

Introductory Neuroscience and Neuro-Instrumentation
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Lecture 49
P300 Demonstration with EEGLAB/ERPLAB (1)

So, introductory Neuroscience and Neuro-Instrumentation. This is a demo on the membrane time constant also called tau. It is denoted by the lower case Greek letter tau.

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Introduction

Hello!

Welcome to a demo of the Membrane Time Constant (τ)

This demo is a complement to the lecture on Axonology and Neuronal Biophysics.

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So, this demo is a compliment to the lecture on Axonology and Neuronal Biophysics.

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Software: METANEURON

Newman MH, Newman EA. *MetaNeuron: A Free Neuron Simulation Program for Teaching Cellular Neurophysiology*. *J Undergrad Neurosci Educ*. 2013;12(1):A11-A17.

Free, standalone program that can be used without restriction.

It is used to conduct Neurophysiology experiments *in silico*.

Works on Windows, Mac and Linux (*via WINE*).

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So again, the software we are using is by Doctor Newman and Newman, it is called MetaNeuron. It is from the University of Minnesota. It is a free neuron simulation program for teaching cellular neurophysiology and was published in a journal of Undergraduate Neuroscience Education, June 2013 and it can be used without restriction. And it is used to conduct neurophysiology experiments in silico. It works on Windows, Mac and Linux. It is a Windows program, but on Linux you use WINE to run it.

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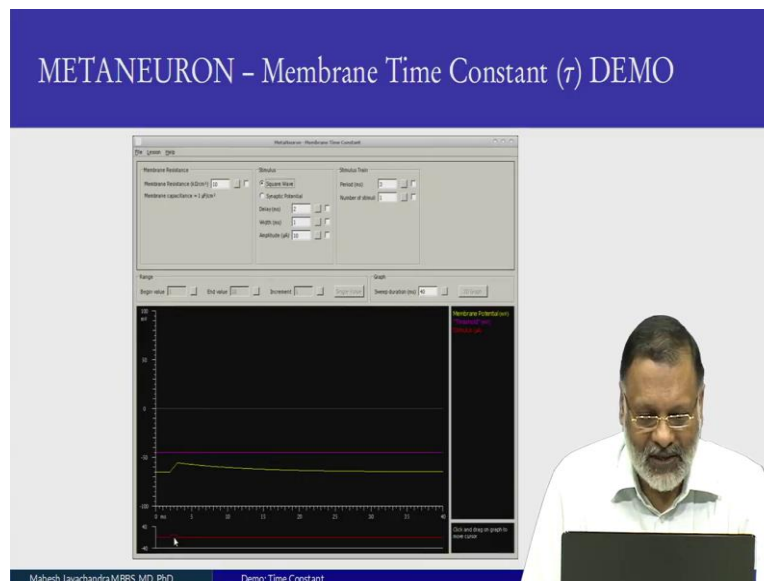
METANEURON (2)

- Neuronal parameters, e.g., Na^+ and K^+ concentrations, equilibrium potentials and conductances can be easily modified.
- A virtual stimulator injects single or double current pulses into the neuron.
- Responses are displayed graphically and can be measured with a cursor.
- Families of traces can be easily generated and viewed in rotatable 3D plots.

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So, as mentioned earlier, the neuronal parameters that is a sodium, potassium concentrations, their equilibrium potentials and conductances can be easily modified. A virtual simulator stimulator injects single or double current pulses into the neuron. Responses are displayed graphically and can be measured with a cursor. And finally, family of traces can be easily generated and viewed in rotatable 3D plots.

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So, here we look at the time constant. So, now, the time constant is the time, suppose consider an axon, so at one end you inject current. So, ignore all the active conductances, just think of it is an electrical phenomenon. So, how long does it take to decay when passively if you inject a particular voltage here, how long does it go the axon and decays? We are not talking about axon potential, we are just talking of just the decay of little bit of current which is injected at one point in the axon.

So, that is what this demon would show you and here you see a current pulse being put in here, it is a little small, this red line which denotes this stimulus. And you have the yellow line which actually shows the membrane potentials. So, when you put in the current, you have a change in the membrane potential, it goes towards depolarisation and then it decays. Now, the purple line is the threshold for it to fire an action potential. We are not modeling the those action potential in this demo. We are just seeing what is the time course of this decay of the potential when you put, inject it at one point in the axon.

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Membrane Time Constant (τ)

The time constant affects many neuronal phenomena:

- 1) The time course of neuron responses
- 2) The propagation of action potentials in axons
- 3) The summation of synaptic potentials



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And this is important, before we get into the demo, little bit of background and also to remind you, the time constant affects many neuronal phenomenon. First of all it affects the time course of the neuron responses, I mean how long does it take to get back to 0. Then it majorly affects the propagation of action potentials in axon. And most importantly, it affects also the summation of synaptic potentials.

For example, if you have one synaptic potential, it does not reach the threshold, but just before it decays, if you have another synaptic potential, again it does not reach threshold, but just before decays if you add a third one, then it hits threshold and then you have an action potential. Now, this depends on tau, you know, how long it takes to decay.

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Membrane Time Constant (τ)

Here the neuron is modeled by a passive membrane resistance, R_m , a membrane capacitance, C_m , and a current source.

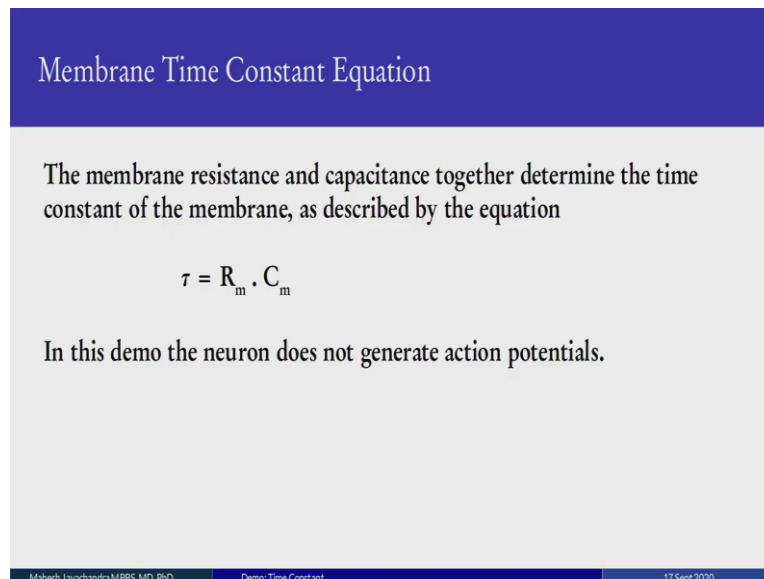
The membrane capacitance equals $1 \mu\text{F}/\text{cm}^2$.

The value of the membrane resistance as well as the time course and amplitude of the current source can be varied.

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And tau is very simply the product of the membrane resistance R_m and the membrane capacitance and a current source. And the membrane capacitance generally is assumed to be 1 microfarad per square centimetre. Membrane resistance, it depends on the axon, the dendrite, the neuron or whatever looking at. And in this demo, the value of the membrane resistance, as well as the time course and the amplitude of the current source, can be varied to get a sense of how it rises and then decays.

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Membrane Time Constant Equation

The membrane resistance and capacitance together determine the time constant of the membrane, as described by the equation

$$\tau = R_m \cdot C_m$$

In this demo the neuron does not generate action potentials.

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So, as mentioned, the membrane resistance and capacitance together determine tau and is described by the simple equation, tau equals R_m into C_m . Again, in this demo the neuron does not generate axon potentials because we are just looking at this passive property of the axon, not active conductances which give rise to the action potential.

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Membrane Time Constant (τ)

Here we see how the membrane resistance, R_m , affects the time constant by varying R_m and the changes in the rise and fall of neuronal responses evoked by injection of a square wave of current.

Using the cursor we can measure the membrane potential at different times during the rising and falling phases of the response and empirically determine τ . We can compare this to the theoretical value $R_m \cdot C_m$.

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So, here we see how the membrane resistance of $\times$ the time constant by varying R_m , and the changes in the rise and fall of neuron responses evoke by injection of a square wave of current. Using the cursor we can measure the membrane potential at different times during the rising and falling phase of the response and empirically determine tau. And then we can compare this to the theoretical value of R_m and C_m and see how they match.

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Membrane Time Constant (τ)

The default value of the stimulus current source, a 1ms depolarizing pulse, is a good approximation of the current generated by a fast excitatory synapse.

Using the default parameters, we see the effect of the membrane time constant on temporal summation of synaptic potentials. The "Threshold" potential indicates the voltage at which action potentials will be initiated.

Note: The neuron model used in this lesson does not include active membrane conductances and will not generate action potentials when the membrane potential exceeds the threshold value

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The default value of the stimulus current is a 1-millisecond depolarizing pulse. This is a very good approximation of the current generated by a fast excitatory synapse. When I say fast excitatory synapse, it assumes there are fast inhibitory synapses and also slow excitatory synapses and slow inhibitory synapses. But here we are looking at a fast excitatory synapse.

Using the default parameters we see the effect of membrane time constant on the temporal summation of axon, synaptic potentials.

The threshold potential indicates the voltage at which action potentials would be initiated. And remember, axon potentials all are nothing, once it reaches threshold, it fires an axon potential. These potentials, the synaptic potentials the graded. So, again, you have the centre play of a an analog system by a greater response and an all or nothing kind of a digital response. So, each neuron is a combination of an analog as well as a digital system.

And just to reiterate, the neuron model used in this lesson does not include active membrane conductances and it will not generate action potentials when the membrane potential exceeds thresholds. Just bear that in mind.

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Membrane Time Constant (τ)

When a constant current is injected into a neuron, the membrane potential depolarizes with an exponential time course (assuming that there are no active membrane conductances).

Similarly, when the stimulus is turned off, the membrane potential returns to the resting membrane potential with an exponential time course.

The rate at which the membrane potential increases/decreases is described by the time constant, τ . τ is defined as the time it takes for the membrane to increase or to decrease to $1-1/e$ (approximately 63%) of its final value.

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Demo: Time Constant

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So, when a constant current is injected into a neuron, the membrane potential depolarizes with an exponential time course (assuming there are no active membrane conductances). Similarly, when the stimulus is turned off, it returns back to the rmp, the resting membrane potential in an exponential, with an exponential time course. So, the rate at which the membrane potential increases or decreases is described by the constant tau. And tau is defined as the time it takes for the membrane to increase or decrease to approximately 63 percent of its final value, $1-1/e$.

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Manipulating the Membrane Time Constant (τ)

- 1) Using the default parameter values, determine the time constant of the membrane by measuring the time it takes for the amplitude of the membrane potential to fall 63% of the way back to the baseline value, after the current source is turned off.
- 2) A family of curves showing the effect of varying the membrane resistance can be displayed by using the range function of MetaNeuron. Check the “Membrane Resistance” range box and choose range values of 0.5, 20, and 2 (begin value, end value, and increment).

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So, there are exercises, again for this lesson, I wish I encourage you to go through. So, some of these are, one is using the default parameter values, determine the tau by measuring the time it takes for the amplitude of the membrane potential to fall to 63 percent way back to baseline value, after the current source is turned off.

You can also generate a family of curves showing the effect of varying the membrane resistance and here you use the range function of MetaNeuron. So, I will show this to you in the demo. So, you essentially you check the membrane resistance range box and choose range values of 0.5, 20 and 2 (begin value, end value and increment) and you get a family of responses like so.

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Effect of varying Membrane Resistance on τ

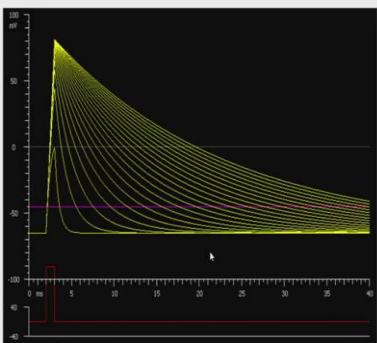
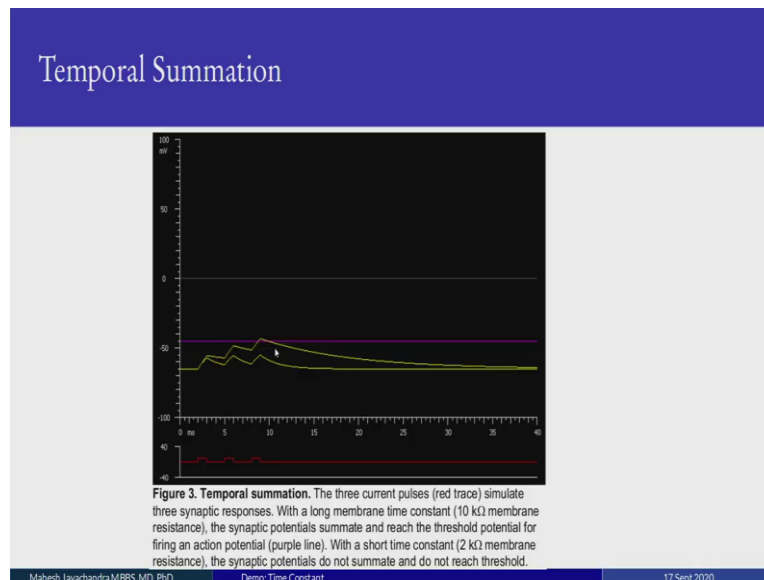


Figure 2. Membrane time constant. A 150 μ A, 1 msec current pulse rapidly depolarizes a neuron. At the end of the pulse, the membrane potential decays back towards the resting membrane potential with an exponential time course. The time constant of decay decreases as the membrane resistance is reduced from 20 k Ω to 0.5 k Ω .

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So, here a 150 microcurrent is injected for 1 millisecond and it rapidly decays over time. Each of these is a family of curves and this is an exponential time course. And at the end of the pulse the decay begins. The time constant of the decay decreases as the membrane resistance is reduced from 20 to 0.5k.

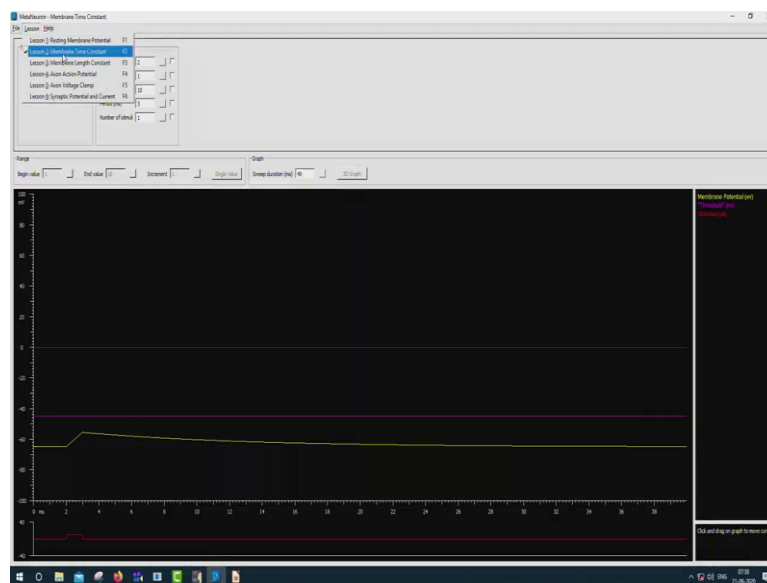
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And here is what I mentioned about temporal summation. You have 3 stimuli, 3 current injections over here. The first one, the second one, and the third one. So, with the long time membrane constant, membrane time constant, here we are talking of 10k ohms, they summate and reach the threshold potential for firing an action potential. So, this is the 10k ohms and when it reaches here you get an action potential.

As I said that is not a model but just assume that happens. But if you have a short time constant, they do not summate enough to reach the threshold. So, you get a sense of how the membrane resistance effects the firing of action potentials.

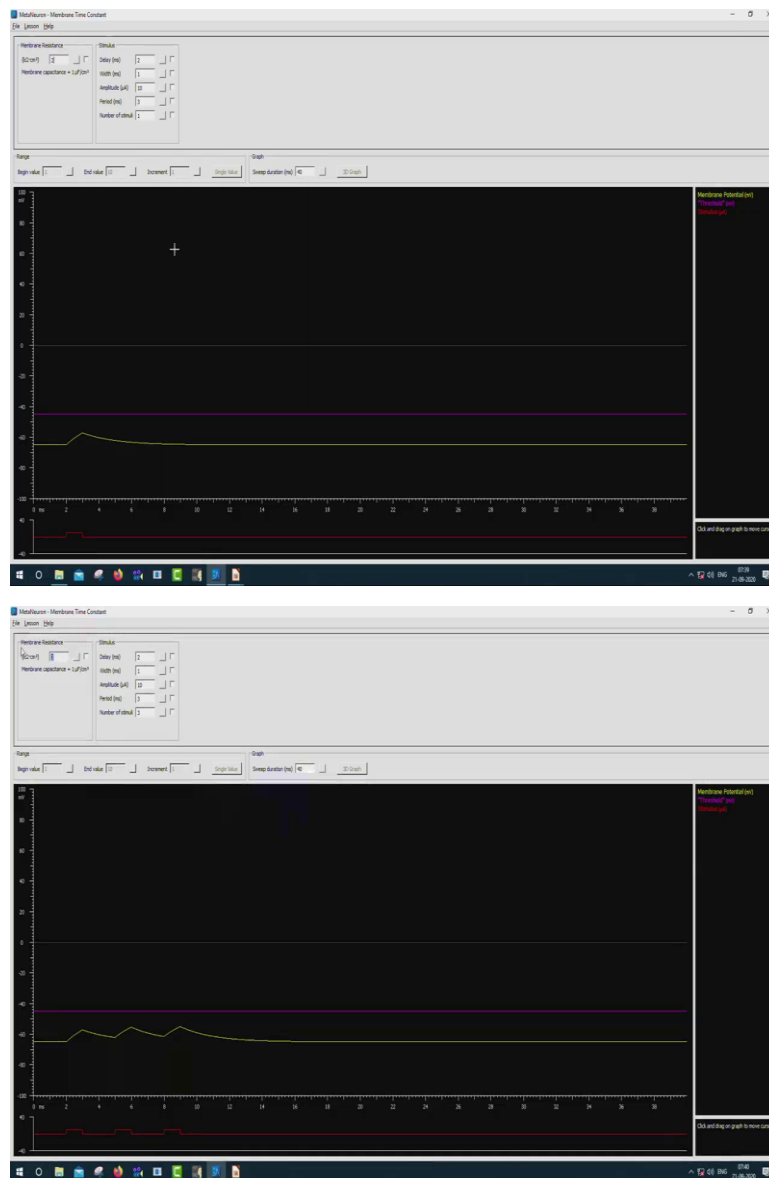
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I open MetaNeuron and I have chosen a lesson 2 which is a membrane time constant. Briefly, on the left you have the membrane resistance and here we have kept with default is 10 kilo ohms into square centimetre and membrane capacitance is constant at 1 microfarad per centimetre square. and the stimulus, we can put in the delay, we can put in the width, we can change the amplitude, we can change the period and we can change the number of stimuli.

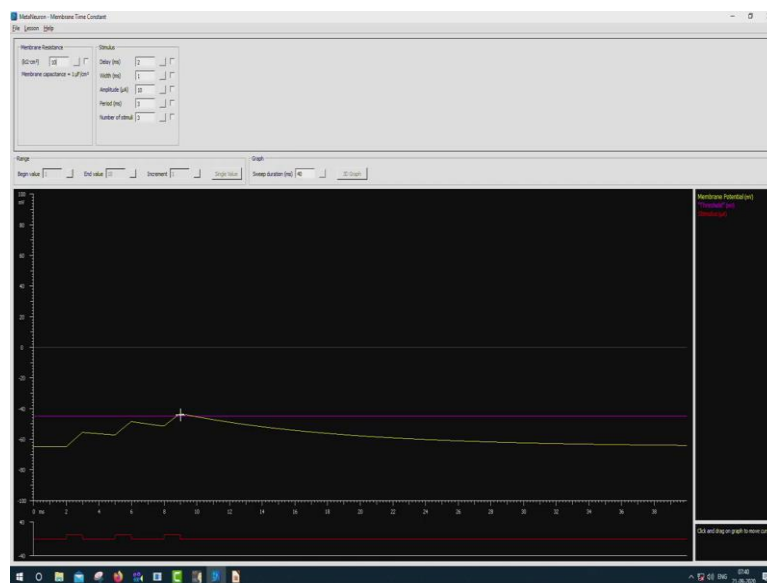
And below is the 3D graph function and I will get to that just in a second. So, briefly, the red line right below the plot, the trace is the current injection, is a stimulus and it is in microamps. The yellow trace is the membrane potential, how it changes and how it decays and purple is the threshold. When it hits threshold, just in your mind think an action potential fires.

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So, we will start simply by changing the membrane resistance from 10 to 2 and you see it comes back to normal much much earlier. Now, over here, let us change the number of stimuli to 3 I hit enter. So, you have a, they sum, this is a little higher, then this because it is coming in before it is completely decayed and this is little higher than this comes back, but it does not and it come back to normal. But it does not hit the purple line. So, it does not hit the threshold, so there are no action potentials.

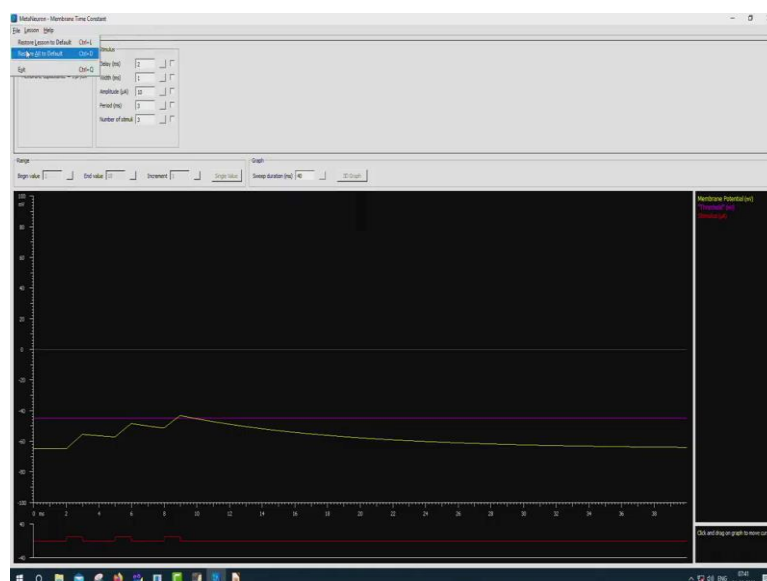
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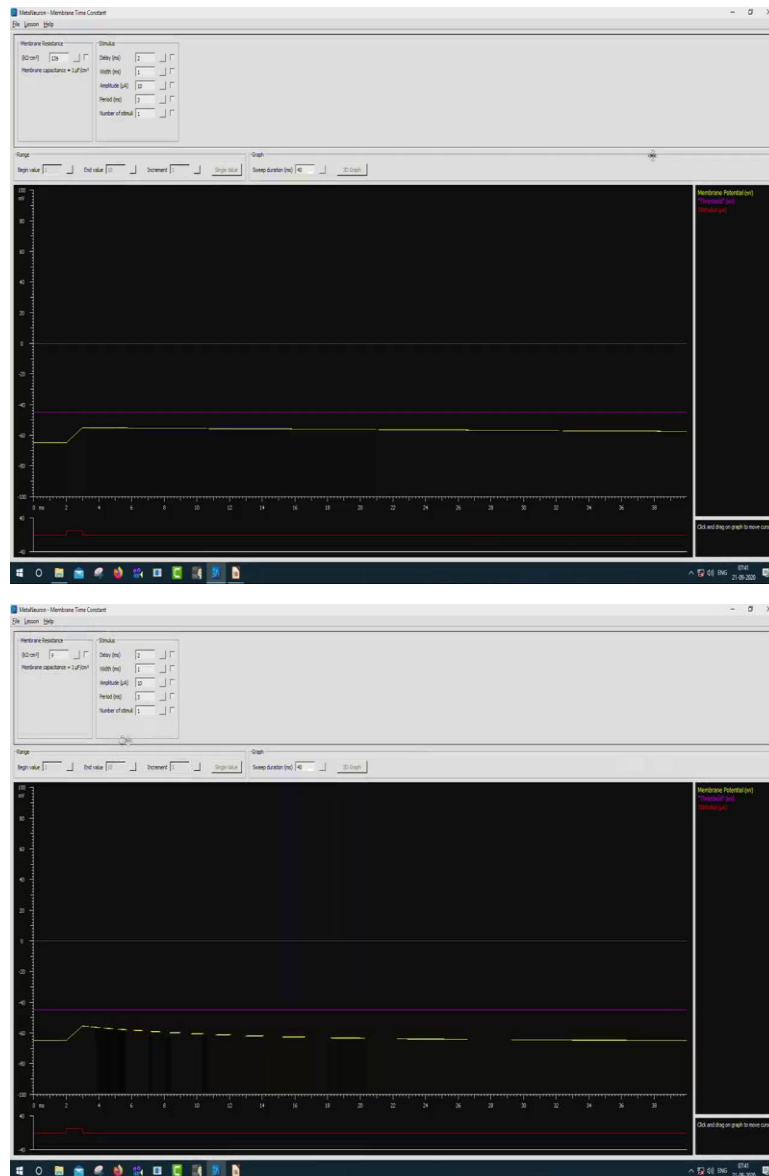


Now if we change it back to 10, there you go. So, the you have nothing else has changed, we have just changed the membrane resistance and you see the tau changes and it takes much longer to decay and by the third stimulus current injection, it reaches threshold. So, why does this happen? Intuitively you can think of some of the current when it is just 2, we will change it back to 2, it leaks out of the membrane, in the sides. It leaks out.

And if it is the resistance is low, more of it leaks out. So, it does not reach threshold, but if it is high, if it goes back to 10, then it is forced to go through the axon on the current. And that is why it is, the reaches threshold. So, now what we can do is we can actually we can change the delay.

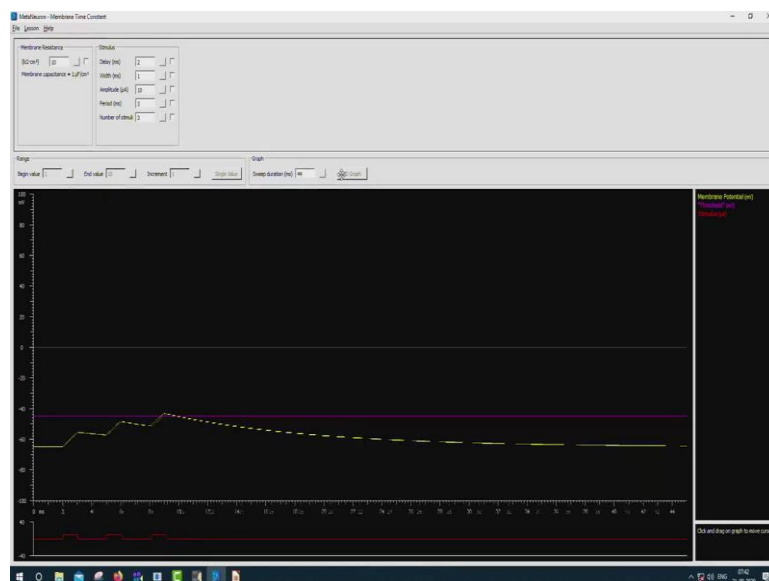
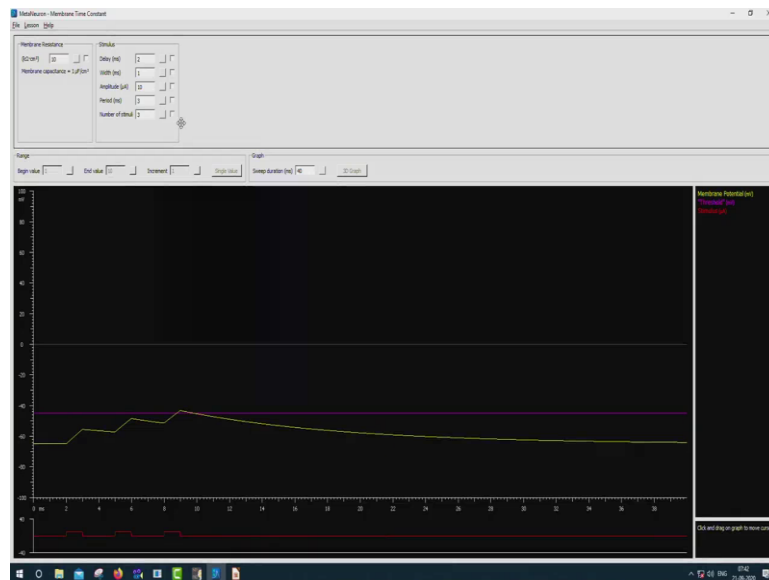
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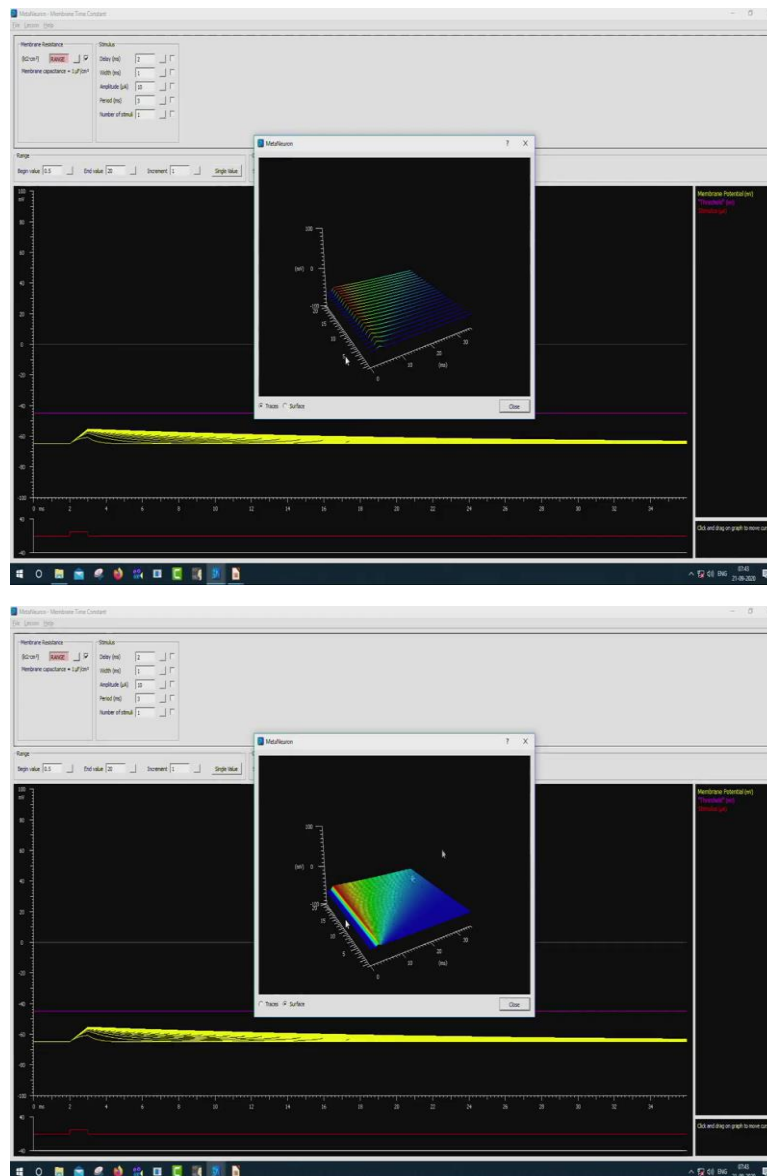
Let me go back to the default values. The default value is, the membrane resistance is 10k ohm centimetre square and one thing I did not mention is the way to change values without actually entering number into the box. So, next to it is this button, so you can hit the button and move it and you can see the tau increasing or you can make it much shorter and it goes. So, that is an easier way to change things rather than entering values each time.

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So, let us go back to default and likewise with the number of stimuli, so you have 1, you have 2, 3, so you can keep doing this way, you do not have to keep entering values and so you see, that when it is 10, by about 3 reaches a threshold and you can easily see that over here. And you can also change this sweep duration if you want to make it much shorter, more tangible or easier to see. So, you can make it much shorter or you can make it much longer. So, let us go back to defaults and we can have range.

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So, we can have range of membrane resistances. So, what you do is, you press click this box over here and then this is activated, this the range panel. So, here you have a begin value of 0.5 and end value of 20 and it increments by 1 and the sweep duration we saw that you can

make it shorter, this is making it longer or you can make it much shorter so you can see it in detail.

And finally, you can 3D graph it. So, well. You can see it, it is not very prominent but you can see the values increasing and this is the voltage and this is the time course, the time course over here and you see the membrane resistance values. Another way of looking at is, this is traces, individual traces with all the increments shown over here, but you can also look at the surface, not so prominent over here but you can, for the action potential stuff, this is the useful way to look at things.

So, thus basically, as far as this demo is concern, please, again I strongly encourage you to download this and it would be very useful if you look at the lecture in tantrum with the demo and play with these values, the you cannot change the capacitance, but the resistance values. If you look at the delay, the width, the amplitude, period, etcetera and get a good sense of how it actually work.

In my experience I found that this is a better way to understand tau rather than you know, dry dreary numbers, you where you keep calculating R_m into C_m .