

ÉCOLE POLYTECHNIQUE
FÉDÉRALE DE LAUSANNE

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EPFL



Week 3 – part 1: Synapses



3.1 Synapses

3.2 Short-term plasticity

3.3 Dendrite as a Cable

3.4 Cable equation

3.5 Compartmental Models - active dendrites

Welcome to week three of the class Neuronal Dynamics. Last week, we talked about the model of Hodgkin-Huxley. This week, we will add more detail.

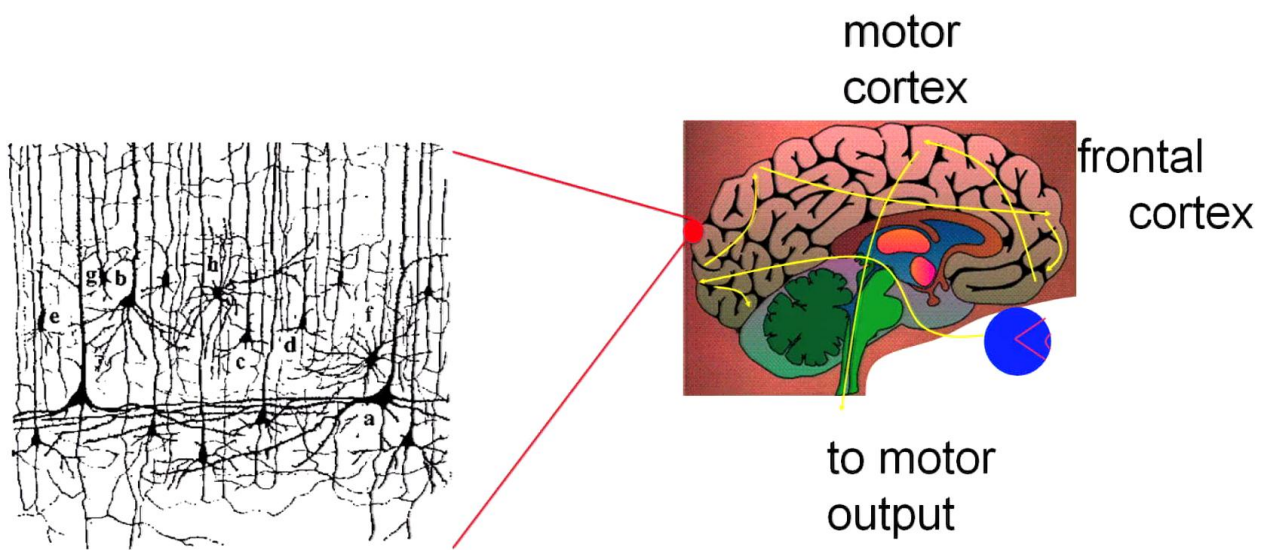
Notes

Summary



0m 04s

Neuronal Dynamics – 3.1. Introduction



Just as in the previous weeks, we'll focus on a single neuron, an isolated neuron, that may be part of the network of neurons in cortex.

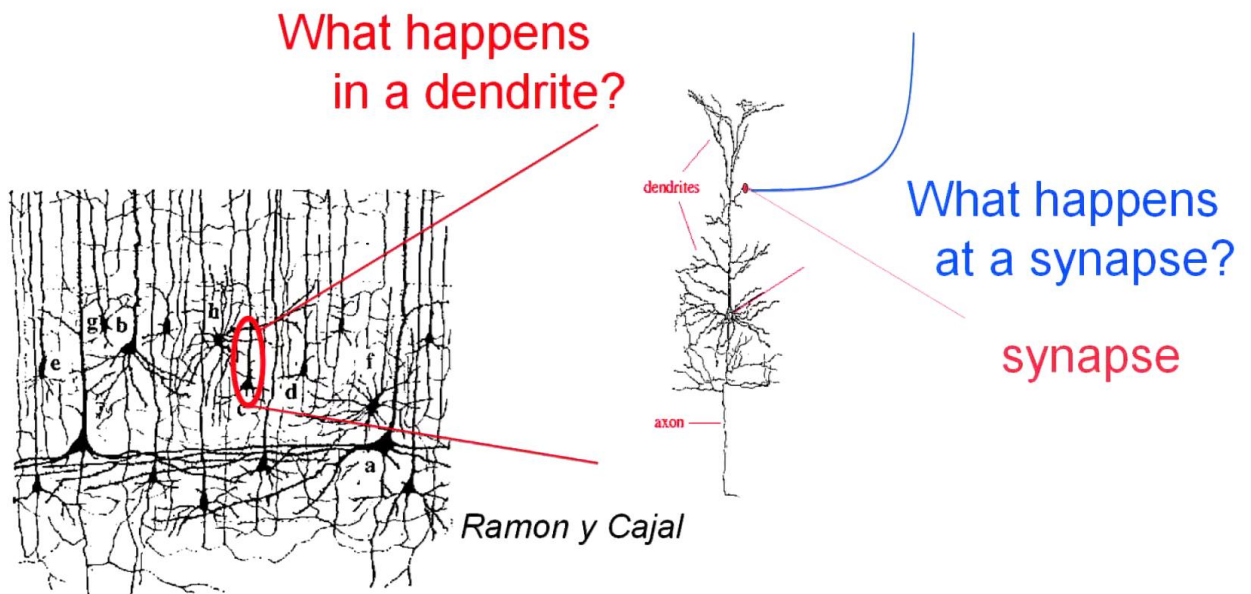
Notes

Summary



0m 15s

Neuronal Dynamics – 3.1 Introduction



Last week, we talked about a biophysical model of the type of Hodgkin and Huxley that included different types of ion channels. However, the neuron was just a point. The neuron did not have any spatial structure. It was a point neuron. Now, real neurons have dendrites. Dendrites have a complicated spatial structure. And so, the natural question is to ask, what is happening in a dendrite? Is there any function? What's the role of the dendrite? That's the first point. The second shortcoming of the model of last week was that input was injected explicitly in the form of stimulating current. You can imagine that the experimentalist injects such a current through an electrode. However, this is not a natural situation. A neuron embedded in a network would receive input from other neurons. And this input would arrive in the form of spikes that arrive at the synapse and cause some response on the postsynaptic side. So the second point I would like to raise this week is, what happens at the synapse? Can we describe the activity of a synapse?

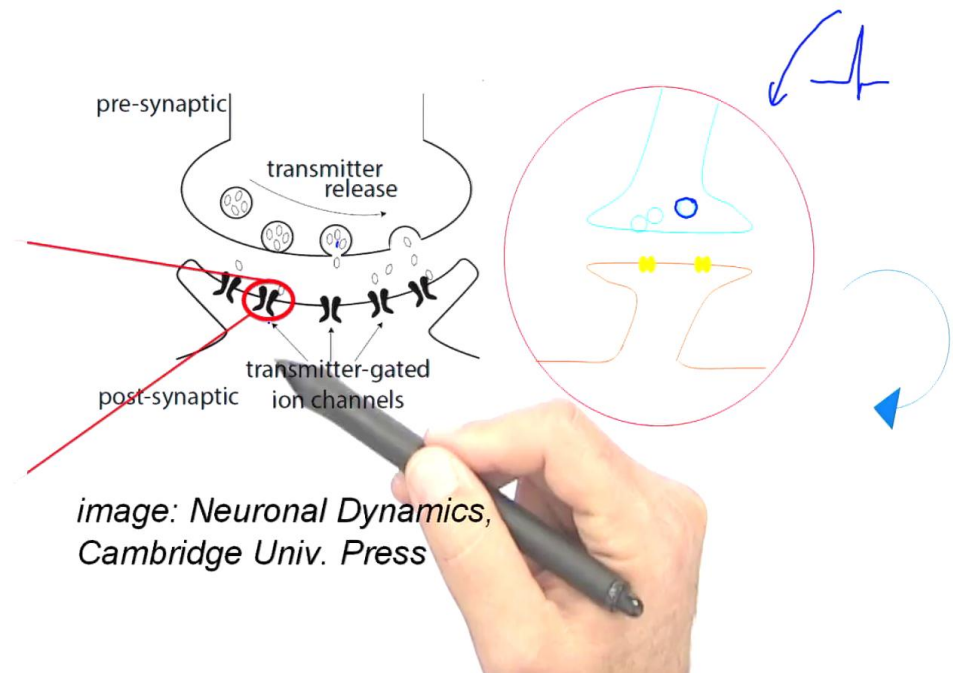
Notes

Summary



0m 25s

Neuronal Dynamics – 3.1 Synapses



And it's with this second point that I would like to start. I would like to start with a discussion of synapses. So here is a zoom onto one synapse. And for the following discussion, let's just focus on this zoomed synapse. And to facilitate the discussion, I would like to turn it around by 90 degrees. And then this is what you'll see. So here on the top part, this is the presynaptic terminal. Inside the terminal, you'll find vesicles. Vesicles are loaded with neurotransmitters. Some sit inside. Some sit on the surface. Now suppose a signal arrives from the presynaptic neuron. The signal would be one of the action potentials that travels along the axon. The axon bifurcates, spreads out, has various ramifications. And one of these ramifications ends at this presynaptic terminal. At the moment when the spike arrives, some of the vesicles fuse with the membrane and eject neurotransmitters into the synaptic cleft. These transmitter molecules are then captured by the channels. So the channels have sensors that can pick up one of these molecules.

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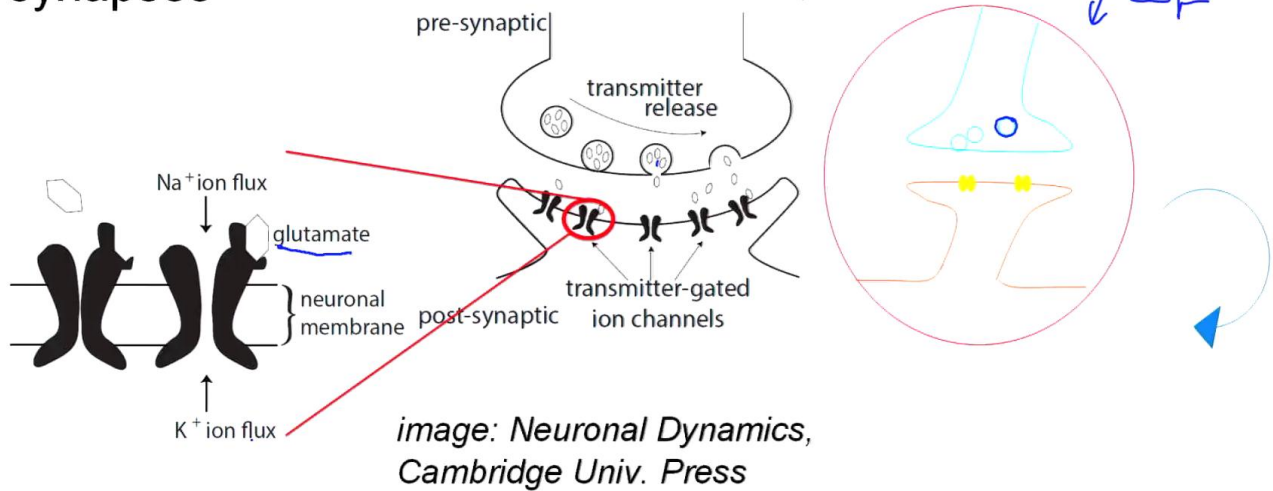
Summary



1m 52s

Neuronal Dynamics – 3.1 Synapses

glutamate: Important neurotransmitter at excitatory synapses



And if one of the molecules is captured, then the channel opens, and sodium ions can flow inside the cell. Potassium ions can flow out of the cell. An important neurotransmitter is glutamate. In fact, this is the most important transmitter at excitatory synapses. One of the excitatory channels is the so-called AMPA channel. If it opens, it makes a thin channel wide enough for sodium and potassium to pass through, but not wide enough for calcium.

Notes

Summary



3m 25s

Neuronal Dynamics – 3.1 Synapses

glutamate: Important neurotransmitter at **excitatory synapses**

-AMPA channel: rapid, calcium cannot pass if open

-NMDA channel: slow, calcium can pass, if open

(*N-methyl-D-aspartate*)

GABA: Important neurotransmitter at **inhibitory synapses** (*gamma-aminobutyric acid*)

Channel subtypes GABA_A and GABA_B

✎ ✏ 📄 ↺

There's another type of channel on excitatory synapses that's the so-called NMDA channel. If it's open, then calcium can pass through. The dynamics of an NMDA is slower than that of the AMPA channel. Excitatory synapses are not the only ones. There are also inhibitory synapses. Inhibitory synapses use the neurotransmitter GABA. And it comes in two subtypes-- GABA A and GABA B.

Notes

Summary



4m 11s

Neuronal Dynamics – 3.1 Synapse types

Model?

$$-I^{syn}(t) = -g_{syn}(t)(u - \underbrace{E_{syn}}_{\text{reversal potential}})$$

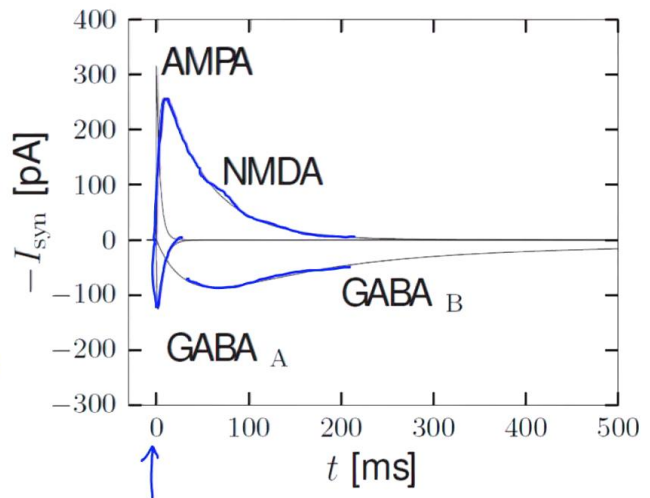


image: Neuronal Dynamics, Cambridge Univ. Press



So here is a model picture of the different synaptic currents caused by neurotransmitter release. So suppose a spike arrives at the synapse at time 0. If it's an excitatory synapse with many AMPA channels, then you would see a very rapid rise, and it decays within a few milliseconds. If the channel also contains NMDA, then the synaptic current through the NMDA channels would be much slower, and it extends over about 100 milliseconds or so. And inhibitory synapses, there are the two channels subtypes, GABA A and GABA B. And one is fast. The other one is slow. So this is the effective current that flows into the cell if a spike arrives at the presynaptic terminal. One of the questions we need to ask is, how can we described such a current? Can we build a model of such a current? And now we have seen the Hodgkin-Huxley model, that an important notion is the synaptic conductance. So let's build this type of model now. The total synaptic current has a drive which is the difference between the momentary voltage and the reversal potential. And the index syn indicates it's the reversal the potential of the synapse. Now, the conductance is time-dependent, because the channel opens if neurotransmitter molecules are bound.

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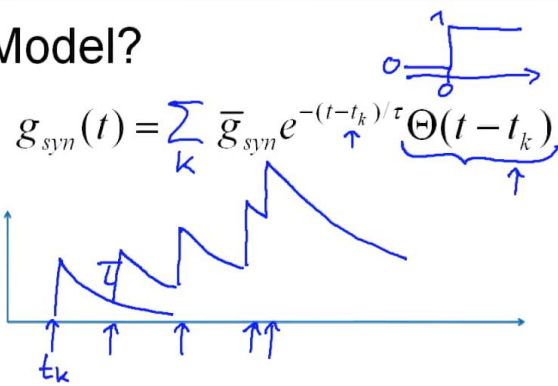
Summary



4m 40s

Neuronal Dynamics – 3.1 Synapse model

Model?

$$g_{syn}(t) = \sum_k \bar{g}_{syn} e^{-(t-t_k)/\tau} \Theta(t-t_k)$$


$$-I^{syn}(t) = -g_{syn}(t)(u - E_{syn})$$

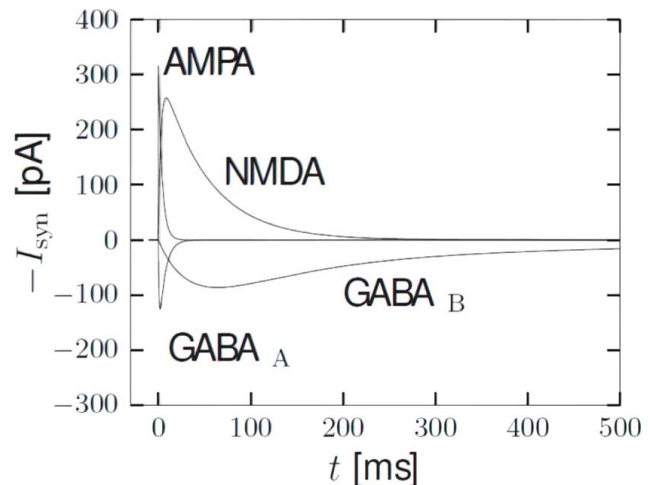


image: Neuronal Dynamics,
Cambridge Univ. Press

And afterwards, it closes again. A very simple model is to say this time dependence is just an exponential pulse. That's the kind of model we have here for the AMPA-- immediate rise, rapid fall afterwards, with some time constant τ for AMPA in the range of a few milliseconds. So suppose a spike arrives here. We have this jump upwards. This says a spike arrives at time t_k . The effect of the spike can only be felt after t_k at times t larger than t_k . So this is just a heavy side step function which jumps from 0 to 1 at 0. So for t smaller than t_k , I have no effect. For t larger than t_k , it's just 1. So essentially, this means the exponential curve here starts at time t_k and then decays with the time constant τ . So this is what we have plotted over there. Now, suppose we have many spikes, spikes arriving at different moments in time. Then the first spike would cause this response. The second spike would cause another response that adds to the first one. A third spike would cause yet another response, the fourth and fifth spike as well. So the total synaptic conductance is the sum of all these different contributions, the sum of all the different firing times t_k . And it's this total synaptic conductance that's inserted here into the equation, multiplied with the drive. And this gives the synaptic current.

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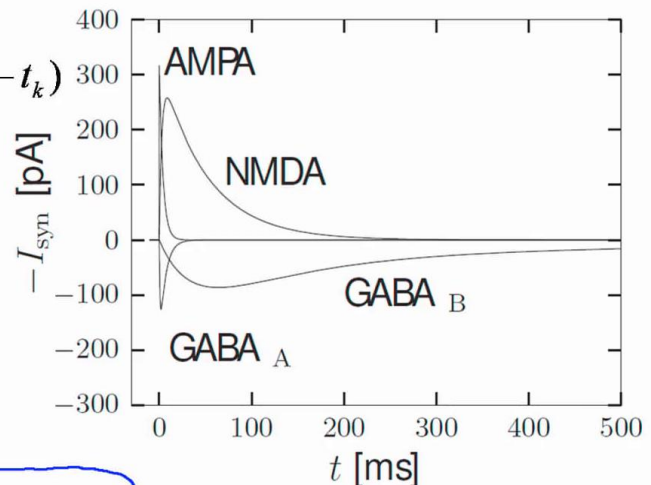
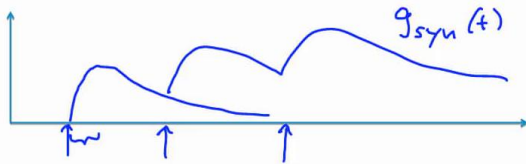
Summary



Neuronal Dynamics – 3.1 Synapse model

Model with rise time

$$g_{syn}(t) = \sum_k \bar{g}_{syn} e^{-(t-t_k)/\tau} [1 - e^{-(t-t_k)/\tau_{rise}}] \Theta(t-t_k)$$



$$-I^{syn}(t) = -g_{syn}(t)(u - E_{syn})$$

$$C \frac{du}{dt} = -g_{Na} m^3 h (u - E_{Na}) - g_K n^4 (u - E_K) - g_l (u - E_l) + I^{stim}(t)$$

image: Neuronal Dynamics, Cambridge Univ. Press

Now, a slightly more complicated model would be to say, well, there's not just this decay time, but there's also a rise time. So a spike comes in here. It has some rise time. And then we decay with the time constant τ . So the rise time corresponds roughly to the time it takes to take off from 0. Now, this current, again, if there are several spikes, would just add up to what I've plotted here as the total conductance. And this total conductance is inserted in the current equation. Now, the current equation could, for example, go into the Hodgkin-Huxley model. And now there are two different interpretations to do this. One would be to say the total stimulating current is this current here with the minus sign. And that's why we have plotted this here. So excitatory synapses with AMPA channels or NMDA channels effectively are equivalent to a positive stimulating current. A different point of view is to say, well, in a real neuron, there is no stimulating current. Rather, there are channels. This is the sodium channel. This is the potassium channel. This is the [INAUDIBLE] channel. And then this here is an additional channel that would naturally have the minus sign. So this is a simple model of synaptic current.

Notes

Summary



8m 50s

Neuronal Dynamics – 3.1 Synapses

glutamate: excitatory synapses

$$I^{stim}(t) = -I^{syn}(t)$$

$$-I^{syn}(t) = -g_{syn}(t)(u - E_{syn})$$

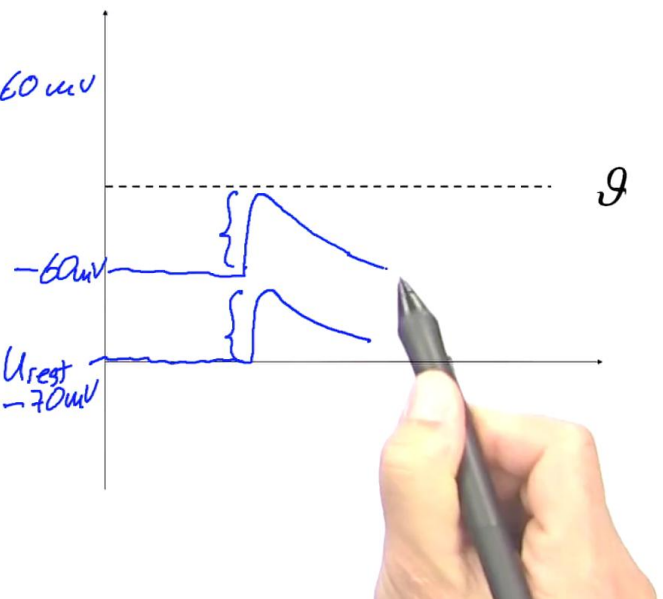
$-70mV // -60mV$

$$E_{syn} \approx 0mV$$

GABA: inhibitory synapses

$$-I^{syn}(t) = -g_{syn}(t)(u - E_{syn})$$

$$E_{syn} \approx -75mV$$



So let me summarize. So we have the neurotransmitter glutamate at excitatory synapses. We have the neurotransmitter GABA at inhibitory synapses. And both are described by the same kind of equation. However, there's a difference, because the reversal potential at excitatory synapses is high, whereas the reversal potential at inhibitory synapses is low. Now, what's the result of this difference in the reversal potential? So let's look at the following graph. Suppose this is about the resting potential. So the membrane potential is fluctuating here. Now, if the voltage is about the resting potential, which is maybe minus 70 millivolts, then this drive here, minus 70 minus 0, means minus 70, multiplied with the minus sign here gives you a big positive driving current. So if a pulse comes in it gives this response to the membrane potential. Now, if the membrane potential momentarily is higher, like here, then this might be minus 60 millivolts. Well, the drive is about the same. The difference between minus 60 and minus 70 is not that big. So the size of the response is roughly the same. Not so at inhibitory synapses. Suppose now I have an inhibitory pulse coming in here.

Notes

Summary



Neuronal Dynamics – 3.1 Synapses

glutamate: excitatory synapses

$$I^{stim}(t) = -I^{syn}(t)$$

$$-I^{syn}(t) = -g_{syn}(t)(u - E_{syn})$$

$-70mV // -60mV$

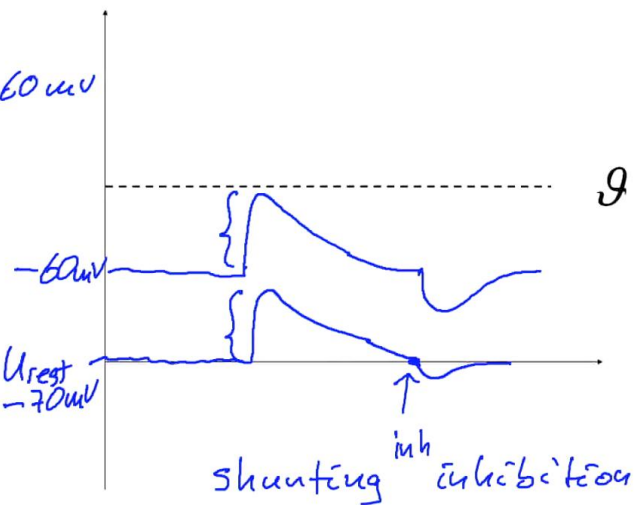
$$E_{syn} \approx 0mV$$

GABA: inhibitory synapses

$$-I^{syn}(t) = -g_{syn}(t)(u - E_{syn})$$

$u_{rest} (-60 - (-75))mV - 70mV$

$$E_{syn} \approx -75mV$$



My current value is minus 60 millivolts. I put in here minus 70 or minus 75. So the total difference is about 50 millivolts. And this is the driving force that's going to multiply the synaptic conductance. And so this gives this kind of response. However, if, at the moment when the inhibitory spike arrives, if, at the moment when the spike arrives at the inhibitory synapse, the membrane potential is roughly at rest, then the driving force, minus 70 minus minus 75, is only about a third of what it was before. So the same spike will have a much smaller effect at the inhibitory synapses if the neuron is at rest. In fact, if the neuron is exactly at the reversal potential, then the driving force is 0. This is called shunting inhibition. The inhibition drives the membrane potential towards the synaptic reversal potential. But if the membrane potential is already close to the synaptic reversal potential, the effect of inhibition is not visible in voltage trace. It's just visible as a change in the conductance.

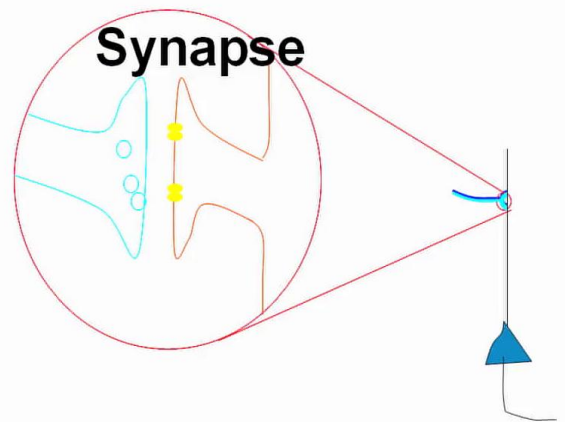
Notes

Summary

12m 46s



Neuronal Dynamics – 3.1 Synapses



So synapses are important contact points between neurons. They are important for signal transmission. If a spike arrives at the presynaptic terminal, a neurotransmitter is emitted. It's captured by the receptors on the postsynaptic side. If it's captured, then the channel opens, which eventually leads to a change in conductance and to an input current into the neuron. And this input current can be described with a simple modeling approach.

Notes

Summary

14m 31s



Neuronal Dynamics – Quiz 3.1

Multiple answers possible!

AMPA channel

- ☐ AMPA channels are activated by AMPA
- ☐ If an AMPA channel is open, AMPA can pass through the channel
- ☐ If an AMPA channel is open, glutamate can pass through the channel
- ☐ If an AMPA channel is open, potassium can pass through the channel
- ☐ The AMPA channel is a transmitter-gated ion channel
- ☐ AMPA channels are often found in a synapse

Synapse types

- ☐ In the subthreshold regime, excitatory synapses always depolarize the membrane, i.e., shift the membrane potential to more positive values
- ☐ In the subthreshold regime, inhibitory synapses always hyperpolarize the membrane, i.e., shift the membrane potential to more negative values
- ☐ Excitatory synapses in cortex often contain AMPA receptors
- ☐ Excitatory synapses in cortex often contain NMDA receptors

Before we go on to Part Two, please have a look at the quiz that we have prepared for you.

Notes

Summary



15m 07s