Biological Modeling of Neural Networks

EPFL

Week 12

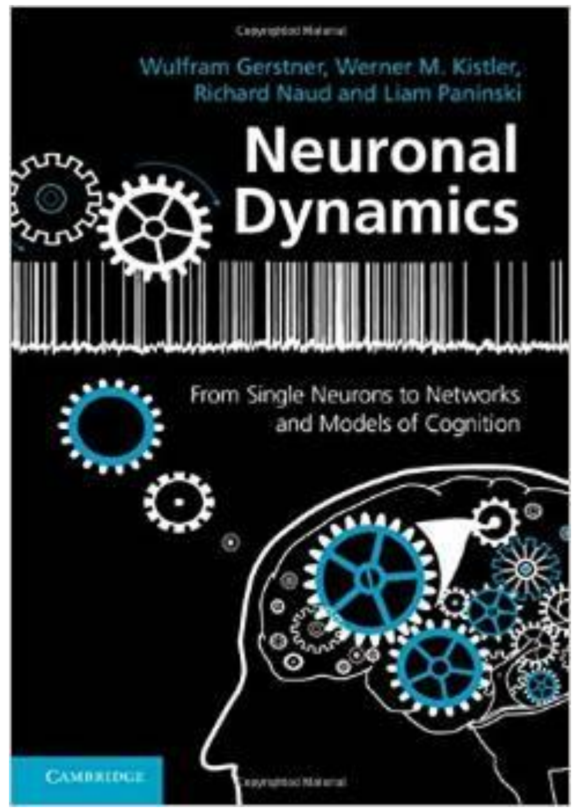
Optimizing Neuron Models

For Coding and Decoding

Wulfram Gerstner

EPFL, Lausanne, Switzerland

Reading for this week:
NEURONAL DYNAMICS
- Ch. 4.6, 6.1,6.2,6.4, 9.2
- Ch. 10.2.3, 11.1. 11.3.3



Cambridge Univ. Press

1 What is a good neuron model?
- Models and data

2 AdEx model
- Firing patterns and adaptation

3 Spike Response Model (SRM)
- Integral formulation

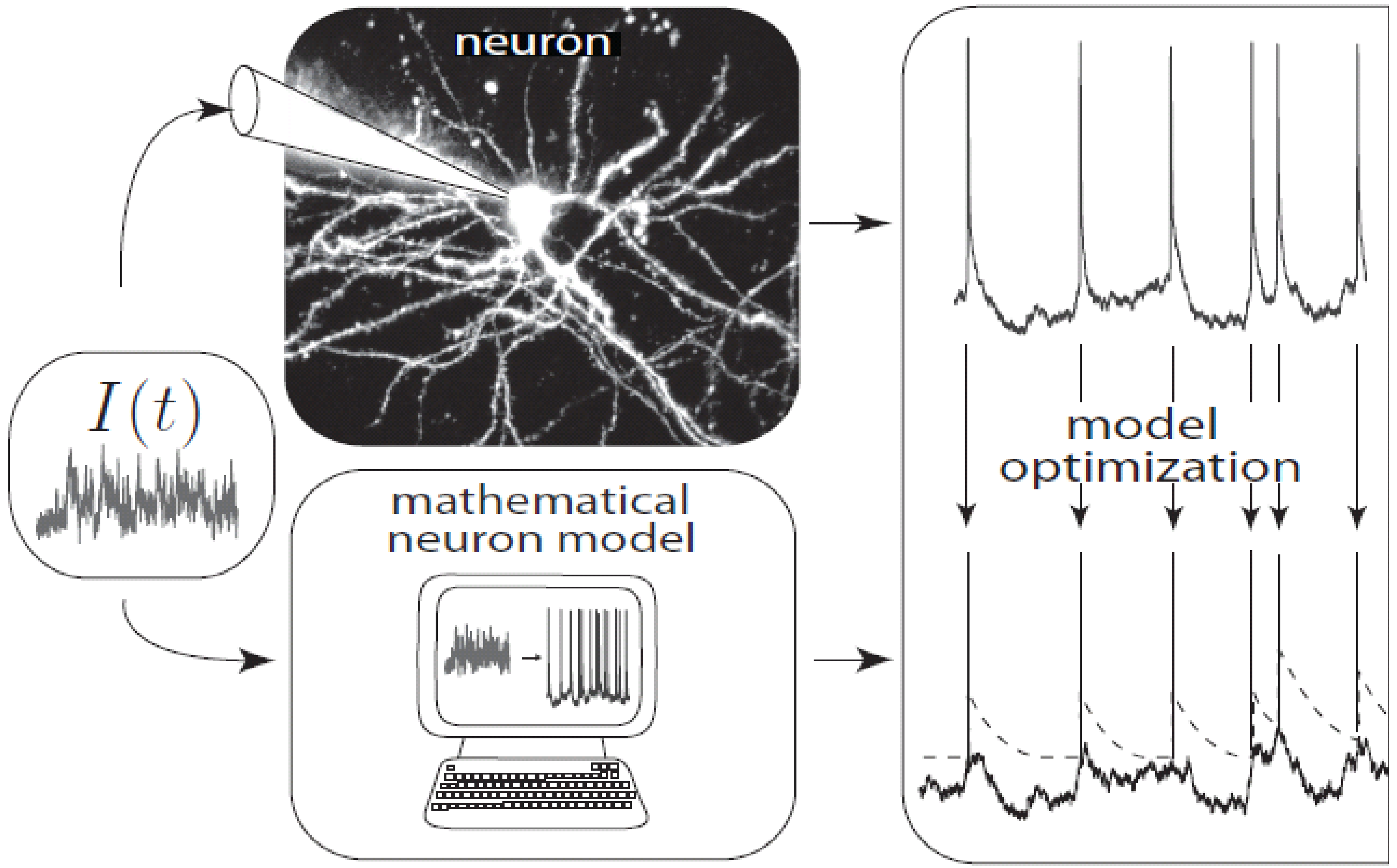
4 Generalized Linear Model
- Adding noise to the SRM
- Likelihood of a spike train

5 Parameter Estimation
(- Quadratic and convex optimization)

6 Modeling in vitro data
- how long lasts the effect of a spike?

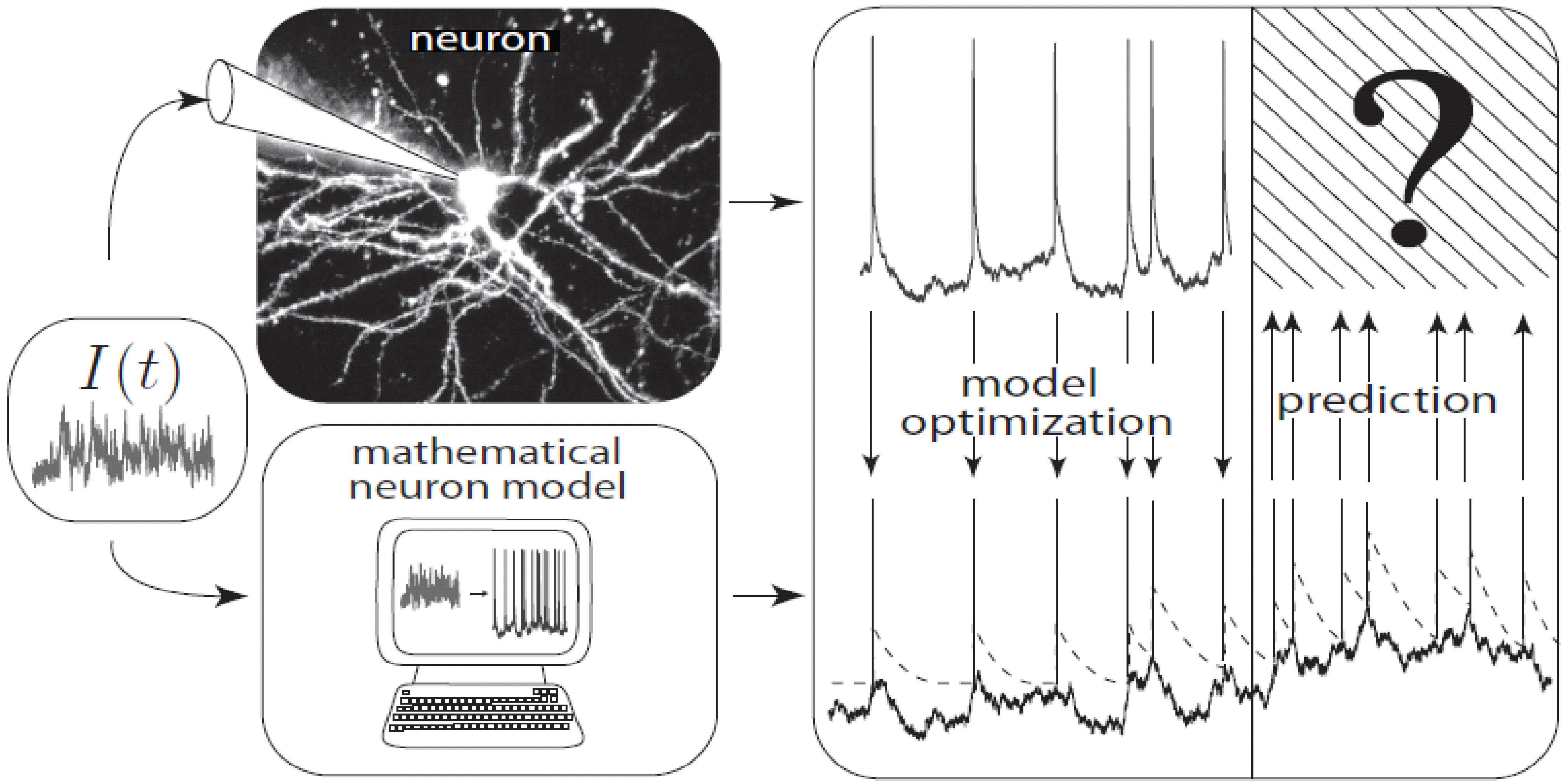
7 Helping humans – in vivo data

1. Neuron Models and Data



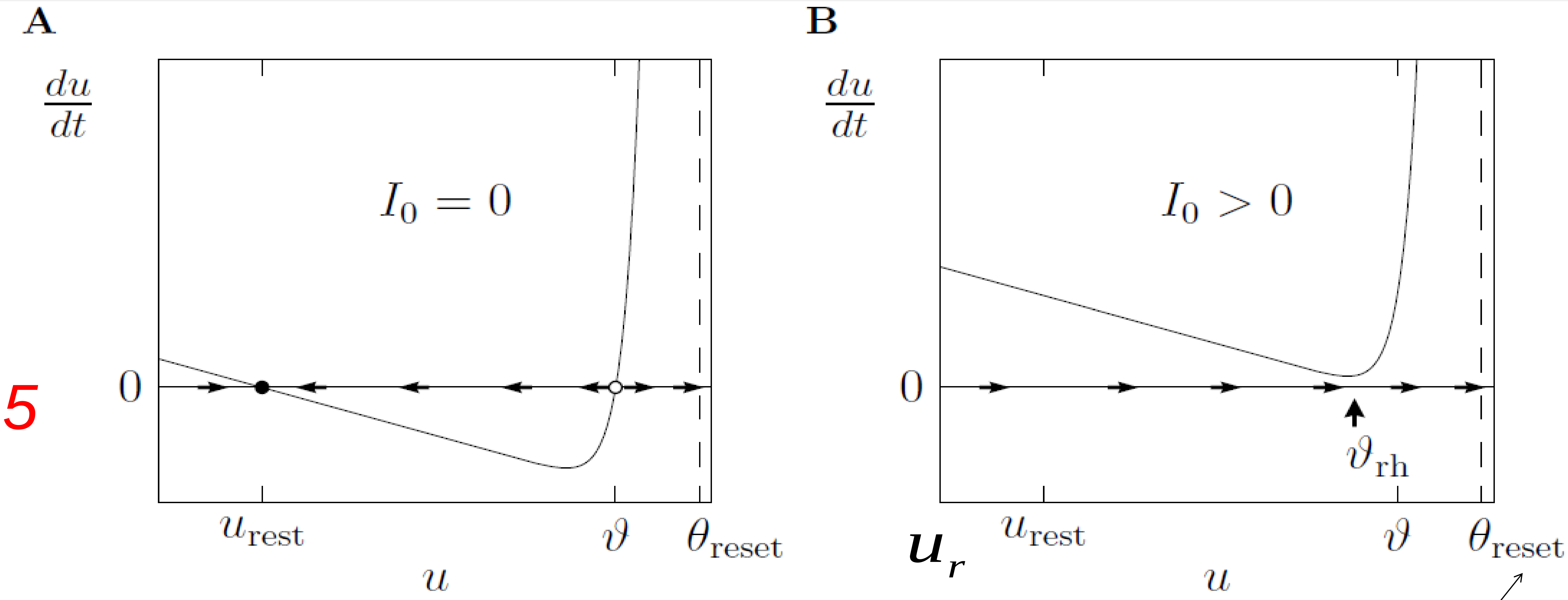
-What is a good neuron model?
-How can we estimate parameters of models?
-What is a neuron model good for?

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

1. Review: Nonlinear Integrate-and-fire



See:
week 1,
lecture 1.5

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

What is a good choice of **f** ?

If $u = \theta_{reset}$

then *reset to*

$$u = u_r$$

1. Review: Nonlinear Integrate-and-fire

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

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

What is a good choice of ***f*** ?

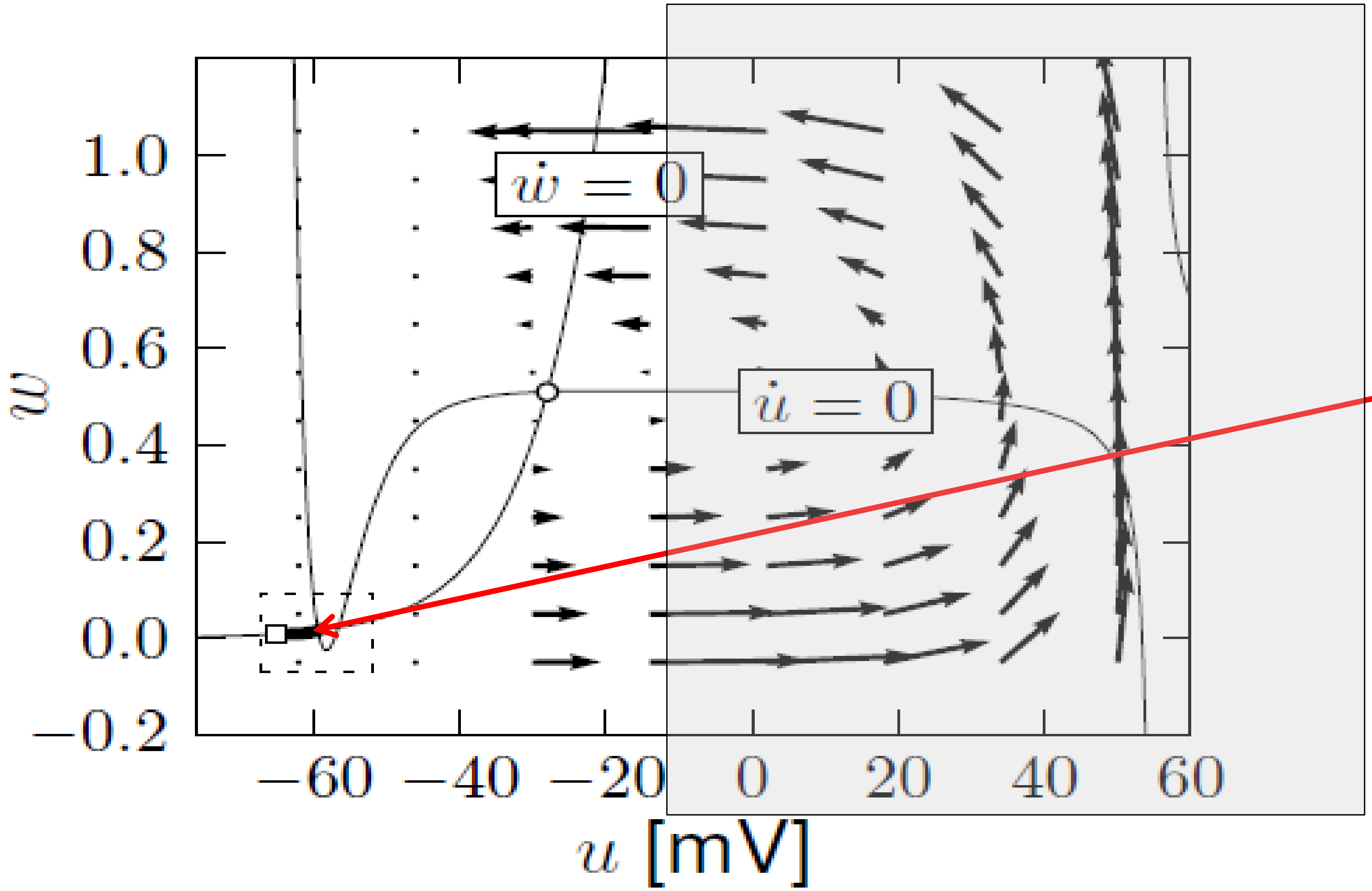
(i) Extract *f* from more complex models

(ii) Extract *f* from data

1. Review: 2-dim neuron models

(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

$$w \approx w_{rest}$$

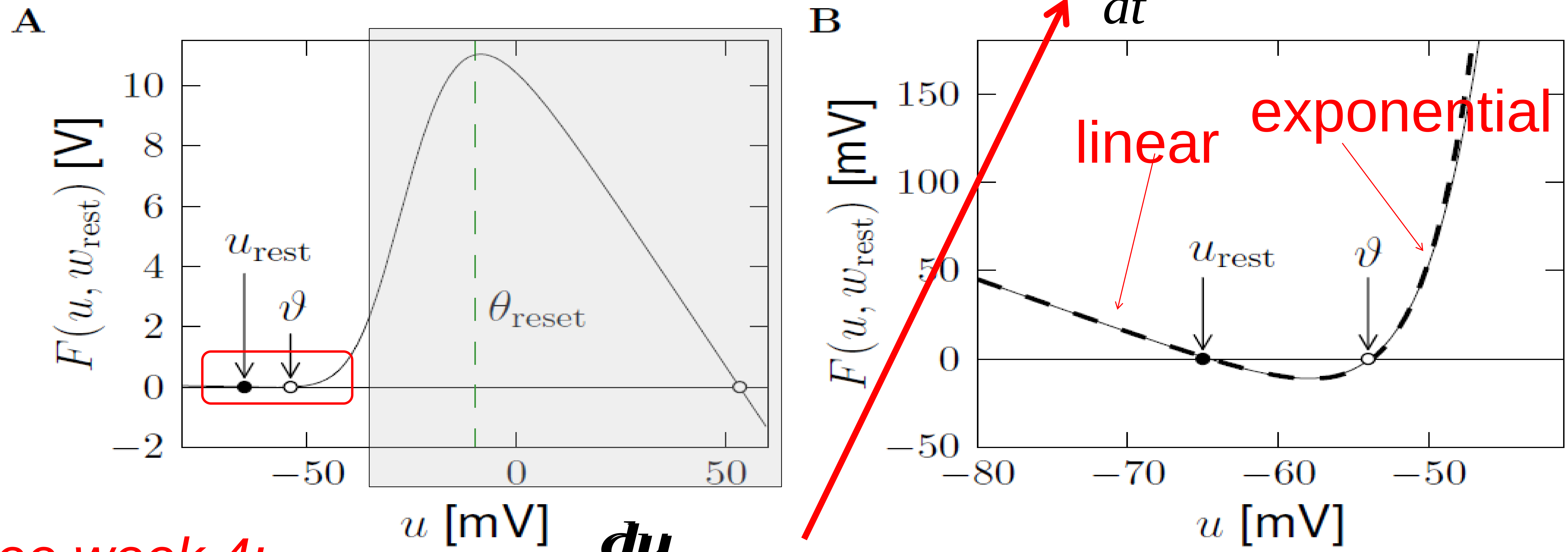
$$\tau \frac{du}{dt} = F(u,w) + RI(t)$$

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

B. Assume $w = w_{rest}$

1. 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

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

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

Separation of time scales

1. Review: Nonlinear Integrate-and-fire

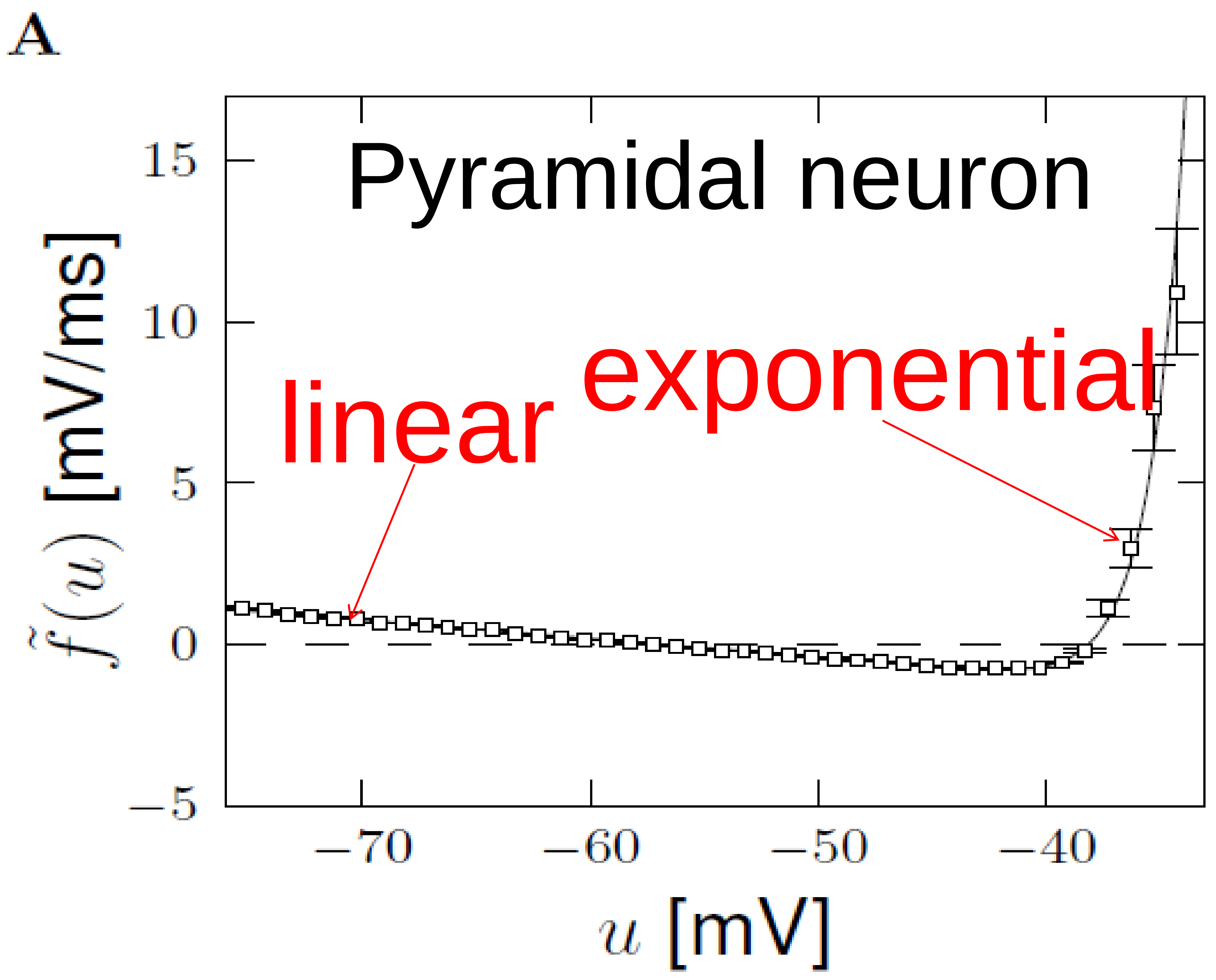
(ii) Extract *f* from data *Badel et al. (2008)*

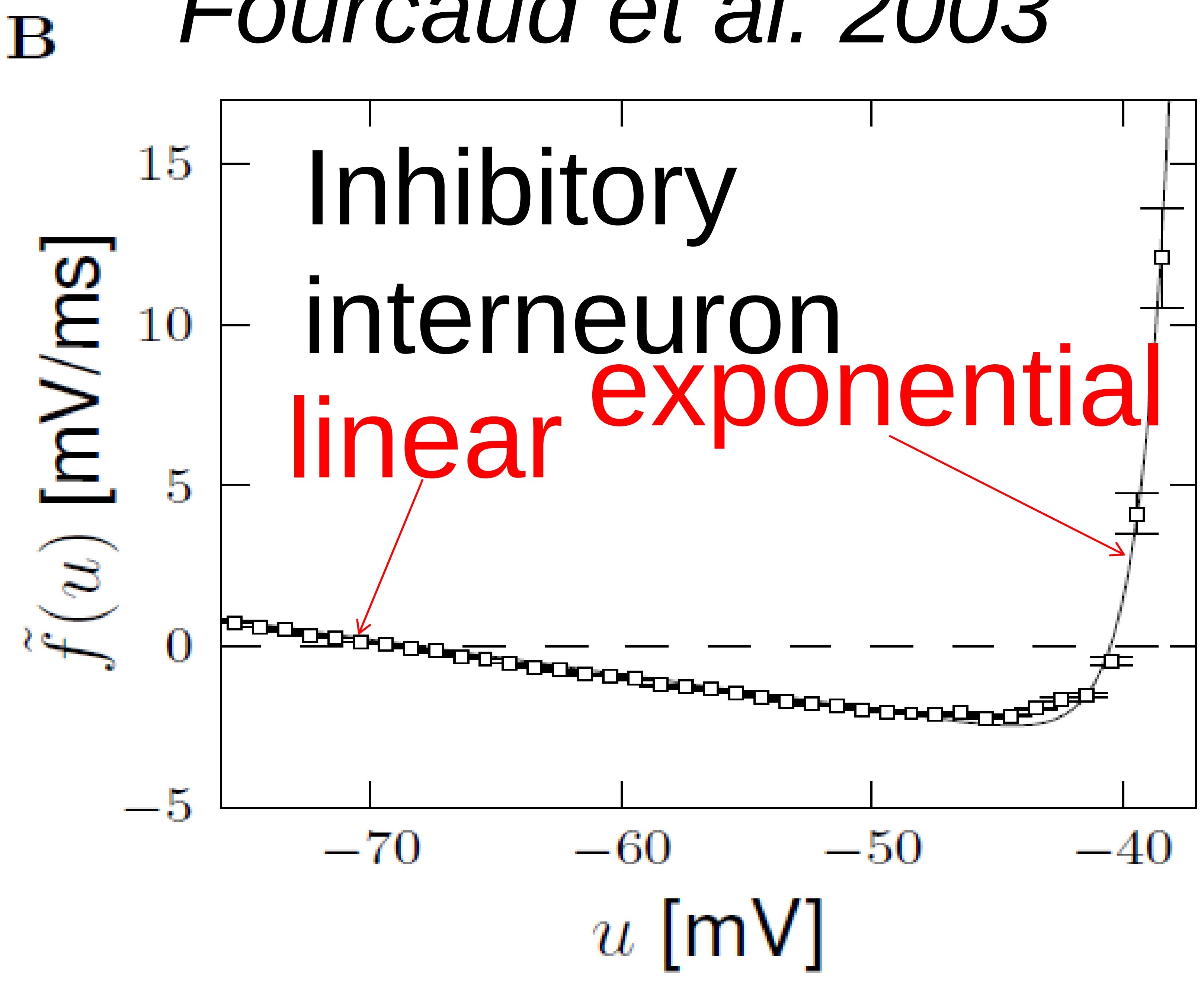
$$\tau \frac{du}{dt} = f(u) + R\,I(t)$$

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

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

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





Badel et al. (2008)

1. Review: Nonlinear Integrate-and-fire

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

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

Best choice of ***f*** : linear + exponential

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

BUT: **Limitations – need to add**

-Adaptation on slower time scales

-Possibility for a diversity of firing patterns

-Increased threshold ϑ after each spike

-Noise

1. Review: Nonlinear Integrate-and-fire

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BUT: **Limitations – need to add**

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-Noise

Conclusion – 1 What is a good neuron model?

A) Predict spike times
B) Predict subthreshold voltage
C) Easy to interpret (not a ‘black box’)
D) Systematic procedure to ‘optimize’ parameters
E) Flexible enough to account for a variety of phenomena
F) Account for adaption and firing patters

How can we find good, but easy-to-interpret neuron models

A) Derived from detailed Hodgkin-Huxley
B) Construct simple phenomenological model

Conclusion – 1 What is a good neuron model?

How can we find good, but easy-to-interpret neuron models

A) Derived from detailed Hodgkin-Huxley

Step 1: reduce to 2 dimensions
Step 2: Separation of time scales.
Step 3: focus on spike initiation zone.
Step 4: During spike initiation keep w constant.

Steps 1 to 4 yield an Exponential I&F model.

Step 5 (next): make w flexible again by giving it a dynamics.

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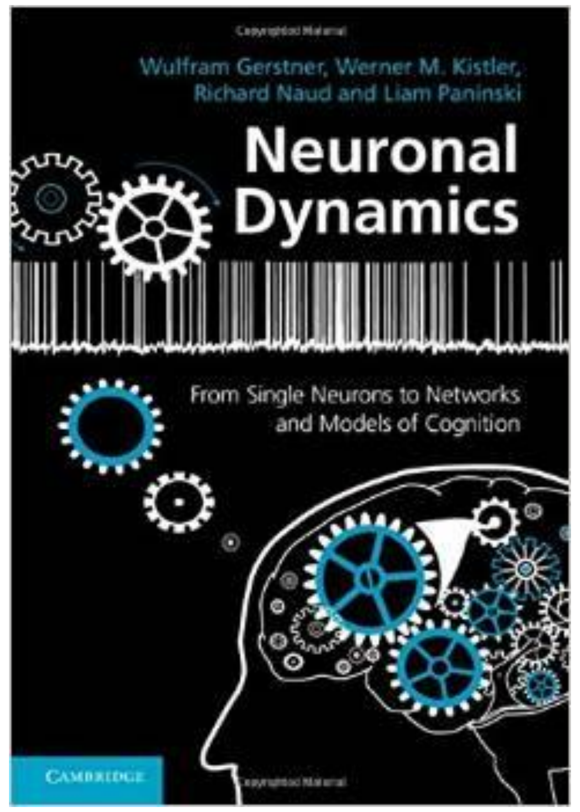

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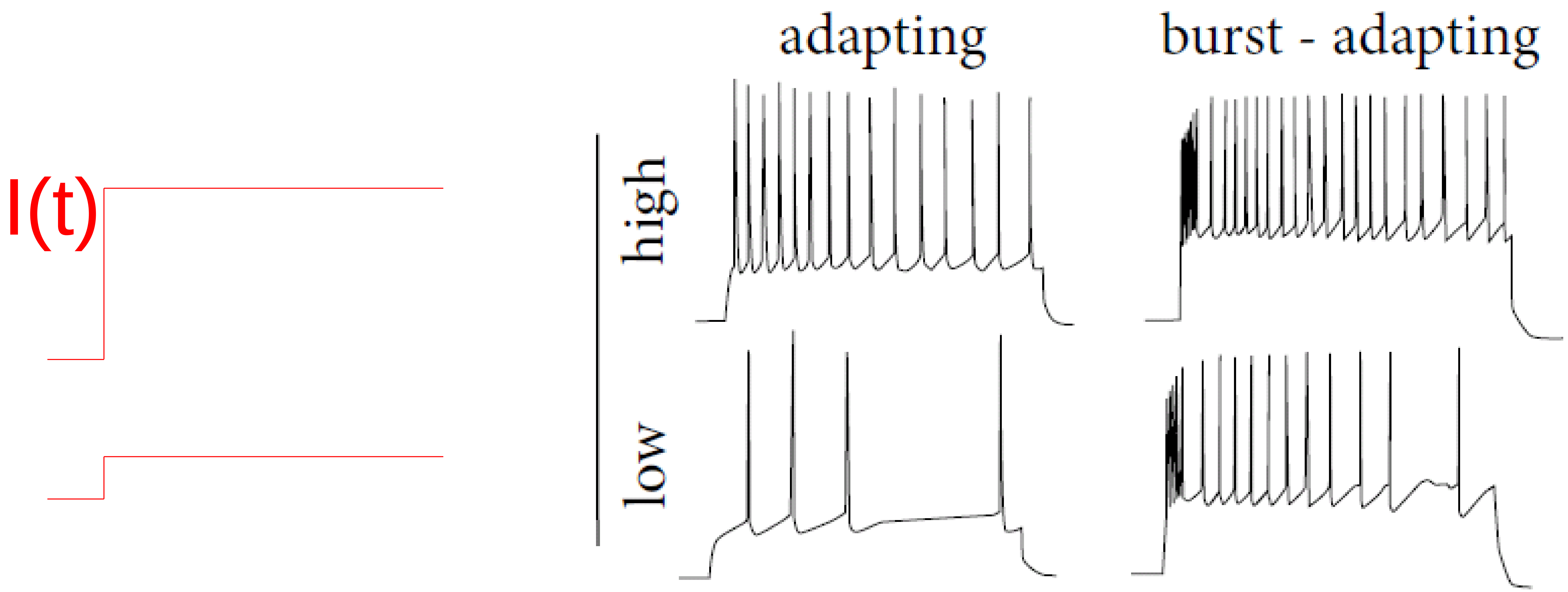
2 Adaptation

Step current input – neurons show adaptation



Data:
Markram et al.
(2004)

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

2 Adaptation

What is adaptation?
‘Firing that slows down in response to step input’
(→ previous slide)

Idea:
Add one (or several) variables to exponential IF model, so as to account for adaptation
(→ next slide)

2 Adaptive Exponential I&F

Add adaptation variables:

Blackboard !

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

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

Exponential I&F
+ **1 adaptation** var.
= AdEx

SPIKE AND RESET

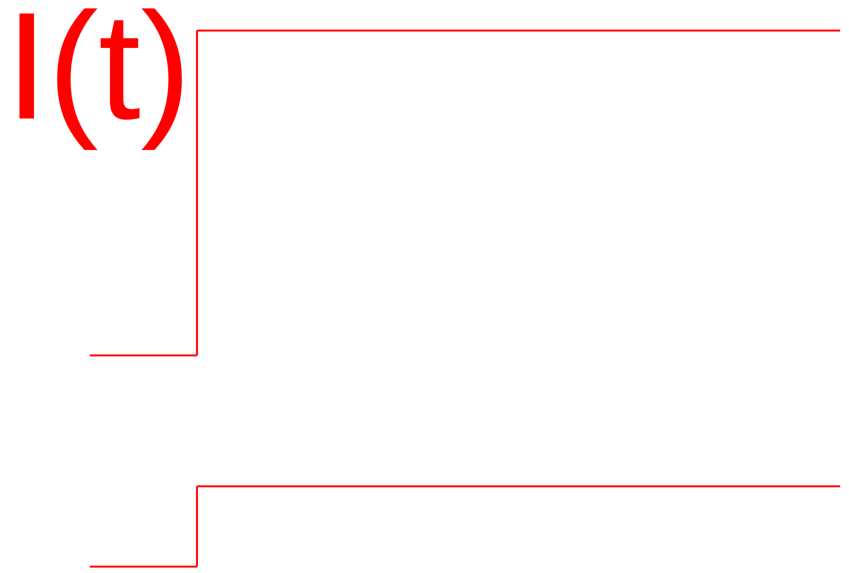
after each spike w_k jumps by an amount b_k

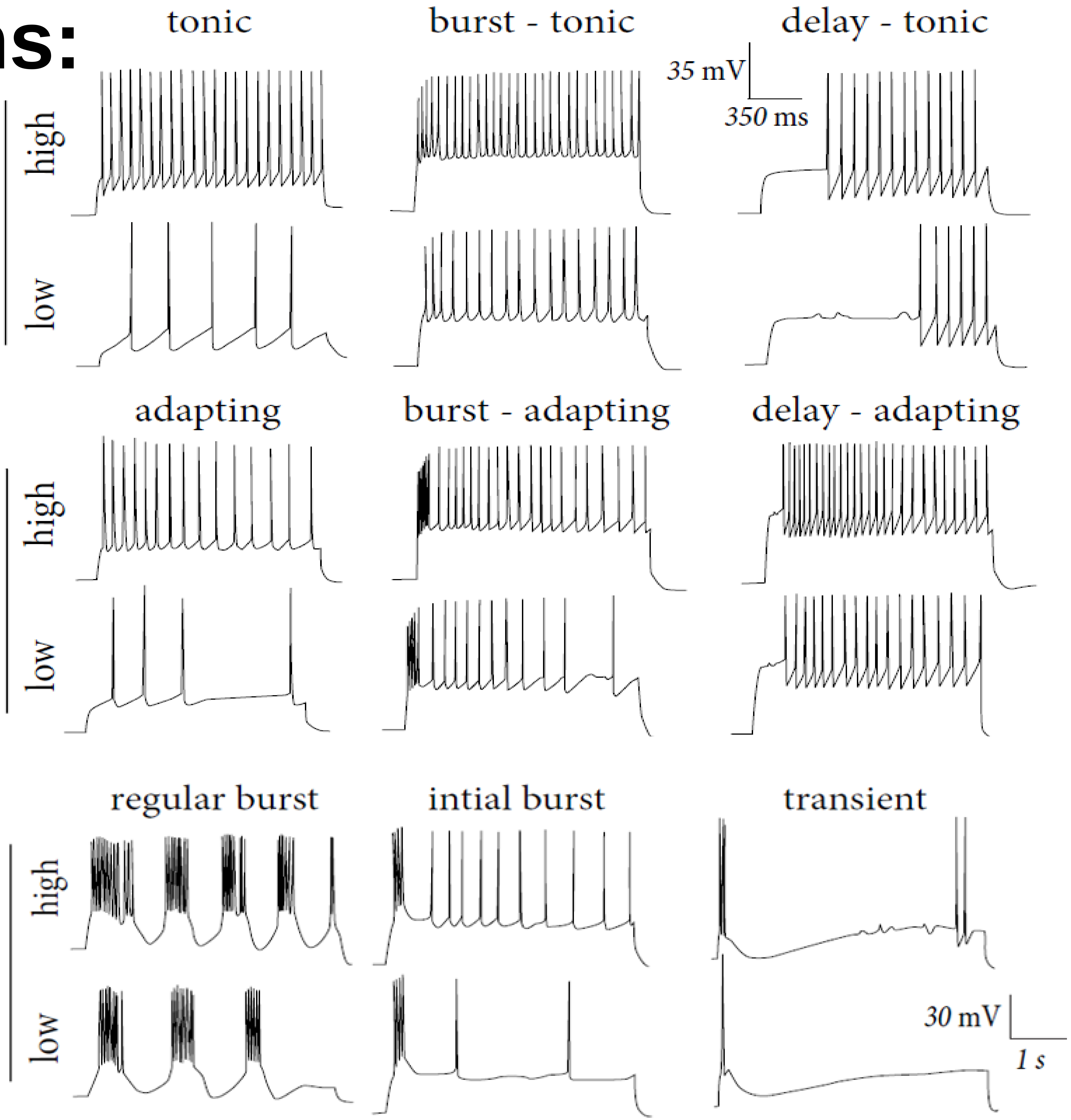
$If \quad u = \theta_{reset} \quad then \quad reset\ to\ u = u_r$

AdEx model, Brette&Gerstner (2005):

Firing patterns:

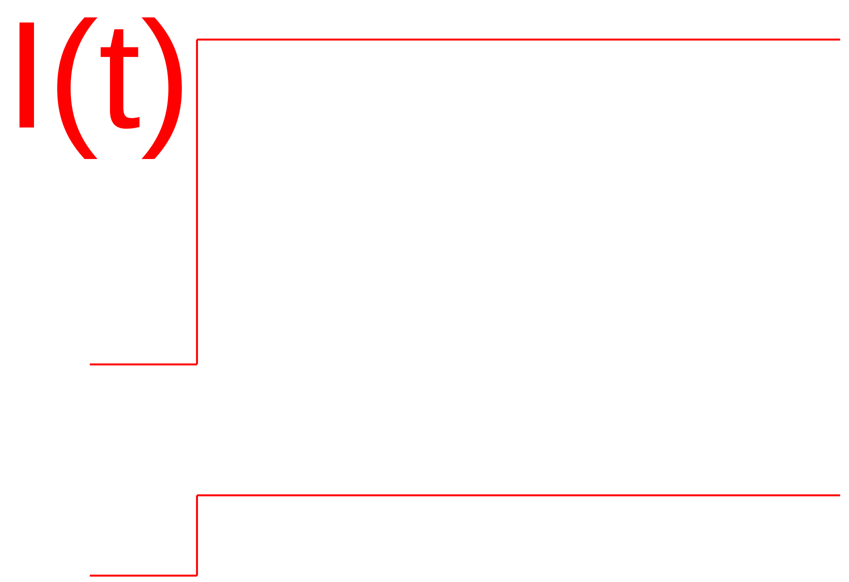
Response to
Step currents,
Exper. Data,
Markram et al.
(2004)





Firing patterns:

Response to
Step currents,
AdEx Model,
Naud&Gerstner



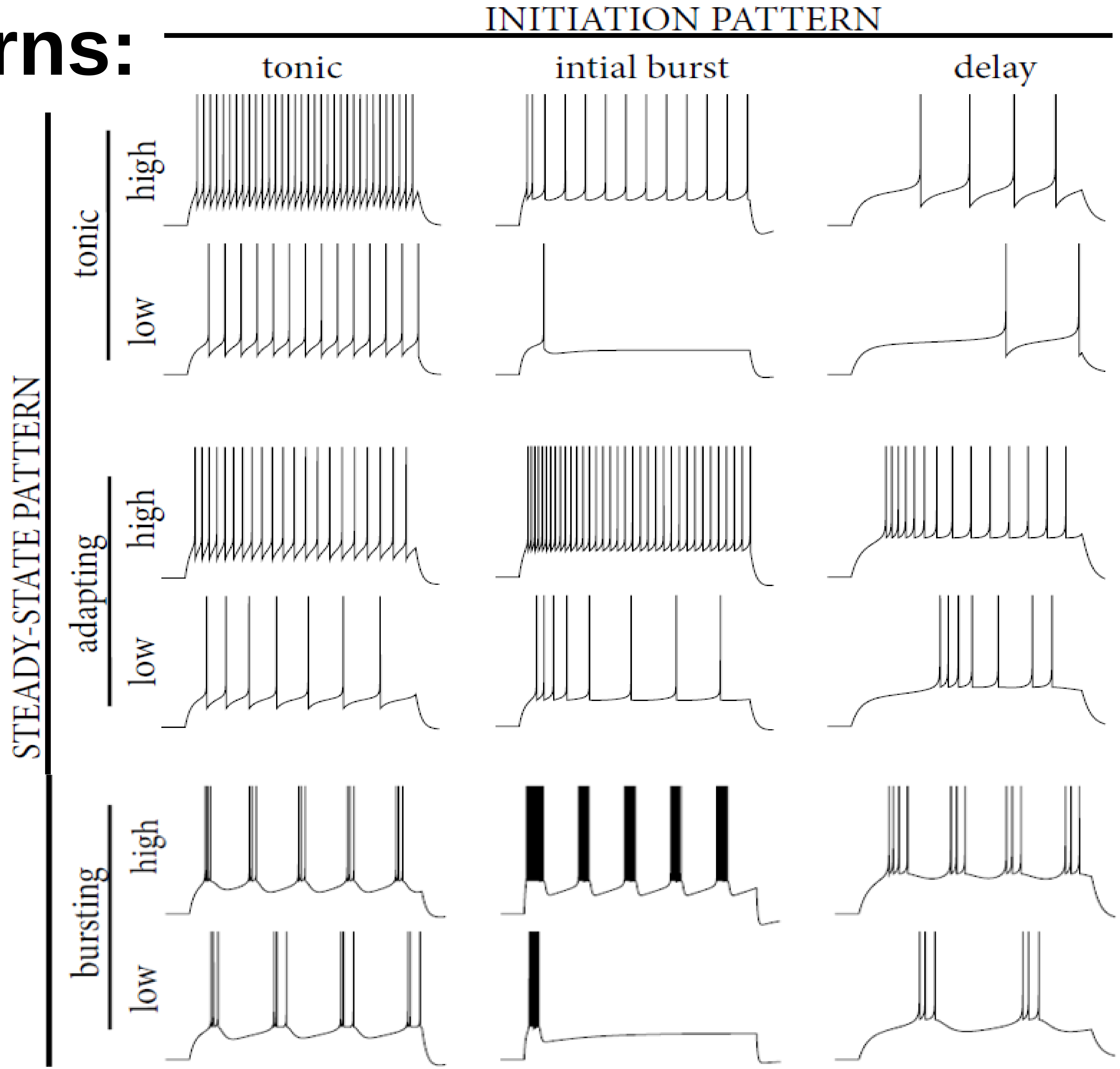


Image:
Neuronal Dynamics,
Gerstner et al.
Cambridge (2002)

Conclusion – 2 Firing patterns

There are many different firing patterns.
Experimentalists have classified them in 9 different groups.
Non-adapting (=tonic), adapting, bursty;
Combined with or without initial burst or delay.

The AdEx model can also account for 9 different types of patterns – changing just 3 parameters!

We will consider parameters a, b, and u_r.

But before we start we need to construct the nullclines.

Week 12 - Firing Patterns

EPFL

Biological Modeling of Neural Networks:

Week `1 – Optimizing Neuron Models For Coding and Decoding

Wulfram Gerstner

EPFL, Lausanne, Switzerland

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2 Adaptive Exponential I&F

AdEx model: exponential I&F plus adaptation variable

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

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

Two variables →Phase plane analysis!

Can we understand the different firing patterns?

Quiz . Nullclines of AdEx

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

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

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 9:45

2. AdEx model

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

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

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

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

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

Can we understand the different firing patterns?

2. AdEx model – phase plane analysis

Next slides: phase plane analysis

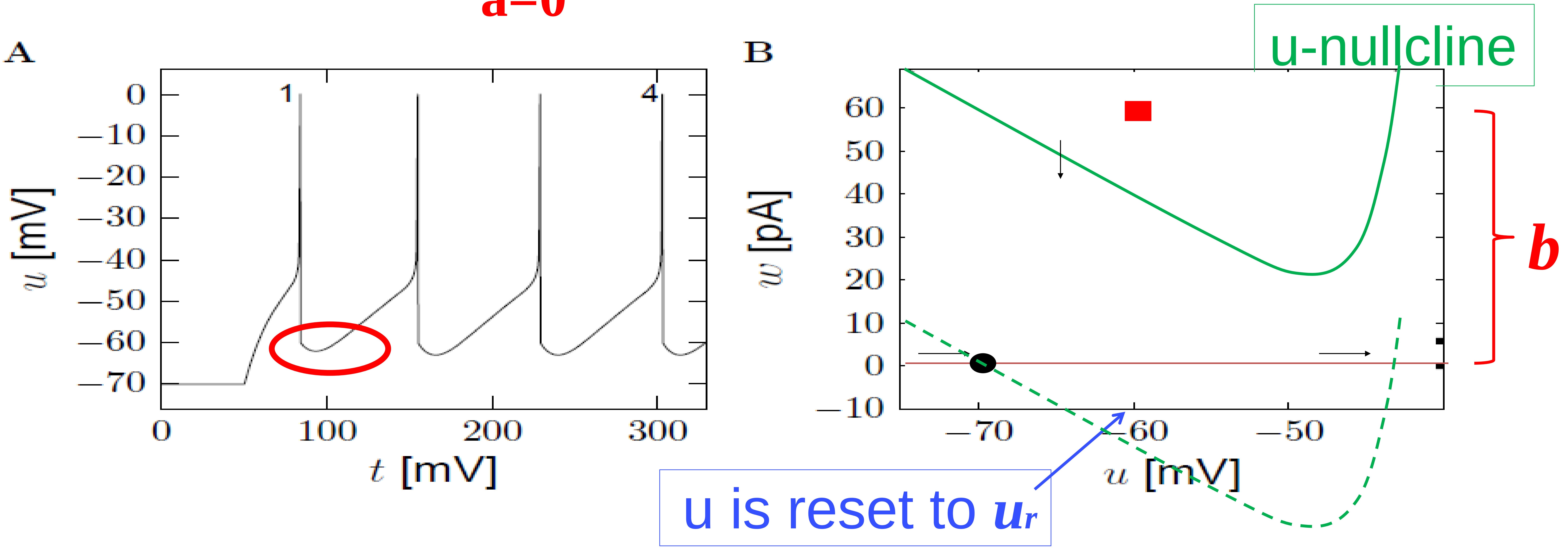
- 3 different examples of firing patterns
- 3 different choices of parameters a and b

2. AdEx model – phase plane analysis: large *b*

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

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

a=0

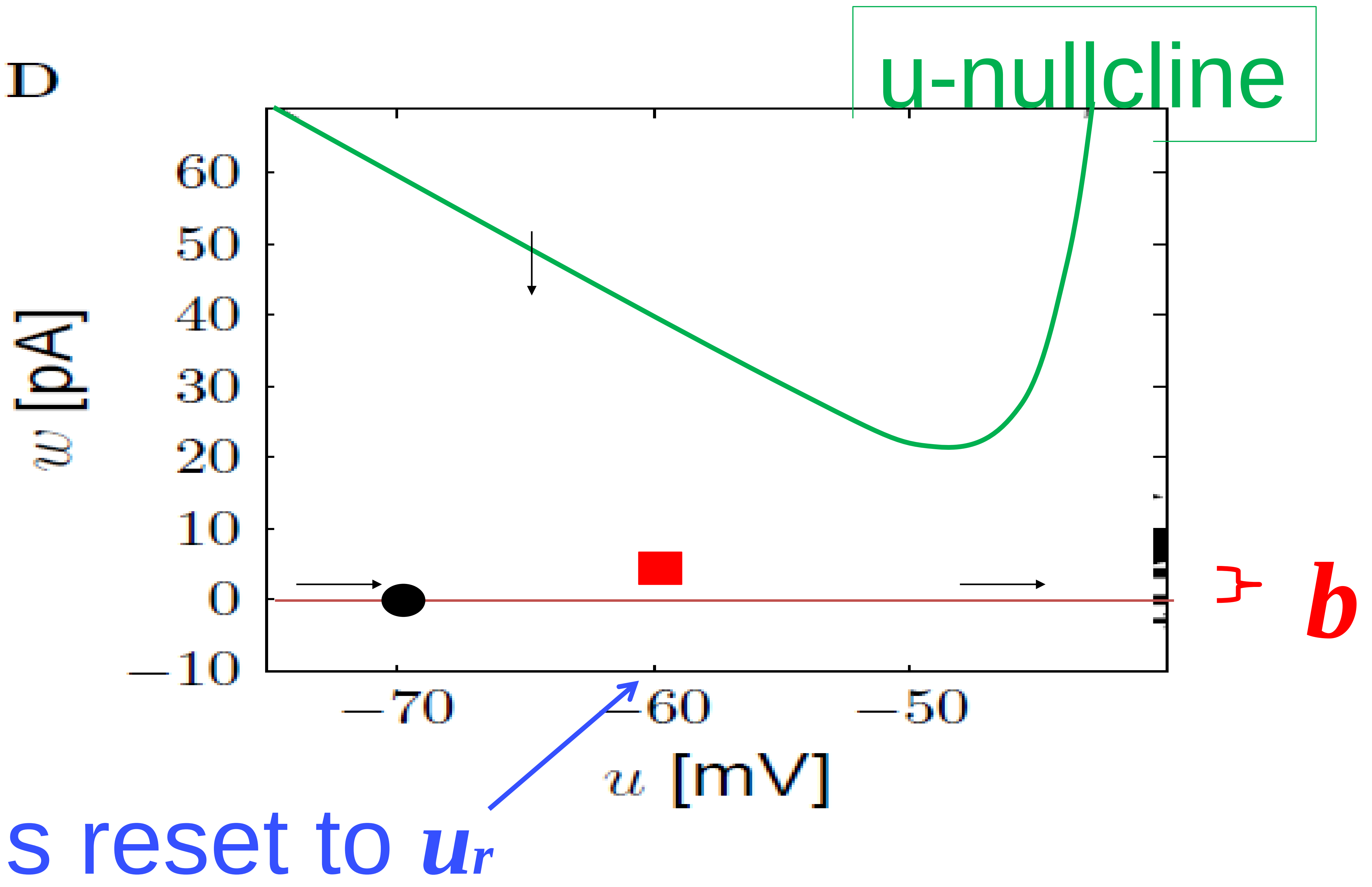


2. AdEx model – phase plane analysis: small *b*

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

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

adaptation



Quiz: AdEx model – phase plane analysis

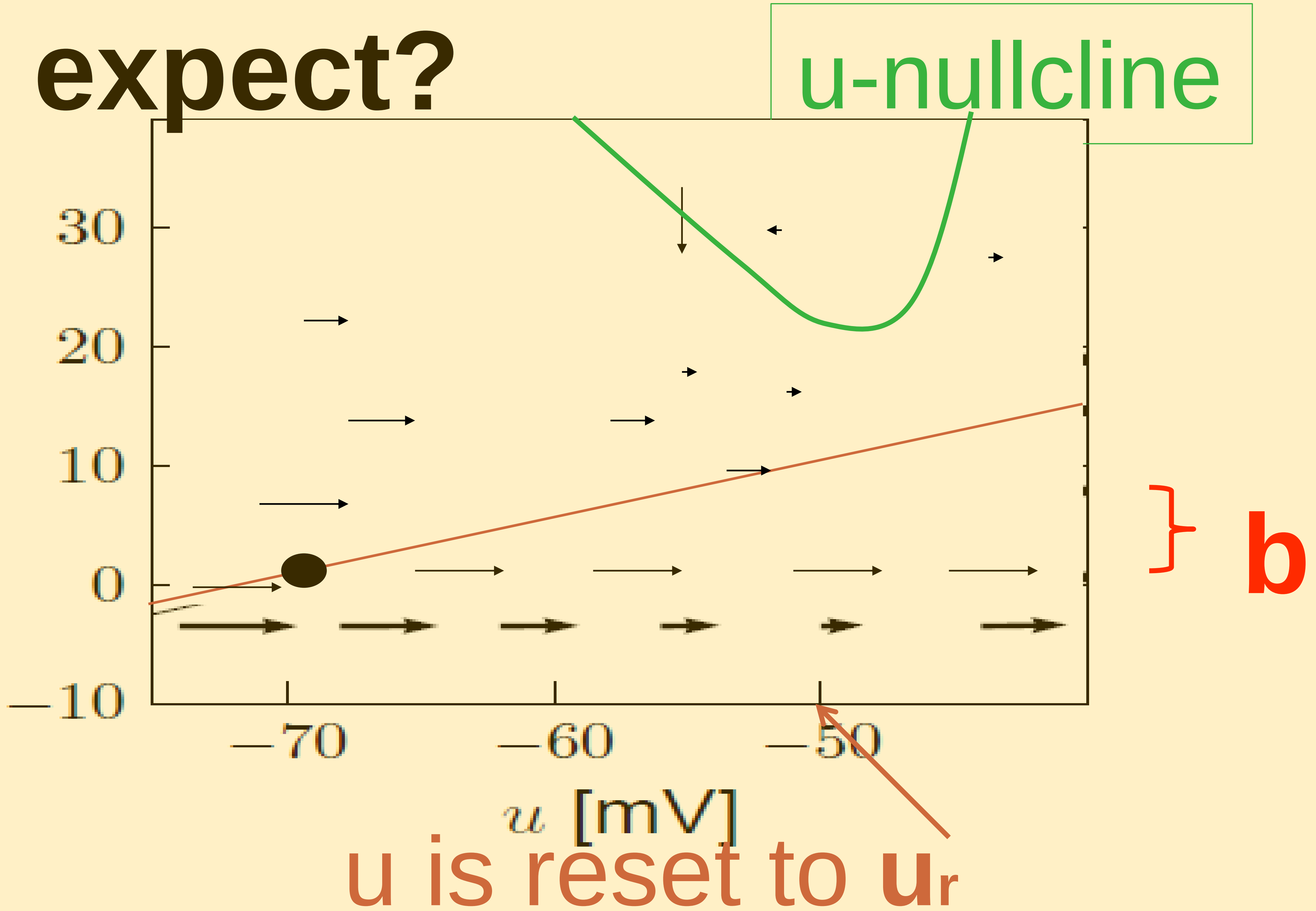
$\tau_w >> \tau$

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

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

What firing pattern do you expect?

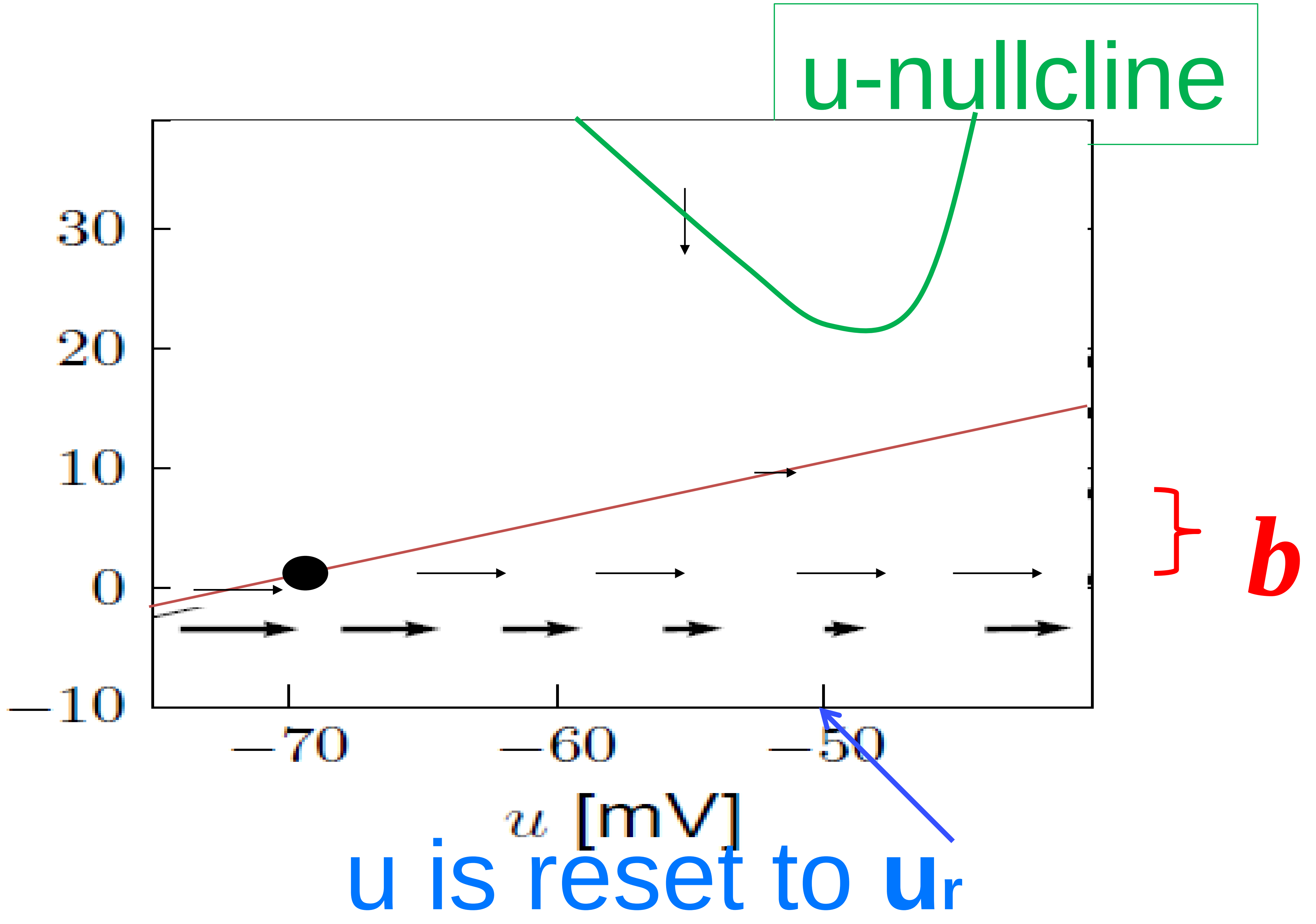
(i) Adapting
(ii) Bursting
(iii) Initial burst
(iv)Non-adapting



2. AdEx model – phase plane analysis: a>0

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

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



2 AdEx model and firing patterns

after each spike u is reset to u_r

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

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

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 Izikhevich (2003)

Review: Nonlinear Integrate-and-fire

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

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

Best choice of ***f*** : linear + exponential

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

BUT: **Limitations – need to add**

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

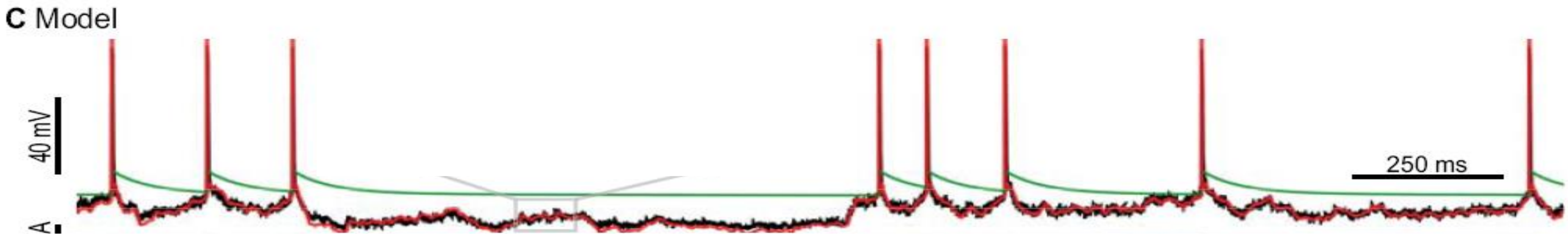
2. AdEx with dynamic threshold

Add dynamic threshold:

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

Threshold increases after each spike

$$\vartheta = \theta_0 + \sum_f \theta_1 (t - t^f)$$



2. Generalized Integrate-and-fire

We started with a one-dimensional nonlinear I&F model

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

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

we added

- ✓ -Adaptation variables
- ✓ -Possibility for firing patterns
- ✓ -Dynamic threshold ϑ
- -Noise → Use 'escape noise' (see earlier lecture) → Section 9.4

Week 12 - Firing Patterns

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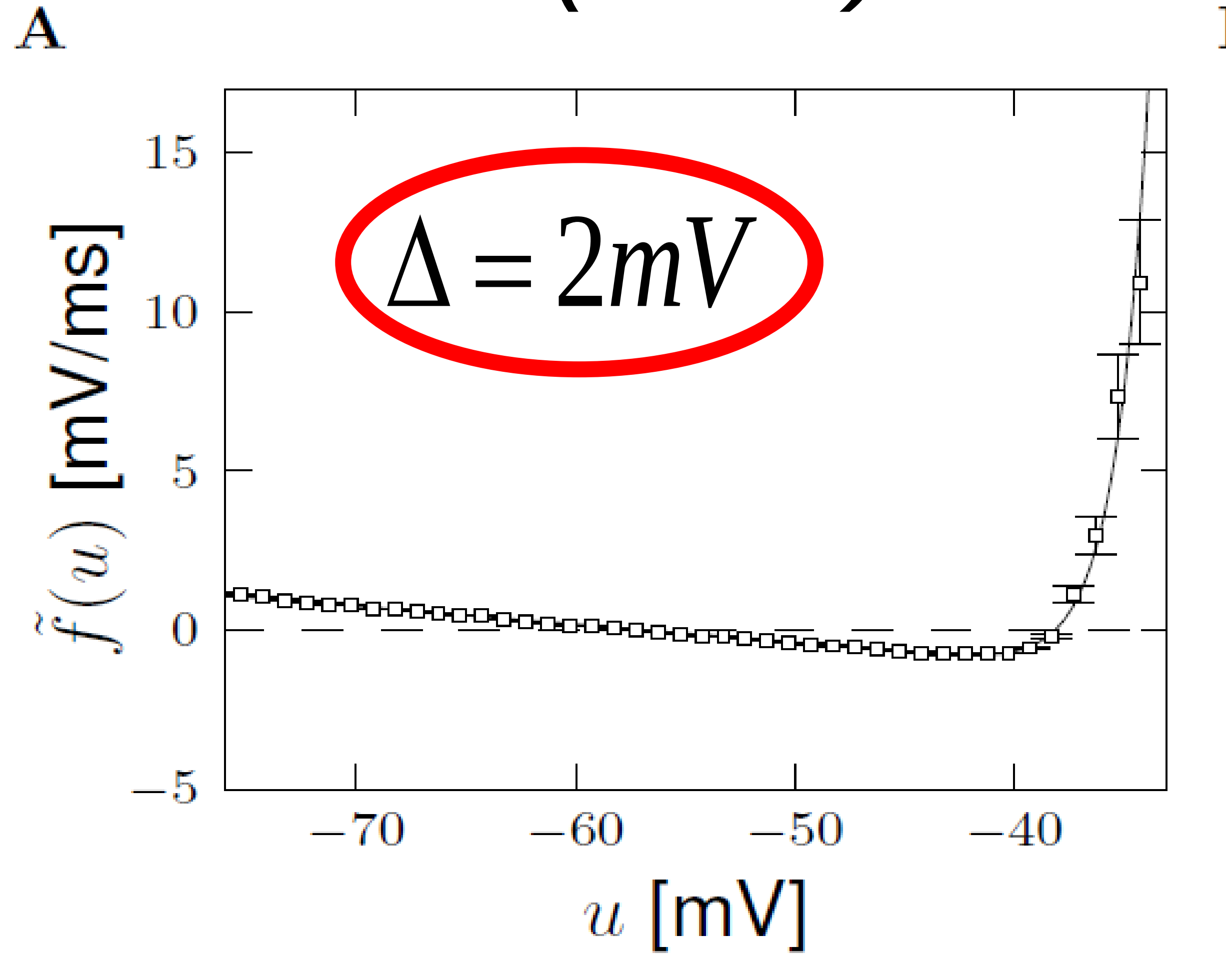
3. Review: Exponential Integrate-and-Fire

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

What is the size of the parameter Δ ?

→ experiments?

Badel et al (2008)

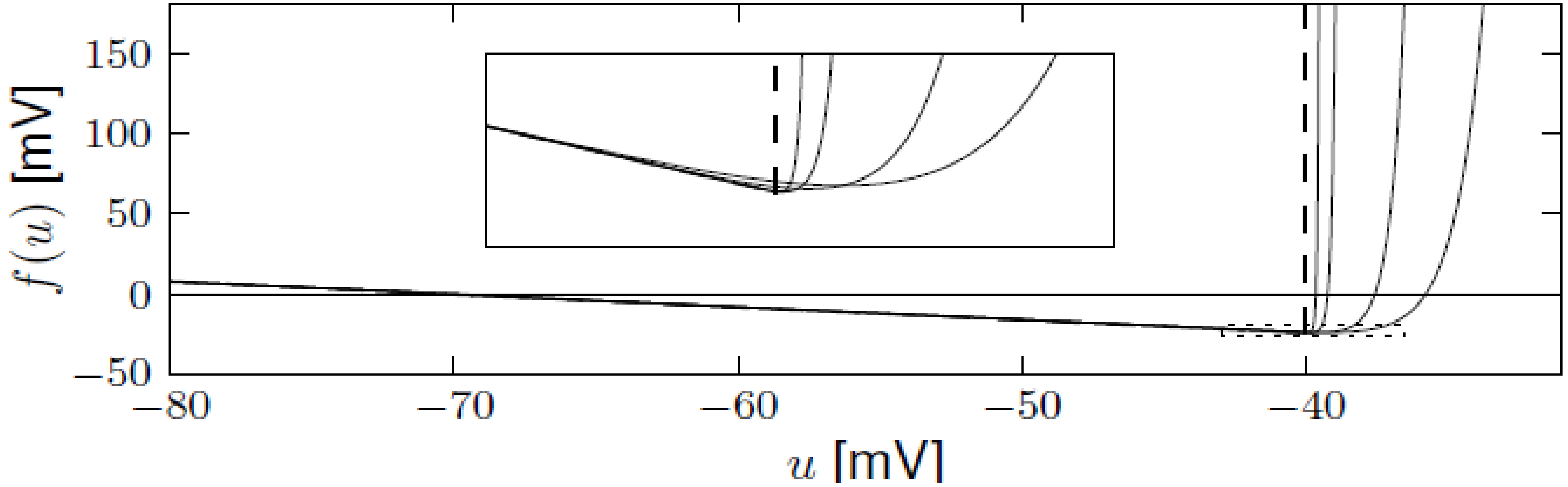


What is the role of the parameter Δ ?

→ make Δ smaller and smaller

3. Exponential versus Leaky Integrate-and-Fire

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



In the limit $\Delta \to 0$ the exponential I&F simplifies to

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

Leaky Integrate-and-Fire

Reset if u= ϑ

3. Adaptive leaky integrate-and-fire

Defined by 1) voltage equation, adaptation variables

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

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

2) spike and reset

If $u = \vartheta(t)$ *then reset to* $u = u_r$

and

w_k *jumps by an amount* b_k

3) Dynamic threshold $\vartheta(t)$

Exercise 1: from adaptive IF to SRM

$$\tau \frac{du}{dt} = -(u - u_{rest}) - R\alpha w + RI(t), \qquad \alpha = \{0,1\}$$

$$If \quad u = \vartheta \; then \;\; reset\, to \; u = u_r$$

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

Start at 10:15

Next lecture at 10:25

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

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

Hint: voltage reset equivalent to short current pulse

A – what is $\varepsilon(s)$ **?** **(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 q $\eta(s)$ **?**

(iii) $x(s) = C[\exp(-\frac{s}{\tau}) - \exp(-\frac{s}{\tau_w})]$ **(iv) Combi of (i) + (iii)**

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!

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

$$\vartheta(t) = \theta_0 + \sum_f \theta_1 (t - t^f)$$

Spike Response Model (SRM)

Representation of potential and threshold by linear filters of arbitrary shape

Firing condition: $u(t) = \vartheta$

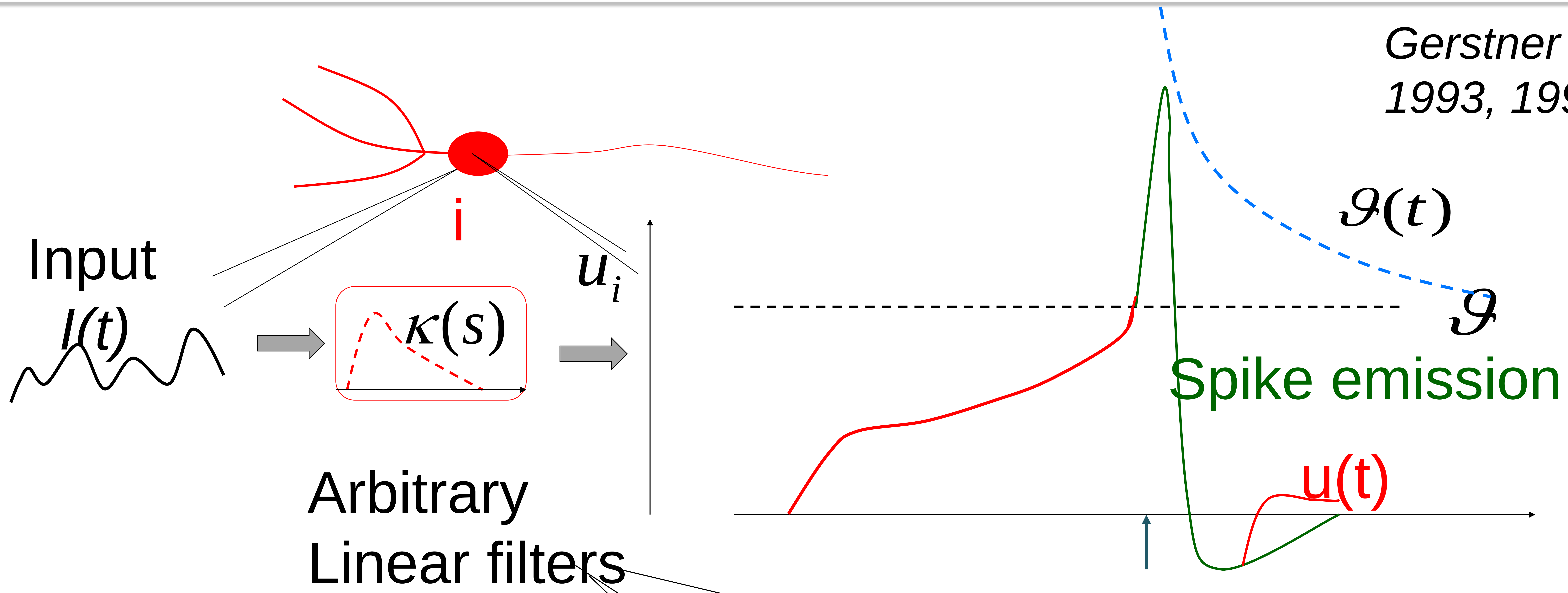
Gerstner et al. (1996)

3. Spike Response Model (SRM)

- Voltage equation in integrated form, includes linear filters
- Linear filters shape neuronal behavior (e.g., bursting)
- Linear filters can result from linear differential equations
- Alternatively linear filters can be directly fitted to experiments
- Simple ‘flow diagram’ (next slide)

3. Spike Response Model (SRM)

Gerstner et al., 1993, 1996



potential

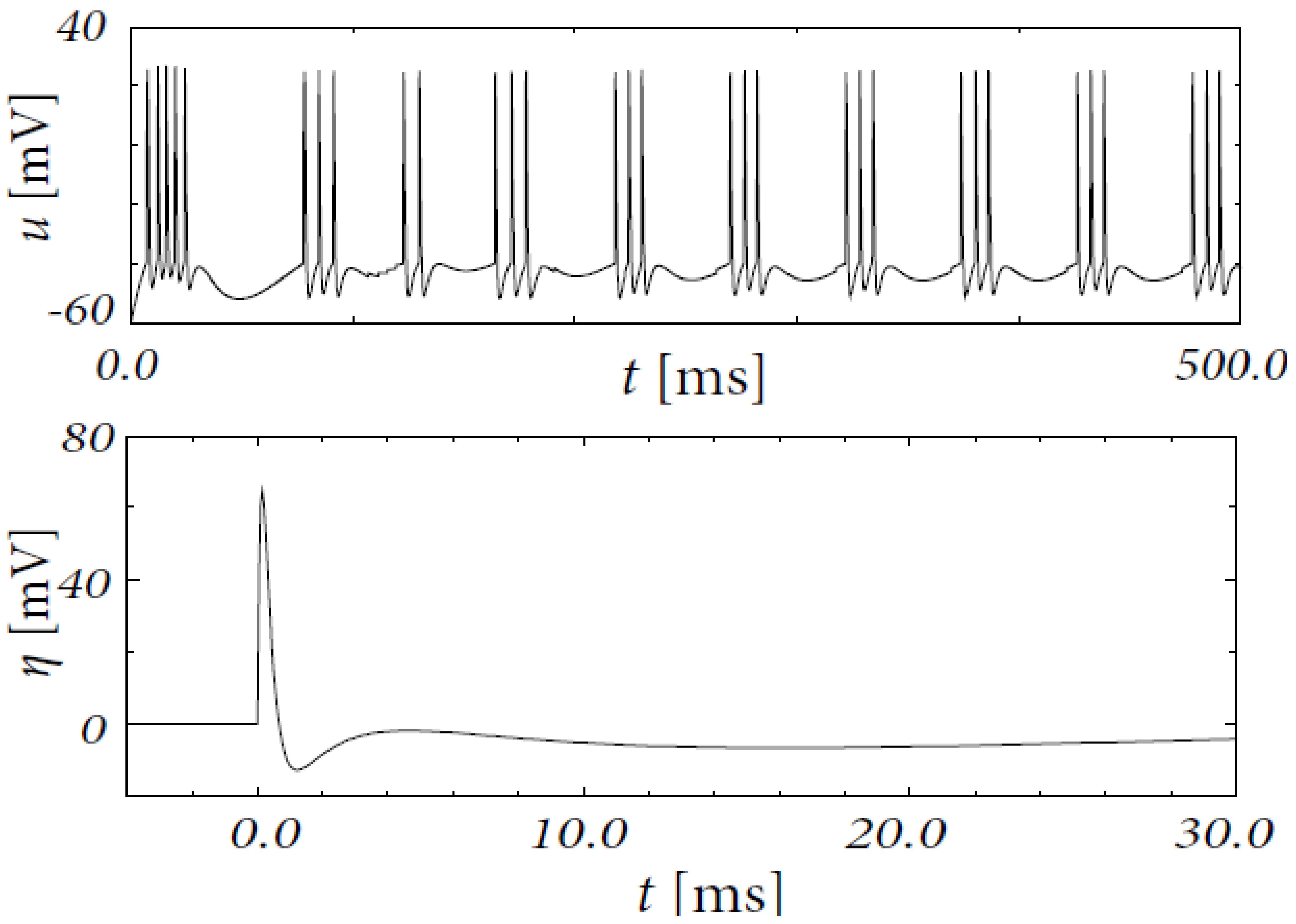
$$u(t) = \sum_{t'} \eta(t - t') + \int_0^{\infty} \kappa(s) I(t-s) ds + u_{rest}$$

threshold

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

3. Bursting in the SRM

SRM with appropriate η leads to bursting

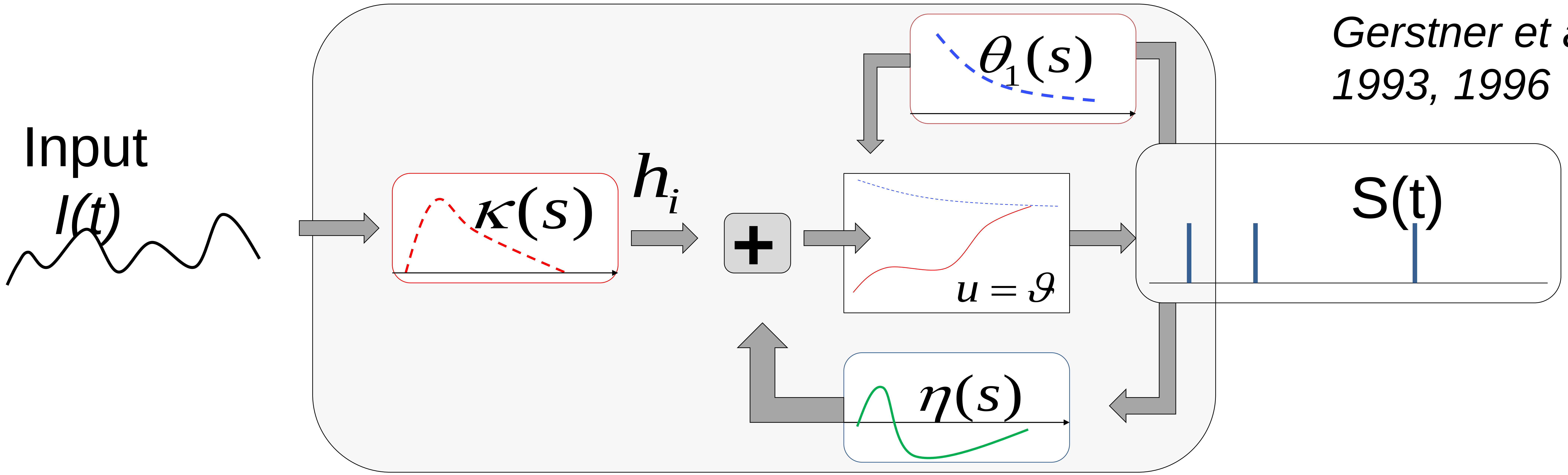


$$u(t) = \sum_f \eta\,(t - t^f) \;+\; \int_0^\infty ds\, \kappa(s) I(t-s) + u_{rest}$$

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

3. Spike Response Model (SRM)

Gerstner et al., 1993, 1996



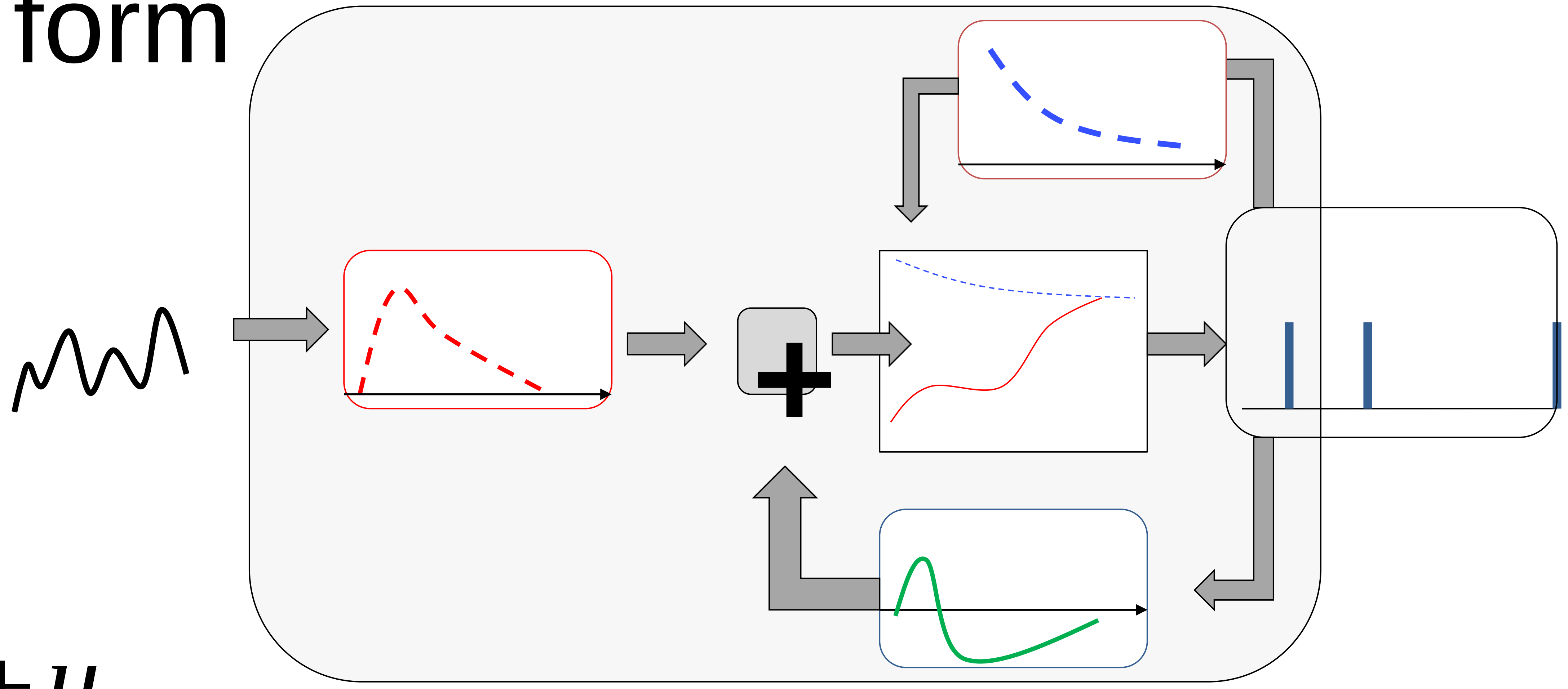
potential $$u(t) = \sum_{t'} \eta(t - t') + \int_0^\infty \kappa(s) I(t-s) ds + u_{rest}$$

threshold $$\vartheta(t) = \theta_0 + \sum_{t'} \theta_1(t - t')$$

firing if $$u(t) = \vartheta(t)$$

3. Summary Spike Response Model (SRM)

- Membrane potential in integral form
- Three arbitrary linear filters
- Threshold condition for firing



potential

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

threshold

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

firing if

$$u(t) = \vartheta(t)$$

Linear filters for
- input: κ
- refractoriness η
- threshold θ

EPFL

Biological Modeling of Neural Networks:

Week 12 – Optimizing Neuron Models For Coding and Decoding

Wulfram Gerstner

EPFL, Lausanne, Switzerland

√ 1 What is a good neuron model?
- Models and data

√ 2 AdEx model
- Firing patterns and adaptation

√ 3 Spike Response Model (SRM)
- Integral formulation

4 Generalized Linear Model
- Adding noise to the SRM

5 Parameter Estimation
- Quadratic and convex optimization

6. Modeling in vitro data
- how long lasts the effect of a spike?

4. Spike Response Model (SRM) = Generalized Linear Model GLM

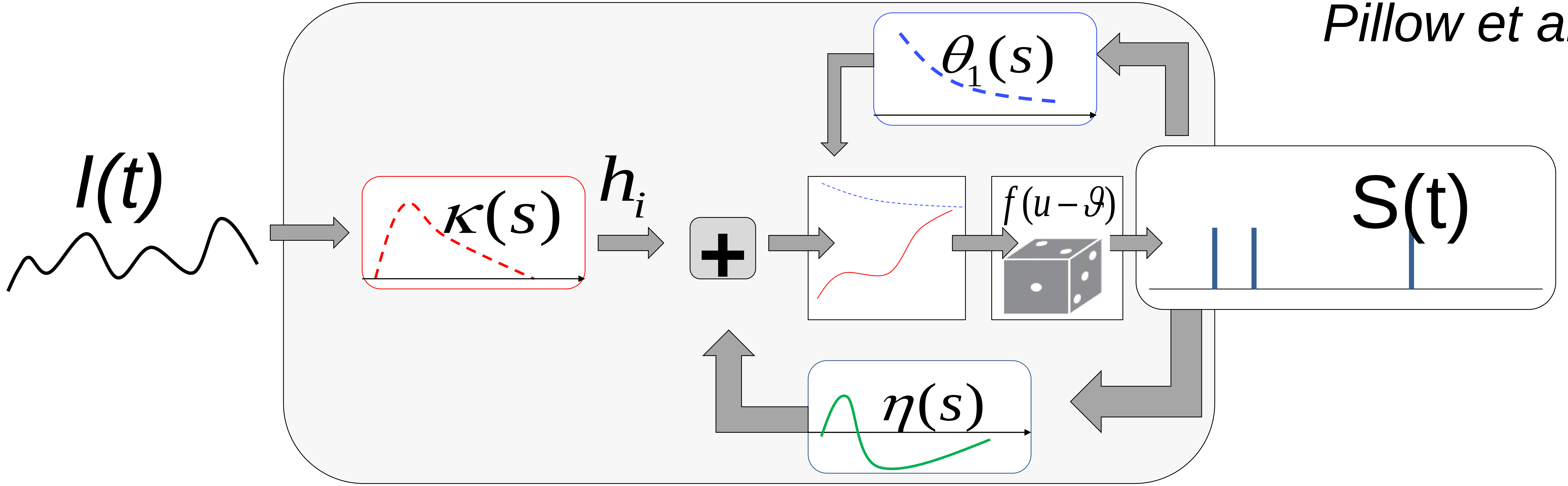
Gerstner et al., 1992,2000
Truccolo et al., 2005
Pillow et al. 2008

- take a (deterministic) spike response model
- add escape nose

→ Generalized Linear Model (GLM)

4. Spike Response Model (SRM)
Generalized Linear Model GLM

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



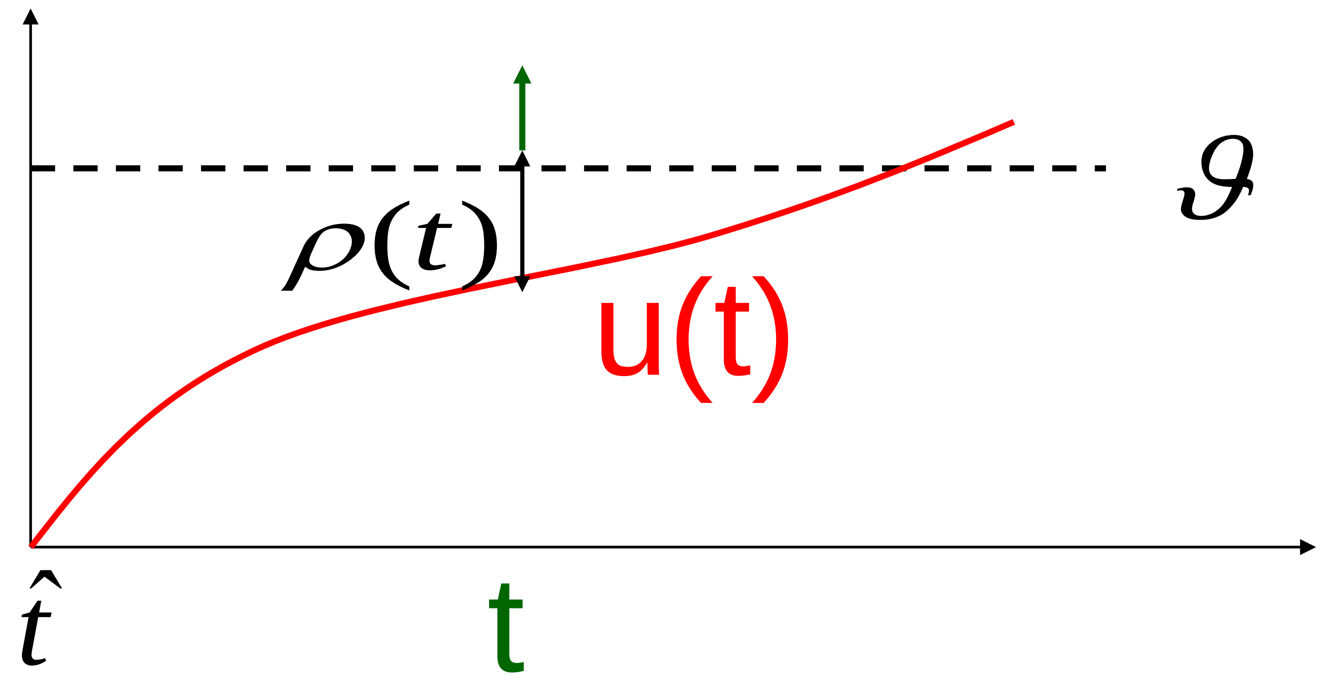
potential $u(t) = \int \eta(s) S(t-s) ds + \int_0^\infty \kappa(s) I(t-s) ds + u_{rest}$

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

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

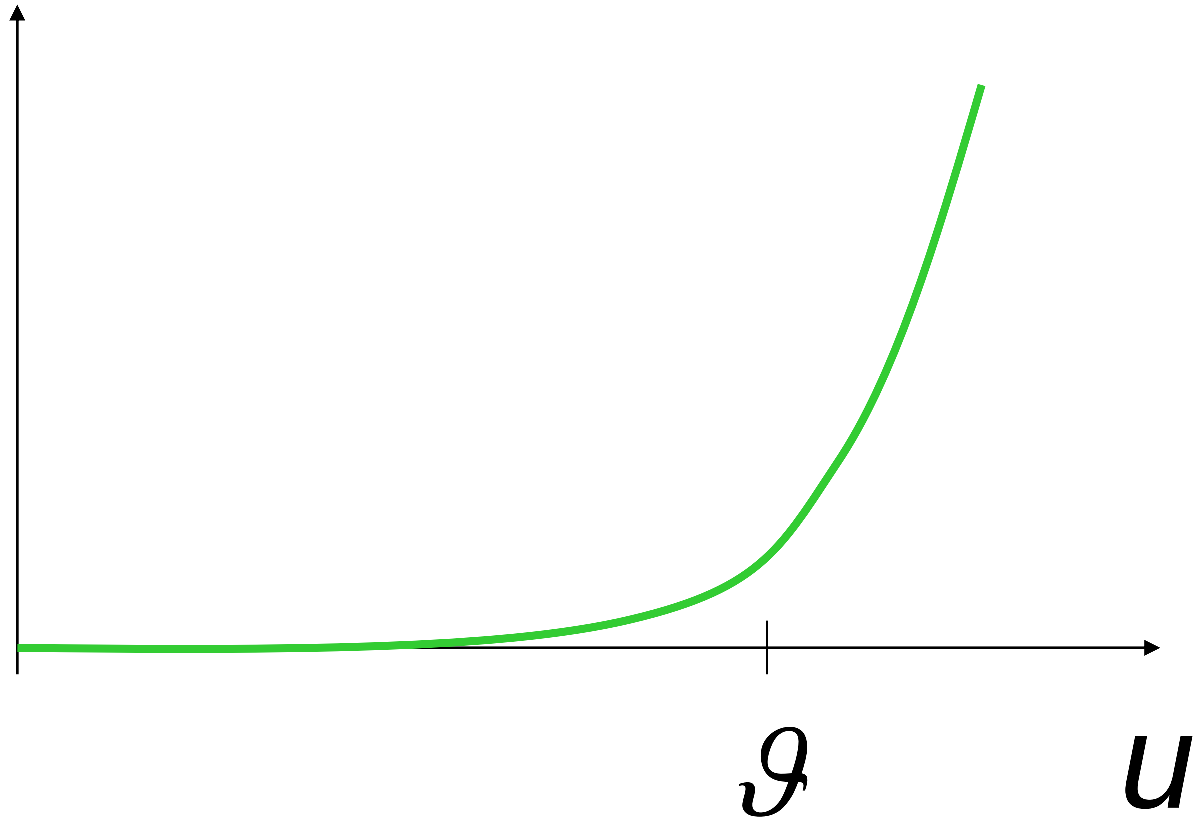
4. Review: Escape noise

escape process



escape rate

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



escape rate

$$\rho(t) = \rho_0 \exp\left(\frac{u(t) - \vartheta}{\Delta}\right)$$

Example: leaky integrate-and-fire model

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

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

Exerc. 2.1: Non-leaky IF with escape rates

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

$$reset\ to\ u_r = 0$$

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

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

Integrate for constant input (repetitive firing)

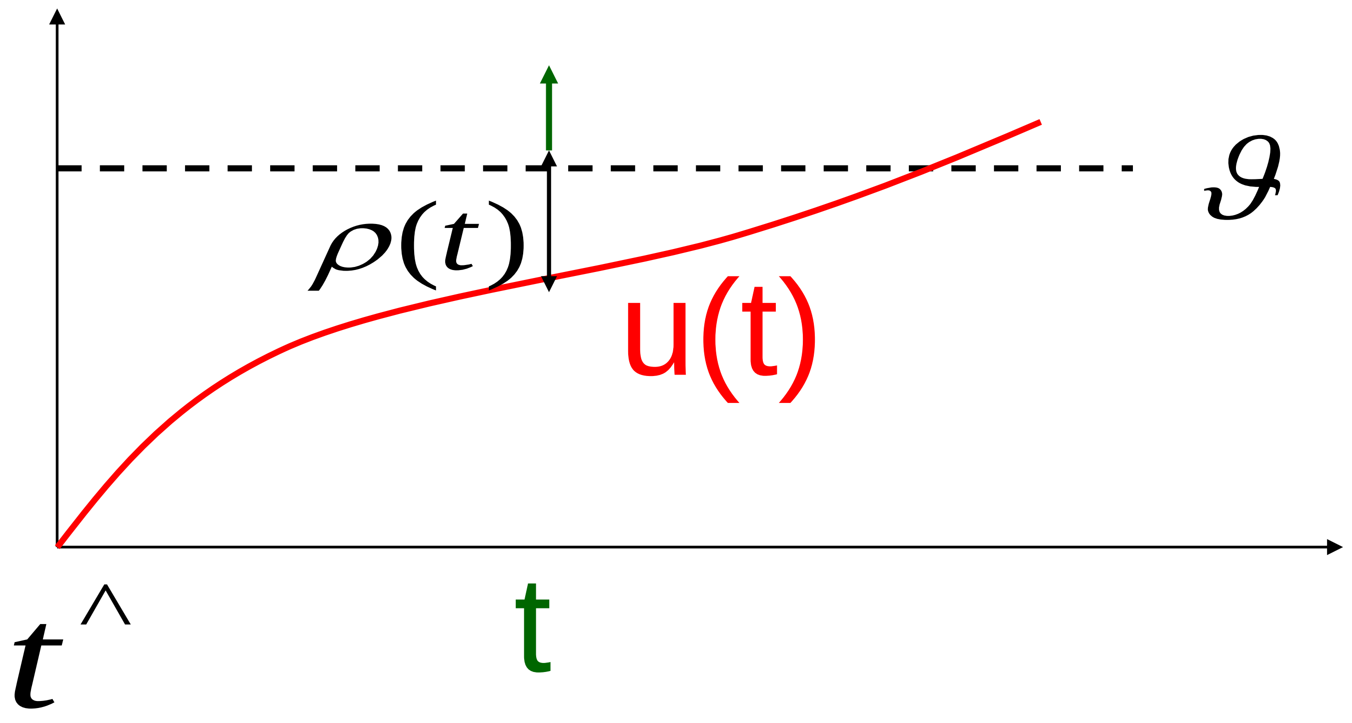
12 minutes,
Next lecture
at 10:51

Calculate

- potential $u(t-\hat{t})$
- hazard $\rho(t-\hat{t}) = \beta \cdot [u(t-\hat{t}) - \vartheta]_+$
- survivor function $S(t-\hat{t})$
- interval distrib. $P_0(t-\hat{t})$

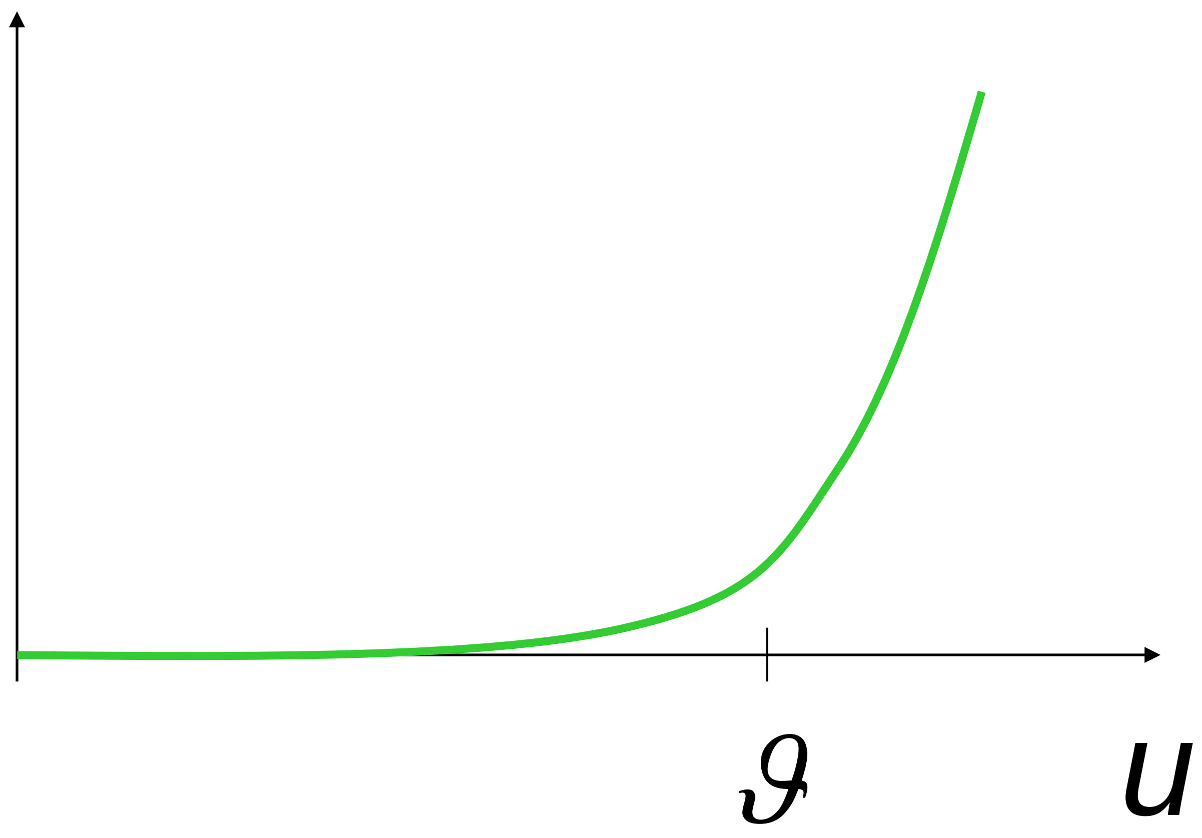
4. Review: Escape noise

escape process



escape rate

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



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

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

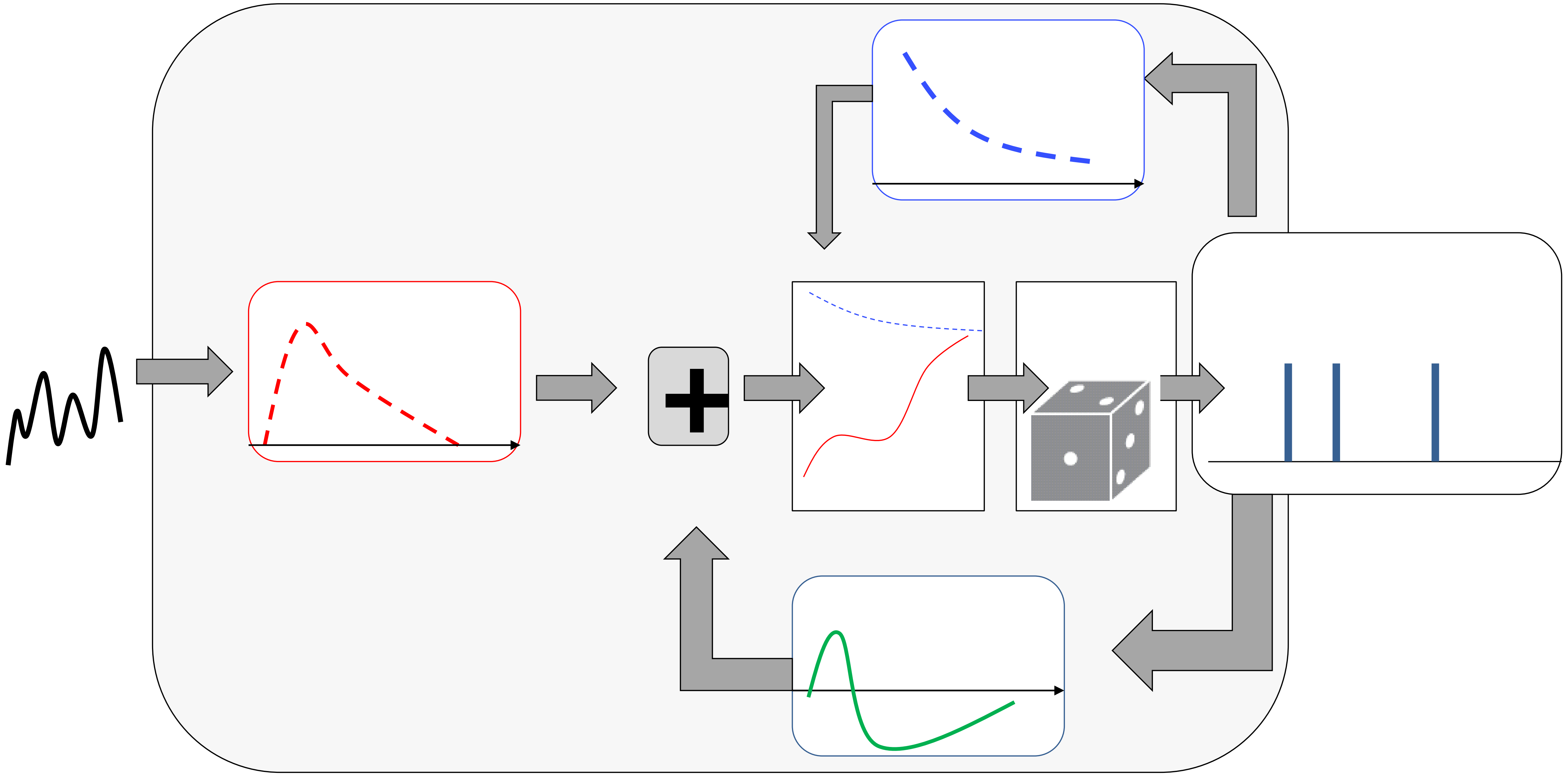
escape rate

Survivor function

Good choice

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

4. Likelihood of spike train



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

4. Likelihood of a spike train in GLMs

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

→Blackboard

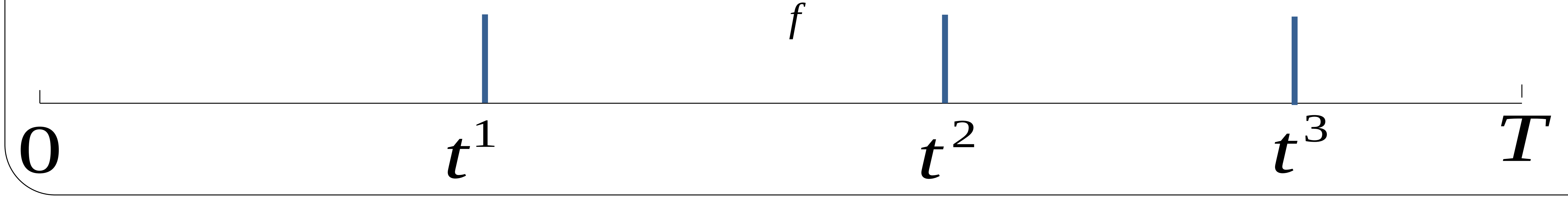
Measured spike train with spike times $t^1, t^2, \ldots t^N$

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

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

4. Log-Likelihood of a spike train

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

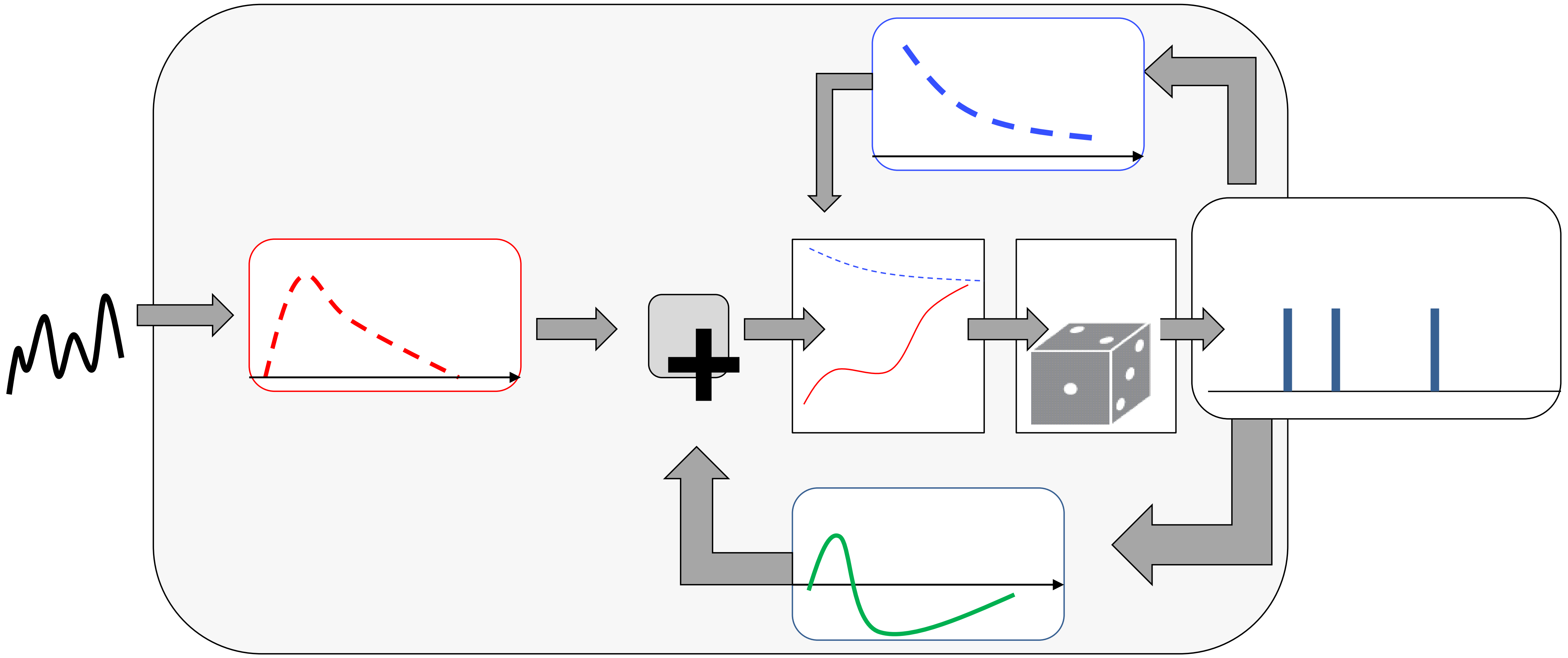


$$L(t^1,\ldots,t^N) = \exp(-\int_0^{t^1} \rho(t')dt')\rho(t^1)\cdot\exp(-\int_{t^1}^{t^2} \rho(t')dt')\rho(t^2)\ldots\cdot\exp(-\int_{t^N}^{T} \rho(t')dt')$$

$$L(t^1,\ldots,t^N) = \exp(-\int_0^{T} \rho(t')dt')\prod_f \rho(t^f)$$

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

4. Summary: SRM with escape noise = GLM



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

we now use this framework for parameter optimization of neuron model

1) A GLM is a Spike Response Model with escape noise. The advantage of the escape noise as a noise model is that we have an explicit mathematical formula for the likelihood of a spike train, given a model.
2) Knowing the input current and past spike times, the model makes a prediction for the difference between voltage and threshold at each moment in time, which gives the intensity $\rho(t)$ and the likelihood of a spike train

Week 12 - Parameter estimation

EPFL

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EPFL, Lausanne, Switzerland

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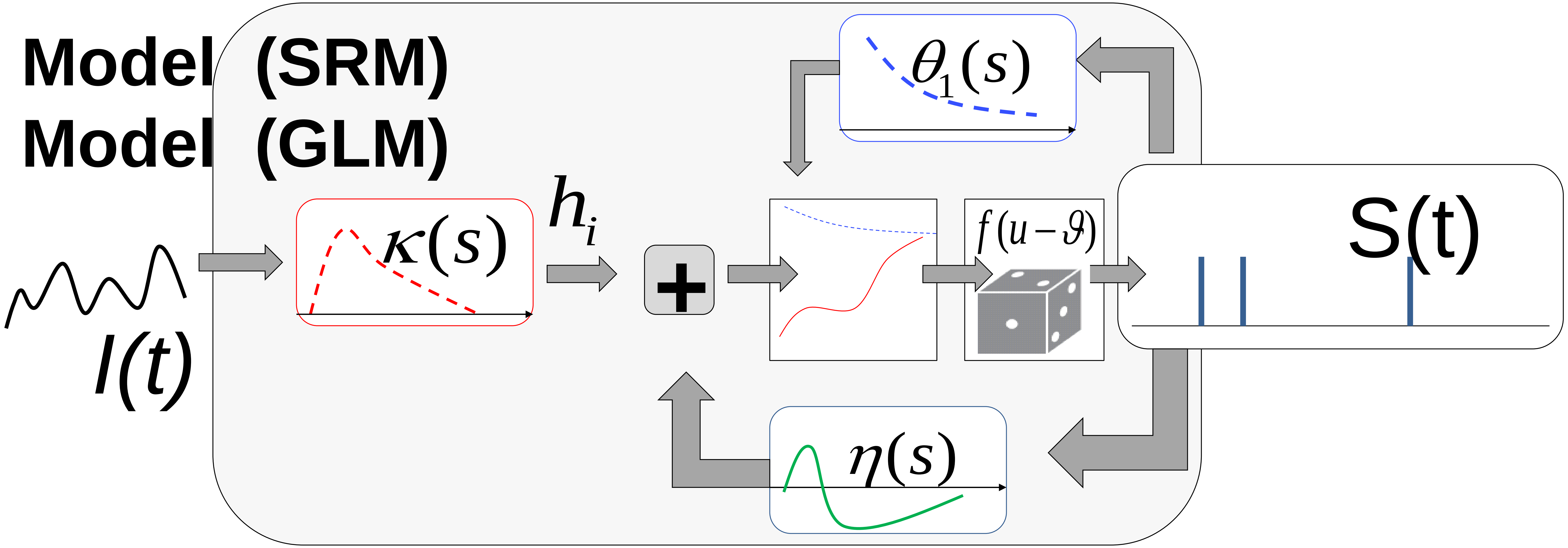
5 Parameter Estimation
- Quadratic and convex optimization

6. Modeling in vitro data
- how long lasts the effect of a spike?

5. Parameter estimation: voltage

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



Subthreshold potential

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

known spike train — known input

Linear filters/linear in parameters

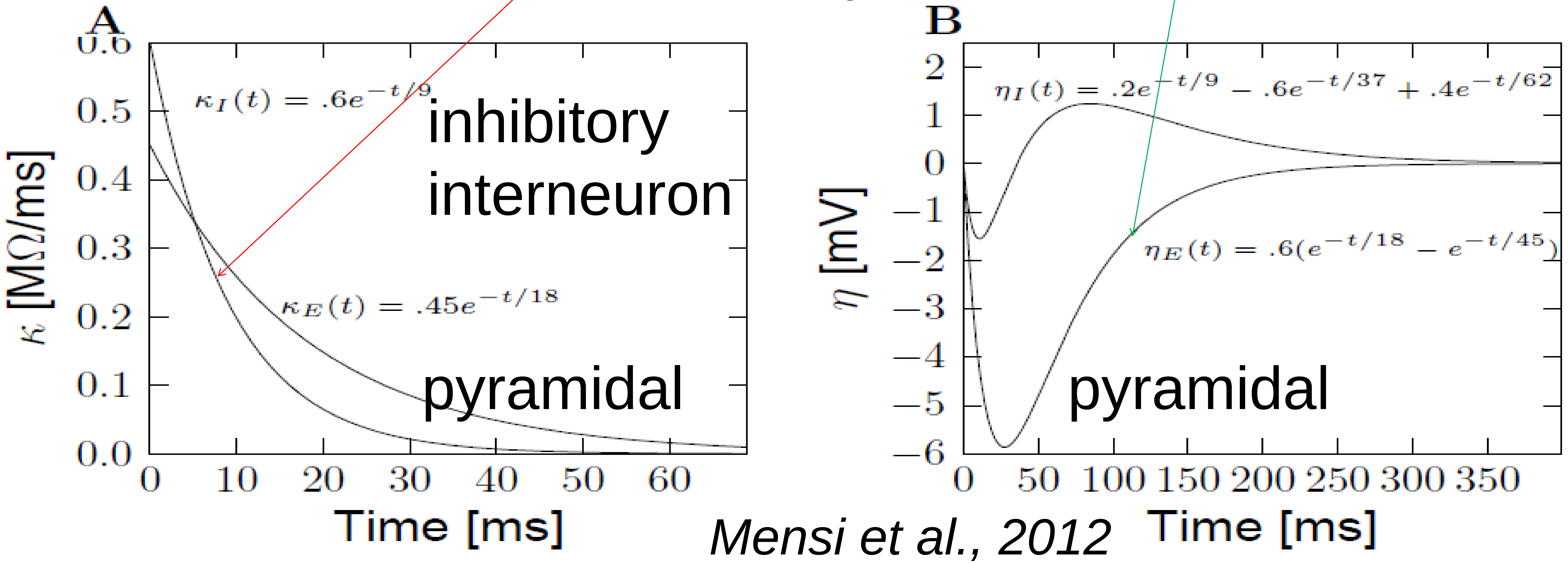
5 Extracted parameters: filter shape extracted from voltage trace

Subthreshold potential

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

known input

known spike train



Mensi et al., 2012

5. Summary: voltage modeling

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

- MODEL: Subthreshold potential between spikes depends on (known) external input and (known) past spikes
- EXPERIMENT: Subthreshold potential is measurable

→ Modify filters κ and η so as to minimize the mean-squared error between model voltage and experimental voltage
→ 'optimal filter' κ is found to be exponential
→ 'optimal filter η is found to be non-trivial

Week 12 - Parameter estimation

EPFL

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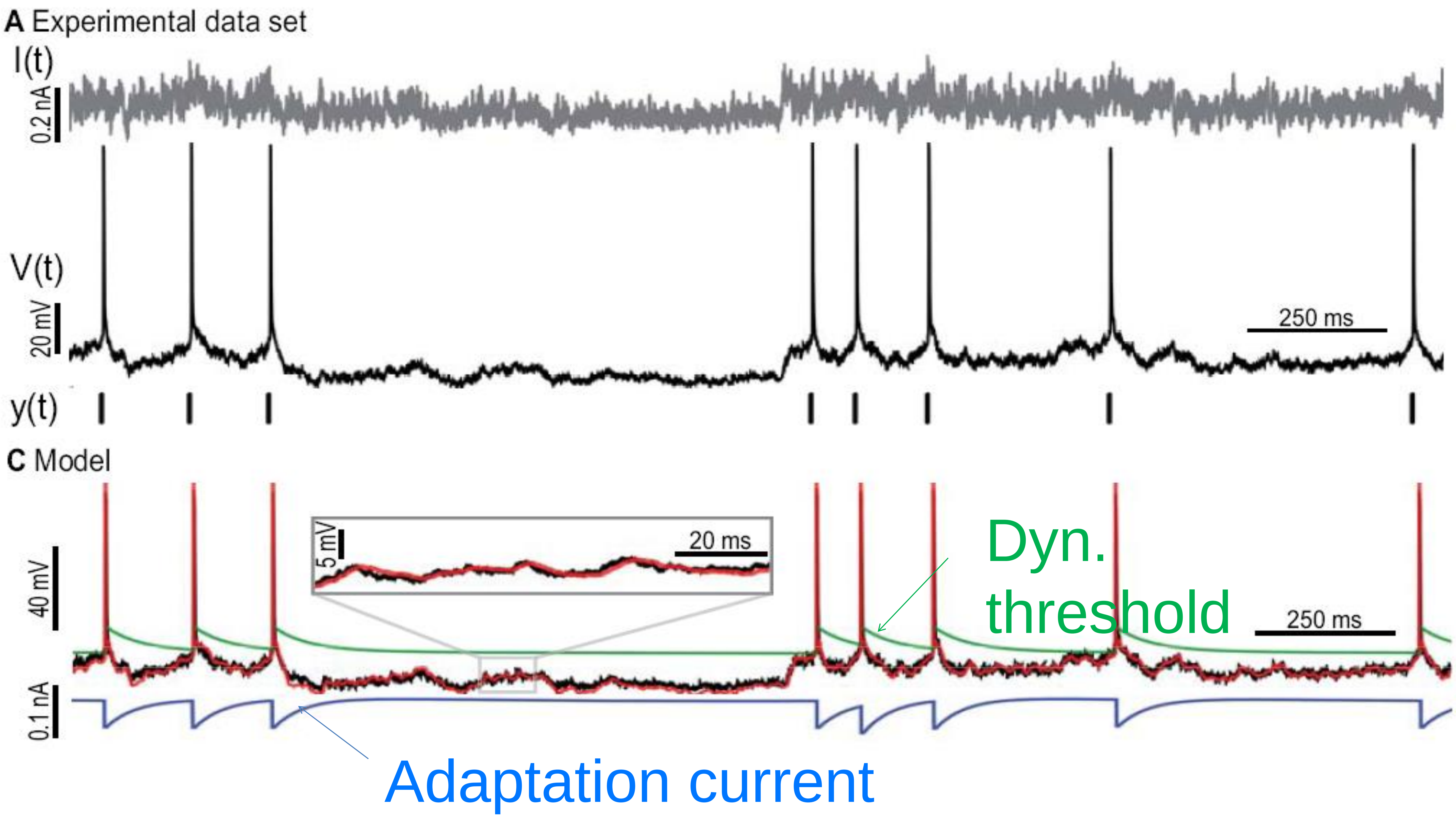
6. Modeling in vitro data
- how long lasts the effect of a spike?

5. Fitting models to data: so far ‘subthreshol



5. Fit Threshold parameters: Predict spike times

Idea:

- use subthreshold voltage to extract filters κ and η
  → previous section

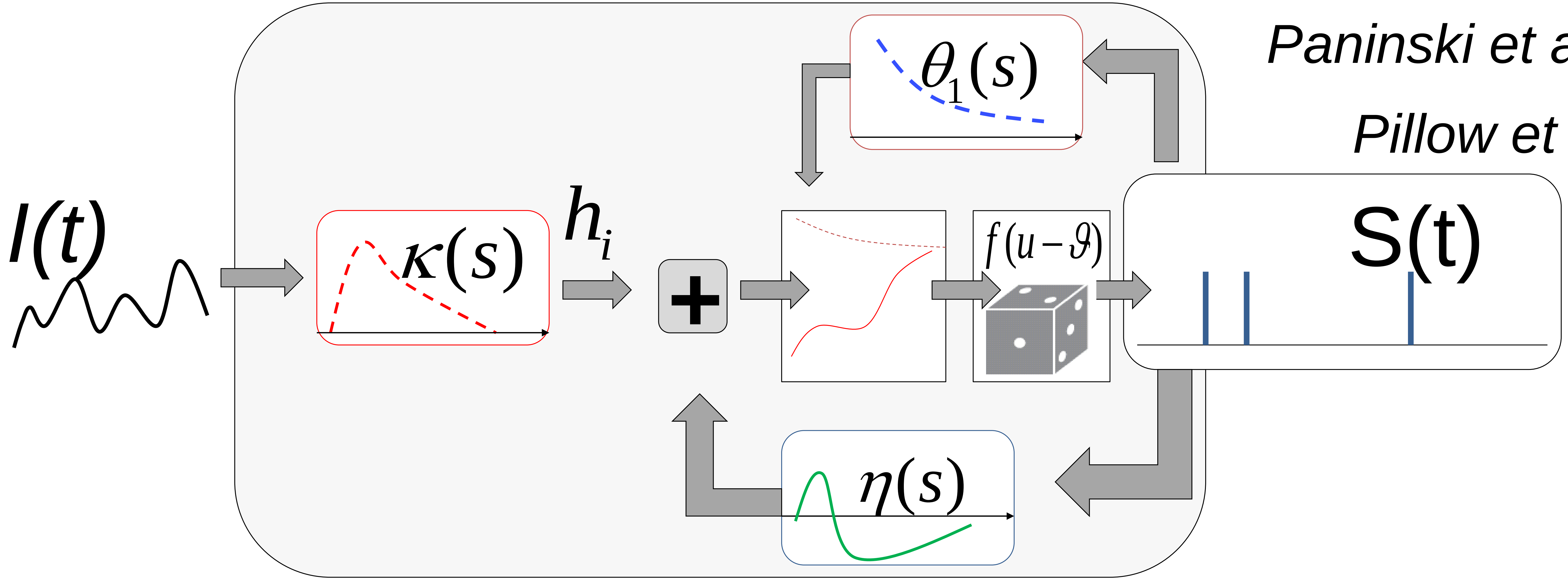
- Use spike times of experimental neuron to extract threshold filters θ

- To do so, maximize likelihood that observed spikes could have been generated by the model
  → now

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

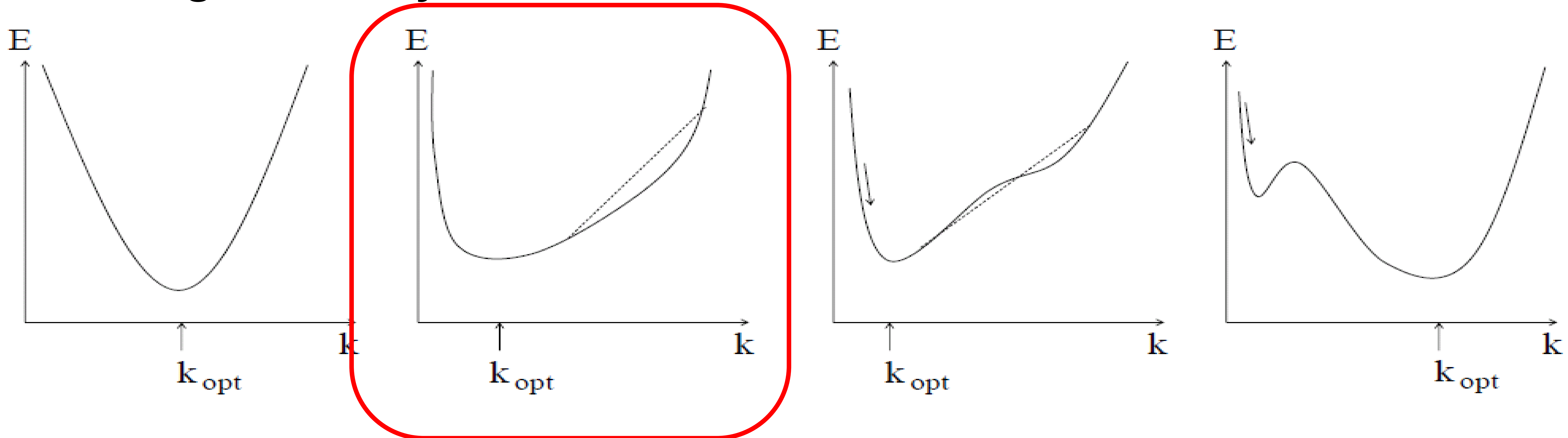
5. Generalized Linear Model (GLM)

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

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



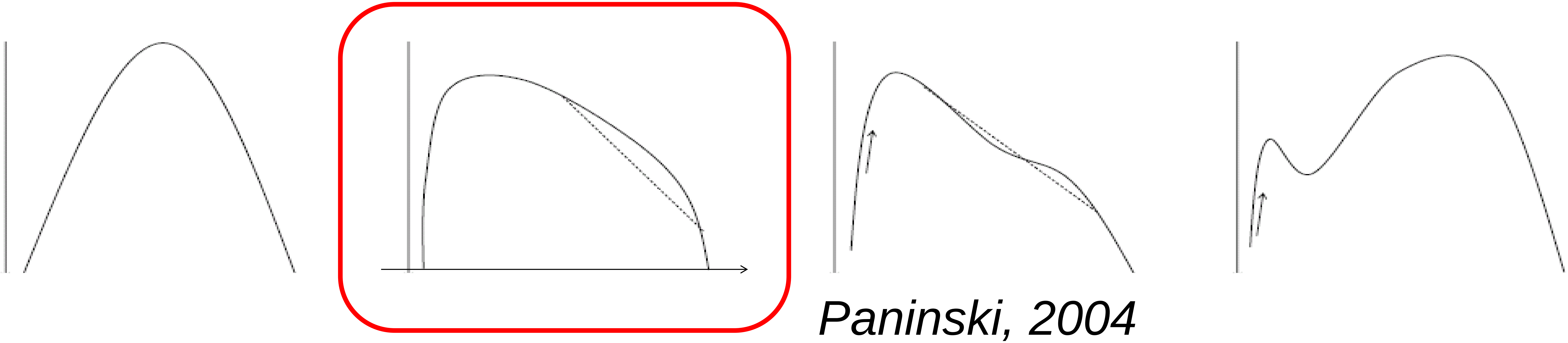
5 GLM: Log-Likelihood induces a concave error function

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

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



Paninski, 2004

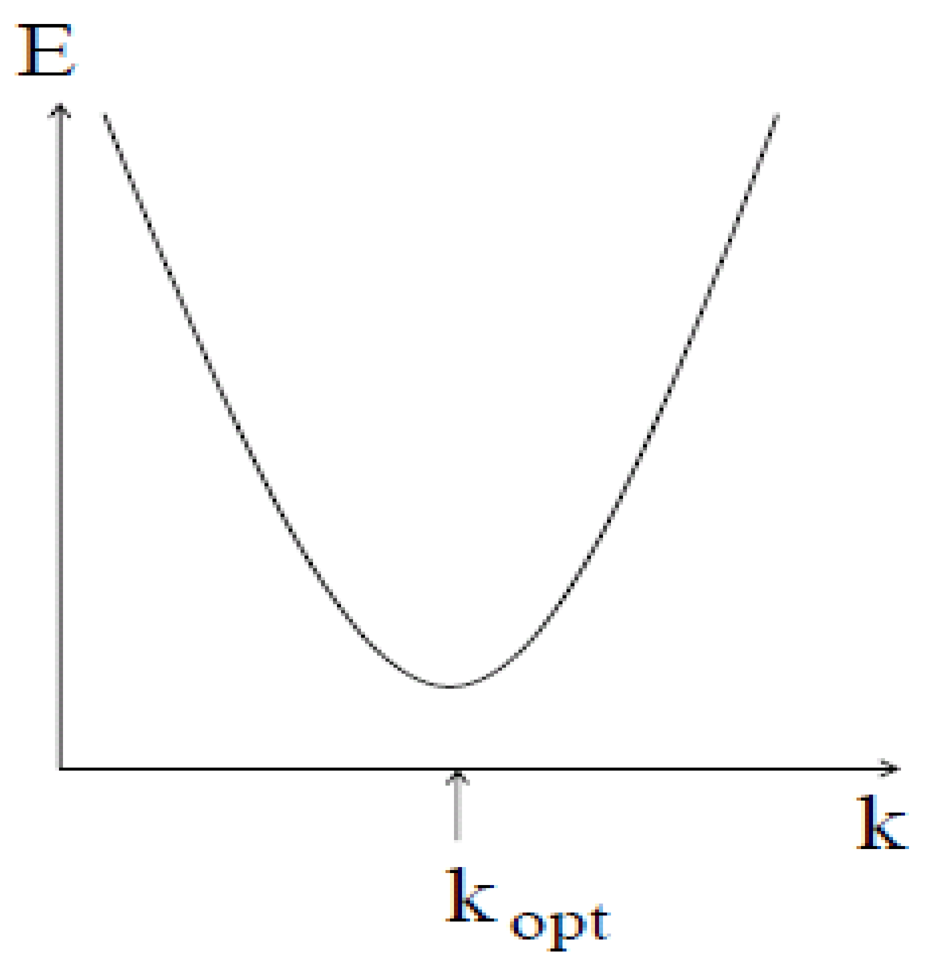
5. quadratic and convex/concave optimization

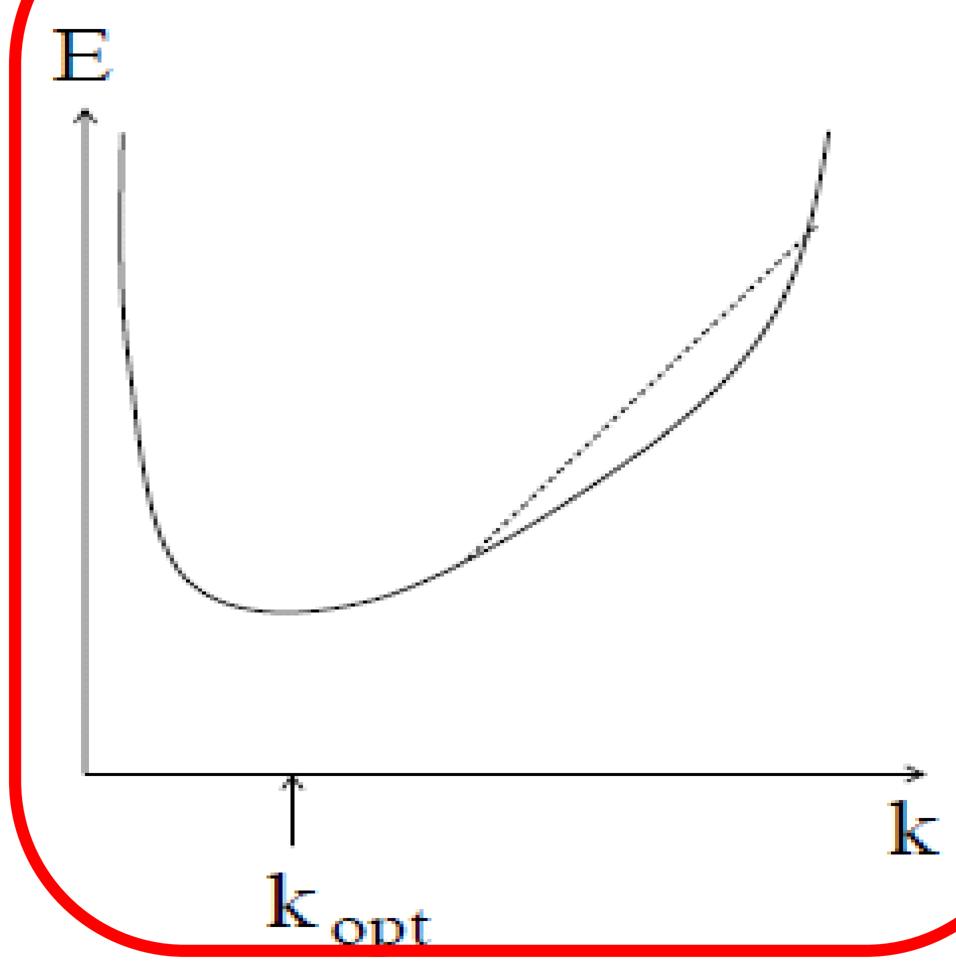
Voltage/subthreshold

- linear in parameters
  → quadratic error function

Spike times

- nonlinear, but GLM,
- negative loglikihood of spikes
  → convex error function



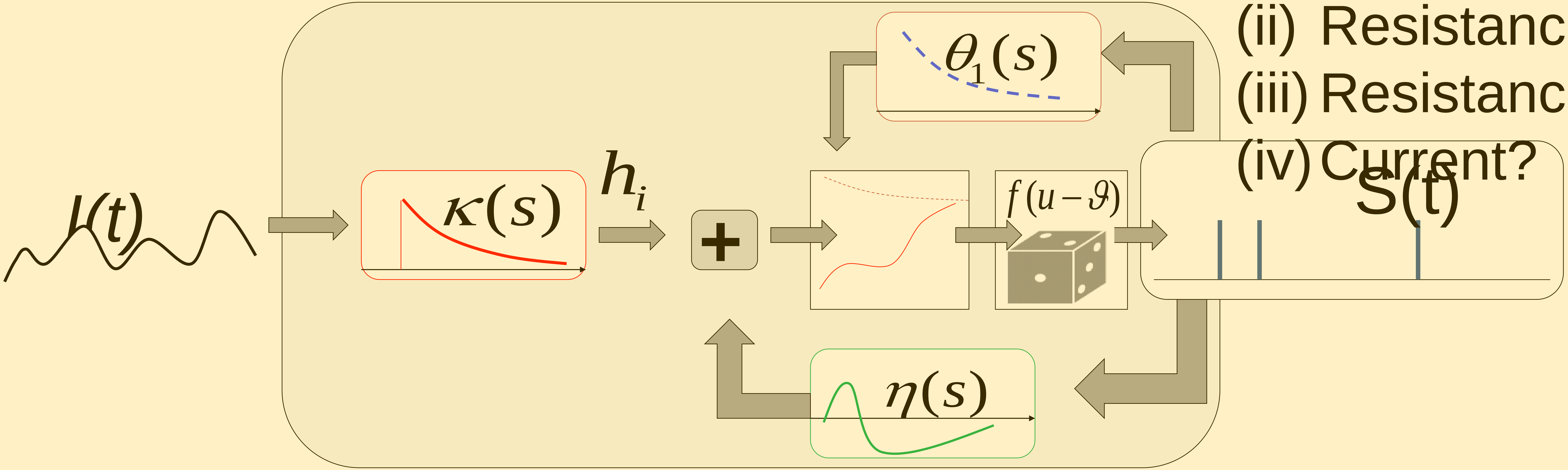


Negative Log-likelihood of spike times is convex as a function of threshold parameters
→ Parameters are easy to extract

Quiz NOW :

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

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



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

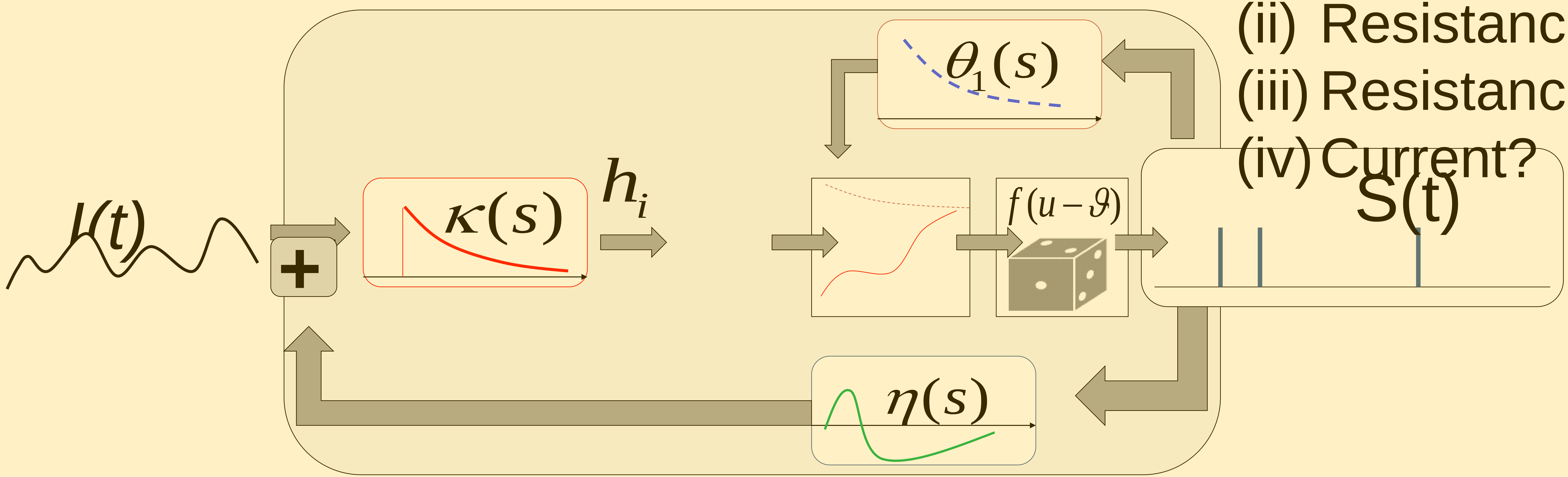
threshold $\vartheta(t) = \theta_0 + \int \theta_1(s) S(t-s) ds$

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

Quiz NOW:

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

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



potential $C\frac{d}{dt}u(t) = -\frac{(u-u_{rest})}{R} + \int \eta(s)S(t-s)ds \quad + I(t-s)$

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

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

Week 12 - Modeling in vitro data

EPFL

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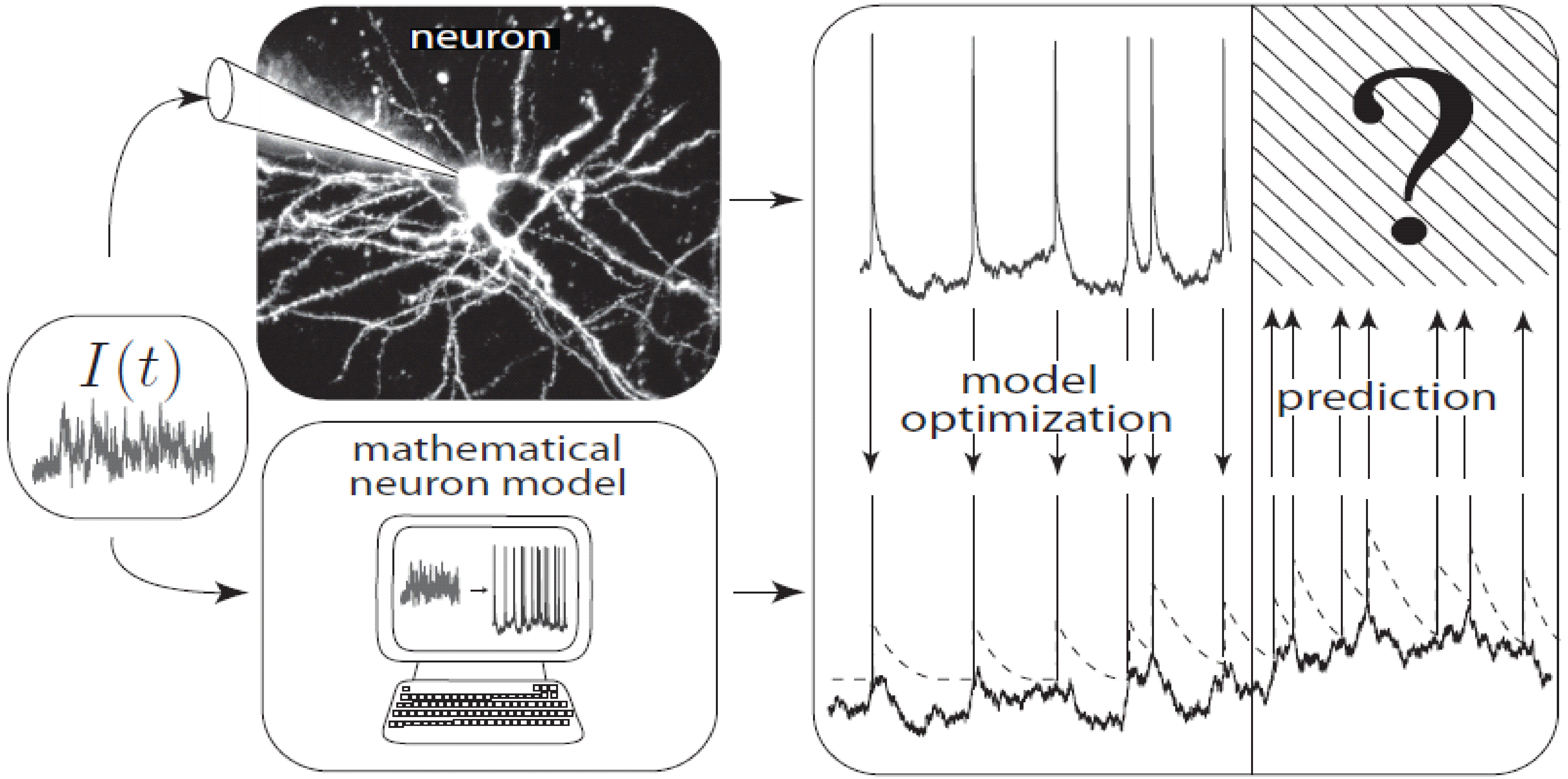
6. Modeling in vitro data
- how long lasts the effect of a spike?

6. Review: Models and Data

comparison model-data



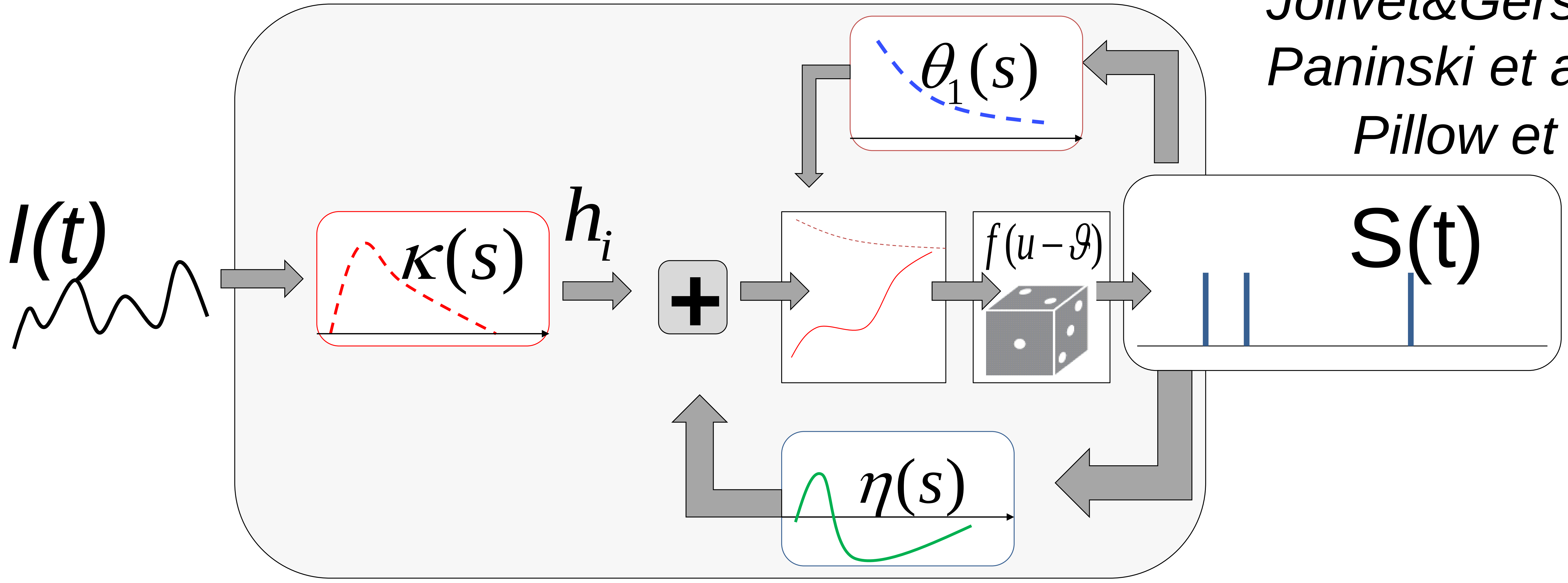
Predict

-Subthreshold voltage

-Spike times

6. Review: GLM/SRM with escape noise

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

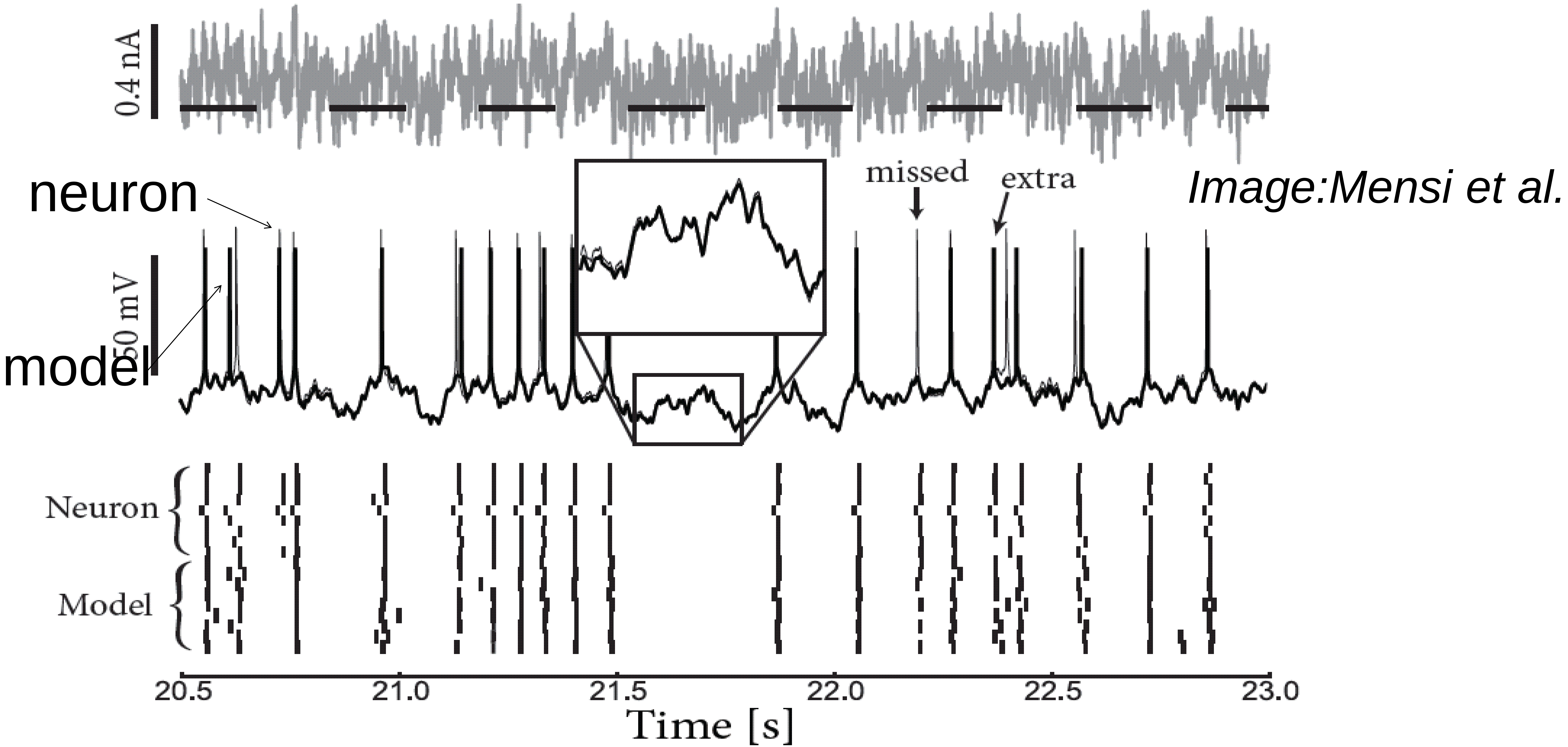


potential $u(t) = \int \eta(s) S(t-s) ds + \int_0^\infty \kappa(s) I(t-s) ds + u_{rest}$

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

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

6. Result: GLM/SRM predict subthreshold voltage and (jittered) spike times

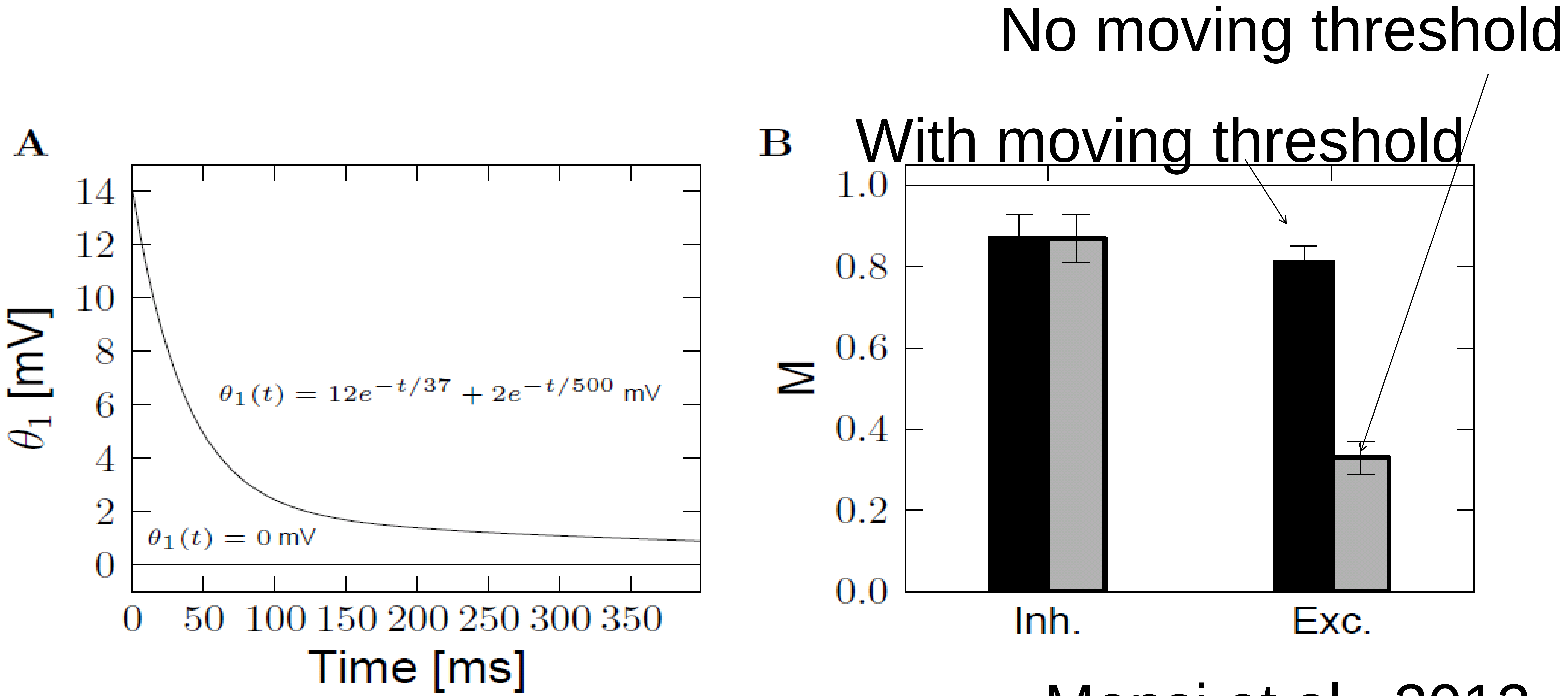


6. Conclusion: GLM/SRM predict neuronal behavior

1) Subthreshold voltage
   → prediction very close to measurements on NEW DATA, not used for parameter optimization

2) Spike times
   → remaining jitter in model very close to jitter in experimental data

Role of moving threshold

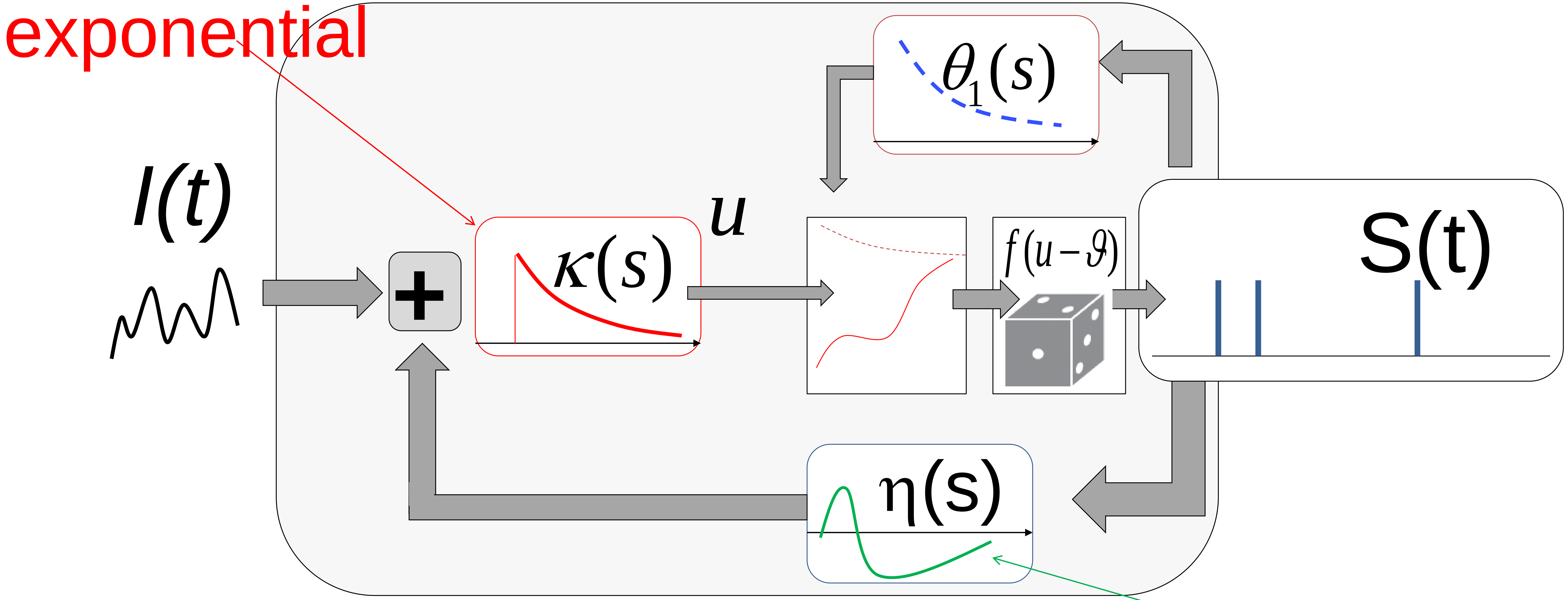


Mensi et al., 2012

Change in model formulation:

What are the units of …. ?

'soft-threshold adaptive IF model'



adaptation current

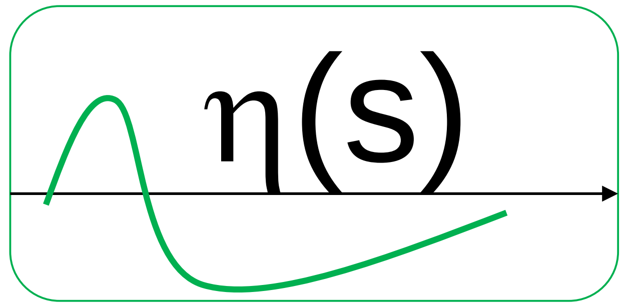
potential $C\frac{d}{dt}u(t) = \int \eta(s)S(t-s)ds \quad + I(t)$

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

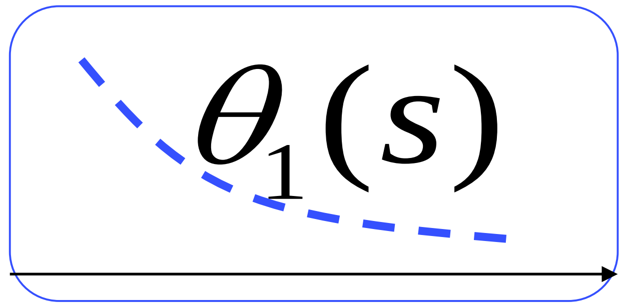
firing intensity $\rho(t) = f(u(t) - \vartheta(t))$

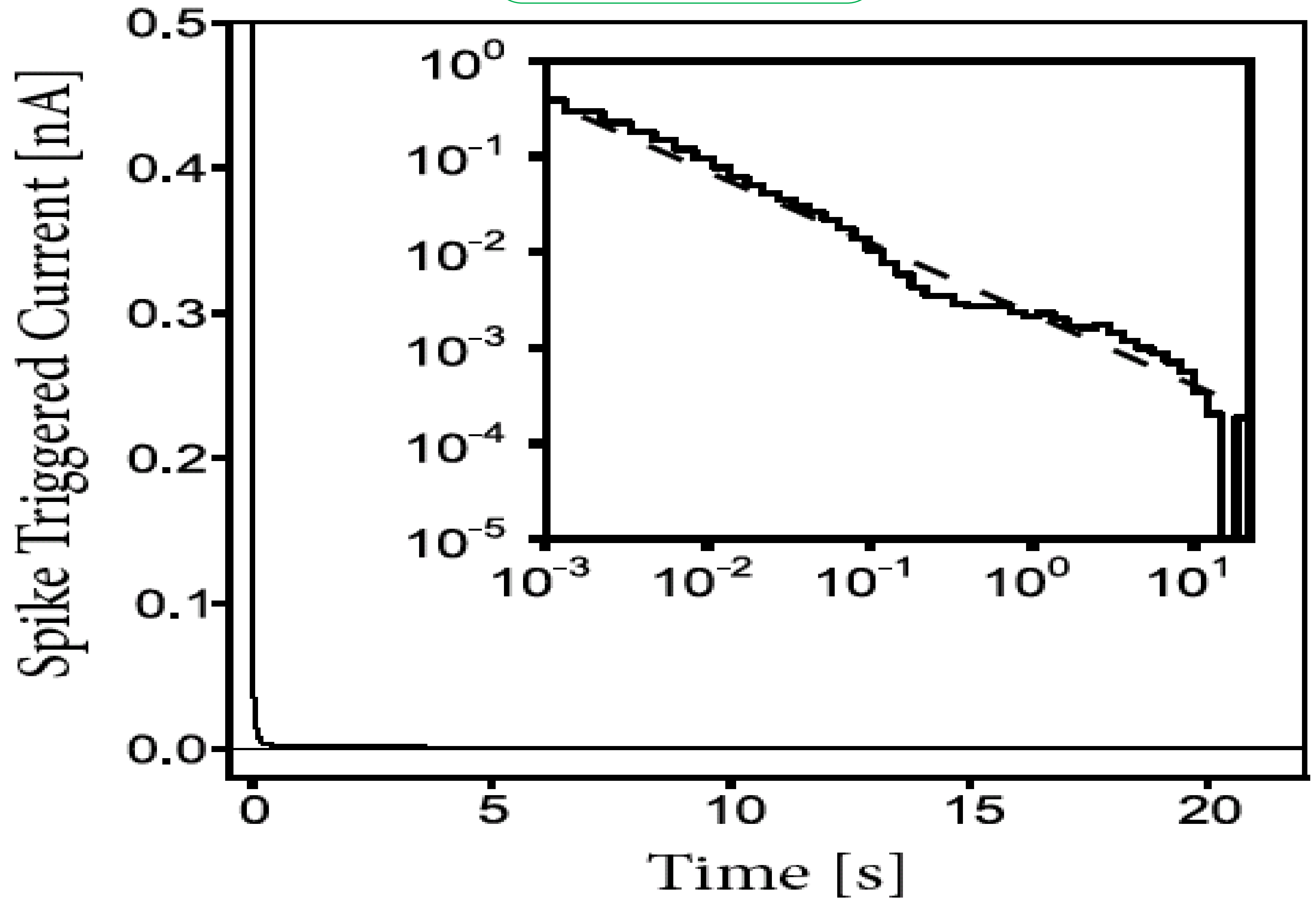
6. How long does the effect of a spike last?

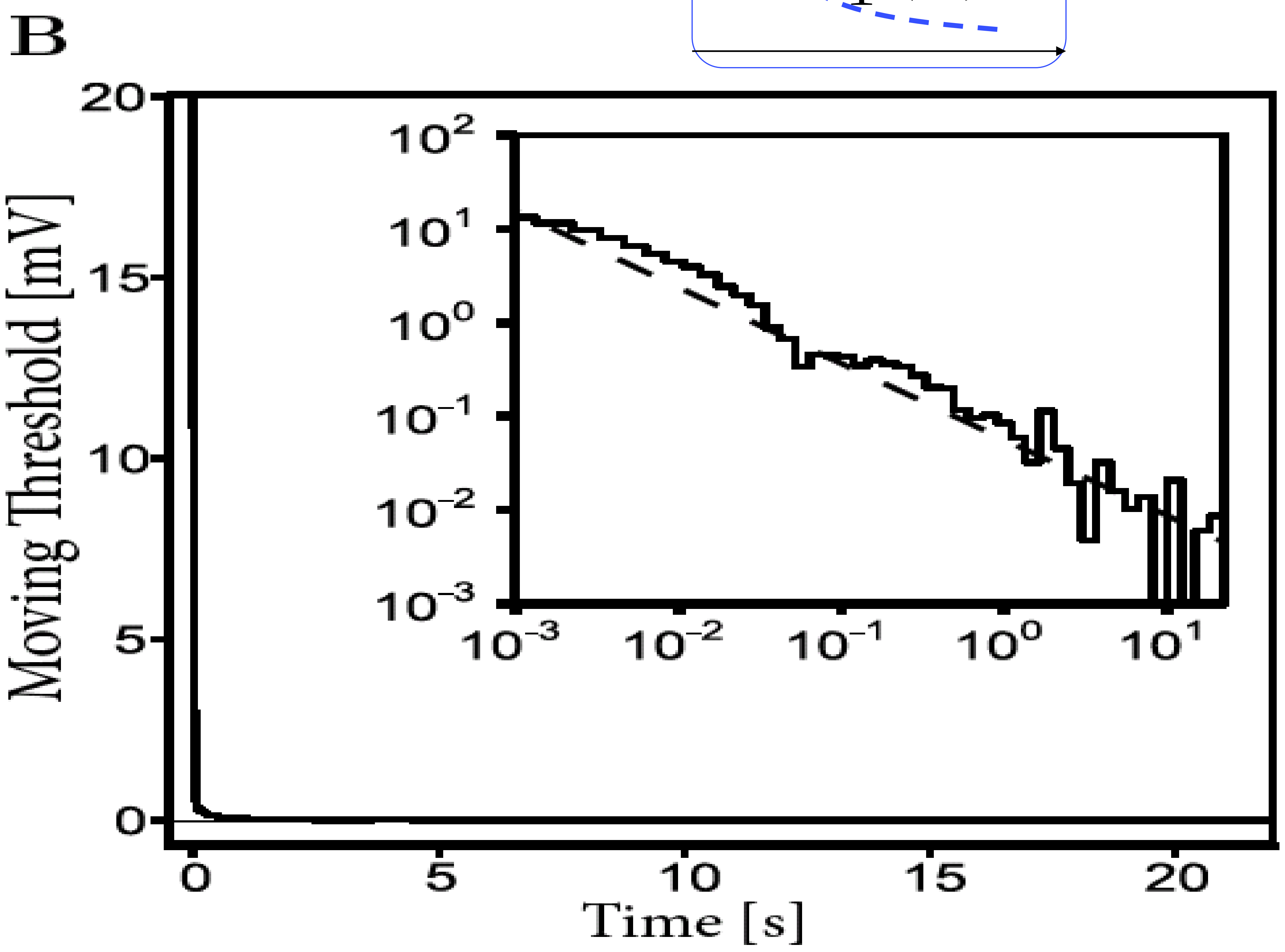
Time scale of filters?



→ **Power law**



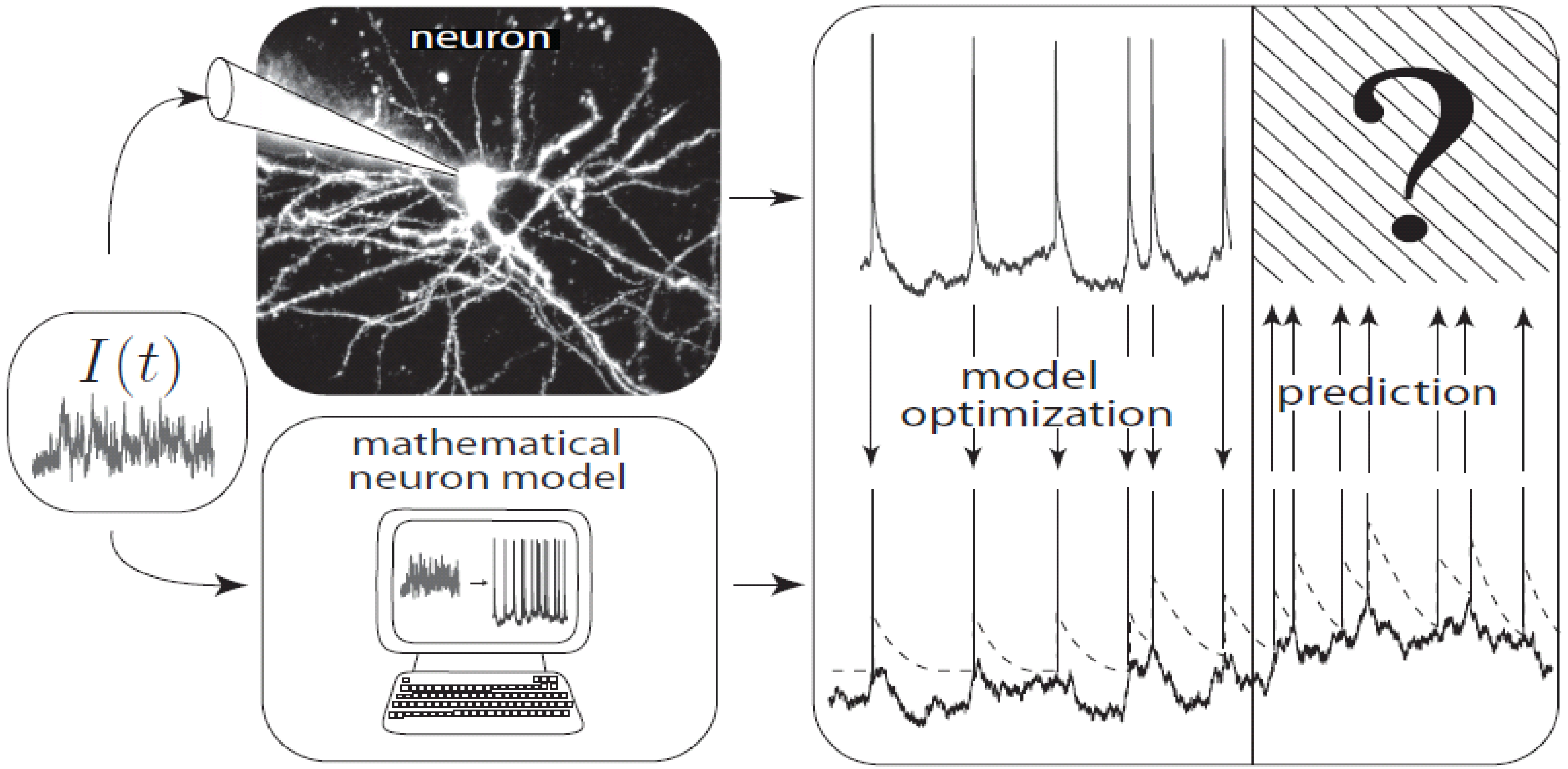




A single spike has a measurable effect more than 10 seconds later!

Pozzorini et al. 2013

6: Conclustion: Models and in vitro Data



The SRM/GLM framework
is able to

-Predict spike times (plus jitter)
-Predict subthreshold voltage
-Easy to interpret (not a ‘black box’)
-optimize parameters systematically
-account forfiring patterns and adaptation

BUT so far limited to in vitro

Week 12 - Helping Humans

EPFL

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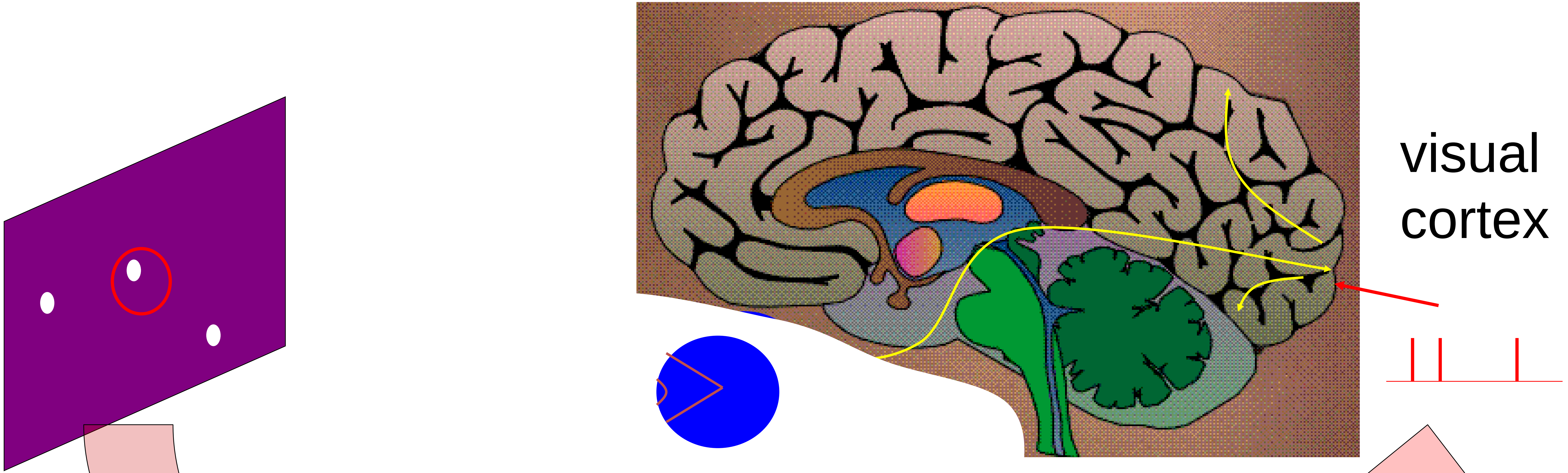
√ 6 Modeling in vitro data
- how long lasts the effect of a spike?

7 Helping Humans: in vivo data

7. Model of ENCODING

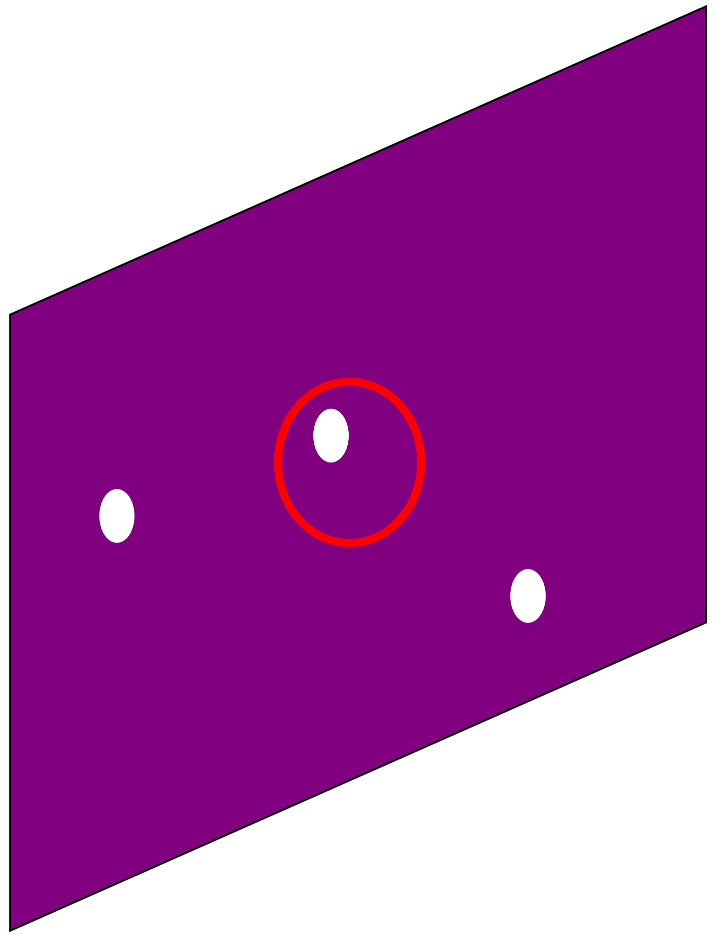


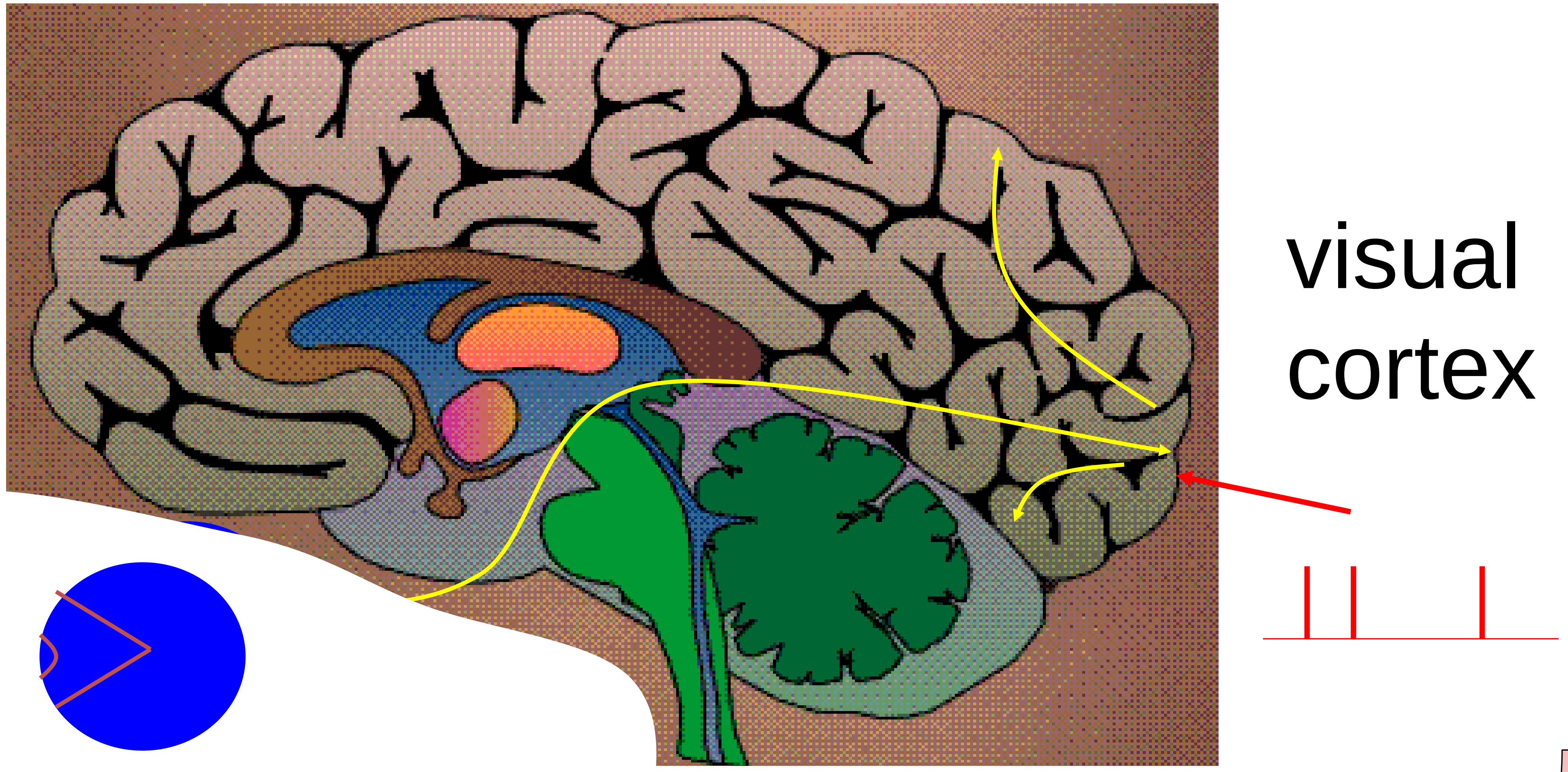
A) Predict spike times, given stimulus
B) ~~Predict subthreshold voltage~~
C) Easy to interpret (not a 'black box')
D) Flexible enough to account for a variety of phenomena
E) Systematic procedure to 'optimize' parameters

Model of 'Encoding'

7. Model of DECODING

Predict stimulus!

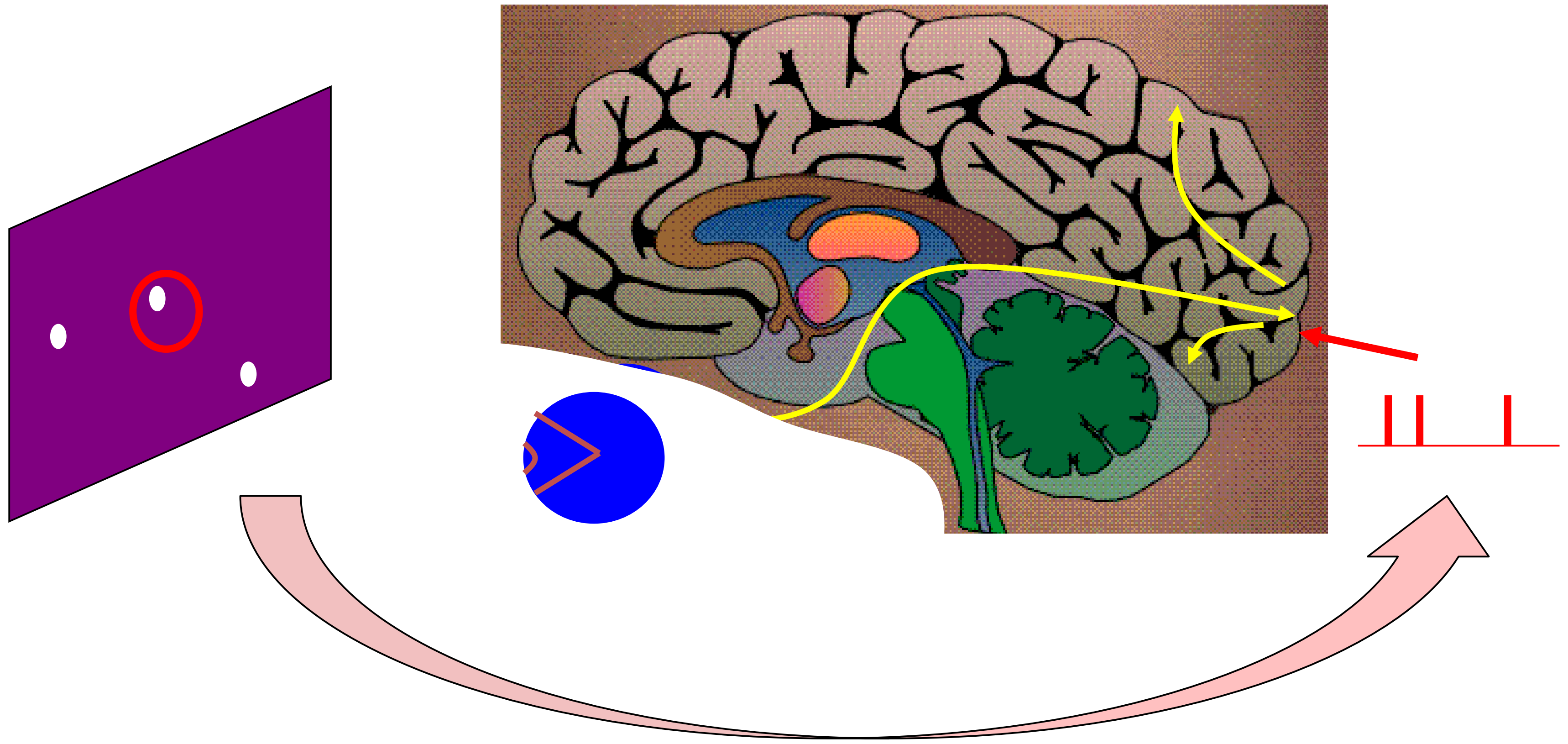




Model of ‘Decoding’:

predict stimulus, given spike times

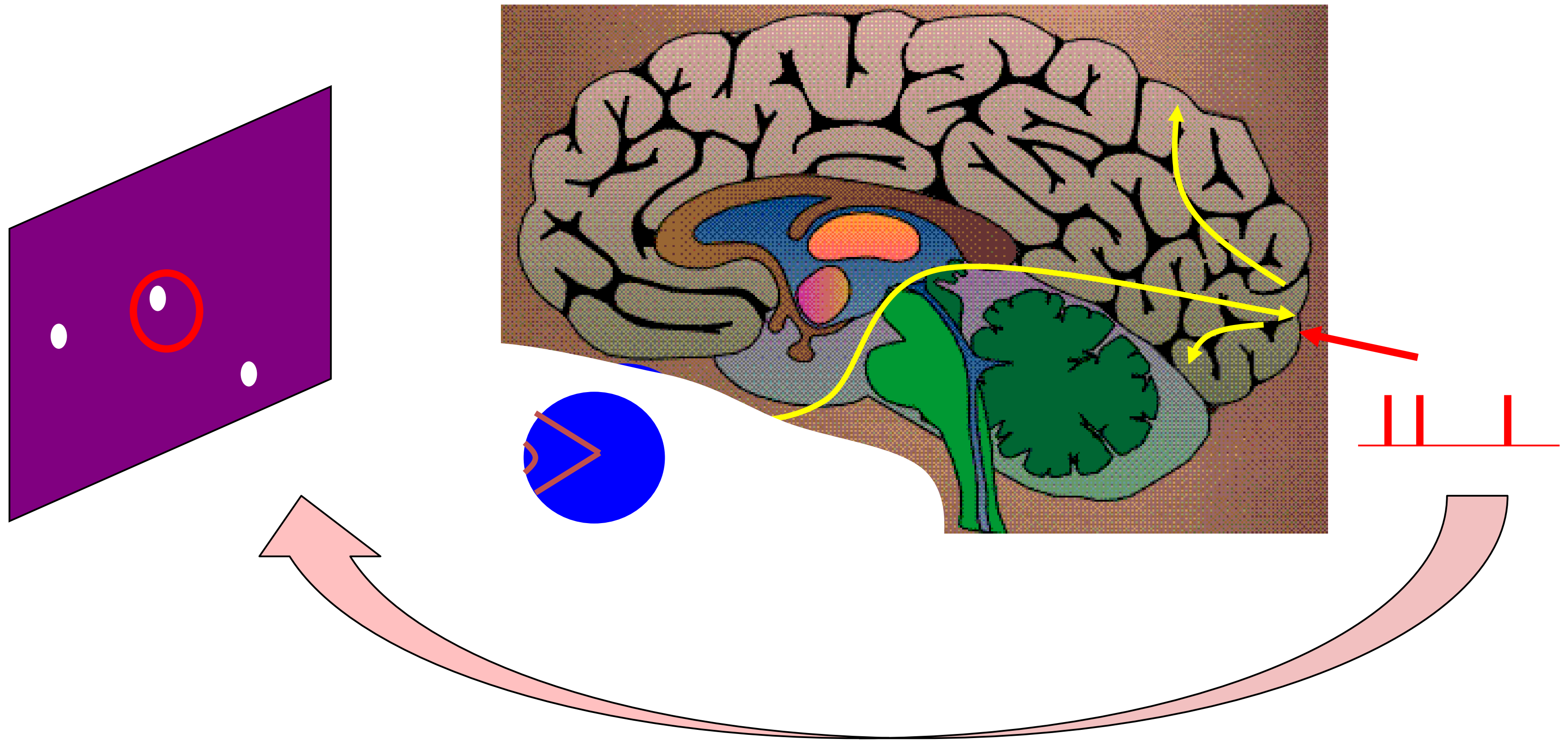
7. ENCODING and Decoding



Model of ‘Encoding’

Generalized Linear Model (GLM)

- flexible model
- systematic optimization of parameters

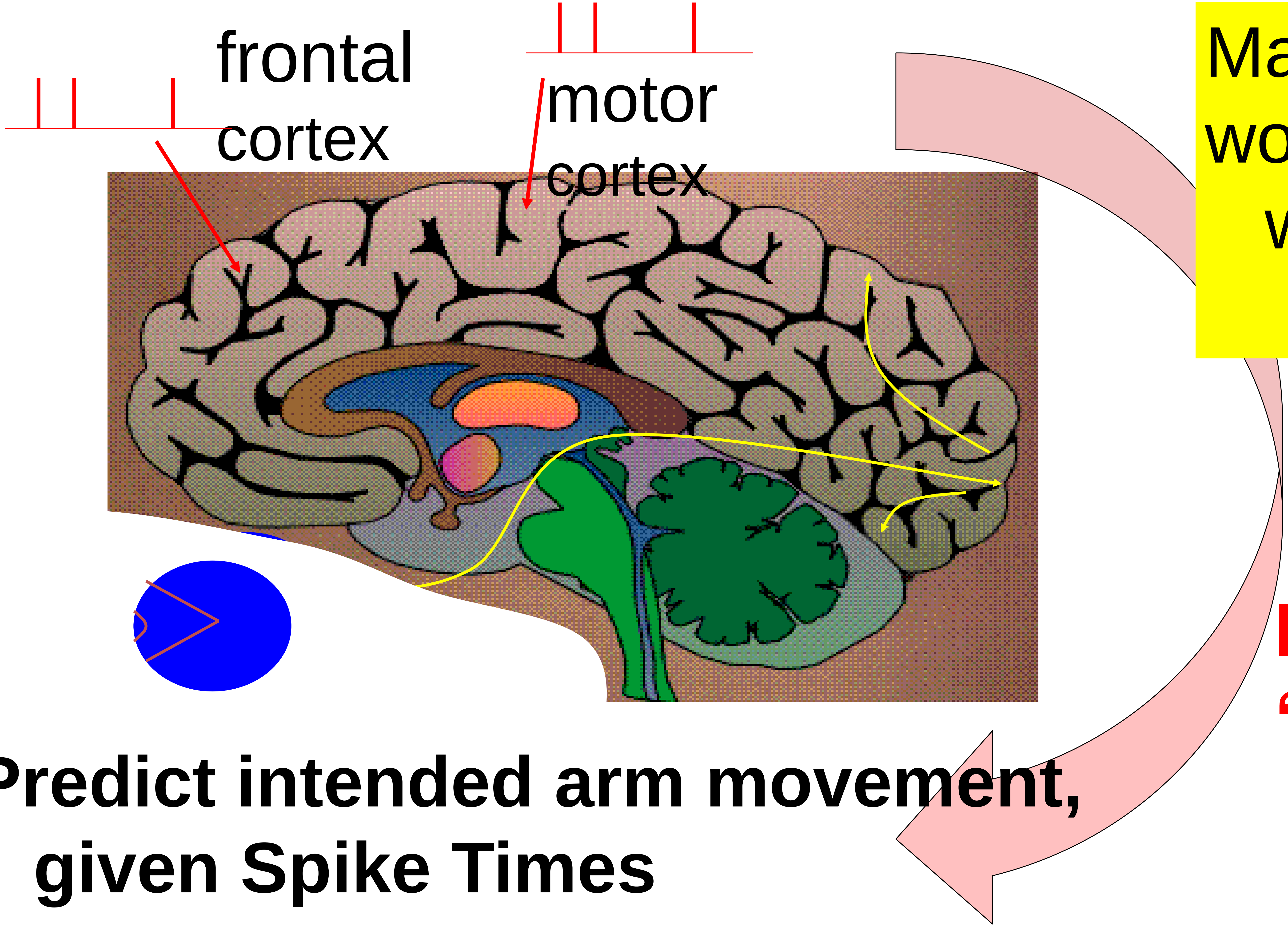


Model of ‘Decoding’

The same GLM works!

- flexible model
- systematic optimization of parameters

Application: Neuroprosthetics



Many groups world wide work on this problem!

Model of 'Decoding'

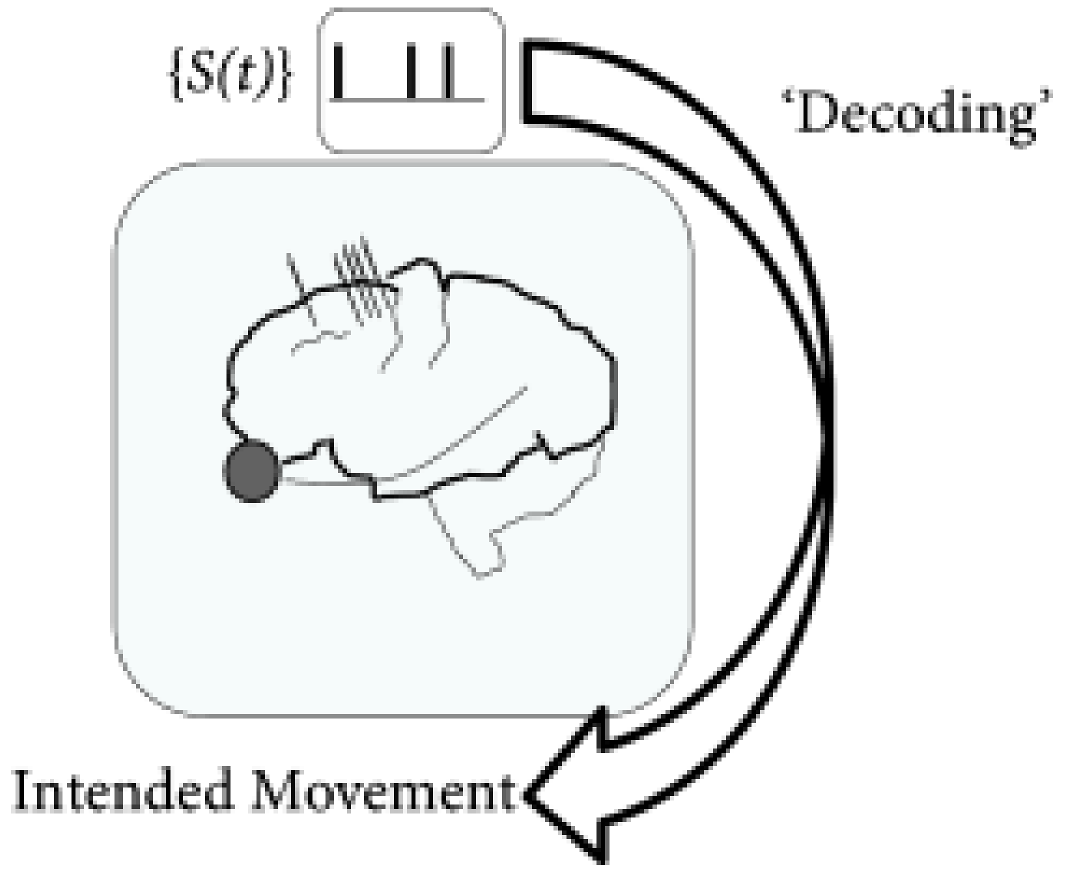
Predict intended arm movement, given Spike Times

Application: Neuroprosthetics

Figure:
Neuronal Dynamics,
Cambridge Univ. Press;
See Truccolo et al. 2005

Decode the intended arm movement

Hand velocity



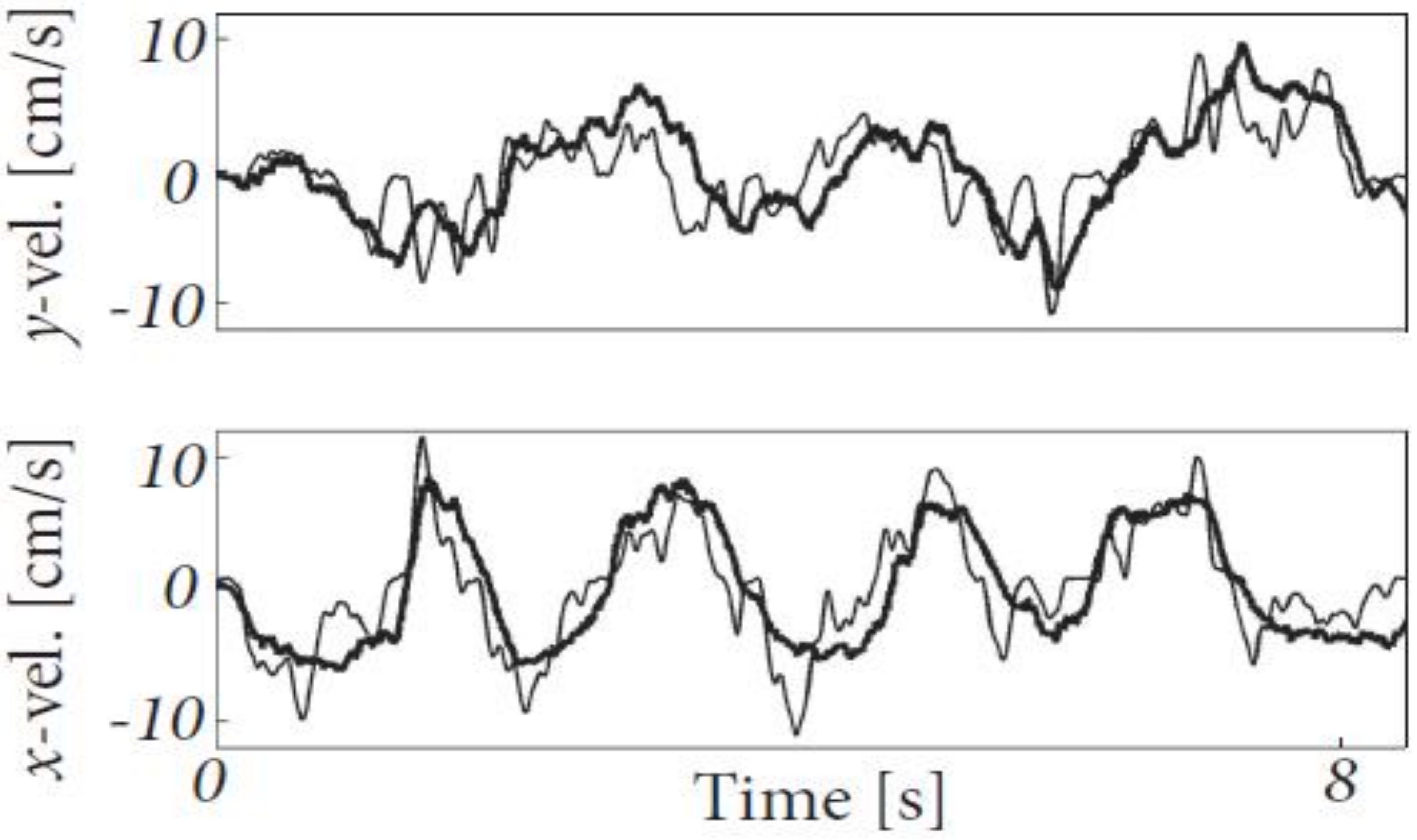


Fig. 11.12: Decoding had velocity from spiking activity in area MI of cortex. The real hand velocity (thin black line) is compared to the decoded velocity (thick black line) for the $x-$ (top) and the $y-$components (bottom). Modified from Truccolo et al. (2005).

7. Conclusion: Basic neuroprosthetics

Complicated math

- Spike Response Model
- Nonlinear Model!
- Survivor Function
- Stochastic Processes
- Likelihood of a spike train

Is all this worth the trouble?

→**yes, because it is used in Important Applications!**

Suggested Reading/selected references

Reading: W. Gerstner, W.M. Kistler, R. Naud and L. Paninski,
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