Systems Biology II: Neural Systems (580.422)

Lecture 8, Linear cable theory

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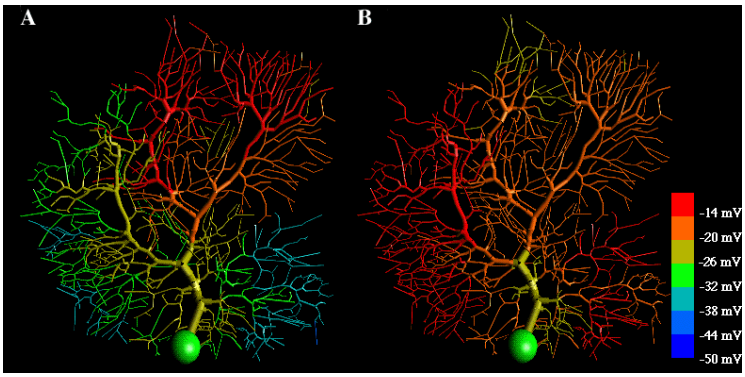
Reading:

Course notes from the website: *Derivation of the Cable Equation*

C. Koch *Biophysics of Computation* (Oxford Press). Chapters 2 and 3.

Neurons are not a single compartment! The figures below show two snapshots of the membrane potential in a model of the dendritic tree of a Purkinje cell from the cerebellum during a dendritic action potential. Note the substantial differences in potential across the dendrites and also how potential spreads through the tree with time.

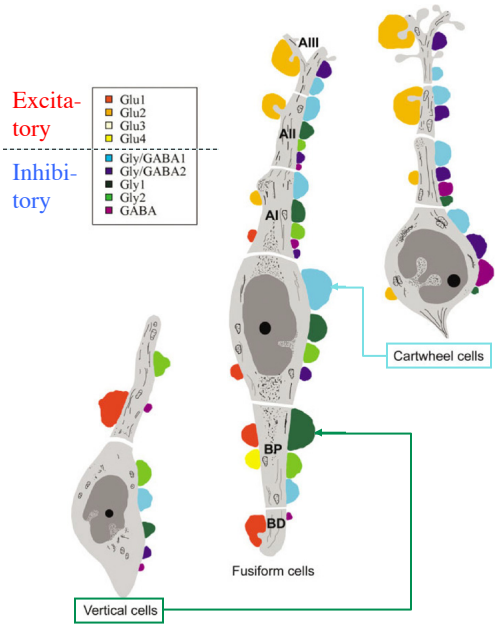


Membrane potential (A-B) during a dendritic Ca2+ spike in the Purkinje cell model. In this example the dendritic spike initiated in the upper right dendrite, but this was not always the case in the model. (This figure has C and D parts that show the calcium concentration during the same simulation; see the website at right).

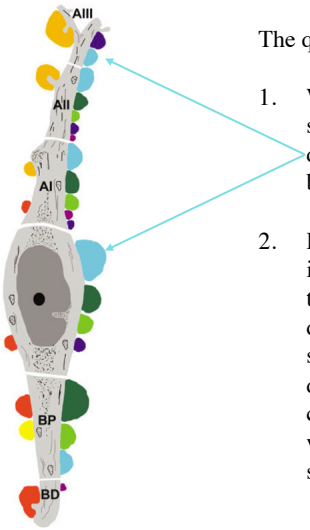
(from De Schutter and colleagues: http://www.tnb.ua.ac.be/models/purkinje.shtml

Synapses do not distribute randomly over the surface of a neuron! For example, inhibitory synapses are often located on the soma and proximal dendrites, whereas excitatory synapses are located further out on the dendrites.

The examples at right show distribution of synaptic terminals of various types (identified by color) on the somas and proximal dendrites of neurons in the dorsal cochlear nucleus (distal dendrites were not reconstructed). Fusiform cells are principal cells and the other two are inhibitory interneurons. Their connections are shown.



Rubio, 2004

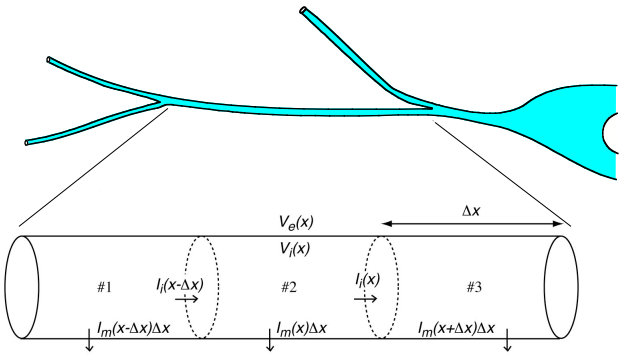


The questions for the next 3 lectures:

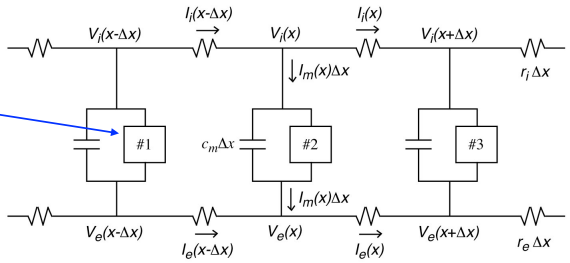
1. What difference does it make where a synaptic terminal is located? Is there a difference between these two terminals because of their locations, for example?

2. How do synapses at different locations interact? Do they interact more strongly if they are close together? Is there a difference between the interactions of synapses located on the same versus different dendritic branches? A component of this question is to explain why inhibitory synapses cluster near the soma.

Distributed properties of dendritic trees are analyzed using the cable model



Ion channels in the membrane go here (later)



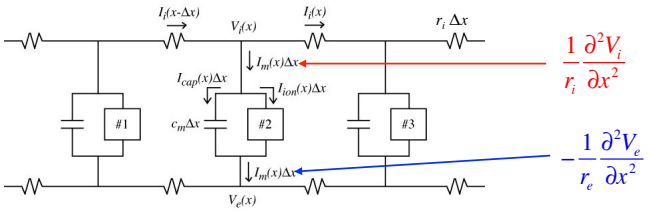
The full derivation of the cable model is given in the notes attached to this lecture. A brief summary is given below.

Applying Kirchoff's current law and Ohm's law at one of the intracellular nodes,

$$I_m(x)\Delta x = I_i(x-\Delta x) - I_i(x) \quad \text{so} \quad I_m(x) = -\frac{\partial I_i}{\partial x}$$

$$I_i(x)\, r_i\Delta x = V_i(x) - V_i(x+\Delta x) \quad \text{so} \quad \mathrm{I_i}(x) = -\frac{1}{r_i}\frac{\partial V_i}{\partial x}$$

and therefore $$\frac{\partial^2 V_i}{\partial x^2} = r_i I_m$$



The same argument applies at the extracellular node, so

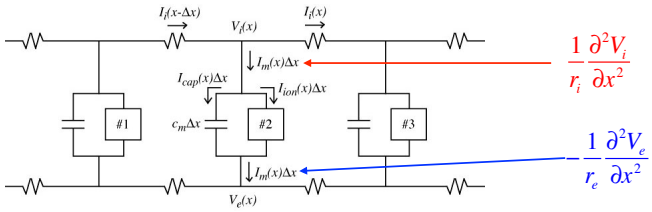
$$-\frac{1}{r_e}\frac{\partial^2 V_e}{\partial x^2} = I_m = \frac{1}{r_i}\frac{\partial^2 V_i}{\partial x^2}$$

Now the transmembrane potential $V = V_i - V_e$ so

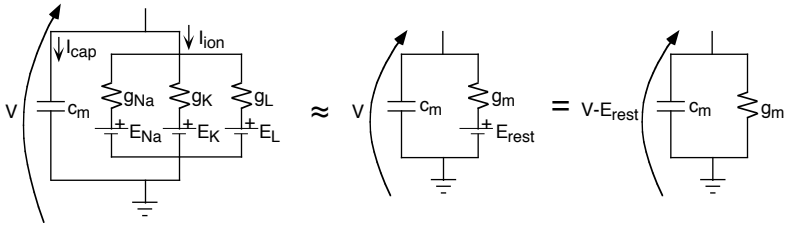
$$\frac{\partial^2 V}{\partial x^2} = \frac{\partial^2 V_i}{\partial x^2} - \frac{\partial^2 V_e}{\partial x^2} = (r_i + r_e) I_m \quad \text{so that} \quad \frac{1}{r_i + r_e}\frac{\partial^2 V}{\partial x^2} = I_m = I_{cap} + I_{ion}$$

The current through the capacitor is $I_{cap}(x)\Delta x = c_m \Delta x \, \partial V_i / \partial t$, which gives the most general form of the cable equation.

$$\frac{1}{r_i + r_e}\frac{\partial^2 V}{\partial x^2} = c_m \frac{\partial V}{\partial t} + I_{ion}$$



To obtain analytical solutions, the membrane is linearized



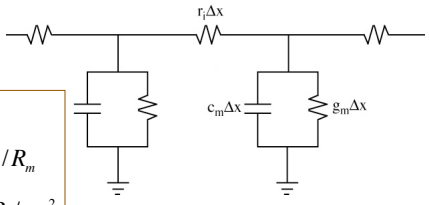
Now the ionic current is given by $I_{ion}=g_m(V-E_{rest})$. Because the differential equation is now linear it is possible to change the reference point for the membrane potential from 0 mV across the membrane to the resting potential. This amounts to a change in variable in the differential equation, replacing $V-E_{rest}$ with V. This gives the linear cable equation:

$$\frac{1}{r_i + r_e}\frac{\partial^2 V}{\partial x^2} = c_m \frac{\partial V}{\partial t} + g_m V$$

Which is usually written as below, defining a length parameter λ and a membrane time constant τ_m.

$$\lambda^2 \frac{\partial^2 V}{\partial x^2} = \tau \frac{\partial V}{\partial t} + V \quad \text{where} \quad \lambda = \sqrt{\frac{1}{g_m (r_i + r_e)}} \quad \text{and} \quad \tau_m = \frac{c_m}{g_m}$$

Parameters: it is useful to relate the parameters of the ladder model to properties of the cylinder membrane.



c_m = cap. per unit length of cylinder = $2\pi aC$

g_m = conductance of unit length of cyl. = $2\pi a / R_m$

r_i = resistance of unit length of cytoplasm = $R_i / \pi a^2$

where C is the capacitance of a unit area of membrane, $\approx 1\ \mu Fd/cm^2$

R_m is the resistance of a unit area of membrane, $\approx 10^3\text{-}10^5\ \Omega\cdot cm^2$

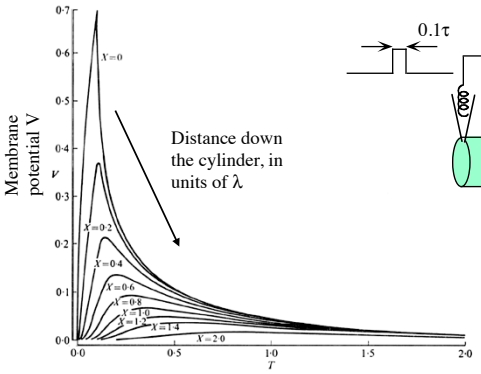
R_i is the resistance of a unit cube of cytoplasm, $\approx 200\ \Omega\cdot cm$

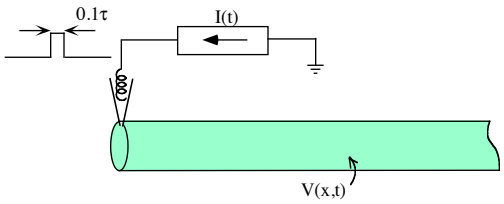
and a is the radius of the cylinder.

THEN the two parameters of the cable equation are given by

$$\lambda = \sqrt{\frac{1}{g_m(r_i + r_e)}} \approx \sqrt{\frac{1}{g_m r_i}} = \sqrt{\frac{a R_m}{2R_i}} \quad \text{and} \quad \tau = \frac{c_m}{g_m} = R_m C$$

Electrotonic processing in dendrites: potentials become smaller in amplitude and more spread out in time as they propagate away from the source





$$\lambda^2 \frac{\partial^2 V}{\partial x^2} = \tau \frac{\partial V}{\partial t} + V$$

$$V(x, t=0) = 0$$

$$\left.\frac{\partial V}{\partial x}\right|_{x=0} = -r_i I(t) \quad \text{and} \quad V(x,t) = \text{finite } \forall x,t$$

Jack, Noble, & Tsien, 1975

Parameters of the cable model:

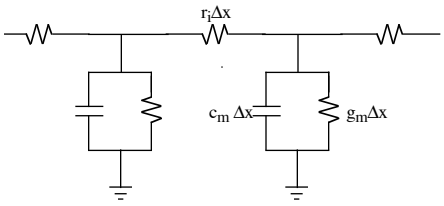
λ is the length constant. To see why, consider the steady-state distribution of membrane potential, say in response to a steady current after a long time. In this situation, $\partial V/\partial t = 0$ and the cable equation becomes

$$\lambda^2 \frac{d^2V}{dx^2} - V = 0$$

The homogeneous solution takes the form

$$V(x) = Ae^{x/\lambda} + Be^{-x/\lambda}$$

where A and B are constants determined from the boundary conditions. The solutions vary exponentially with distance x divided by λ, showing that λ determines the distance through which disturbances spread along a cable.



$$\lambda = \sqrt{\frac{1}{g_m r_i}} = \sqrt{\frac{R_m}{2R_i}}a$$

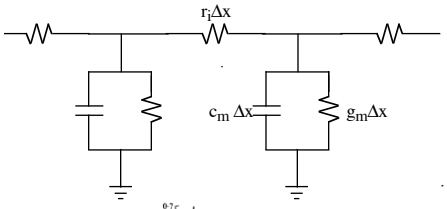
Note that the length constant is proportional to $a^{1/2}$, so potentials spread further in larger cylinders.

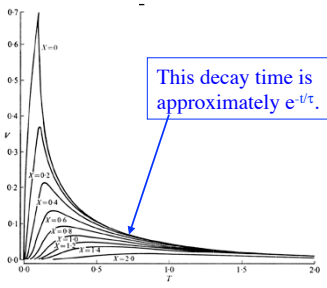
For a 1 μm dendrite with R_m=3x10^4 Ω·cm^2, λ = 866 mm

Parameters of the cable model:

τ is the time constant. In all solutions to the cable equation, time appears as t/τ, so that τ determines the time scale of solutions, e.g. how long it takes membrane potential to change in response to an injected current.

$$\tau = \frac{c_m}{g_m} = R_m C$$

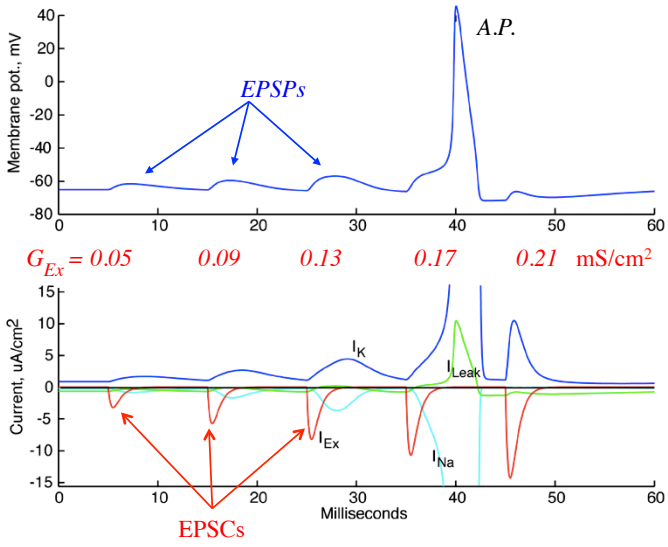




This decay time is approximately $e^{-t/\tau}$.

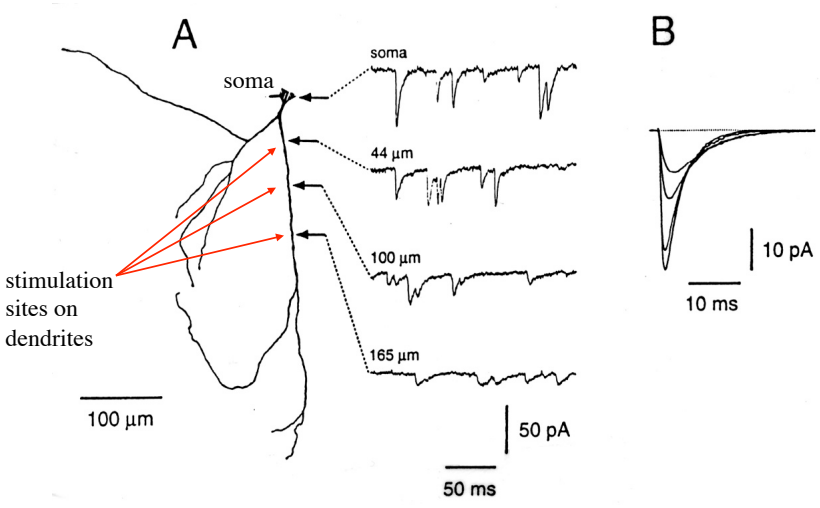
Note that the time constant does not depend on the cylinder size. For a process with R_m=3x10^4 Ω·cm^2, τ= 30 ms.

As a reminder, inputs to neurons come through *synapses* which produce conductance changes in the postsynaptic membrane. The result can be observed as *excitatory postsynapic currents* (EPSCs) or *excitatory postsynaptic potentials* (EPSPs).



simp.m

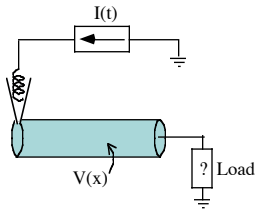
The cable model at work: EPSCs recorded in the soma show the effects expected, depending on the dendritic source (smaller and slower if initiated further away)

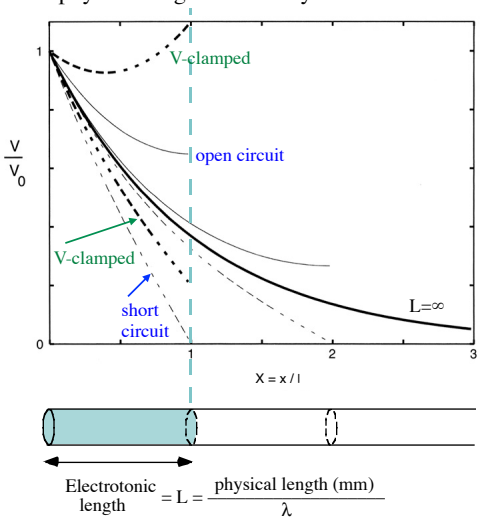


Bekkars and Stevens, 1996

The distance that a potential propagates in a membrane cylinder is set by the length constant λ. For this reason, a meaningful measure of the length of a membrane cylinder is its electrotonic length, equal to physical length divided by λ.

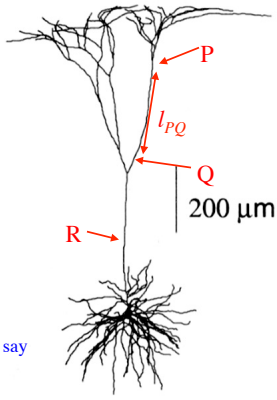
For a semi-infinite cylinder, the potential decays as $e^{-x/\lambda}$ with distance. For finite cylinders, the decay depends on the boundary condition (or load) at the second end.





Koch, 1999

How large is a cell? This can be answered in terms of physical length, as in the picture at right. A more meaningful answer is in terms of electrical size, some measure of the electrical coupling between two points.



Two measures:

1. Electrotonic length (as defined previously)

$$L_{PQ} = \frac{l_{PQ}}{\lambda}$$

2. The morphoelectrotonic transform (MET), in which distance is defined in terms of voltage attenuation A as follows:

$$A_{PR} = \frac{V_R}{V_P}$$

V_R: resulting potential observed at point R

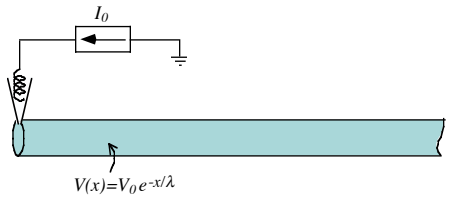
V_P: membrane potential produced at point P, say by a synapse

then the MET is

$$\Lambda_{PR} = -\ln A_{PR}$$

Note that Λ_{PR} incorporates both the exponential decay of potential with distance and the effects of branching (which the cumulative electrotonic length $L_{PQ}+L_{QR}$ would not) .

Justification for the MET: Consider again a semi-infinite cylinder driven by a constant current I_0 at one end, at times where the potential is in steady state.



The voltage gain from the point of current injection to point x is

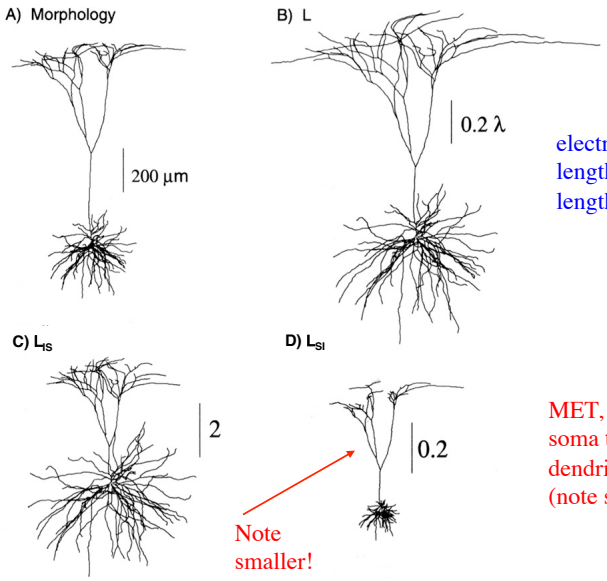
$$A(x) = \frac{V(x)}{V_0} = e^{-x/\lambda}$$

and the MET is

$$\Lambda(x) = -\ln\left(e^{-x/\lambda}\right) = \frac{x}{\lambda} = L(x)$$

so in this special case, the MET corresponds to the electrotonic length. Again, the advantage of the MET is that it takes into account the effects of branching, not relevant in this example.

How large is the dendritic tree? Note that the MET is different depending on the direction in which it is defined.



physical size

electrotonic length, equal to length/length const

MET, dendrite to soma

MET, soma to dendrites (note scale!)

Note smaller!

Zador, 1993

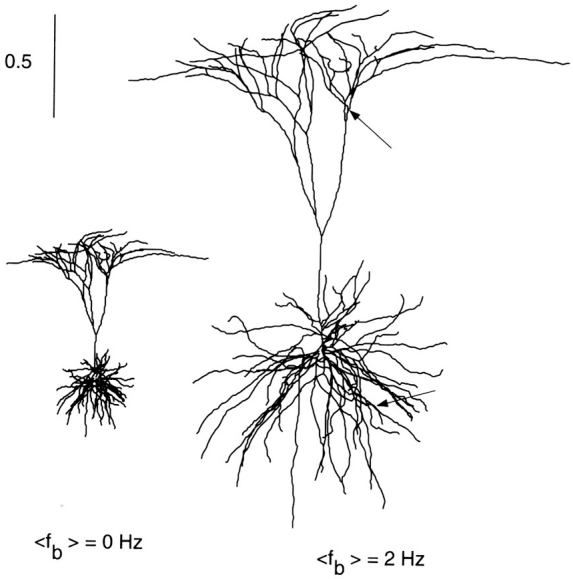
A cell's electrical size depends on the amount of synaptic input it receives.

The somaward METs at right are for a cell with no synaptic input (left) and a cell with substantial, randomly occurring, input (right).

Note the cell is electrically larger with synaptic input. This is explained as an effect of synaptic input on R_m and therefore on λ, since

$$\lambda = \sqrt{\frac{R_m}{2R_i}}a$$

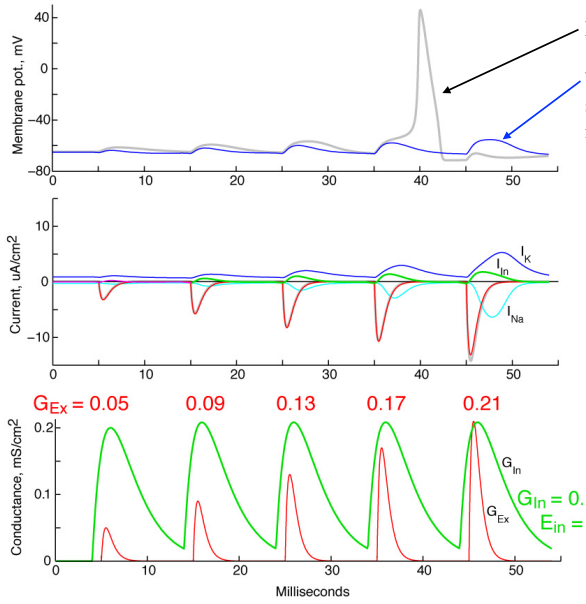
(λ decreases as R_m decreases, making the cell electrically larger.)



Bernander et al., 1991

end lect 8

Adding shunting inhibitory inputs blocks the response to the excitatory input. The effect is mainly due to the inhibitory conductance change.



Response with no inhibition.

With inhibition, EPSPs are subthreshold (threshold is now G_{Ex}=0.23)

E_{in} = -65 mV = the rest potential. Thus inhibitory currents flow only during the EPSP. However, they make the EPSPs smaller by diverting current from the other membrane components. This is **shunting inhibition**.

simp1.m