Introductory Neuroscience & Neuro-Instrumentation
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Lecture No. 57
Demonstration Synaptic Potentials & Current

So, introductory neuroscience and neuro instrumentation, this is a demo on synaptic potentials and occurrence.

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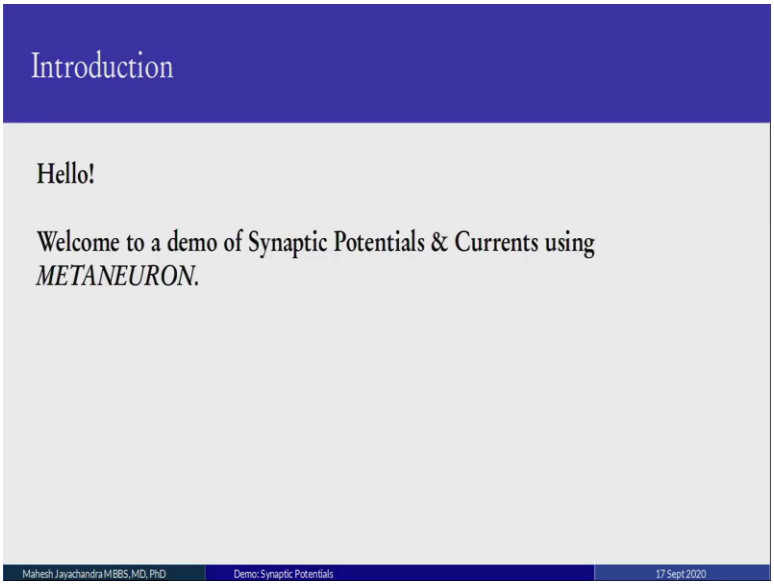

So, welcome to our demo of synaptic potentials and currents and we are going to be using MetaNeuron.

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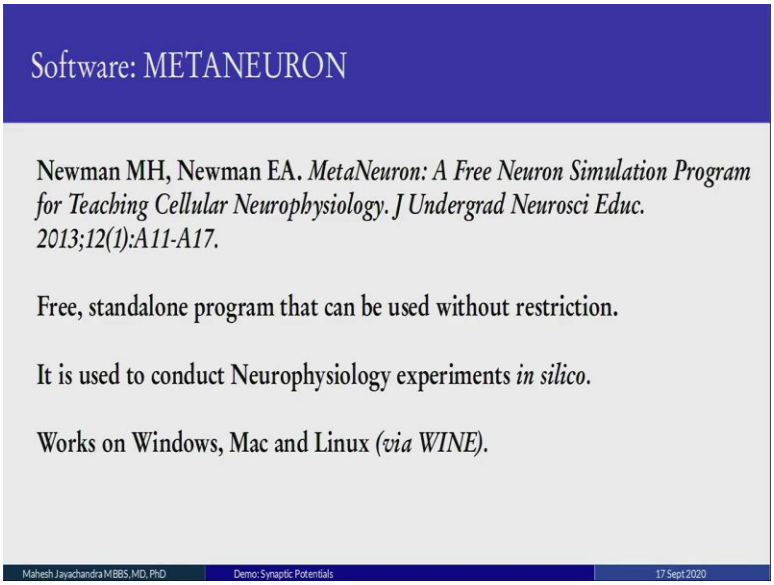

This is software created and published by Professors Newman and Newman at the University of Minnesota in the journal of Undergrad Neuroscience Education June in 2013. As said earlier with a free standalone program that can be used without restriction, it is used to conduct cellular neurophysiology experiments in silico and it works on windows Mac and on Linux via WINE.

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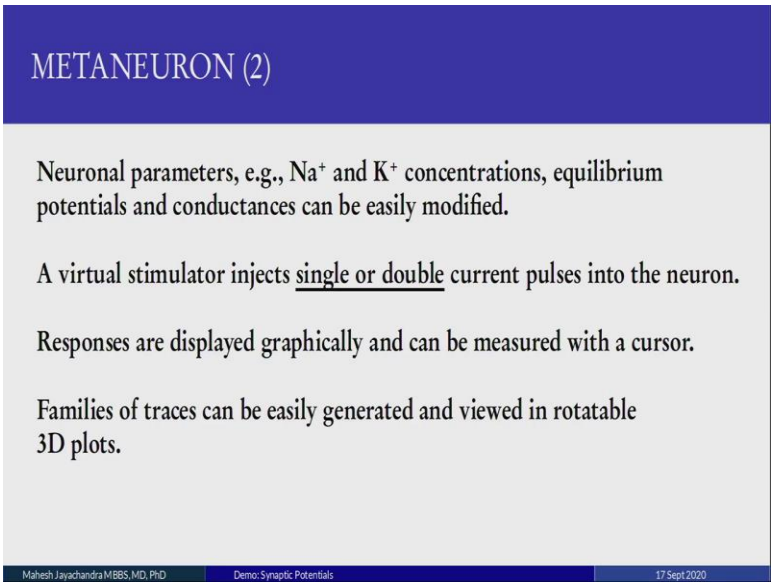

So, as mentioned neuronal parameters that is sodium and potassium concentrations, their equilibrium potentials and conductances can be easily modified. A virtual stimulator injects single or double current pulses into the neuron. Responses are displayed graphically and can be

measured with the cursor. And finally families of traces can be easily generated and viewed in a rotatable 3D plot.

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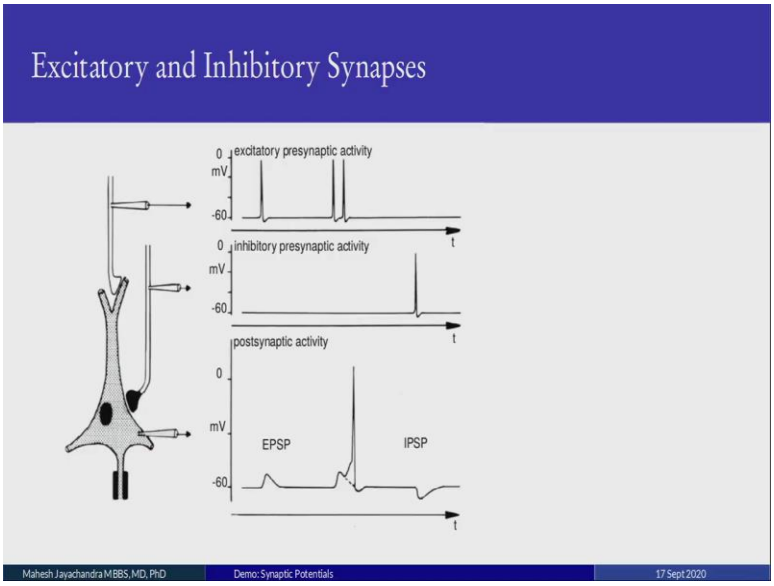

So, a little a reminder of what exactly we mean by excitatory and inhibitory synapses. So, consider a pyramidal cell in the central nervous system on the left, a classic pyramidal cell. Now, I have chopped off all the dendritic trees because that would make it very confusing. So, we are just looking at excitatory synapses and inhibitory synapses. So, this is a dendrite from an adjacent interneuron or a pyramidal cell which comes and forms an excitatory synapse over here.

So, if you remember a synapse consists of a presynaptic process, a cleft, synaptic cleft which is a discontinuity of 20 nanometers and a postsynaptic process over here. So, here we are recording intracellularly from the presynaptic process, presynaptic axon before it goes to the synapse and you see excitatory presynaptic activity axons firing action potential is one over here, there is two over here and if you look at the postsynaptic activity which is what is happening in the pyramidal cell, this is the post-synaptic activity.

If you just consider the presynaptic activity changing the resting membrane potential of the pyramidal cell. So, you have an excitatory postsynaptic potential EPSP. And if remember these are mediated by the neurotransmitter glutamate. So, you have this little synaptic process and then it decays. And how does it decay? This follows lambda chop all the principles of passive neuron, neuronal conduction.

When you have two of them and very close to each other they summate, they summate temporally and the first one is the same as here but the second one comes in and it reaches it adds on to it and it reaches the threshold, it meaning the resting membrane potential and then you have an all or nothing action potential and then the action potential goes down within about a millisecond or 2, then you have the after hyperpolarization and then it comes back to normal.

So, that was excitation but you can also have inhibition mediated if you remember via GABA gamma-aminobutyric acid and this is a intracellular recording of the inhibitory pre-synaptic axonal process, this is the inhibitory synapse and that looks the same the inhibitory action potentials are action potentials they look the same. But what it causes in the membrane is the resting membrane potential goes below. So, obviously there is no action potential because it is hyper polarizing, this is depolarizing.

Now, the excitatory post synaptic potentials this is what causes EEG just to remind you, not the inhibition, not the action potentials of the post synaptic process but the EPSPs that is what gives rise to EEG, it looks so small but that is the, that is what we record from the scalp.

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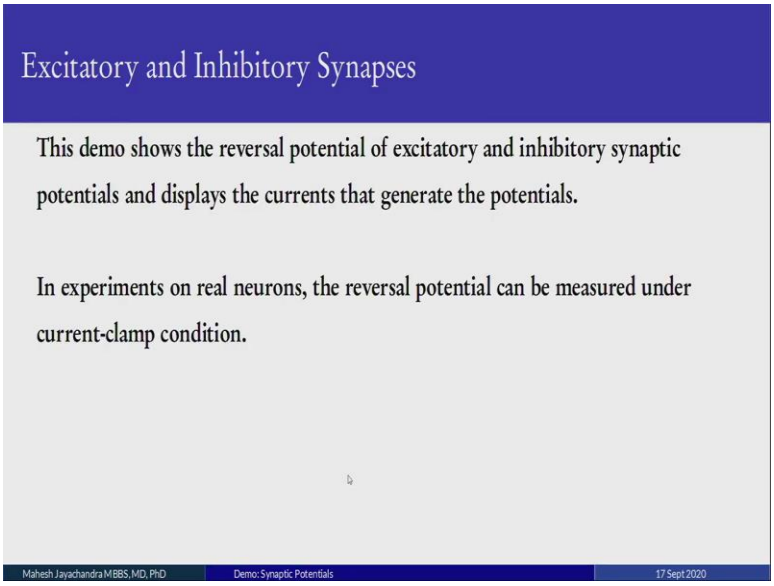

So, moving on the our demo will show the reversal potential, where it reverses of the excitatory and the inhibitory synaptic potentials and it also displays the currents that generate these potentials. In experiments on real neurons, the reversal potential can be measured under current clamp conditions, not voltage clamp but current clamp.

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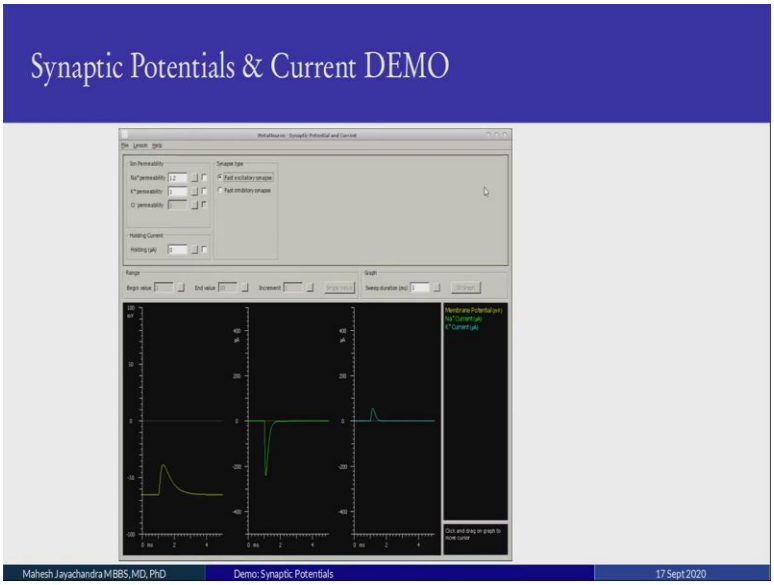

So, this is the demo opening panel for synaptic potentials and currents and we will go through it in detail when we actually do the demo.

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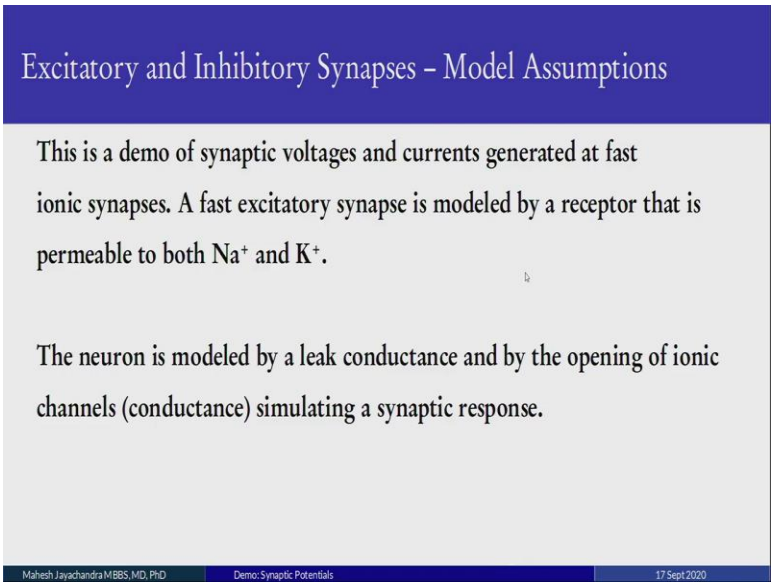

And this demo of synaptic voltages and currents generated as a demo generated at fast ionic synapses there are many many different kinds of synapses, some of them are fast, some of them are slow, so we are looking at the fast guys. A fast excitatory synaptic potential is modeled by a receptor that is permeable to both sodium and potassium and the neuron is modeled by a leak

conductance and by the opening of ionic channels or conductance then this simulates a synaptic response.

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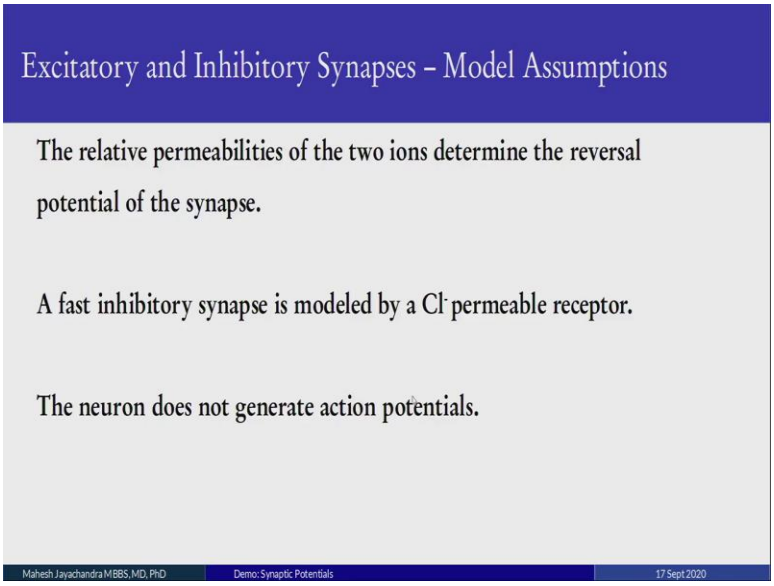

So, there are certain assumptions in this model. So, one is the relative permeabilities of the two ions determine the reversal potential of the synapse. A fast inhibitory synapse is modeled by a chloride permeable receptor. And finally this neuron does not generate action potentials.

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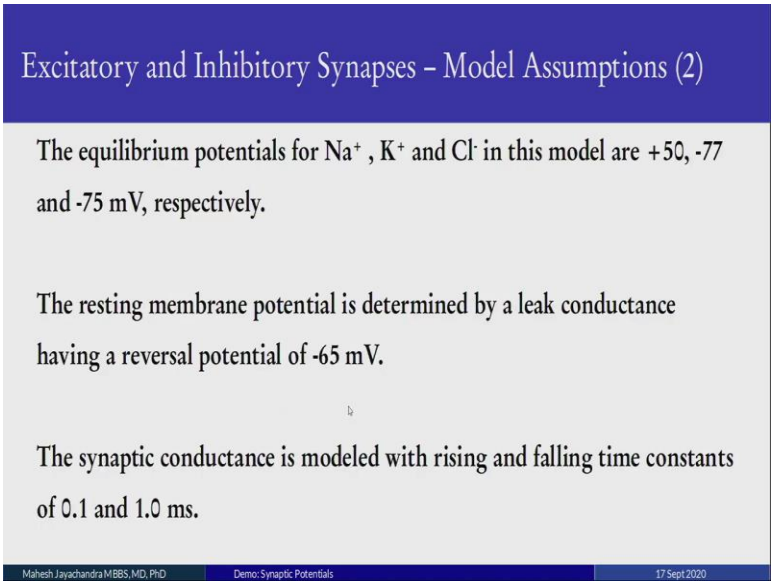

So, the other assumptions are the equilibrium potentials, equilibrium potentials of sodium, potassium and chloride, in this model are plus 50, minus 77 and minus 75 respectively. The resting membrane potential is determined by a leak conductance having a reversal potential of minus 65 millivolts and the synaptic conductance is modeled with a rising and falling time constant of 0.1 to 1 milliseconds.

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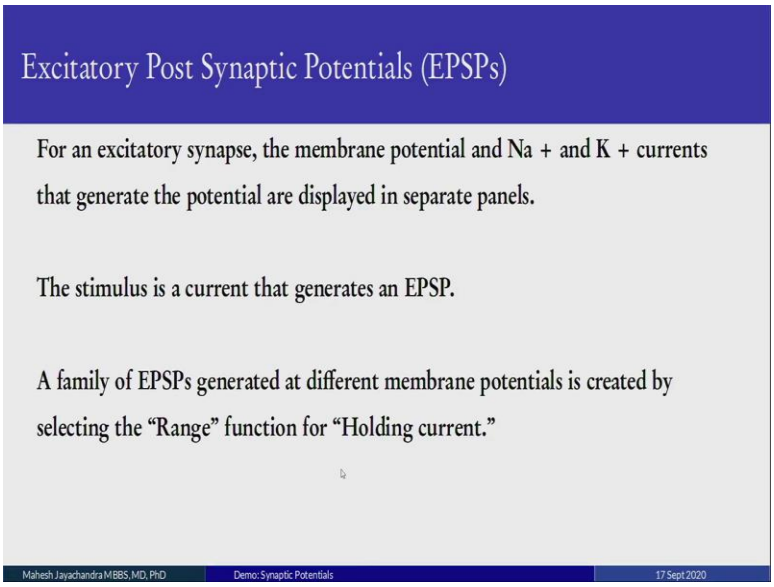

So, EPSPs. For an excitatory synapse, the membrane potential sodium and potassium currents are generated and they are displayed in separate channels. The stimulus is a current which generates an EPSP and a family of EPSPs are generated at different membrane potentials is created by selecting the range function for the holding current.

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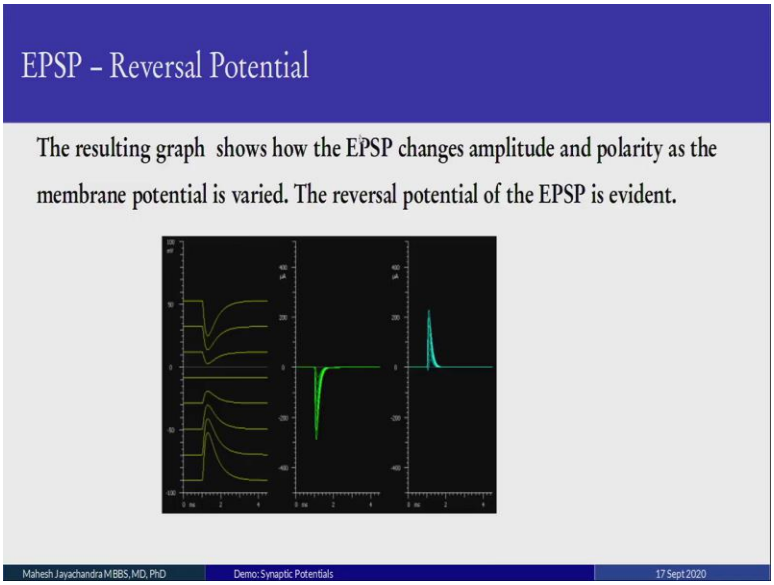

So, this graph shows how the EPSP changes amplitude and polarity as the membrane potential is varied. So, you see the reversal potential it is quite evident over here, this is where it reverses. And this is the sodium channel kinetics where you see the inward currents happening and this is the potassium channel kinetics where you see the outward currents happening.

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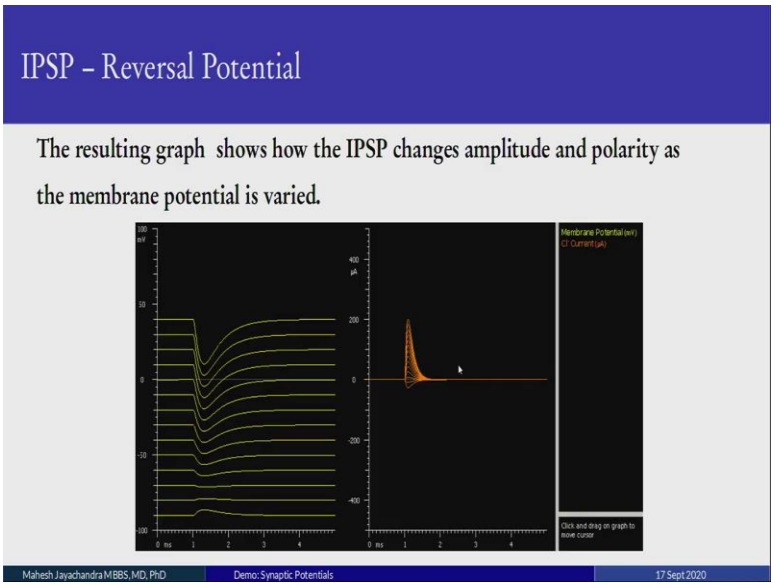

So, similarly the IPSP the inhibitory postsynaptic potential, here it is modeled by chloride and again you see a reversal potential happening pretty low over here and you see actually the currents in the next panel.

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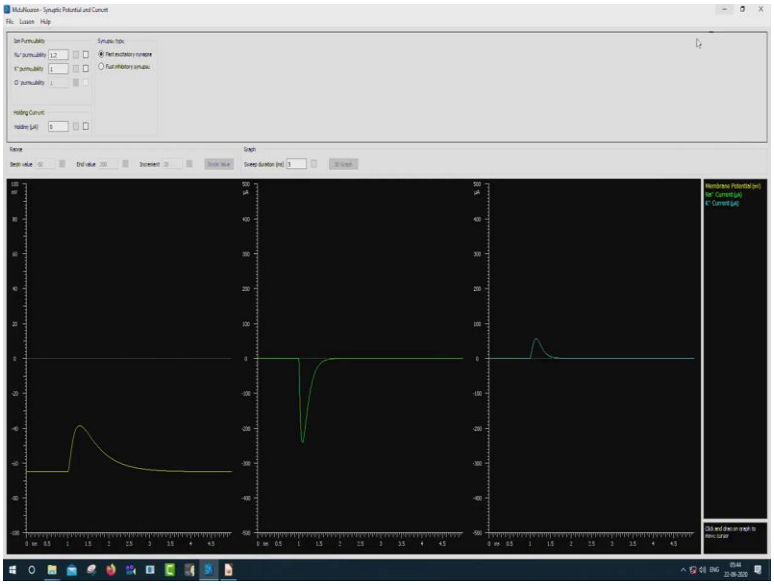

So, I will enter the demonstration, the demonstration is the lesson 6 synaptic potentials and currents, it is already open over here. So, just to go over the panel above, so we just have ionic permeabilities, so we have sodium permeability kept at 1.2, potassium permeability kept at 1, and chloride permeability does not, is not relevant here because we are looking at excitatory synapses, and we have a holding current over here.

And the membrane potential is the guy in yellow, the sodium current is green and the potassium current is blue. So, a couple of things, one is of course this shows the spread, the temporal spread of the potential and this follows tau and depending on the, it also depends on the physical structure of the axon or the dendrite whatever we are modeling. But you see how the potassium current occurs, so this is the EPSP what we showed earlier, so the potassium sodium current, is the current going inside, the potassium current is the current going outside. So, the holding current right now is 0.

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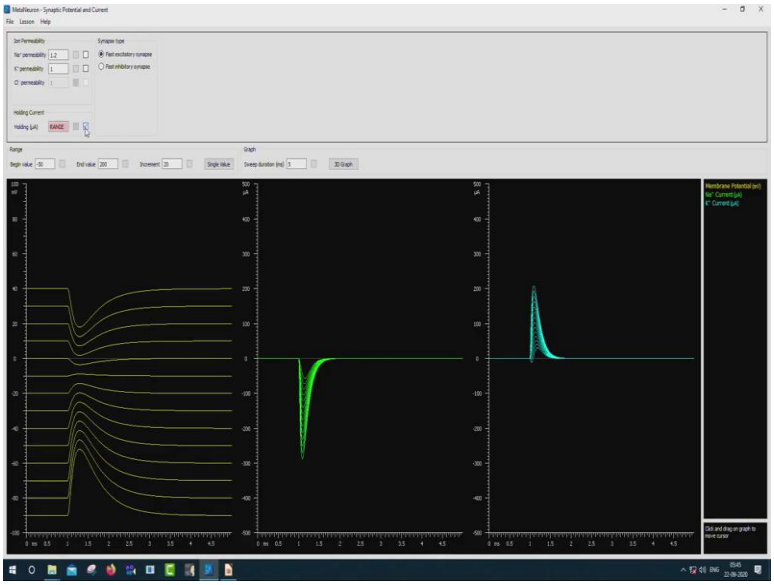

So, if we can use a range over here we can very easily see where the membrane potential reverses for an EPSP, this is a fast EPSP as I mentioned fast excitatory synapse. So, at different currents and we are a begin value is minus 50, the end value is 200 and these are the increments we are talking about microamps, you see how the membrane potential changes, inward currents is happening and the membrane potential approximately reverses somewhere here.

So, likewise with the potassium current, potassium current is happening at the same time so that is an outward current and as you change it, you, the reversal potential is an interplay of both these conductances.

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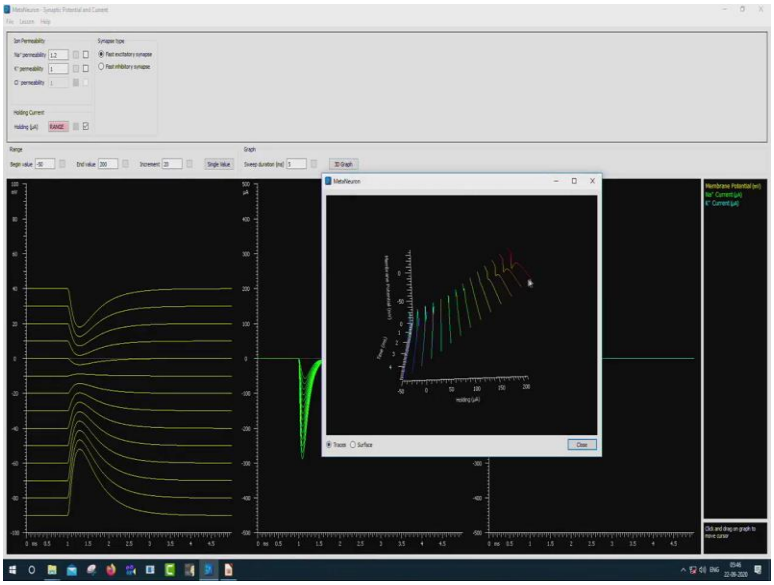

And the good old 3D graph well traces are much better. So, you can see it is starting over here and then it reverses. So, this was an excitatory synapse. So, let us look at an inhibitory synapse, a fast inhibitory synapse.

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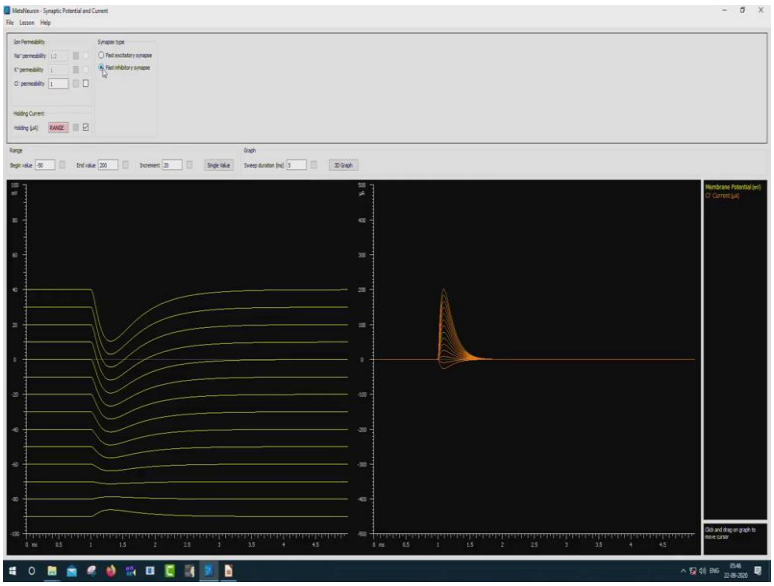

So, basically when you say fast that implies slow, so there are many possibilities you have fast excitatory synapses, fast inhibitory synapses and slow excitatory synapses and slow inhibitory synapses. So, they all work the same way generally but the kinetics are different. So, here you have a range let us take the range off, so that we just see.

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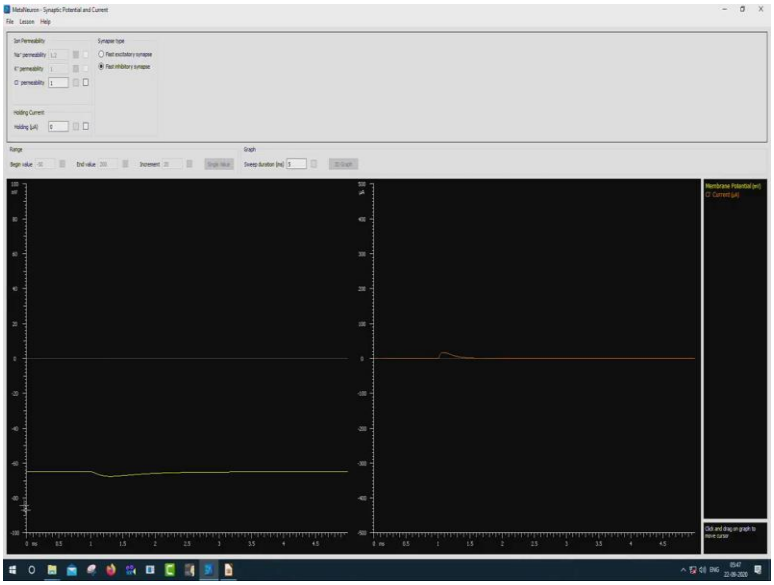

So, this is the inhibitory when a inhibition occurs through synapse the membrane potential goes slightly down but it is hyperpolarized so there is no question of action potentials firing. So, in a cell you have an interplay of the excitation inhibition, so this is the analog part of computation in a neuron, the interplay of these if it reaches threshold, then it starts firing action potentials. Now, the action potentials are all or nothing while these can be graded like so let us look at some inhibitory potential grading.

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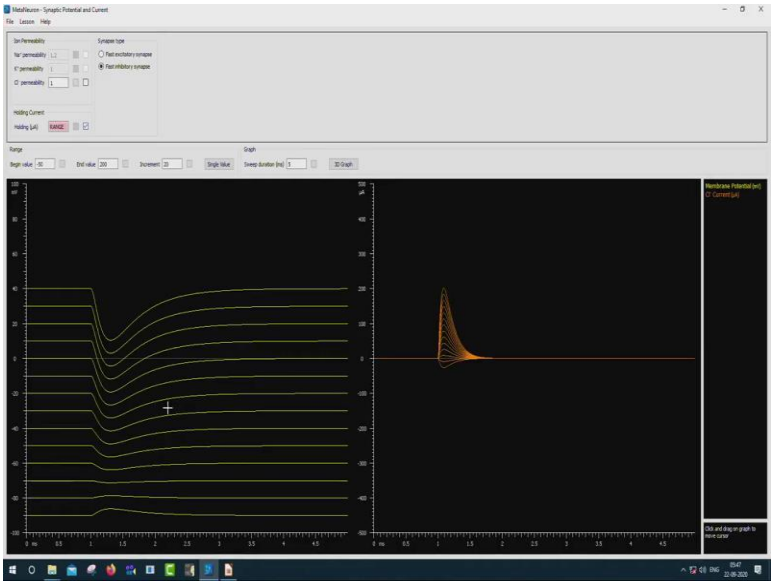

So, we start a range and again, so here we are looking only at chloride conductances, the chloride current, sodium and potassium are not activated because for sodium to activate it has to reach threshold and once that changes then you have the delayed rectifier happening, this happens only with depolarization excitation, here there is inhibition, so sodium and potassium are quiescent, while the action is at the chloride channels.

So, here again its range is minus 50 to 20 and you see it going up from minus 50 to plus 20 and the reversal potential occurs somewhere here and this is the equivalent currents going through the chloride currents.

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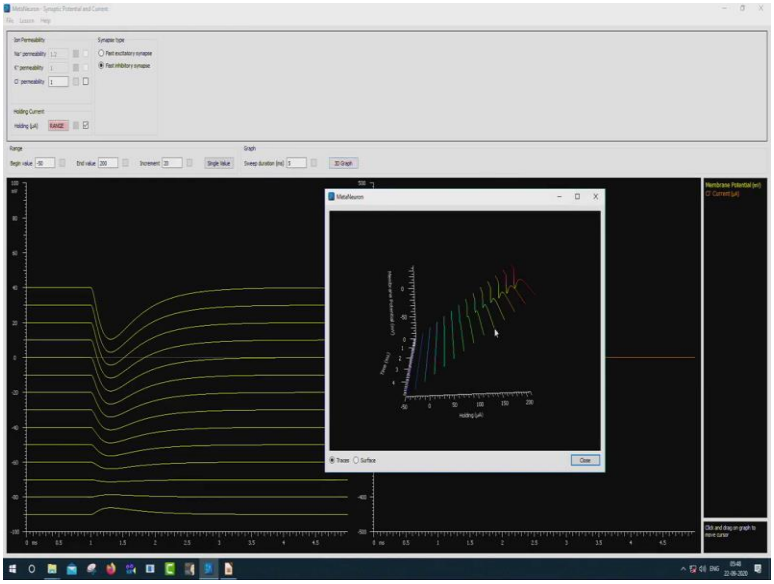

So, if you look at the 3D graph. You can see it. So, this kind of ends the MetaNeuron tutorials and I encourage you to again download this and systematically play with all the parameters, this actually is a using MetaNeuron and cellular for understanding cellular neurophysiology is actually a 3 to 6 month course and that is why we just wanted to give you a flavor of what is possible.

So, two things, one is download the papers and also download the MetaNeuron manual, they are freely available on internet and if you systematically go through it and persevere and go through all the exercises you will have a fairly good knowledge of what is happening with all these phenomena the resting membrane potential, how things change when you change the membrane

time constant, what is the effect of lambda and that is the membrane length constant, what happens when you change the diameter of the axon.

And then of course the action potential experiments and the voltage clamp techniques. And finally the synaptic potentials and currents. If you go through all this systematically and I promise you none of these things are going to be asked on your test, this is for your information, you will have a very good knowledge of what happens in the cell when you manipulate it in this fashion. So, thank you very much.