

# Week 9 – part 1 : Models and data



## Biological Modeling of Neural Networks:

### Week 9 – Optimizing Neuron Models For Coding and Decoding

Wulfram Gerstner

EPFL, Lausanne, Switzerland

#### 9.1 What is a good neuron model?

- Models and data

#### 9.2 AdEx model

- Firing patterns and adaptation

#### 9.3 Spike Response Model (SRM)

- Integral formulation

#### 9.4 Generalized Linear Model

- Adding noise to the SRM

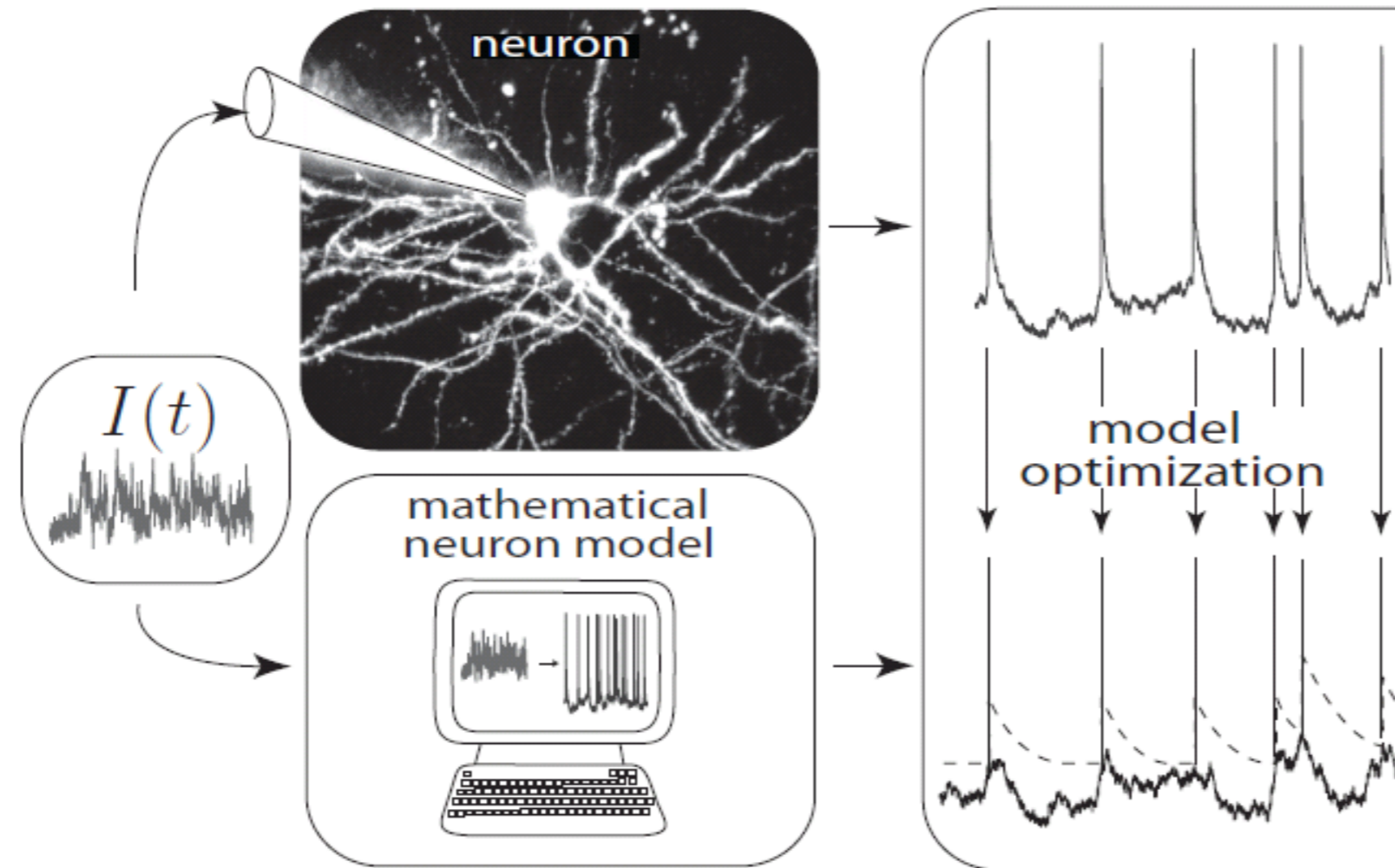
#### 9.5 Parameter Estimation

- Quadratic and convex optimization

#### 9.6. Modeling in vitro data

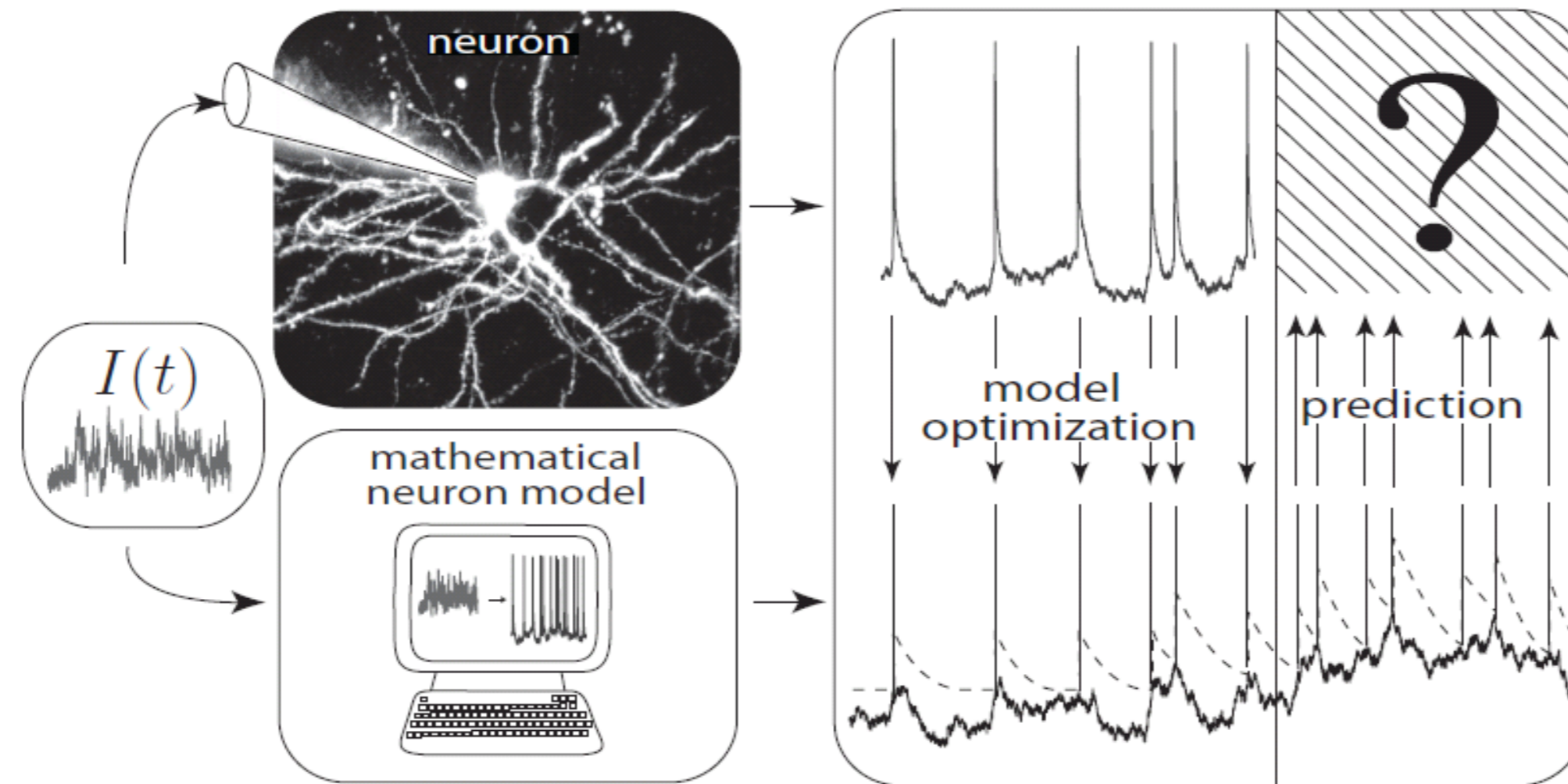
- how long lasts the effect of a spike?

# Neuronal Dynamics – 9.1 Neuron Models and Data



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

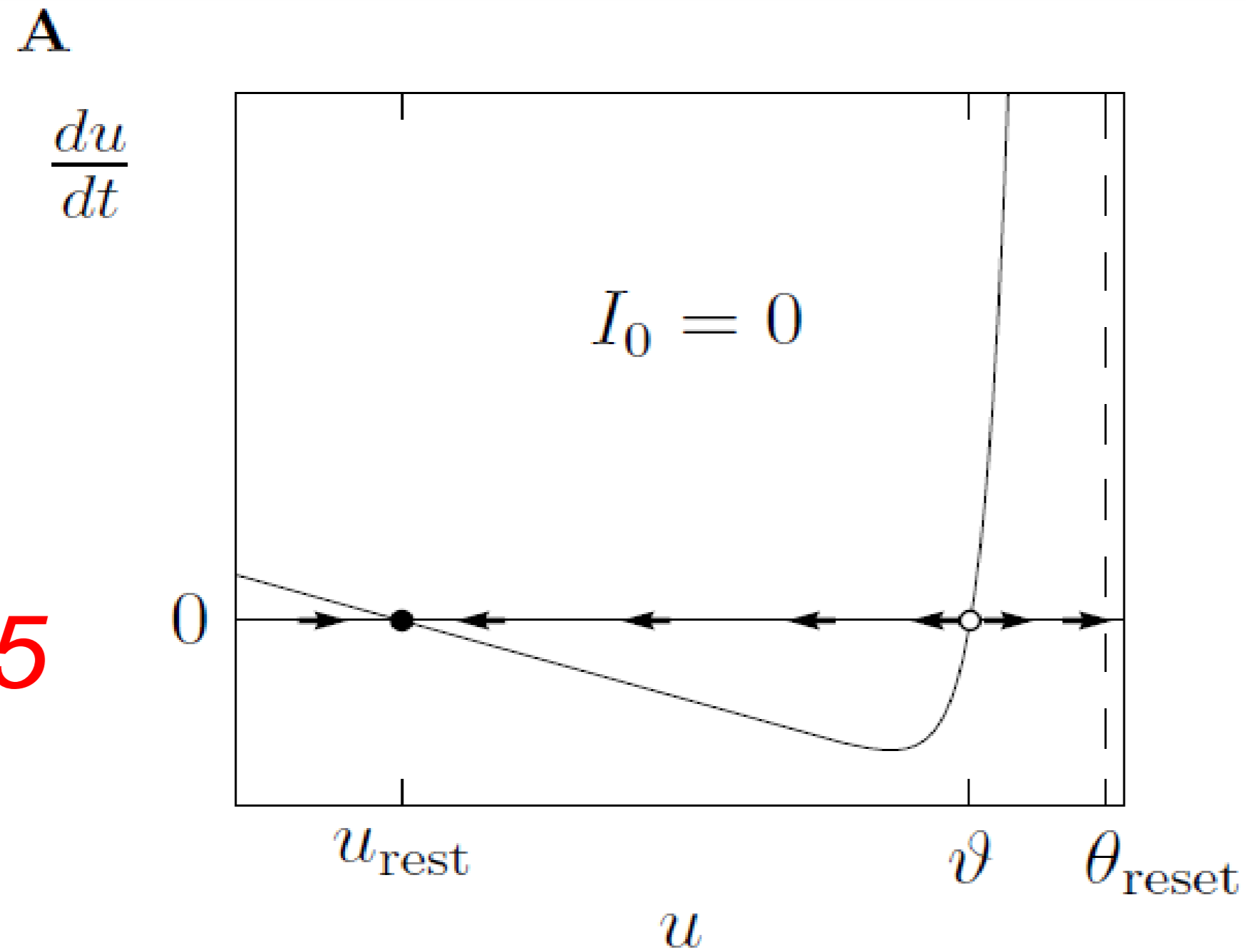
# Neuronal Dynamics – 9.1 What is a good neuron model?



- 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

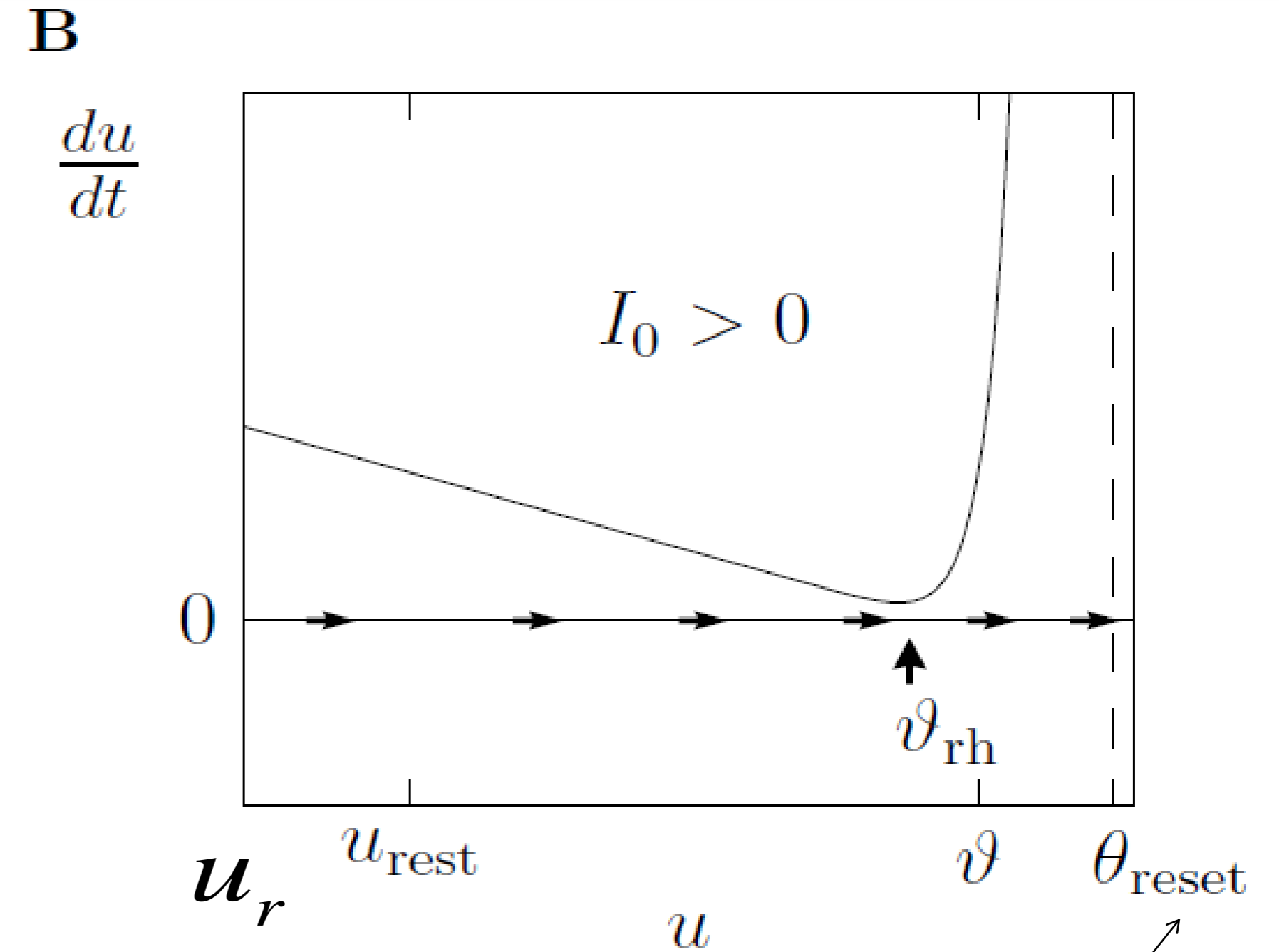
# Neuronal Dynamics – Review: Nonlinear Integrate-and-fire

See:  
week 1,  
lecture 1.5



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

What is a good choice of  $f$  ?



If  $u = \theta_{reset}$

then reset to

$$u = u_r$$

# 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  $f$  ?

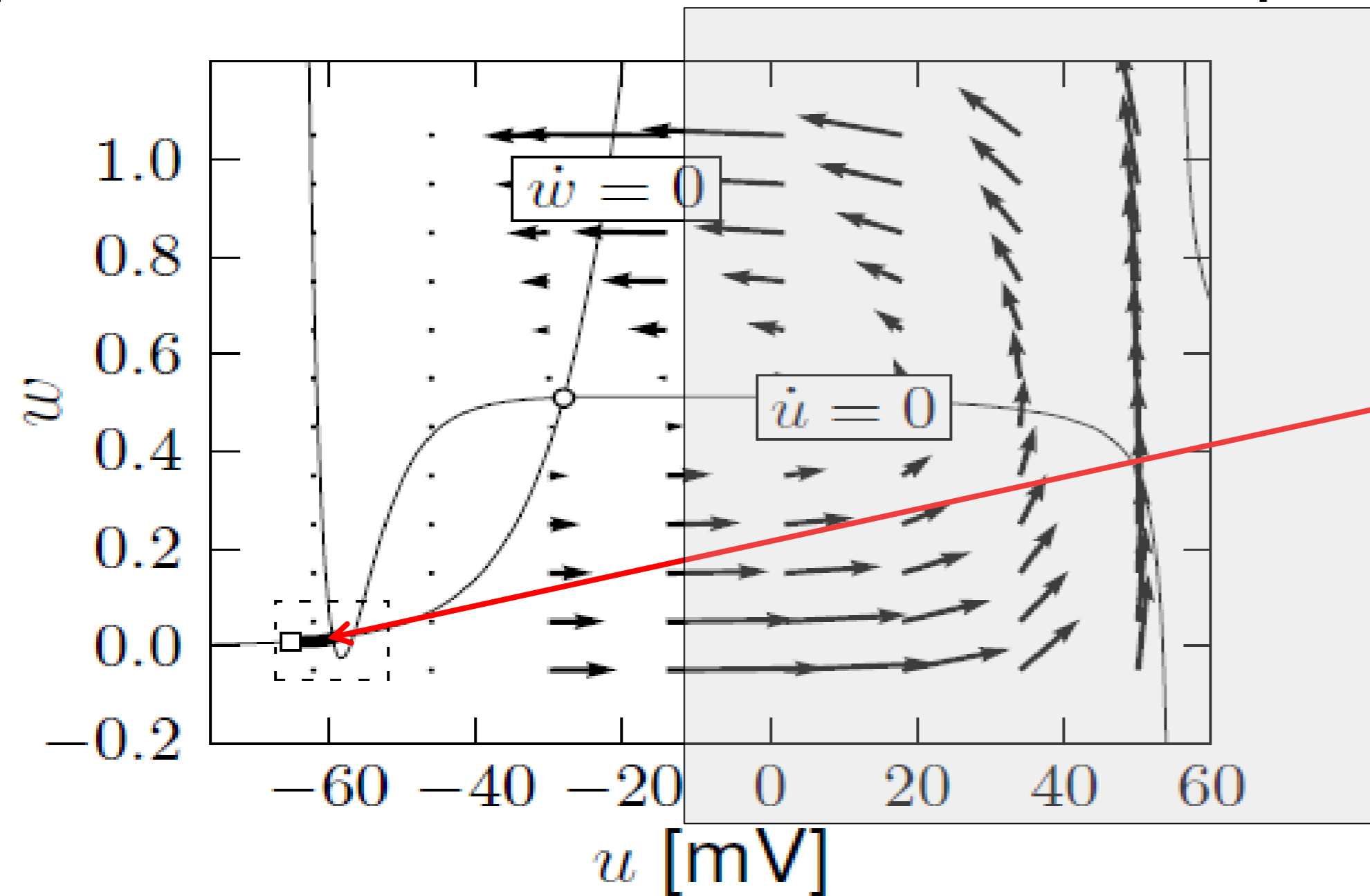
- (i) Extract  $f$  from more complex models
- (ii) Extract  $f$  from data



# 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 3:  
2dim version of  
Hodgkin-Huxley

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

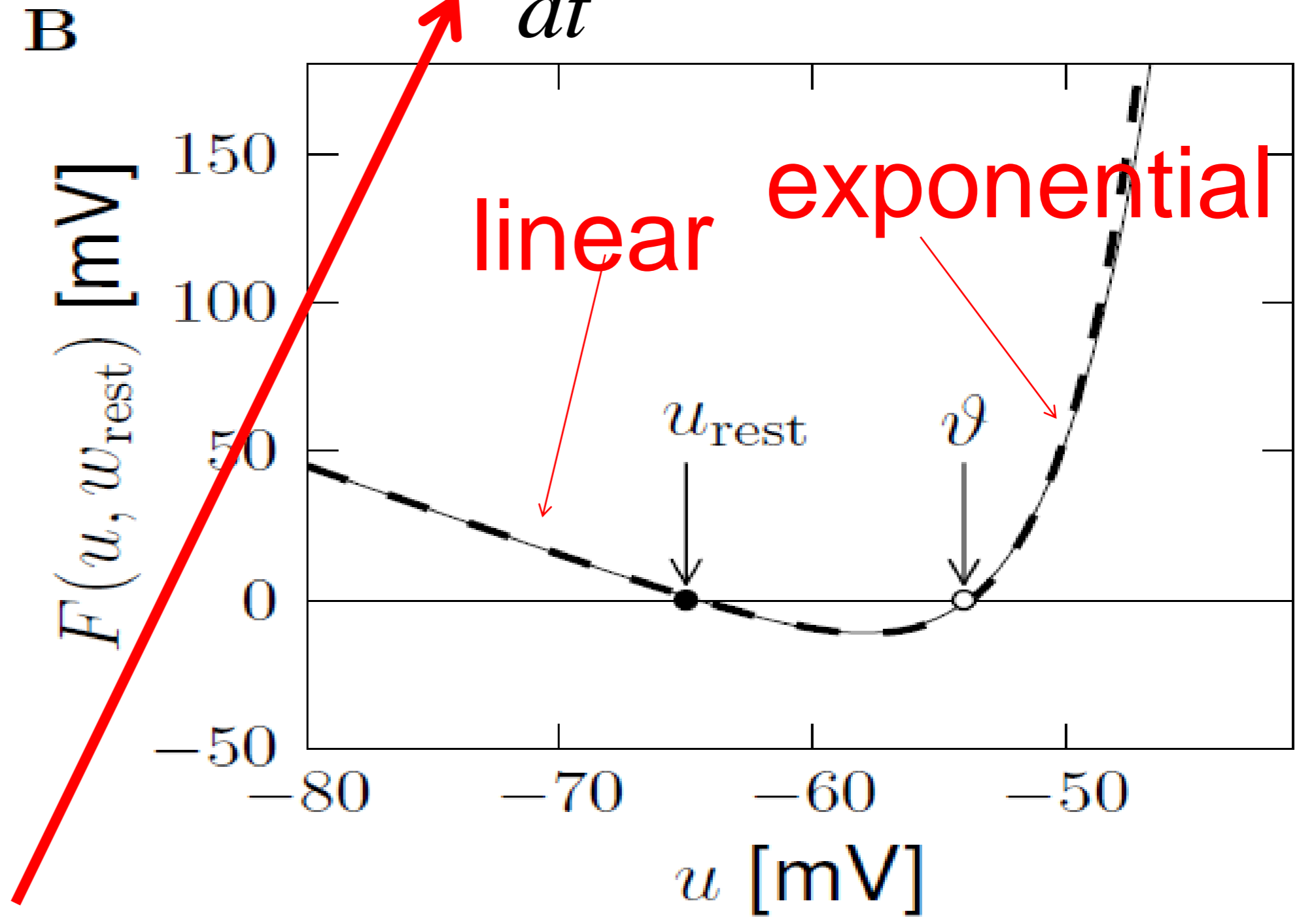
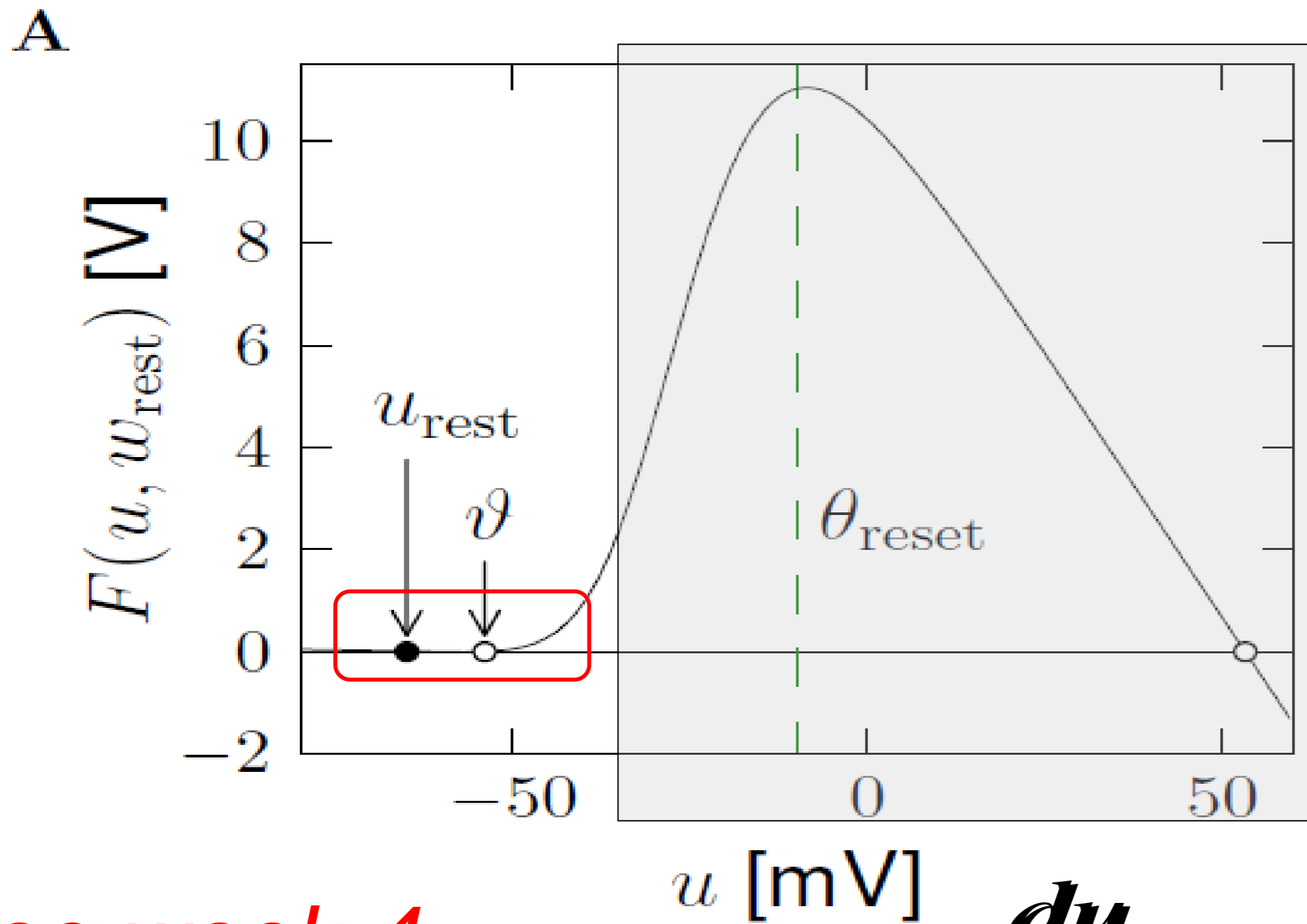
$$w \approx w_{rest}$$

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

B. Assume  $w = w_{rest}$

# 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

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

Separation of time scales

$$\tau_w \frac{dw}{dt} = G(u, w) \longrightarrow w \approx w_{rest}$$

# Neuronal Dynamics – Review: Nonlinear Integrate-and-fire

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

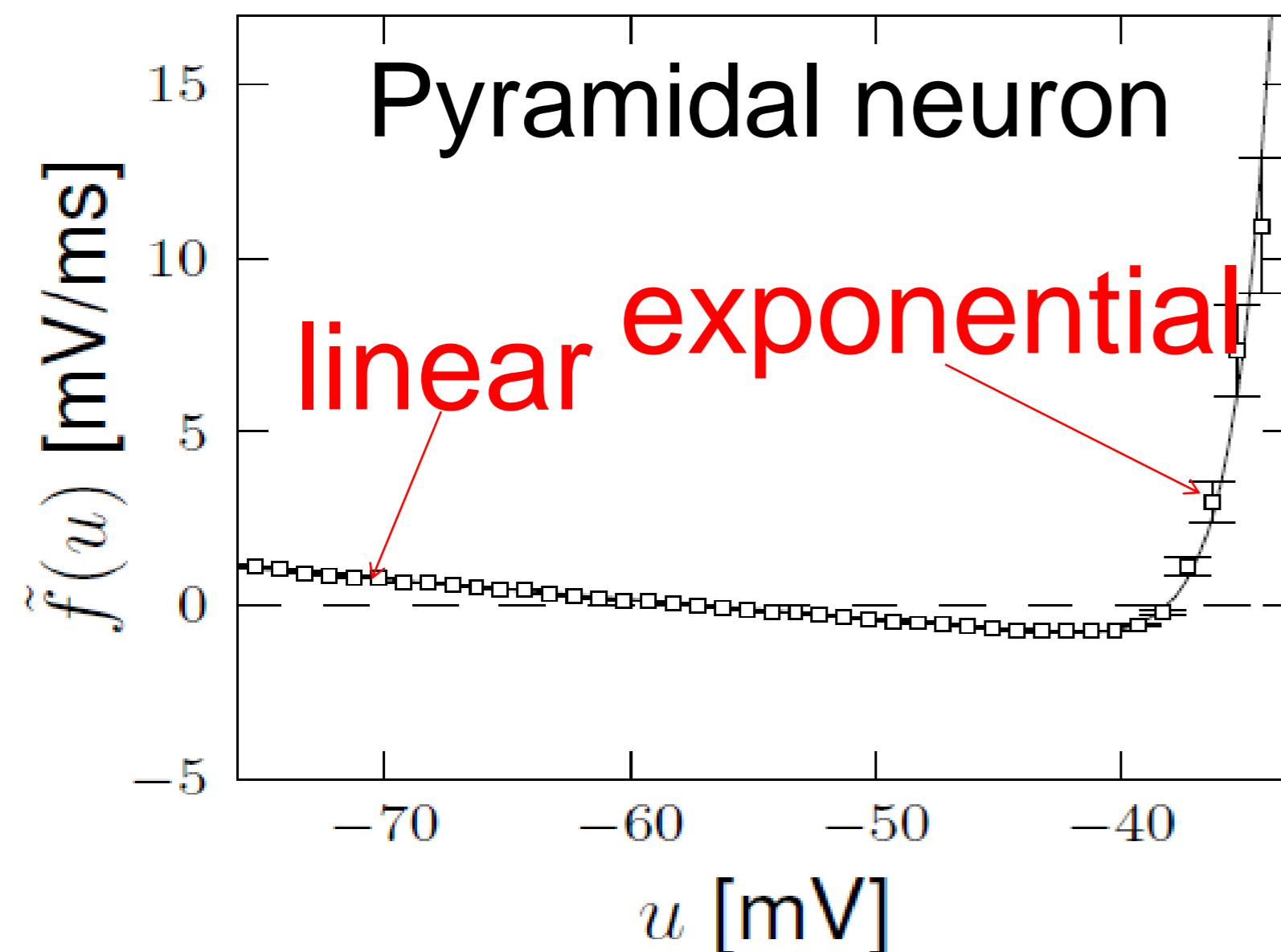
$$\tau \frac{du}{dt} = f(u) + RI(t)$$

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

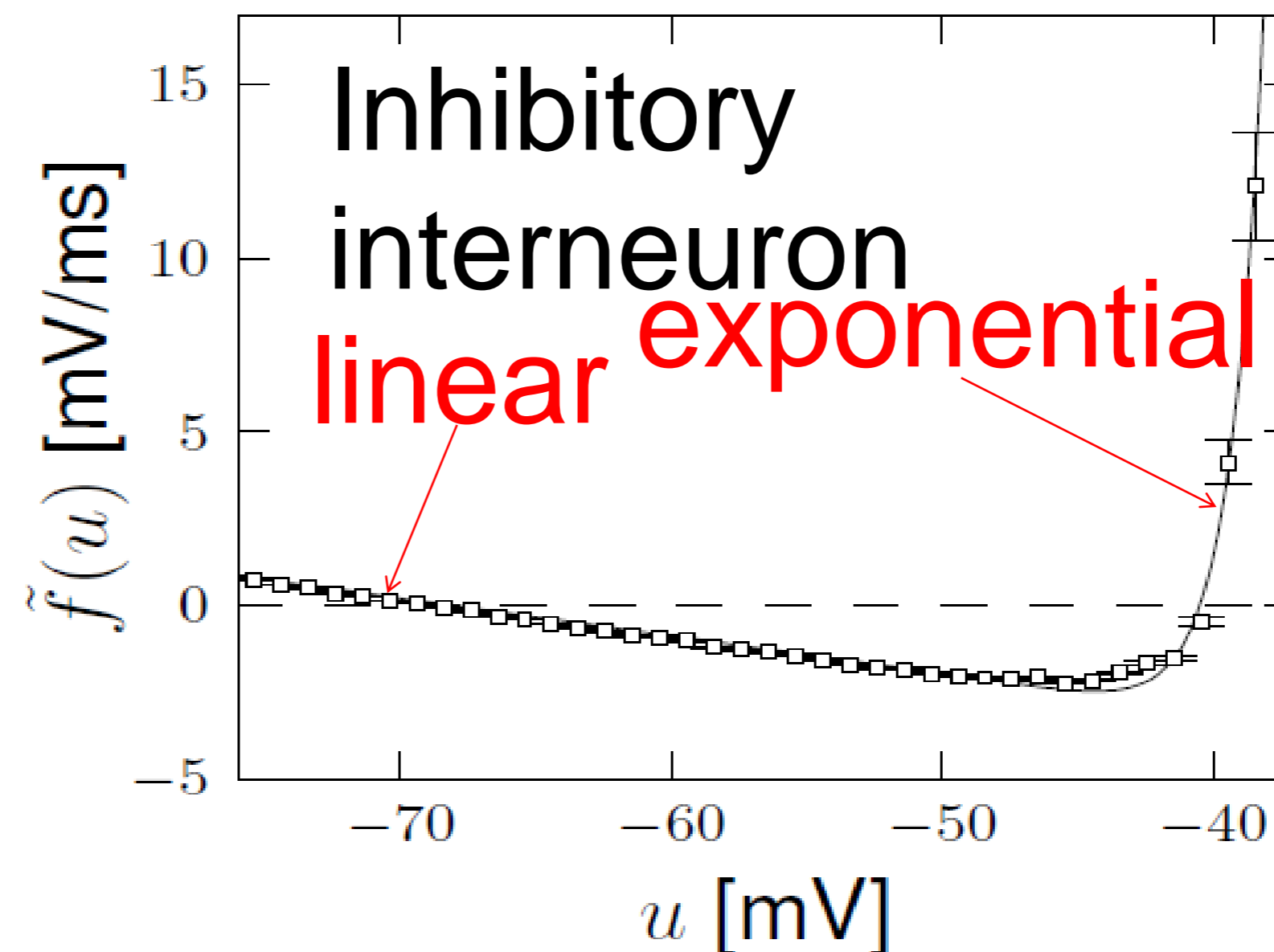
$$\tilde{f}(u) = \frac{f(u)}{\tau}$$

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

A



B



*Badel et al. (2008)*



# 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  $u = u_r$*

Best choice of  $f$ : linear + exponential

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

**BUT: Limitations – need to add**

- Adaptation on slower time scales
- Possibility for a diversity of firing patterns
- Increased threshold  $\mathcal{I}$  after each spike
- Noise

# Week 9 – part 2 : Adaptive Exponential Integrate-and-Fire Model



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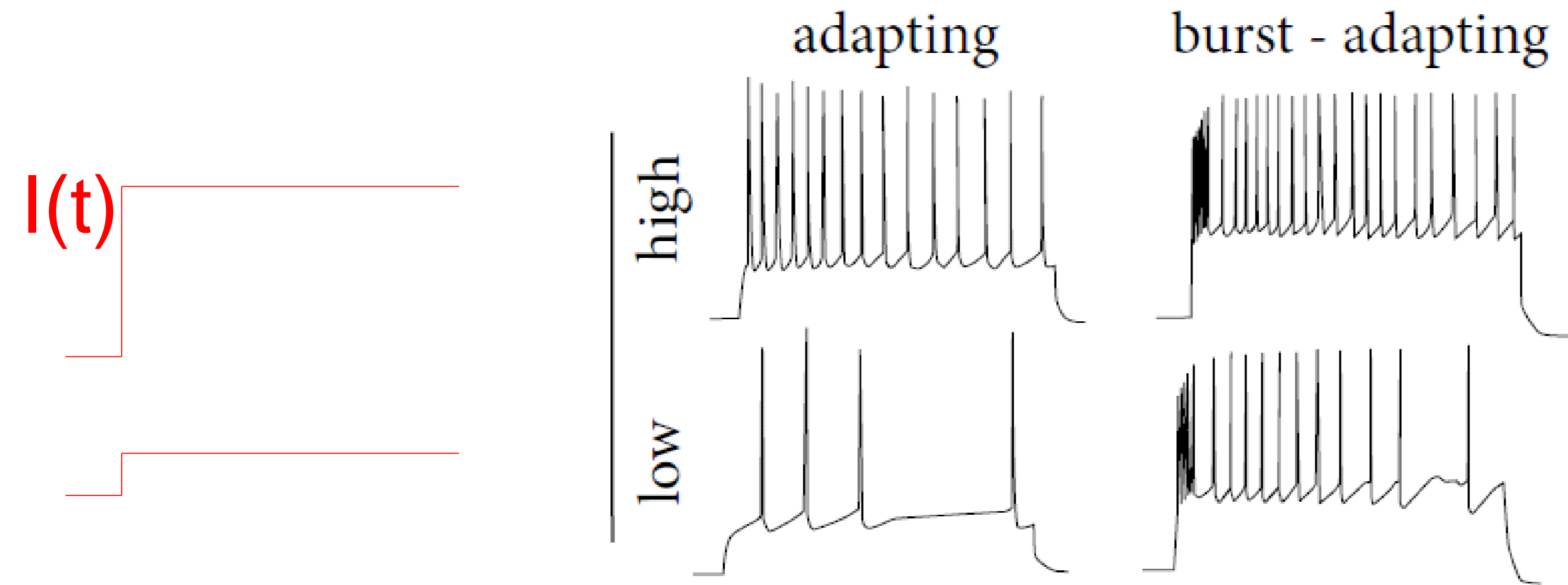
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# Neuronal Dynamics – 9.2 Adaptation

## Step current input – neurons show adaptation



*Data:  
Markram et al.  
(2004)*

**1-dimensional (nonlinear) integrate-and-fire model cannot do this!**

# Neuronal Dynamics – 9.2 Adaptive Exponential I&F

Add adaptation variables:

Blackboard !

$$\tau \frac{du}{dt} = -(u - u_{rest}) + \Delta \exp\left(\frac{u - \mathcal{I}}{\Delta}\right) - R \sum_k w_k$$

$$\tau_k \frac{dw_k}{dt} = a_k (u - u_{rest}) - w_k + b_k \tau_k \sum_f \delta(t - t^f)$$

Exponential I&F  
+ 1 adaptation var.  
= AdEx

**SPIKE AND  
RESET**

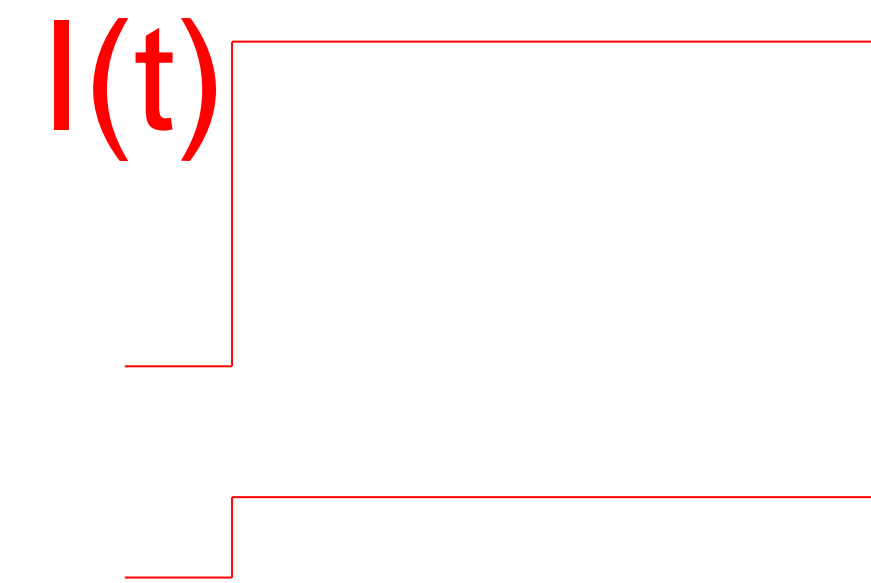
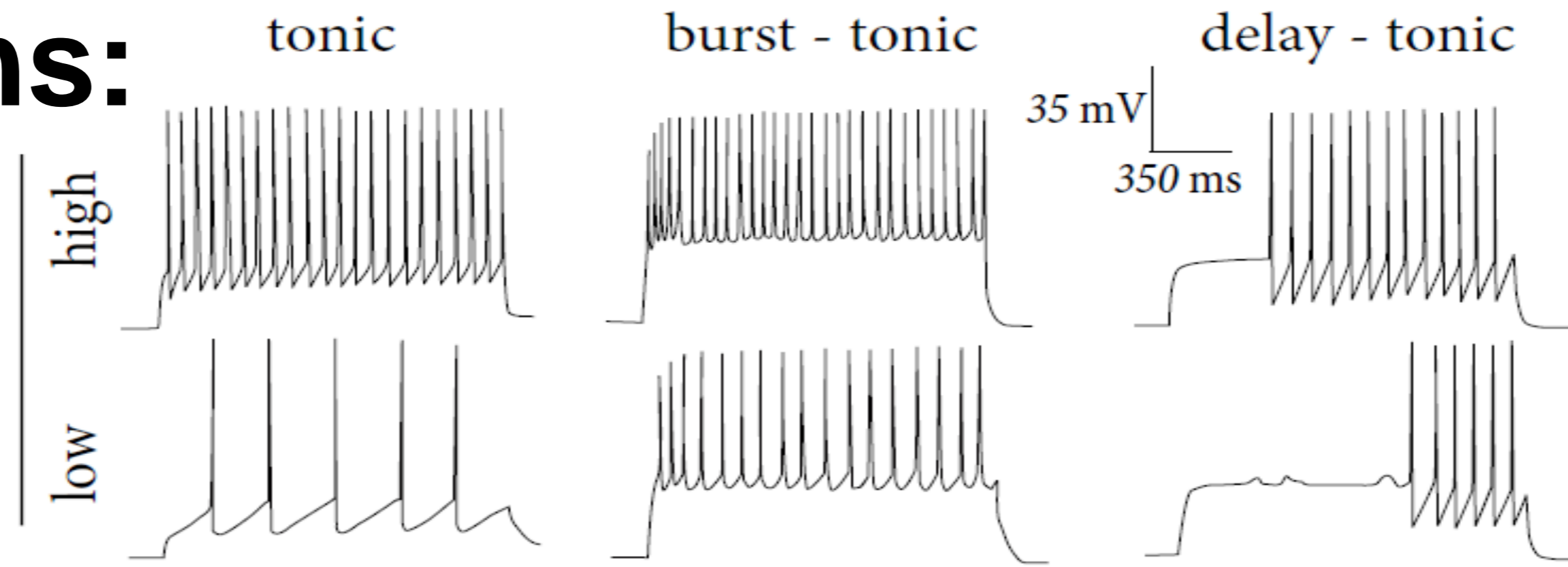
after each spike  $w_k$   
jumps by an amount  $b_k$

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

*AdEx model,  
Brette & Gerstner (2005):*

# Firing patterns:

Response to  
Step currents,  
*Exper. Data,*  
*Markram et al.*  
*(2004)*

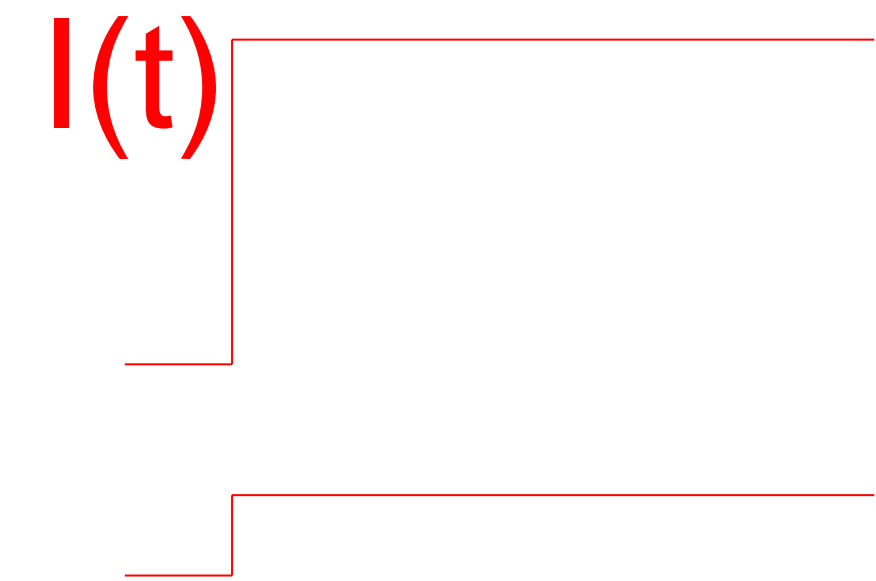
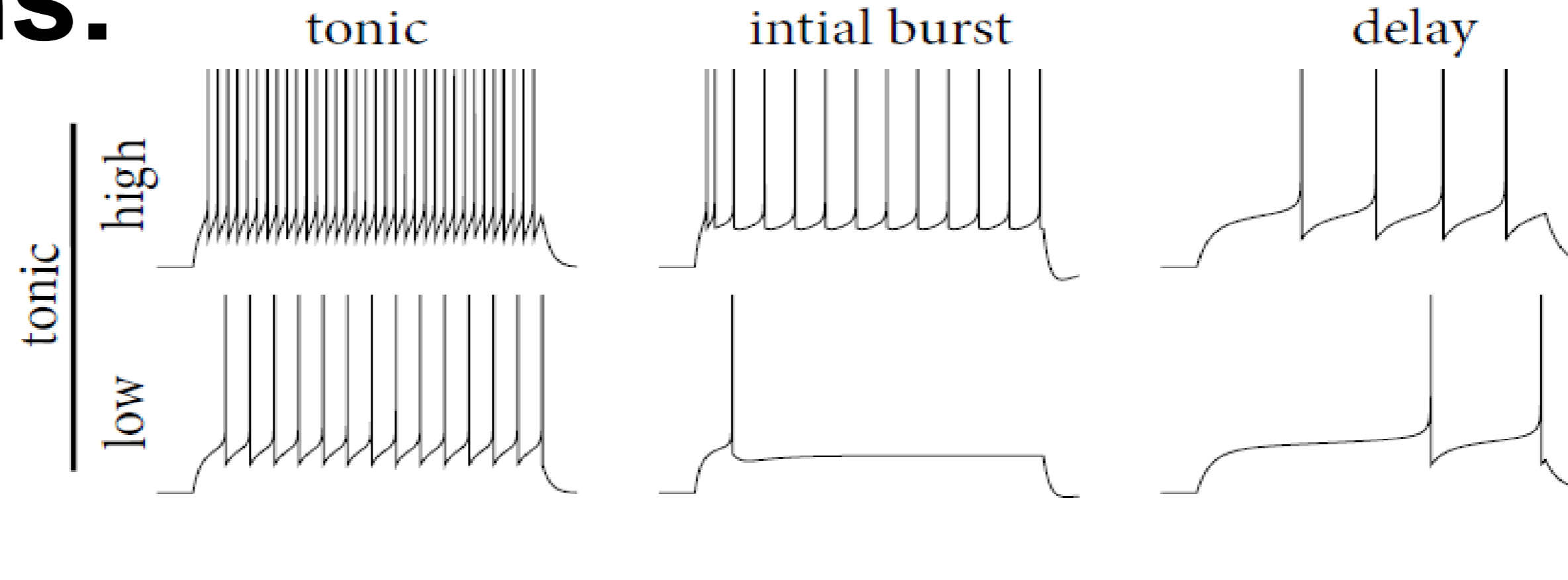


# Firing patterns:

Response to  
Step currents,  
**AdEx Model,**  
**Naud & Gerstner**

ERN

## INITIATION PATTERN



*Image:*  
*Neuronal Dynamics,*  
*Gerstner et al.*  
*Cambridge (2002)*



# Neuronal Dynamics – 9.2 Adaptive Exponential I&F

$$\tau \frac{du}{dt} = -(u - u_{rest}) + \Delta \exp\left(\frac{u - \mathcal{G}}{\Delta}\right) - R w + R I(t)$$
$$\tau_w \frac{dw}{dt} = a (u - u_{rest}) - w + b \tau_w \sum_f \delta(t - t^f)$$

**AdEx model**

**Phase plane analysis!**

Can we understand the different firing patterns?

# Neuronal Dynamics – 9.2. Adaptive Exponential I&F

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

$$\tau_w \frac{dw}{dt} = a (u - u_{rest}) - w$$

-linear + exponential  
-adaptation variable

→ Various firing patterns

# Neuronal Dynamics – Quiz 9.1. Nullclines of AdEx

$$\tau \frac{du}{dt} = -(u - u_{rest}) + \Delta \exp\left(\frac{u - \mathcal{I}}{\Delta}\right) - R w + R I(t)$$

$$\tau_w \frac{dw}{dt} = a (u - u_{rest}) - w$$

**A - What is the qualitative shape of the w-nullcline?**

- constant
- linear, slope a
- linear, slope 1
- linear + quadratic
- linear + exponential

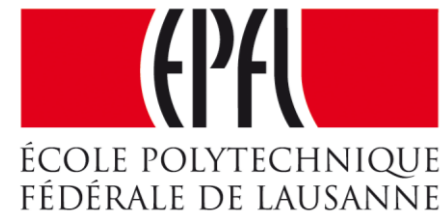
**B - What is the qualitative shape of the u-nullcline?**

- linear, slope 1
- linear, slope 1/R
- linear + quadratic
- linear w. slope 1/R+ exponential

2 minutes

Restart at 9:38

# Week 9 – part 2b : Firing Patterns



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Wulfram Gerstner

EPFL, Lausanne, Switzerland

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#### 9.6. Modeling in vitro data

- how long lasts the effect of a spike?

# AdEx model

after each spike  
 $u$  is reset to  $u_r$

$$\tau \frac{du}{dt} = -(u - u_{rest}) + \Delta \exp\left(\frac{u - \mathcal{G}}{\Delta}\right) - R_w + RI(t)$$

$$\tau_w \frac{dw}{dt} = a (u - u_{rest}) - w + b \tau_w \sum_f \delta(t - t^f)$$

after each spike  
 $w$  jumps by an amount  $b$

parameter  $a$  – slope of  $w$ -nullcline

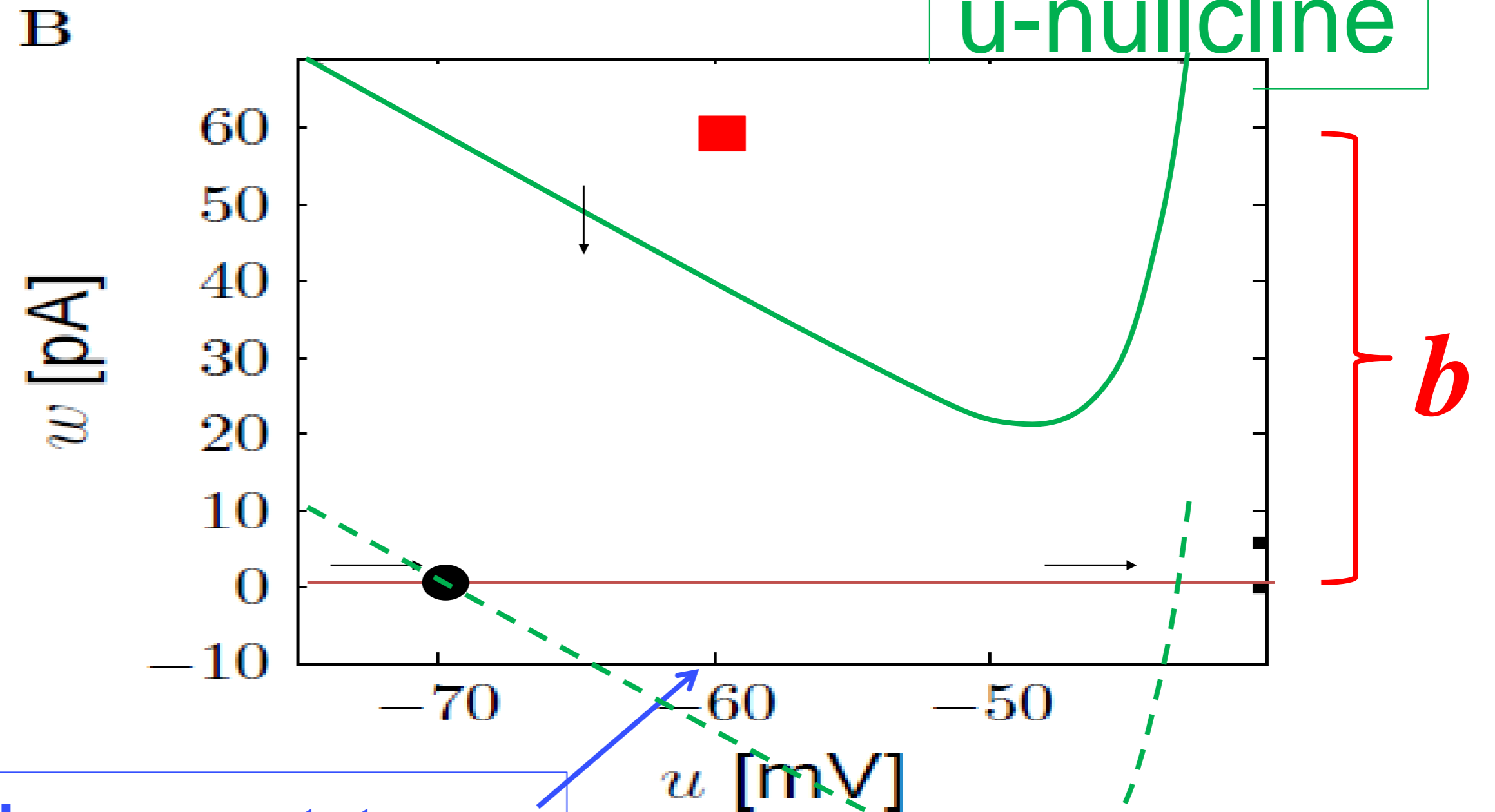
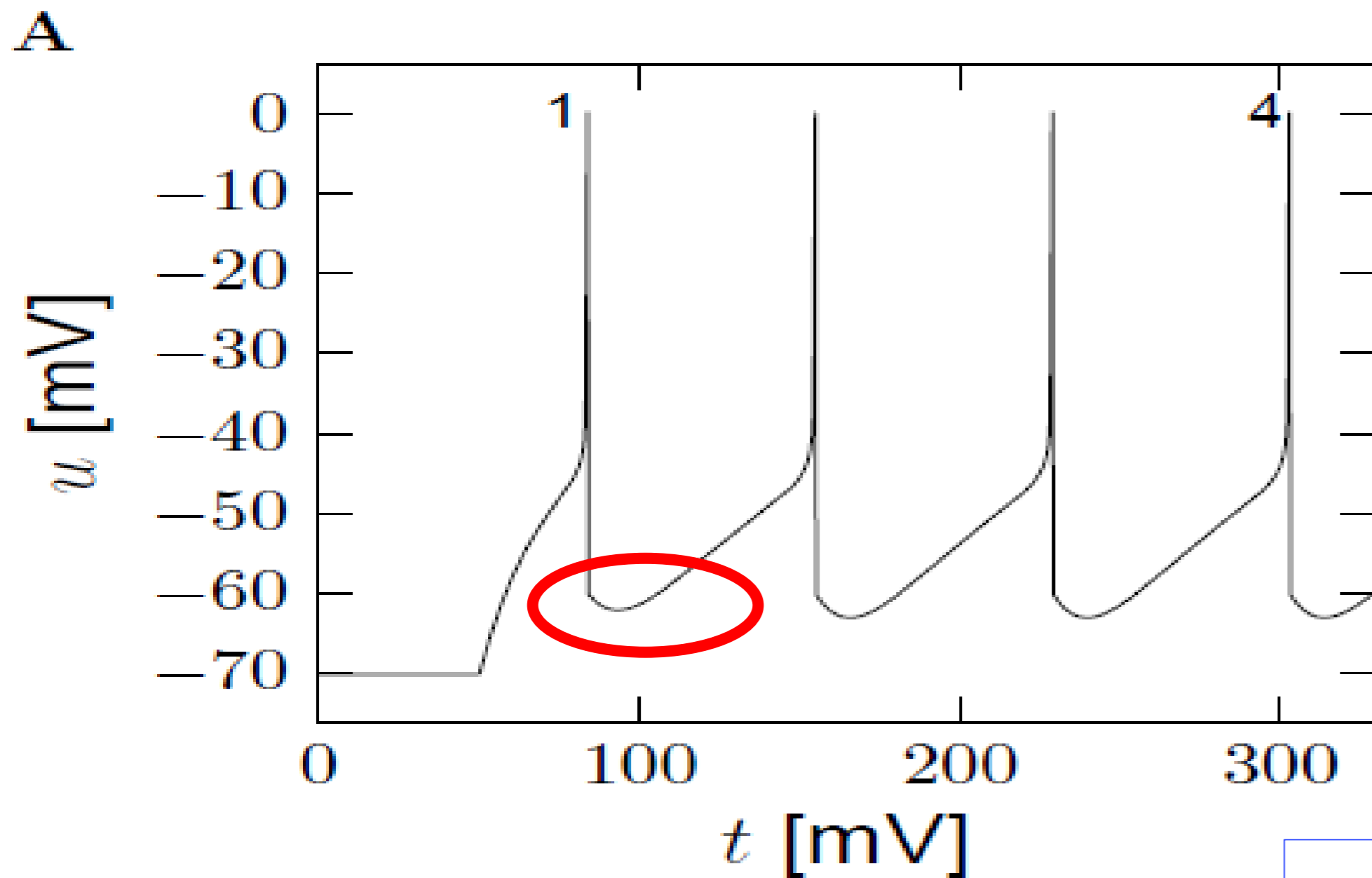
Can we understand the different firing patterns?

# AdEx model – phase plane analysis: **large $b$**

$$\tau \frac{du}{dt} = -(u - u_{rest}) + \Delta \exp\left(\frac{u - \mathcal{G}}{\Delta}\right) + w + RI(t)$$

$$\tau_w \frac{dw}{dt} = \cancel{a(u - u_{rest})} - w + b \tau_w \sum_f \delta(t - t^f)$$

**$a=0$**





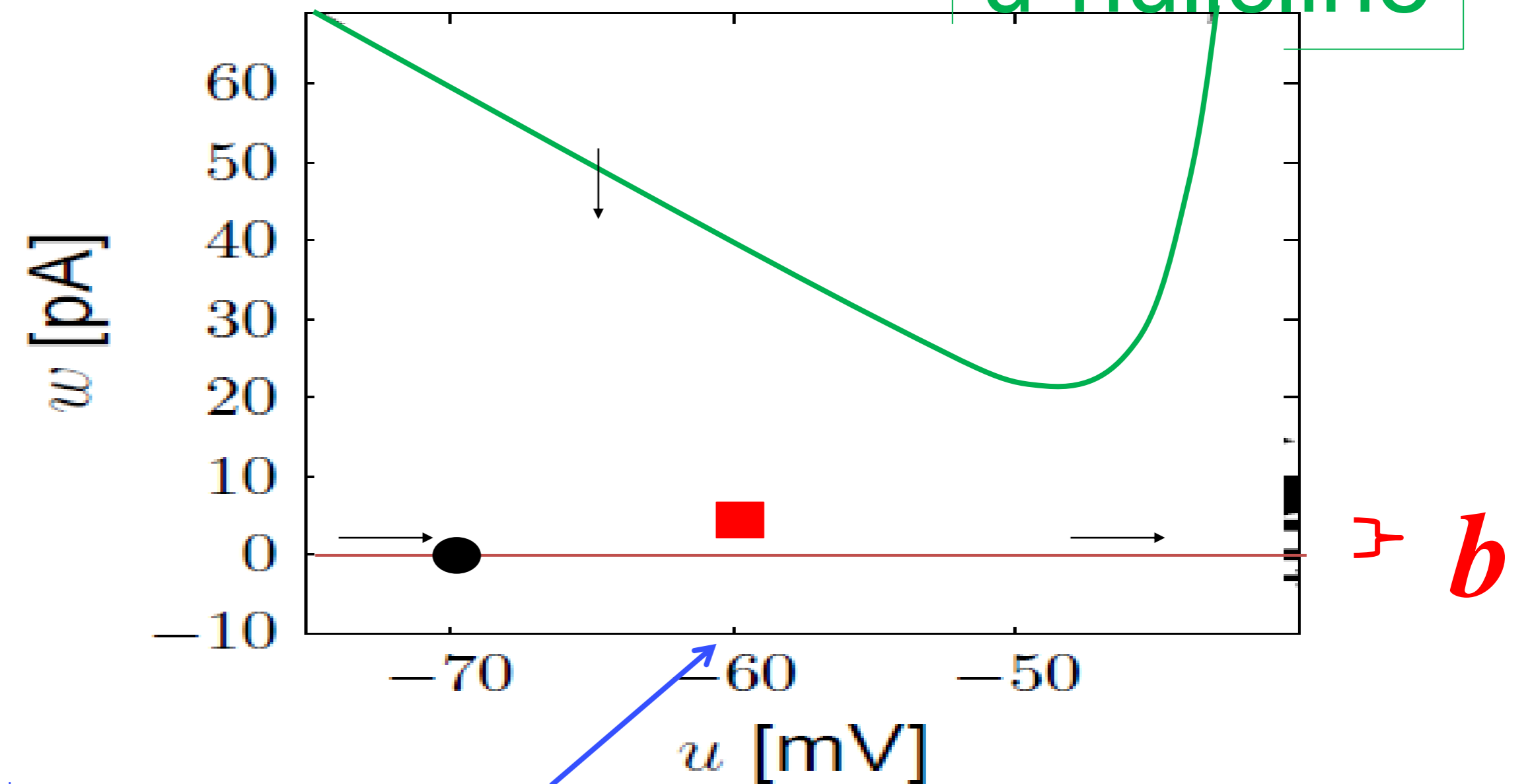
# AdEx model – phase plane analysis: **small $b$**

$$\tau \frac{du}{dt} = -(u - u_{rest}) + \Delta \exp\left(\frac{u - \mathcal{G}}{\Delta}\right) + w + RI(t)$$

$$\tau_w \frac{dw}{dt} = a (u - u_{rest}) - w + b \tau_w \sum_f \delta(t - t^f)$$

**adaptation**

D

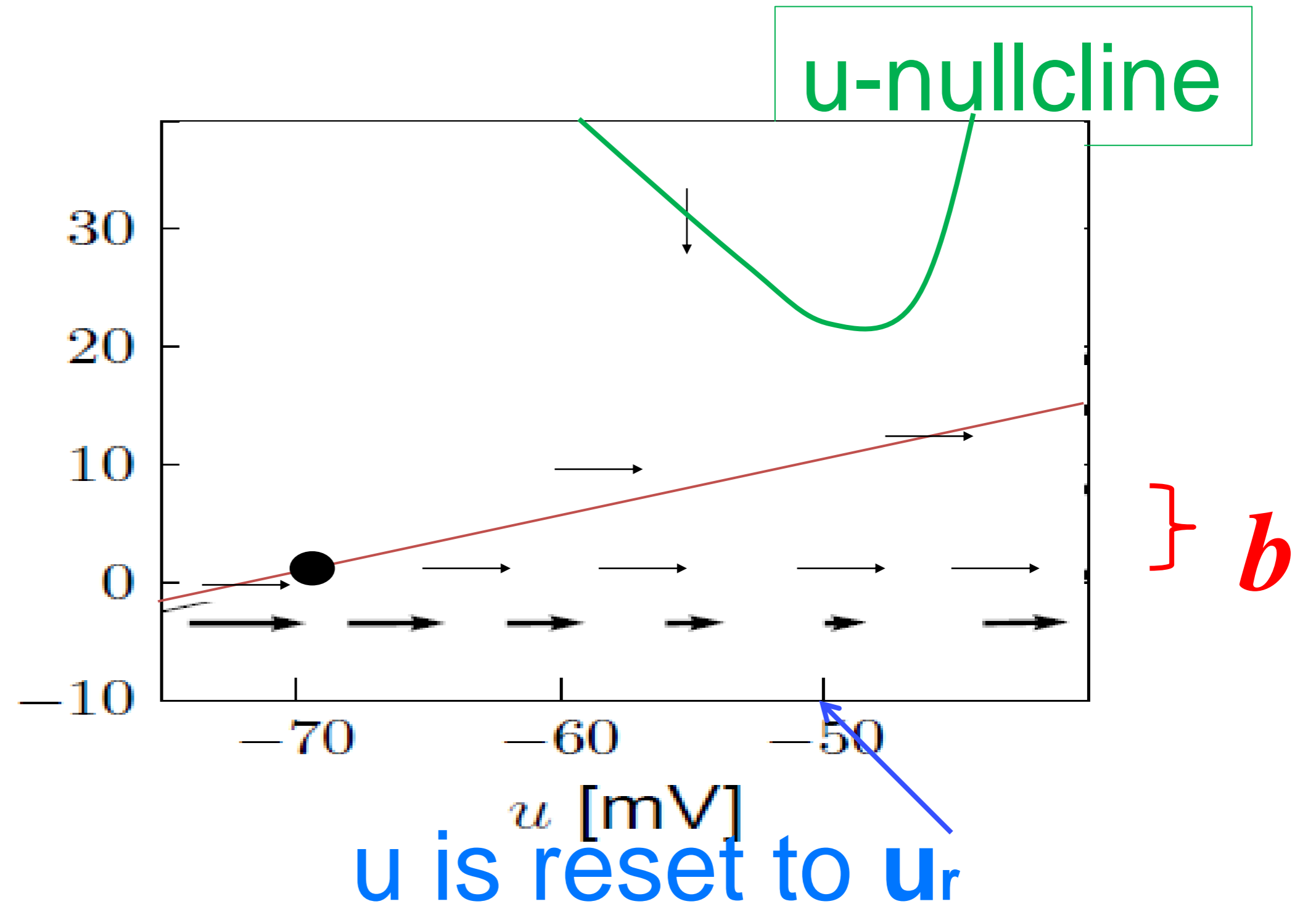


u is reset to  $u_r$

# AdEx model – phase plane analysis: $a > 0$

$$\tau \frac{du}{dt} = -(u - u_{rest}) + \Delta \exp\left(\frac{u - \mathcal{G}}{\Delta}\right) + w + RI(t)$$

$$\tau_w \frac{dw}{dt} = a(u - u_{rest}) - w + b \tau_w \sum_f \delta(t - t^f)$$



# Neuronal Dynamics – 9.2 AdEx model and firing patterns

after each spike  $u$  is reset to  $u_r$

$$\tau \frac{du}{dt} = -(u - u_{rest}) + \Delta \exp\left(\frac{u - \mathcal{I}}{\Delta}\right) - Rw + RI(t)$$

$$\tau_w \frac{dw}{dt} = a (u - u_{rest}) - w + b \tau_w \sum_f \delta(t - t^f)$$

after each spike

$w$  jumps by an amount  $b$

parameter  $a$  – slope of  $w$  nullcline

**Firing patterns arise from different parameters!**

*See Naud et al. (2008), see also Izhikheich (2003)*

# 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  $u = u_r$*

Best choice of  $f$ : linear + exponential

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

**BUT: Limitations – need to add**

- ✓ -Adaptation on slower time scales
- ✓ -Possibility for a diversity of firing patterns
- Increased threshold  $\mathcal{I}$  after each spike
- Noise

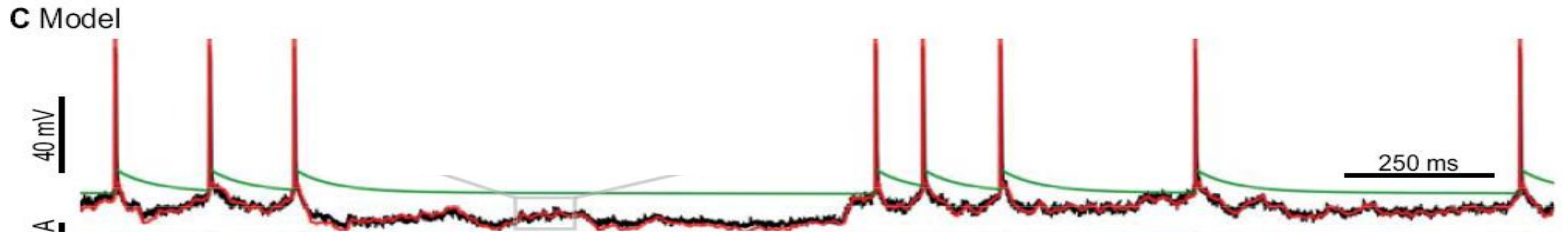
# Neuronal Dynamics – 9.2 AdEx with dynamic threshold

Add dynamic threshold:

$$\tau \frac{du}{dt} = -(u - u_{rest}) + \Delta \exp\left(\frac{u - \mathcal{I}}{\Delta}\right) - R \sum_k w_k + RI(t)$$

Threshold increases after each spike

$$\mathcal{I} = \theta_0 + \sum_f \theta_1 (t - t^f)$$



# Neuronal Dynamics – 9.2 Generalized Integrate-and-fire

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

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

**add**

- ✓ -Adaptation variables
- ✓ -Possibility for firing patterns
- ✓ -Dynamic threshold  $\mathcal{I}$
- Noise



# Neuronal Dynamics – Quiz 9.2. Nullclines for constant input

$$\tau \frac{du}{dt} = -(u - u_{rest}) + \Delta \exp\left(\frac{u - \mathcal{G}}{\Delta}\right) + w + RI(t)$$

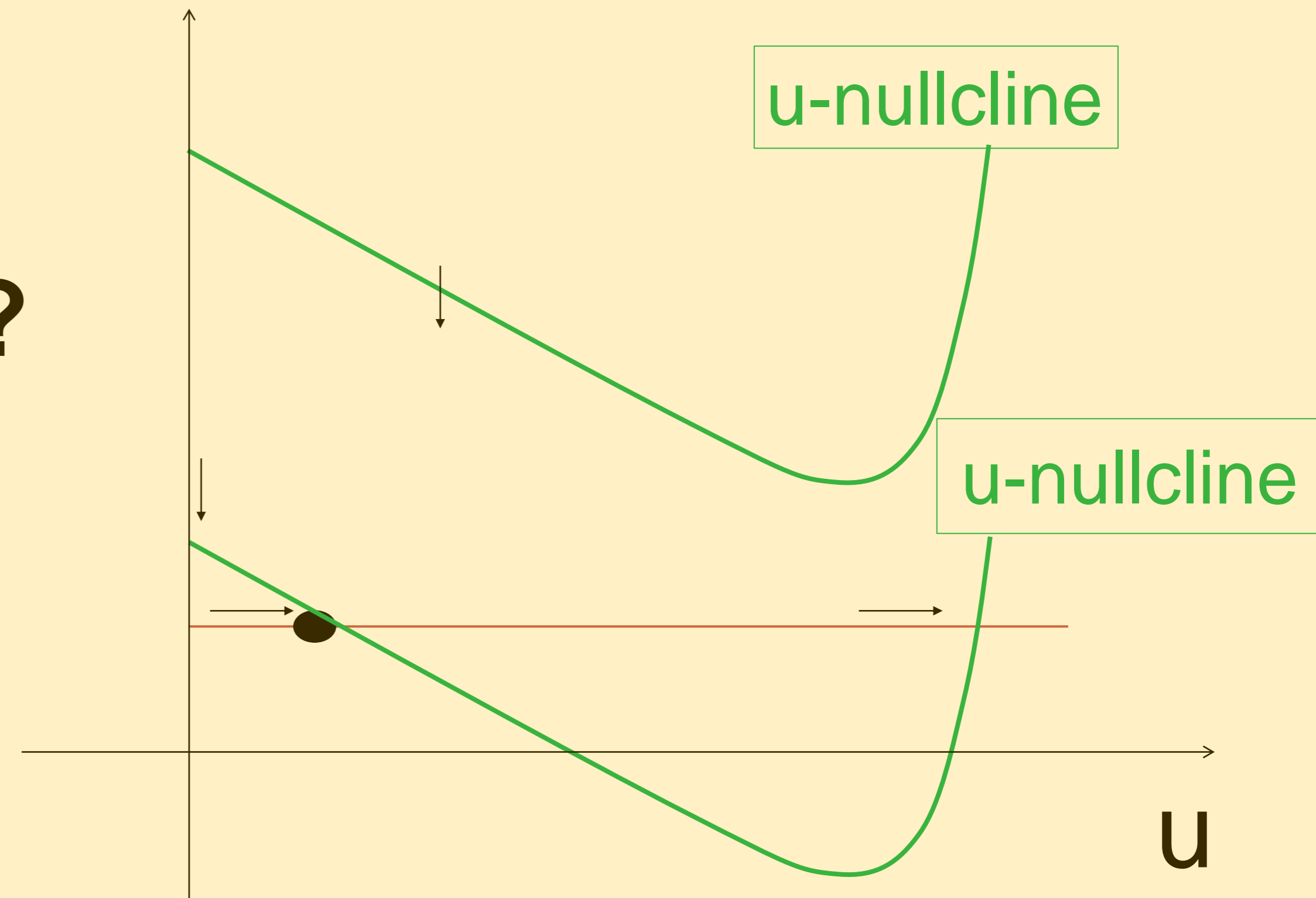
$$\tau_w \frac{dw}{dt} = a(u - u_{rest}) - w + b \tau_w \sum_f \delta(t - t^f)$$

~~$a(u - u_{rest})$~~   
 $a=0$

Only during reset

**What happens if input switches from  $I=0$  to  $I>0$ ?**

- u-nullcline moves horizontally
- u-nullcline moves vertically
- w-nullcline moves horizontally
- w-nullcline moves vertically



# Week 9 – part 3: Spike Response Model (SRM)



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- Adding noise to the SRM

#### 9.5 Parameter Estimation

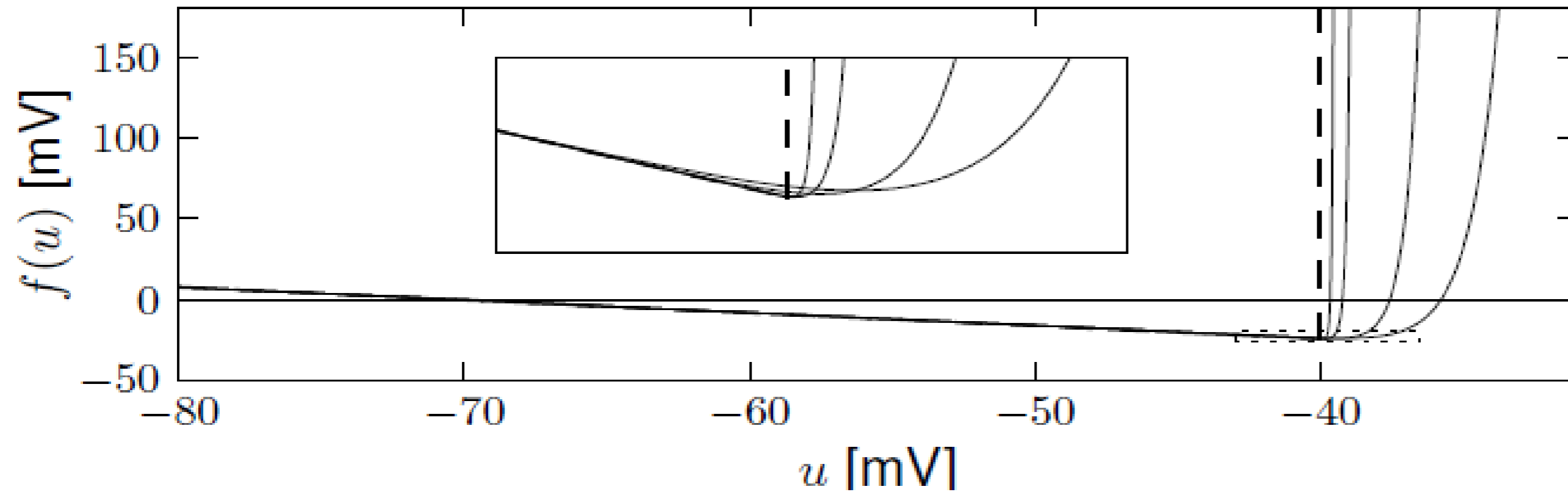
- Quadratic and convex optimization

#### 9.6. Modeling in vitro data

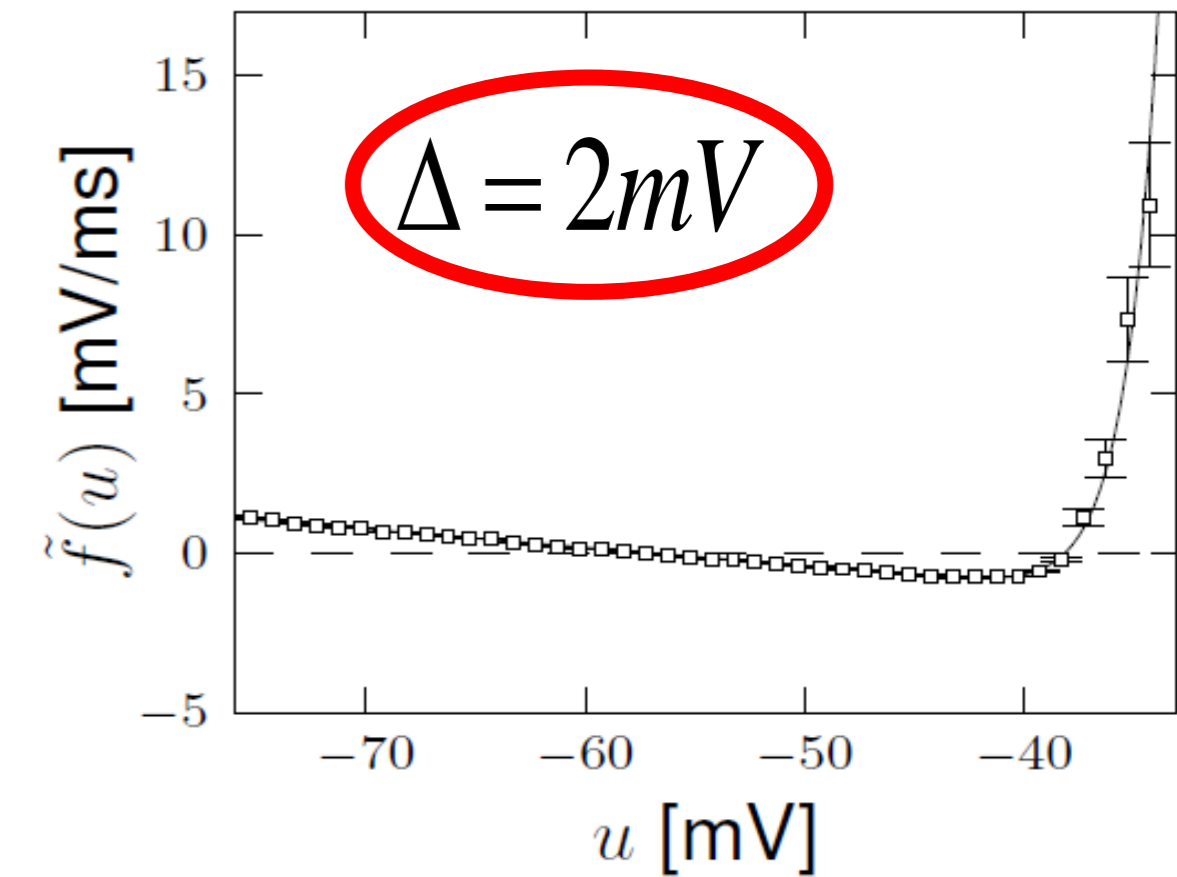
- how long lasts the effect of a spike?

# Exponential versus Leaky Integrate-and-Fire

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



*Badel et al (2008)*  
A



$$\tau \frac{du}{dt} = -(u - u_{rest}) + RI(t)$$

Reset if  $u = \mathcal{I}$

**Leaky Integrate-and-Fire**

# Neuronal Dynamics – 9.3 Adaptive leaky integrate-and-fire

$$\tau \frac{du}{dt} = -(u - u_{rest}) - R \sum_k w_k + RI(t)$$

$$\tau_k \frac{dw_k}{dt} = a_k (u - u_{rest}) - w_k + b_k \tau_k \sum_f \delta(t - t^f)$$

SPIKE AND  
RESET

after each spike

$w_k$  jumps by an amount  $b_k$

If  $u = \mathcal{G}(t)$  then reset to  $u = u_r$

Dynamic threshold

# Neuronal Dynamics – 9.3 Adaptive leaky I&F and SRM

$$\tau \frac{du}{dt} = -(u - u_{rest}) - R \sum_k w_k + RI(t)$$

$$\tau_k \frac{dw_k}{dt} = a_k (u - u_{rest}) - w_k + b_k \tau_k \sum_f \delta(t - t^f)$$

Adaptive  
leaky I&F

**Linear equation → can be integrated!**

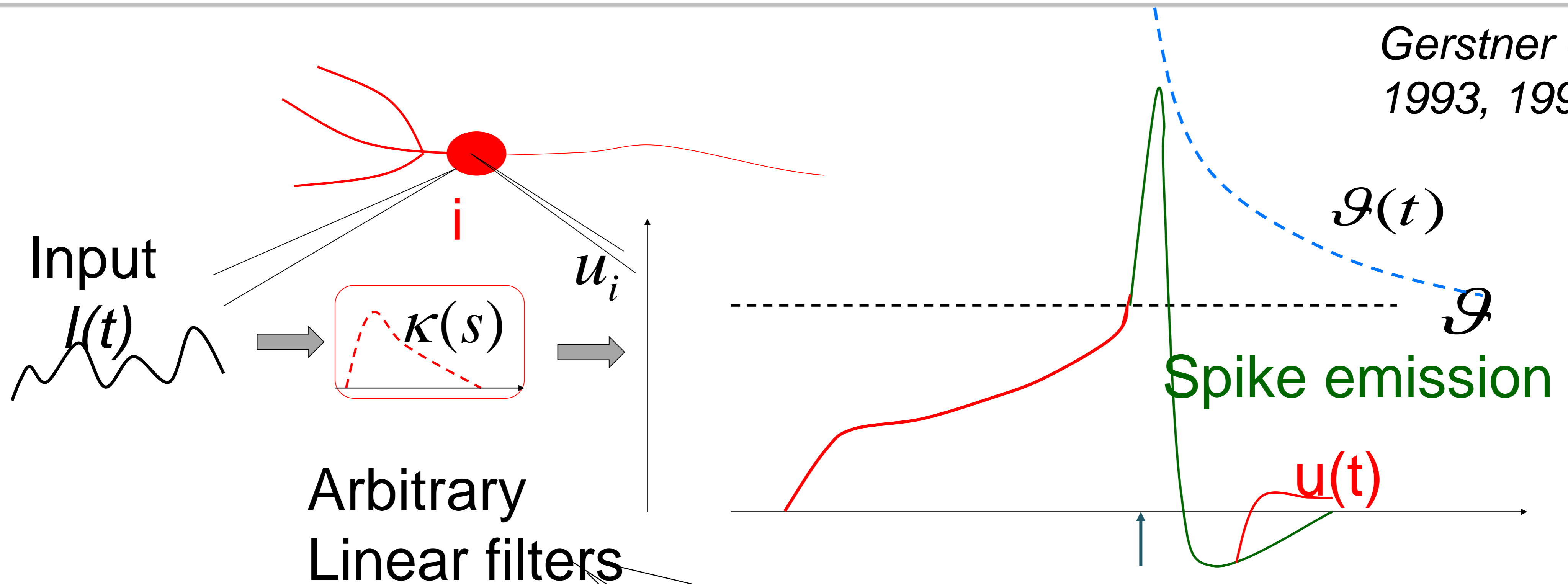
$$u(t) = \sum_f \eta (t - t^f) + \int_0^\infty ds \kappa(s) I(t - s)$$

$$\mathcal{G}(t) = \theta_0 + \sum_f \theta_1 (t - t^f)$$

**Spike Response Model (SRM)**  
Gerstner et al. (1996)

# Neuronal Dynamics – 9.3 Spike Response Model (SRM)

Gerstner et al.,  
1993, 1996



potential

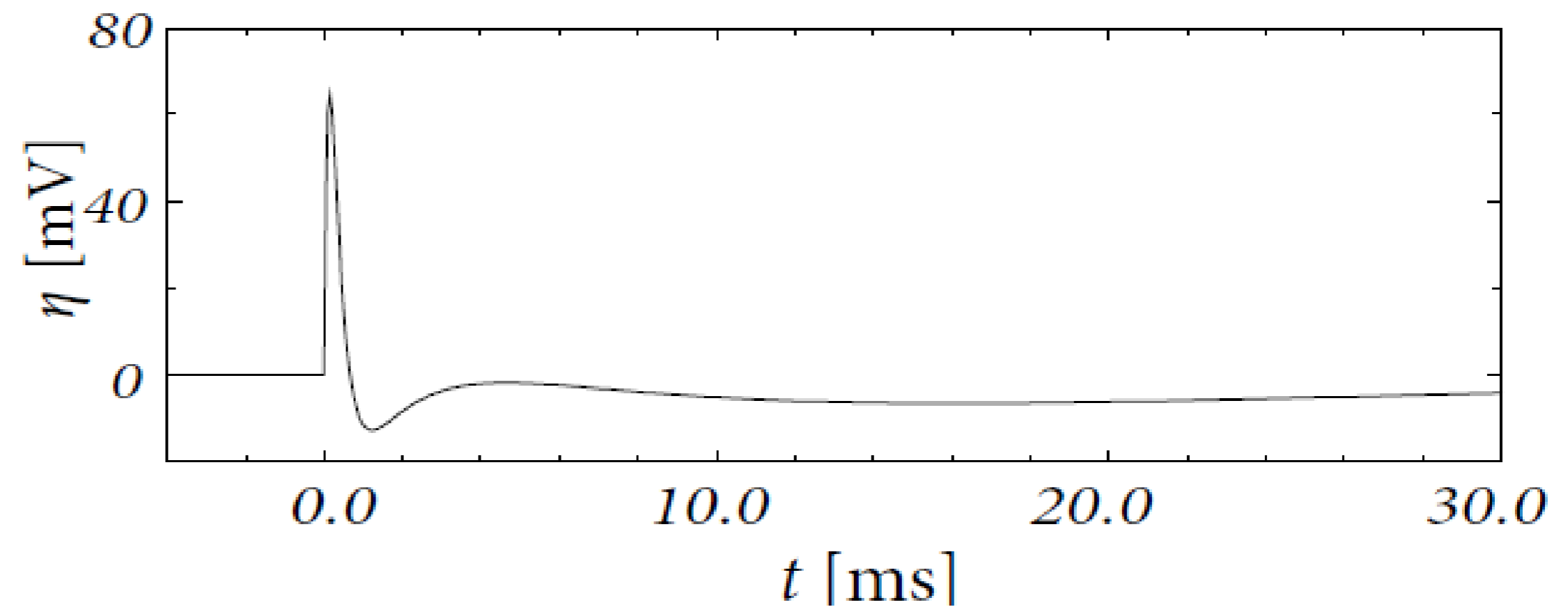
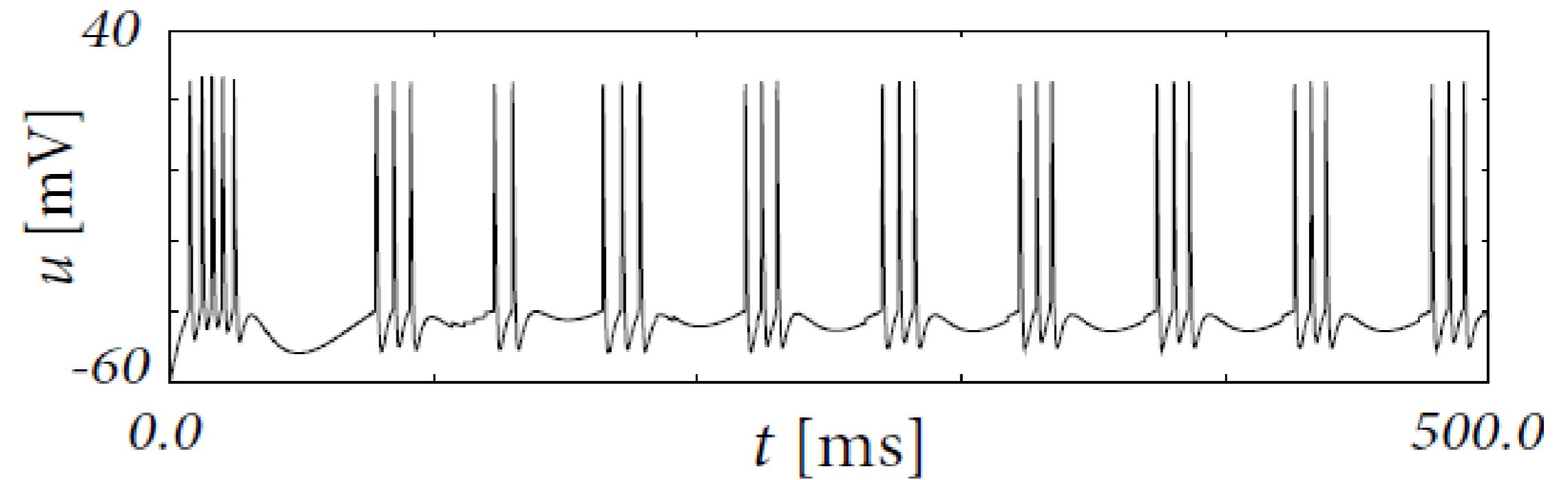
$$u(t) = \sum_{t'} \eta(t-t') + \int_0^\infty \kappa(s) I(t-s) ds + u_{rest}$$

threshold

$$\mathcal{G}(t) = \theta_0 + \sum_{t'} \theta_1(t-t')$$

# Neuronal Dynamics – 9.3 Bursting in the SRM

SRM with appropriate  $\eta$   
leads to bursting



$$u(t) = \sum_f \eta(t - t^f) + \int_0^\infty ds \kappa(s) I(t - s) + u_{rest}$$
$$u(t) = \int_0^\infty ds \eta(s) S(t - s) + \int_0^\infty ds \kappa(s) I(t - s) + u_{rest}$$



# Quiz 9.3: from adaptive IF to SRM

$$\tau \frac{du}{dt} = -(u - u_{rest}) - w + RI(t)$$

If  $u = \mathcal{I}$  then reset to  $u = u_r$

$$\tau_w \frac{dw}{dt} = -w + b \tau_w \sum_f \delta(t - t^f)$$

Next lecture  
at 9:57

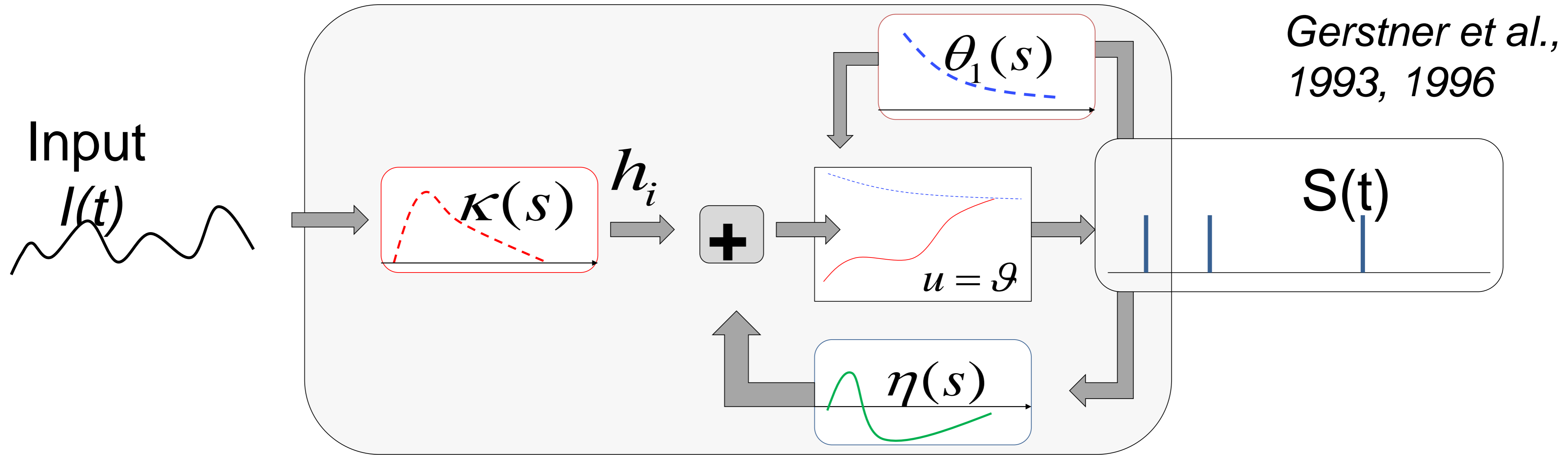
Integrate the above system of two differential equations so as to rewrite the equations as

**potential**  $u(t) = \int_0^{\infty} \underline{\eta(s)} S(t-s) ds + \int_0^{\infty} \underline{\varepsilon(s)} I(t-s) ds + u_{rest}$

**A – what is  $\underline{\eta(s)}$  ?** (i)  $x(s) = \frac{R}{\tau} \exp(-\frac{s}{\tau})$  (ii)  $x(s) = \frac{R}{\tau_w} \exp(-\frac{s}{\tau_w})$

**B – what is  $\underline{\varepsilon(s)}$  ?** (iii)  $x(s) = C[\exp(-\frac{s}{\tau}) - \exp(-\frac{s}{\tau_w})]$  (iv) **Combi of (i) + (iii)**

# Neuronal Dynamics – 9.3 Spike Response Model (SRM)



potential

$$u(t) = \sum_{t'} \eta(t-t') + \int_0^\infty \kappa(s) I(t-s) ds + u_{rest}$$

threshold

$$\mathcal{G}(t) = \theta_0 + \sum_{t'} \theta_1(t-t')$$

firing if

$$u(t) = \mathcal{G}(t)$$

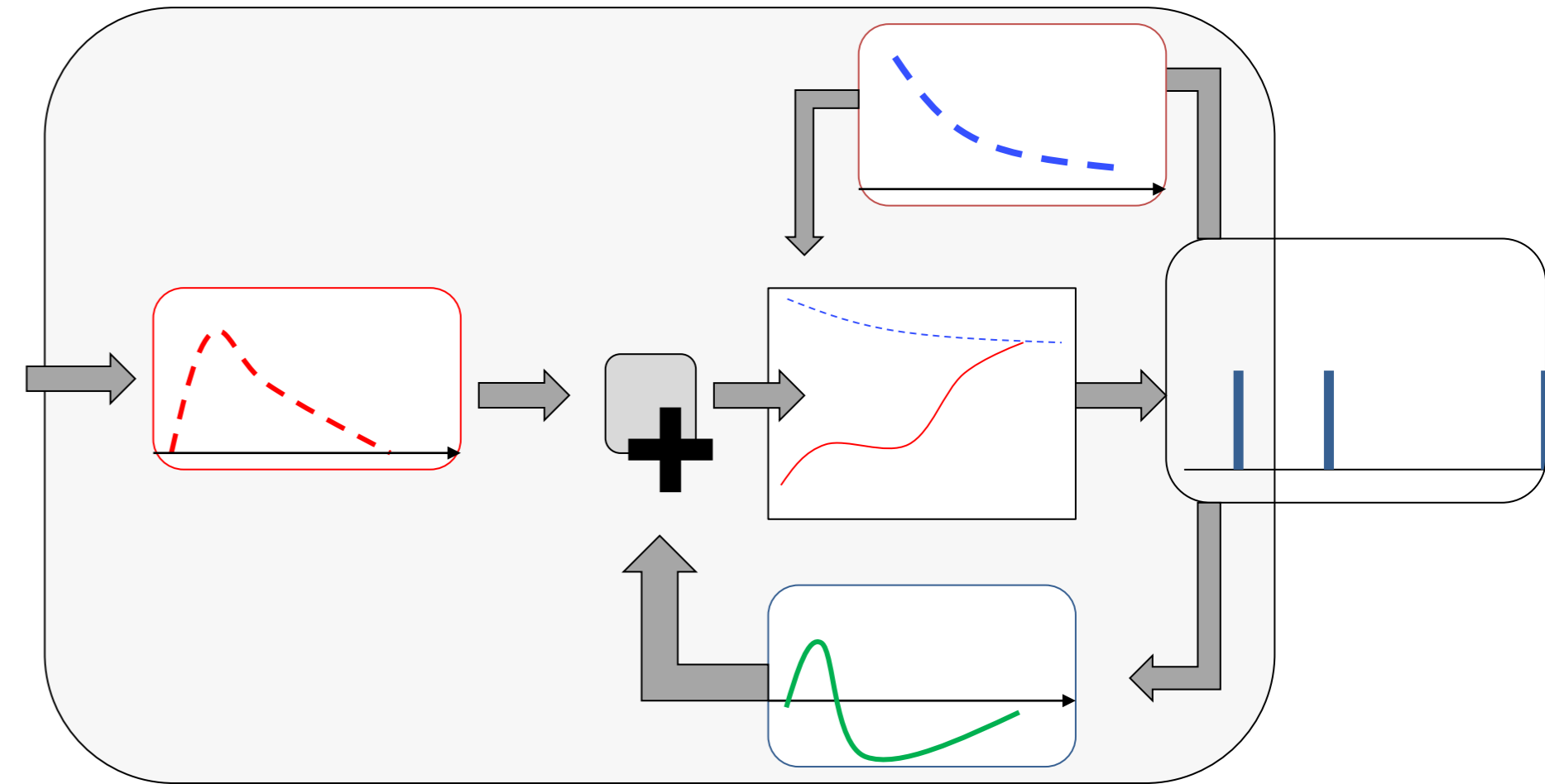
# Neuronal Dynamics – 9.3 Spike Response Model (SRM)

potential

$$u(t) = \sum_{t'} \underline{\eta(t-t')} + \int_0^\infty \underline{\kappa(s)} I(t-s) ds + u_{rest}$$

threshold

$$\mathcal{G}(t) = \theta_0 + \sum_{t'} \underline{\theta_1(t-t')}$$



Linear filters for

- input
- threshold
- refractoriness

# Week 9 – part 4: Generalized Linear Model (GLM)



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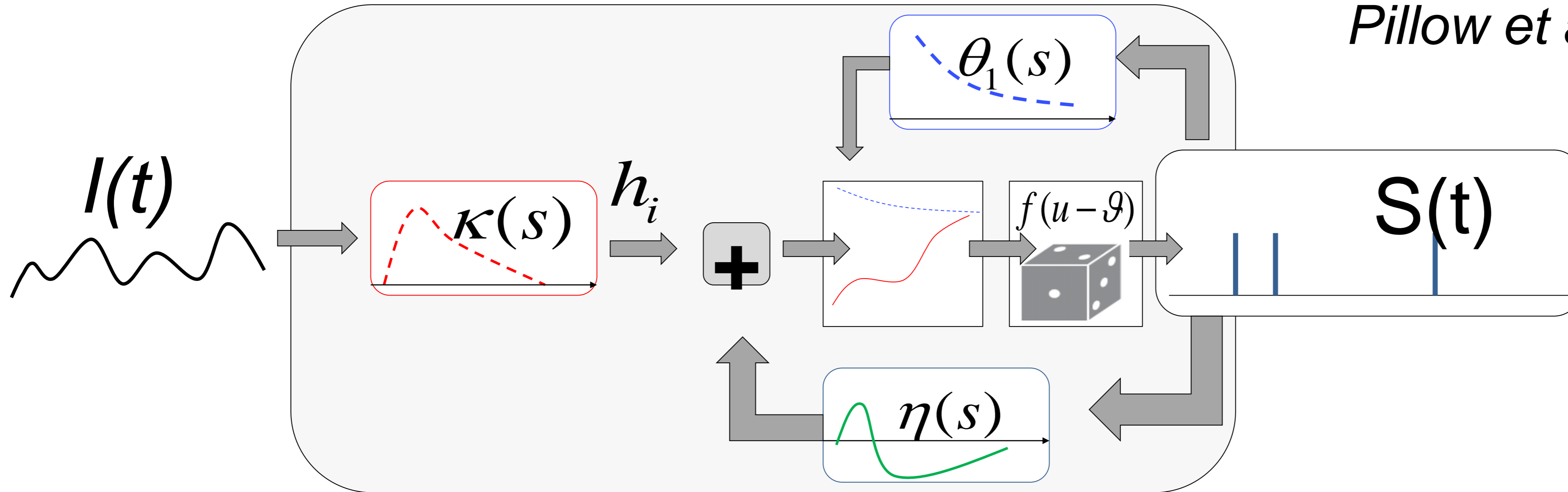
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- how long lasts the effect of a spike?

# Spike Response Model (SRM)

## Generalized Linear Model GLM

*Gerstner et al.,  
1992, 2000*  
*Truccolo et al., 2005*  
*Pillow et al. 2008*



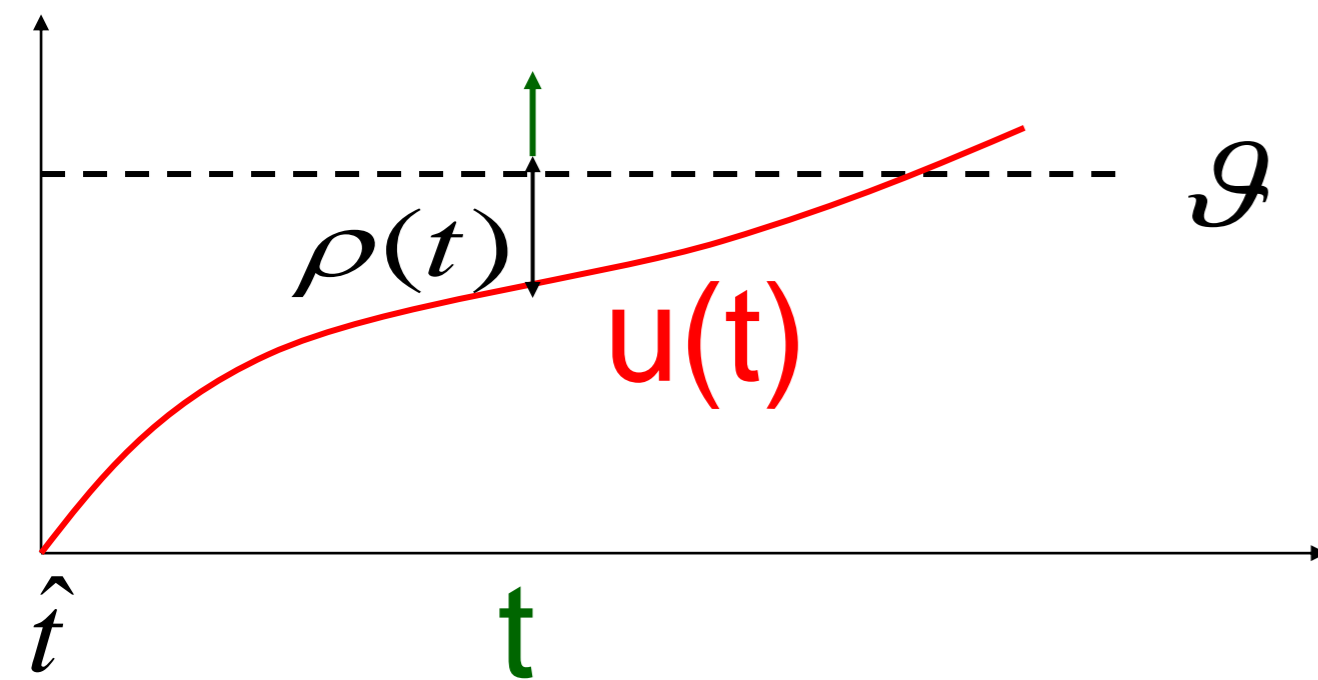
**potential**  $u(t) = \int \underline{\eta(s)} S(t-s) ds + \int_0^\infty \underline{\kappa(s)} I(t-s) ds + u_{rest}$

**threshold**  $\vartheta(t) = \theta_0 + \int \underline{\theta_1(s)} S(t-s) ds$

firing intensity  $\rho(t) = f(u(t) - \vartheta(t))$

# Neuronal Dynamics – review from week 8: Escape noise

escape process

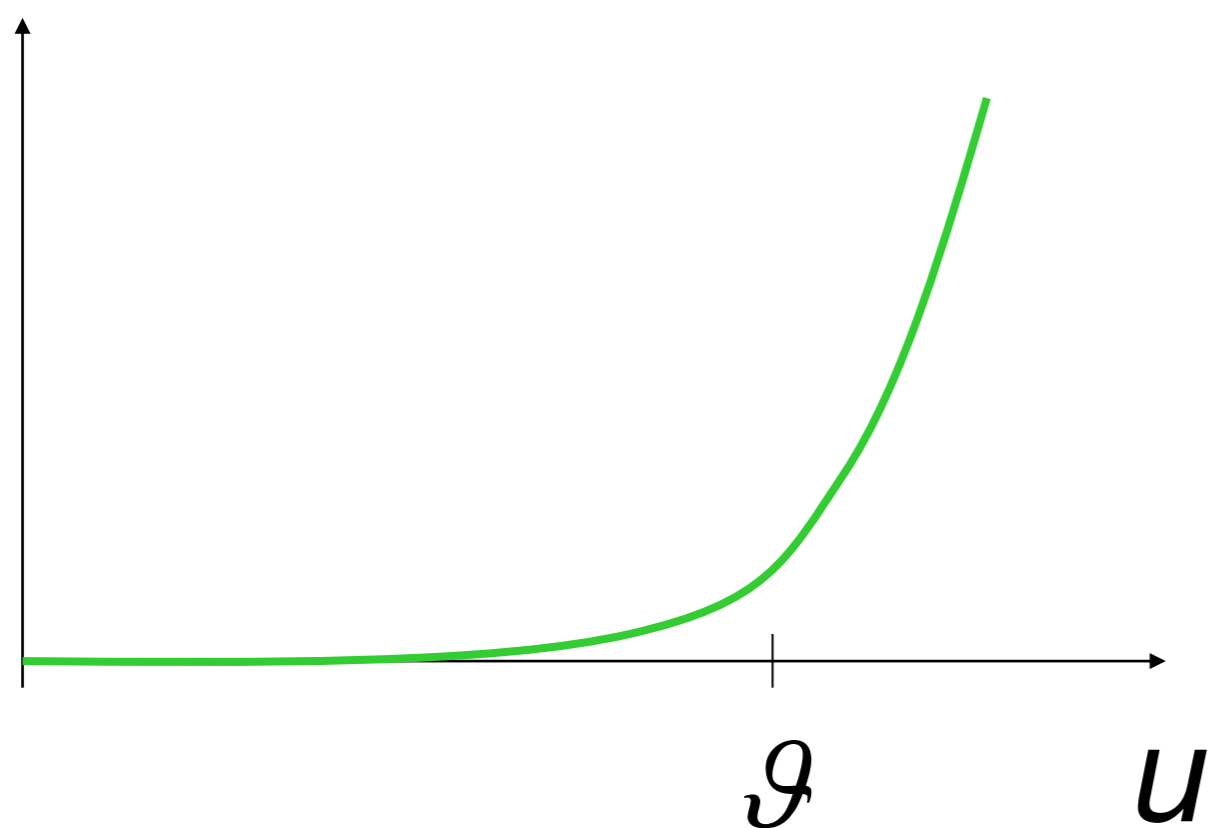


escape rate

$$\rho(t) = \frac{1}{\Delta} \exp\left(\frac{u(t) - \mathcal{G}}{\Delta}\right)$$

escape rate

$$\rho(t) = f(u(t) - \mathcal{G})$$



Example: leaky integrate-and-fire model

$$\tau \cdot \frac{d}{dt} u = -(u - u_{rest}) + RI(t)$$

$$\text{if spike at } t^f \Rightarrow u(t^f + \delta) = u_r$$

# Exerc. 1: leaky and non-leaky IF with escape rates

$$\tau \frac{du}{dt} = -(u - u_{rest}) + RI(t)$$

$$\text{reset to } u_{rest} = u_r = 0$$

$$\frac{du}{dt} = \frac{R}{\tau} I(t) = \frac{1}{C} I(t)$$

$$\text{reset to } u_r = 0$$

**Integrate for constant input (repetitive firing)**

**Next lecture  
at 10:40**

Calculate

- potential

$$u(t - \hat{t})$$

- hazard

$$\rho(t - \hat{t}) = \beta \cdot [u(t - \hat{t}) - \mathcal{G}]_+$$

- survivor function

$$S(t - \hat{t})$$

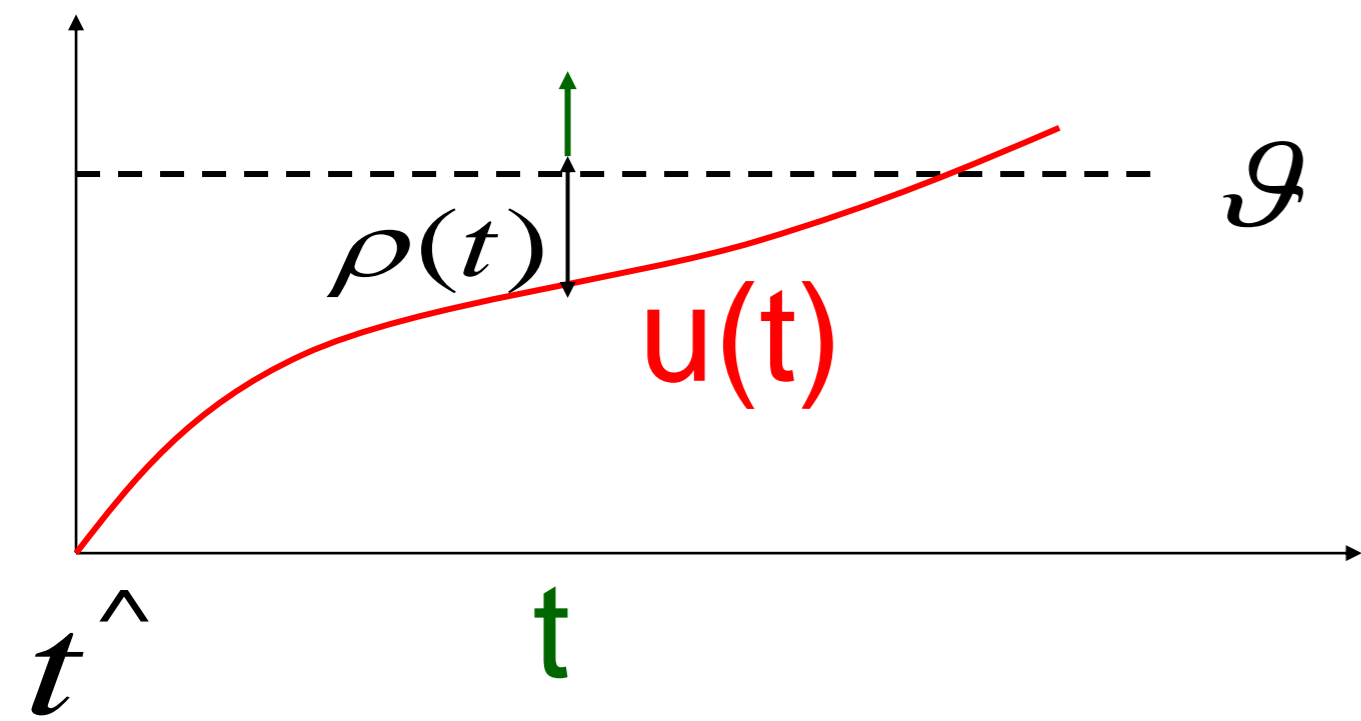
- interval distrib.

$$P_0(t - \hat{t})$$



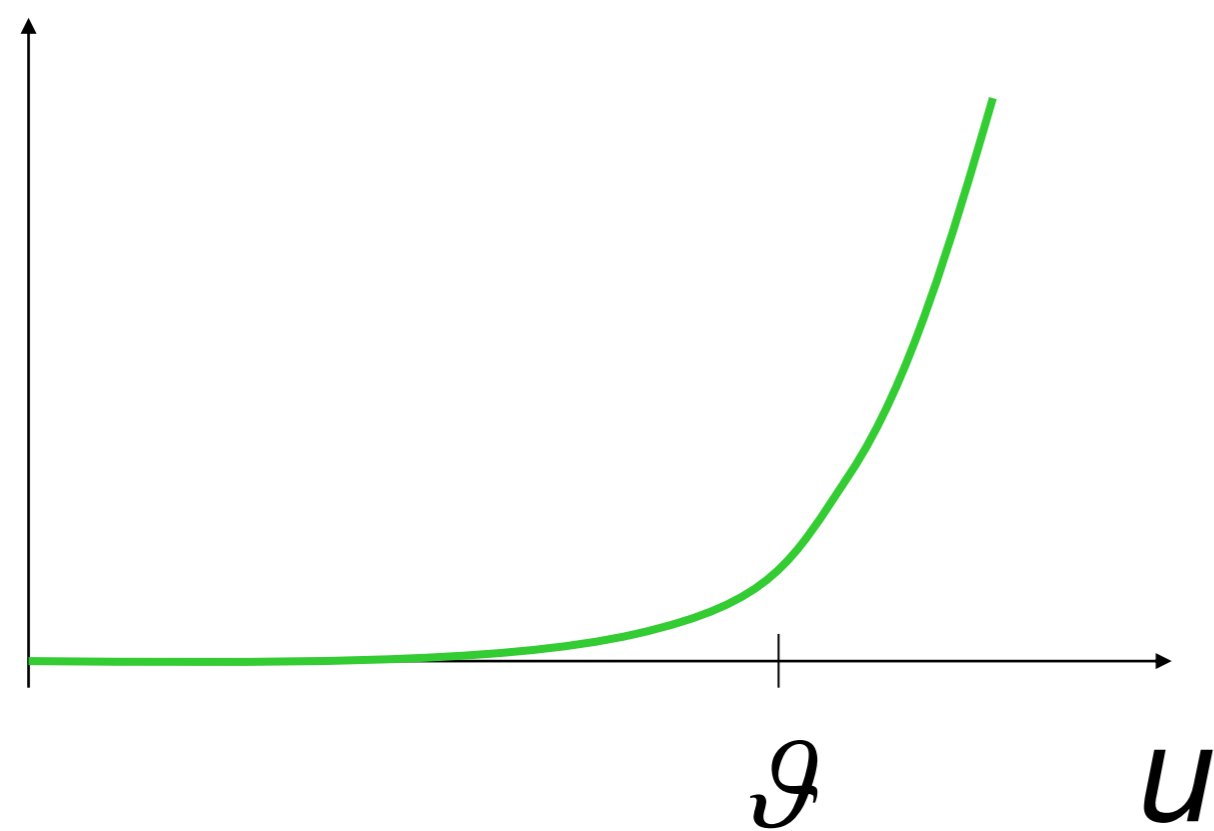
# Neuronal Dynamics – review from week 8: Escape noise

escape process



escape rate

$$\rho(t) = f(u(t) - \mathcal{G}(t))$$



Survivor function

$$\frac{d}{dt} S_I(t|\hat{t}) = -\rho(t) S_I(t|\hat{t})$$

$$S_I(t|\hat{t}) = \exp\left(-\int_{\hat{t}}^t \rho(t') dt'\right)$$


Interval distribution

$$P_I(t|\hat{t}) = \underbrace{\rho(t)}_{\text{escape rate}} \cdot \underbrace{\exp\left(-\int_{\hat{t}}^t \rho(t') dt'\right)}_{\text{Survivor function}}$$

Good choice

$$\rho(t) = f(u(t) - \mathcal{G}(t)) = \rho_0 \exp\left[\frac{u(t) - \mathcal{G}(t)}{\Delta u}\right]$$

# Neuronal Dynamics – 9.4 Likelihood of a spike train in GLMs

$$S(t) = \sum_f \delta(t - t^f)$$


→ Blackboard

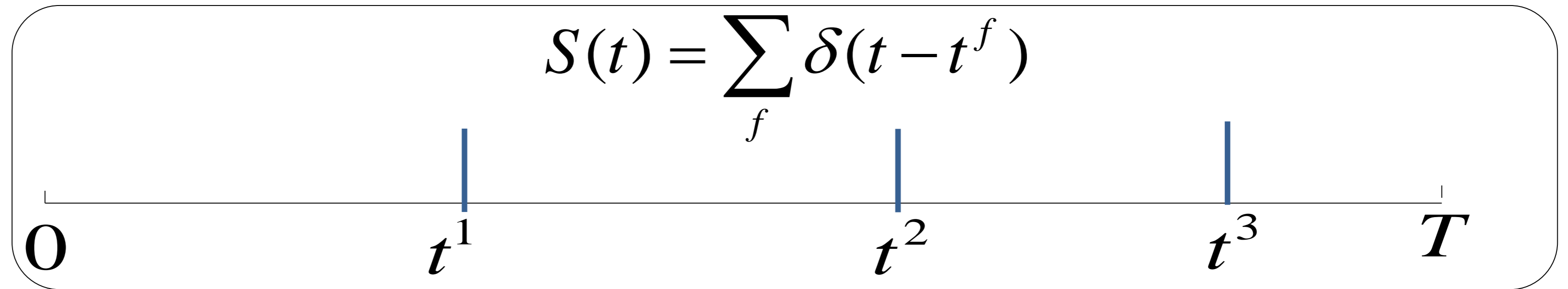
$t^1, t^2, \dots, t^N$

**Measured spike train with spike times**

Likelihood  $L$  that this spike train  
could have been generated by model?

$$L(t^1, \dots, t^N) = \exp\left(-\int_0^{t^1} \rho(t') dt'\right) \rho(t^1) \cdot \exp\left(-\int_{t^1}^{t^2} \rho(t') dt'\right) \dots$$

# Neuronal Dynamics – 9.4 Likelihood of a spike train

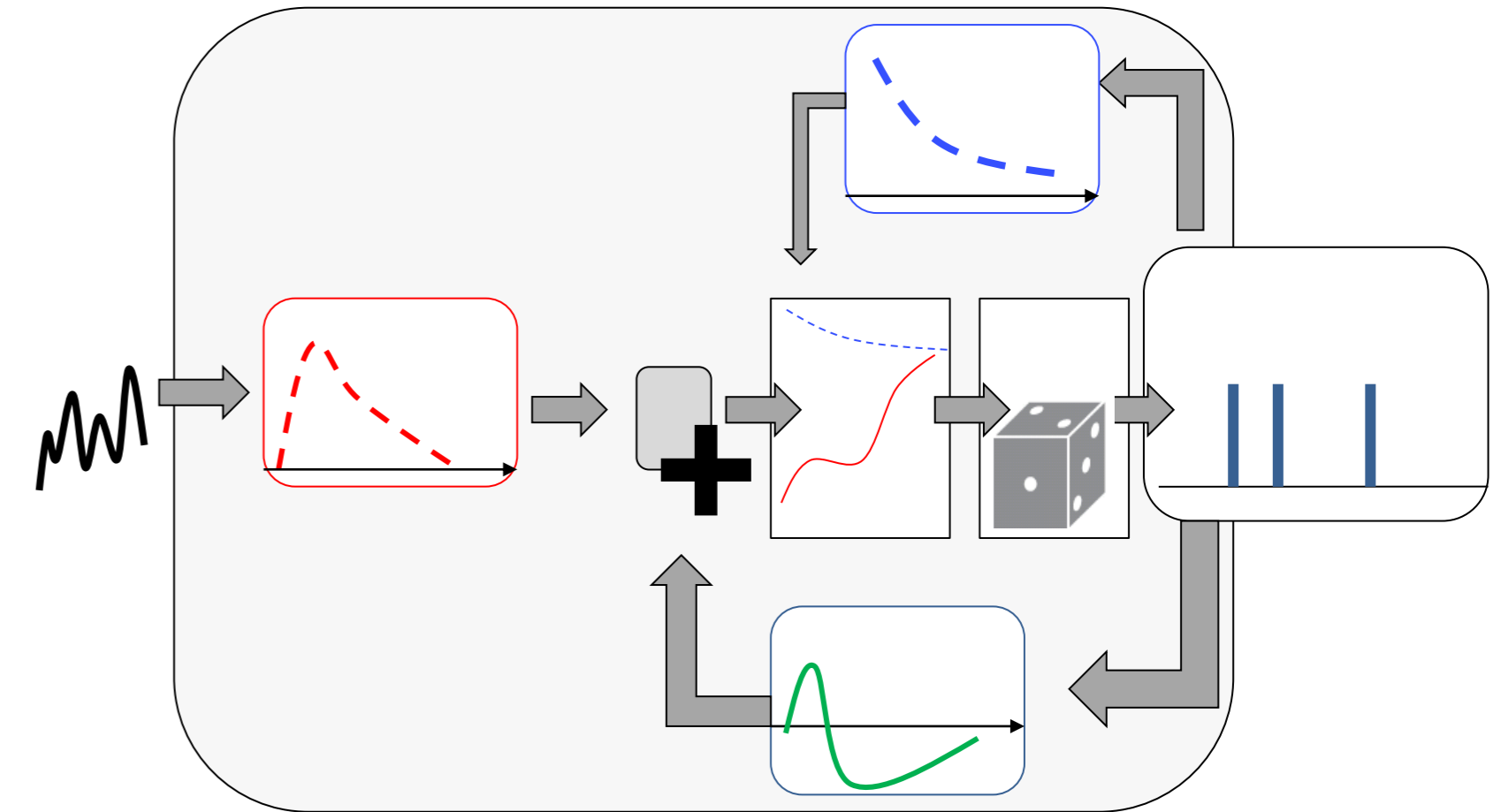


$$L(t^1, \dots, t^N) = \exp\left(-\int_0^{t^1} \rho(t') dt'\right) \rho(t^1) \cdot \exp\left(-\int_{t^1}^{t^2} \rho(t') dt'\right) \rho(t^2) \dots \exp\left(-\int_{t^N}^T \rho(t') dt'\right)$$

$$L(t^1, \dots, t^N) = \exp\left(-\int_0^T \rho(t') dt'\right) \prod_f \rho(t^f)$$

$$\log L(t^1, \dots, t^N) = -\int_0^T \rho(t') dt' + \sum_f \log \rho(t^f)$$

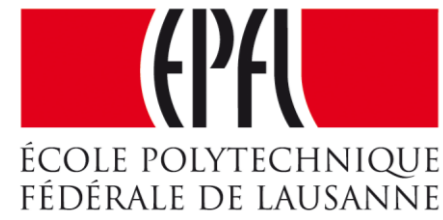
# Neuronal Dynamics – 9.4 SRM with escape noise = GLM



- linear filters
- escape rate
- likelihood of observed spike train

→ parameter optimization of neuron model

# Week 9 – part 5: Parameter Estimation



## Biological Modeling of Neural Networks:

### Week 9 – Optimizing Neuron Models For Coding and Decoding

Wulfram Gerstner

EPFL, Lausanne, Switzerland

#### ✓ 9.1 What is a good neuron model?

- Models and data

#### ✓ 9.2 AdEx model

- Firing patterns and adaptation

#### ✓ 9.3 Spike Response Model (SRM)

- Integral formulation

#### ✓ 9.4 Generalized Linear Model

- Adding noise to the SRM

#### 9.5 Parameter Estimation

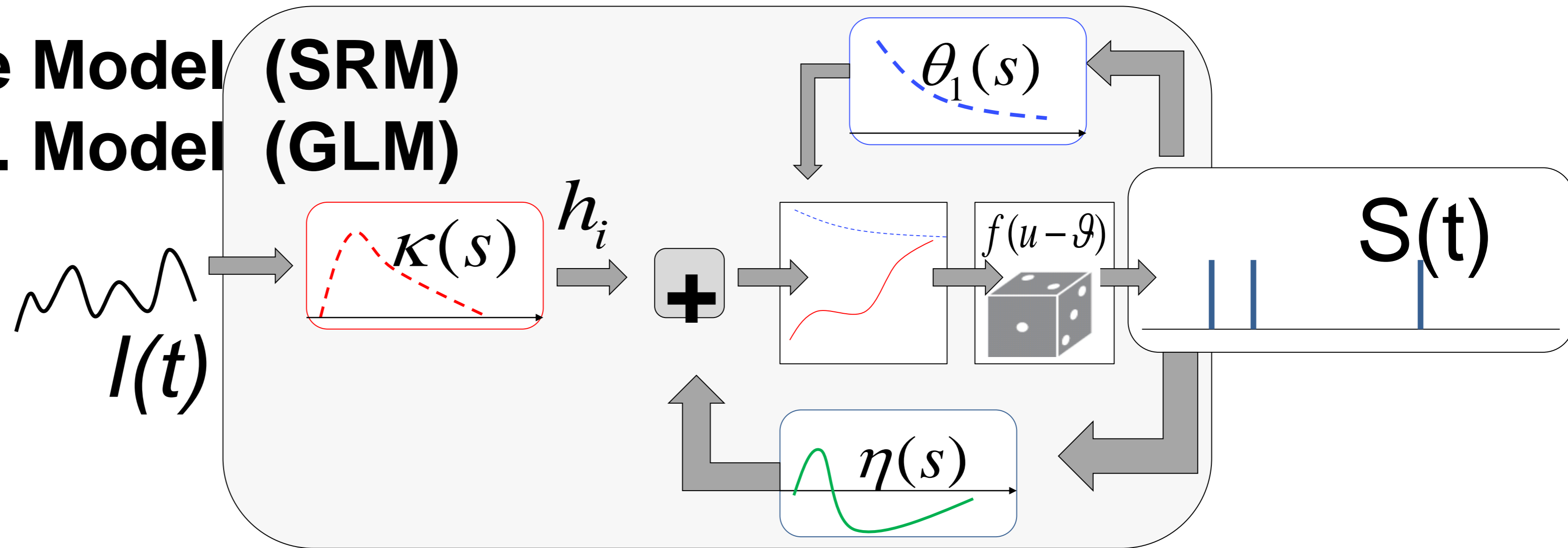
- Quadratic and convex optimization

#### 9.6. Modeling in vitro data

- how long lasts the effect of a spike?

# Neuronal Dynamics – 9.5 Parameter estimation: voltage

**Spike Response Model (SRM)**  
**Generalized Lin. Model (GLM)**



**Subthreshold potential**

$$u(t) = \int \underbrace{\eta(s)}_{\text{known spike train}} S(t-s) ds + \int_0^\infty \underbrace{\kappa(s)}_{\text{known input}} I(t-s) ds + u_{rest}$$

known spike train

known input

**Linear filters/linear in parameters**

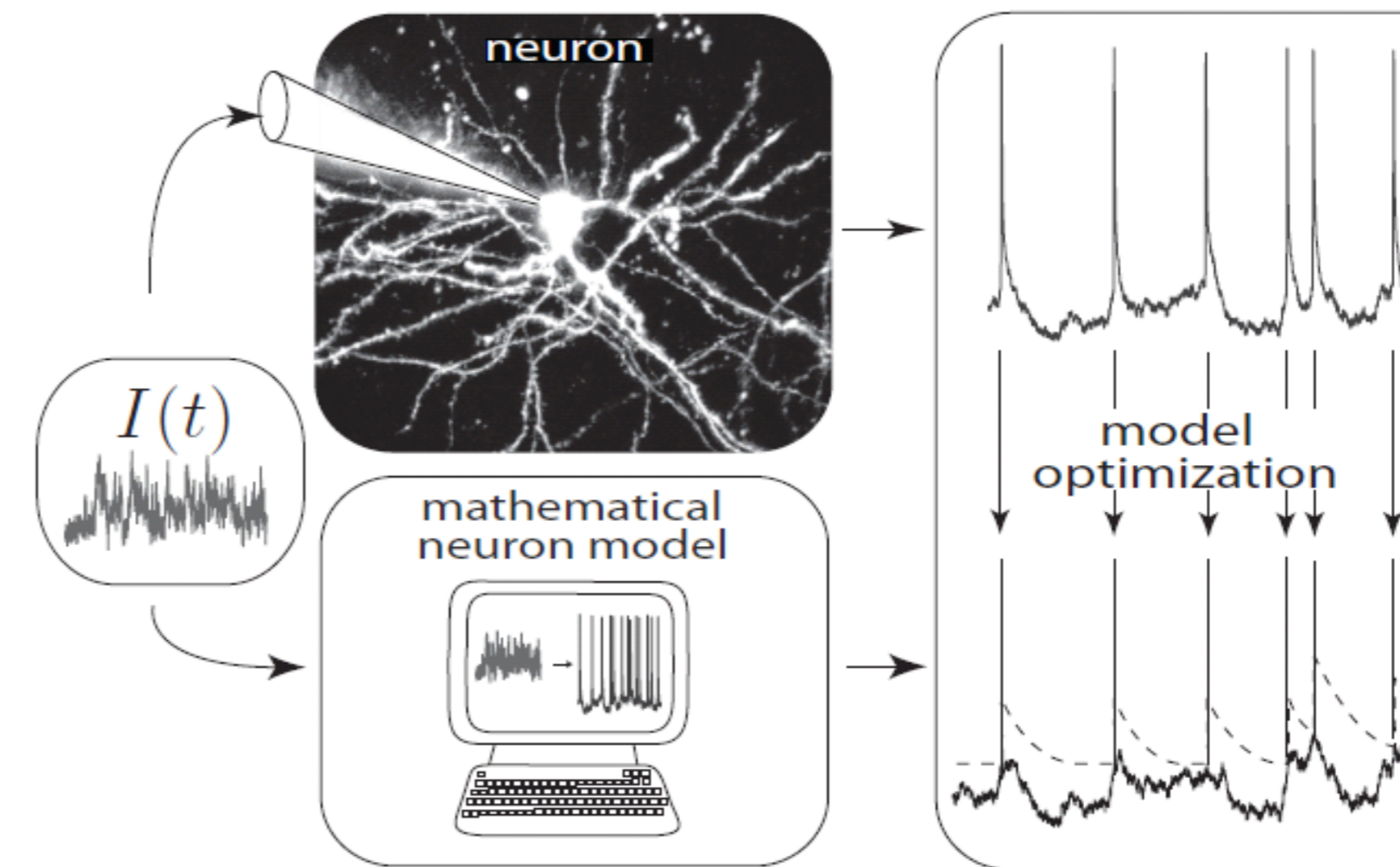
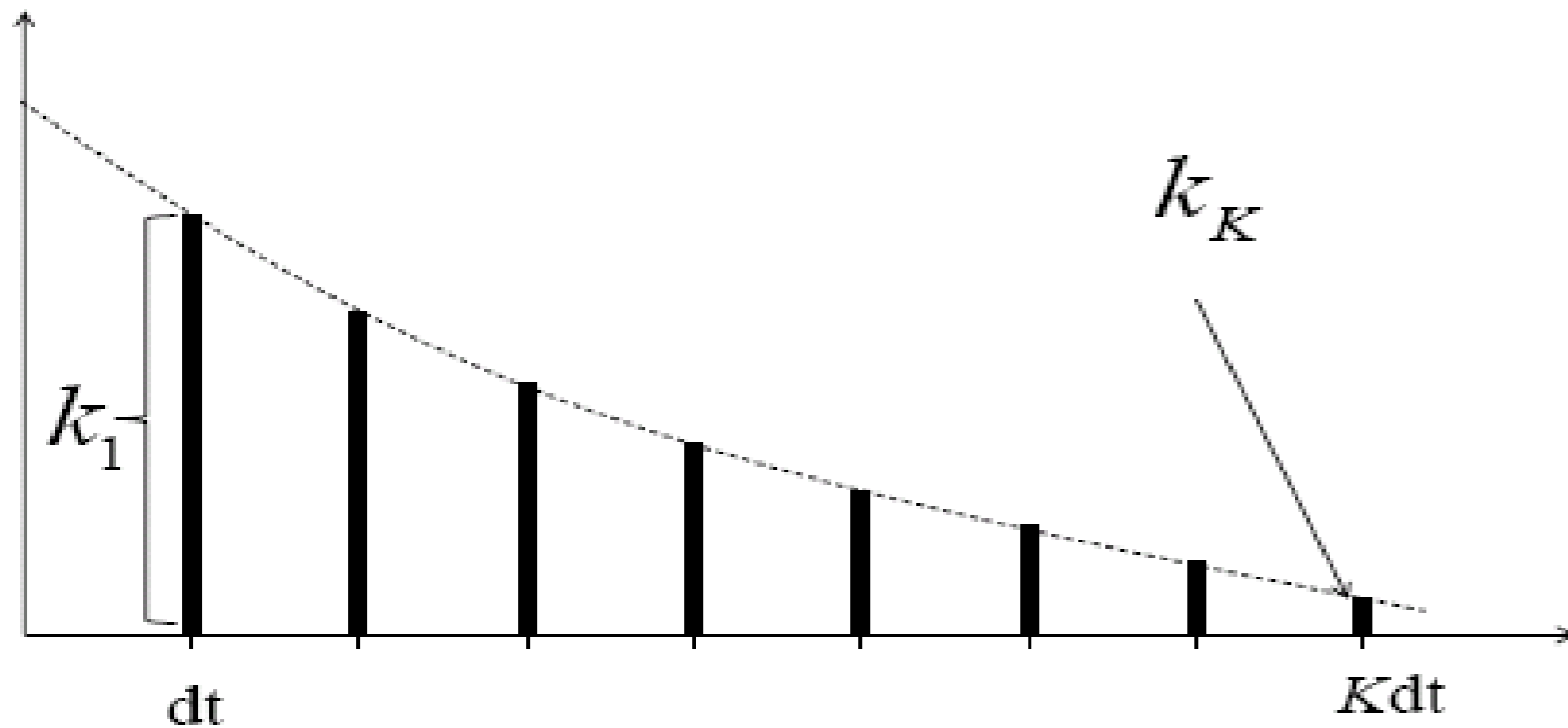
# Neuronal Dynamics – 9.5 Parameter estimation: voltage

Linear in parameters = linear fit = quadratic problem

$$u(t) = \int_0^{\infty} \kappa(s) I(t-s) ds + u_{rest}$$

$$u(t_n) = \sum k_k I_{n-k} + u_{rest}$$

comparison model-data



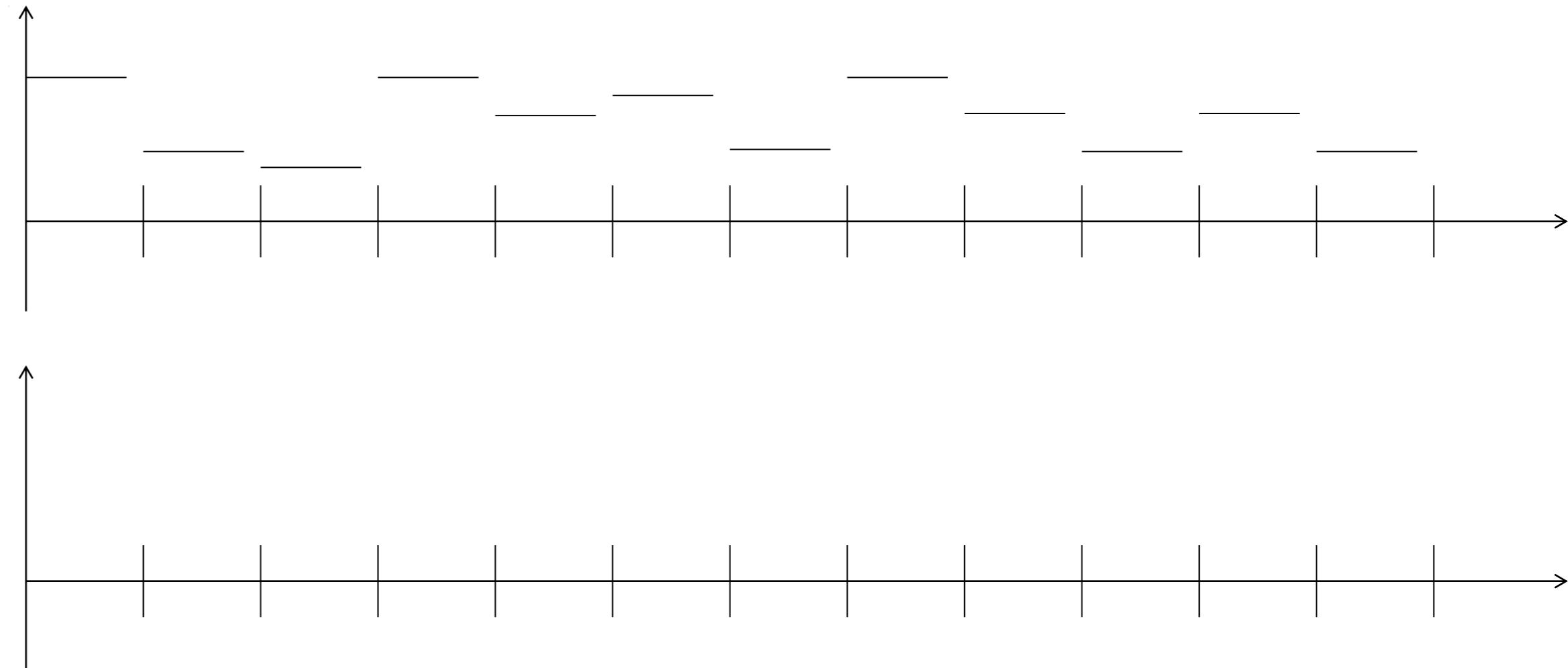
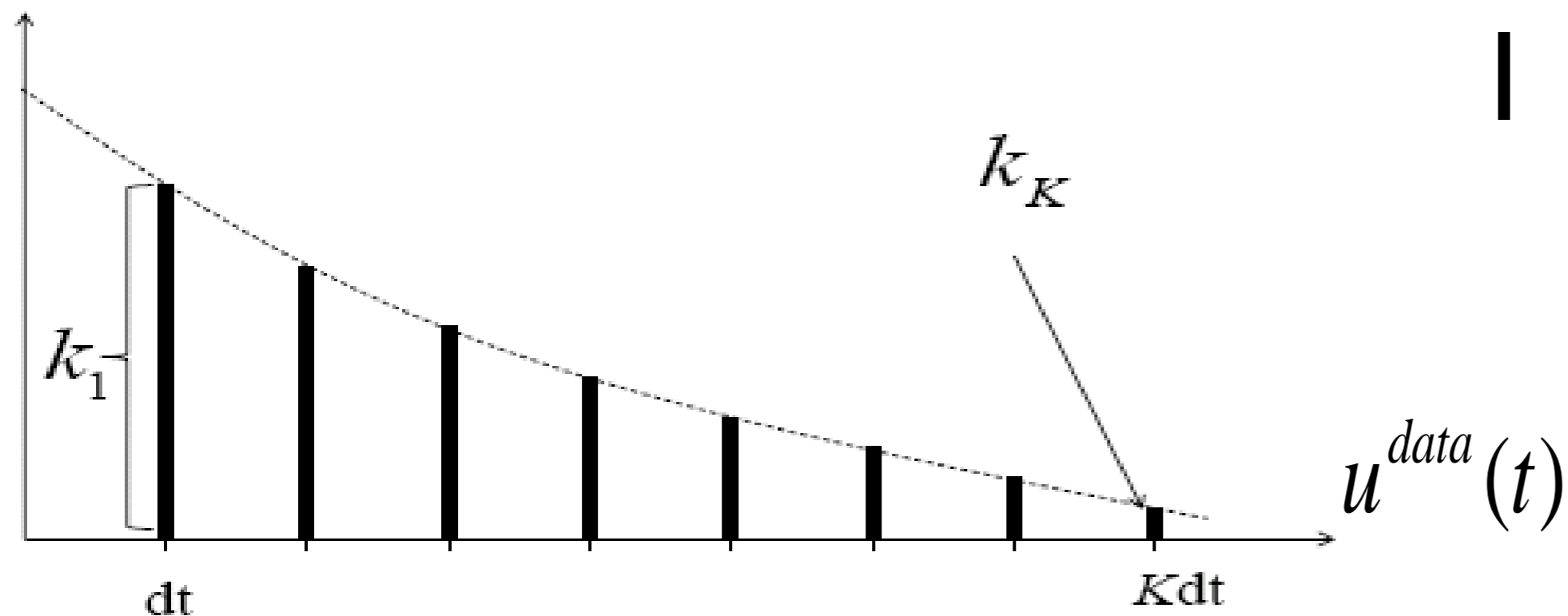


# Neuronal Dynamics – 9.5 Parameter estimation: voltage

Linear in parameters = linear fit

$$u(t) = \int_0^{\infty} \kappa(s) I(t-s) ds + u_{rest}$$

$$u(t_n) = \sum k_k I_{n-k} + u_{rest}$$



$$E = \sum_n \left[ u^{data}(t_n) - \sum_{k=1}^K k_k I_{n-k} - u_{rest} \right]^2$$

# Neuronal Dynamics – 9.5 Parameter estimation: voltage

Linear in parameters = linear fit = quadratic optimization

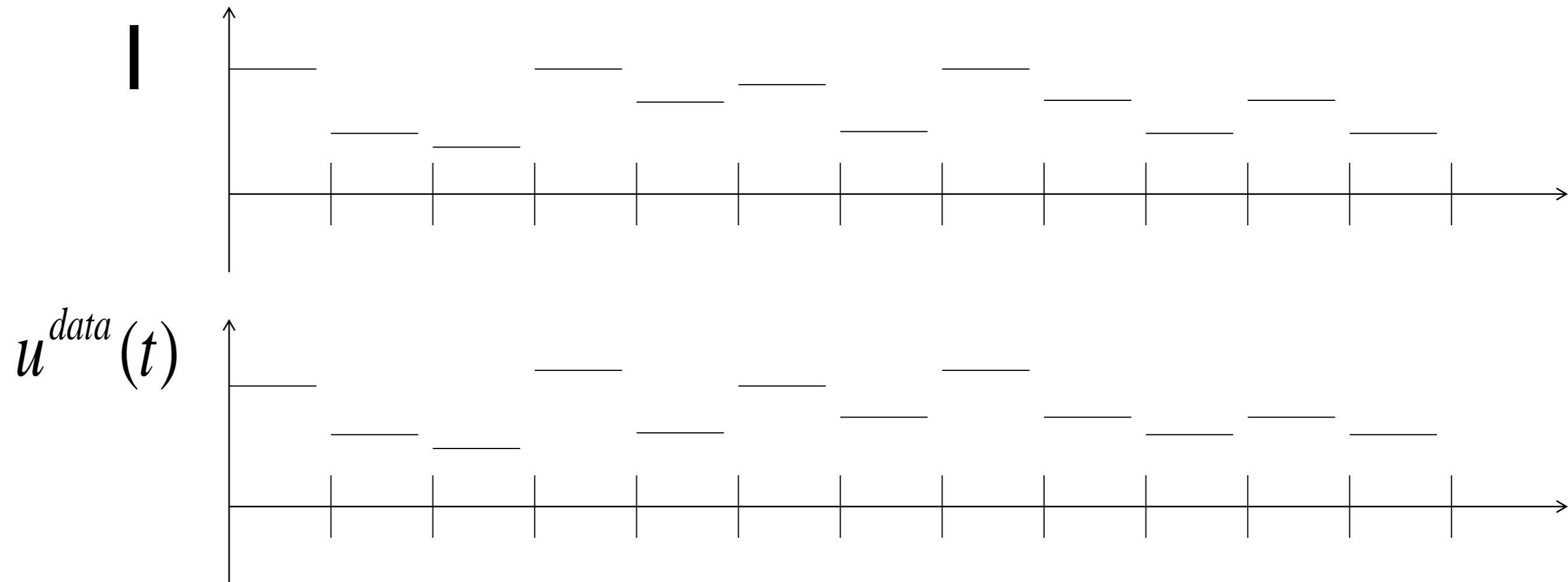
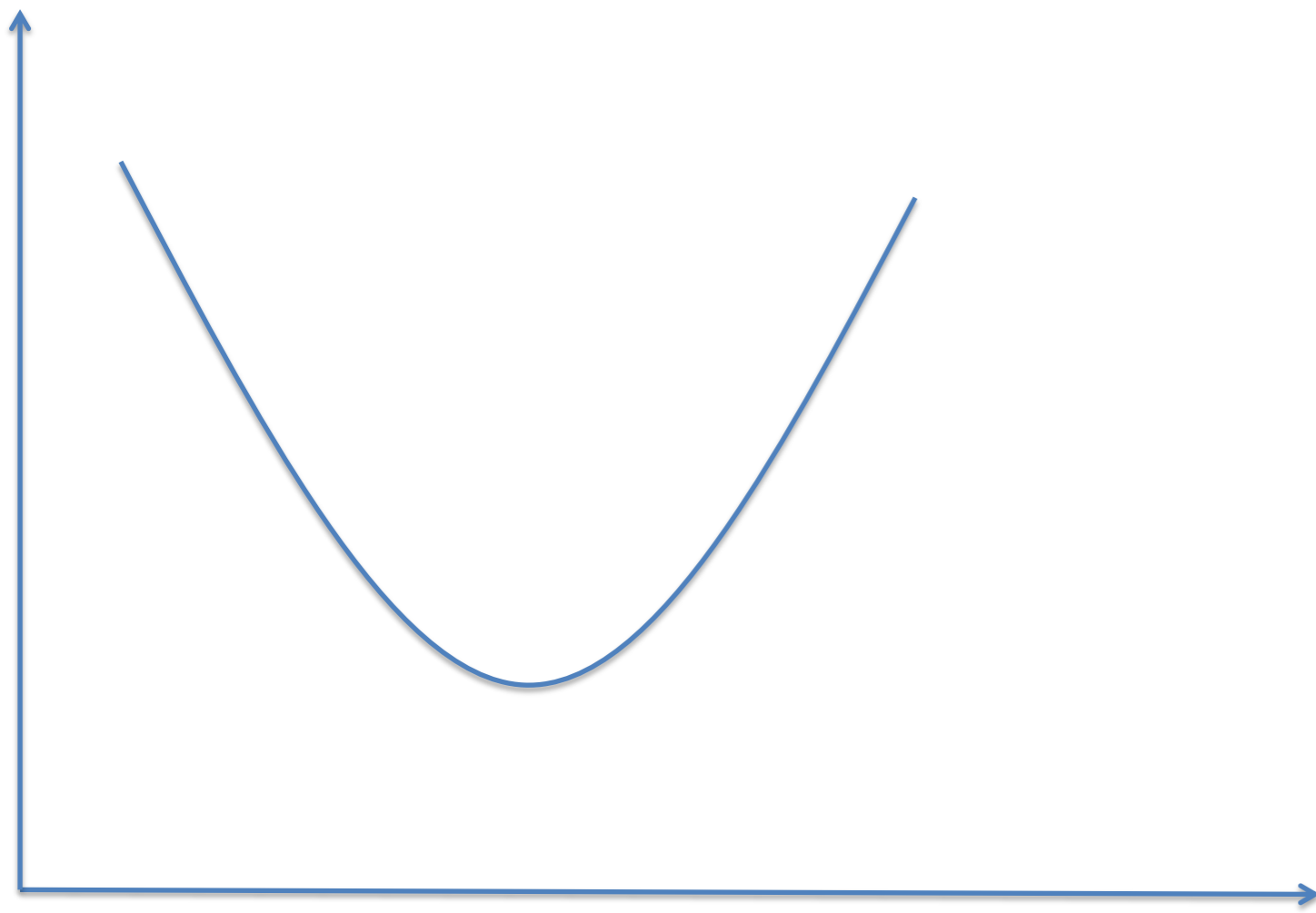
Model

$$u(t) = \int_0^{\infty} \kappa(s) I(t-s) ds + u_{rest}$$

$$u(t_n) = \sum_k k_k I_{n-k} + u_{rest}$$

Data

$u^{data}(t)$



$$E = \sum_n \left[ u^{data}(t_n) - \sum_{k=1}^K k_k I_{n-k} - u_{rest} \right]^2$$

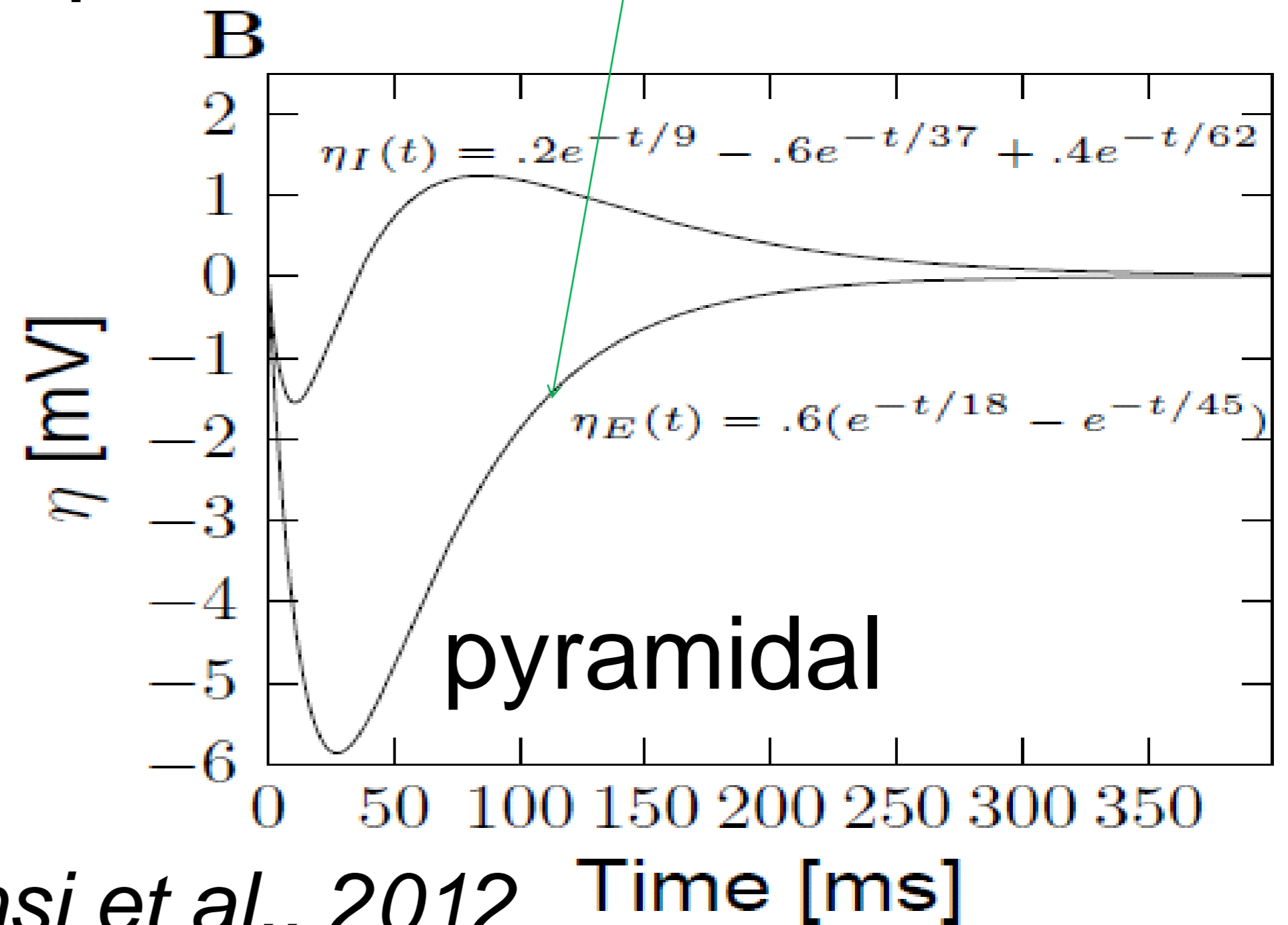
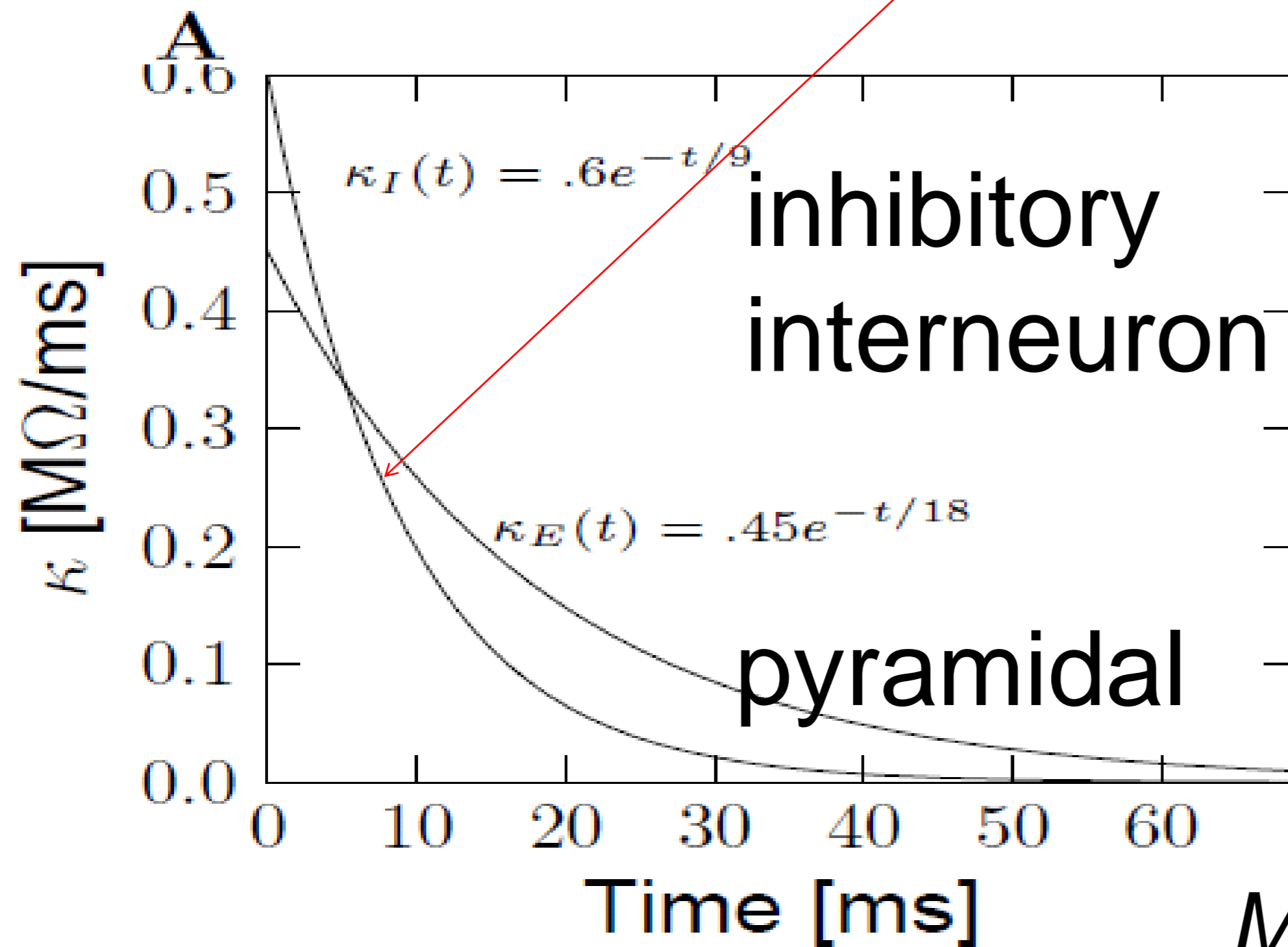
# Neuronal Dynamics – 9.5 Extracted parameters: voltage

Subthreshold potential

$$u(t) = \int_0^\infty \underbrace{\kappa(s)}_{\text{known input}} I(t-s) ds + u_{rest} + \int \underbrace{\eta(s)}_{\text{known spike train}} S(t-s) ds$$

known input

known spike train



Mensi et al., 2012

# Exercise 3 NOW: optimize 1 free parameter

Model

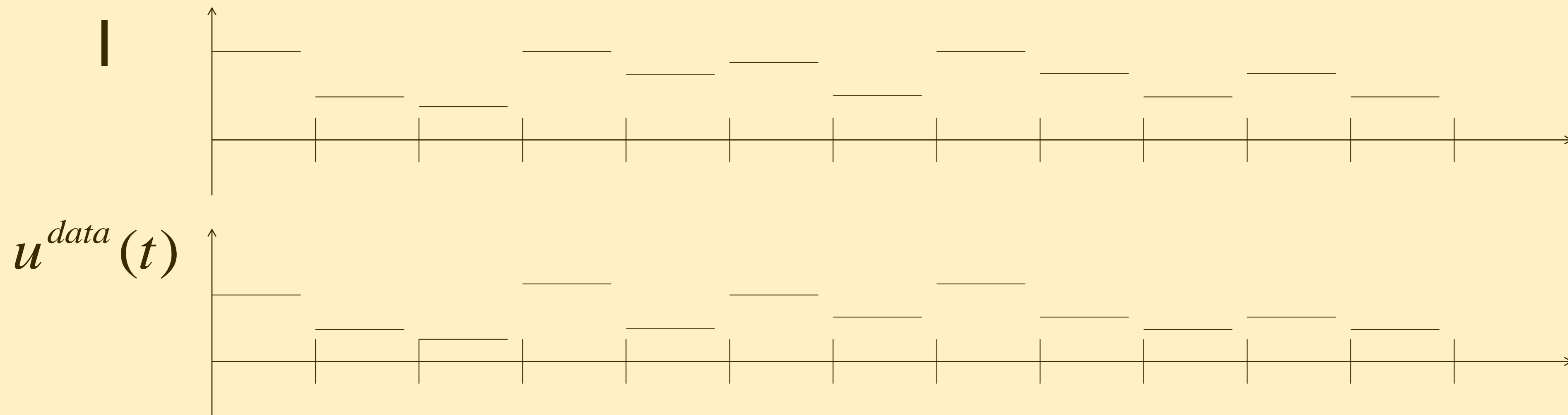
$$u_n = RI_n$$

Data

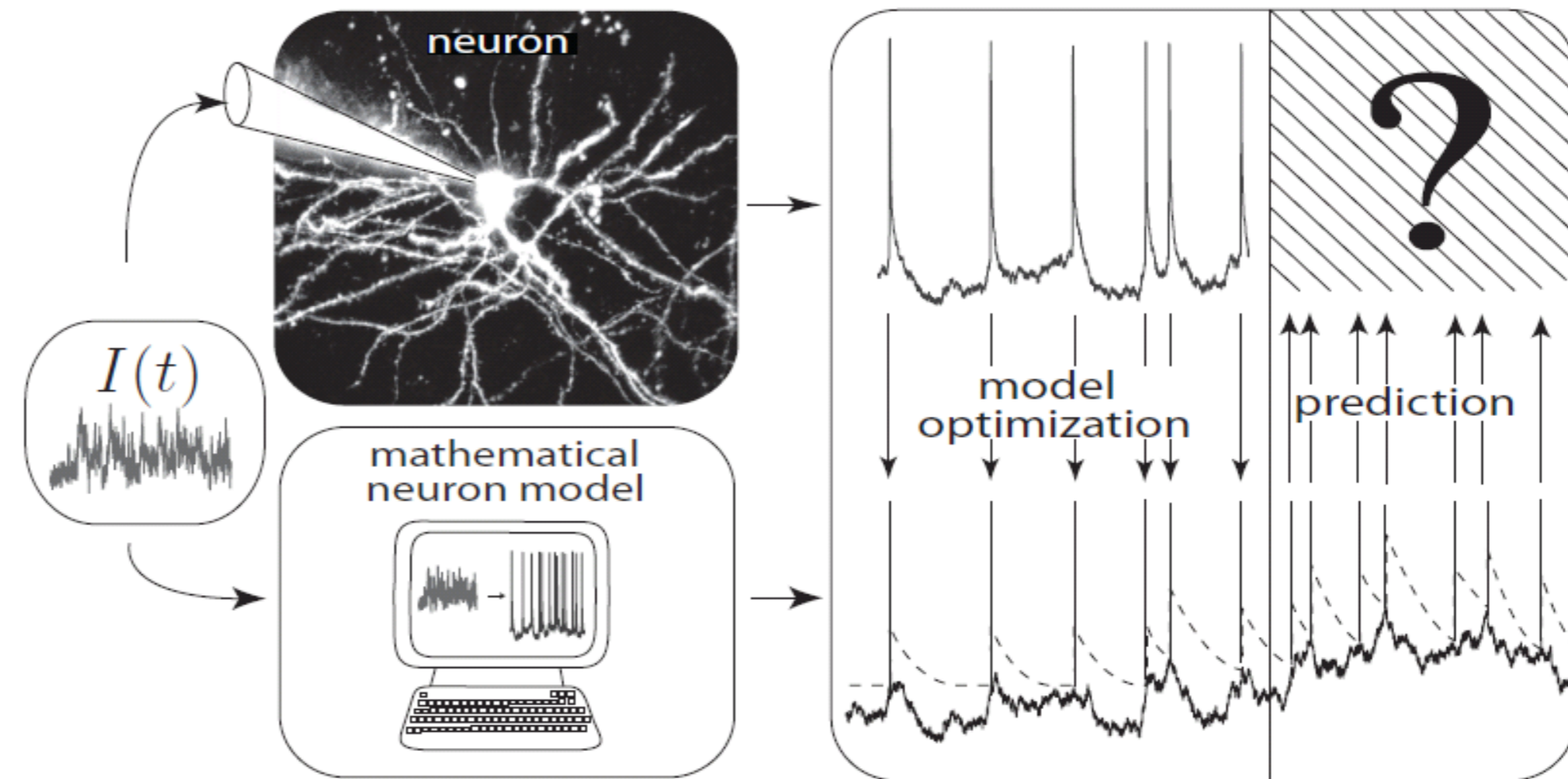
$$u^{data}(t_n)$$

**Optimize parameter R, so as to have a minimal error**

$$E = \sum_n [u^{data}(t_n) - RI_n]^2$$



# Neuronal Dynamics – What is a good neuron model?



- A) Predict spike times
- B) Predict subthreshold voltage
- C) Easy to interpret (not a 'black box')
- D) Flexible
- E) Systematic: 'optimize' parameters

# Week 9 – part 5b: Quadratic and Convex Optimization



## Biological Modeling of Neural Networks:

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Wulfram Gerstner

EPFL, Lausanne, Switzerland

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- Quadratic and convex optimization

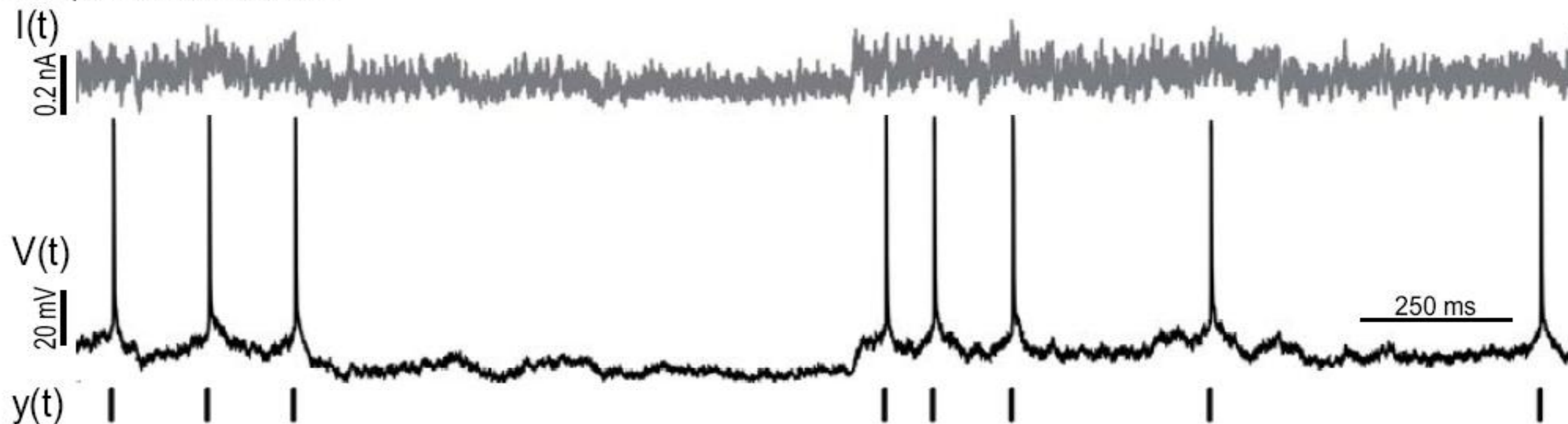
#### 9.6. Modeling in vitro data

- how long lasts the effect of a spike?

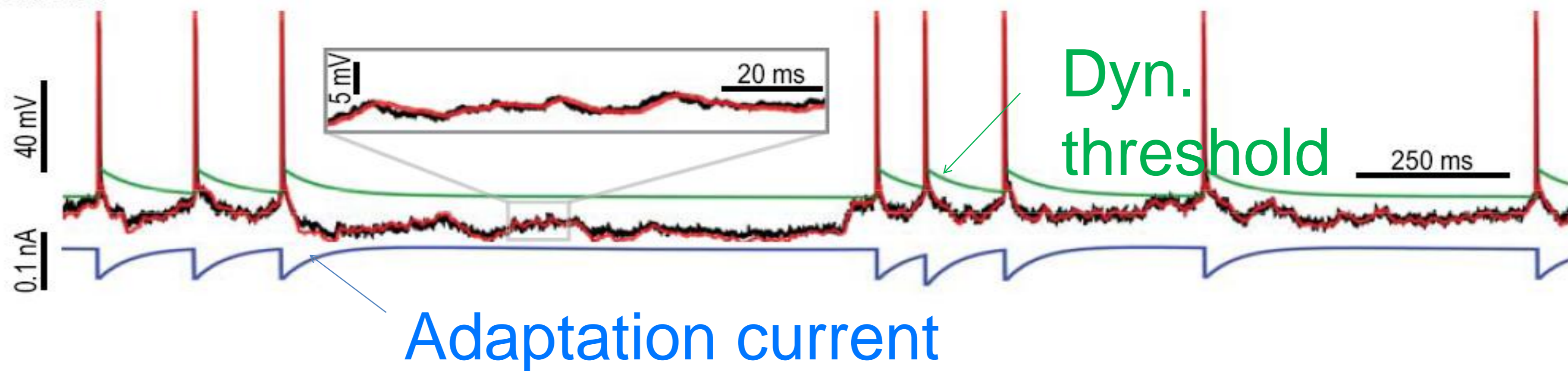


# Fitting models to data: so far 'subthreshold'

A Experimental data set



C Model



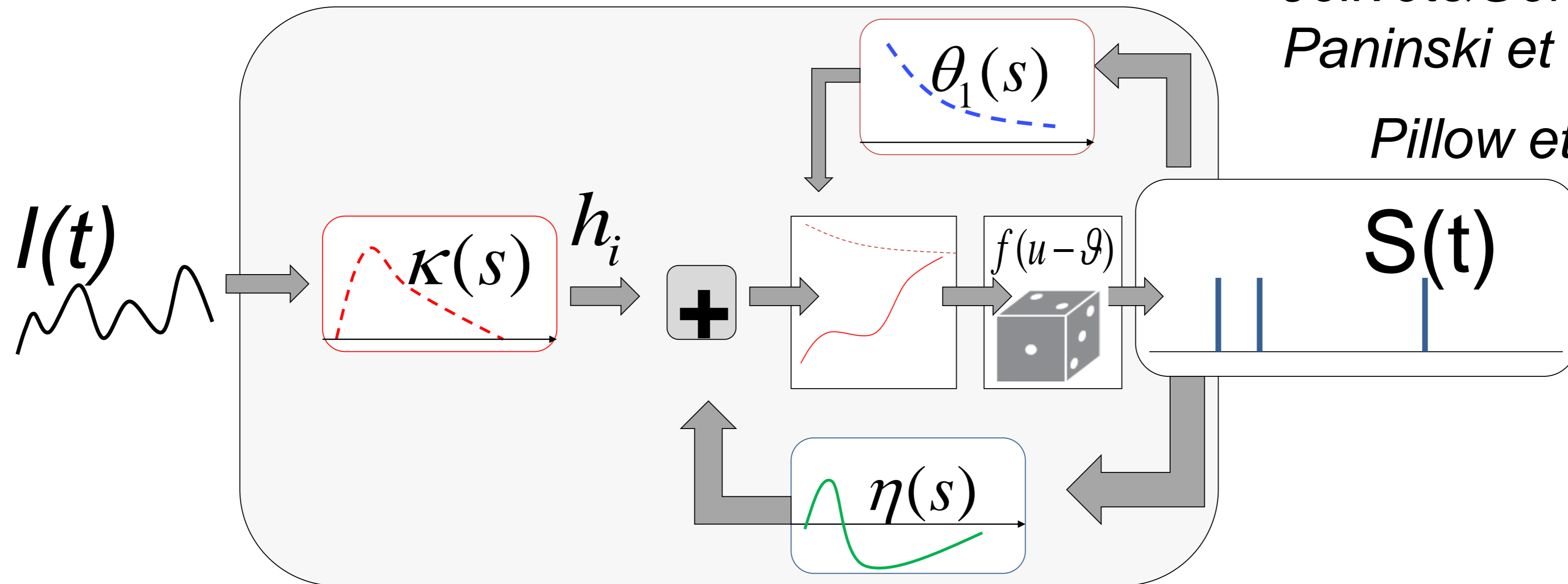


# Neuronal Dynamics – 9.5 Threshold: Predicting spike times

*Jolivet & Gerstner, 2005*

*Paninski et al., 2004*

*Pillow et al., 2008*



**potential**  $u(t) = \int \eta(s) S(t-s) ds + \int_0^\infty \kappa(s) I(t-s) ds + u_{rest}$

**threshold**  $\vartheta(t) = \theta_0 + \int \theta_1(s) S(t-s) ds$

**firing intensity**  $\rho(t) = f(u(t) - \vartheta(t))$

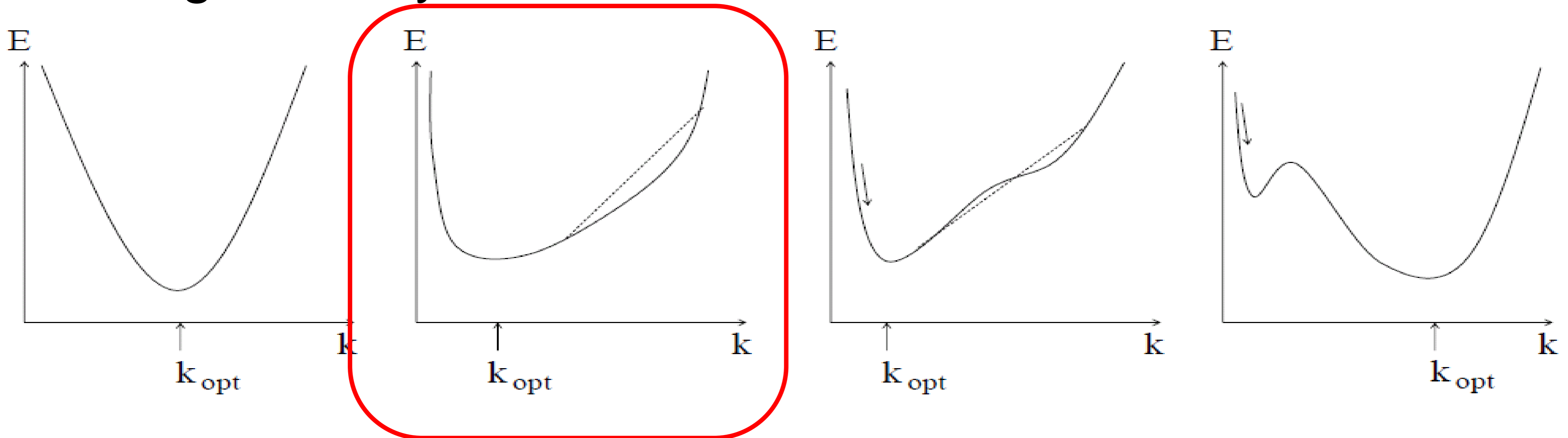
# Neuronal Dynamics – 9.5 Generalized Linear Model (GLM)

$$\log L(t^1, \dots, t^N) = -\int_0^T \rho(t') dt' + \sum_f \log \rho(t^f) = -E$$

potential  $u(t) = \int \underline{\eta(s)} S(t-s) ds + \int_0^\infty \underline{\kappa(s)} I(t-s) ds + u_{rest}$

threshold  $\mathcal{G}(t) = \theta_0 + \int \underline{\theta_1(s)} S(t-s) ds$

firing intensity  $\rho(t) = f(u(t) - \mathcal{G}(t))$



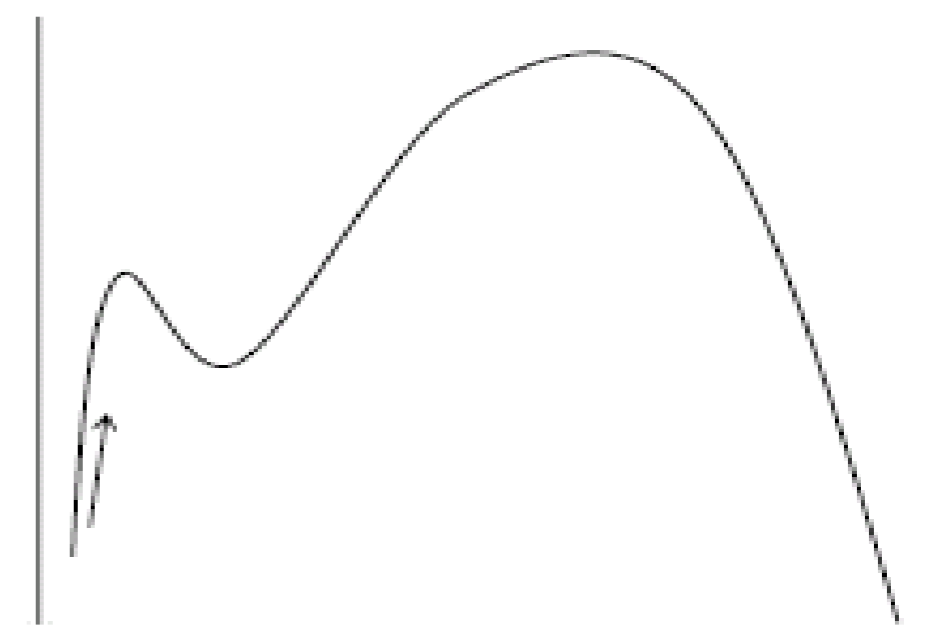
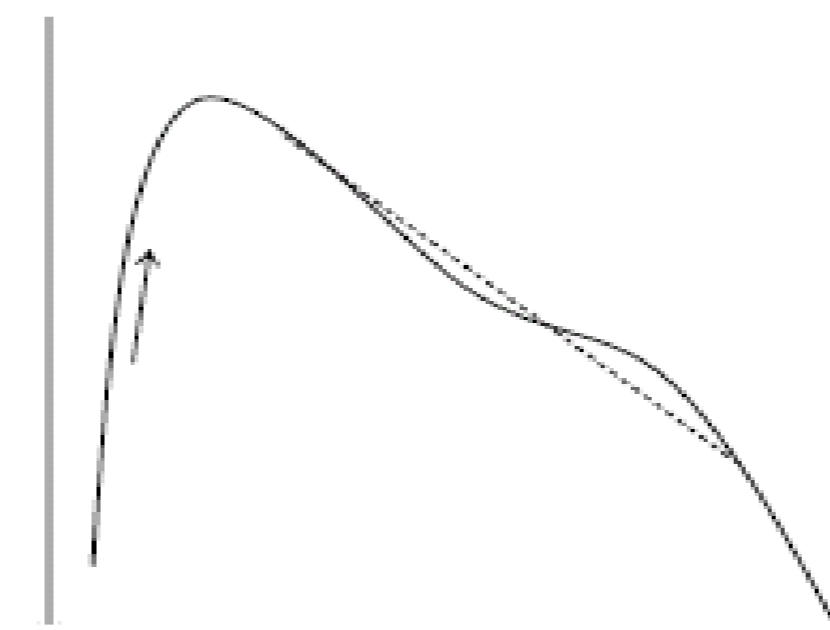
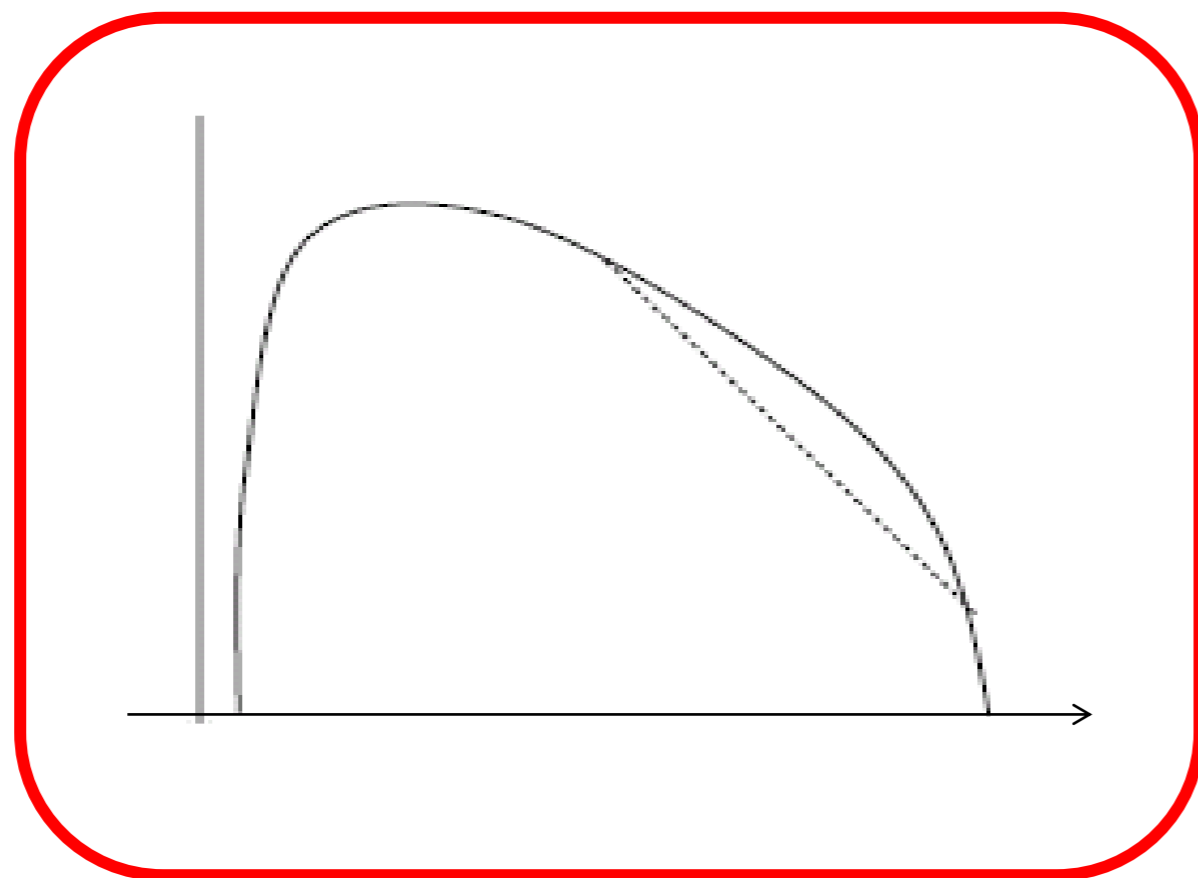
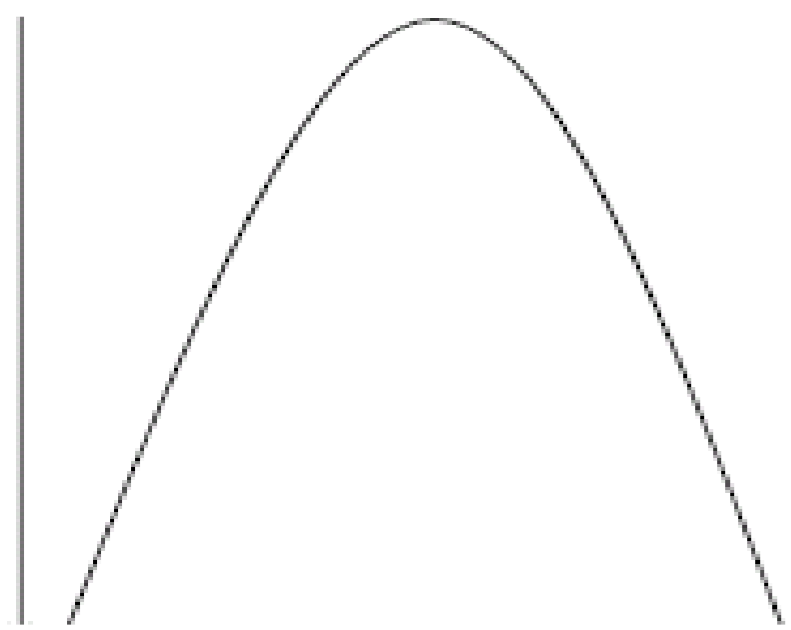
# Neuronal Dynamics – 9.5 GLM: concave error function

potential  $u(t) = \int \underline{\eta(s)} S(t-s) ds + \int_0^\infty \underline{\kappa(s)} I(t-s) ds + u_{rest}$

threshold  $\mathcal{G}(t) = \theta_0 + \int \underline{\theta_1(s)} S(t-s) ds$

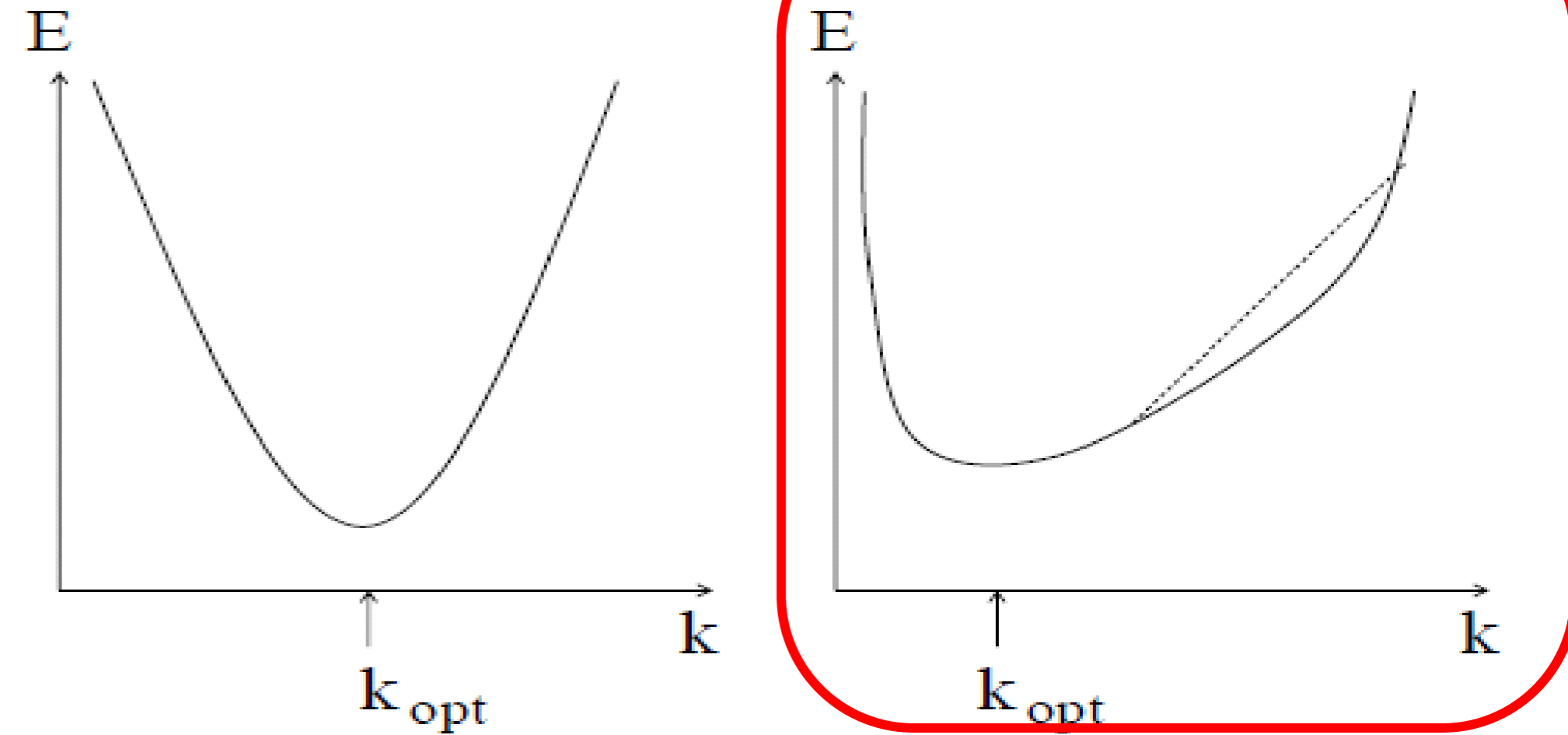
firing intensity  $\rho(t) = f(u(t) - \mathcal{G}(t))$

$$\log L(t^1, \dots, t^N) = -\int_0^T \rho(t') dt' + \sum_f \log \rho(t^f)$$



*Paninski, 2004*

# Neuronal Dynamics – 9.5 quadratic and convex/concave optimization



Voltage/subthreshold

- linear in parameters  
→ quadratic error function

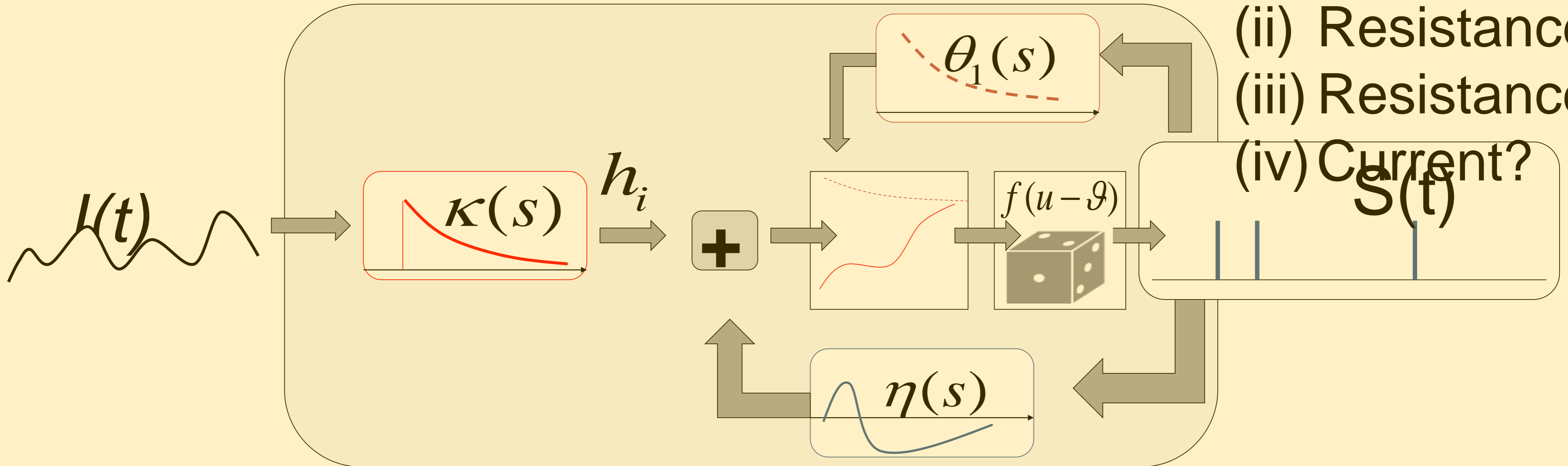
Spike times

- nonlinear, but GLM  
→ convex error function

# Quiz 3 NOW :

What are the units of  $\eta(s)$  ?

- (i) Voltage?
- (ii) Resistance?
- (iii) Resistance/s?
- (iv) Current?



**potential**  $u(t) = \int \eta(s) S(t-s) ds + \int_0^\infty \kappa(s) I(t-s) ds + u_{rest}$

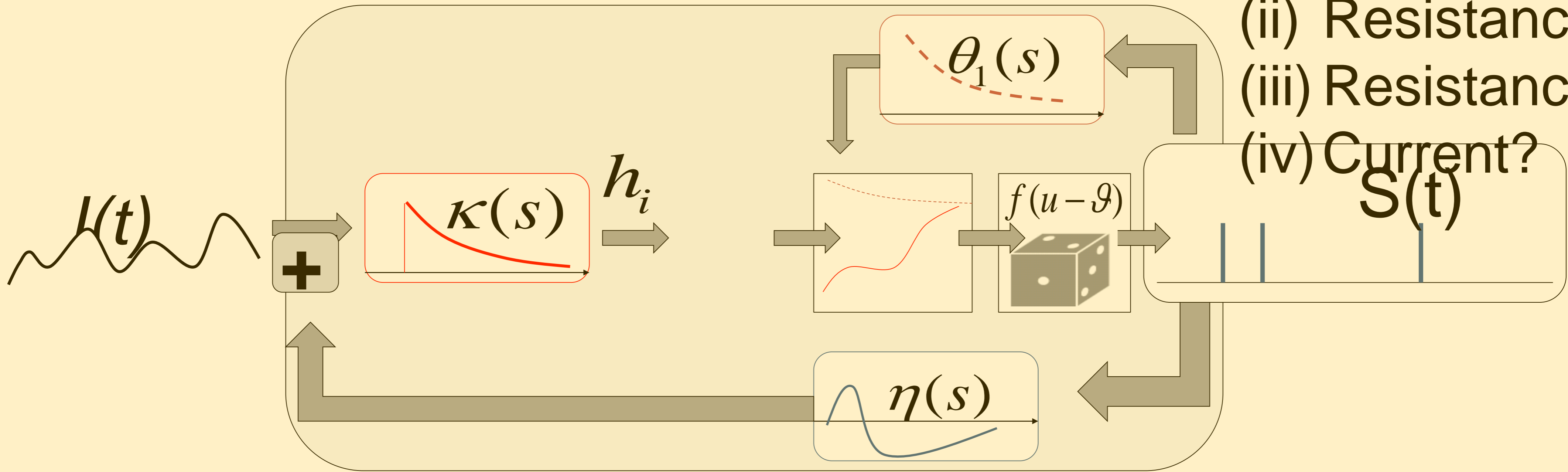
**threshold**  $\mathcal{G}(t) = \theta_0 + \int \theta_1(s) S(t-s) ds$

**firing intensity**  $\rho(t) = f(u(t) - \mathcal{G}(t))$

# Quiz NOW:

What are the units of  $\kappa(s)$  ?

- (i) Voltage?
- (ii) Resistance?
- (iii) Resistance/s?
- (iv) Current?

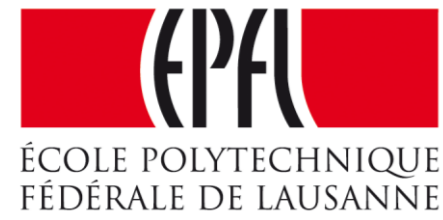


**potential**  $u(t) = \int \underline{\eta(s)} S(t-s) ds + \int_0^\infty \underline{\kappa(s)} I(t-s) ds + u_{rest}$

**threshold**  $\mathcal{G}(t) = \theta_0 + \int \underline{\theta_1(s)} S(t-s) ds$

**firing intensity**  $\rho(t) = f(u(t) - \mathcal{G}(t))$

# Week 9 – part 6: Modeling in vitro data



## Biological Modeling of Neural Networks:

### Week 9 – Optimizing Neuron Models For Coding and Decoding

Wulfram Gerstner

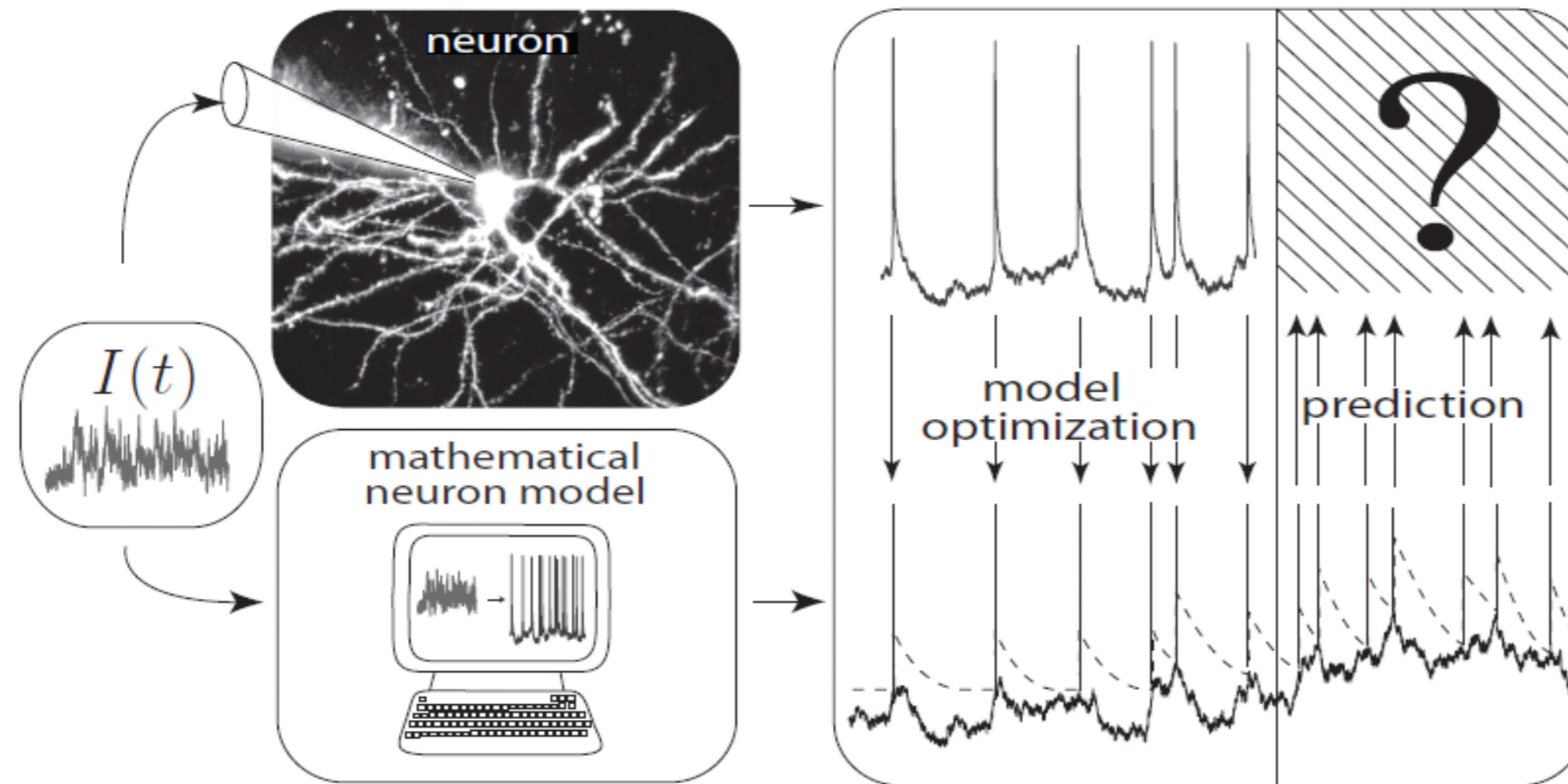
EPFL, Lausanne, Switzerland

- ✓ **9.1 What is a good neuron model?**
  - Models and data
- ✓ **9.2 AdEx model**
  - Firing patterns and adaptation
- ✓ **9.3 Spike Response Model (SRM)**
  - Integral formulation
- ✓ **9.4 Generalized Linear Model**
  - Adding noise to the SRM
- ✓ **9.5 Parameter Estimation**
  - Quadratic and convex optimization
- 9.6. Modeling in vitro data**
  - how long lasts the effect of a spike?
- 9.7. Helping Humans**



# Neuronal Dynamics – 9.6 Models and Data

comparison model-data



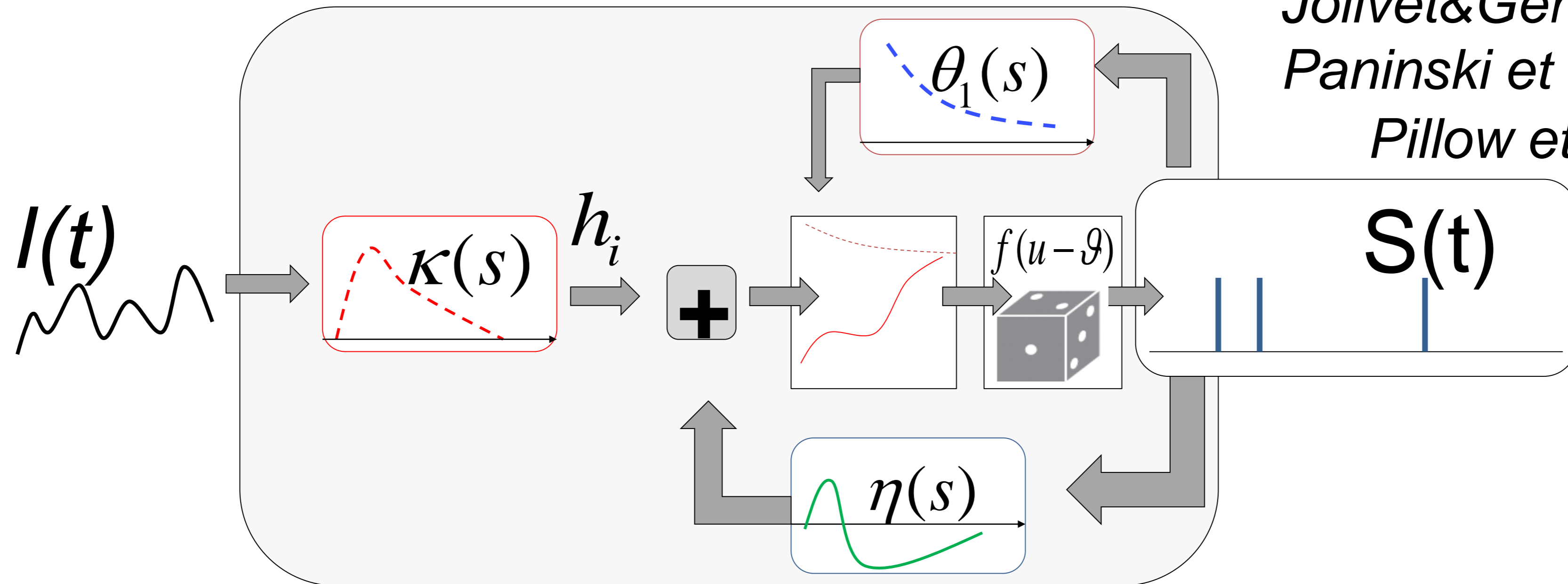
**Predict**

-Subthreshold voltage

-Spike times

# Neuronal Dynamics – 9.6 GLM/SRM with escape noise

*Jolivet & Gerstner, 2005*  
*Paninski et al., 2004*  
*Pillow et al., 2008*

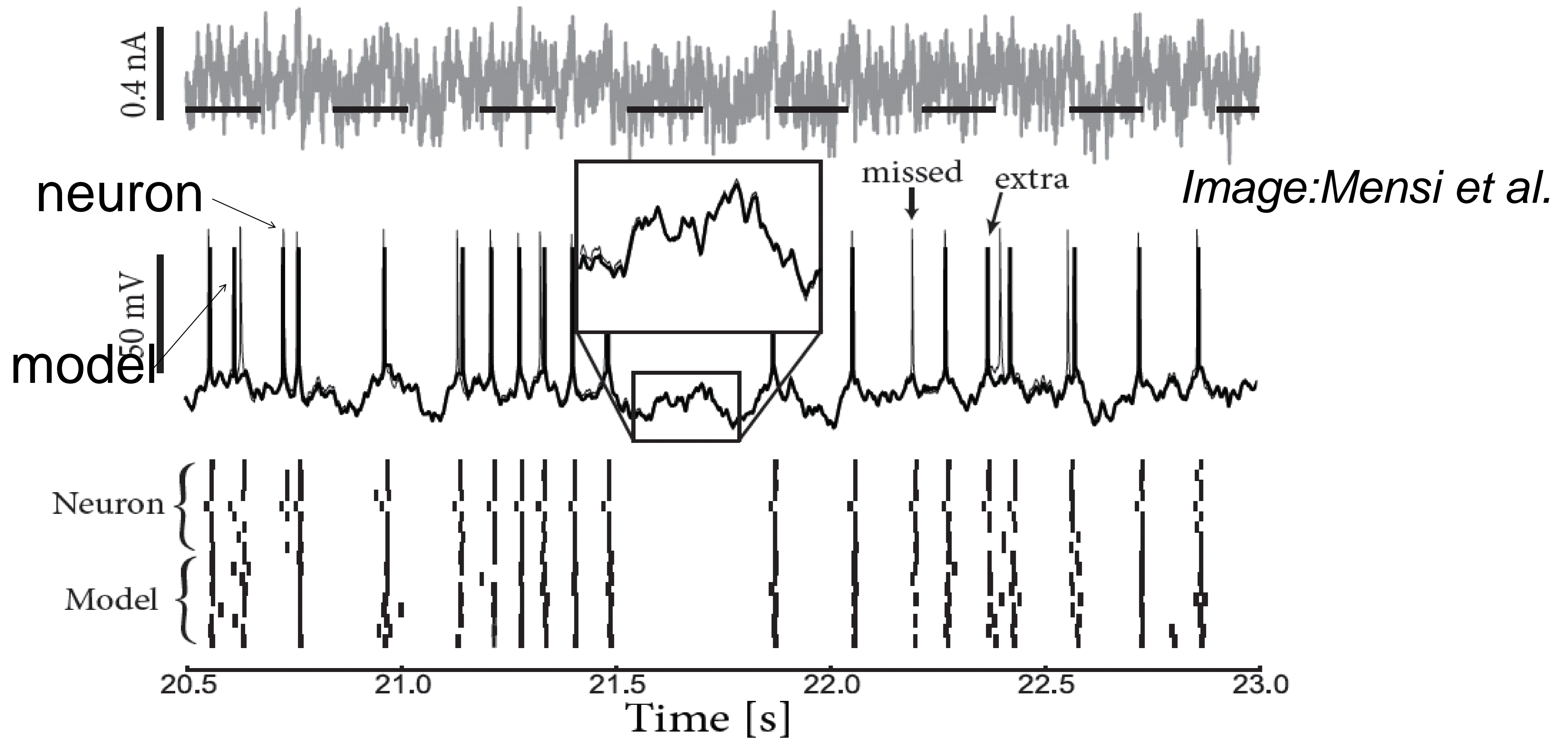


**potential**  $u(t) = \int \eta(s) S(t-s) ds + \int_0^\infty \kappa(s) I(t-s) ds + u_{rest}$

**threshold**  $\mathcal{G}(t) = \theta_0 + \int \theta_1(s) S(t-s) ds$

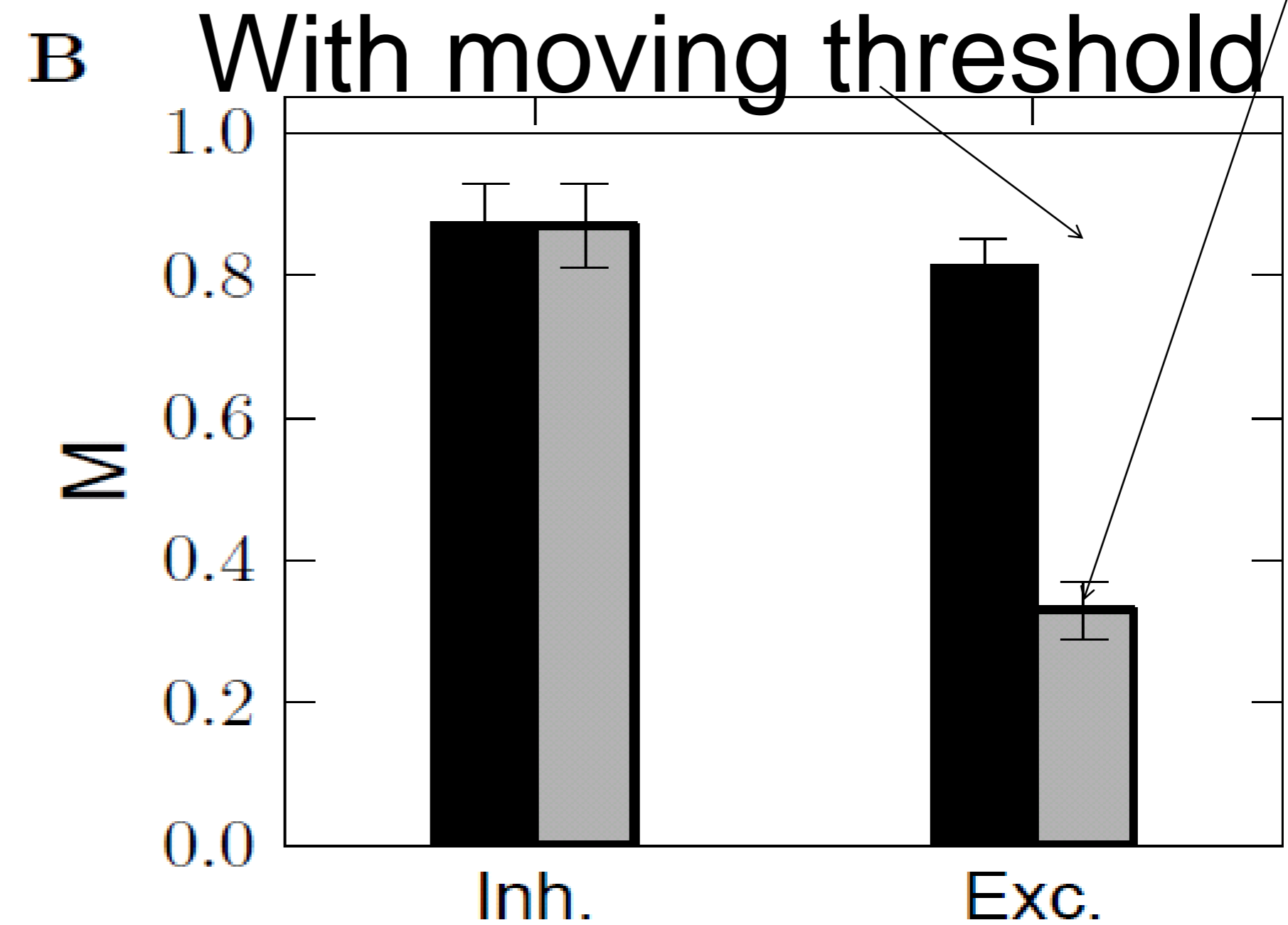
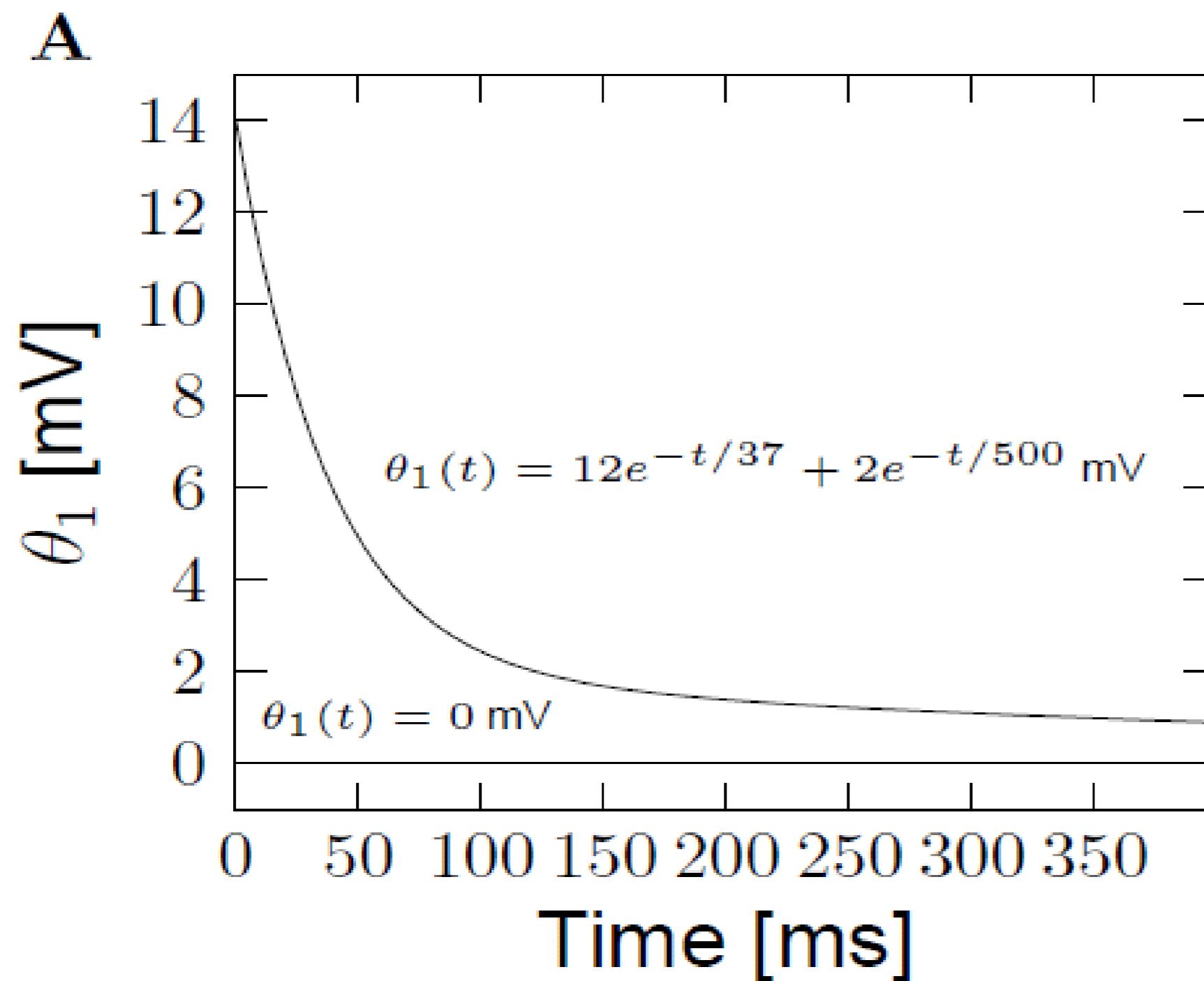
**firing intensity**  $\rho(t) = f(u(t) - \mathcal{G}(t))$

# Neuronal Dynamics – 9.6 GLM/SRM predict subthreshold voltage



## Role of moving threshold

No moving threshold



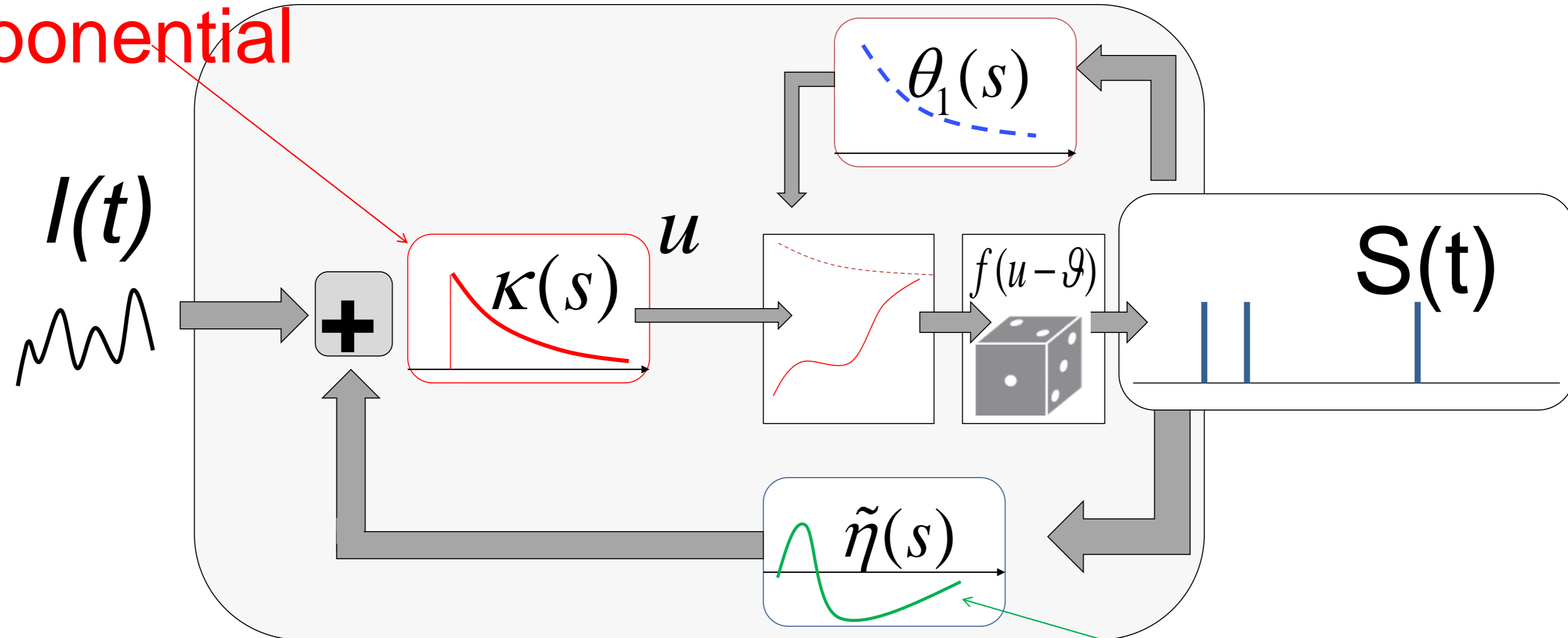
Mensi et al., 2012

# Change in model formulation:

What are the units of .... ?

'soft-threshold  
adaptive IF model'

exponential



potential

$$C \frac{d}{dt} u(t) = \int \tilde{\eta}(s) S(t-s) ds + I(t)$$

threshold

$$\mathcal{G}(t) = \theta_0 + \int \theta_1(s) S(t-s) ds$$

firing intensity

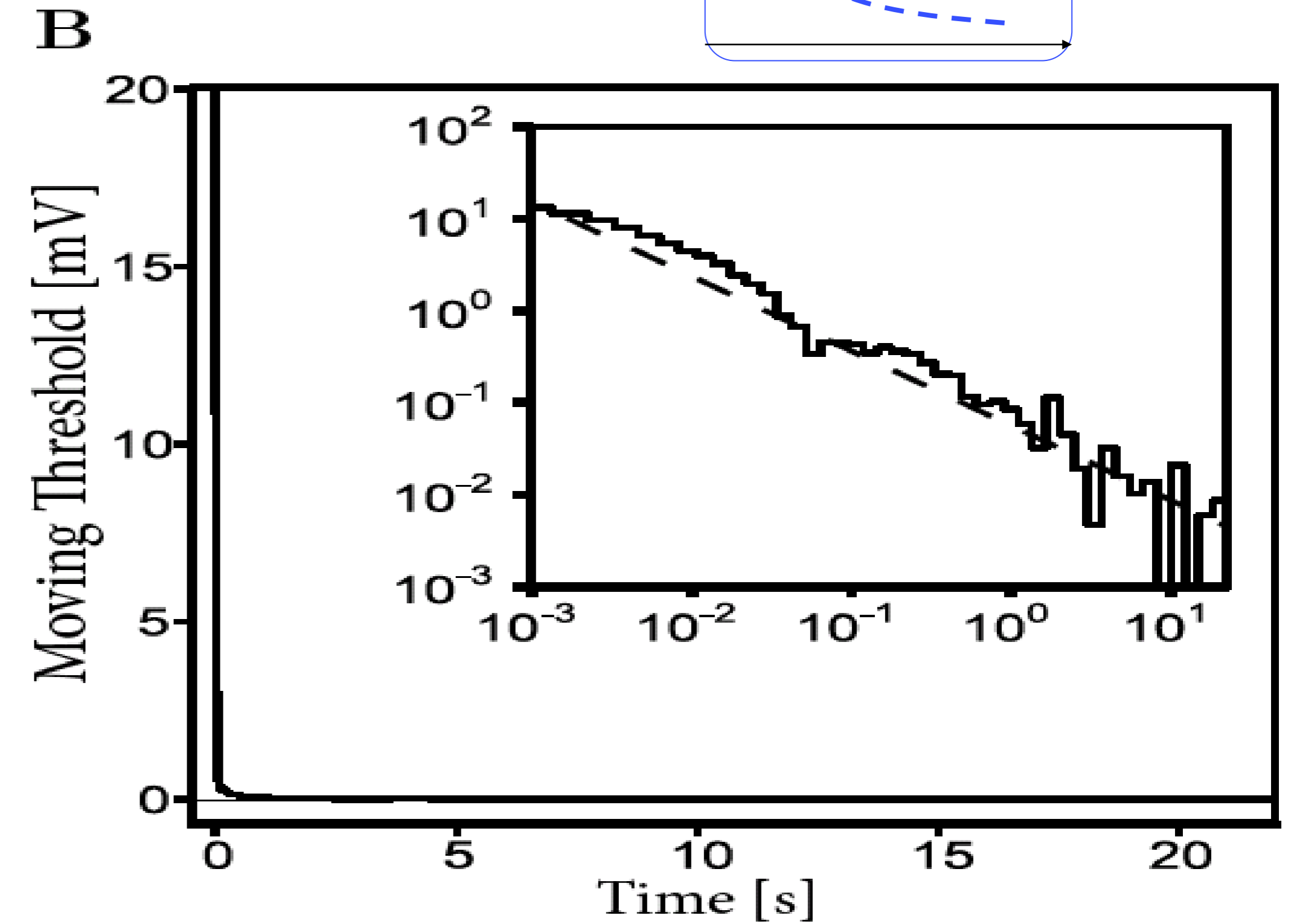
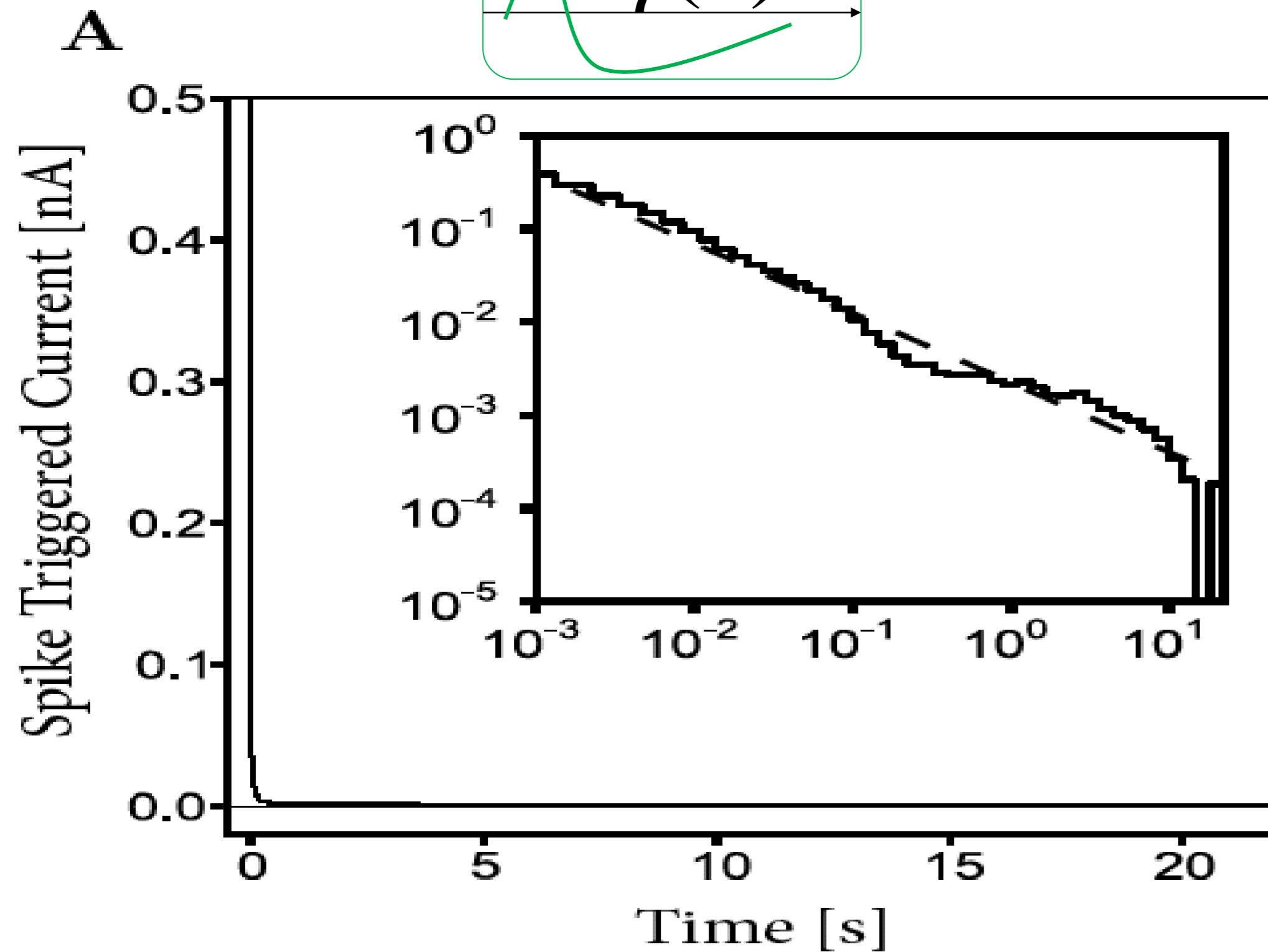
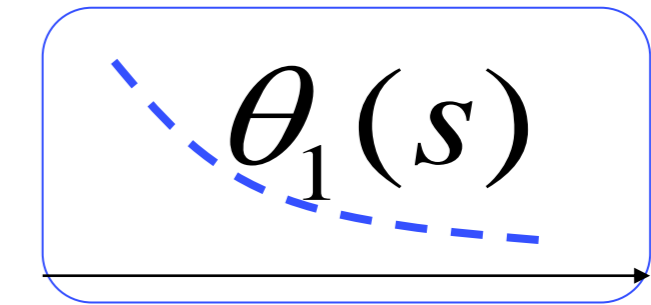
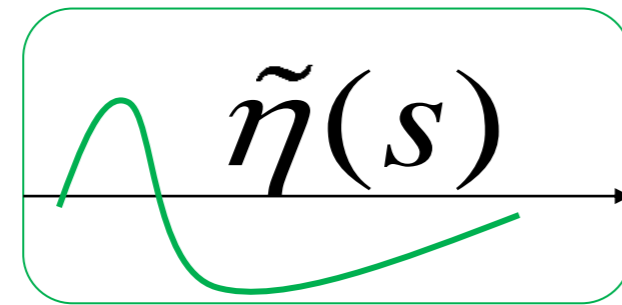
$$\rho(t) = f(u(t) - \mathcal{G}(t))$$

adaptation  
current

# Neuronal Dynamics – 9.6 How long does the effect of a spike last?

*Time scale of filters?*

→ **Power law**

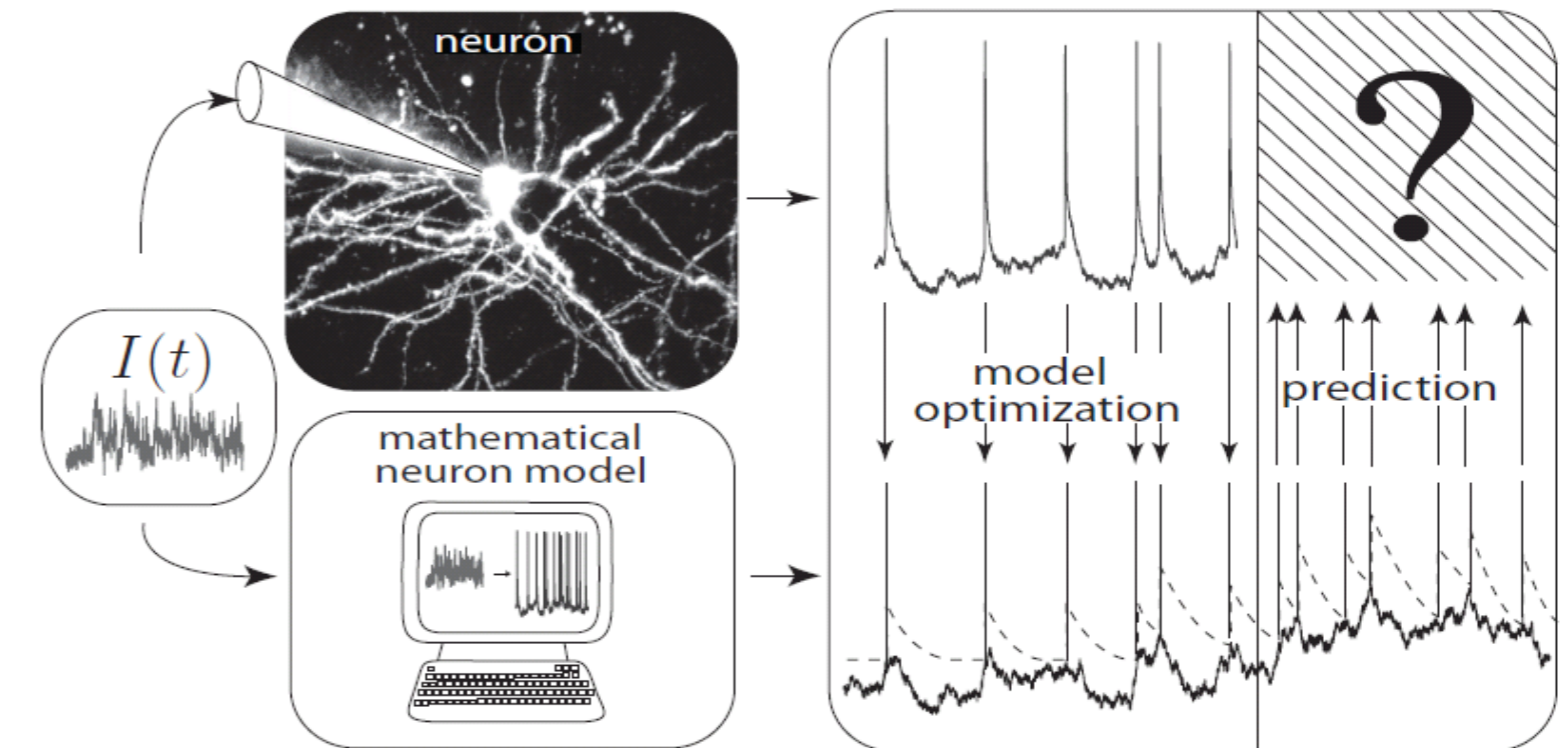


***A single spike has a measurable effect more than 10 seconds later!***

*Pozzorini et al. 2013*



# Neuronal Dynamics – 9.6 Models and Data



- Predict spike times
- Predict subthreshold voltage
- Easy to interpret (not a 'black box')
- Variety of phenomena
- Systematic: 'optimize' parameters

**BUT so far limited to in vitro**



# Neuronal Dynamics week 7 – Suggested Reading/selected references

**Reading:** W. Gerstner, W.M. Kistler, R. Naud and L. Paninski,  
*Neuronal Dynamics: from single neurons to networks and models of cognition*. Ch. 6,10,11: Cambridge, 2014

## Nonlinear and adaptive IF

- Fourcaud-Trocme, N., Hansel, D., van Vreeswijk, C., and Brunel, N. (2003). How spike .... *J. Neuroscience*, 23:11628-11640.
- Badel, L., et al. (2008a). Extracting nonlinear integrate-and-fire, *Biol. Cybernetics*, 99:361-370.
- Brette, R. and Gerstner, W. (2005). Adaptive exponential integrate-and-fire *J. Neurophysiol.*, 94:3637- 3642.
- Izhikevich, E. M. (2003). Simple model of spiking neurons. *IEEE Trans Neural Netw*, 14:1569-1572.
- Gerstner, W. (2008). Spike-response model. *Scholarpedia*, 3(12):1343.

## Optimization methods for neuron models, max likelihood, and GLM

- Brillinger, D. R. (1988). Maximum likelihood analysis of spike trains of interacting nerve cells. *Biol. Cybern.*, 59:189-200.
- Truccolo, et al. (2005). A point process framework for relating neural spiking activity to spiking history, neural ensemble, and extrinsic covariate effects. *Journal of Neurophysiology*, 93:1074-1089.
- Paninski, L. (2004). Maximum likelihood estimation of ... *Network: Computation in Neural Systems*, 15:243-262.
- Paninski, L., Pillow, J., and Lewi, J. (2007). Statistical models for neural encoding, decoding, and optimal stimulus design. In Cisek, P., et al. , *Comput. Neuroscience: Theoretical Insights into Brain Function*. Elsevier Science.
- Pillow, J., ET AL.(2008). Spatio-temporal correlations and visual signalling... . *Nature*, 454:995-999.

## Encoding and Decoding

- Rieke, F., Warland, D., de Ruyter van Steveninck, R., and Bialek, W. (1997). *Spikes - Exploring the neural code*. MIT Press,
- Keat, J., Reinagel, P., Reid, R., and Meister, M. (2001). Predicting every spike ... *Neuron*, 30:803-817.
- Mensi, S., et al. (2012). Parameter extraction and classification .... *J. Neurophys.*,107:1756-1775.
- Pozzorini, C., Naud, R., Mensi, S., and Gerstner, W. (2013). Temporal whitening by . *Nat. Neuroscience*,
- Georgopoulos, A. P., Schwartz, A.,Kettner, R. E. (1986). Neuronal population coding of movement direction. *Science*, 233:1416-1419.
- Donoghue, J. (2002). Connecting cortex to machines: recent advances in brain interfaces. *Nat. Neurosci.*, 5:1085-1088.

The END