Mark Mikhly
3/2/09
Intro to Computational Modeling of Neurons
Professor John Rinzel

The Passive Axon

General Goal: Explore how different factors affect the spread of voltage in axons without voltage-sensitive channels

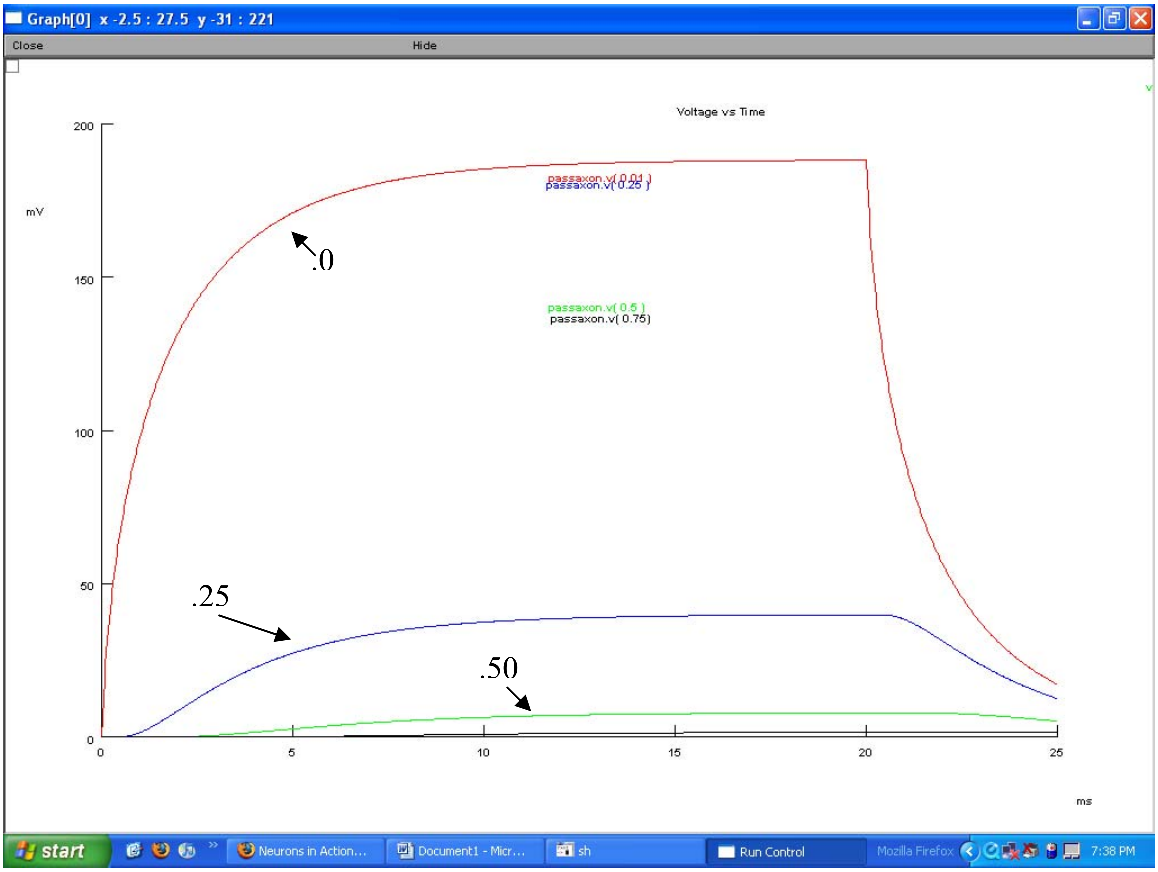
We will be looking at axons with no voltage gated channels and closed ends. Though most neurons have mechanisms in place to allow enhancement of signals to allow the spread of voltage, this tutorial will show the necessity of these mechanisms. Furthermore, there are indeed neurons – retinal photoreceptors and the hair cells of the inner ear – which are able to use passive voltage spread because of their size.

Specific Goals:

- Observing how voltage spreads passively when current is injected
- Discuss and measure the length constant, lambda.
- See how membrane resistance and axonal diameter affect lambda and the spread of voltage
- Investigate whether capacitance changes affect the spread
- Explore the affect of stimulus placement on passive spread

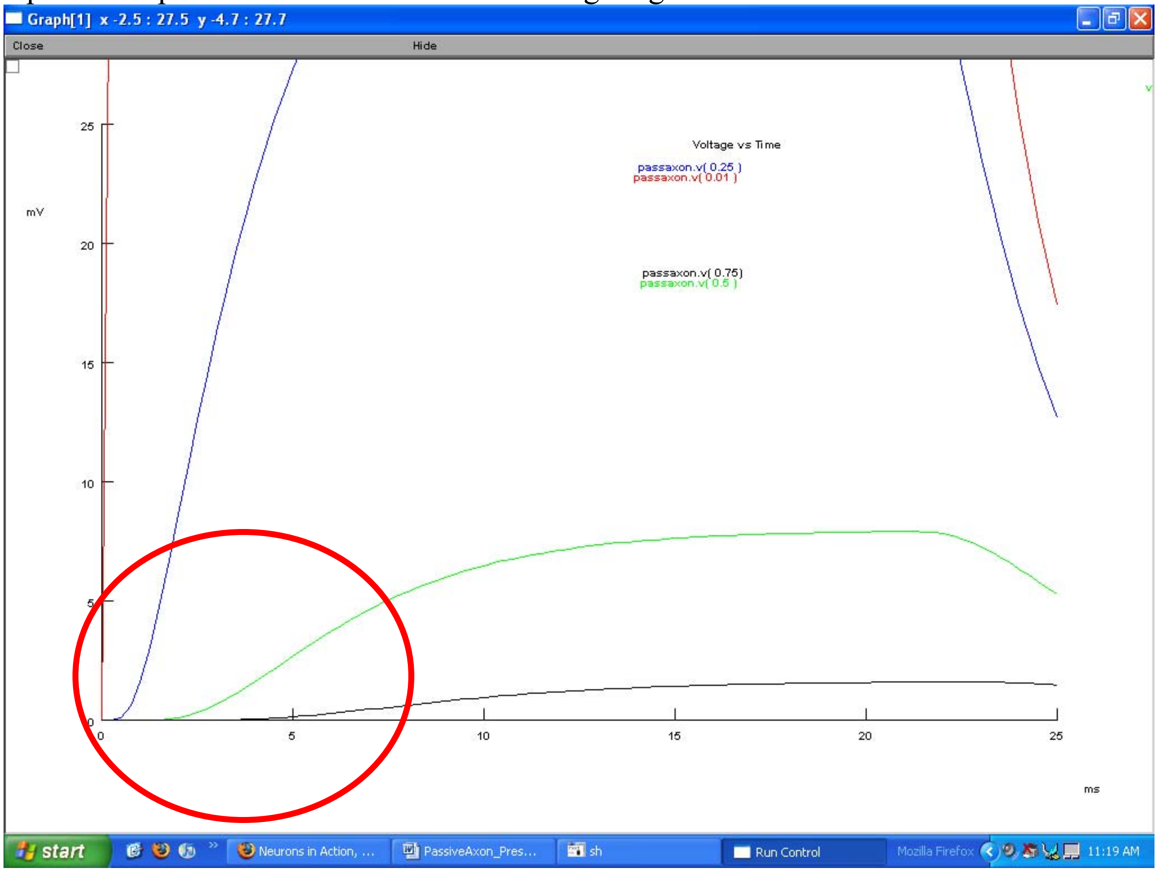
Task 1: Looking at Passive Spread of Voltage

Depolarize the axon at its left end and looking at the voltage spread town the axon.



Not only does the amplitude of steady state voltage get lower as you get farther from the point of stimulation, the rate of rise towards that amplitude gets smaller as well.

Open the expanded V vs. time to view it at higher gain:



We can see more clearly the delay in voltage spread that is caused by attenuation of the voltage as it spreads down the axon.

Task 2: Observing the steady state distribution of voltage along an axon

Open the voltage vs. space window and watch a movie of voltage changing along the length of the axon.
To change the speed of the simulation, move the bar along the control box.

To freeze the simulation as it approaches steady state, set the total ms box to 1 second below the stimulus length.

Task 3: Measuring the length constant

The length constant, lambda, is not really a constant but a measure of how charge is distributed down a specific axon. The number is the length down the axon from the stimulus at which the voltage is 1/e, or approximately .368, of the voltage at the point of stimulus.

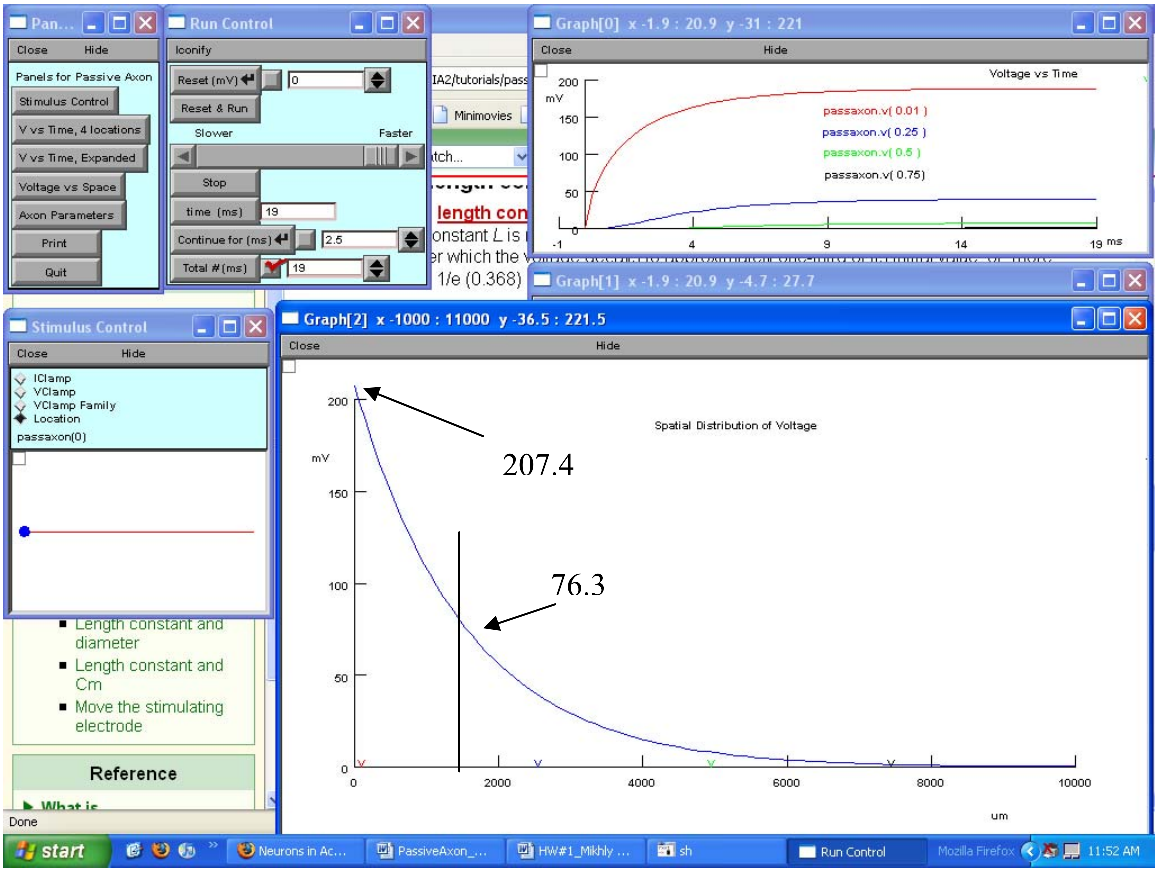
It is a product of the interplay of how easily current flows across the axon membrane against the ease of passage down the axon itself.

Mathematically we can find lambda:

L (lambda) = $\sqrt{}$ (r_m / r_a)
(1) $r_m = R_m / (pi * r)$ is the membrane resistance of a cm length of axon;
[R_m is membrane resistivity in ohm-cm^2 and r is the radius in cm.]
(2) $r_a = R_i/(pi * r^2)$is the axial resistance per cm length of axon.
[R_i is the intracellular resistivity in ohm-cm.]

r_m has units of ohm-cm^2 * cm.
r_a has units of ohm-cm.
Thus the ratio r_m/r_i has units of cm^2 and L has units of cm.

We can use neuron to measure lambda empirically by taking a look at the axon in steady state.



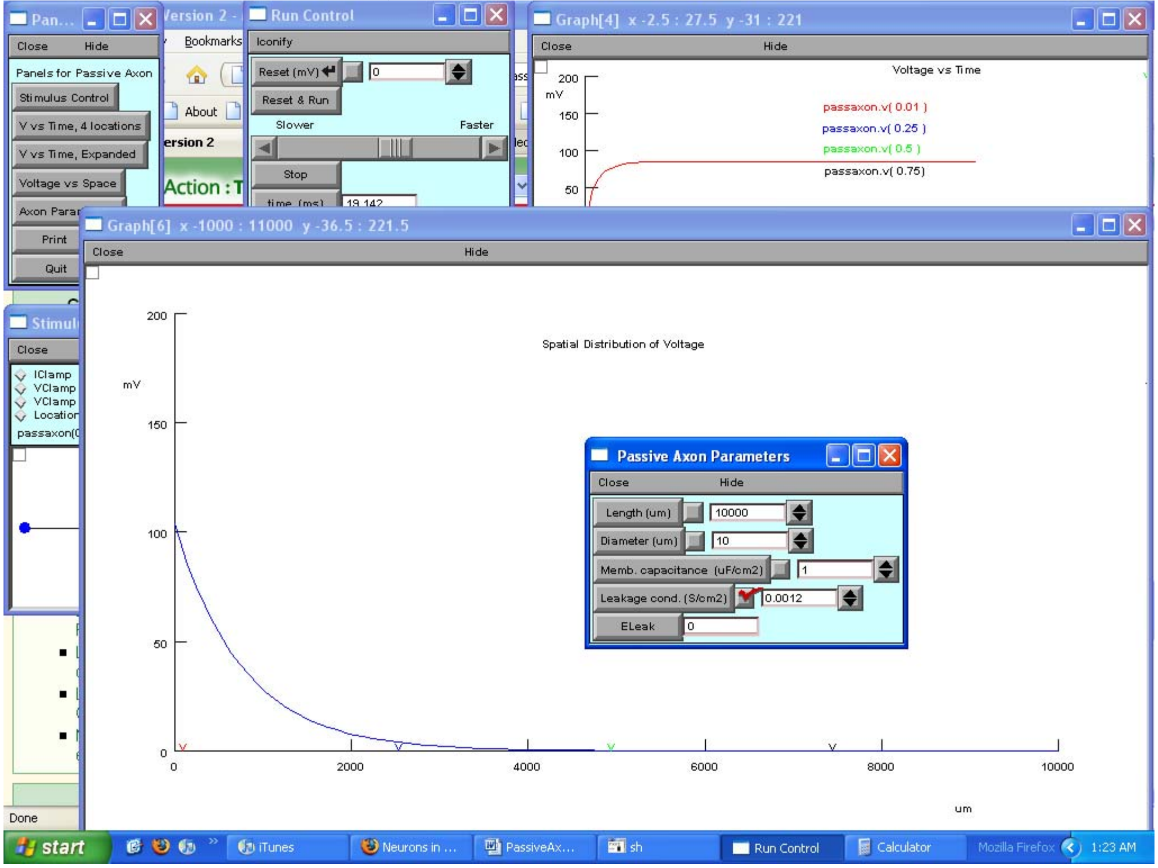
207.4

76.3

Measure V at x = 0 um: 207.4 mV
207*1/e= 76.3
X at which v = 76.3 mV : 1534.7 um

Task 4: The impact of membrane resistance on lambda

Decreasing the **membrane resistance** (or increasing the leakage conductance) leads to a smaller lambda as predicted by the above equation.



Reset (mV) 0

time (ms) 19.142

Length (um) 10000

Diameter (um) 10

Memb. capacitance (uF/cm2) 1

Leakage cond. (S/cm2) 0.0012

ELeak 0

mV at x =0 : 104
104*1/e= 38.3
X at which v = 38.3 mV : 742.6 um

Since L (lambda) = $\sqrt{(r_m / r_a)}$, quartering r_m halves lambda.
This is logical as the more current that flows out through the membrane, the less that is allowed to flow down the axon.

Task 5: The impact of axonal diameter on lambda.

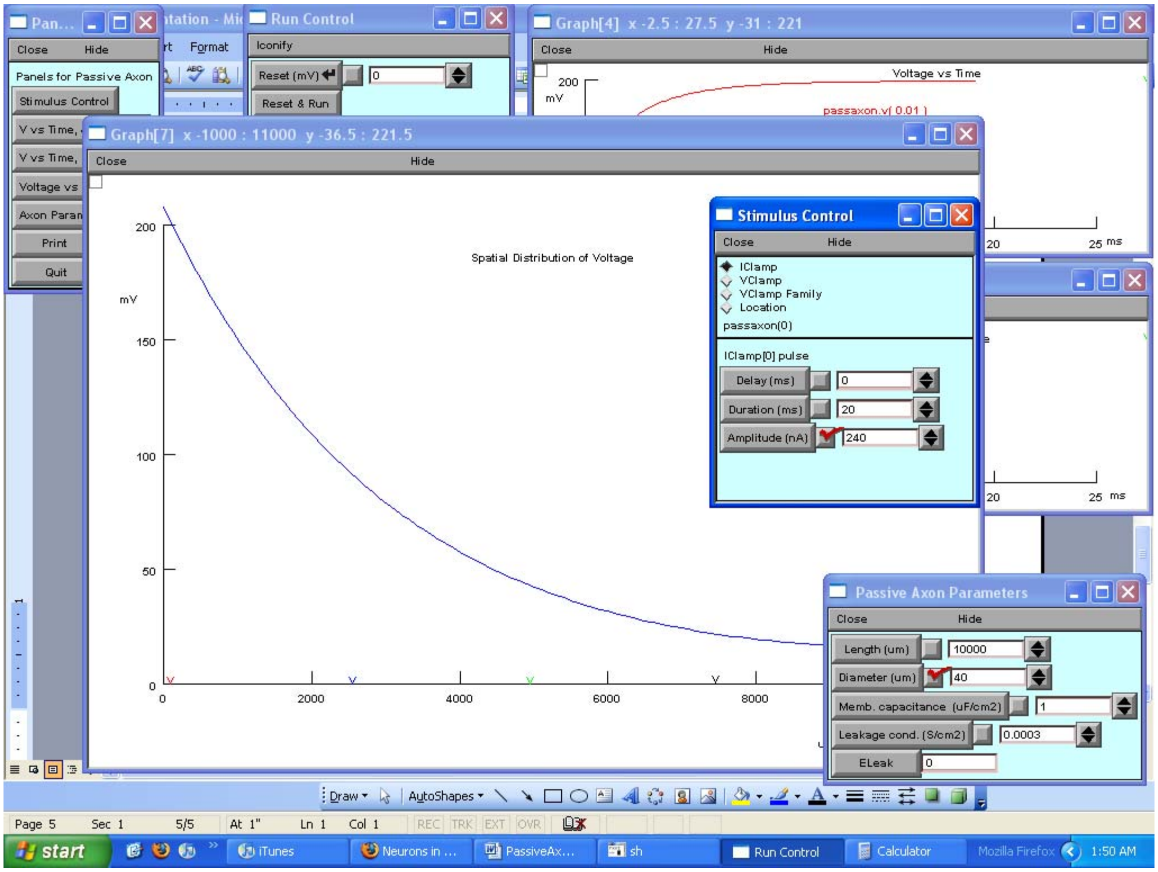
What about adjustments in the **axon's diameter**? Increasing the diameter of the axon decreases the axial resistance.

Lambda = square root of r_m/r_a and $r_m = R_m / (\text{pi} * r)$ and $r_a = R_i/(\text{pi} * r^{2)}$

$$\frac{\text{Ohm*cm}^2}{\text{Cm}} \quad \text{x} \quad \frac{\text{cm}^2}{\text{Ohm*cm}} \quad = \text{cm}^2$$

There is thus a direct relationship between radius and the ration of r_m to r_a. If r is quadrupled r_m/r_a would be quadrupled… and the square root of that (lambda) would be doubled.

Looking at Neuron:



Reset (mV) 0

Delay (ms) 0

Duration (ms) 20

Amplitude (nA) 240

Length (um) 10000

Diameter (um) 40

Memb. capacitance (uF/cm2) 1

Leakage cond. (S/cm2) 0.0003

ELeak 0

Measure V at x = 0 cm: 207.9 mV

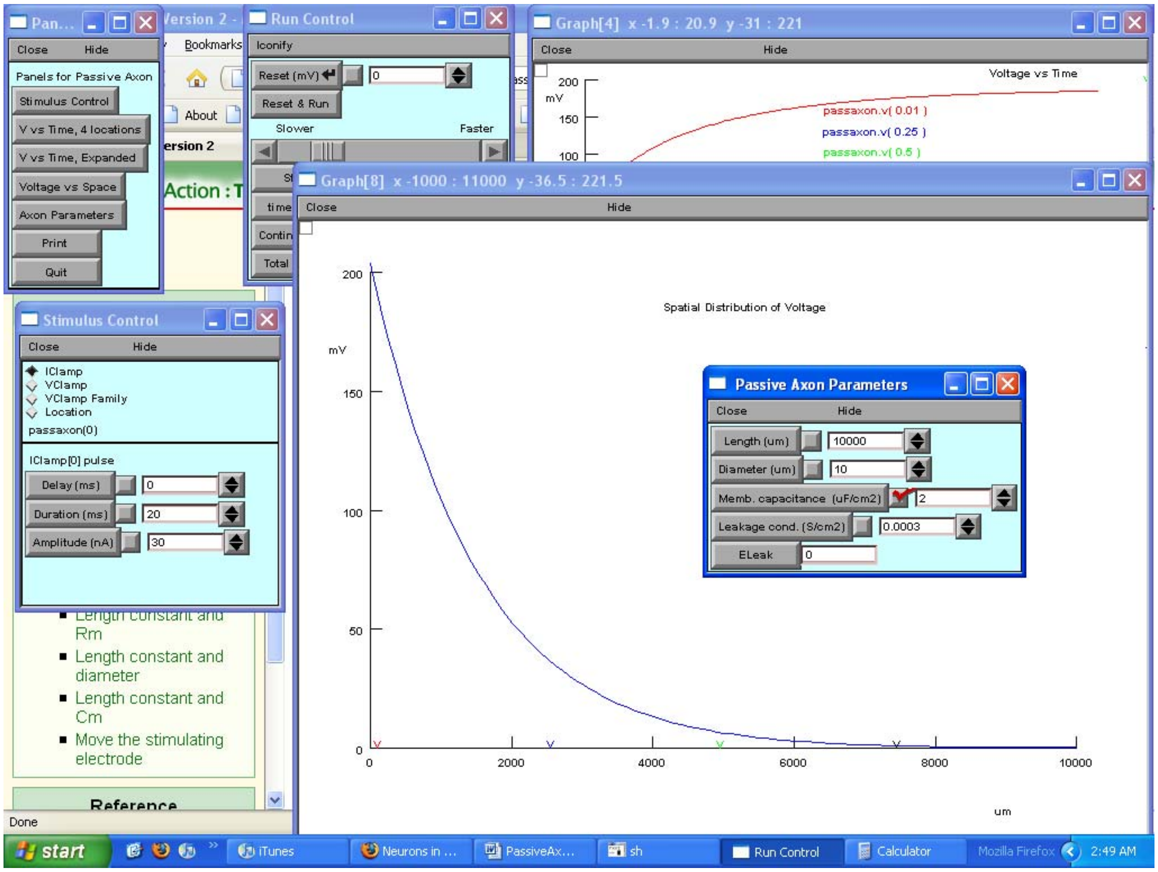
207.9 mV *1/e= 76.5 mV

X at which v = 76.5 mV : ~ 3118um [which is roughly double the original lambda of 1534]

Task 6: Capacitance and the length constant.

We've explored how changes in membrane and axial resistance affect lambda.
What about changes in membrane capacitance? In the body, myelin greatly decreases membrane capacitance. How do changes in capacitance affect the length constant?

Lets double the capacitance:



Reset (mV): 0

● IClamp

passaxon(0)

IClamp[0] pulse

Delay (ms): 0

Duration (ms): 20

Amplitude (nA): 30

Length (um): 10000

Diameter (um): 10

Memb. capacitance (uF/cm2): 2

Leakage cond. (S/cm2): 0.0003

ELeak: 0

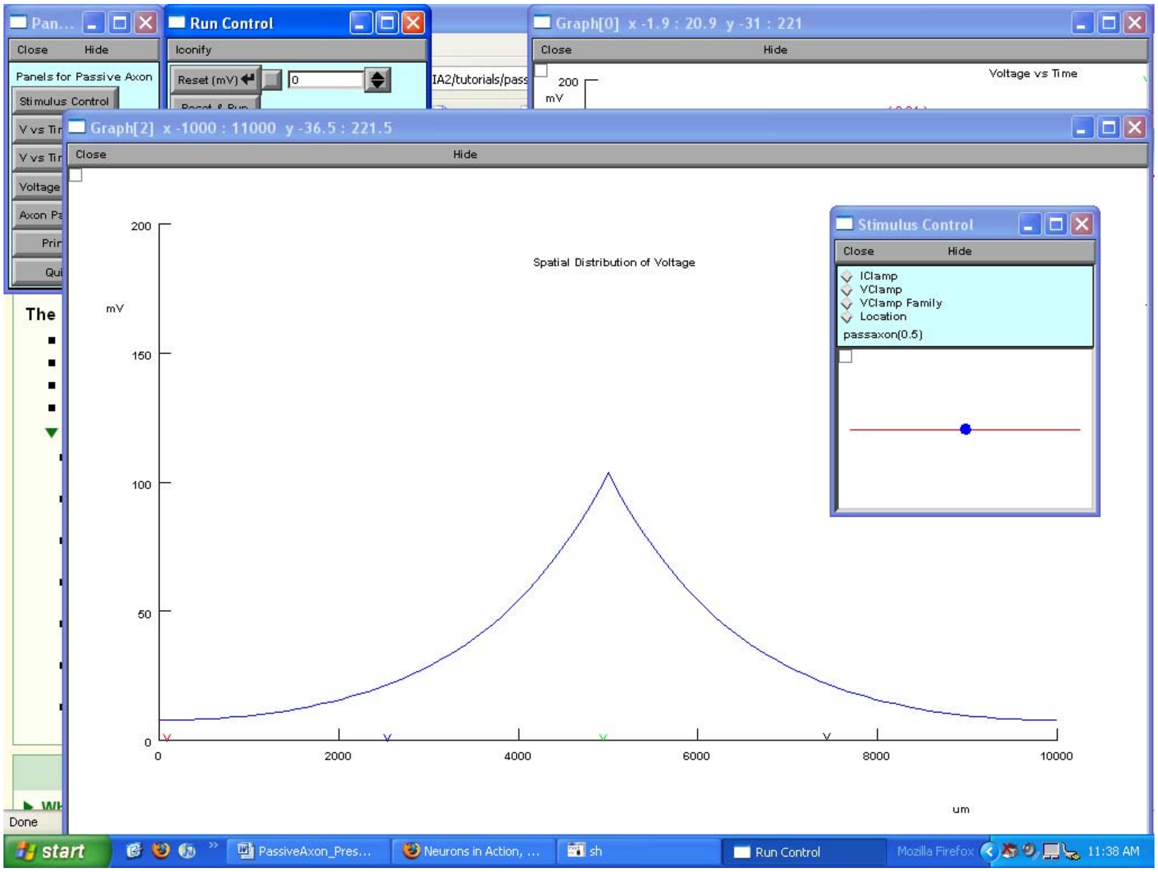
Measure V at x = 0 cm: 204 mV
204 mV *1/e= 75 mV
X at which v = 75 mV : ~ 1534um

There is no change in lambda. This shouldn't be a surprise since capacitance is not in the equation for lambda. What is effected is the time course of the voltage rise at the point of current entry, as the time constant tau (the time which it takes to rise to 1-1/e of its steady state voltage) is directly affected by capacitance: $t = r_m c_m$.

Increasing the capacitance increased the rate of voltage rise. Decreasing does the opposite. That is how myelination, which decreases conductance by putting more space between the capacitors, promotes the speed of voltage spread and salutatory conduction.

Task 7: Moving the stimulus electrode

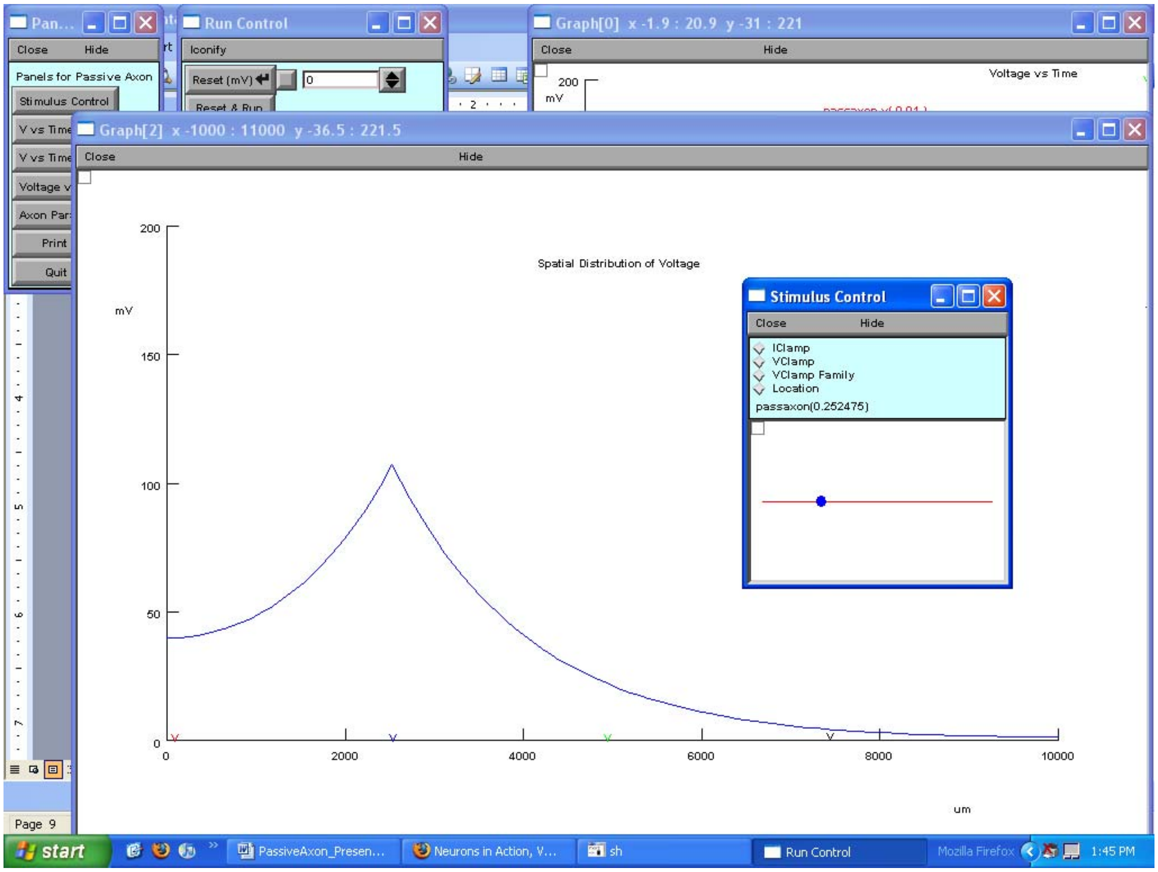
Place the stimulus electrode at the center of the axon’s length



passaxon(0.5)

Note that the Vmax is half what it previously was, since the voltage can now diffuse in two directions.

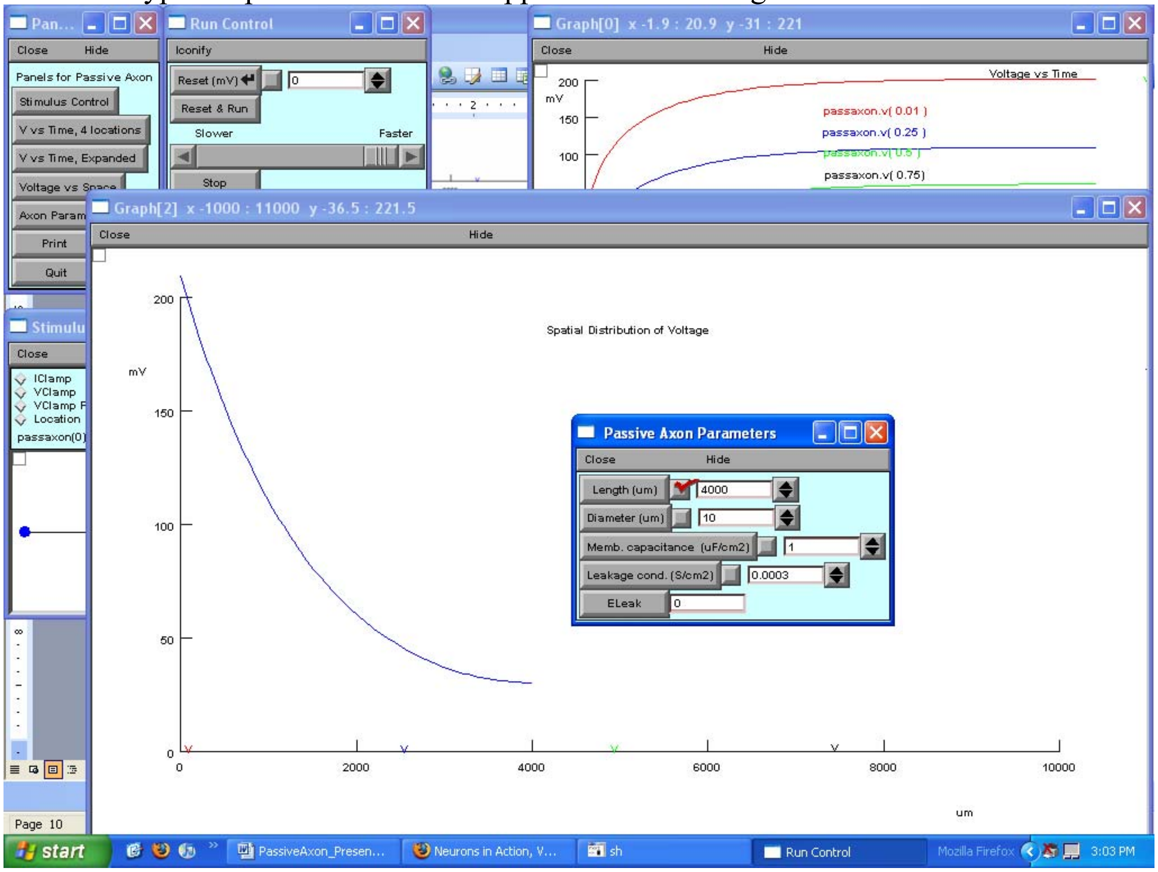
Placed at ~2500 um from the end of the axon:



passaxon(0.252475)

The voltage on the near side doesn't decay normally because there is nowhere for the current to go but back upon itself. The simulation uses an axon with closed ends of infinite resistance. Without current there is no gradient.

The same type of spatial summation happens when the length of the axon is shortened:



Passive Axon Parameters

Length (um) 4000

Diameter (um) 10

Memb. capacitance (uF/cm2) 1

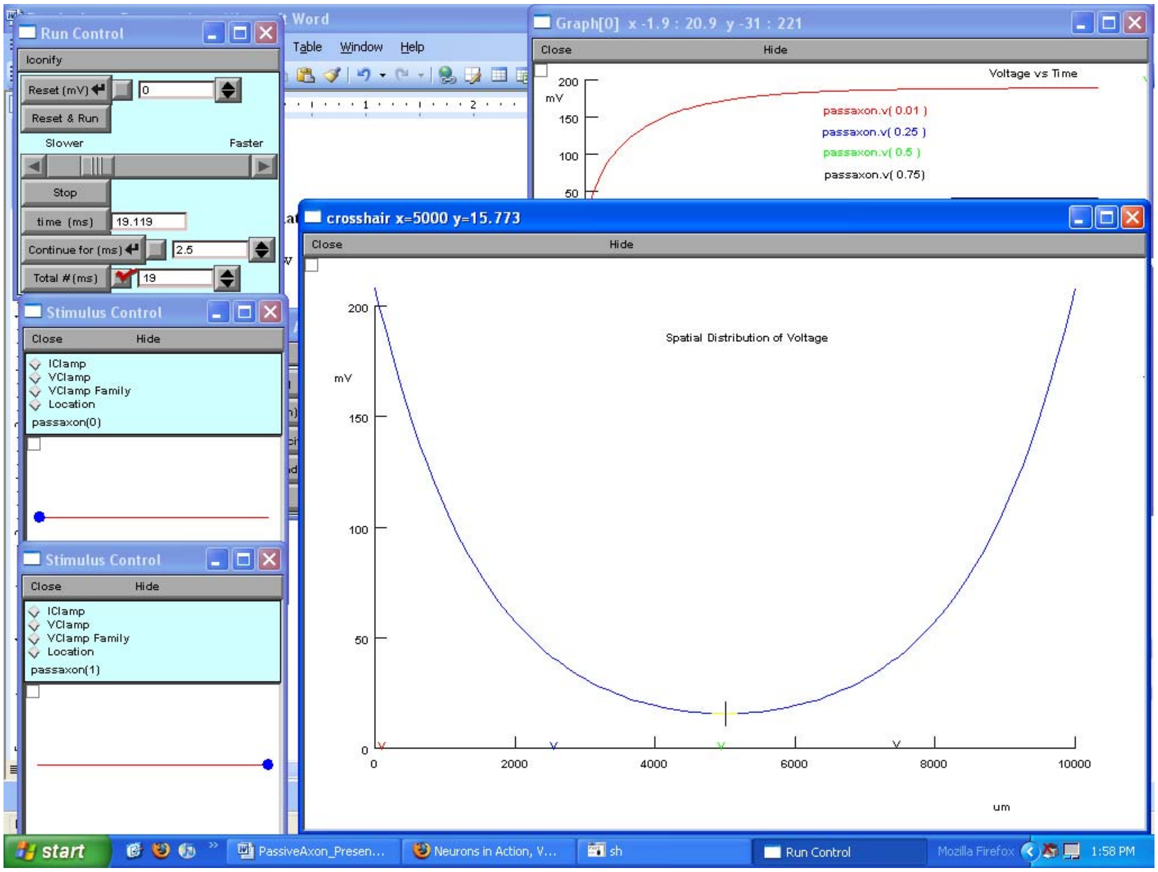
Leakage cond. (S/cm2) 0.0003

ELeak 0

What if there were two stimulating electrodes?

How would the voltage gradient be affected by currents diffusing from different points?

Stimulating from opposite ends:



Reset (mV) 0

time (ms) 19.119

Continue for (ms) 2.5

Total # (ms) 19

crosshair x=5000 y=15.773

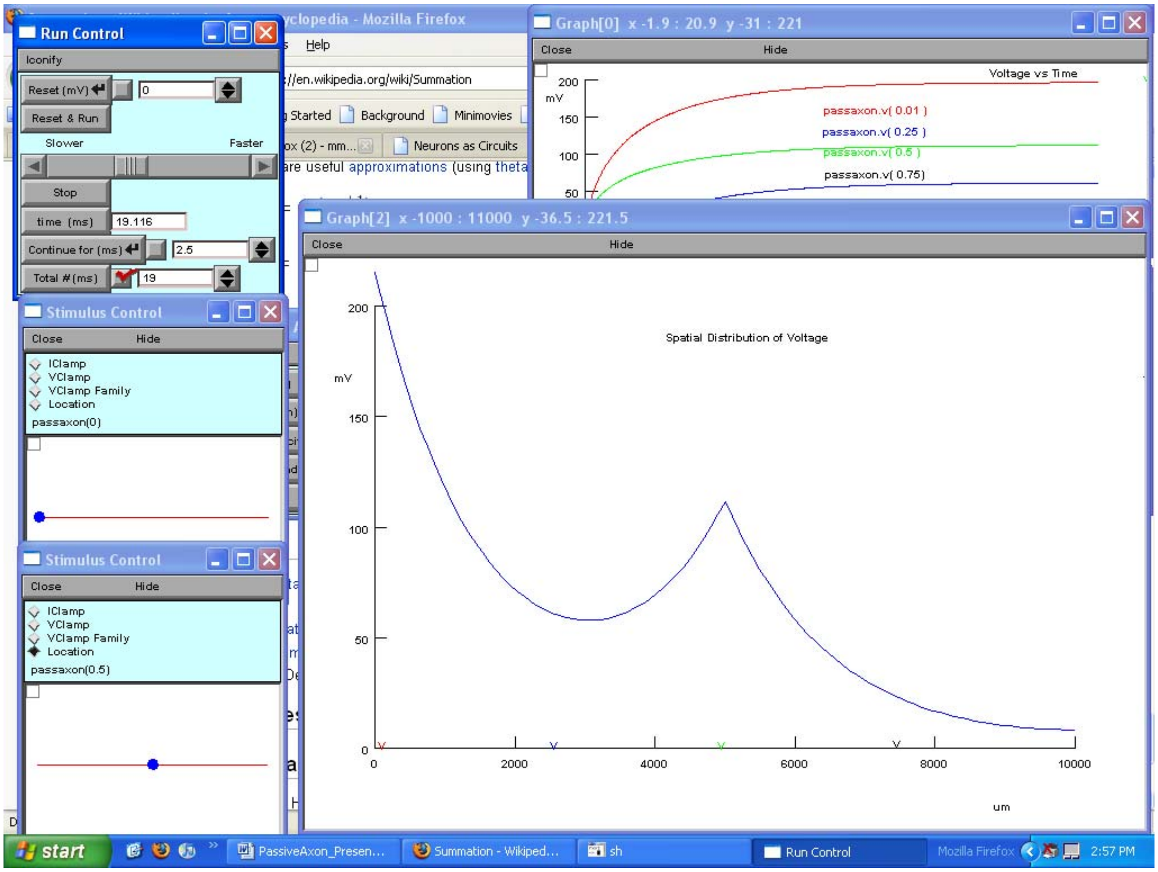
Graph[0] x -1.9 : 20.9 y -31 : 221

passaxon(0)

passaxon(1)

At the midpoint of the axon the voltage is double what it would be with only a single electrode – the voltages sum spatially.

This can also be seen in the case of one electrode on an end with another in the middle.



Reset (mV) 0

time (ms) 19.116

Continue for (ms) 2.5

Total # (ms) 19

passaxon(0)

passaxon(0.5)