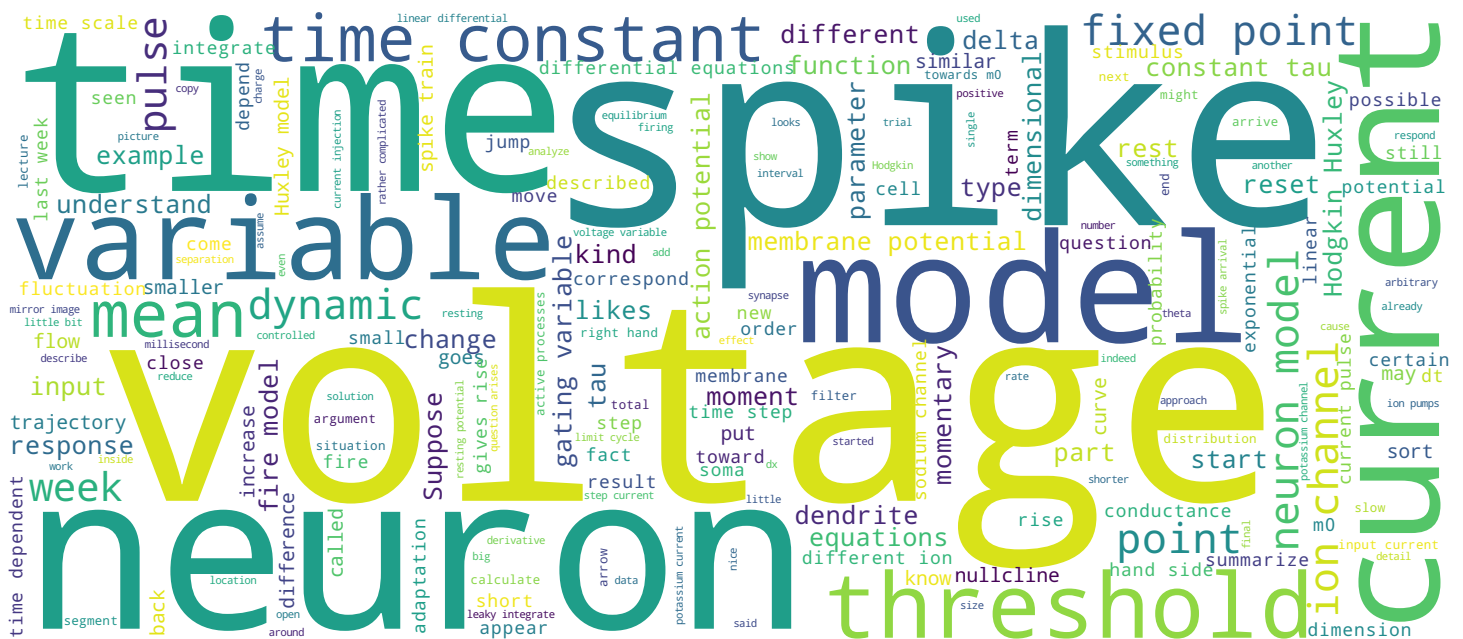


ÉCOLE POLYTECHNIQUE
FÉDÉRALE DE LAUSANNE

EPFL, Lausanne, Switzerland

- from two to one dimension



EPFL



Week 4 – part 1 : Reduction of the Hodgkin-Huxley Model



4.1 From Hodgkin-Huxley to 2D

- Overview: From 4 to 2 dimensions
- MathDetour 1: Separation of time scales
- MathDetour 2: Exploiting similarities

4.2 Phase Plane Analysis

- Role of nullclines

4.3 Analysis of a 2D Neuron Model

- MathDetour 3: Stability of fixed points

4.4 Type I and II Neuron Models

- where is the firing threshold?
- MathDetour 4: separation of time scales

4.5. Nonlinear Integrate-and-fire

- from two to one dimension

Welcome to week four of the class Neural Dynamics. In the previous two weeks, we have developed rather detailed biophysical neuron models. We started off with models of the Hodgkin-Huxley type with different ion channels. Last week, we added synapses and added dendrites.

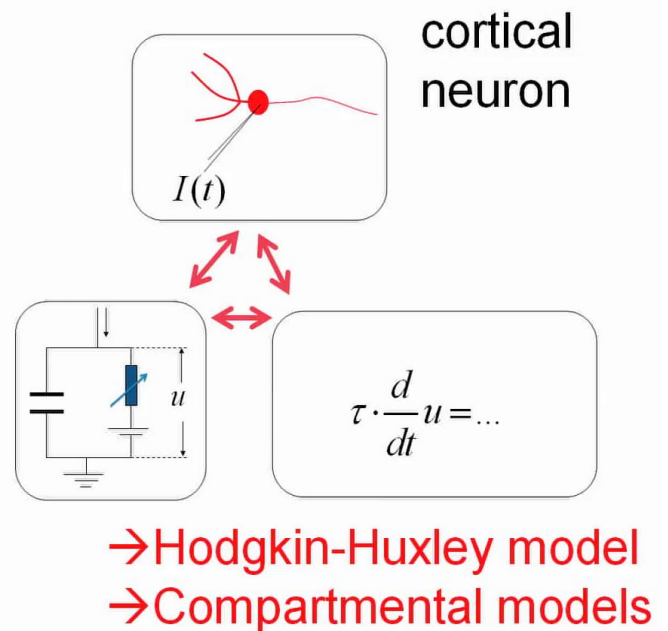
Notes

Summary



0m 04s

Neuronal Dynamics – 4.1. Review :Hodgkin-Huxley Model



So, if you look at one of these detailed models, it has a rather complicated structure. There are maybe 75 different ion channel types. There might be many different ion channels distributed across the dendrite with many, many compartments. And such a detailed neuron model is indeed capable of reproducing many phenomena of real neurons. However, the aim of a model is to understand what's going on in nature, to describe natural phenomena. If the neuron model itself is so complicated it becomes hard to understand it, then the question arises, what can we do? Is it possible to arrive at a simplified description which is easier to understand, where we can grasp the essence of phenomena, where we can develop mathematical tools to really analyze what's going on? And that's the topic for this week.

Notes

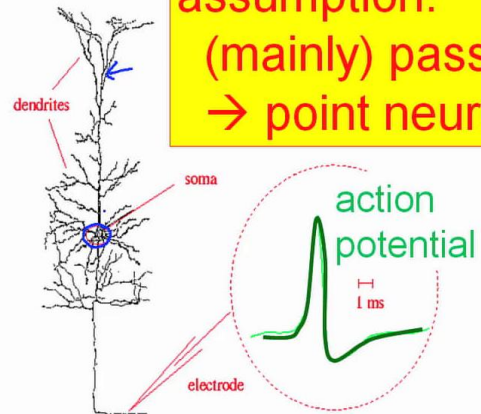
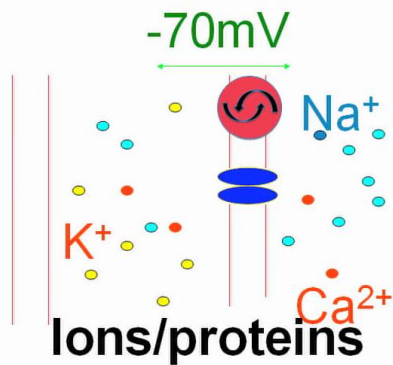
Summary



0m 24s

Neuronal Dynamics – 4.1 Review :Hodgkin-Huxley Model

Dendrites (week 3):
Active processes?



assumption:
(mainly) passive
→ point neuron

So, last week we looked at detailed neuron models. For example, we made a model of such a pyramidal neuron in cortex. Now, such a parietal neuron has a rich dendritic structure. And we have seen last week that there are active processes in a dendrite that give rise to a ping pong between back-propagating action potentials generated in the soma and dendritic spikes. Now, these active processes exist. The question arises whether these and other neurons would show such active ping pong-like processing in an in vivo situation, if the neuron is embedded in a real brain, involved in a real processing task, sensory processing, memory retrieval. Are these active processes important? We don't really know. Other neurons might not have these active processes at all. If you assume that the dendrite is passive, then indeed, the main function of the dendrite is to provide a filtering. Signals that arrive in the upper branches of the dendrite give rise to a filtered input at the soma. But all the decisions about generating the action potential or not are taken at the soma. And in this case, in the case of a passive or mainly passive dendrite, it's possible to reduce the description to that of a point neuron model.

Notes

Summary



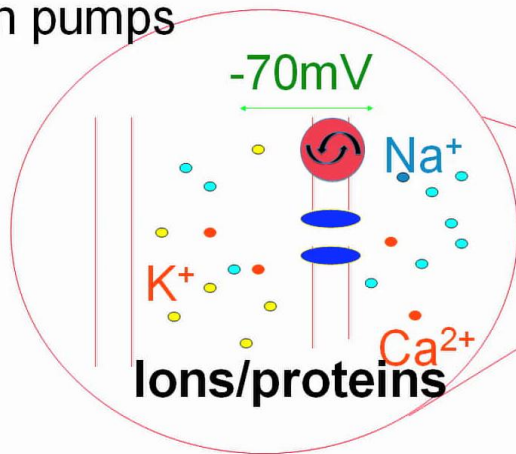
1m 24s

Neuronal Dynamics – 4.1 Review :Hodgkin-Huxley Model

Week 2:

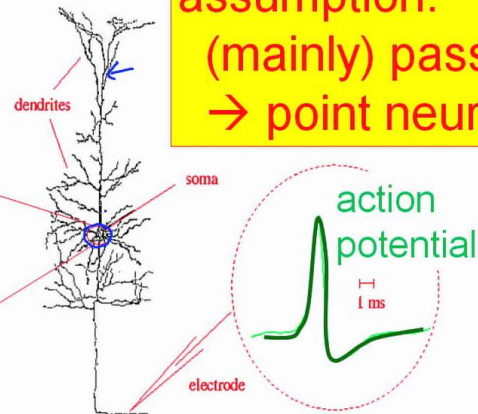
Cell membrane contains

- ion channels
- ion pumps



Dendrites (week 3):
Active processes?

assumption:
(mainly) passive
→ point neuron



Now, even a Hodgkin-Huxley type point neuron model may have many different ion channels embedded in the membrane. And these ion channels open and close depending on the state of the environment. Now, with 75 different ion channel types, such a model is still a rather complicated model. Ion pumps and ion channels give rise to complicated behavior.

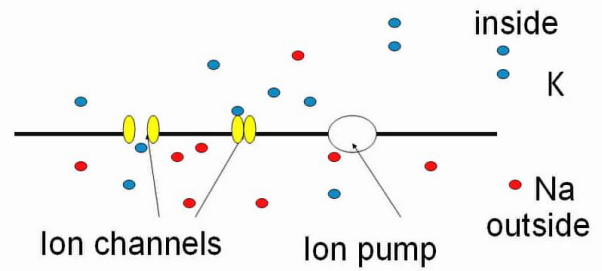
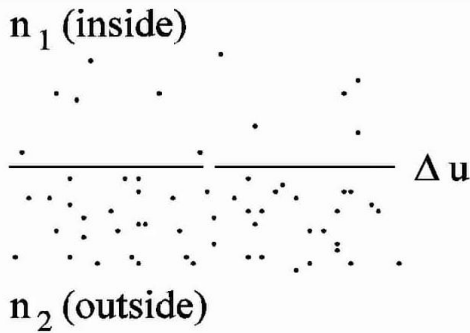
Notes

Summary



3m 02s

Neuronal Dynamics – 4.1. Review :Hodgkin-Huxley Model



$$\Delta u = u_1 - u_2 = \frac{-kT}{q} \ln \frac{n(u_1)}{n(u_2)}$$

Reversal potential

ion pumps → concentration difference ⇔ voltage difference

⌂ / ☰ ➡

As we have seen, ion pumps gives rise to a difference in voltage via a concentration difference.

Notes

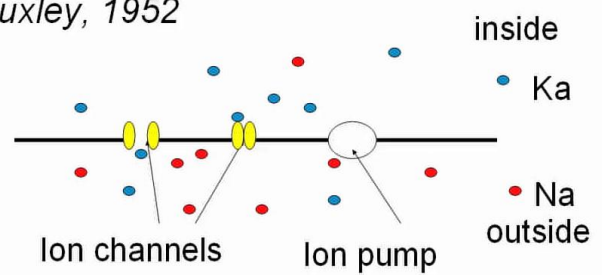
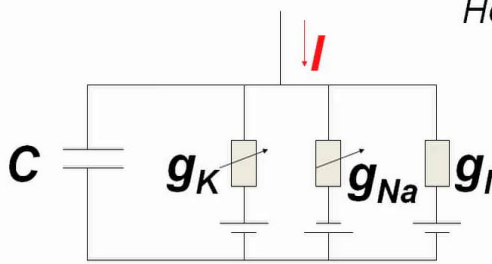
Summary



3m 26s

Neuronal Dynamics – 4.1. Review: Hodgkin-Huxley Model

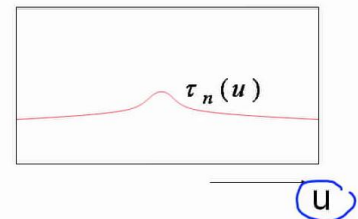
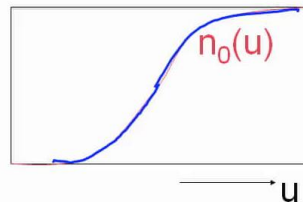
Hodgkin and Huxley, 1952



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

4 equations
= 4D system

$$\frac{dn}{dt} = - \frac{n - n_0(u)}{\tau_n(u)}$$



And this, in the end, gives rise to the reversal potential. Ion channels can be described by their conductances. And these conductances-- for example, a conductance for the sodium channel or the potassium channel or the leak channel-- the conductance of a sodium channel depends on these gating variables, like m and h . And each of these gating variables has a complicated dynamics. m likes to go towards m_0 , with some time constant τ_m . h likes to go towards h_0 , with some time constant τ_h . And n , for the potassium current, n likes to go towards n_0 , with some time constant τ_n . Now, I say "time constant τ_n ," but it's not really a constant because this time constant depends on the voltage u . Similarly, the target value, or equilibrium value, depends on the voltage u that's presently valid in the membrane. So, with three different types of ions, sodium, potassium, and leak, one type of ion channel for each type of ion, we have already four differential equations. We can also say we have a four dimensional system of differential equations.

Notes

Summary



Neuronal Dynamics – 4.1. Overview and aims

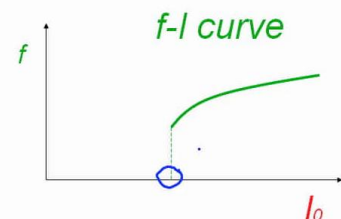
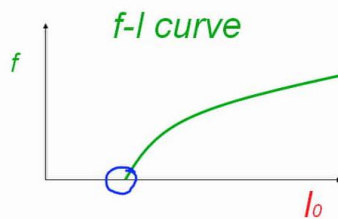
Can we understand the dynamics of the HH model?

→ Reduce from 4 to 2 equations

Type I and

type II models

ramp input/
constant input



Now, four dimensional differential equations are still rather complicated. It's not easy to understand the dynamics in such high dimensions, and four is a big number in that context. So, how can we understand the dynamics of the Hodgkin-Huxley model given that it's formulated in four dimensions? How can it be that some Hodgkin-Huxley models show a smooth f-i curve, of the type one, others show a jumpy f-i curve, which means type two, with just a small change of parameters? Can we understand these different types of neuron model? Can we understand the threshold behavior? When does the model will send out a spike? When does it not respond with a spike? Well, all of these phenomena can be understood if you reduce the system from four to two equations. And that's the aim for this first lecture.

Notes

Summary



5m 09s

Neuronal Dynamics – 4.1. Overview and aims

Toward a two-dimensional neuron model

-Reduction of Hodgkin-Huxley to 2 dimension

-step 1: separation of time scales

-step 2: exploit similarities/correlations



Now, in order to go from four dimensions to two, you have to use two mathematical tools, two mathematical tricks. And the first one is the separation of time scale.

Notes

Summary

6m 20s

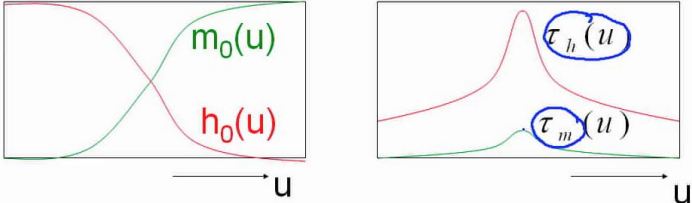


Neuronal Dynamics – 4.1. Reduction of Hodgkin-Huxley model

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

$$\rightarrow \frac{dm}{dt} = - \frac{m - m_0(u)}{\tau_m(u)}$$

$$\rightarrow \frac{dh}{dt} = - \frac{h - h_0(u)}{\tau_h(u)}$$

$$\rightarrow \frac{dn}{dt} = - \frac{n - n_0(u)}{\tau_n(u)}$$


So, here are the four equations of the Hodgkin-Huxley model in their full beauty, written out. There's a voltage equation. And there's the equation of the variable m , which enters into the sodium channel. There's an equation for the variable h , which also enters into the sodium channel. And then there's a variable n , which controls the potassium channel. m likes to go towards m_0 , its equilibrium value, with some time constant τ_m . h likes to go towards its equilibrium value with some time constant τ_h . No, these time constants, as I mentioned before, are voltage dependent. And the first observation we make is that the time constant for m is much, much shorter, it's smaller, than that for h . It's also smaller than that for n . So in that sense, m is fast. So if, for the moment, we assume that the stimulus is some constant drive, then the whole dynamics is controlled by the interaction between the voltage variable, the gating variable m , the gating variable h , the gating variable n . Now, the m variable reacts with the time constant τ_m , which is small, to changes in the voltage. τ_m is much smaller than all the other time constants in the system. And therefore, we can say m is a fast variable.

Notes

Summary



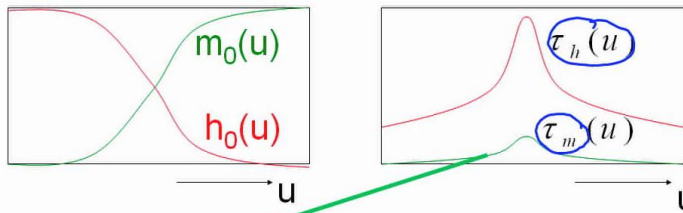
6m 35s

Neuronal Dynamics – 4.1. Reduction of Hodgkin-Huxley model

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

$$\rightarrow \frac{dm}{dt} = - \frac{m - m_0(u)}{\tau_m(u)}$$

$$\rightarrow \frac{dh}{dt} = - \frac{h - h_0(u)}{\tau_h(u)}$$

$$\rightarrow \frac{dn}{dt} = - \frac{n - n_0(u)}{\tau_n(u)}$$


MathDetour 4.1

1) dynamics of m is fast $\longrightarrow \underline{m(t)} = \underline{m_0(u(t))}$

It's faster than the others. And m approaches its value-- m likes to go towards m_0 with a time constant τ_m . And τ_m is short, so m sort of goes instantaneously towards m_0 . That means at any moment in time, we can imagine that m has already approached its value m_0 for the momentary voltage u . So, this is the idea of separation of time scale. One of the variables is fast, or a group of variables are fast, and these fast variables have already approached their instantaneous equilibrium value. The details of this argument will be given in the next lecture.

Notes

Summary



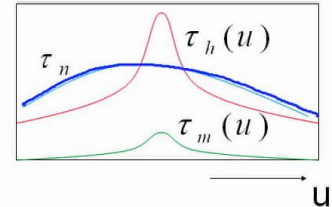
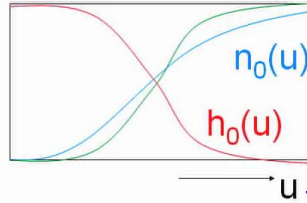
Neuronal Dynamics – 4.1. Reduction of Hodgkin-Huxley model

$$C \frac{du}{dt} = - \overbrace{g_{Na} m^3 h (u - E_{Na})}^{I_{Na}} - \overbrace{g_K n^4 (u - E_K)}^{I_K} - \overbrace{g_l (u - E_l)}^{I_{leak}} + \overset{\text{stimulus}}{\downarrow} I(t)$$

$$\frac{dm}{dt} = - \frac{m - m_0(u)}{\tau_m(u)}$$

$$\frac{dh}{dt} = - \frac{h - h_0(u)}{\tau_h(u)}$$

$$\frac{dn}{dt} = - \frac{n - n_0(u)}{\tau_n(u)}$$



- 1) dynamics of m are fast $\longrightarrow m(t) = m_0(u(t))$
- X2) dynamics of h and n are similar

So, the dynamics of m are fast. Now, the second observation is that the dynamics of h and n are sort of of similar speed. If I compare τ_n here, some hand-drawn trigger, with τ_h , it's not the same. But it's roughly in the same range. n approaches n_0 , and h approaches h_0 . And both do that with a time constant which is similar. τ_h and τ_n are similar. Now, obviously the curves, the equilibrium curves for n_0 and for h_0 are not similar at all.

Notes

Summary

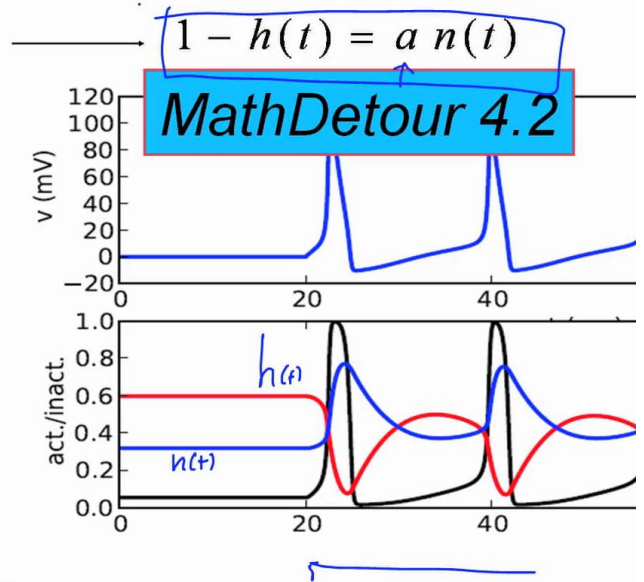
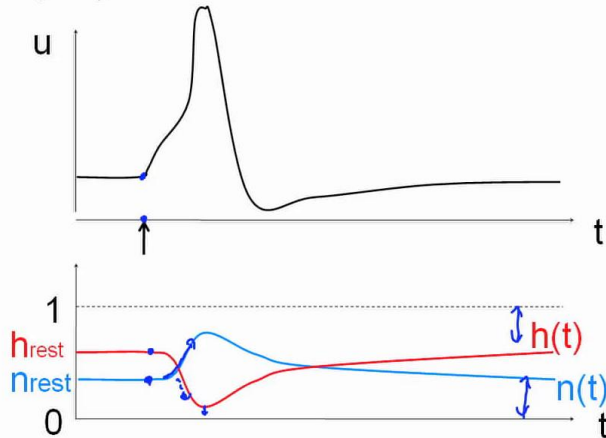


9m 27s

Neuronal Dynamics – 4.1. Reduction of Hodgkin-Huxley model

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

2) dynamics of h and n are similar



However, they are sort of a mirror image of each other. Suppose I'm here at a resting value of the voltage. There is no external current. The system has equilibrated. And at this resting state, n has a certain value and h has a certain value. Now, while n goes up, h will go down. So, they behave one in a mirror image of the other. And while h gets small, n gets big. Or, while n gets small, h gets big. If you compare the value here-- that's the momentary value of n -- with the value 1 minus h , then they are sort of similar to each other, not perfectly similar. That's why I've put an arbitrary constant a , a scaling constant, between the two. So here's, again, the same kind of picture, but during constant current injection. The current injection starts here at time 20 milliseconds. And you see that n of t increases periodically during the spikes. And, at the same moment, h of t decreases. So the two curves form mirror images. The dynamics of the two is sort of similar. And that's what we have expressed by this equation here. The details of the argument will be given in the third lecture.

Notes

Summary

10m 11s



Neuronal Dynamics – 4.1. Reduction of Hodgkin-Huxley model

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

$$= -g_{Na} [m_0(u(t))]^3 [1 - w(t)] (u(t) - E_{Na}) - g_K$$

1) dynamics of m are fast

2) dynamics of h and n are similar

$$m(t) = m_0(u(t))$$

$$1 - h(t) = w(t) \quad n(t) = w(t)$$

$$h = 1 - w$$

$$h = \frac{w}{a}$$

But let's put these insights together. So, the Hodgkin-Huxley model has a sodium current. It's controlled by the momentary value, m of t of the gating variable m and by the momentary value of the gating variable h . The potassium current is controlled by the momentary value of the gating variable n . I stress momentary value, and that's why I've written explicitly n of t . This is one of the variables. Other variables are u of t . And then there's an external input which can be constant or time dependent. Now, we said the dynamics of m are fast, so m can be replaced by its momentary value, m_0 . So, I put that in, m_0 of u of t . Now, before, m was an independent variable. Now, m_0 of u is just a readout of a look up table, m_0 of u evaluated at the momentary value u of t . And then, m goes to the third power. Now, the dynamics of h and n are similar. And so, both, I will introduce a new variable. $1 - h$ will be written as w . a times n will be written as w . So, $1 - h$ is equal to w , then h is $1 - w$. And that's what I put in here, $1 - w$ of t . And then I copy u of t minus E_{Na} . Now, n . a times n is w , so n is w/a . Let's insert this in here, w of t over a constant a to the power of 4.

Notes

Summary



12m 08s

Neuronal Dynamics – 4.1. Reduction of Hodgkin-Huxley model

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

$$= -g_{Na} [m_0(u(t))]^3 [1-w(t)] (u(t) - E_{Na}) - g_K \left[\frac{w(t)}{a} \right]^4 (u(t) - E_K) - g_l (u(t) - E_l) + I(t)$$

voltage

$$C \frac{du}{dt} = -g_{Na} m_0(u)^3 (1-w)(u - E_{Na}) - g_K \left[\frac{w}{a} \right]^4 (u - E_K) - g_l (u - E_l) + I(t)$$

1) dynamics of m are fast

$$\longrightarrow m(t) = m_0(u(t))$$

2) dynamics of h and n are similar

$$\longrightarrow 1-h(t) = an(t) \quad h = 1-w \quad w(t) \quad w(t) \quad n = \frac{w}{a}$$

u of t minus E_K . And the rest does not change. I can copy it. u of t minus E_l plus I of t . Let's rewrite this like a voltage equation. This is the voltage variable. And the voltage variable appears here. On the right hand side, it appears here. It appears here. And it appears there. This is my first variable. And then I have a second variable. The secondary level is w . It appears here. And it appears here. And that's it in terms of variables. We started off with four variables, m , h , n , and the voltage u . We end up with two variables, one for the voltage and one for w .

Notes

Summary



14m 47s

Neuronal Dynamics – 4.1. Reduction of Hodgkin-Huxley model

voltage

$$C \frac{du}{dt} = -g_{Na} m_0(u)^3 (1-w)(u - E_{Na}) - g_K \left(\frac{w}{a}\right)^4 (u - E_K) - g_l (u - E_l) + I(t)$$

w-equation

$$\frac{dw}{dt} = -\frac{w - w_0(u)}{\tau_{eff}(u)}$$

2-dim

$$\begin{cases} C \frac{du}{dt} = f(u(t), w(t)) + I(t) \\ \frac{dw}{dt} = g(u(t), w(t)) \end{cases}$$

Now, each of the gating variables, n and h, had an equation. n likes to go towards n0. h likes to go towards h0. And so, it's not surprising that there should be some dynamics for this new variable w. w likes to go towards w0 with some effective time constant, which itself is voltage dependent. So I have here my voltage equation. And here I have my w equation. And together they form a two dimensional system of equations, some function on the right hand side of the momentary voltage, the momentary w. Again, here is the voltage. Here is the voltage. Here is the voltage. Here is the voltage. Here is w, and here is w. And the w equation is also-- it depends on the voltage. Here is the voltage. And it depends on w. Here is w. So, we have a two dimensional system of equations as a result.

Notes

Summary



15m 45s

Neuronal Dynamics – 4.1. Reduction to 2 dimensions

2-dimensional equation

$$C \frac{du}{dt} = f(u(t), w(t)) + I(t)$$

$$\frac{dw}{dt} = g(u(t), w(t))$$

Enables graphical analysis!

- Discussion of threshold
- Type I and II
- Repetitive firing



So, let me summarize what we have seen. Exploiting the difference of time scales, we can use the mathematical trick, separation of time scales, so as to replace the m variable by its instantaneous value. Moreover, w represents an effective variable. And that w variable exploits the similarities in the dynamics between h and n . As a result, a four dimensional system of equations has been reduced to two dimensions. As we will see in the following, two dimensional systems of equations are beautiful. They are nice. They are nice because you can use graphical tools to analyze the system. You can understand the difference between a type one and a type two neuron model. You can understand threshold behaviors. You can understand repetitive firing. So, once you are in two dimensions, you have an immense amount of tools available in order for you to understand the dynamics of action potential generation in neurons.

Notes

Summary



17m 04s

Neuronal Dynamics – Quiz 4.1.

A- Assumptions: In order to reduce a detailed compartmental neuron model to two dimensions we have to assume that

- ☐ dendrites can be approximated as passive
- ☐ the neuron model has no dendrite
- ☐ the neuron model has at most 2 types of ion channels
- ☐ all gating variables are fast
- ☐ no gating variable is fast
- ☐ gating variables fall in two groups:
 - those that are fast and those that are slow
- ☐ at least one of the ion channels is inactivating
- ☐ the neuron does not generate spikes

B - A biophysical point model with 3 ion channels, each with activation and inactivation, has a total number of equations equal to
☐ 3 or ☐ 4 or ☐ 6 or ☐ 7 ; ☐ 8 or more

C- Separation of time scales:

We start with two equations

$$\tau_1 \frac{dx}{dt} = -x + I(t)$$

$$\tau_2 \frac{dy}{dt} = -y + x^2 + A$$

We assume that $\tau_1 \ll \tau_2$

In this case a reduction of dimensionality

☐ is not possible

☐ is possible and the result is

$$\tau_2 \frac{dy}{dt} = -y + [I(t)]^2 + A$$

☐ is possible and the result is

$$\tau_1 \frac{dx}{dt} = -x + x^2 + A$$

Before we continue, please have a look at our quiz.

Notes

Summary



18m 24s