

Week 7 – part 1 : Models and data



7.1 What is a good neuron model?

- Models and data

7.2 AdEx model

- Firing patterns and adaptation

7.3 Spike Response Model (SRM)

- Integral formulation

7.4 Generalized Linear Model

- Adding noise to the SRM

7.5 Parameter Estimation

- Quadratic and convex optimization

7.6. Modeling in vitro data

- how long lasts the effect of a spike?

7.7. Helping Humans

Welcome to the final week of the class, Neuronal Dynamics. Thanks for staying with me for such a long time. In the previous weeks, we have covered different aspects of neuron modeling. This week, they'll put the different strands together, and I hope I can show the we will arrive at some exciting results.

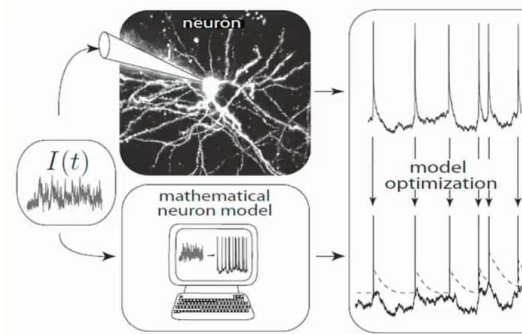
Notes

Summary



0m 05s

Neuronal Dynamics – 7.1 Neuron Models and Data



- What is a good neuron model?
- Estimate parameters of models?

The question I would like to ask this week is actually what is good neuron model? And how can we compare a neuron model with data? How can we optimize parameters of neuron model so that it really describes biology.

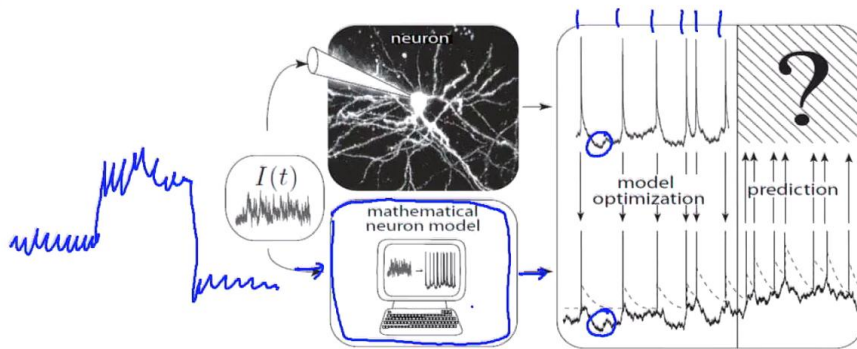
Notes

Summary



0m 30s

Neuronal Dynamics – 7.1 What is a good neuron model?



- A) Predict spike times ✓
- B) Predict subthreshold voltage
- C) Easy to interpret (not a 'black box')
- D) Flexible enough to account for a variety of phenomena
- E) Systematic procedure to 'optimize' parameters

So let's start with the first question. Let's suppose we inject an input current into a real neuron. The input should look like the one, a neuron that's likely to receive in vivo. Say it has a fluctuating part and suppose you suddenly see the image of the signal per house, the mean of the input changes, and you look at something else, so that's the kind of input current one could inject in a real neuron. The real neuron emits spikes. What I would like as a first condition for a good neuron model, that if I inject the very same current into a mathematical neuron model, I would find the spikes at the same moments in time. But moreover, I could ask, well, in this region where there are no spikes, in the subthreshold region, do the model and the neuron have the same kind of behavior? And then ideally, I don't want a model that's just a black box. Just a books where I get some input and an output. But ideally, I would like to be able to interpret variables in the model in terms of biological phenomena. Well, the model should be flexible so it accounts for a variety of fired behavior, and at the same time, the mathematical structure of the model should be such that there exists a systematic procedure to optimize parameters.

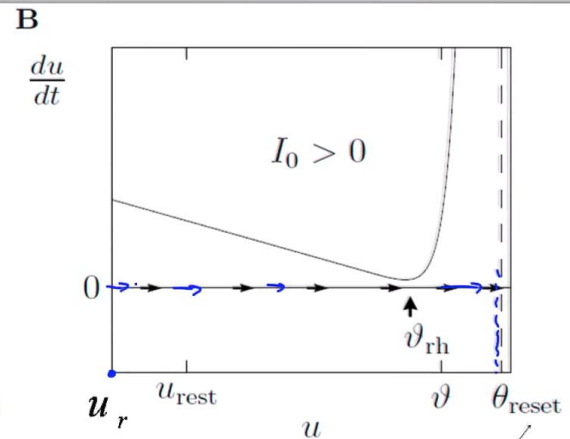
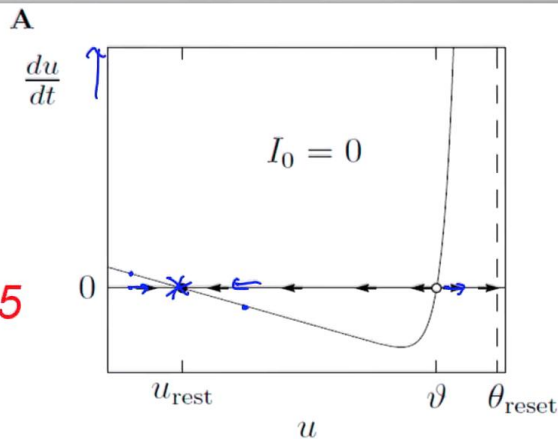
Notes

Summary



Neuronal Dynamics – Review: Nonlinear Integrate-and-fire

See:
week 1,
lecture 1.5



$$\tau \frac{du}{dt} = \underbrace{f(u)}_{\text{non-linear}} + R I(t)$$

$\uparrow I_0 > 0$

If $u = \theta_{\text{reset}}$
then reset to

$$u = u_r$$

What is a good choice of f ?

Now, in week one, we have seen a very simple neuron model. The neuron model consist of just one differential equation and this can be described by some non-linear function. And if you look here the derivative, the du/dt , then this means if this function f is positive, I have movement to the right. If it's negative, I have movement to the left, so this would be a stable fixed point of the dynamics. There's an unstable fixed point up here. If I apply a constant input, then the du/dt curve is shifted vertically upwards, and I've no fixed points anymore. I have a flow that's always towards the right. And then if it hits this formal reset threshold, then we reset the voltage to some value u_r , and the whole process starts again. So that's a non-linear integrate-and-fire model. And the first question is, compared to real data, now, what would be a good choice of this non-linear function f ?

Notes

Summary



2m 37s

Neuronal Dynamics – Review: Nonlinear Integrate-and-fire

$$(1) \quad \tau \frac{du}{dt} = f(u) + RI(t)$$

(2) If $u = \theta_{reset}$ then reset to $u = u_r$

What is a good choice of f ?

(i) Extract f from more complex models ✖

(ii) Extract f from data

✎ ✎ ✎ ✎

And we have seen in week one that there is a natural choice related to data. So one can extract this function f from data. We've also seen that one can try to extract this function f for more complex models. Let's review this first.

Notes

Summary

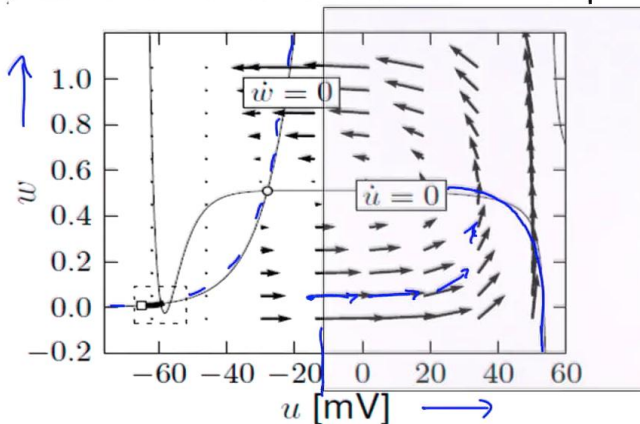


3m 56s

Neuronal Dynamics – Review: Nonlinear Integrate-and-fire

(i) Extract f from more complex models

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



A. detect spike and reset

Separation of time scales:
Arrows are nearly horizontal

See week 4:
2dim version of
Hodgkin-Huxley

$$\begin{cases} \tau \frac{du}{dt} = F(u, w) + RI(t) \\ \tau_w \frac{dw}{dt} = G(u, w) \end{cases}$$

Suppose in a first step we reduce a model like the four dimensional Hodgkin-Huxley model to two dimensions. That would be this system of equations. And we have seen in week four that we can analyze this in the phase plane where the horizontal axis is the voltage and the vertical axis is this auxiliary variable w . Now, what I have plotted here are the node lines. So this curve here is the u node line and this curve here is the w node line. The arrows indicate the direction of the flux, and we see here that arrows are nearly horizontal. In fact, once the system is here, we know that it will continue along a trajectory, which I can construct. And this trajectory, this detour, corresponds to a spike. So instead of each time modeling this trajectory in the phase plane, you can say, well, there's some kind of threshold. Let's call this the threshold, where we detect the spike. And then instead of integrating the two dimensional differential equation, we just reset. Moreover, we see here that arrows are nearly horizontal. Why? Because the dynamics of w is much slower than that of the voltage. Normally, the membrane potential hovers around in the neighborhood of the fixed point, of the stable fixed point.

Notes

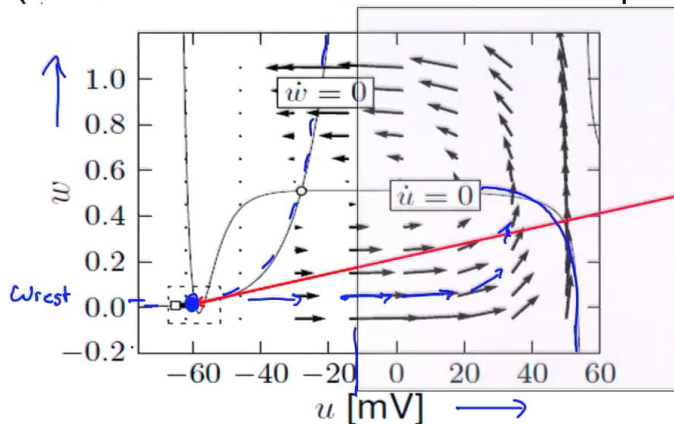
Summary



Neuronal Dynamics – Review: Nonlinear Integrate-and-fire

(i) Extract f from more complex models

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



A. detect spike and reset

resting state

Separation of time scales:
Arrows are nearly horizontal

Spike initiation, from rest

See week 4:
2dim version of
Hodgkin-Huxley

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

$$\underline{w \approx w_{rest}}$$

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

B. Assume $w = w_{rest}$

That's where the resting potential is. And there's also a resting value of the auxiliary variable w . Now, if the input is big enough to kick it out of this regime, then it will start a horizontal flow. So we can say that sharing the initial increase of the voltage, w remains still close to its resting value. And that means, we may assume that in this region here, just in this region, w is equal to w_{rest} .

Notes

Summary



Neuronal Dynamics – Review: Nonlinear Integrate-and-fire

(i) Extract f from more complex models $\tau \frac{du}{dt} = f(u) + RI(t)$

See week 4:
2dim version of
Hodgkin-Huxley

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

We blocked this back into this equation, w equal to w_{rest} , so this becomes w_{rest} , and the second equation just disappears. So now we have just one equation, a voltage equation, with some non-linear function, and this is the function that's plotted here.

Notes

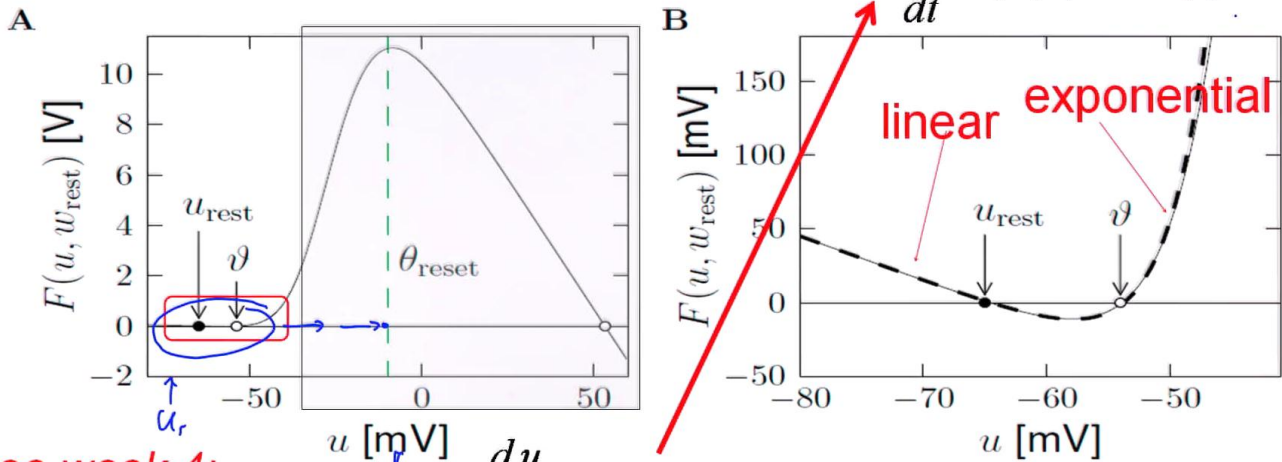
Summary



6m 58s

Neuronal Dynamics – Review: Nonlinear Integrate-and-fire

(i) Extract f from more complex models $\tau \frac{du}{dt} = f(u) + RI(t)$



See week 4:
2dim version of
Hodgkin-Huxley

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

Above the same range as before, and here I have indicated the threshold, the numerical threshold for reset. Once the voltage reaches this point here, we reset to a value u_r , say, this value here. Now the decision whether a spike is triggered or not, actually happens in this region down here. So let's zoom on this region, and then this function looks like a linear curve followed by an exponential increase. That means the correct one-dimensional nonlinearity is a combination of a linear and exponential term.

Notes

Summary

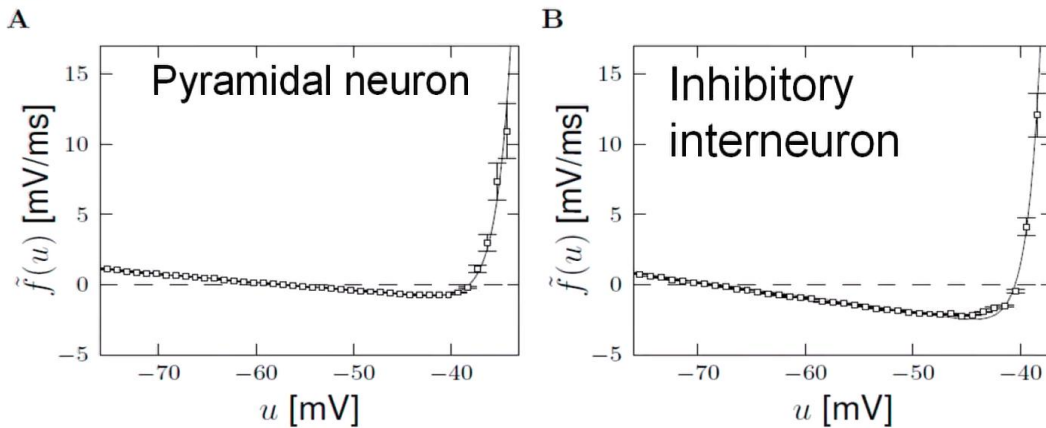


Neuronal Dynamics – Review: Nonlinear Integrate-and-fire

(ii) Extract f from data *Badel et al. (2008)*

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

$$\underbrace{\tilde{f}(u)} = \frac{f(u)}{\tau}$$



*Badel et al.
(2008)*

And this is called the exponential integrate-and-fire model. Alternatively, as we have seen in week one, I can also extract this function f directly from data. If I divide the voltage equation by τ , I have this effective function $\tilde{f}$, which is plotted here, and you see that the solid line-- it's a very nice fit.

Notes

Summary



8m 20s

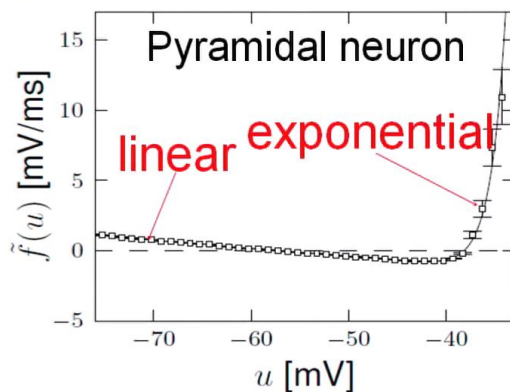
Neuronal Dynamics – Review: Nonlinear Integrate-and-fire

(ii) Extract f from data *Badel et al. (2008)*

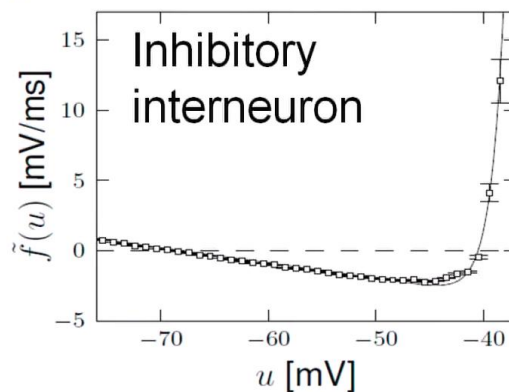
$$\tau \frac{du}{dt} = \underbrace{f(u)} + RI(t)$$

$$\underbrace{\tilde{f}(u)} = \frac{f(u)}{\tau}$$

A



B



Badel et al. (2008)

The solid line consists of a linear term and an exponential. And that's true for different types of neurons. It's true for pyramidal neuron.

Notes

Summary



8m 48s

Neuronal Dynamics – Review: Nonlinear Integrate-and-fire

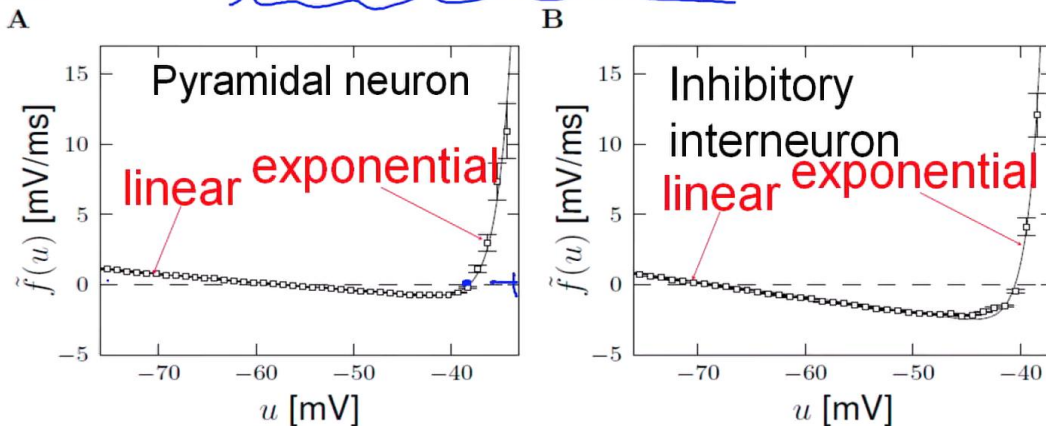
(ii) Extract f from data *Badel et al. (2008)*

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

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

$$\tilde{f}(u) = \frac{f(u)}{\tau}$$

Exp. Integrate-and-Fire, *Fourcaud et al. 2003*



Badel et al. (2008)

It's also true for the inhibitory interneuron. Thus, if we restrict ourselves to just one voltage equation and combine with reset, the best function is the one that has a linear term and an exponential term, and this is called the exponential integrate-and-fire model. If the voltage reaches some value above this unstable fixed point here, say, at this point here, we may reset the voltage and integration may start again.

Notes

Summary



8m 58s

Neuronal Dynamics – Review: Nonlinear Integrate-and-fire

$$(1) \quad \tau \frac{du}{dt} = f(u) + R I(t)$$

(2) *If $u = \theta_{reset}$ then reset to $u = u_r$*

Best choice of f : linear + exponential

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

⏮ ⏪ ⏩ ⏭

Thus, for one-dimensional neuron models, you can identify the best non-linearity, it's linear plus exponential. It looks like this. This is called the exponential integrate-and-fire model.

Notes

Summary



9m 40s

Neuronal Dynamics – Review: Nonlinear Integrate-and-fire

$$(1) \quad \tau \frac{du}{dt} = f(u) + R I(t)$$

$$(2) \quad \text{If } u = \theta_{\text{reset}} \text{ then reset to } u = u_r$$

Best choice of f : linear + exponential

$$\tau \frac{du}{dt} = -(u - u_{\text{rest}}) + \Delta \exp\left(\frac{u - \vartheta}{\Delta}\right)$$

BUT: Limitations – need to add

- Adaptation on slower time scales
- Possibility for a diversity of firing patterns
- Increased threshold ϑ after each spike
- Noise

✎ ✎ ✎ ✎

However, that's not sufficient. Such a model completely neglects adaptation, processes that happen on a slower time scale. It's impossible to use such a model to account for the diversity of firing patterns. There's a fixed threshold. However, we need to make this parameter, theta, somewhat dynamic, and then this is a deterministic model. It has no noise. Now, these additional points will be discussed in the next lectures of this week. We'll get rid of these limitations.

Notes

Summary



9m 57s

Neuronal Dynamics – 7.1. Nonlinear Integrate-and-fire

$$(1) \quad \tau \frac{du}{dt} = f(u) + R I(t)$$

$$(2) \quad \text{If } u = \theta_{\text{reset}} \text{ then reset to } u = u_r$$

f : linear + exponential

$$\tau \frac{du}{dt} = -(u - u_{\text{rest}}) + \Delta \exp\left(\frac{u - \vartheta}{\Delta}\right)$$

Limitations

- Adaptation
- firing patterns
- Increased threshold ϑ
- Noise



To summarize, thus, if we restrict ourselves to one-dimensional integrate-and-fire models, then the best model is exponential integrate-and-fire, a linear term in the voltage equation combined with an exponential. However, this model has limitations, and they'll get rid of these limitations in this series of lectures for this final week. Please, have a look at the quiz.

Notes

Summary



10m 42s

Neuronal Dynamics – Quiz 7.1.

The exponential integrate-and-fire model

- ☐ can be extracted from data
- ☐ can be extracted from two-dimensional neuron model under the assumption of a separation of time scales
- ☐ has a linear and an exponential term in the voltage equation
- ☐ accounts for adaptation
- ☐ accounts for bursting

Notes

Summary

11m 15s

