilic.

  Ions are the charged versions of certain elements, such as sodium, potassium, chloride, and calcium.

- They are charged because they have either lost or gained an electron, which carries a negative charge.

- The little plus or minus signs tell you how many electrons were lost or gained: Na^{+}, K^{+}, Cl^{-}, Ca^{++}.

- Positive and negative ions stick together to make a salt; NaCl is table salt.

- Many proteins are charged as well.

  Charge makes a compound hydrophilic since the hydrogen of H_2O will stick comfortably to a negative charge and the oxygen will stick comfortably to a positive charge.

- Fat will stick only to uncharged molecules.

- Therefore, ions and charged proteins can move around freely in either extracellular or intracellular space but can't pass through the fatty part of the membrane.

- Some proteins and various other compounds are hydrophobic and can float around the interior of the membrane but not move into the water on either side.
- There are also information-carrying compounds that are gases. These don't care whether they're in fat or water. They can pass through anything.
- The most well known of these is nitric oxide (NO), a former molecule-of-the-year winner and the functional basis of Viagra.
- Proteins are the active components of cells, involved in metabolism, cell reproduction, and practically every other function.
- Transporters and pores are transmembrane proteins (e.g., the pore in Fig. 11.3).
- Although ions cannot move directly across the fatty membrane, they can flow through these pores.
- Ions will move passively from a high concentration to low concentration, a process of diffusion down a concentration gradient.
- Other proteins can provide ion pumps or transporters that push ions up against a concentration gradient.
- Additionally, proteins provide transport and structure within both the extracellular and intracellular spaces.
- Although the extracellular and intracellular space are usually, thought of as being salt water, the large amount of protein gives it structure, making it more like jello than seawater.

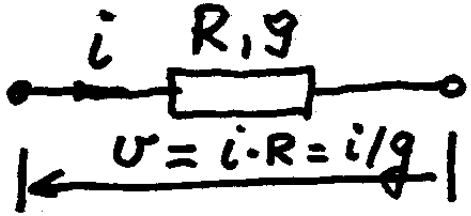
8.3 Morphing soap and salt to batteries and resistors

- Descriptions like the above are both model and metaphor: the extracellular space is jello, the membrane is an inside-out soap bubble, the proteins form holes.
- By switching to another representation, another language, we can describe the same thing in different terms.

  A particular model/metaphor will be better than another for a particular purpose.
- In this case, translation of the model into the language of electronics (batteries, resistors, capacitors) will allow us to describe neural signaling much more easily than we would be able to do just chewing the salt and the fat.
- Morphing from a membrane and salt representation to an electrical engineering representation obscures the biology somewhat.
- Any representation offers trade-offs and compromises.

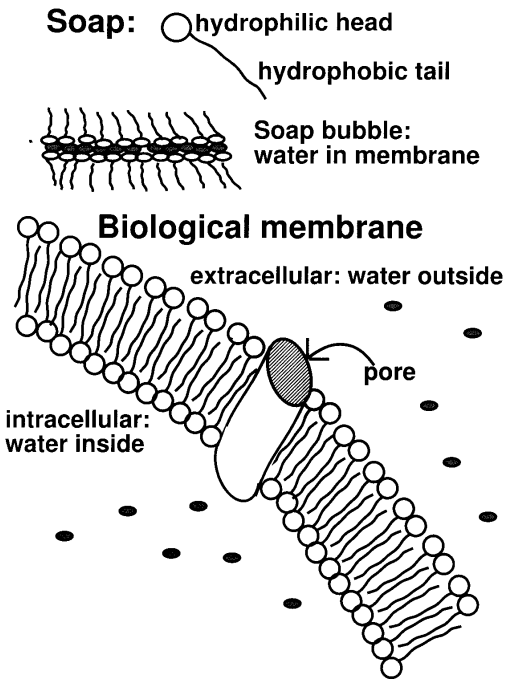
  The advantage of the electrical representation is that we can now use the many mathematical tools developed for electrical circuit analysis.

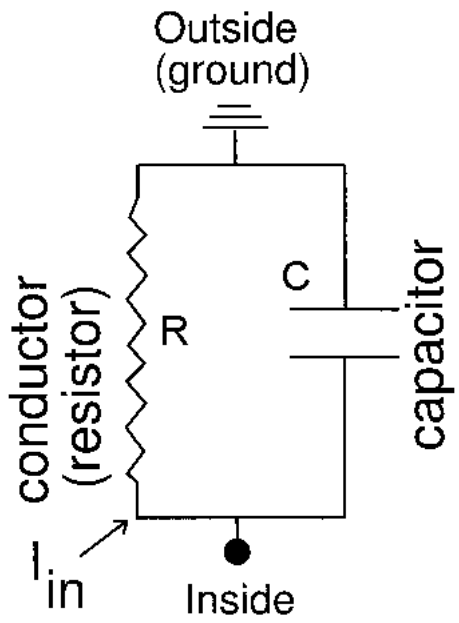
- Ions moving through water carry charge.
- The movement of charge is electrical current.
- Current can flow through the cytoplasm and extracellular fluid freely.
- The pores in the membrane provide conduits (conductors) for current to go through the membrane as well.
- Protein pores of a particular type provide conductors through the membrane that are selective for a particular ion.
- These pores are parallel conductors providing parallel paths for current.
- A conductor/resistor is defined by its tendency to resist the flow of current.
- Resistance is expressed in ohms (Ω) and is represented by R. Conductance is measured in siemens (S) and is represented by g.



- Mathematically, conductance is the inverse of resistance, $g = \dfrac{1}{R}$
- We can say that the **voltage** v across a resistor is proportional to the **current** i flowing through the resistor:

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





- In the circuit diagram (left) all of the pores of a single type are jumped together as a single big conductor (resistor).
- The membrane is represented as an RC (resistor-capacitor) circuit.

  Current can be injected inside the cell (arrow) by using a hollow glass electrode.

- This ubiquitous conductance is known as the leak conductance (g_{leak} or R_{leak}).
- Made of fat, the membrane acts as an insulator.
- Charge that does not flow through one of the pores will just sit next to the membrane.
- Charge acts at a distance to **attract unlike** charge or **repel like** charge.
- Charge that is sitting on one side of the membrane will cause equal but opposite charge to sit on the other side of the membrane.
- This phenomenon is known as **capacitance**.

- In electronics, a **capacitor** is built by placing an insulating material between two parallel metal plates that are attached to the wire leads of the capacitor.
- Since these plates do not touch, electricity cannot pass directly through the capacitor.
- However, electricity can flow indirectly as one plate induces electrical flow in the other plate.
- In the biological situation, the two plates are just thin accumulations of ions in the water adjacent to either side of the membrane.
- Capacitance is a measure of the capacity of the plates to hold charge.
- This capacity will have to do with the size of the plates, the distance separating them, and the nature of the material between them (its dielectric constant).
- A capacitor, or membrane, with high capacitance has the ability to hold a lot of charge with only a small voltage difference between the plates.
- Voltage times charge is a measure of energy.
- A high capacitance means that charge can be stored easily, i.e., without requiring as much energy.
- As you put more voltage across a capacitor, it will hold more charge and more energy.
- Capacitance tells how much the capacitor can hold at a given voltage.
- In electrophysiology, we insert an electrode through the membrane and then inject current into the inside of the cell.

This current will pass out of the cell through the resistor or the capacitor (through the pores or via the capacitance).

- Once the current reaches the outside of the cell it will disperse to the rest of the body and the surrounding world.
- In the diagram this is represented by the **ground symbol**.
- The human body is big enough and the currents are small enough that the body can easily sink (conduct away) the current that cells produce.
- When we put a cell in a dish and inject current, we place a wire in the dish to conduct the current out to ground.
- This wire is attached to something metal that leads to the physical ground.

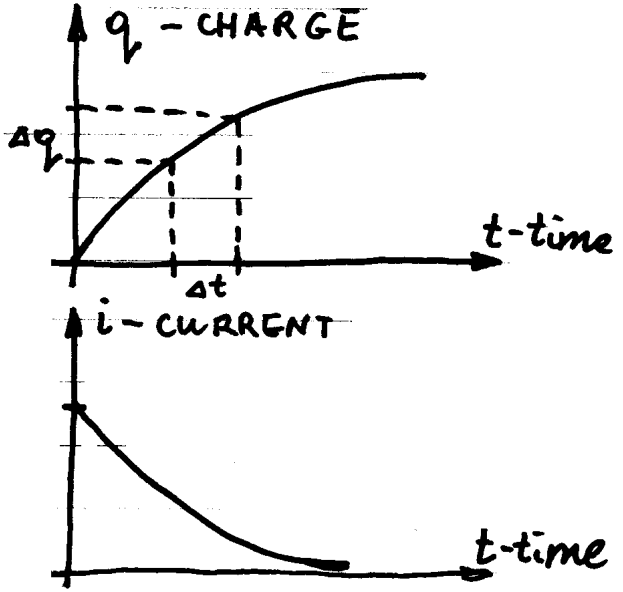
8.4 Analysis of the RC circuit

- Modeling the neuron as an electrical circuit involves predicting

  voltage changes based on current flow.
- One can also model an electrical circuit the other way around: given the voltages, predict the currents.
- 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.

8.4.1 Charge and current

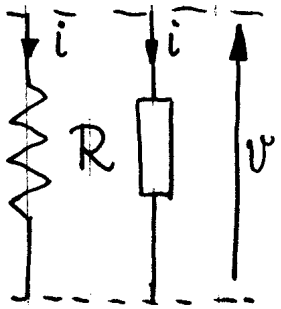
- Electric current is a rate of change of charge.
- Typical charges are: electrons, ions and charged proteins
- If the charge is compared to water flowing through a pipe, than the current will be compared to amount of water flowing through the pipe in a time unit.
- Mathematically, the current i is a time derivative of charge q.
- Imagine that the charge $q(t)$ varies with time as in the following plot:



$$i = \frac{dq}{dt} = \dot{q} \approx \frac{\Delta q}{\Delta t}$$

- Time derivative of the charge (current in this case) can be approximated as the ratio of the change of charge Δq over a small time interval Δt.
- Note that the rate of change of the charge is slowing down. Therefore the current, charge's derivative is being reduced.
- Derivative of a function is also called the gradient (slope) of the function.

8.4.2 Resistors

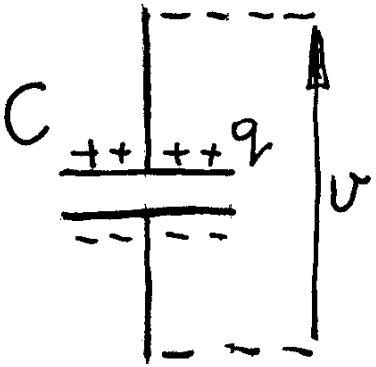


- Voltage across a resistor is proportional to the current flowing through the resistor.

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

- 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.

8.4.3 Capacitors

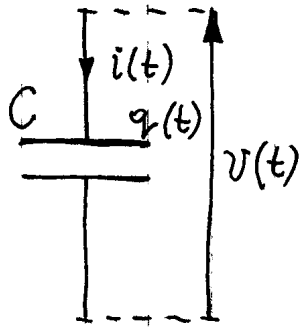


- Charge on a capacitor is proportional to the voltage applied to the capacitor.

$$q = C \cdot v$$

- 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

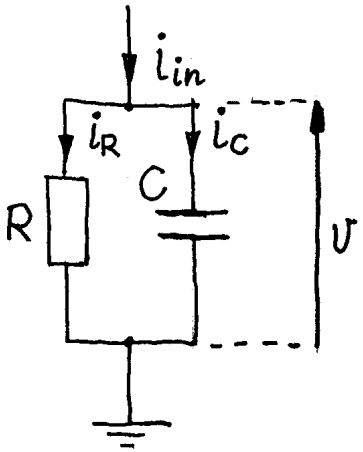


- If the charge stored in the capacitor varies, then the current (derivative of charge) flows and can be calculated as

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

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

8.4.4 Summing currents — Kirchhoff's law



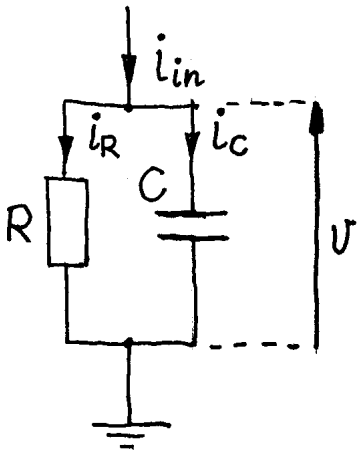
- Kirchhoff's law on conservation of charge says that the sum of currents incoming into an electric node and outgoing from the node is equal.

  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

8.4.5 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:

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

Let us denote

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

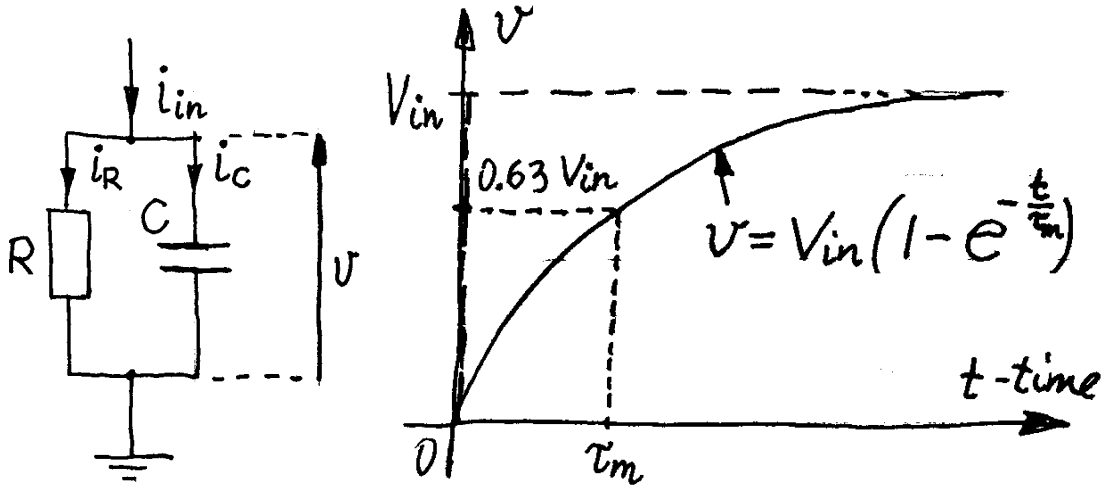
The equation for the voltage across the membrane can now be written as:

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

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.

8.4.6 Time constant of the RC circuit

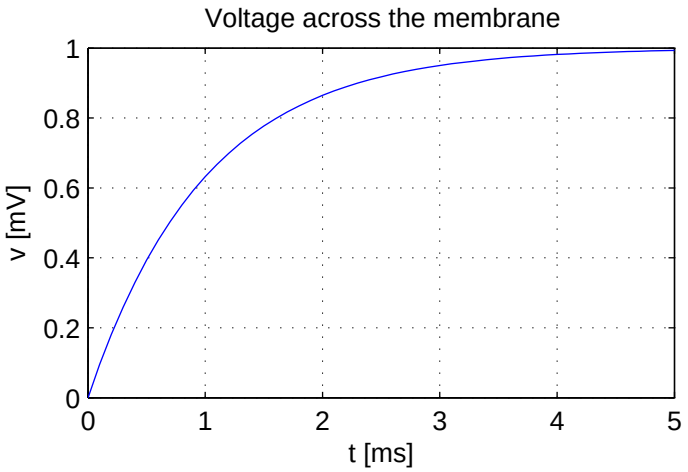


- If a constant current is injected, the voltage across the membrane (RC circuit) grows exponentially, until it saturates at the value $V_{in} = R\, i_{in}$

  ($e \approx 2.7183$ 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 : $g = 1$ mS/cm^2
- capacitance : $C = 1\mu$F/cm^2
- time constant : $\tau_m = \frac{C}{g} = 1$ ms
- injected current : $i_{in} = 1\mu$A/cm^2
- max voltage : $V_{in} = \frac{i_{in}}{g} = 1$ mV

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
```

8.5 Rate (frequency) coding

- Most information processed by the brain is temporal, that is, time varying.
- To understand speech, the brain processes strings of phonemes to understand words and then strings of words to understand the whole idea.
- Internally the temporal information is represented by the train of spikes of varying frequency.
- This is the frequency or rate coding.
- The frequency translates the train of spikes into a single number.
- Such a number is used in our artificial neural networks to represent information.
- The frequency coded temporal information is utilized through the temporal integration performed by the neuronal membrane.

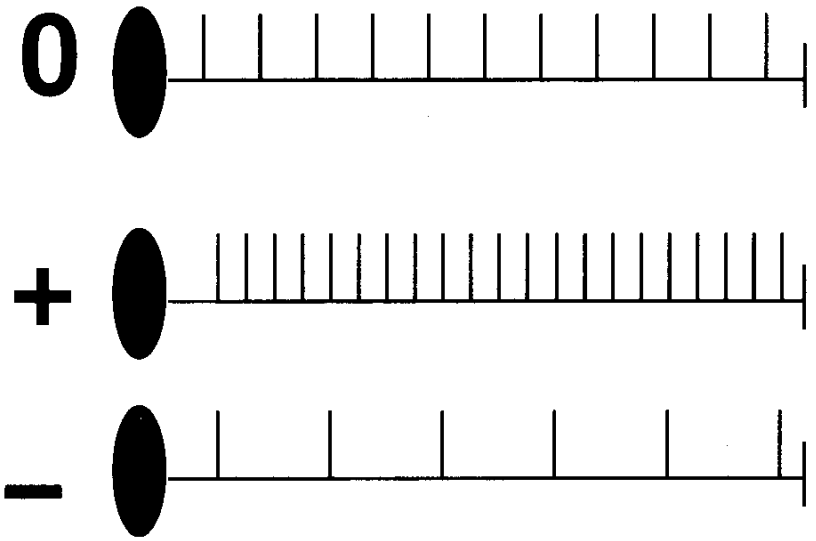


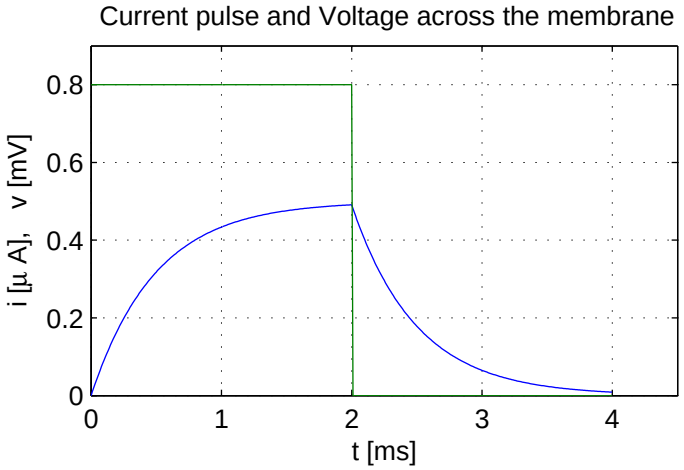
Fig. 7.2: Spontaneous rate represents a scalar state of 0. Increased rate is positive state and decreased rate is a negative state. Spikes are represented as short vertical lines atop the horizontal axons. At bottom: negative state times negative weight equals positive state.

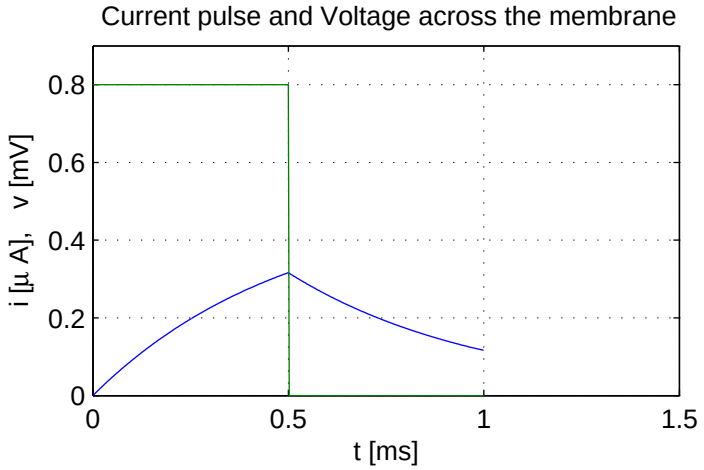
- The spikes can be thought of as current pulses injected to the neuron through its membrane.

8.6 Temporal integration

- Consider a **current pulse** of duration t_p ms **injected through the membrane**,
- It is possible to get an analytical expression for the resulting membrane voltage, but it is easier to do computer simulation and plot the the signals.
- Results depends on the relative ration of the current pulse duration t_p and the membrane's time constant τ_m

$\tau_m = 0.25\, t_p$ "fast"/high conductance membrane $\tau_m = t_p$ "slow"/low conductance membrane






```
v = zeros(1,2*K+1);
% during the pulse
for k = 1:K
  v(k+1)=r*v(k)+(1-r)*Vm;
end
% after the pulse
for k = (1:K)+K
  v(k+1)=r*v(k);
end
```

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

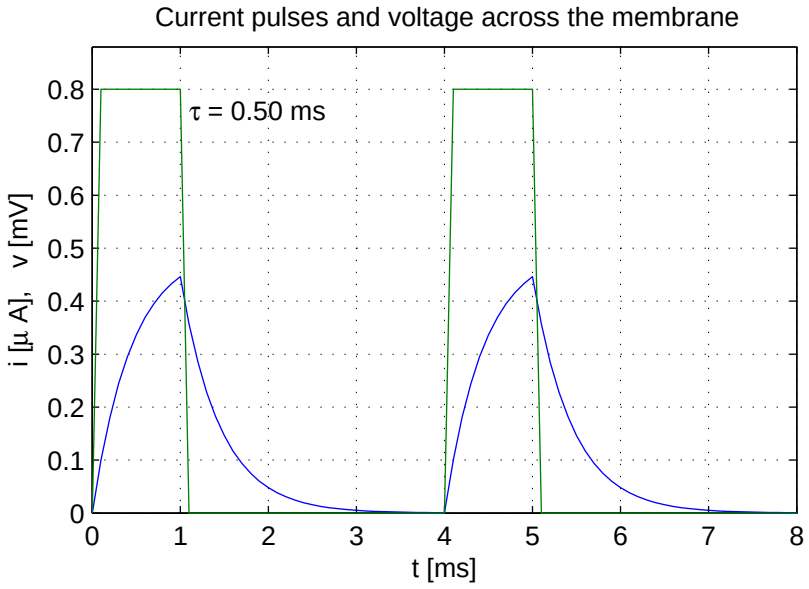
- the voltage across the membrane does not reach its maximum value during the pulse, and
- does not go back to zero in the period equal to the current pulse duration.

8.6.1 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

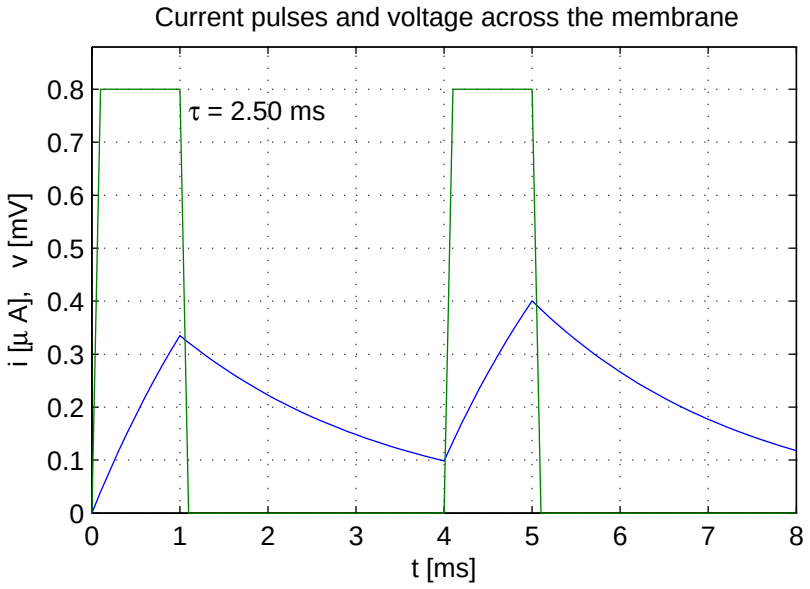
$\tau_m = 0.5\text{ms} = 0.5\, t_p$



The membrane voltage is NOT integrated.

Long membrane time constant

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

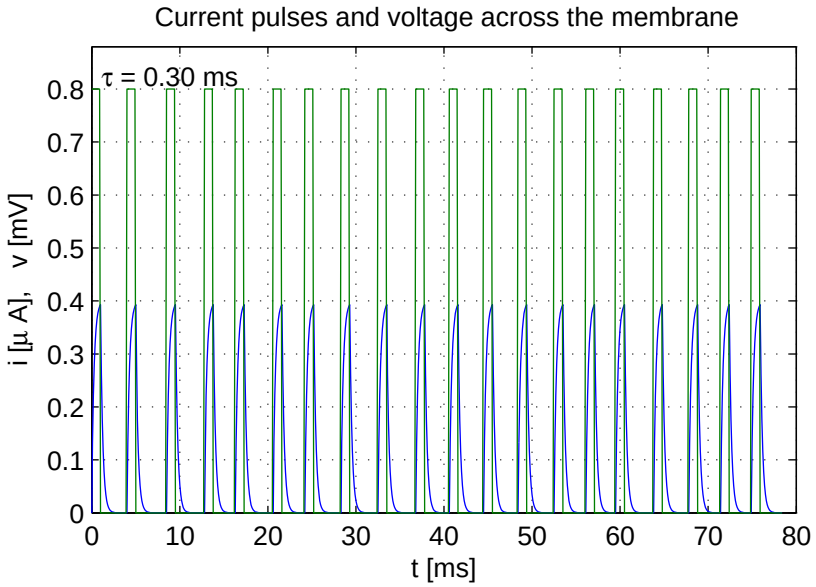


The membrane voltage is integrated (summed up).

8.6.2 Temporal integration of many current pulses

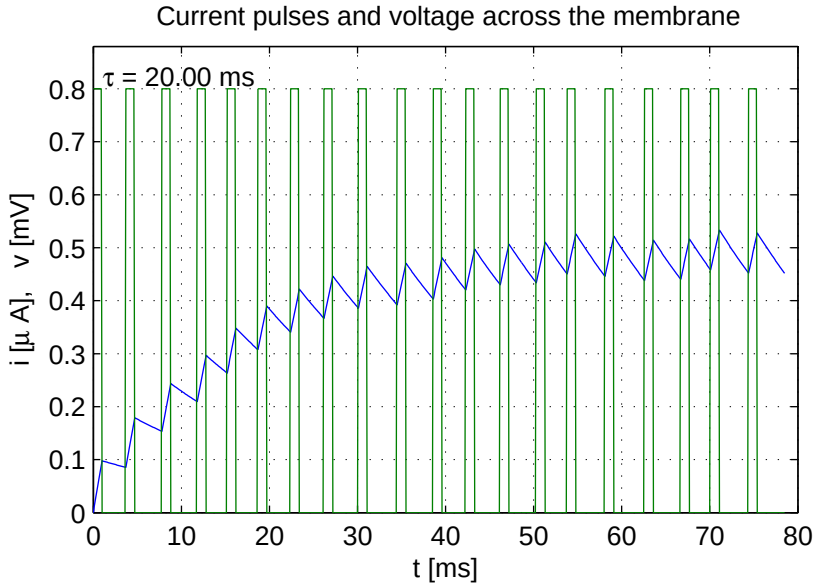
- To investigate further the problem of temporal integration let us observe the membrane voltage after injection of 20 pulses of duration $t_p = 1$ms.
- The time intervals between pulses randomly vary by 20% from its average value of 3ms.

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.

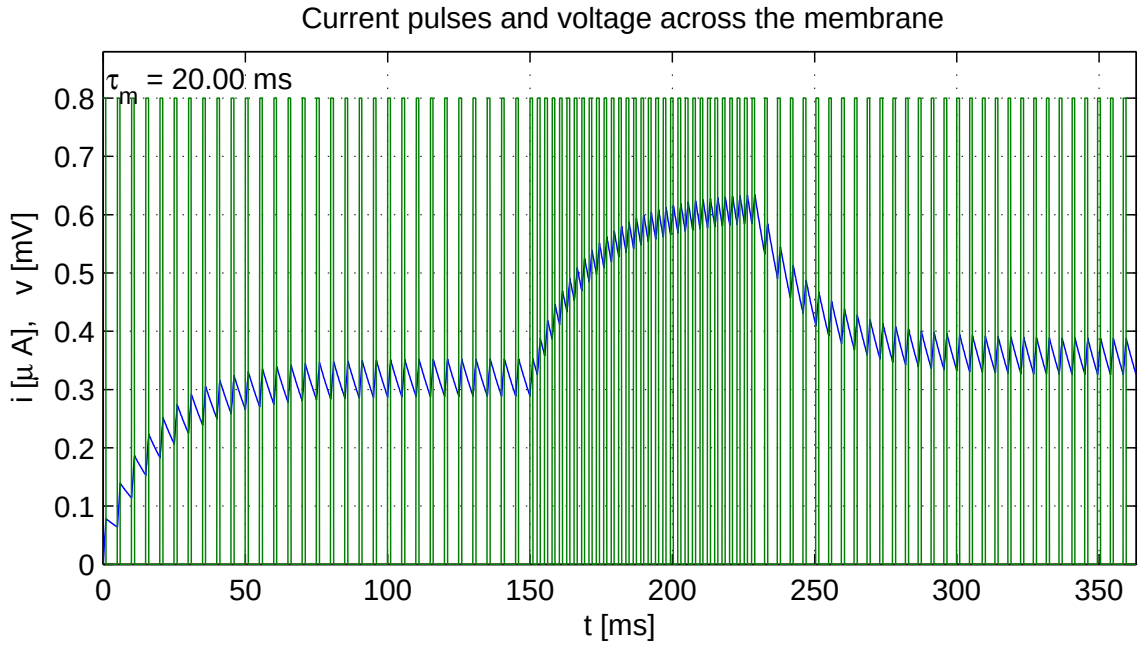
Long membrane time constant
$\tau_m = 20\text{ms} = 20\, t_p$



- Here the membrane reacts slower to the pulses — the voltages caused by each current pulse are "stretched out" in time and therefore add up.
- This is **temporal integration**.

8.6.3 Membrane as a frequency detector

- In this example the pulses have been generated with three different frequencies.
- We can observe that withe 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)

8.7 Slow potential theory

- Slow potential theory describes how signal integration is performed as spikes trigger postsynaptic potentials (PSPs), which add up to produce a voltage that estimates the average presynaptic frequency.
- These PSPs are the slow potentials. They have to be relatively slow, long in duration, in order to give a reliable estimate.
- Temporal summation occurs as more spikes come in during the time while previous PSPs are still active.
- From listening to the radio, you know that amplitude modulation (AM) and frequency modulation (FM) are two methods of transmitting information using an oscillatory signal.
- Since biological spikes do not vary meaningfully in height, the system is not using AM.
- Rate coding theory assumes that the system is using FM.
- To describe an FM signal, we need to discuss two different frequencies: the carrier frequency of the spikes and the frequency at which the rate changes.

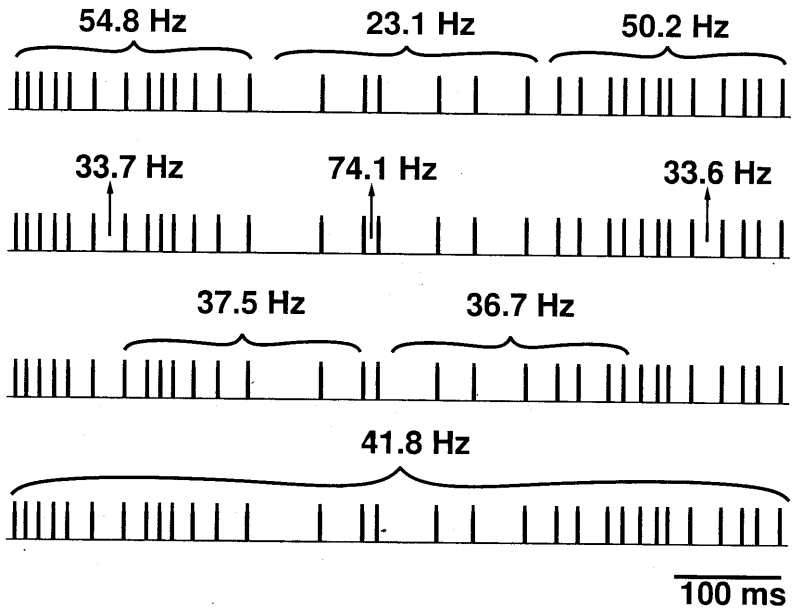
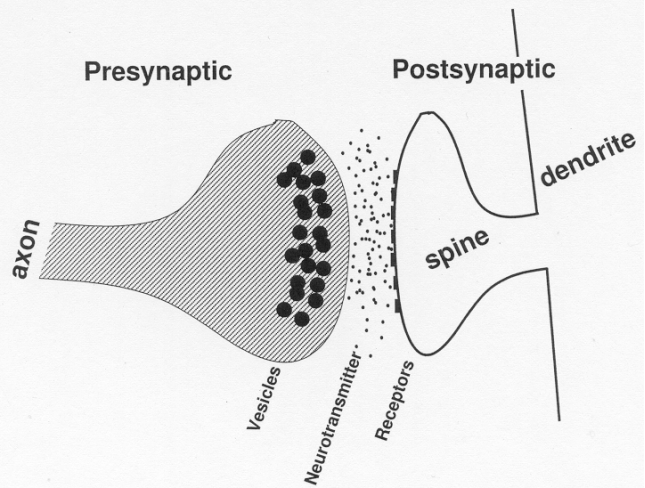


Fig. 11.11:
Different frequency estimates from a noisy FM spike train. Top trace: estimates are fairly accurate reflections of the underlying $50 \rightarrow 25 \rightarrow 50$ frequencies.
Second trace: Measurements of instantaneous frequency can be highly inaccurate.
Third trace: Averaging with correct duration but wrong phase (timing of start of average) also gives bad estimates.
Fourth trace: averaging for too long a duration misses the modulation entirely.

- It is a noisy spike train with carrier frequency varying between 25 and 50 Hz.
- This frequency is modulated at a rate of 4 Hz, meaning that we have a shift in frequency every quarter second (250 ms – the length of the brackets at the top of Fig. 11.11).
- Clearly, the frequency of modulation must be considerably lower than the carrier frequencies.
- In Fig. 11.11, rates for a single artificial noisy frequency modulated spike train are estimated correctly, and then incorrectly in several ways.
- Biologically, it is not possible to be confident of whether a particular signal estimation is correct or incorrect.

8.8 A synapse — Postsynaptic potential

- At this stage we have to realize that in reality the origin of the current spikes and subsequent post-synaptic potentials (PSPs)is through a synapse that links an axon of one neuron with the dendrite of another one



  - An electrical signal, an **action potential** produced by an afferent neuron, invades the presynaptic axon terminal.
  - This causes vesicles to release neurotransmitter into the **synaptic cleft** between the neurons.
  - The neurotransmitter molecules float across and bind to receptors on the postsynaptic neuron.
  - These receptors are linked to channels that open up and create an electrical signal, a **postsynaptic potential**, on the membrane of a spine or dendrite of the postsynaptic neuron.
- We can see that assigning just one weight to the synapse seems to be an oversimplification.

  Simplicity was an obvious attraction.
- At this stage we concentrate on a possible model of postsynaptic potentials.

  We add more complexity when we need it.
- We study generation an action potential in the next chapter.

8.8.1 Realistic model of Post-Synaptic Potentials

- We used square waves (pulses) as models of artificial current injections.
- Real biological signals are more curvy.
- One of a more realistic models of a postsynaptic potential (PSP) is described by the alpha function.

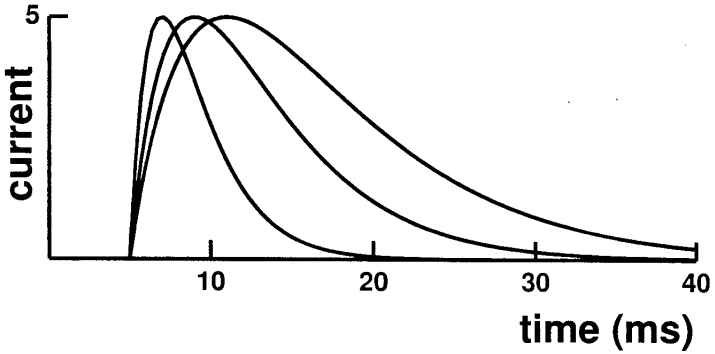


Fig. 11.12: Alpha functions with onset at 5 ms and amplitude of 5 μA/cm^2. Three curves with $\tau_\alpha = 2, 4, 6$ ms.
Note that τ_α equals the time from onset to peak. τ_α also determines decay time.
This is used as a model of a postsynaptic potential (PSP).

We start with the following function:

$$y = t \cdot e^{-\frac{t}{\tau_\alpha}}$$

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

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

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

- Note that we now have a couple of time constants to discuss:

  the alpha function time constant τ_α and

  the membrane time constant τ_m

- The time constant of the slow potential must be chosen so that the PSPs are long enough to average a reasonable number of spikes.
- Choice of too short a τ_α, will not allow integration to occur — the PSP will end after only one or two impulses so that only instantaneous frequency can be measured.
- An overly long τ_α, will not allow enough PSP decay during the arrival of many spikes, and will therefore average across the frequency modulation.

8.9 More on frequency coding

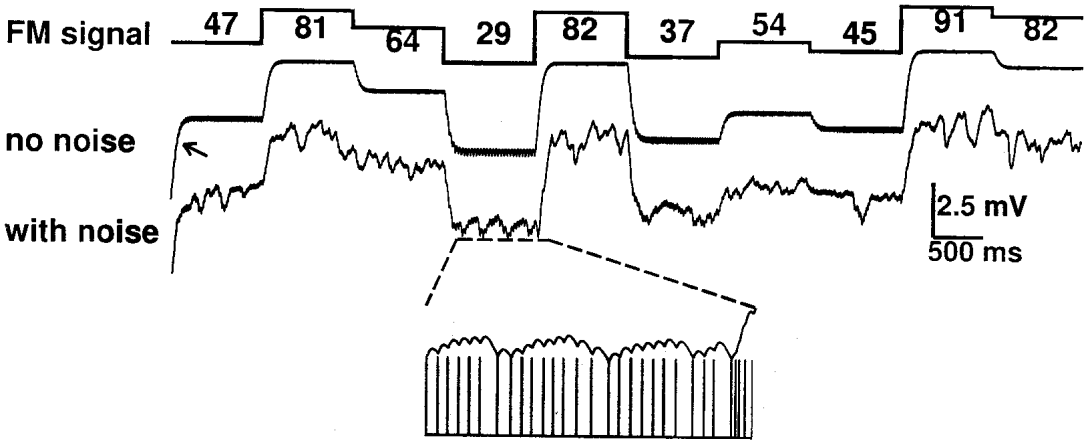
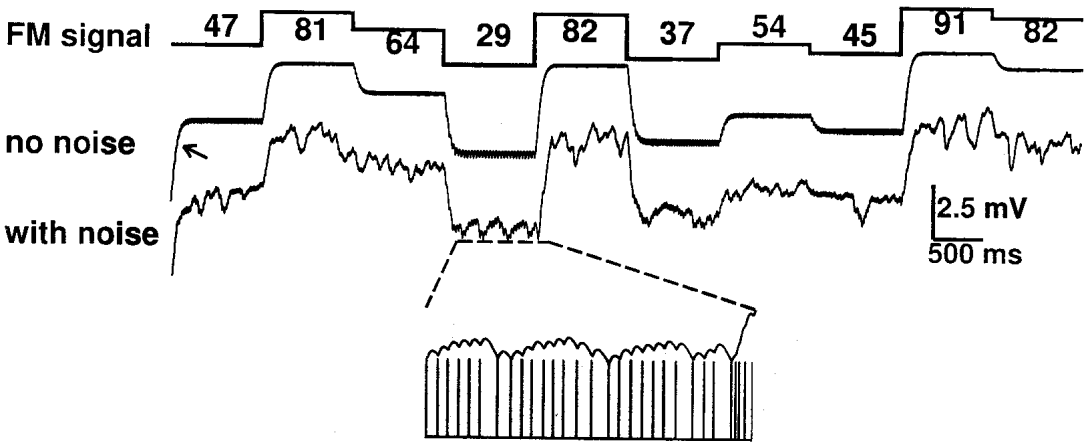


Fig. 11.13: Slow PSP response to FM square wave (carrier frequencies shown in Hz). PSP parameters: $\tau_\alpha = 30$ms; $\tau_m = 1$ms

- An FM signal with spike-train frequencies varied randomly between 20 and 100 Hz.

- The frequency changed every second (1 Hz modulation frequency) for 10 seconds.
- The carrier frequencies are shown graphically in the top trace with the values given in Hertz.
- I didn't show all the spikes since at this scale they would just scrunch together into an indistinguishable blob.
- However, at the bottom of the figure I expanded an 800-ms period to show the spikes and membrane response together.
- With carrier frequency between 20 and 100 Hz, the interspike intervals (ISIs) ranged from 50 to 10 ms (period is inverse of frequency: ISI = $\frac{1}{f}$).
- A good choice of τ_α, would be somewhere in this range; I used 30 ms.

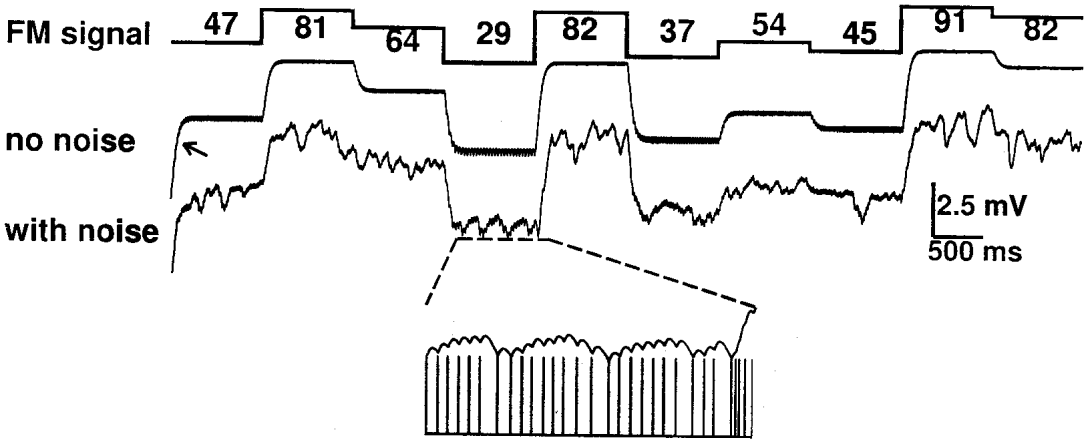
- Membrane time constant, τ_m is 1 ms, which allows the membrane to follow the PSP without substantial lag and without adding any additional delay.



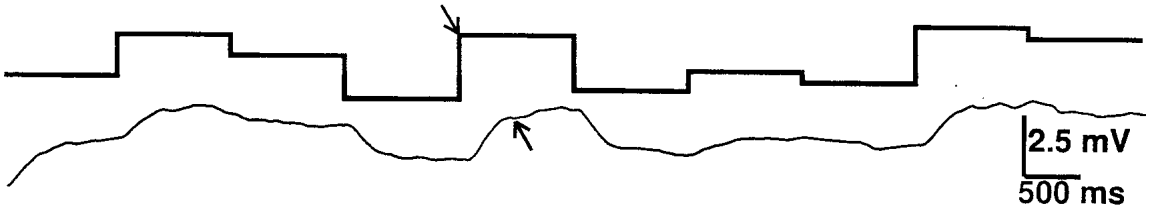
- Fig. 11.13 shows membrane potential in response to two spike trains with the same underlying frequencies but without and with noise.

- There is an initial charging period (arrow) when the membrane rises from resting membrane potential by about 3 mV.
- Then the potential plateaus in response to the constant-frequency input.
- When the input frequency shifts upward from 47 to 81 Hz there is another charging period as the membrane rises another 2 mV and plateaus.
- The correspondence between shifts in frequency and shifts in membrane voltage can be easily appreciated.
- The scaling is arbitrary: the change in millivolts as a number is not the same as the change in frequency as a number.

- However, the relationship is linear: a doubling of input frequency leads to a doubling of potential.



- During the plateau there is a low-amplitude oscillation from the waveforms of the constituent alpha functions.
- In the absence of noise, membrane potential closely reflects frequency modulation, even reflecting small frequency shifts such as the shift at right from 91 to 82 Hz.
- Once noise is added to the FM signal (Fig. 11.13, with noise), frequency estimation suffers.
- It is no longer possible to reliably identify frequency shifts of under 10 Hz.
- Even the shift from 81 to 64 Hz is hard to see.
- The expanded trace below shows the alpha function responses to individual spikes up to the shift from 29 to 82 Hz.



- Fig. 11.14: Slower PSP response to noisy FM signal of Fig. 11.13. $\tau_\alpha = 100$ms.

- With τ_α increased to 100 ms, averaging occurs over a greater number of spikes and most of the noise is filtered out.
- As well as averaging over a greater period, the longer τ_α also produces longer charging delays.
- This means, a longer wait for the voltage to stabilize on an estimate of the incoming signal (arrows).
- With a charging delay of nearly half a second and frequency modulation of 1 Hz (period of 1 second), the frequency estimate barely registers as a plateau before the frequency shifts again.

8.10 Summary and thoughts

- In this chapter, I started with salt, water, and soap, the basic ingredients of the brain.
- Out of these, the body builds **capacitors and resistors**.
- In the next chapter we'll see that it builds **batteries** as well.
- The physical limitations of these building blocks makes neurons very slow compared to transistors.
- In particular, the relatively large capacitance translates into slow signaling.
- Rather than be dismayed by this slowness, I presented models that use it to advantage.
- The slowness allows the membrane to hold onto a signal, permitting temporal summation.
- The amount of summation has to do with the length of the membrane time constant.
- **Slow potential theory** is a model that makes slowness a feature, using long time constants to do signal averaging that blurs out noise.
- This chapter showed how the parameters of the membrane and of the signal itself determine the influence a signal has on the neuron.
- These interactions explained **signal transduction from presynaptic spike rate to postsynaptic membrane potential**.
- They also explained the signal summation and formation of the total postsynaptic activity.