

ÉCOLE POLYTECHNIQUE
FÉDÉRALE DE LAUSANNE

EPFL, Lausanne, Switzerland

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EPFL



Week 4 – part 5: Nonlinear Integrate-and-Fire Model



✓ 4.1 From Hodgkin-Huxley to 2D

✓ 4.2 Phase Plane Analysis

✓ 4.3 Analysis of a 2D Neuron Model

✓ 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

Whoa. This has been a long series of lectures for me to teach, for you to watch and listen. And yes, this is the final lecture of week four of the class neuronal dynamics. I will use this final lecture to make a transition from the two dimensional neuron models to the nonlinear integrate-and-fire type models that we have seen in week one. And this is important because it's with these reduced models that we will work for the following two or three weeks.

Notes

Summary



0m 04s

Neuronal Dynamics – 4.5. Further reduction to 1 dimension



2-dimensional equation

$$\tau \frac{du}{dt} = F(u, w) + RI(t)$$

stimulus
↓

$$\tau_w \frac{dw}{dt} = G(u, w)$$

slow!

Separation of time scales

**-w is nearly constant
(most of the time)**

In order to make this transition, I will do yet another separation of time scales. I will assume that the auxiliary variable w is slow. And that means that most of the time, w is indeed constant, and you can exploit that. Now before I go into the mathematical details, let me remind you of the motivation. Why do we do all this?

Notes

Summary

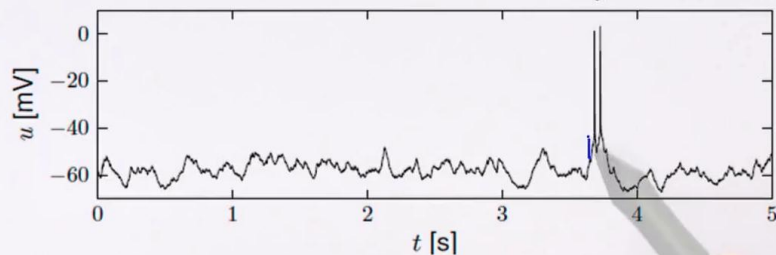


0m 41s

Neuronal Dynamics – 4.5 sparse activity in vivo

Spontaneous activity *in vivo*

awake mouse, cortex, freely whisking,



-spikes are rare events

Crochet et al., 2011

-membrane potential fluctuates around 'rest'

Well, cortical neurons spontaneously emit spikes. And you see here in the total period of five seconds, there are only two spikes. That means spikes are sparse. They are rare events. Most of the time, the membrane potential is fluctuating in some regime subthreshold. It's fluctuating around some reference potential, or maybe you could say around the resting potential. And then, the aim of modeling is to say, when is the moment? When is one of these rare moments that the neuron is going to emit a spike?

Notes

Summary

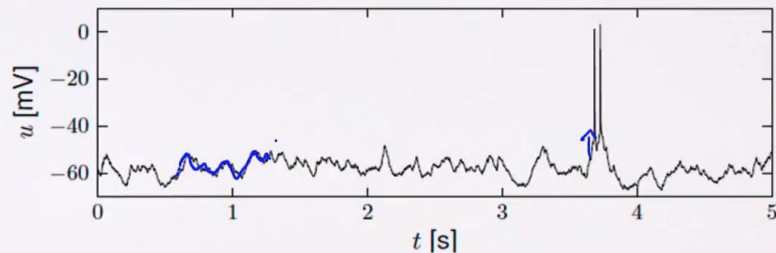


1m 03s

Neuronal Dynamics – 4.5 sparse activity in vivo

Spontaneous activity *in vivo*

awake mouse, cortex, freely whisking,



-spikes are rare events

Crochet et al., 2011

-membrane potential fluctuates around 'rest'

Aims of Modeling:

- predict spike initiation times
- predict subthreshold voltage

Moreover why do we see these fluctuations? Why do we see this move up and down? Can we predict the subthreshold voltage with a neuron model?

Notes

Summary



1m 44s

Neuronal Dynamics – 4.5. Further reduction to 1 dimension

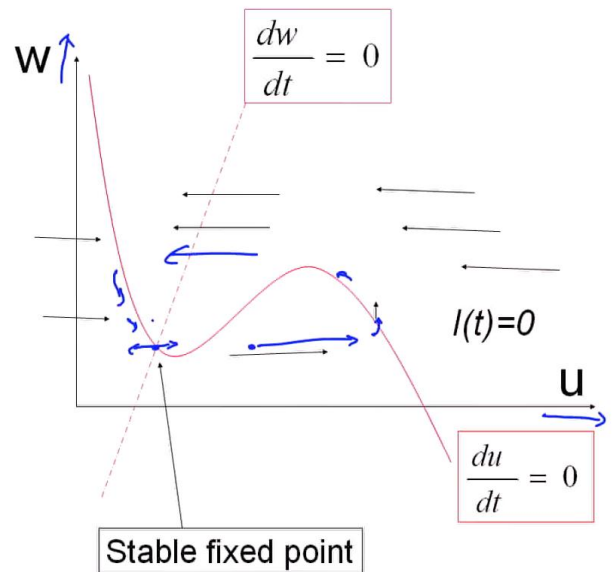
$$\tau \frac{du}{dt} = F(u, w) + \overset{\text{stimulus}}{I(t)}$$

$$\tau_w \frac{dw}{dt} = G(u, w) \quad \text{slow!}; \quad \frac{dw}{dt} = \frac{G}{\tau_w}$$

Separation of time scales

$$\tau_w \gg \tau_u$$

→ Flux nearly horizontal



So we have seen a class of two-dimensional neuron models. And these neuron models can be analyzed in the phase plane. This is the first variable, the voltage variable, horizontal axis, second variable, auxiliary variable w , vertical axis. And now separation of time scale means that the time constant for the second variable is much slower than that of the voltage. So this is our slow variable. That means w only changes a little bit. If you look at the derivative, $\frac{dw}{dt}$, then is-- this is G over τ_w . But τ_w is big, so the change in a small time step of w is small. And this means that the flow arrows are nearly horizontal all the time. So if this is a stable, fixed point, then in the presence of some time dependent stimulating current, the membrane potential would fluctuate up and down while the w variable hardly changes. If you have a big input, then the voltage variable might be kicked up here, from which it goes very rapidly afterwards. And it turns around, it follows the u note line, and then it has a rapid jump down before it goes back. And then it will again stay a long time close to this resting state. So the flux, most of the time, is nearly horizontal except in the neighborhood of the note line.

Notes

Summary



Neuronal Dynamics – 4.5. Further reduction to 1 dimension

Hodgkin-Huxley reduced to 2dim

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

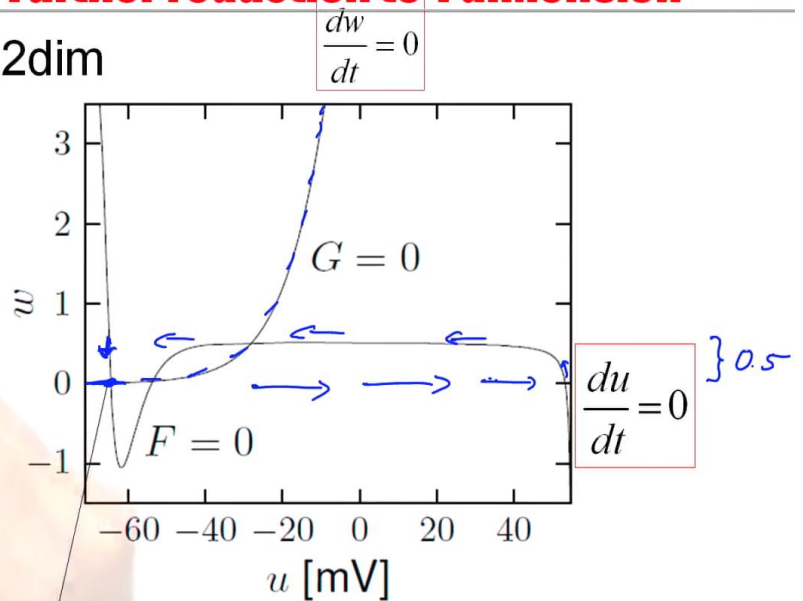
$$\tau_w \frac{dw}{dt} = G(u, w) \quad \text{slow}$$

Separation of time scales

$$\tau_w \gg \tau_u \quad w \approx w_{rest}$$

$$\tau_w \frac{dw}{dt} \approx 0 \rightarrow w \approx w_{rest}$$

$$\tau \frac{du}{dt} = F(u, w_{rest}) + RI(t)$$



As we have seen, if you reduce the Hodgkin-Huxley model to two dimensions, then we have exactly this kind of diagram, with a u note line and a w note line. And these note lines will have several fixed points, and this is the stable fixed point. Now suppose I give a strong stimulus. If there's a separation of time scales, if w is slow, that means all the arrows are nearly horizontal. So there's a rapid rise towards a high voltage, high positive voltage. And this is the peak of the action potential. And it stays a little bit up here. And it's at this moment that w starts to change. w starts to increase. And then you have rapid downward movement. And then, this is vertical here, and then w decreases again. So you see the total range of w in this scale is about 0.5 during a spike. But if the neuron is not spiking, if it's just receiving weak time-dependent input, then it's basically sitting here. And w is always equal to its resting value. So you can exploit this. w is always close to its resting value. That means in the first equation, the voltage equation, where I have a dependence on the voltage u , w , I don't really need this second variable. I can replace this by its constant value.

Notes

Summary



Neuronal Dynamics – 4.5. Further reduction to 1 dimension

Hodgkin-Huxley reduced to 2dim

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

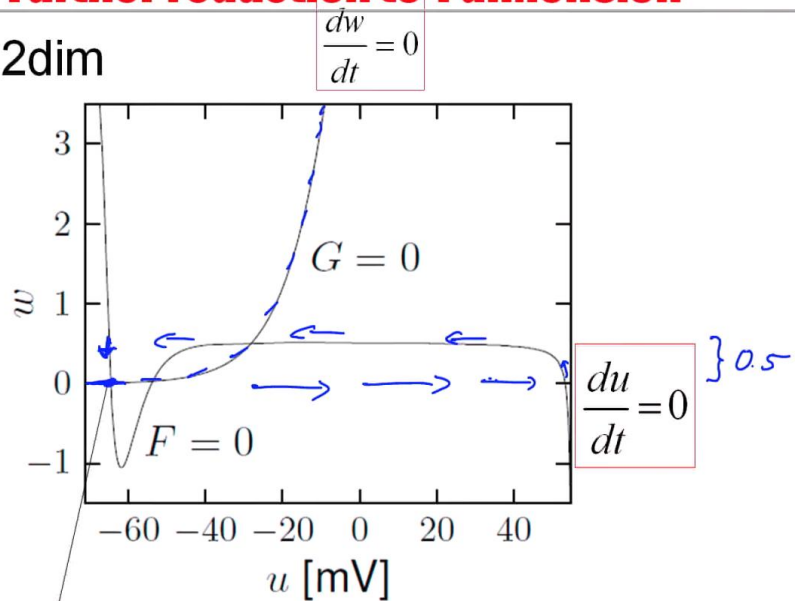
$$\tau_w \frac{dw}{dt} = G(u, w) \quad \text{slow}$$

Separation of time scales

$$\tau_w \gg \tau_u \quad w \approx w_{rest}$$

$$\tau_w \frac{dw}{dt} \approx 0 \rightarrow w \approx w_{rest}$$

$$\tau \frac{du}{dt} = F(u, w_{rest}) + RI(t)$$



Stable fixed point

And this replacement should be true in the neighborhood of this resting state here. it's not true up here during a spike, but down here, where the neuron spends most of its time, down here, it's true. W is always very close to w rest.

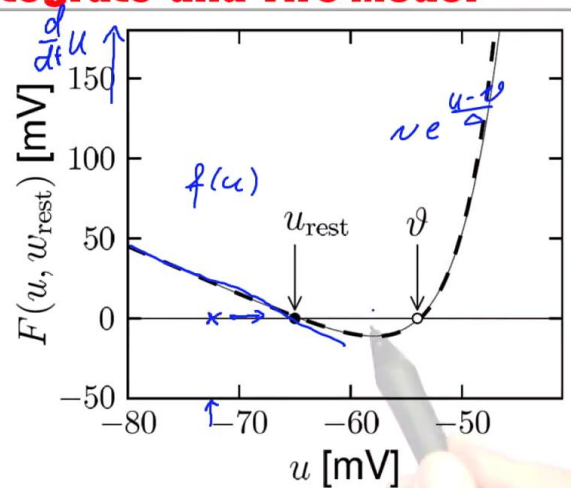
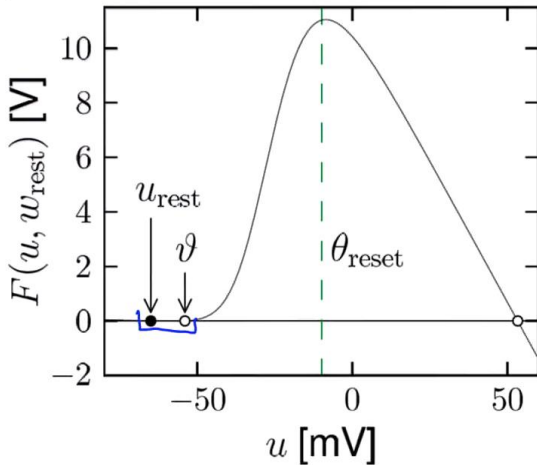
Notes

Summary



5m 38s

Neuronal Dynamics – 4.5. Nonlinear Integrate-and-Fire Model



$$\tau \frac{du}{dt} = F(u, w_{rest}) + RI(t) = f(u) + RI(t)$$

$\uparrow$ $\uparrow$ $\uparrow$
 fixed $I=0$

→ Nonlinear I&F (see week 1!)

Image: Neuronal Dynamics,
Gerstner et al.,
Cambridge Univ. Press (2014)

Now we can plot this function now. I evaluate for fixed w_{rest} . I evaluate the function f of u . And now this is now a function of a single variable. It's a function just of the voltage. That's a fixed parameter. That means I can rewrite this as a one-dimensional differential equation with some non-linear function f of u . And this is how this function looks like. Now If we zoom in just into this region here, then what we find is that this function f of u has a linear part, and then it bends over quite rapidly. And in fact, this rapid increase can be described as an exponential part. Now this is, in fact, a non-linear integrate-and-fire model. And the specific nonlinear integrate-and-fire model would be one, which is a combination of this linear part plus an exponential part. In other words, an exponential integrate-and-fire model. Now we can interpret this vertical axis, which is f of u plus r times i . For the moment, set i equals 0. Then this vertical axis is the derivative of the voltage. And then I can use the arguments of week one and say, well, if the present voltage is here, then the change is positive and it will flow towards the resting potential. The voltage is here.

Notes

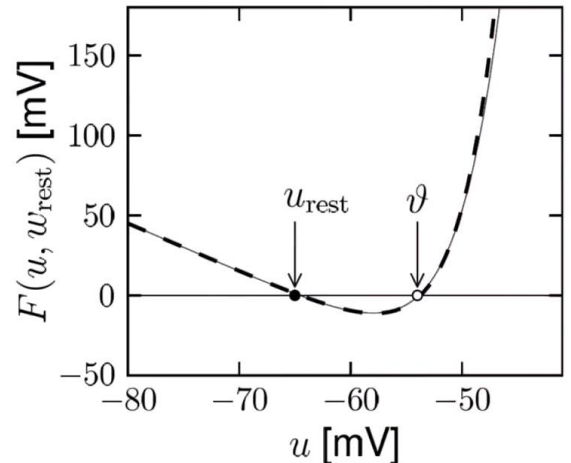
Summary



Neuronal Dynamics – 4.5. Nonlinear Integrate-and-Fire Model

Exponential integrate-and-fire model (EIF)

$$f(u) = -(u - u_{rest}) + \Delta \exp\left(\frac{u - \vartheta}{\Delta}\right)$$



$$\tau \frac{du}{dt} = F(u, w_{rest}) + RI(t) = f(u) + RI(t)$$

→ Nonlinear I&F (see week 1!)

Image: Neuronal Dynamics,
Gerstner et al.,
Cambridge Univ. Press (2014)

⏮ ⏪ ⏩ ⏭

The change is negative. We are below zero, $ddtu$ is negative, flow in this direction. If you are here, it will increase further. Now let's now jump back to this model here. It will increase further. Now in this reduced one-dimensional model, it would in fact flow up to this additional fixed point up here. That's in fact the moment when the action potential reaches its maximum. And at this point, you should go back to the two-dimensional neuron model, and say now it does flow in the two-dimensional face plane, w increases, we have to downswing, and so forth. And all this change of w , all this downswing, is replaced by a threshold process. If this variable hits the threshold θ , then the voltage is reset to some new value u_r which might be below the resting potential or above the resting potential depending on the type of neuron we are describing. Thus, during spike initiation, a two-dimensional neuron model can be replaced by just a single one-dimensional, non-linear integrate-and-fire model. And the specific integrate-and-fire model that results from this kind of analysis is exponential integrate-and-fire model, which has a linear part and an exponential part.

Notes

Summary



7m 54s

Neuronal Dynamics – 4.5. Exponential Integrate-and-Fire Model

Exponential integrate-and-fire model (EIF)

$$f(u) = -(u - u_{rest}) + \Delta \exp\left(\frac{u - \vartheta}{\Delta}\right)$$

linear

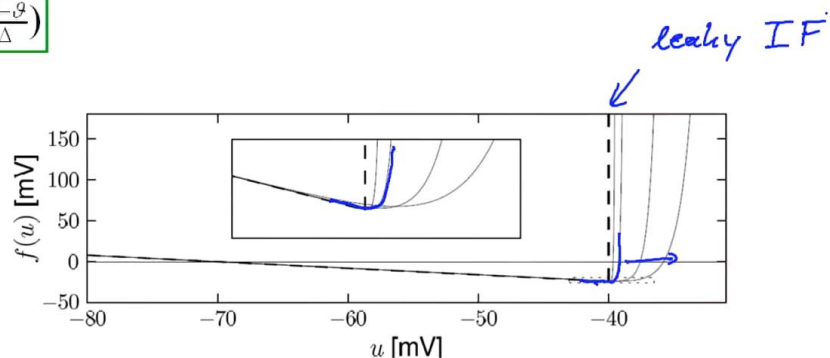


Image: Neuronal Dynamics,
Gerstner et al.,
Cambridge Univ. Press (2014)

Now interestingly, if you do this analysis, the exponential part is rather sharp. We have changed here this parameter, delta. If delta is a big number, say, 10 millivolt, then you get a slow increase. If delta is a small number, like 2 millivolt, then we get a very rapid increase here. And this is the zoom into this kind of picture. That means as soon as the voltage is above this turning point, the change [$\frac{df(u)}{du}$] is very, very rapid. It's like a very rapid upswing of the action potential, and it doesn't really matter where we stop it. Now in the limit, the delta becomes smaller and smaller. It becomes really a sharp threshold-like transition, and we are back to the leaky integrate-and-fire model. The standard linear integrate-and-fire model with a dictator.

Notes

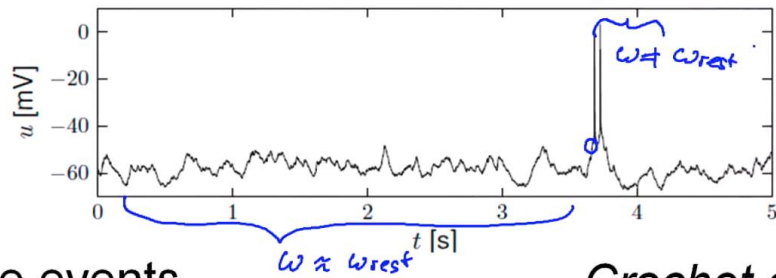
Summary



Neuronal Dynamics – 4.5 sparse activity in vivo

Spontaneous activity *in vivo*

awake mouse, cortex, freely whisking,



-spikes are rare events

Crochet et al., 2011

-membrane potential fluctuates around 'rest'

⌂ / ☐ ➡

Now let's come back to our spontaneous activity picture of the awake mouse in vivo. The aim is to predict the spike initiation points. Now the spike initiation points are well predicted by this model. That's what I would expect because during all this time here in this subthreshold regime, w stays very close to the resting value. And it's only during the downswing of the spike and during this phase afterwards, after a spike, the w is not equal to w_{rest} .

Notes

Summary

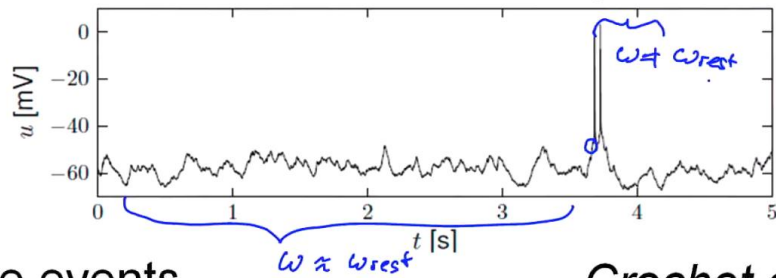
10m 44s



Neuronal Dynamics – 4.5 sparse activity in vivo

Spontaneous activity *in vivo*

awake mouse, cortex, freely whisking,



-spikes are rare events

Crochet et al., 2011

-membrane potential fluctuates around 'rest'

**Aims of Modeling: - predict spike initiation times
- predict subthreshold voltage**

Now if our aim is just to predict the spike initiation point and maybe also to predict the subthreshold fluctuations, then we don't need the w variable. We can replace the w variable by a reset.

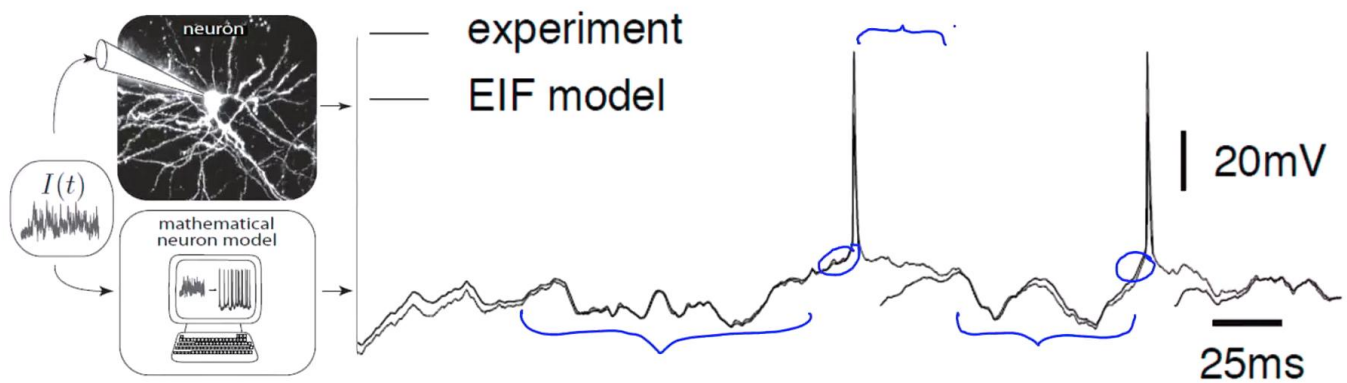
Notes

Summary

11m 33s



Neuronal Dynamics – 4.5. How good are integrate-and-fire models?



Badel et al., 2008

- Aims:
- predict spike initiation times
 - predict subthreshold voltage

Add adaptation and refractoriness (week 7)

And this is essentially why such an exponential integrate-and-fire model works so well to predict spike times. The same current is injected into a real neuron and an exponential integrate-and-fire model. The real neuron emits a spike here, and so does the exponential integrate-and-fire model. Spike initiation is perfectly well predicted. Here again, spike initiation is well predicted. The subthreshold membrane potential is well predicted by the model. It's only during the phase after the spike where we expect that additional processes come into play. That exponential integrate-and-fire model is not as good. But if you add adaptation and refractoriness, as we will do in week seven, then this part can be covered as well.

Notes

Summary



11m 50s

Neuronal Dynamics – 4.5. Exponential Integrate-and-Fire Model

Direct derivation from Hodgkin-Huxley

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

$$C \frac{du}{dt} = -g_{Na} [m_0(u)]^3 h_{rest} (u - E_{Na}) - g_K [n_{rest}]^4 (u - E_K) - g_l (u - E_l) + I(t)$$

Fourcaud-Trocme et al, J. Neurosci. 2003

$$f(u) = -(u - u_{rest}) + \Delta \exp\left(\frac{u - \theta}{\Delta}\right)$$

$$\tau \frac{du}{dt} = F(u, h_{rest}, n_{rest}) + RI(t) = \underbrace{f(u)}_{\text{gives expon. I\&F}} + RI(t)$$

gives expon. I&F
+ threshold + reset

So we have reduced the two-dimensional model to arrive at the exponential integrate-and-fire model. However, we could have done this in a single step coming from the Hodgkin-Huxley model. All Let's replace the m variable, the [? fast-gating ?] variable, by its instantaneous value. H and n are slow. Let's replace h by its reference value at rest and n by its reference value at rest. Then, we have just a function which depends on the membrane potential. And these are parameters. For fixed parameters, I just have a function f of u. And this function is the exponential integrate-and-fire type model. It has a linear term and an exponential term. Now this nonlinear integrate-and-fire model needs to be complemented by a threshold and reset mechanism and then we are done.

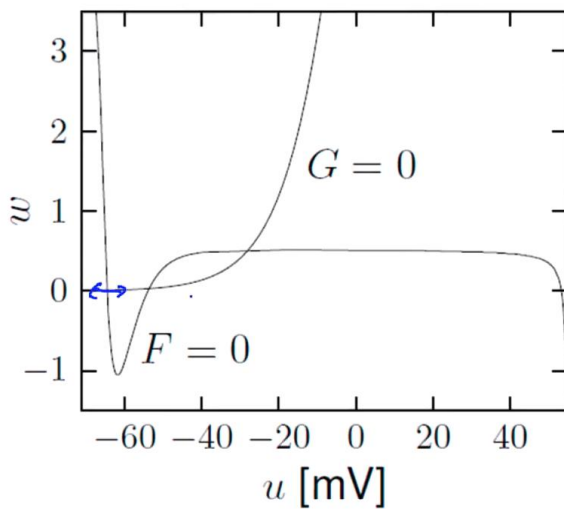
Notes

Summary



12m 48s

Neuronal Dynamics – 4.5. Nonlinear Integrate-and-Fire Model



2-dimensional equation

$$\tau \frac{du}{dt} = F(u, w) + RI(t)$$

$$\tau_w \frac{dw}{dt} = G(u, w) \quad \text{slow}$$

Separation of time scales

-w is constant (if not firing)

$$\tau \frac{du}{dt} = f(u) + RI(t)$$

⌕ / ☐ ➡

So let me summarize what I said. If you have this separation of time constants so that w is the slow variable, then the neuron that stays most of the time close to its resting state can be treated by a model where w is treated as a constant. w comes into play mainly during the downstream of the action potential, not during the initiation of the action potential.

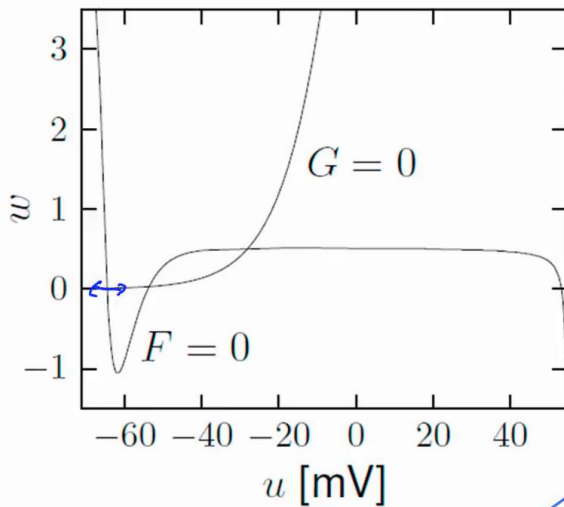
Notes

Summary



14m 01s

Neuronal Dynamics – 4.5. Nonlinear Integrate-and-Fire Model



Relevant during spike and downswing of AP

2-dimensional equation

$$\tau \frac{du}{dt} = F(u, w) + RI(t)$$

$$\tau_w \frac{dw}{dt} = G(u, w) \quad \text{slow}$$

Separation of time scales

-w is constant (if not firing)

$$\tau \frac{du}{dt} = \underline{f(u)} + RI(t)$$

threshold+reset for firing

This kind of bouncing of the action potential is replaced in this nonlinear integrate-and-fire model by an explicit reset. The non-linearity that we find here is that of the exponential integrate-and-fire model. So let me summarize.

Notes

Summary



Neuronal Dynamics – 4.5. Nonlinear Integrate-and-Fire Model



2-dimensional equation

$$\tau \frac{du}{dt} = F(u, w) + RI(t)$$

$$\tau_w \frac{dw}{dt} = G(u, w)$$

Separation of time scales

-w is constant (if not firing)

$$\tau \frac{du}{dt} = f(u) + RI(t)$$

Linear plus exponential

This week, we have reduced the Hodgkin-Huxley model to two dimensions, and we arrived at a model where spike initiation and spike formation can be nicely analyzed in the phase plane. Now in this last lecture, I've made a further reduction to one dimension. We arrived at a non-linear integrate-and-fire model, which has a large linear subthreshold part and the exponential non-linearity. And in this one-dimensional nonlinear integrate-and-fire model, the bouncing of the action potential, that is modeling the two-dimensional case by the w variable, the downswing of the action potential is replaced by a simple reset of the voltage variable. Now this kind of model with a broad, linear subthreshold regime will be the starting point for the discussions of coding and noise in the next few weeks.

Notes

Summary



14m 59s

Neuronal Dynamics – Quiz 4.7.

A. Exponential integrate-and-fire model.

The model can be derived

- ☐ from a 2-dimensional model, assuming that the auxiliary variable w is constant.
- ☐ from the HH model, assuming that the gating variables h and n are constant.
- ☐ from the HH model, assuming that the gating variable m is constant.
- ☐ from the HH model, assuming that the gating variable m is instantaneous.

B. Reset.

- ☐ In a 2-dimensional model, the auxiliary variable w is necessary to implement a reset of the voltage after a spike
- ☐ In a nonlinear integrate-and-fire model, the auxiliary variable w is necessary to implement a reset of the voltage after a spike
- ☐ In a nonlinear integrate-and-fire model, a reset of the voltage after a spike is implemented algorithmically/explicitly

Please take a moment for the quiz, and don't forget the assignments.
Hope to see again next week for exciting new material.

Notes

Summary



16m 08s