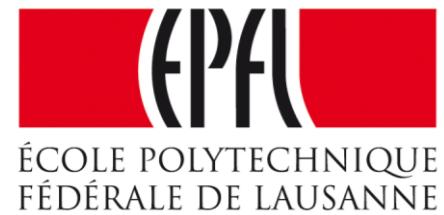


# Week 4 – part 2: More Detail – compartmental models



## Biological Modeling of Neural Networks

### Week 4

- Reducing detail
- Adding detail

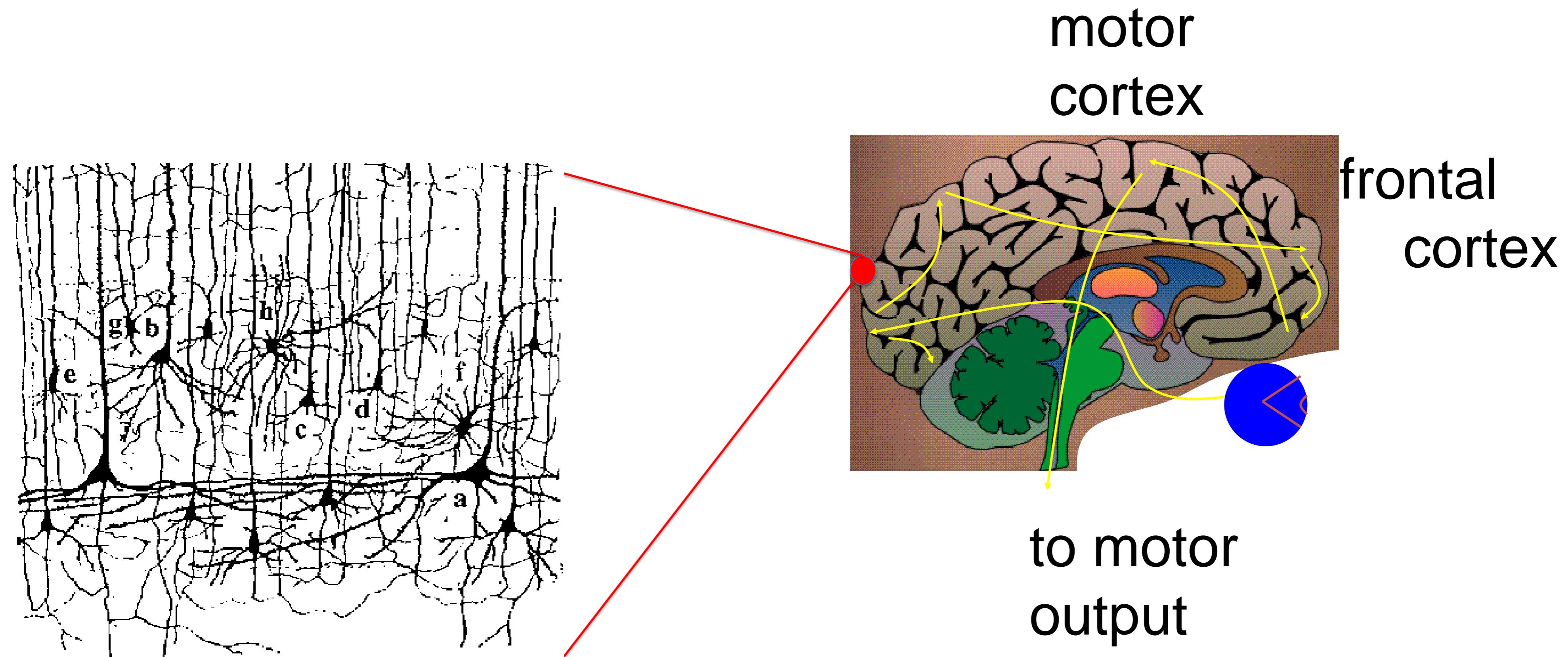
### 4.2. Adding detail

- synapse
- cable equation

Wulfram Gerstner

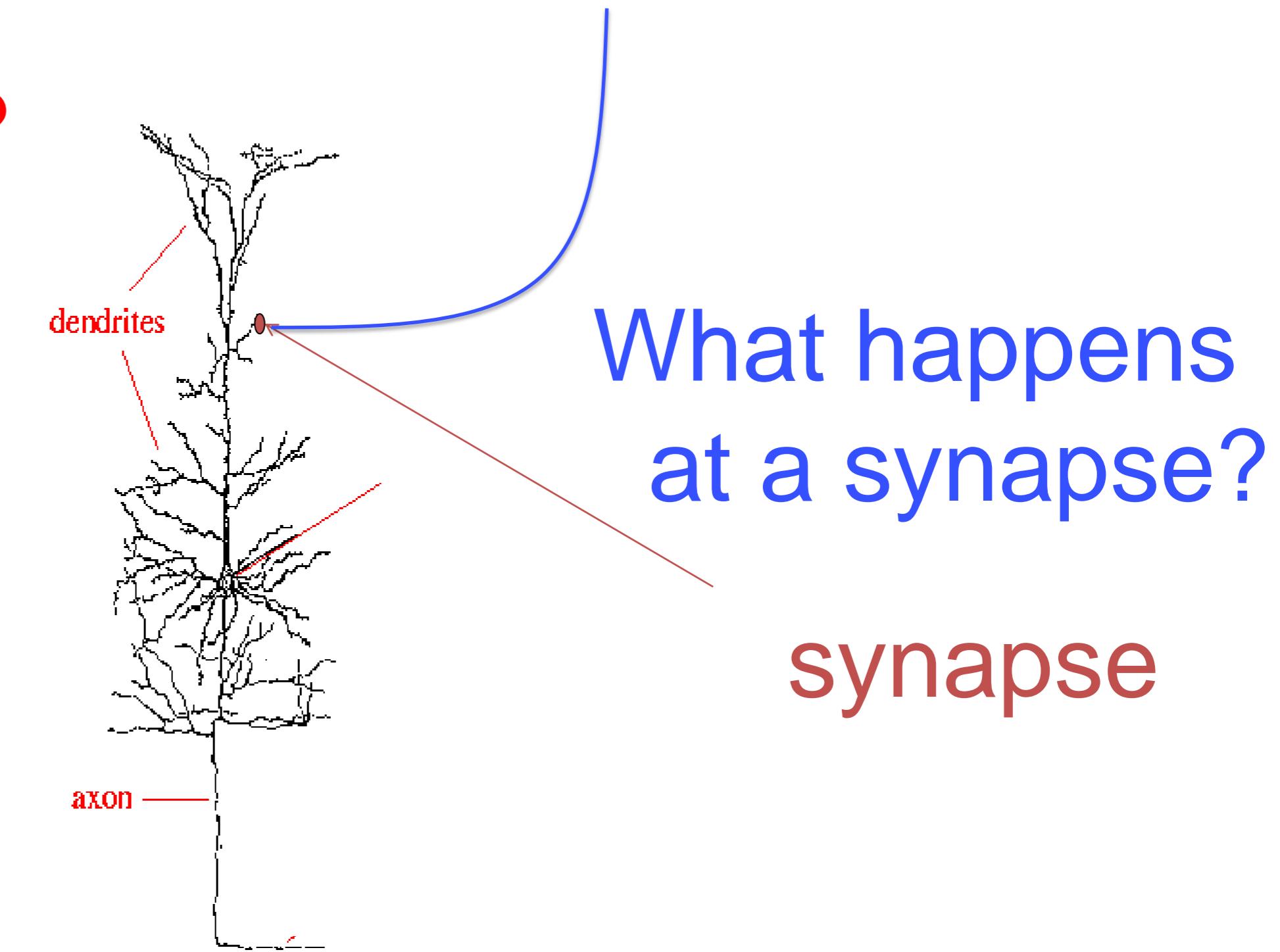
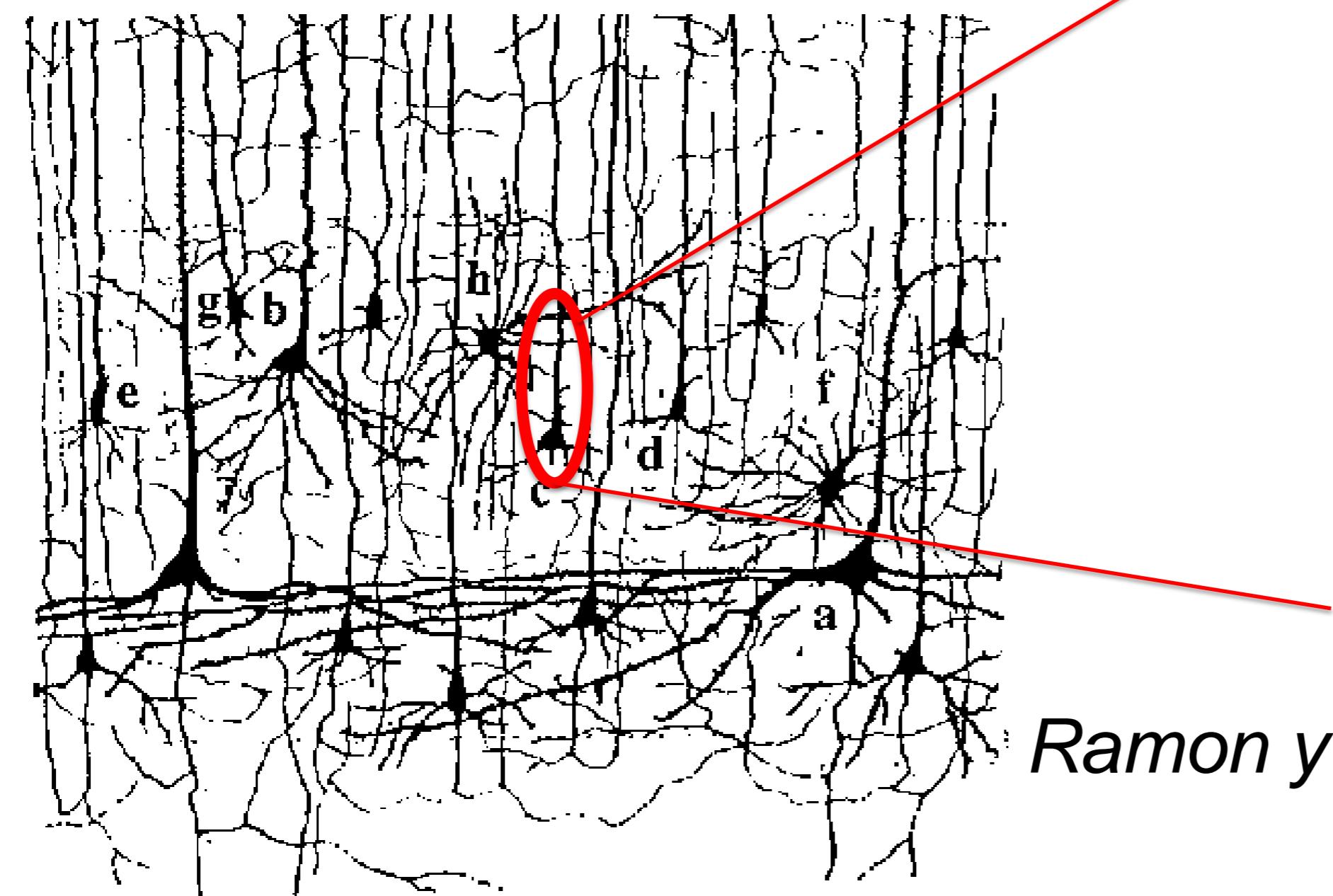
EPFL, Lausanne, Switzerland

# Neuronal Dynamics – 4.2. Neurons and Synapses

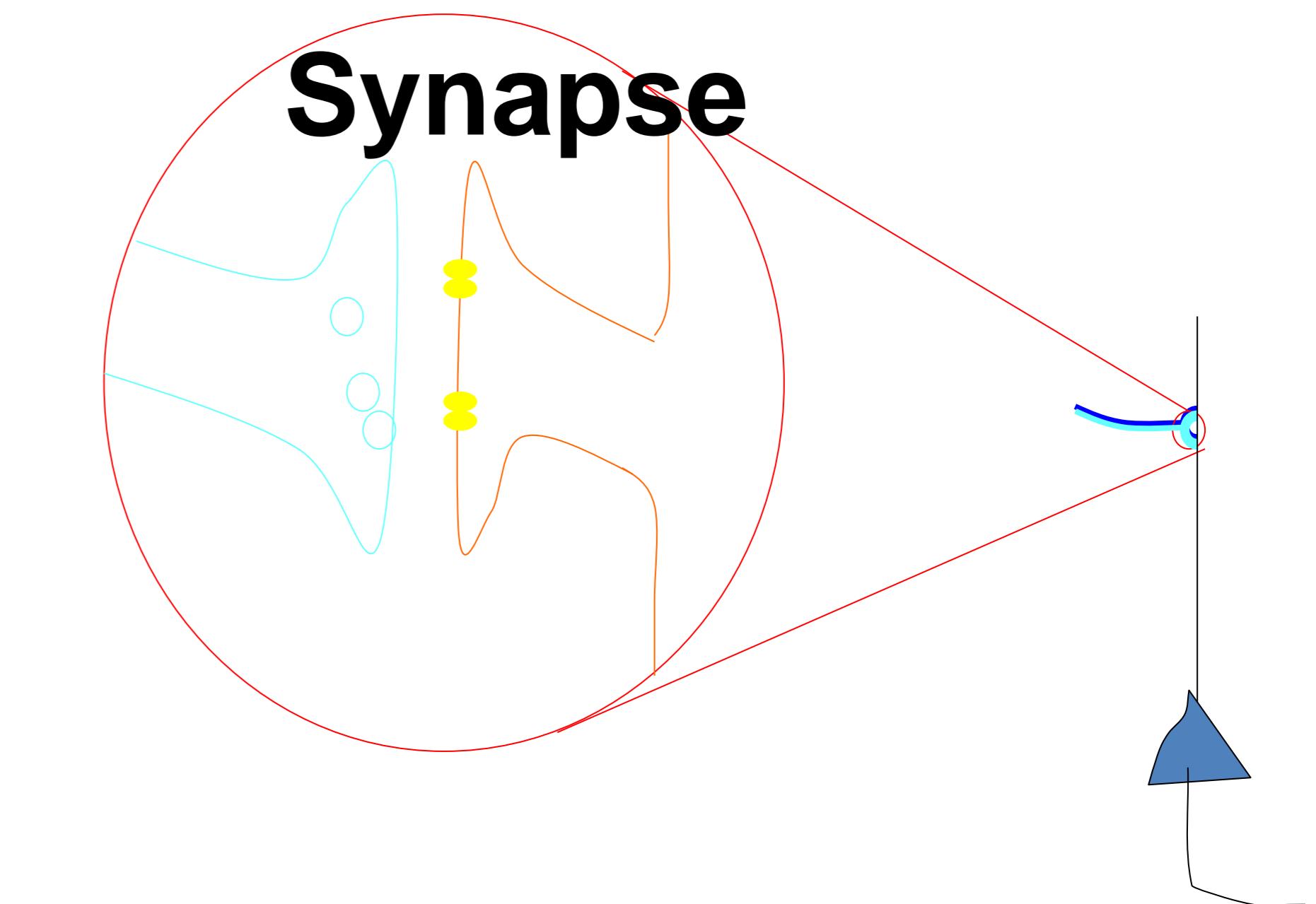


# Neuronal Dynamics – 4.2 Neurons and Synapses

What happens  
in a dendrite?

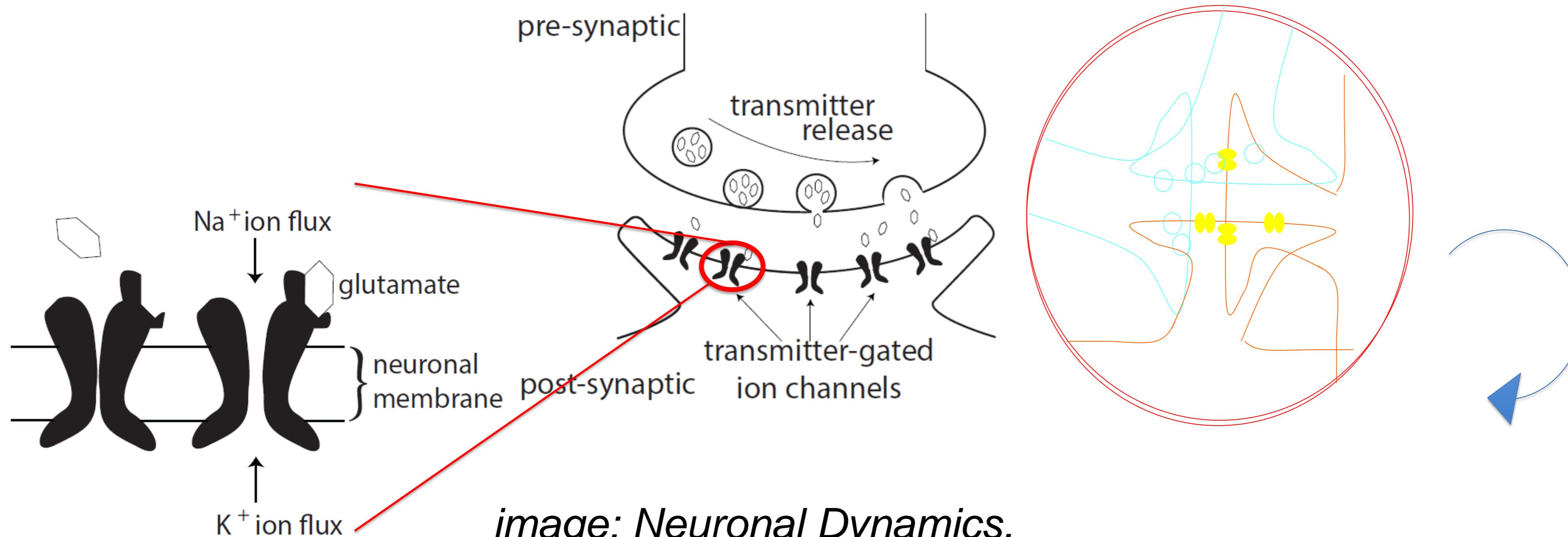


# Neuronal Dynamics – 4.2. Synapses



# Neuronal Dynamics – 4.2 Synapses

glutamate: Important neurotransmitter at excitatory synapses



# Neuronal Dynamics – 4.2. Synapses

**glutamate:** Important neurotransmitter at **excitatory synapses**

-AMPA channel: rapid, calcium cannot pass if open

-NMDA channel: slow, calcium can pass, if open  
*(N-methyl-D-aspartate)*

**GABA:** Important neurotransmitter at **inhibitory synapses**

*(gamma-aminobutyric acid)*

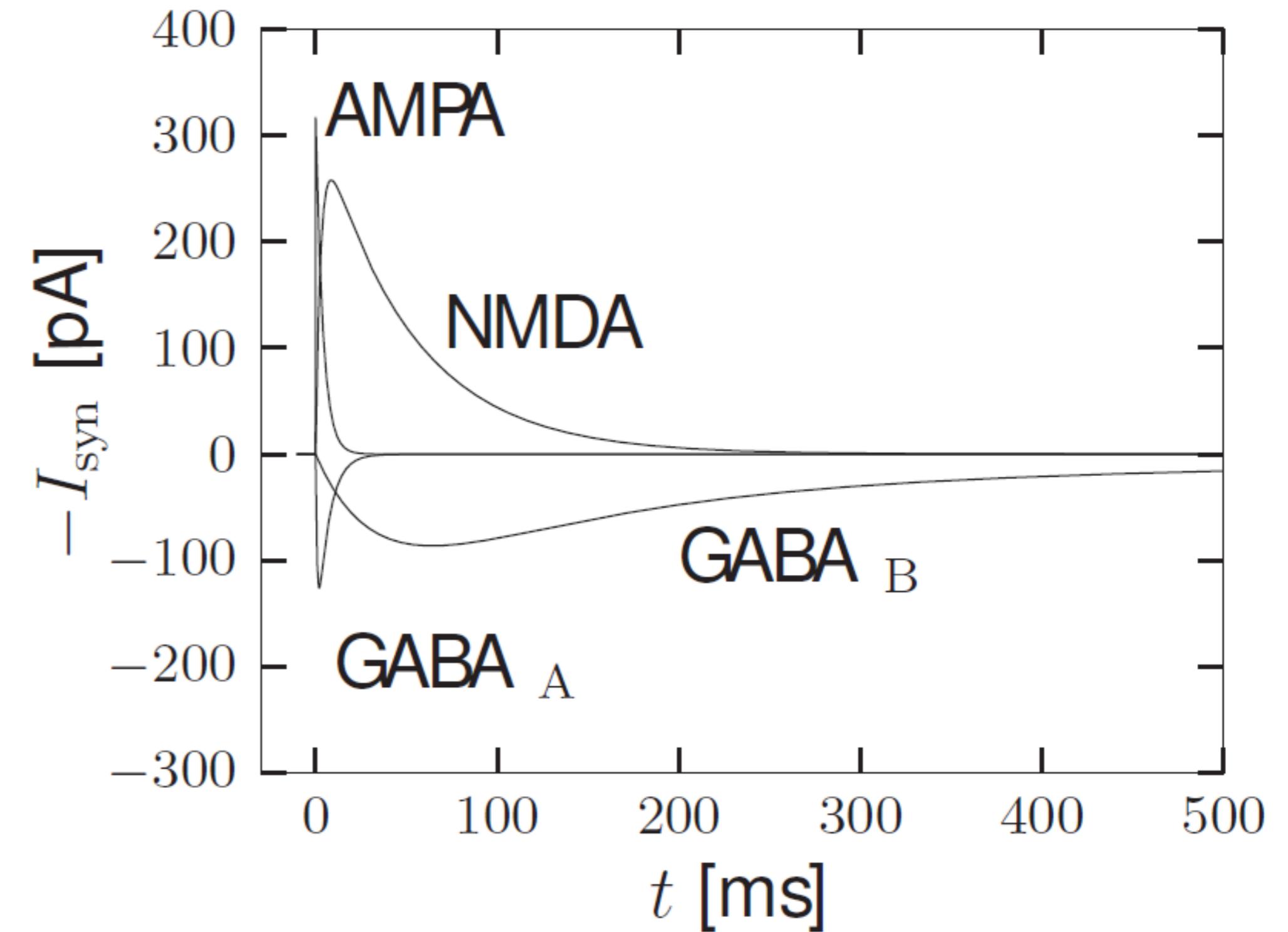
Channel subtypes GABA<sub>A</sub> and GABA<sub>B</sub>

# Neuronal Dynamics – 4.2. Synapse types

Model?

$$g_{syn}(t) = \bar{g}_{syn} e^{-(t-t_k)/\tau} \Theta(t - t_k)$$

$$-I^{syn}(t) = -g_{syn}(t)(u - E_{syn})$$



*image: Neuronal Dynamics,  
Cambridge Univ. Press*

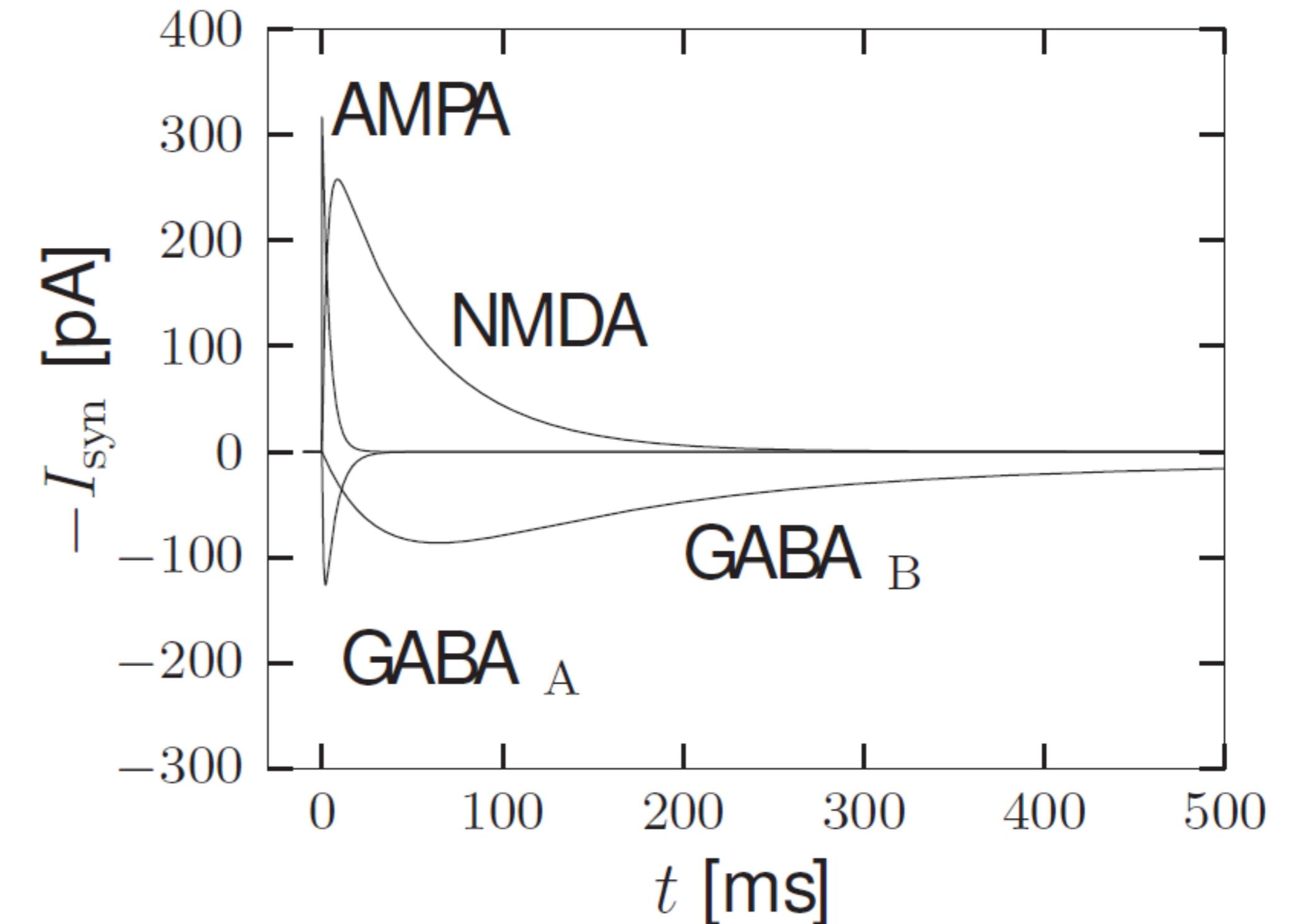
# Neuronal Dynamics – 4.2. Synapse model

Model?

$$g_{syn}(t) = \bar{g}_{syn} e^{-(t-t_k)/\tau} \Theta(t - t_k)$$



$$-I^{syn}(t) = -g_{syn}(t)(u - E_{syn})$$



*image: Neuronal Dynamics,  
Cambridge Univ. Press*

# Neuronal Dynamics – 4.2. Synapse model

Model with rise time

$$g_{syn}(t) = \sum_k \bar{g}_{syn} e^{-(t-t_k)/\tau} [1 - e^{-(t-t_k)/\tau_{rise}}] \Theta(t - t_k)$$

$$-I^{syn}(t) = -g_{syn}(t)(u - E_{syn})$$

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

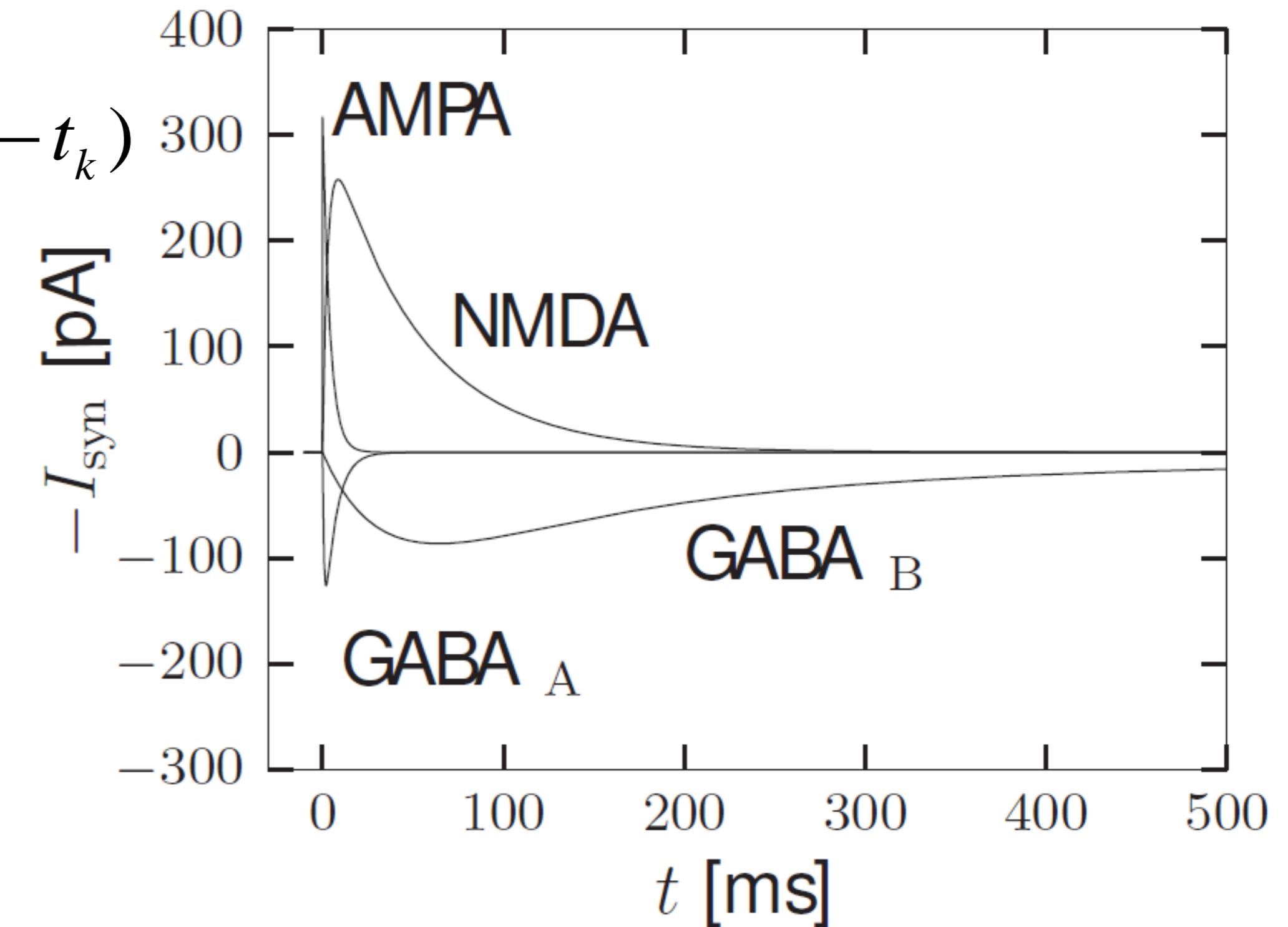


image: *Neuronal Dynamics*,  
Cambridge Univ. Press

# Neuronal Dynamics – 4.2. Synaptic reversal potential

glutamate: excitatory synapses

$$-I^{syn}(t) = -g_{syn}(t)(u - E_{syn})$$

$$E_{syn} \approx 0mV$$

GABA: inhibitory synapses

$$-I^{syn}(t) = -g_{syn}(t)(u - E_{syn})$$

$$E_{syn} \approx -75mV$$

# Neuronal Dynamics – 4.2. Synapses

glutamate: excitatory synapses

$$-I^{syn}(t) = -g_{syn}(t)(u - E_{syn})$$

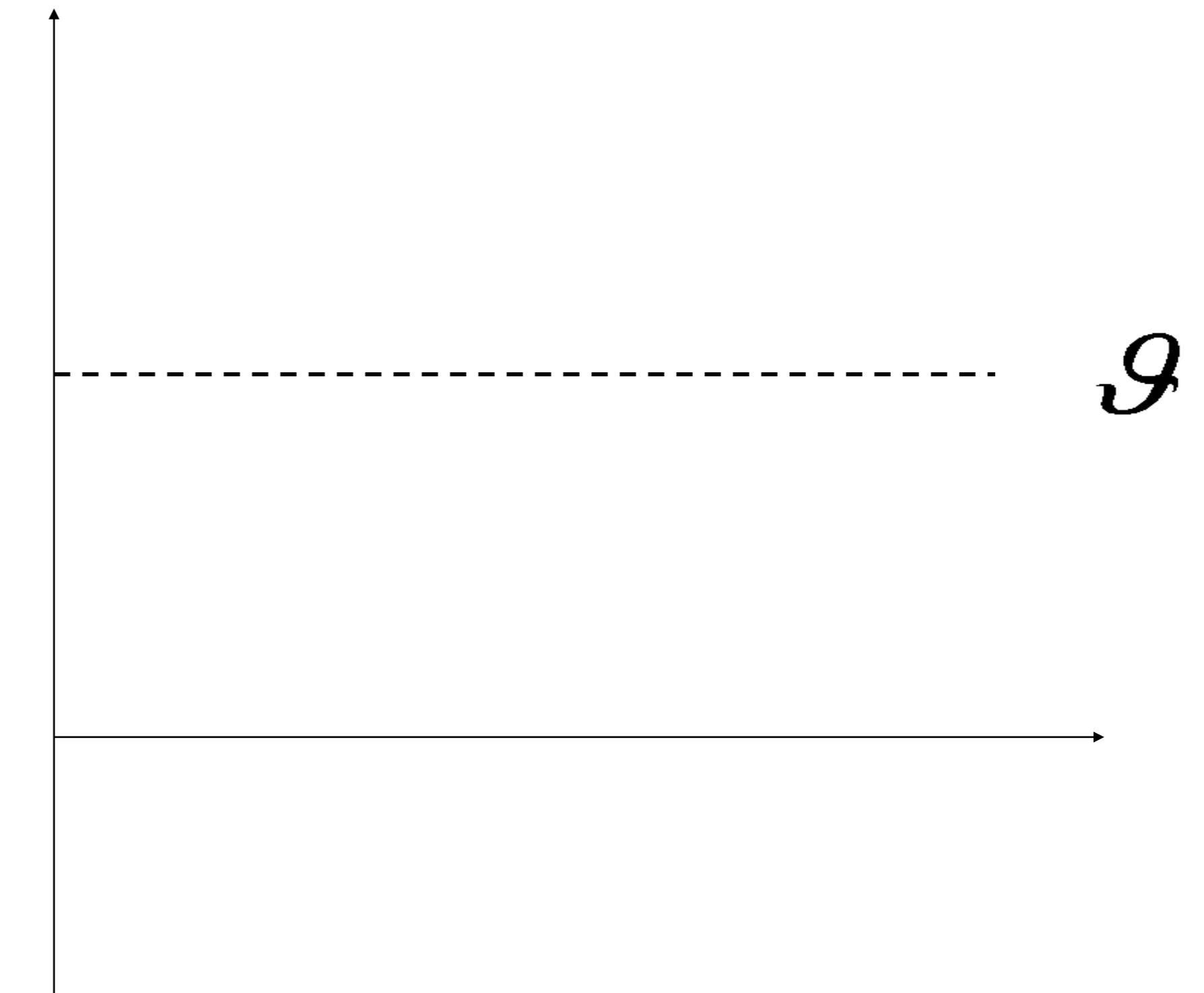
$$E_{syn} \approx 0mV$$

GABA: inhibitory synapses

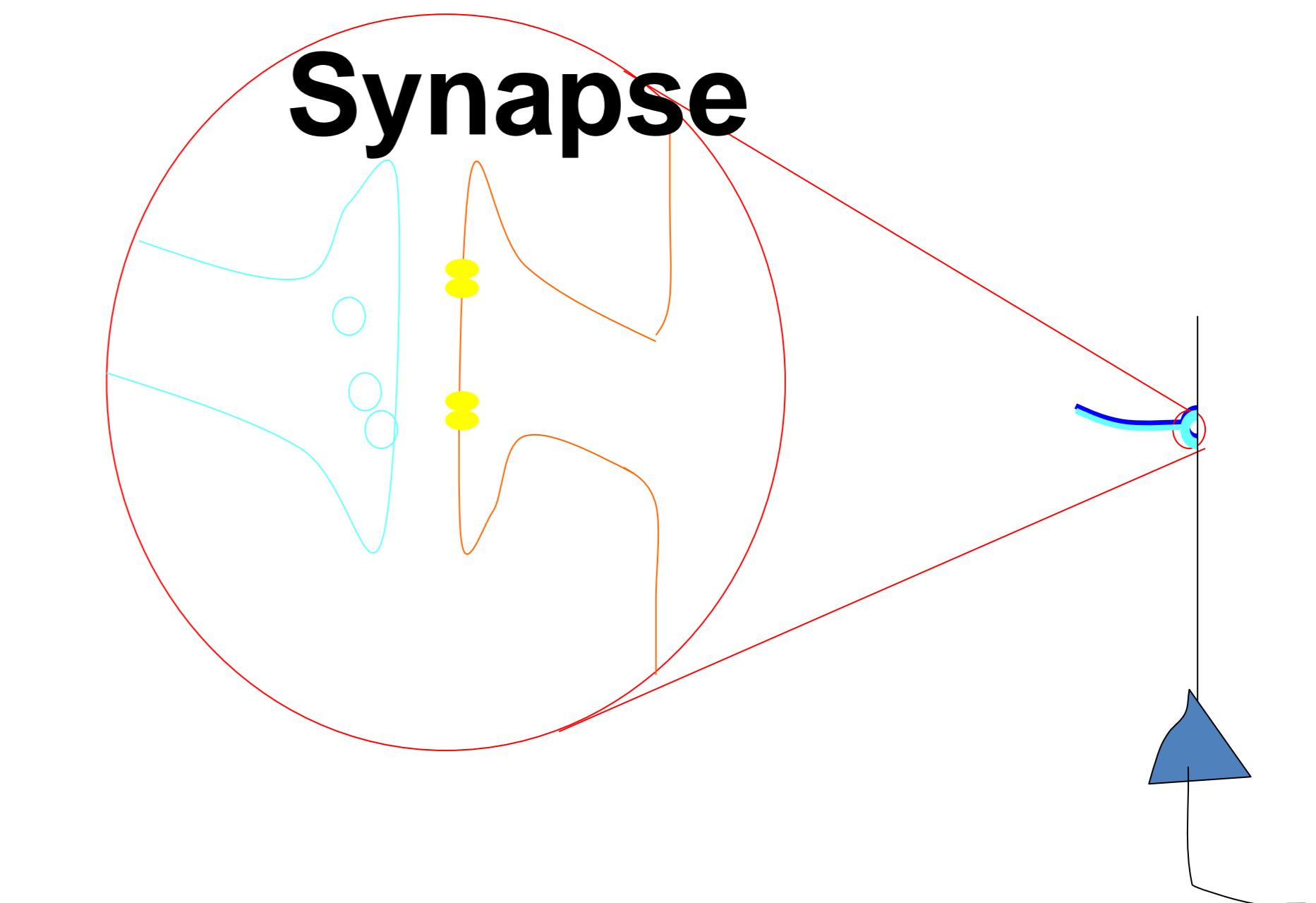
$$-I^{syn}(t) = -g_{syn}(t)(u - E_{syn})$$

$$E_{syn} \approx -75mV$$

$$I^{stim}(t) = -I^{syn}(t)$$



# Neuronal Dynamics – 4.2.Synapses



# Neuronal Dynamics – Quiz 4.3

*Multiple answers possible!*

## AMPA channel

- [ ] AMPA channels are activated by AMPA
- [ ] If an AMPA channel is open, AMPA can pass through the channel
- [ ] If an AMPA channel is open, glutamate can pass through the channel
- [ ] If an AMPA channel is open, potassium can pass through the channel
- [ ] The AMPA channel is a transmitter-gated ion channel
- [ ] AMPA channels are often found in a synapse

## Synapse types

- [ ] In the subthreshold regime, excitatory synapses always depolarize the membrane, i.e., shift the membrane potential to more positive values
- [ ] In the subthreshold regime, inhibitory synapses always hyperpolarize the membrane, i.e., shift the membrane potential more negative values
- [ ] Excitatory synapses in cortex often contain AMPA receptors
- [ ] Excitatory synapses in cortex often contain NMDA receptors

## Week 4 – part 2: More Detail – compartmental models



# Biological Modeling of Neural Networks

## Week 4

- Reducing detail
- Adding detail

Wulfram Gerstner

EPFL, Lausanne, Switzerland

↓ 3.1 From Hodgkin-Huxley to 2D

↓ 3.2 Phase Plane Analysis

↓ 3.3 Analysis of a 2D Neuron Model

↓ 4.1 Type I and II Neuron Models

- limit cycles
- where is the firing threshold?
- separation of time scales

## 4.2. Dendrites

- synapses
- cable equation

# Neuronal Dynamics – 4.2. Dendrites

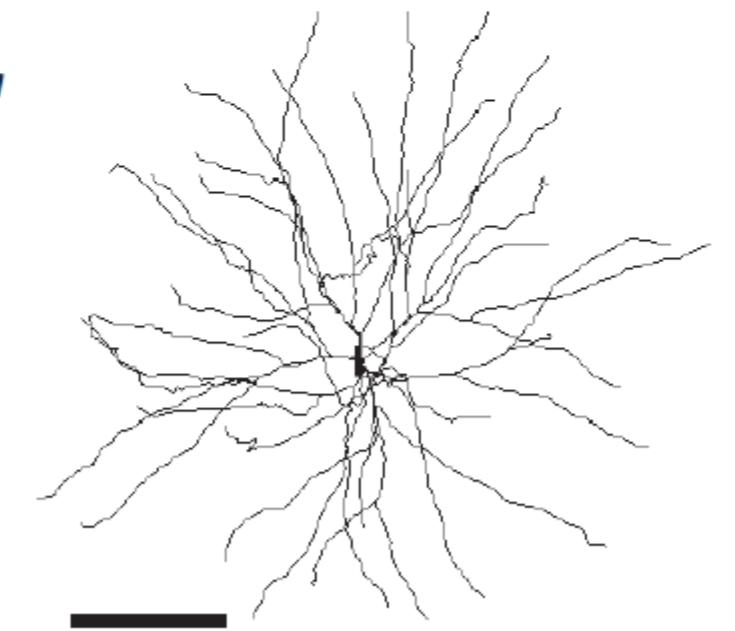
C



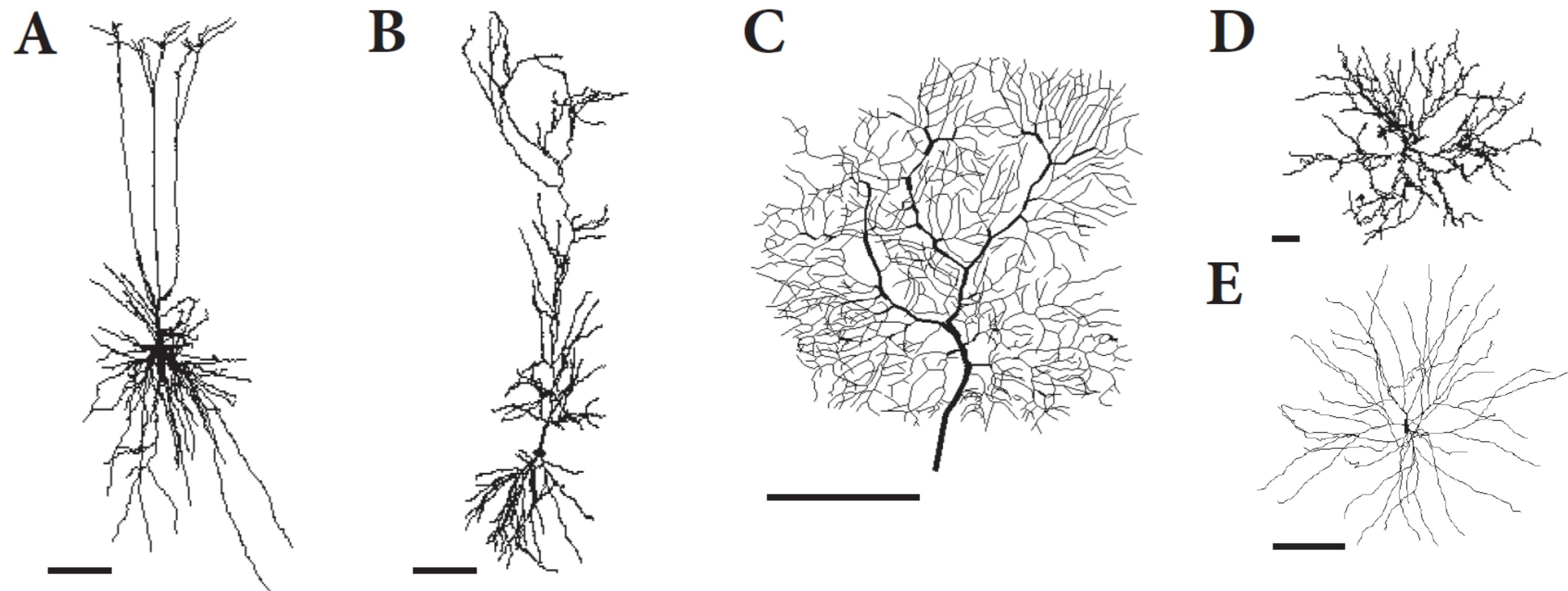
D



E



# Neuronal Dynamics – 4.2 Dendrites



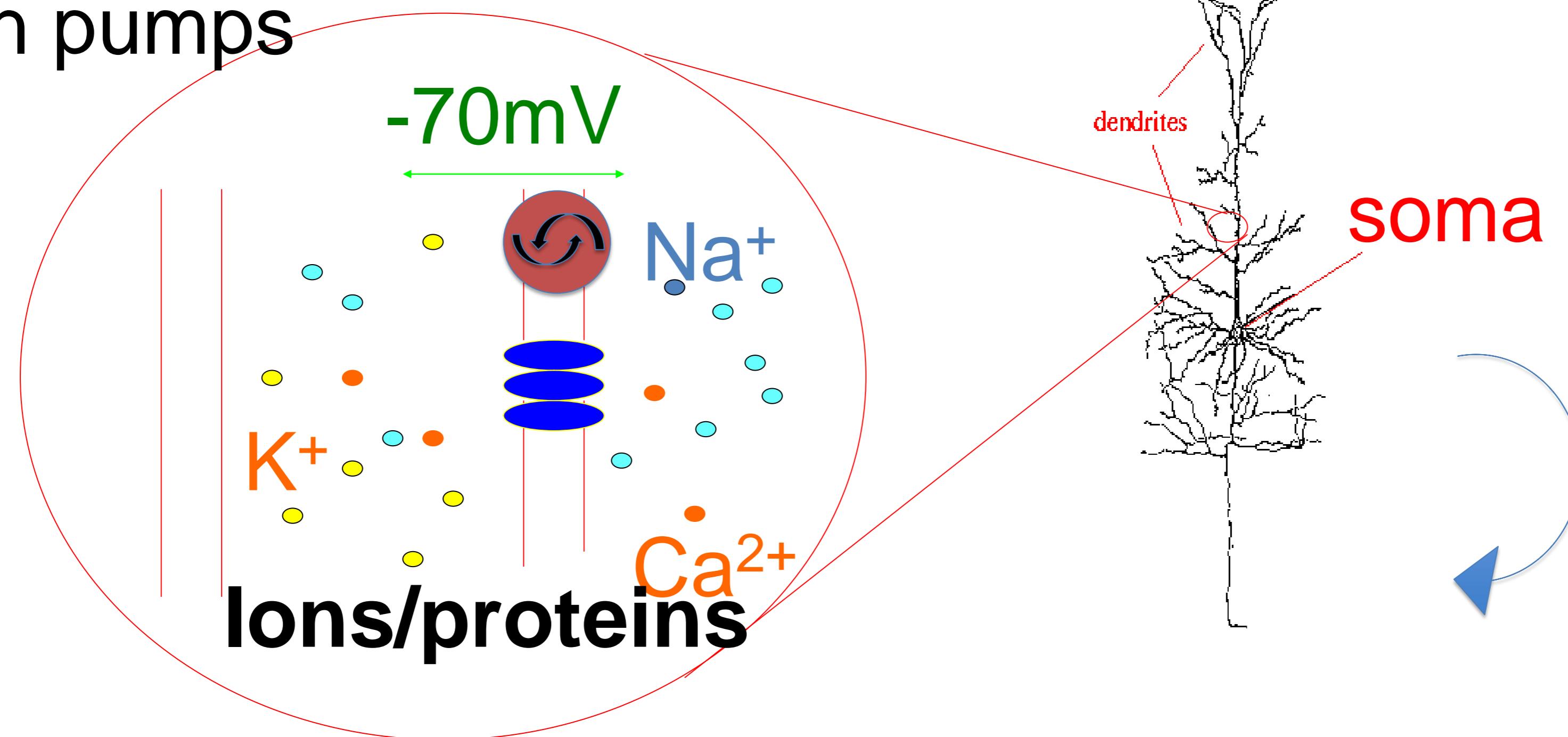
**Fig. 3.4:** Reconstructed morphology of various types of neurons. **A.** Pyramidal neuron from a deep cortical layer(Contreras et al., 1997). **B.** Pyramidal neuron from the CA1 of the hippocampus (Golding et al., 2005). **C.** Purkinje cell from the cerebellum (Rapp et al., 1994). **D.** Motoneuron from the spinal cord (Cullheim et al., 1987). **E.** Stellate neuron from the neocortex (Mainen and Sejnowski, 1996). Reconstructed morphologies can be downloaded from <http://NeuroMorpho.Org>. Scale bars represents 100  $\mu$ m.

# Neuronal Dynamics – Review: Biophysics of neurons

Cell surrounded by membrane

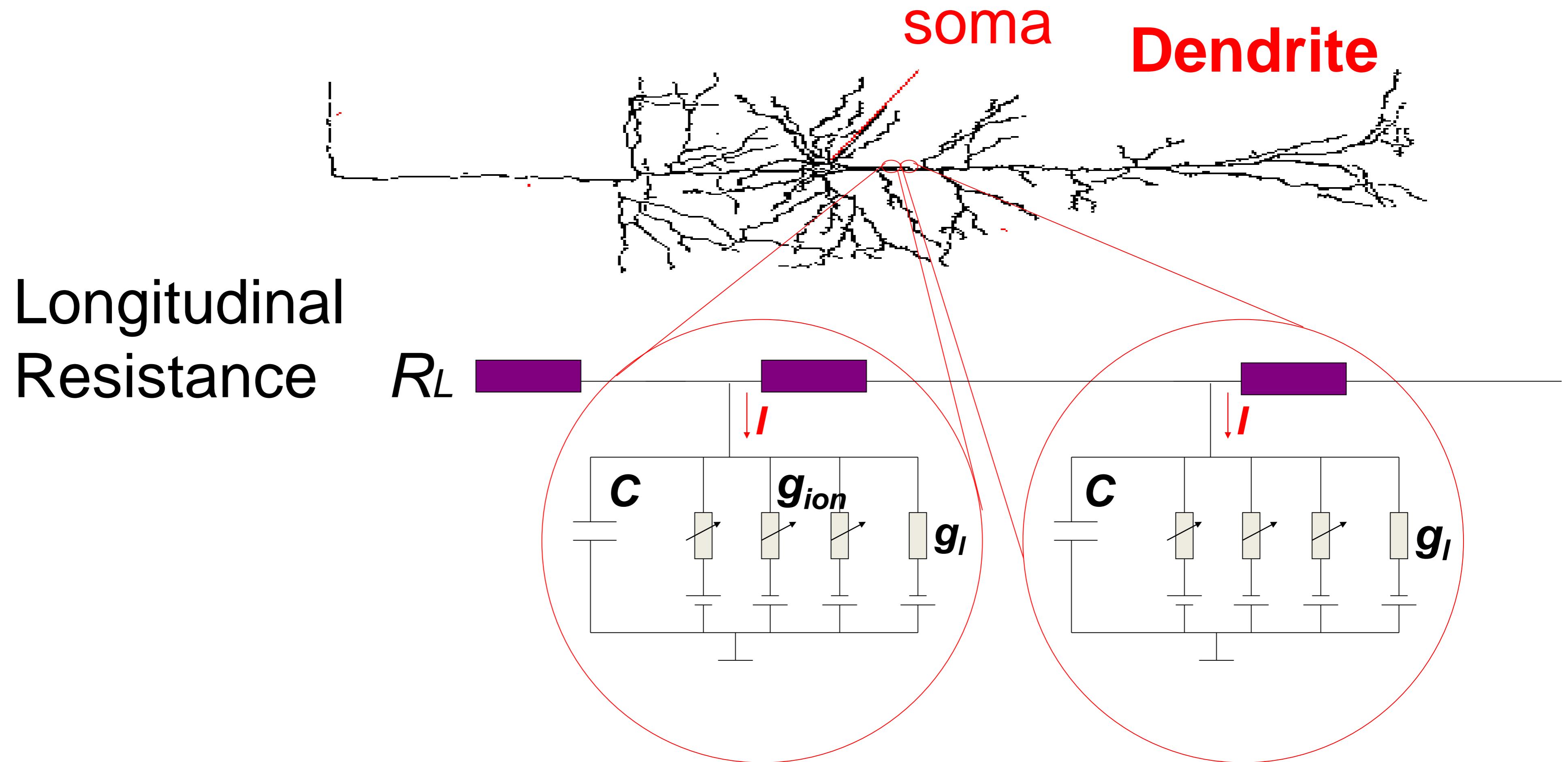
Membrane contains

- ion channels
- ion pumps



Dendrite and axon:  
Cable-like extensions  
Tree-like structure

# Neuronal Dynamics – Modeling the Dendrite

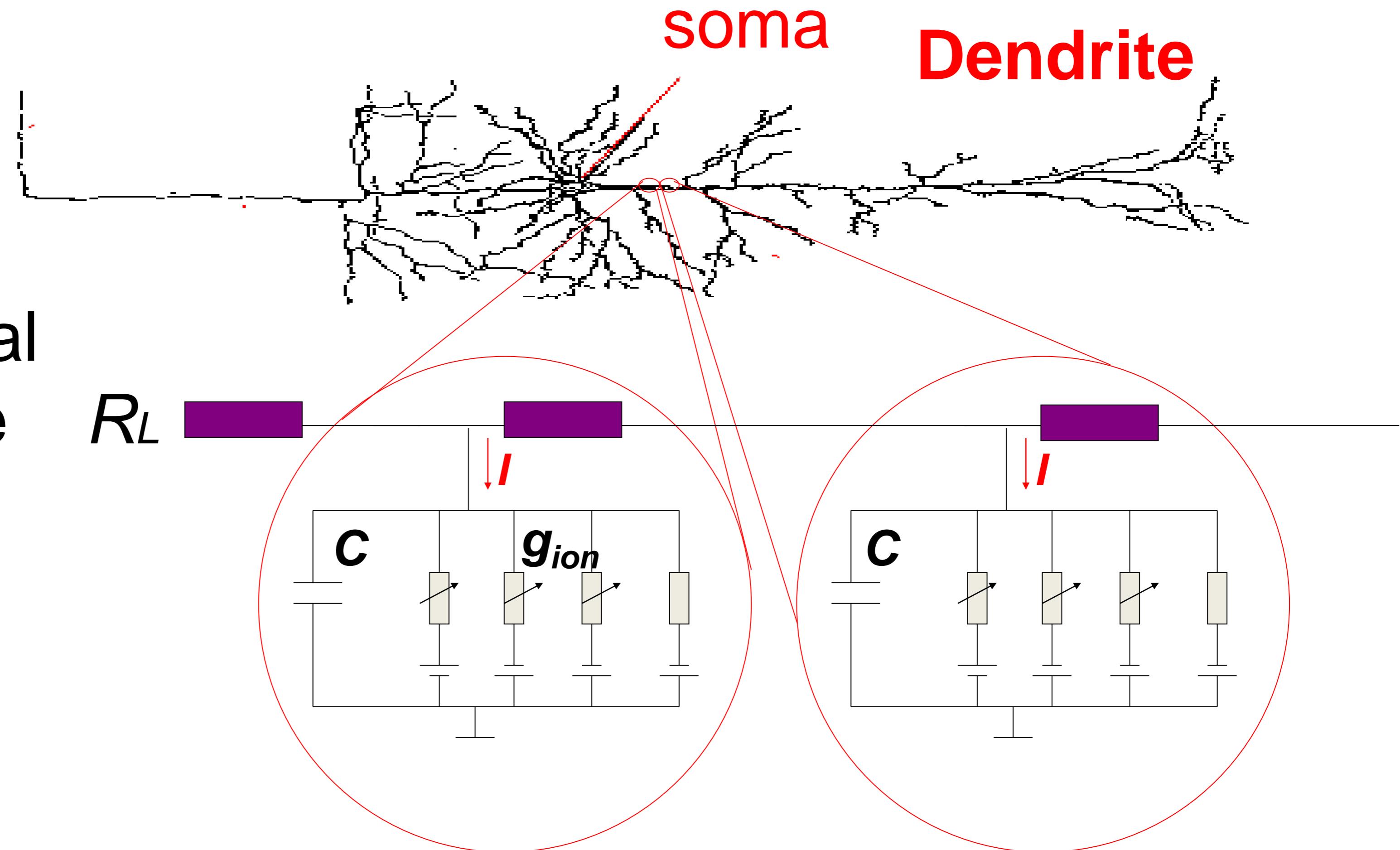


# Neuronal Dynamics – Modeling the Dendrite

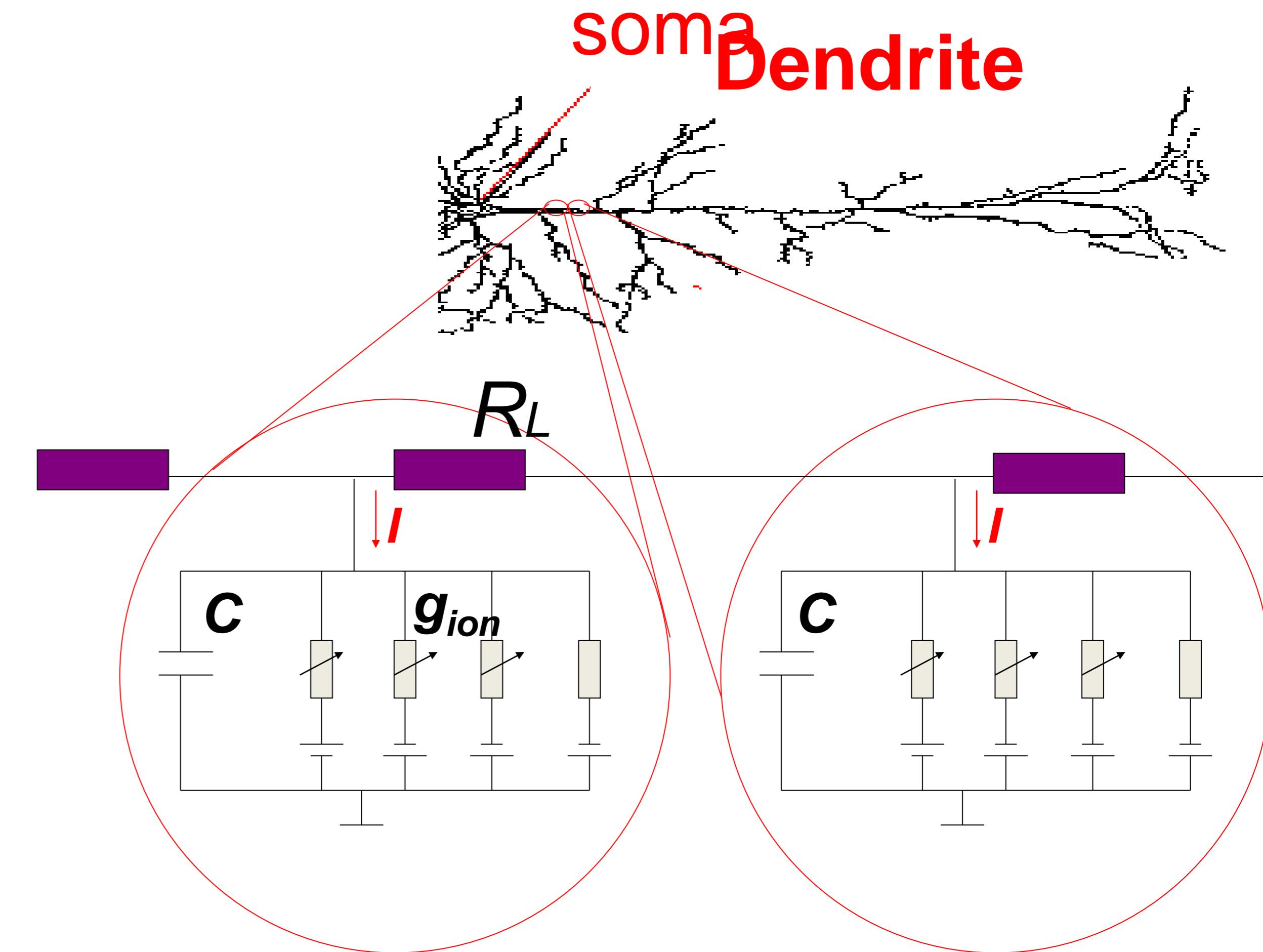
Longitudinal  
Resistance

$R_L$

*Calculation*



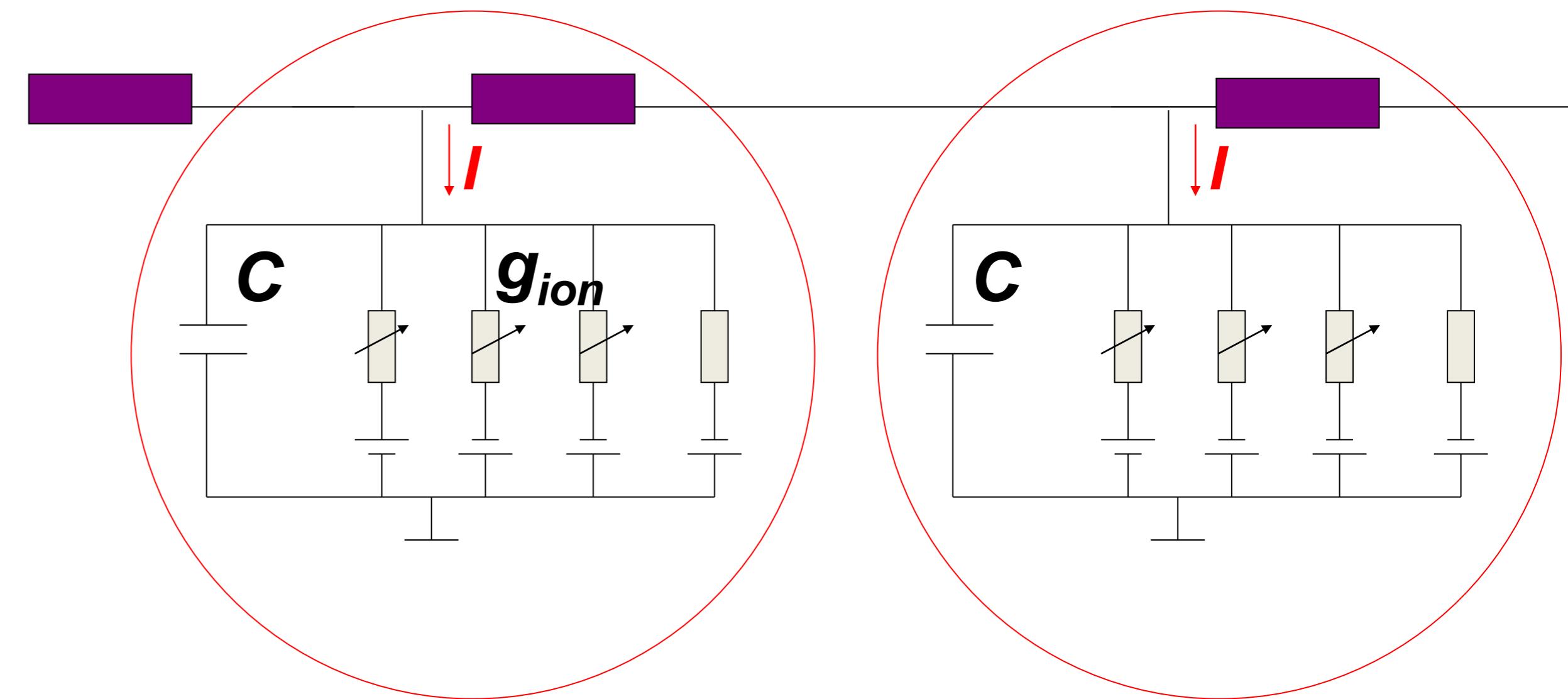
# Neuronal Dynamics – Conservation of current



# Neuronal Dynamics – 4.2 Equation-Coupled compartments

$$\frac{u(t, x - dx) - 2u(t, x) + u(t, x + dx)}{R_L} = C \frac{d}{dt} u(t, x) + \sum_{ion} I_{ion}(t, x) - I^{ext}(t, x)$$

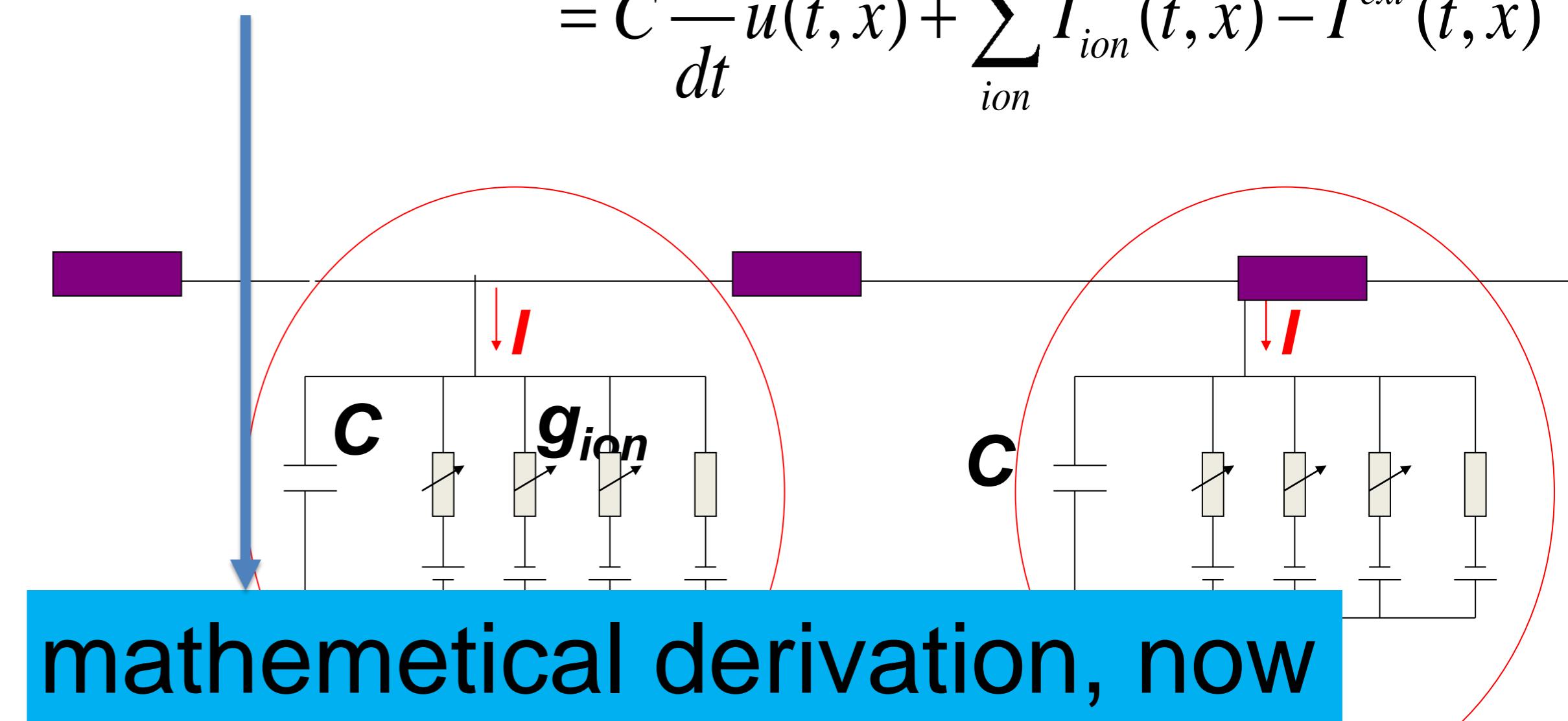
Basis for  
-Cable equation  
-Compartmental models



# Neuronal Dynamics – 4.2 Derivation of Cable Equation

$$\frac{u(t, x - dx) - 2u(t, x) + u(t, x + dx)}{R_L}$$

$$= C \frac{d}{dt} u(t, x) + \sum_{ion} I_{ion}(t, x) - I^{ext}(t, x)$$

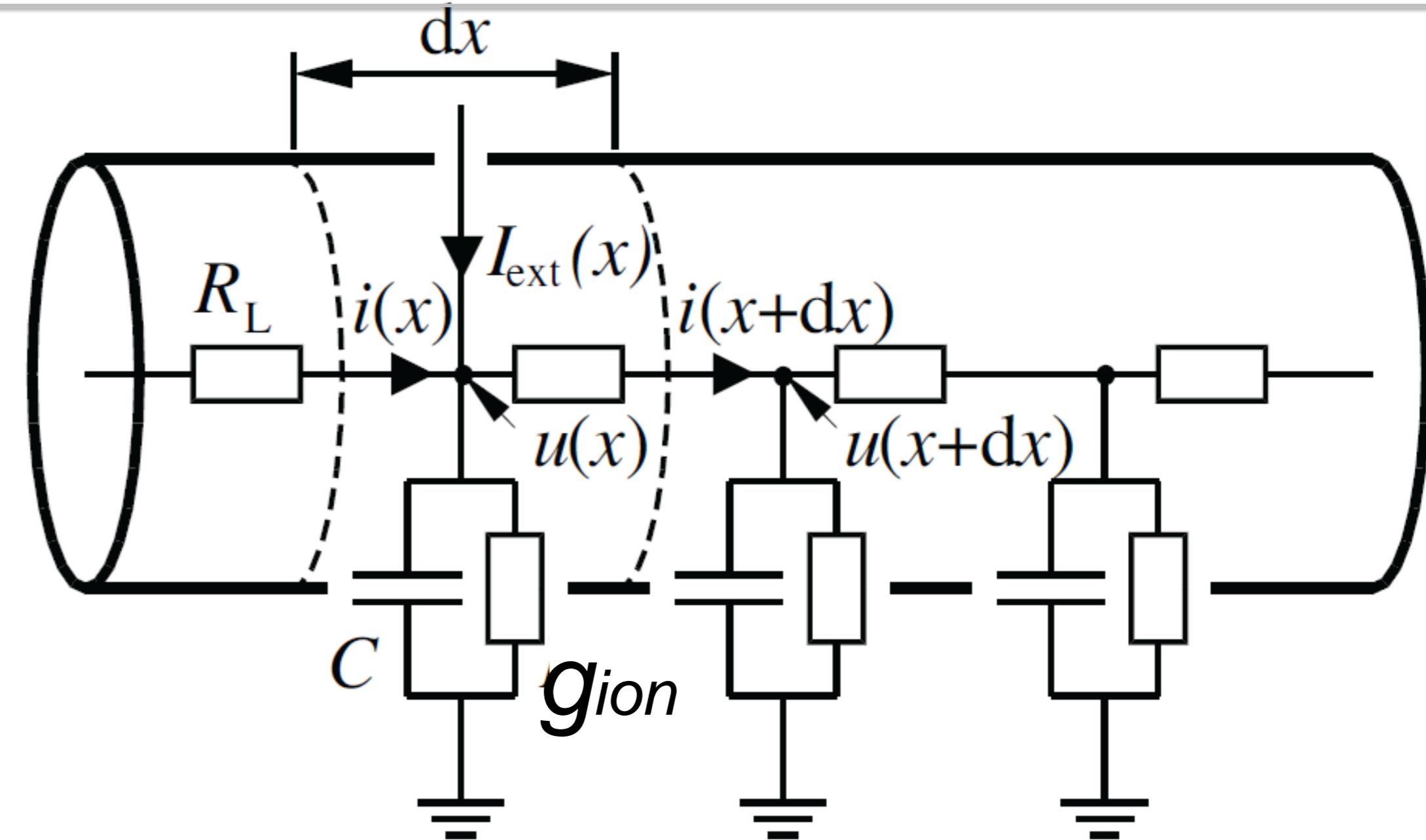


$$\frac{d^2}{dx^2} u(t, x) = cr_L \frac{d}{dt} u(t, x) + r_L \sum_{ion} i_{ion}(t, x) - r_L i^{ext}(t, x)$$

# Neuronal Dynamics – 4.2 Modeling the Dendrite

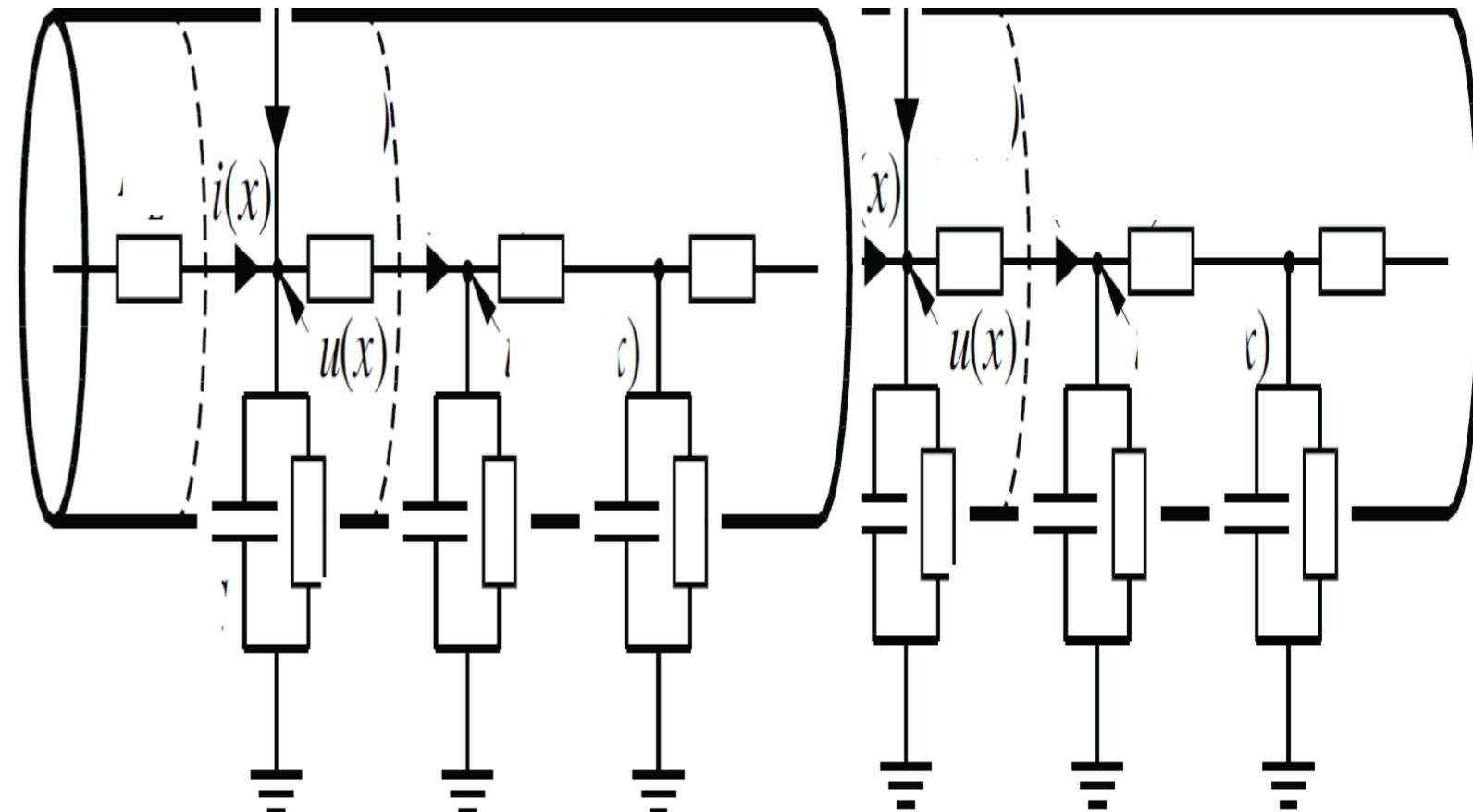
$$R_L = r_L dx$$

$$C = c dx$$



$$I_{ion} = i_{ion} dx$$

$$I^{ext} = i^{ext} dx$$



# Neuronal Dynamics – 4.2 Derivation of cable equation

$$\frac{u(t, x - dx) - 2u(t, x) + u(t, x + dx)}{R_L} = C \frac{d}{dt} u(t, x) + \sum_{ion} I_{ion}(t, x) - I^{ext}(t, x)$$

$$R_L = r_L dx$$

$$C = c dx$$

$$I_{ion} = i_{ion} dx$$

$$I^{ext} = i^{ext} dx$$

$$\frac{d^2}{dx^2} u(t, x) = cr_L \frac{d}{dt} u(t, x) + r_L \sum_{ion} i_{ion}(t, x) - r_L i^{ext}(t, x)$$

# Neuronal Dynamics – 4.2 Dendrite as a cable

$$\frac{d^2}{dx^2} u(t, x) = cr_L \frac{d}{dt} u(t, x) + r_L \sum_{ion} i_{ion}(t, x) - r_L i^{ext}(t, x)$$

$\sum_{ion} i_{ion}(t, x) = leak$       passive dendrite

$\sum_{ion} i_{ion}(t, x) = Ca, Na, \dots$  active dendrite

$\sum_{ion} i_{ion}(t, x) = Na, K, \dots$  axon

# Neuronal Dynamics – Quiz 4.4

*Multiple answers possible!*

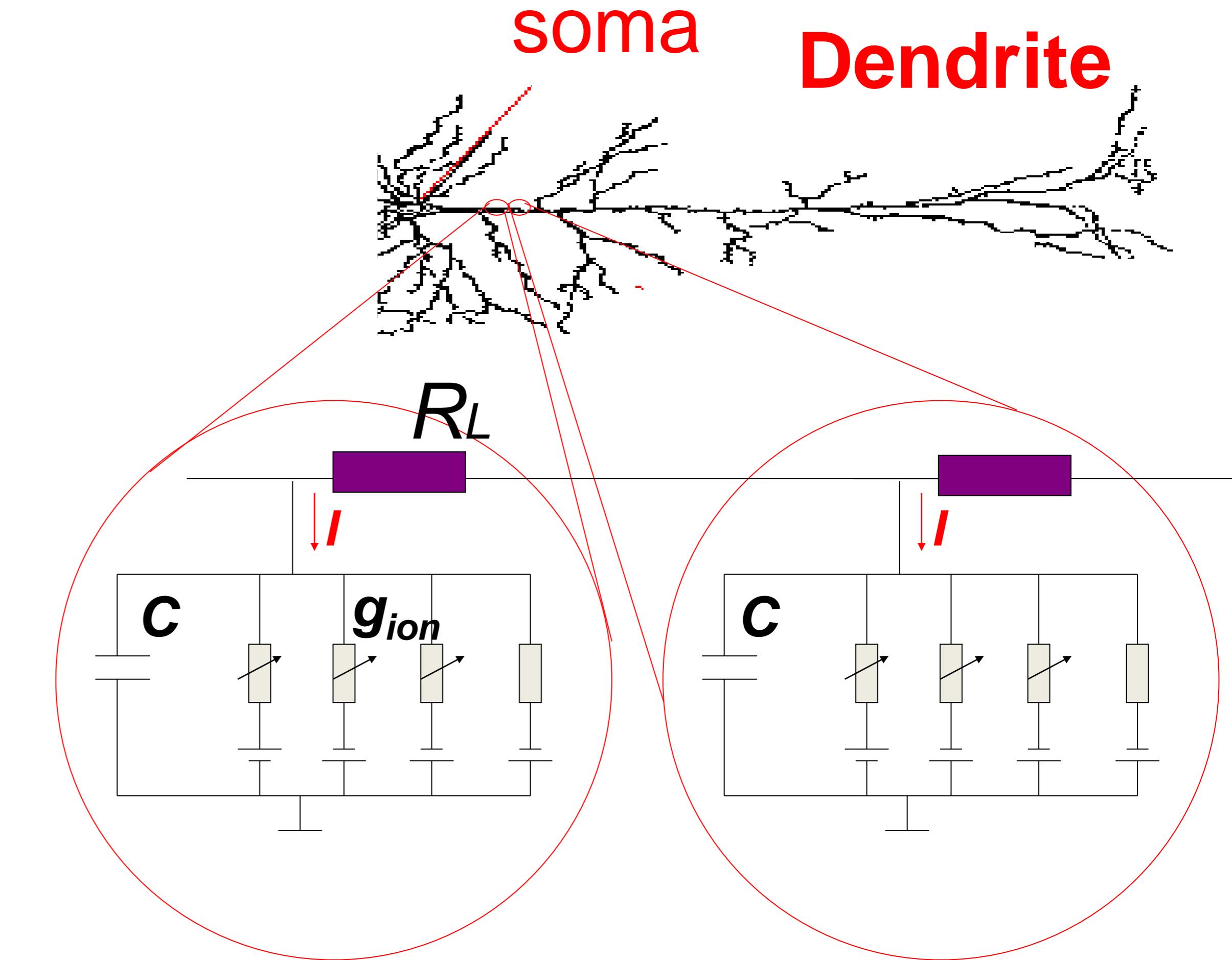
## Scaling of parameters.

Suppose the ionic currents through the membrane are well approximated by a simple leak current. For a dendritic segment of size  $dx$ , the leak current is through the membrane characterized by a membrane resistance  $R$ . If we change the size of the segment

From  $dx$  to  $2dx$

- the resistance  $R$  needs to be changed from  $R$  to  $2R$ .
- the resistance  $R$  needs to be changed from  $R$  to  $R/2$ .
- $R$  does not change.
- the membrane conductance increases by a factor of 2.

# Neuronal Dynamics – 4.2. Cable equation



# Neuronal Dynamics – 4.2 Cable equation

$$\frac{d^2}{dx^2} u(t, x) = cr_L \frac{d}{dt} u(t, x) + r_L \sum_{ion} i_{ion}(t, x) - r_L i^{ext}(t, x)$$

$\sum_{ion} i_{ion}(t, x) = leak$       passive dendrite

$\sum_{ion} i_{ion}(t, x) = Ca, Na, \dots$  active dendrite

$\sum_{ion} i_{ion}(t, x) = Na, K, \dots$  axon

# Neuronal Dynamics – 4.2 Cable equation

## Mathematical derivation

$$\frac{d^2}{dx^2} u(t, x) = cr_L \frac{d}{dt} u(t, x) + r_L \sum_{ion} i_{ion}(t, x) - r_L i^{ext}(t, x)$$

$$\sum_{ion} i_{ion}(t, x) = leak \quad \text{passive dendrite}$$

$$\sum_{ion} i_{ion}(t, x) = Ca, Na, \dots \quad \text{active dendrite}$$

$$\sum_{ion} i_{ion}(t, x) = Na, K, \dots \quad \text{axon}$$

# Neuronal Dynamics – 4.2 Derivation for passive cable

$$\frac{d^2}{dx^2} u(t, x) = cr_L \frac{d}{dt} u(t, x) + r_L \sum_{ion} i_{ion}(t, x) - r_L i^{ext}(t, x)$$

$$\sum_{ion} i_{ion}(t, x) = leak$$

passive dendrite

$$I_{ion} = i_{ion} dx$$

$$I^{ext} = i^{ext} dx$$

See exercise 3

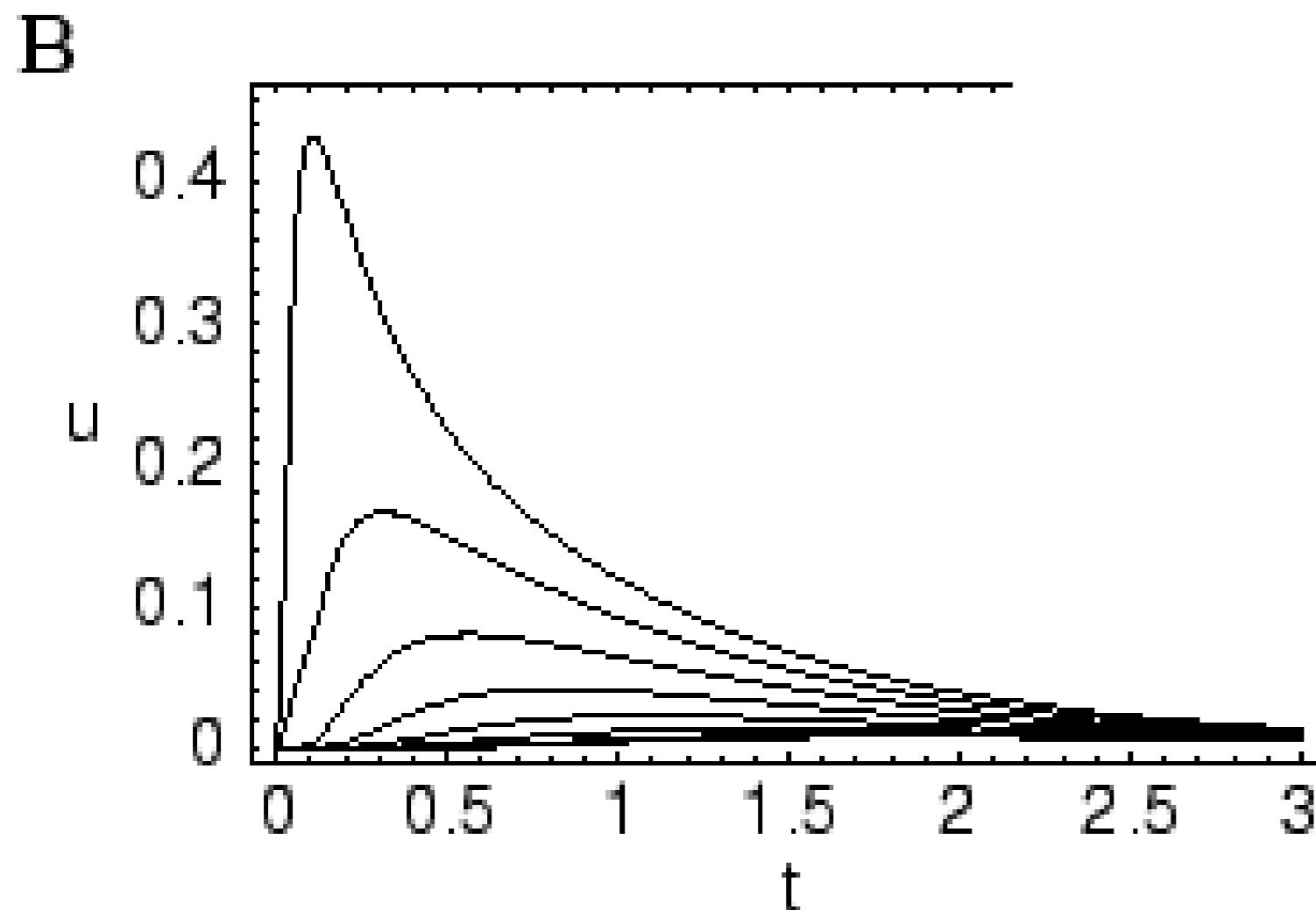
$$\lambda^2 \frac{d^2}{dx^2} u(t, x) = \tau_m \frac{d}{dt} u(t, x) + u - r_m i^{ext}(t, x)$$

$$\sum_{ion} i_{ion}(t, x) = \frac{u}{r_m}$$

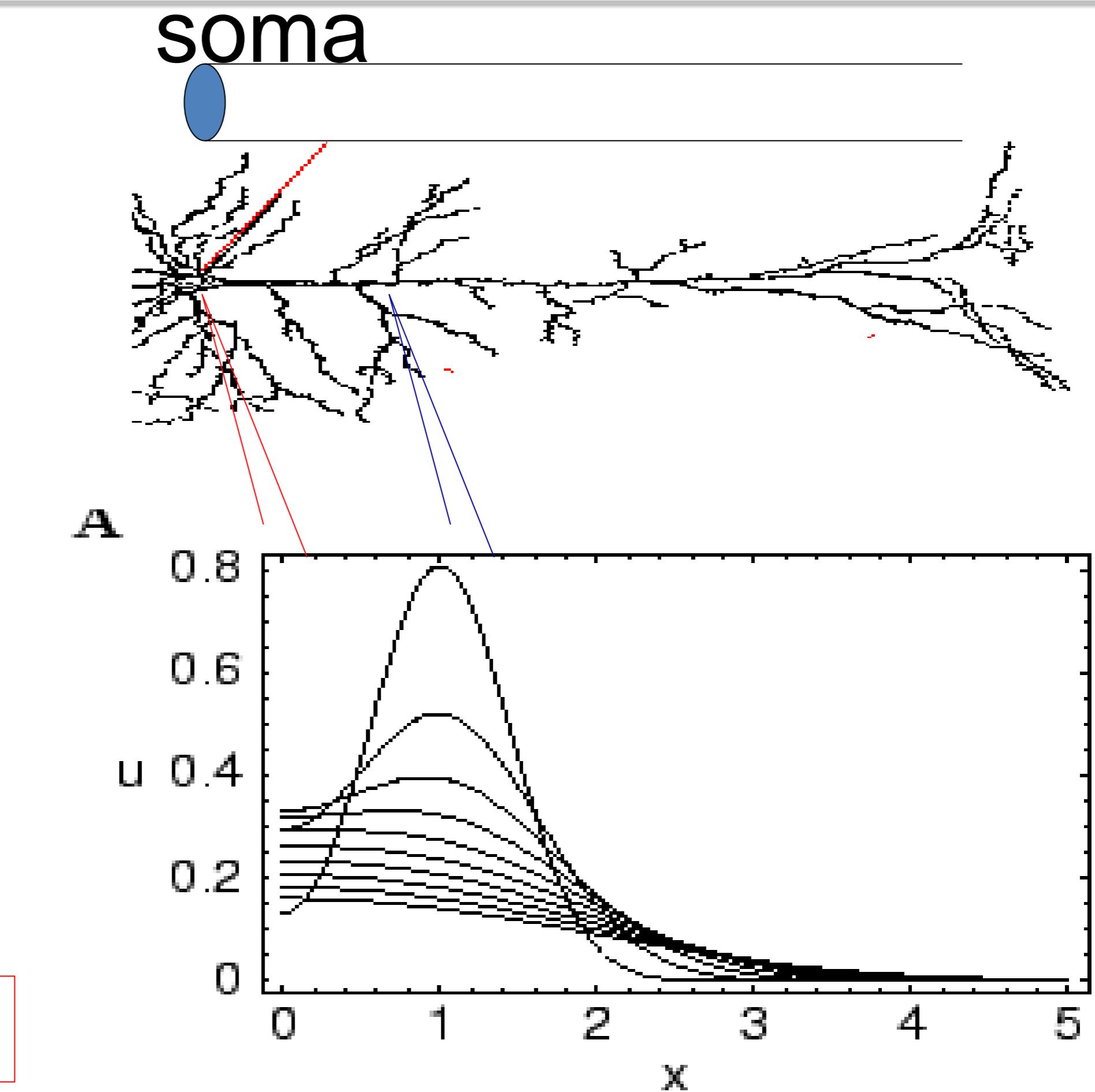
# Neuronal Dynamics – 4.2 dendritic stimulation

passive dendrite/passive cable

$$\lambda^2 \frac{d^2}{dx^2} u(t, x) = \tau_m \frac{d}{dt} u(t, x) + u - r_m i^{ext}(t, x)$$

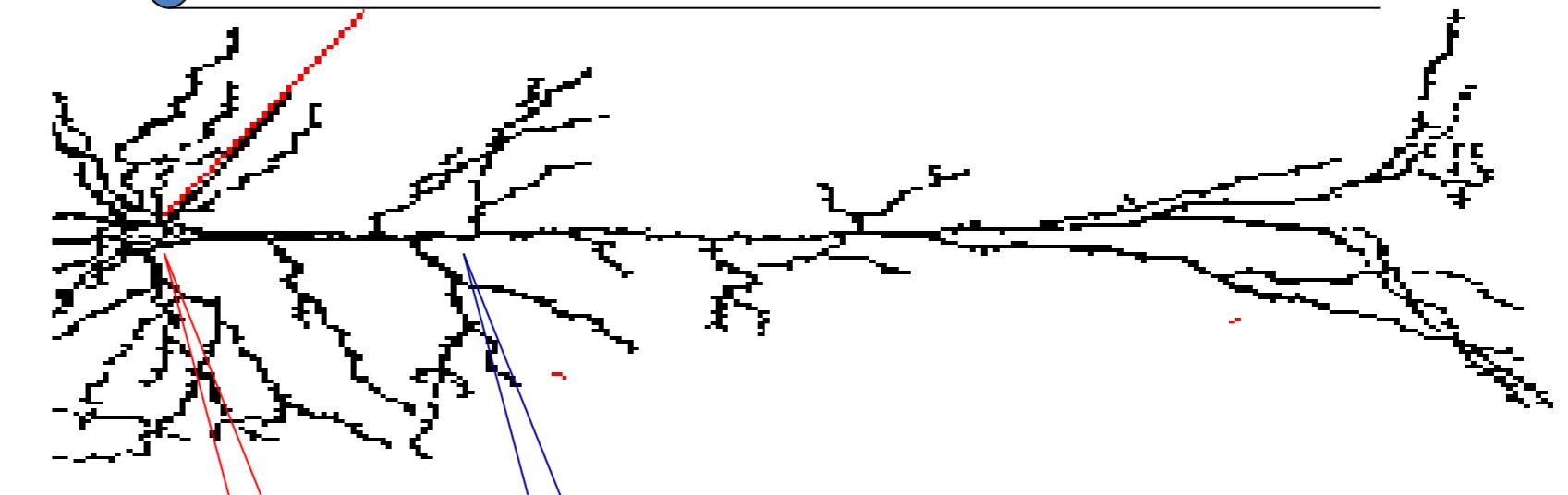


Stimulate dendrite, measure at soma

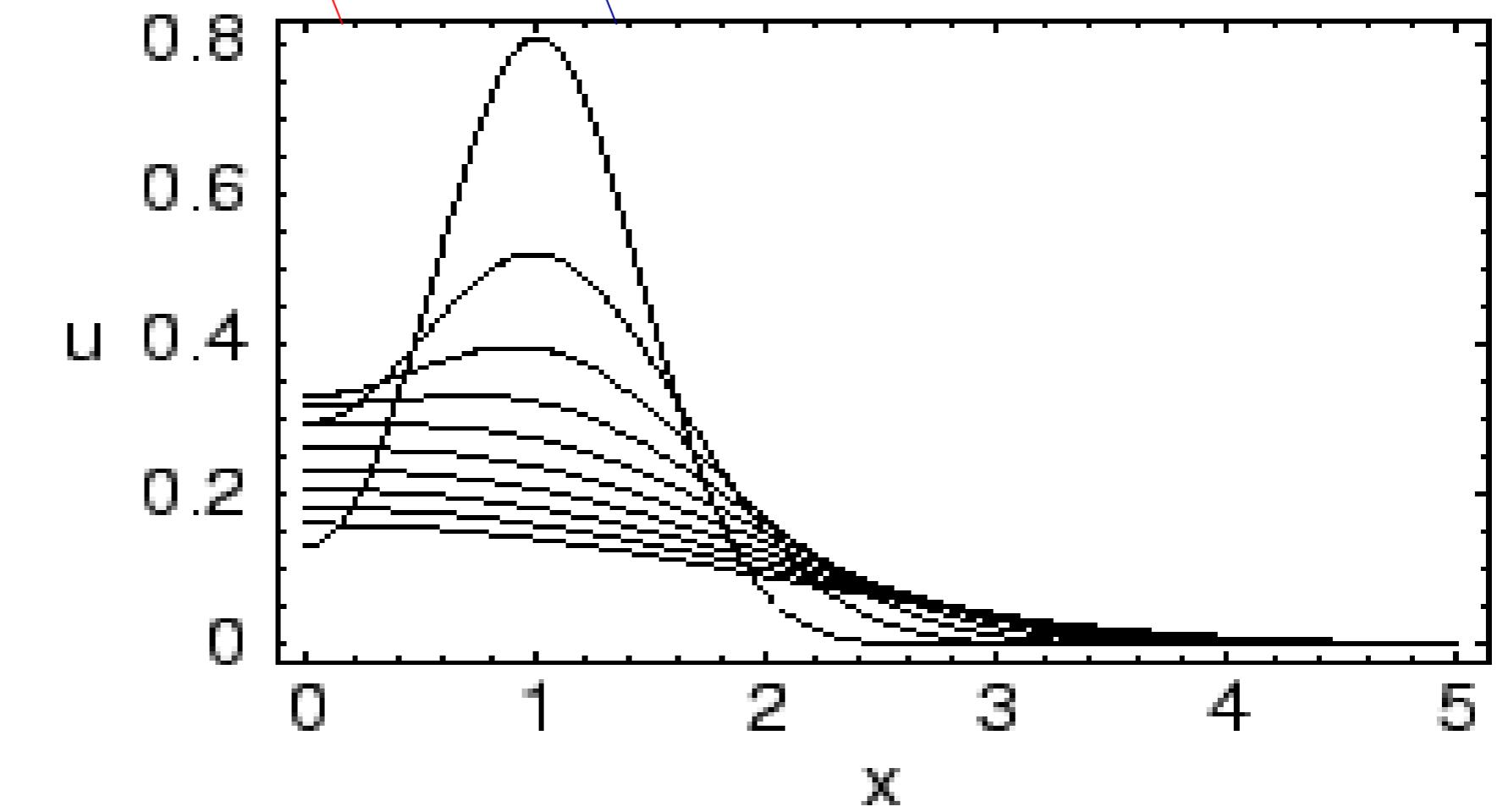


# Neuronal Dynamics – 4.2 dendritic stimulation

soma



The END



# Neuronal Dynamics – Quiz 4.5

*Multiple answers possible!*

**The space constant of a passive cable is**

[ ]  $\lambda = \frac{r_m}{r_L}$

[ ]  $\lambda = \frac{r_L}{r_m}$

[ ]  $\lambda = \sqrt{\frac{r_L}{r_m}}$

[ ]  $\lambda = \sqrt{\frac{r_m}{r_L}}$

**Dendritic current injection.**

- If a short current pulse is injected into the dendrite
- [ ] the voltage at the injection site is maximal immediately after the end of the injection
  - [ ] the voltage at the dendritic injection site is maximal a few milliseconds after the end of the injection
  - [ ] the voltage at the soma is maximal immediately after the end of the injection.
  - [ ] the voltage at the soma is maximal a few milliseconds after the end of the injection

**It follows from the cable equation that**

- [ ] the shape of an EPSP depends on the dendritic location of the synapse.
- [ ] the shape of an EPSP depends only on the synaptic time constant, but not on dendritic location.

# Neuronal Dynamics – Homework

Consider

$$(*) \quad u(t, x) = \frac{1}{\sqrt{4\pi t}} \exp\left[-t - \frac{(x - x_0)^2}{4t}\right] \quad \text{for } t > 0$$
$$u(t, x) = 0 \quad \text{for } t < 0$$

(i) Take the second derivative of (\*) with respect to  $x$ . The result is

$$\frac{d^2}{dx^2} u(t, x) = \dots$$

(ii) Take the derivative of (\*) with respect to  $t$ . The result is

$$\frac{d}{dt} u(t, x) = \dots$$

(iii) Therefore the equation is a solution to

$$\lambda^2 \frac{d^2}{dx^2} u(t, x) = \tau_m \frac{d}{dt} u(t, x) + u - r_m i^{ext}(t, x)$$

with  $\tau_m = \dots$  and  $\lambda = \dots$

(iv) The input current is [ ]  $i^{ext}(t, x) = \delta(t)\delta(x - x_0)$

$$[ ] \quad i^{ext}(t, x) = i_0 \quad \text{for } t > 0$$

# Neuronal Dynamics – Homework

Consider the two equations

$$(1) \quad \lambda^2 \frac{d^2}{dx^2} u(t, x) = \tau_m \frac{d}{dt} u(t, x) + u - r_m i^{ext}(t, x)$$

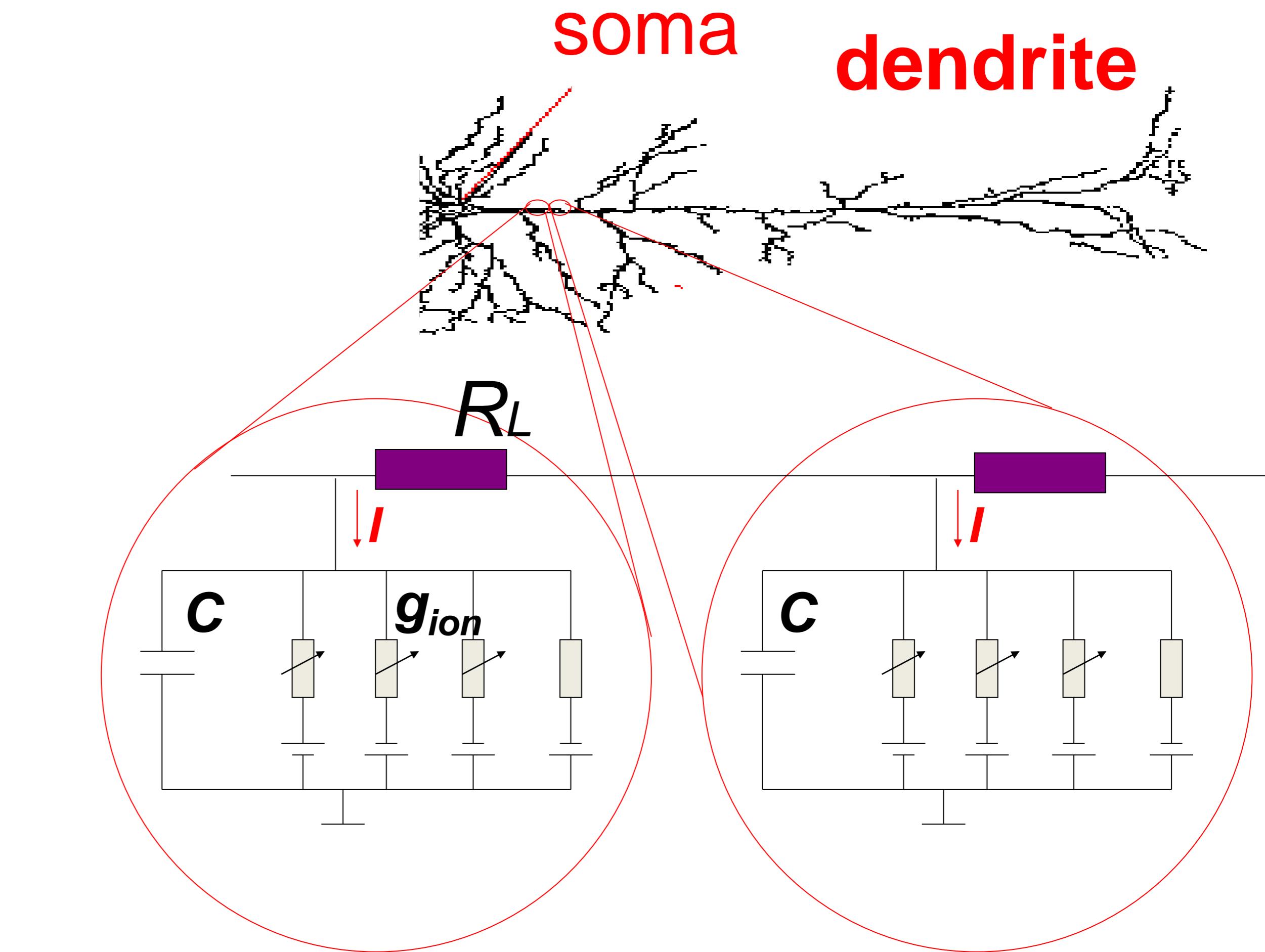
$$(2) \quad \frac{d^2}{d\tilde{x}^2} u(t', \tilde{x}) = \frac{d}{dt'} u(t', \tilde{x}) + u - i^{ext}(t', \tilde{x})$$

The two equations are equivalent under the transform

$$\tilde{x} = cx \text{ and } t' = at$$

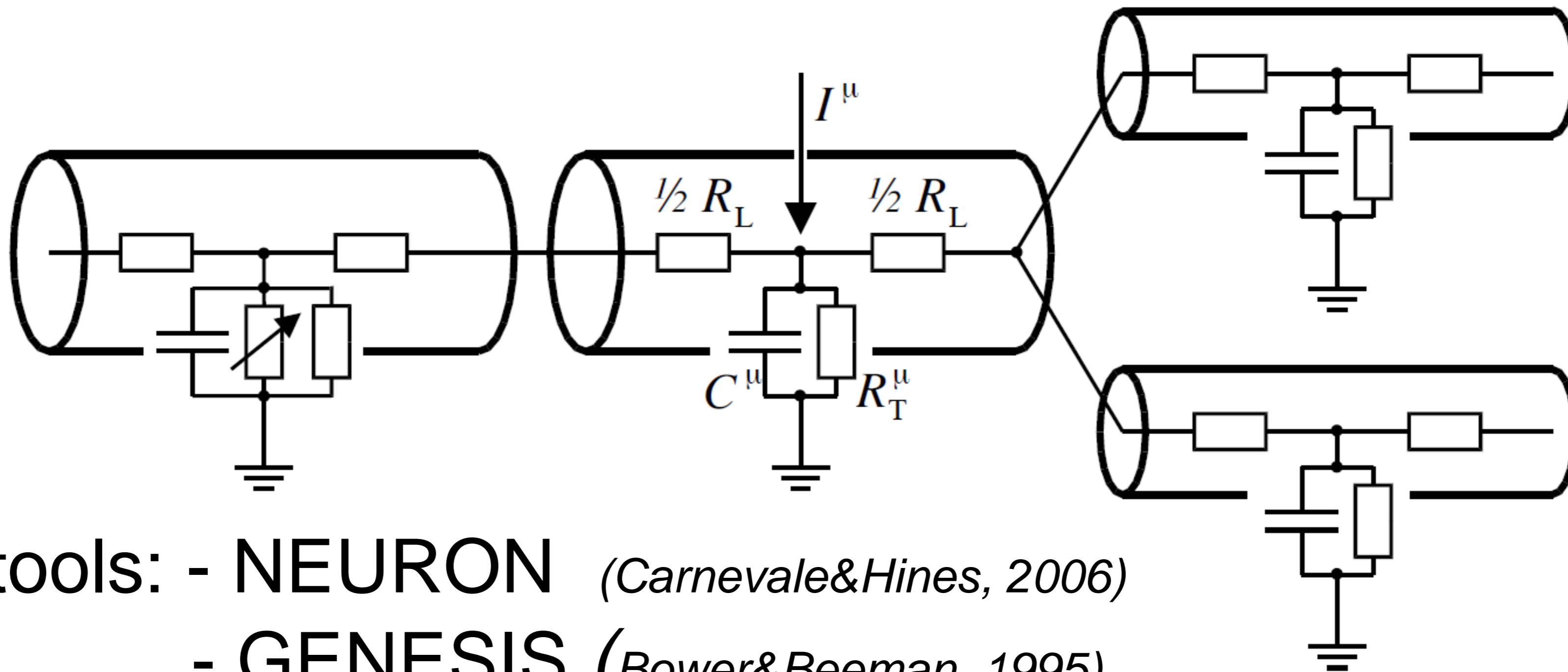
with constants  $c = \dots$  and  $a = \dots$

# Neuronal Dynamics – 4.3. Compartmental models



# Neuronal Dynamics – 4.3. Compartmental models

$$\frac{u(t, \mu-1) - u(t, \mu)}{0.5(R_L^\mu + R_L^{\mu-1})} - \frac{u(t, \mu) - u(t, \mu+1)}{0.5(R_L^\mu + R_L^{\mu+1})} = C^\mu \frac{d}{dt} u(t, \mu) + \sum_{ion} I_{ion}(t, \mu) - I^\mu(t)$$

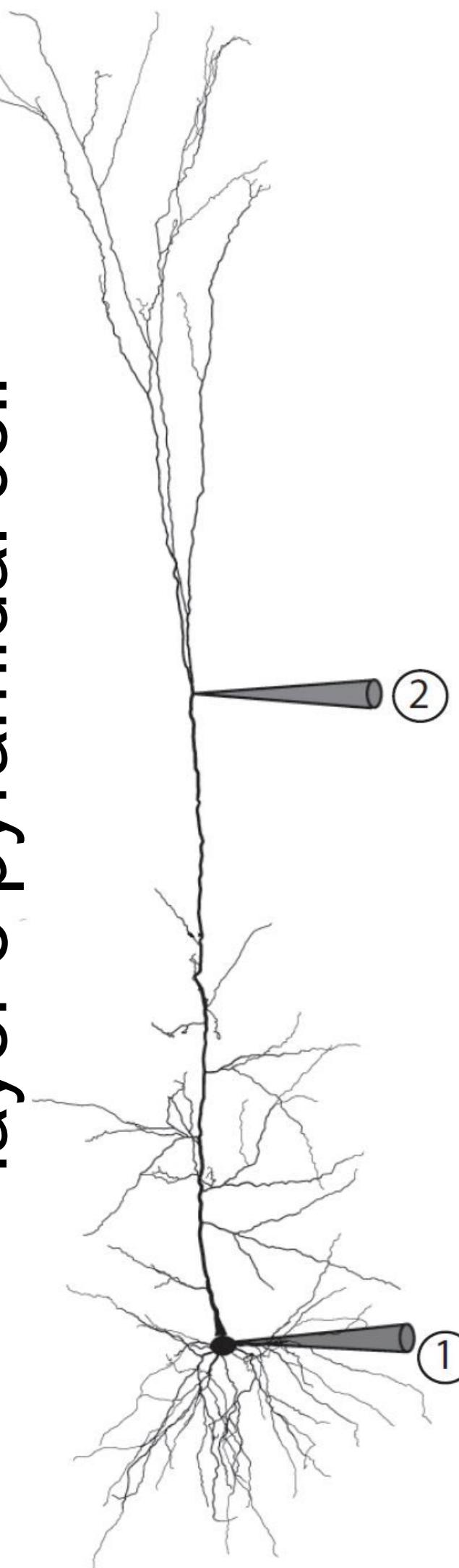


Software tools:

- NEURON (*Carnevale & Hines, 2006*)
- GENESIS (*Bower & Beeman, 1995*)

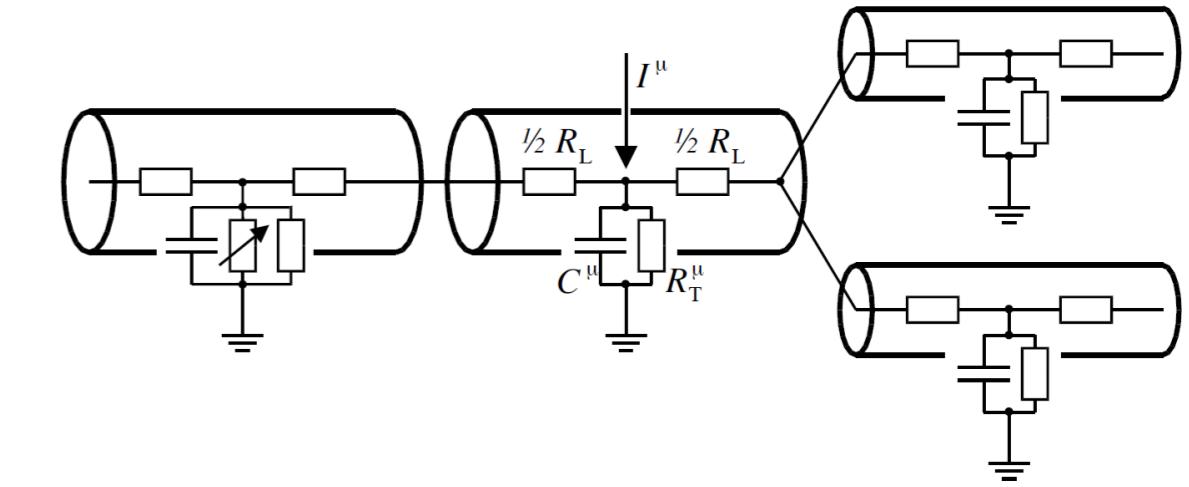
# Neuronal Dynamics – 4.3. Model of Hay et al. (2011)

layer 5 pyramidal cell



## Morphological reconstruction

- Branching points
- 200 compartments ( $\leq 20\mu m$ )
- spatial distribution of ion currents



'hotspot'

*Ca currents*

## Sodium current (2 types)

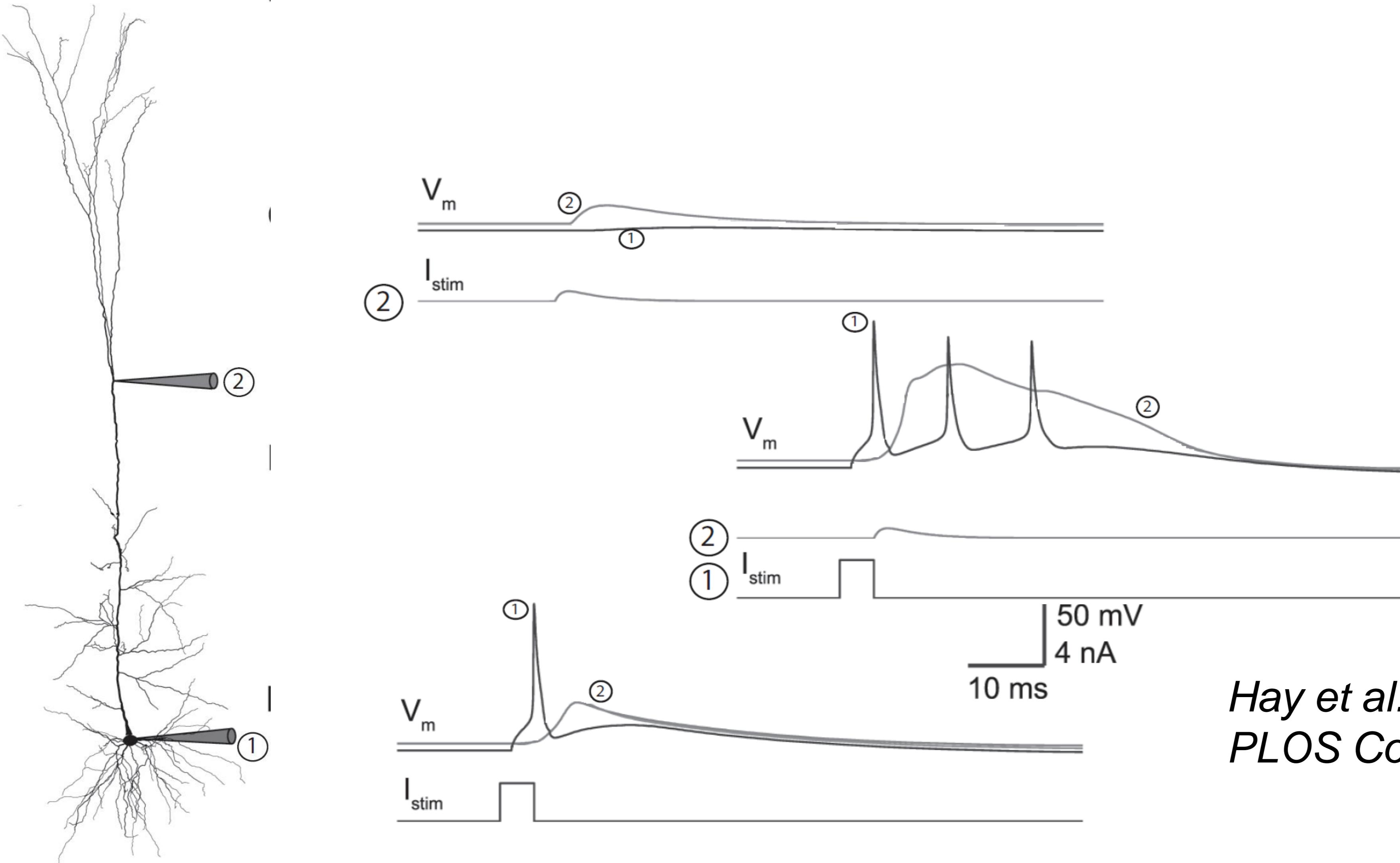
- $I_{Na,transient}$  HH-type (inactivating)
- $I_{NaP}$  persistent (non-inactivating)

## Calcium current (2 types and calcium pump)

## Potassium currents (3 types, includes $I_M$ )

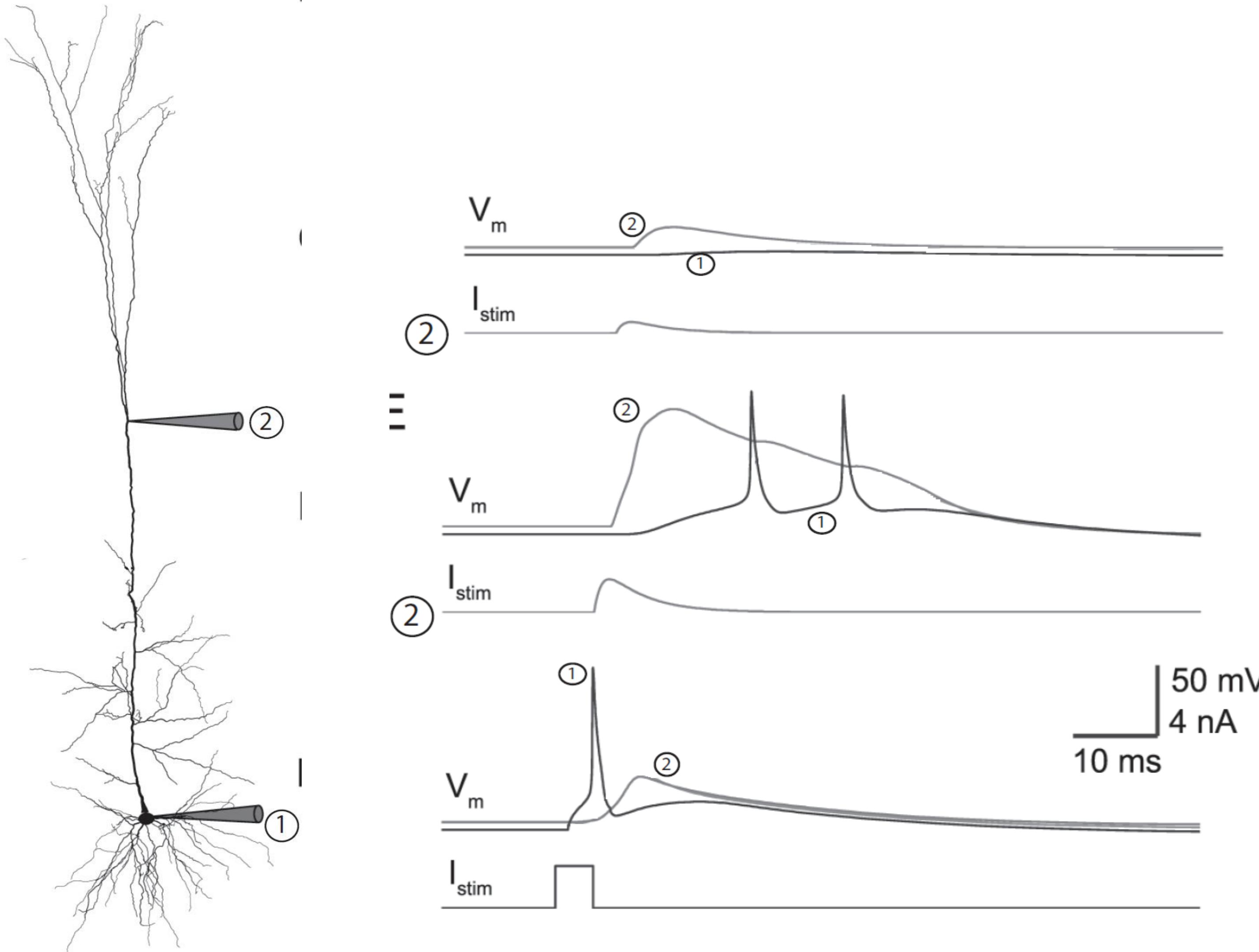
## Unspecific current

# Neuronal Dynamics – 4.3. Active dendrites: Model



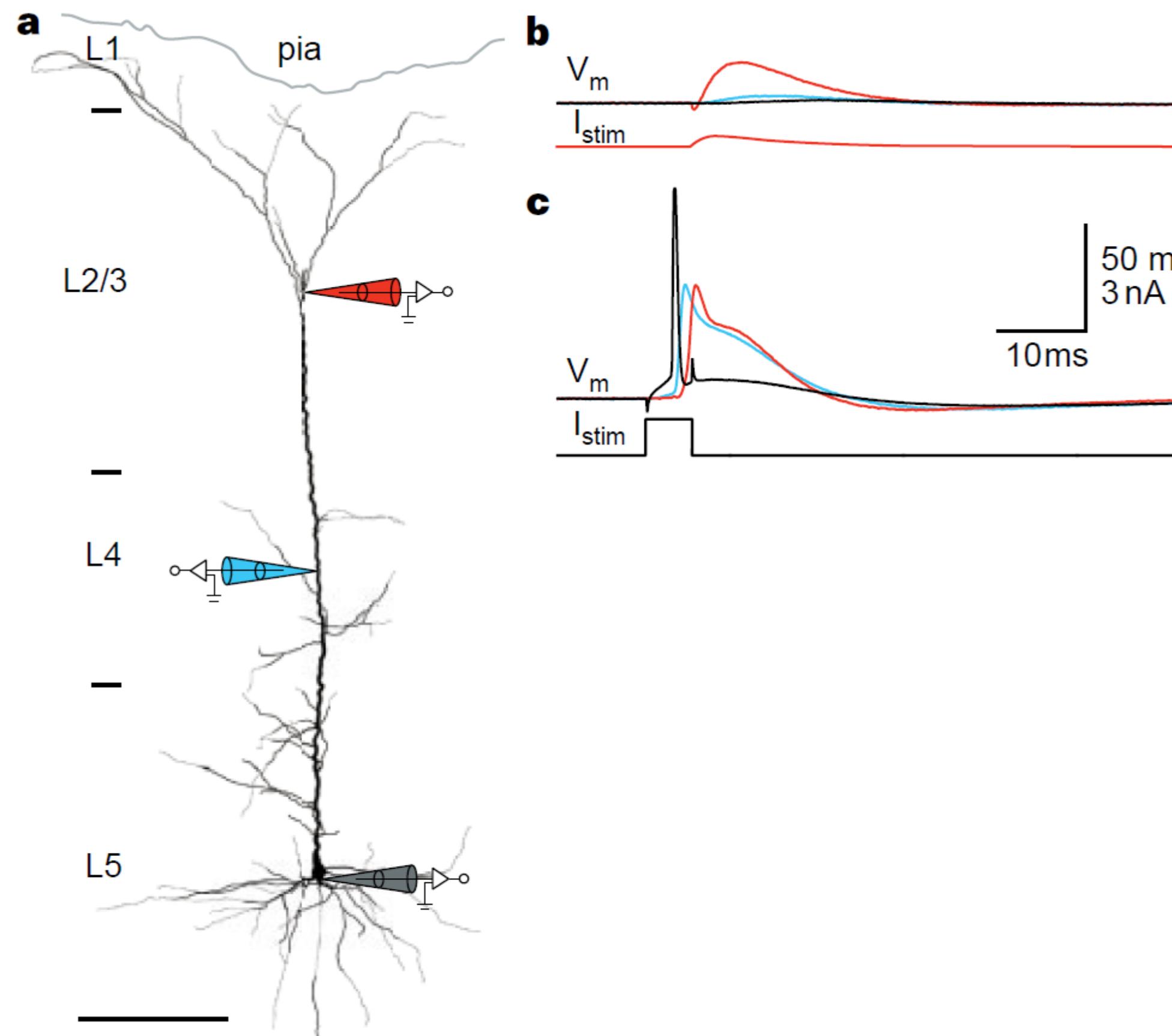
Hay et al. 2011,  
PLOS Comput. Biol.

# Neuronal Dynamics – 4.3. Active dendrites: Model



*Hay et al. 2011,  
PLOS Comput. Biol.*

# Neuronal Dynamics – 4.3. Active dendrites: Experiments



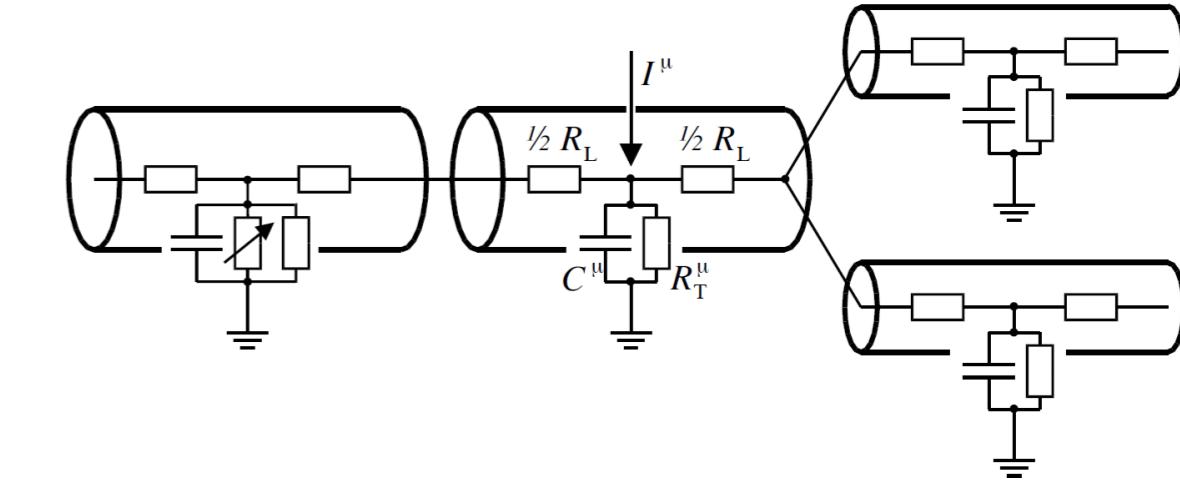
BPAP:  
backpropagating action potential

Dendritic Ca spike:  
activation of Ca channels

Ping-Pong:  
BPAP and Ca spike

*Larkum, Zhu, Sakman  
Nature 1999*

# Neuronal Dynamics – 4.3. Compartmental models



**Dendrites are more than passive filters.**

- Hotspots
- BPAPs
- Ca spikes

**Compartmental models**

- can include many ion channels
- spatially distributed
- morphologically reconstructed

BUT

- spatial distribution of ion channels difficult to tune

# Neuronal Dynamics – Quiz 4.5

*Multiple answers possible!*

## BPAP

- [ ] is an acronym for BackPropagatingActionPotential
- [ ] exists in a passive dendrite
- [ ] travels from the dendritic hotspot to the soma
- [ ] travels from the soma along the dendrite
- [ ] has the same duration as the somatic action potential

## Dendritic Calcium spikes

- [ ] can be induced by weak dendritic stimulation
- [ ] can be induced by strong dendritic stimulation
- [ ] can be induced by weak dendritic stimulation combined with a BPAP
- [ ] can only be induced by strong dendritic stimulation combined with a BPAP
- [ ] travels from the dendritic hotspot to the soma
- [ ] travels from the soma along the dendrite

# Neuronal Dynamics – week 4 – Reading

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

*Neuronal Dynamics: from single neurons to networks and models of cognition.* Chapter 3: *Dendrites and Synapses*, Cambridge Univ. Press, 2014

OR W. Gerstner and W. M. Kistler, *Spiking Neuron Models*, Chapter 2, Cambridge, 2002

OR P. Dayan and L. Abbott, *Theoretical Neuroscience*, Chapter 6, MIT Press 2001

## References:

M. Larkum, J.J. Zhu, B. Sakmann (1999), *A new cellular mechanism for coupling inputs arriving at different cortical layers*, *Nature*, 398:338-341

E. Hay et al. (2011) *Models of Neocortical Layer 5b Pyramidal Cells Capturing a Wide Range of Dendritic and Perisomatic Active Properties*, *PLOS Comput. Biol.* 7:7

Carnevale, N. and Hines, M. (2006). *The Neuron Book*. Cambridge University Press.

Bower, J. M. and Beeman, D. (1995). *The book of Genesis*. Springer, New York.

Rall, W. (1989). *Cable theory for dendritic neurons*. In Koch, C. and Segev, I., editors, *Methods in Neuronal Modeling*, pages 9{62, Cambridge. MIT Press.

Abbott, L. F., Varela, J. A., Sen, K., and Nelson, S. B. (1997). Synaptic depression and cortical gain control. *Science* 275, 220–224.

Tsodyks, M., Pawelzik, K., and Markram, H. (1998). Neural networks with dynamic synapses. *Neural. Comput.* 10, 821–835.

# Week 3 – part 2: Synaptic short-term plasticity



## Neuronal Dynamics: Computational Neuroscience of Single Neurons

Week 3 – Adding Detail:  
Dendrites and Synapses

Wulfram Gerstner  
EPFL, Lausanne, Switzerland

### ↓ 3.1 Synapses

### 3.2 Short-term plasticity

### 3.3 Dendrite as a Cable

### 3.4 Cable equation

### 3.5 Compartmental Models - active dendrites

# Week 3 – part 2: Synaptic Short-Term plasticity



## ↓ 3.1 Synapses

### 3.2 Short-term plasticity

### 3.3 Dendrite as a Cable

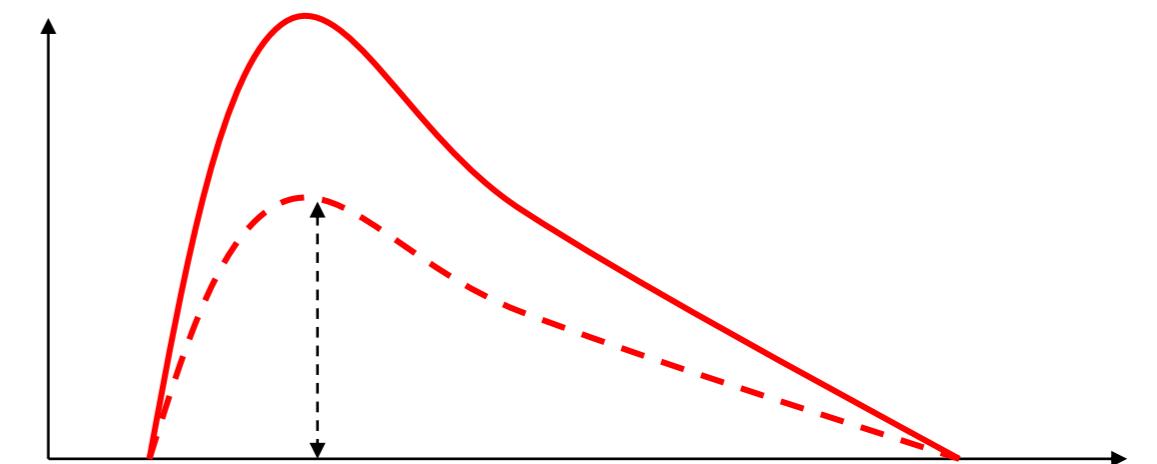
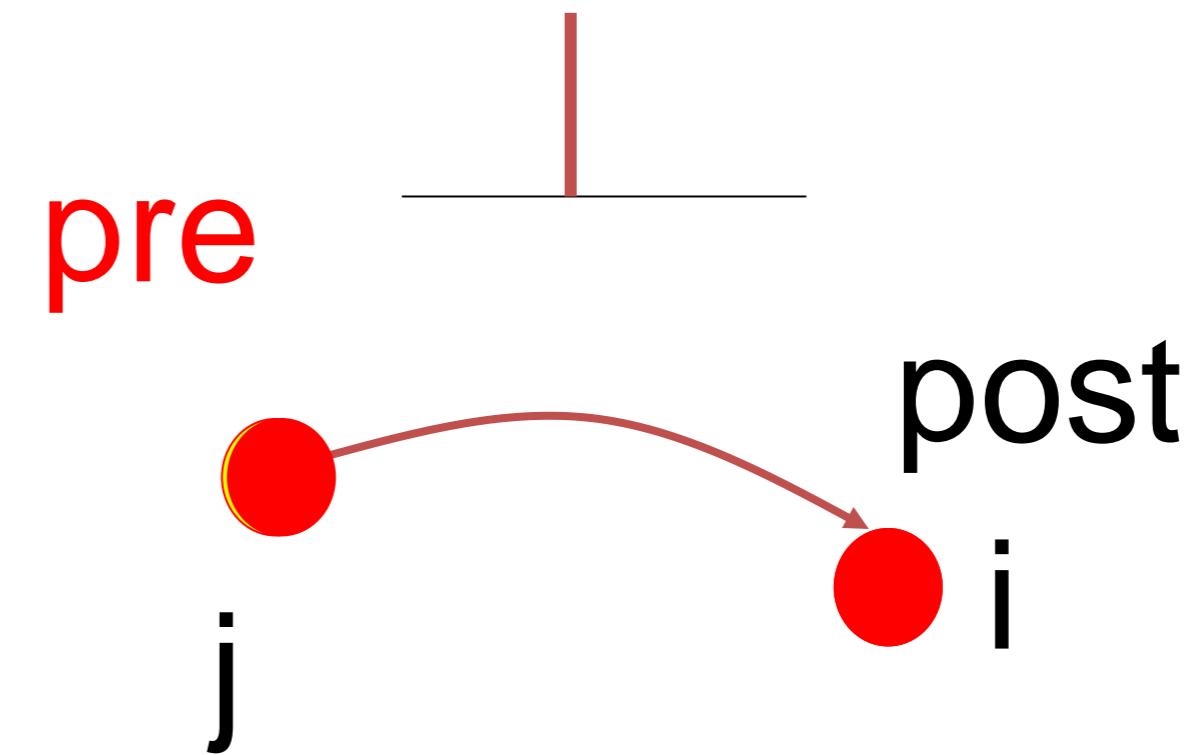
### 3.4 Cable equation

### 3.5 Compartmental Models - active dendrites

# Neuronal Dynamics – 3.2 Synaptic Short-Term Plasticity

$$I^{syn}(t) = g_{syn}(t)(u - E_{syn})$$

$$C \frac{du}{dt} = -g_l(u - u_{rest}) - I^{syn}(t)$$



# Neuronal Dynamics – 3.2 Synaptic Short-Term Plasticity

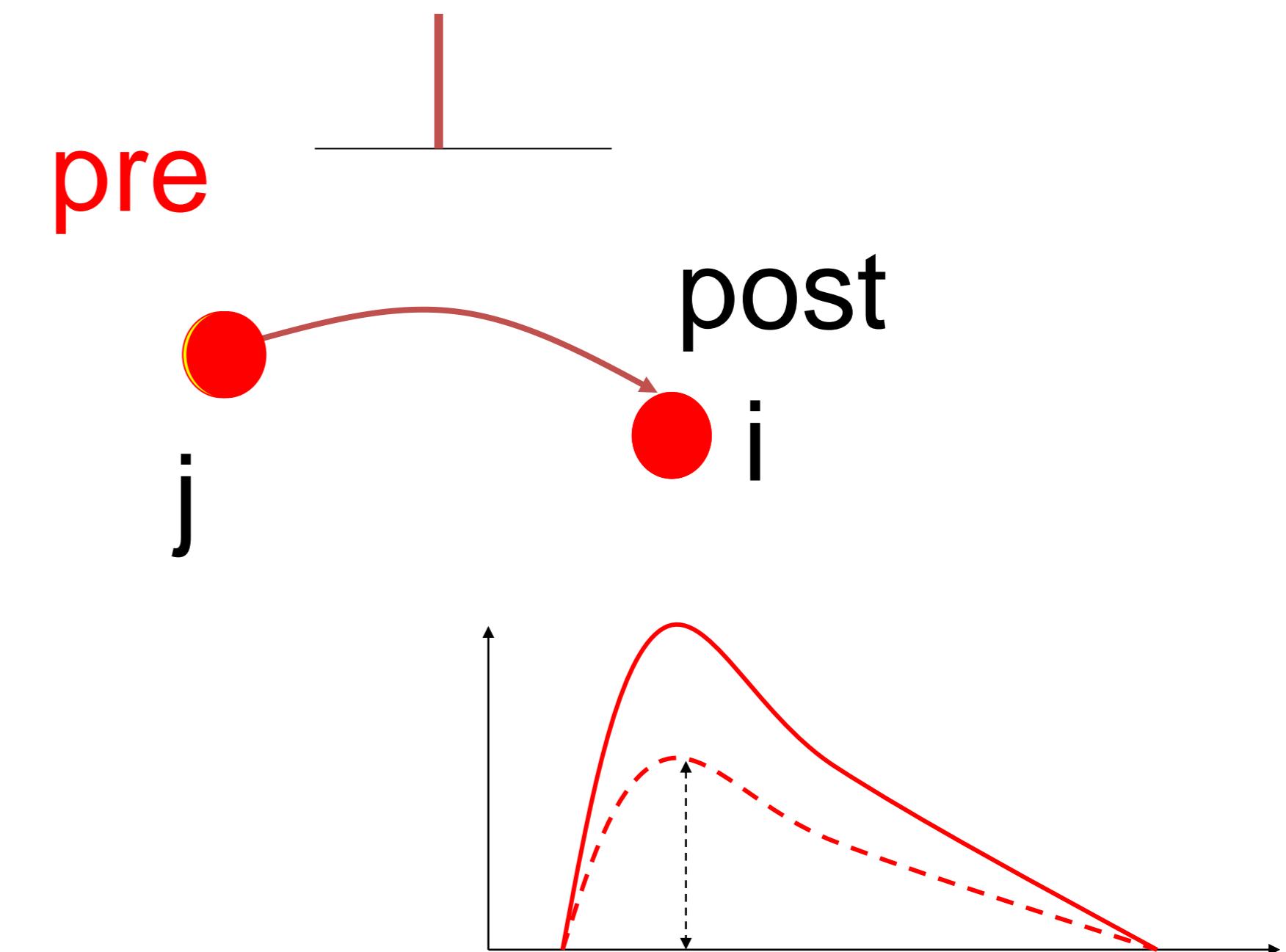
## Short-term plasticity/ fast synaptic dynamics

*Thomson et al. 1993*

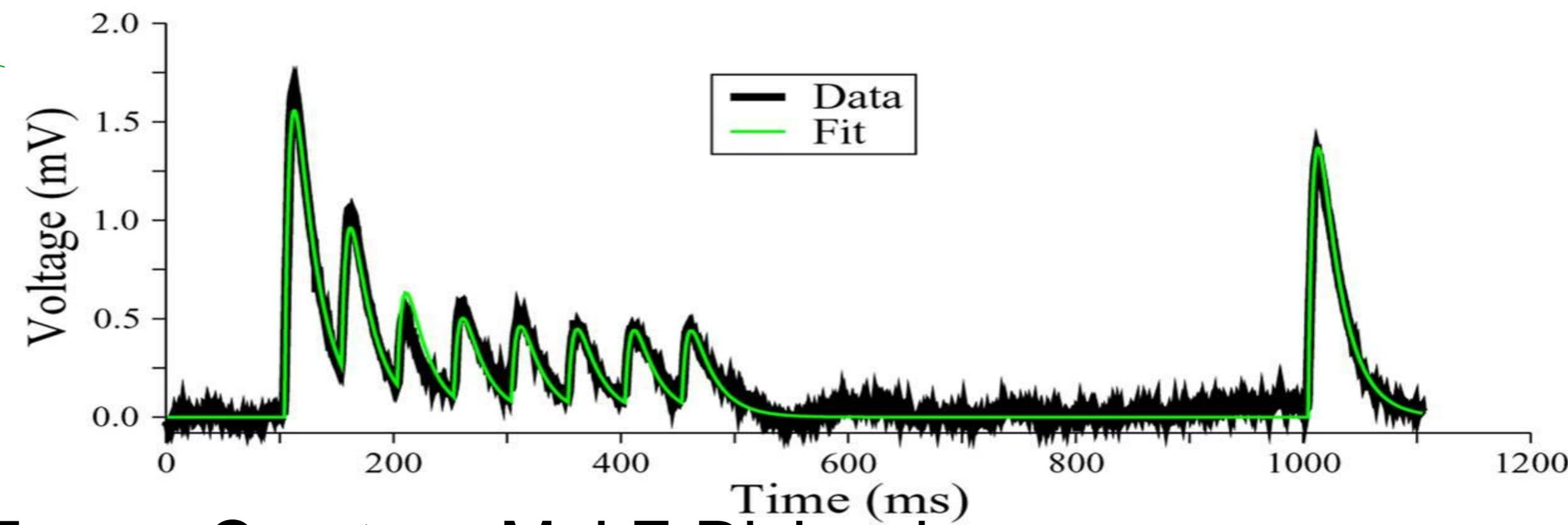
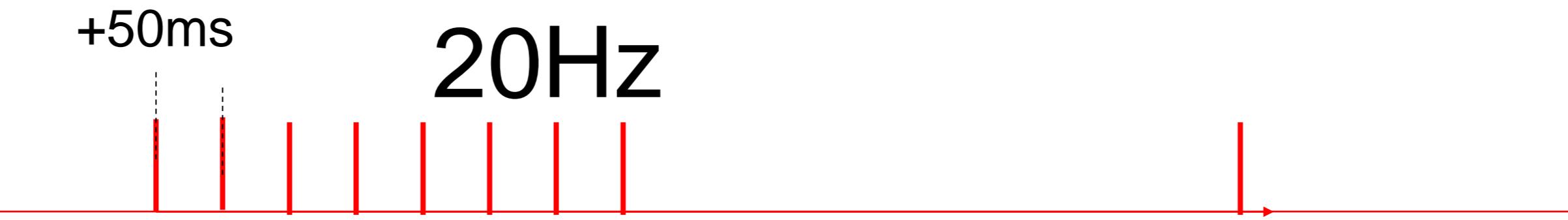
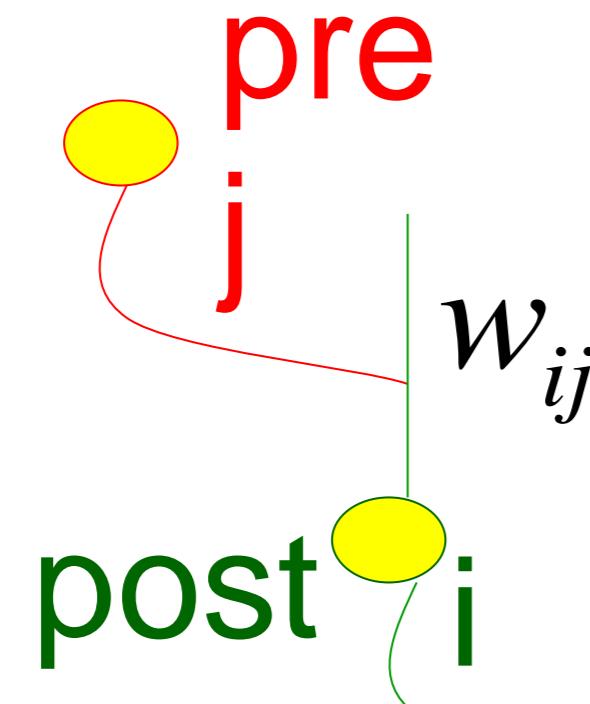
*Markram et al 1998*

*Tsodyks and Markram 1997*

*Abbott et al. 1997*



# Neuronal Dynamics – 3.2 Synaptic Short-Term Plasticity



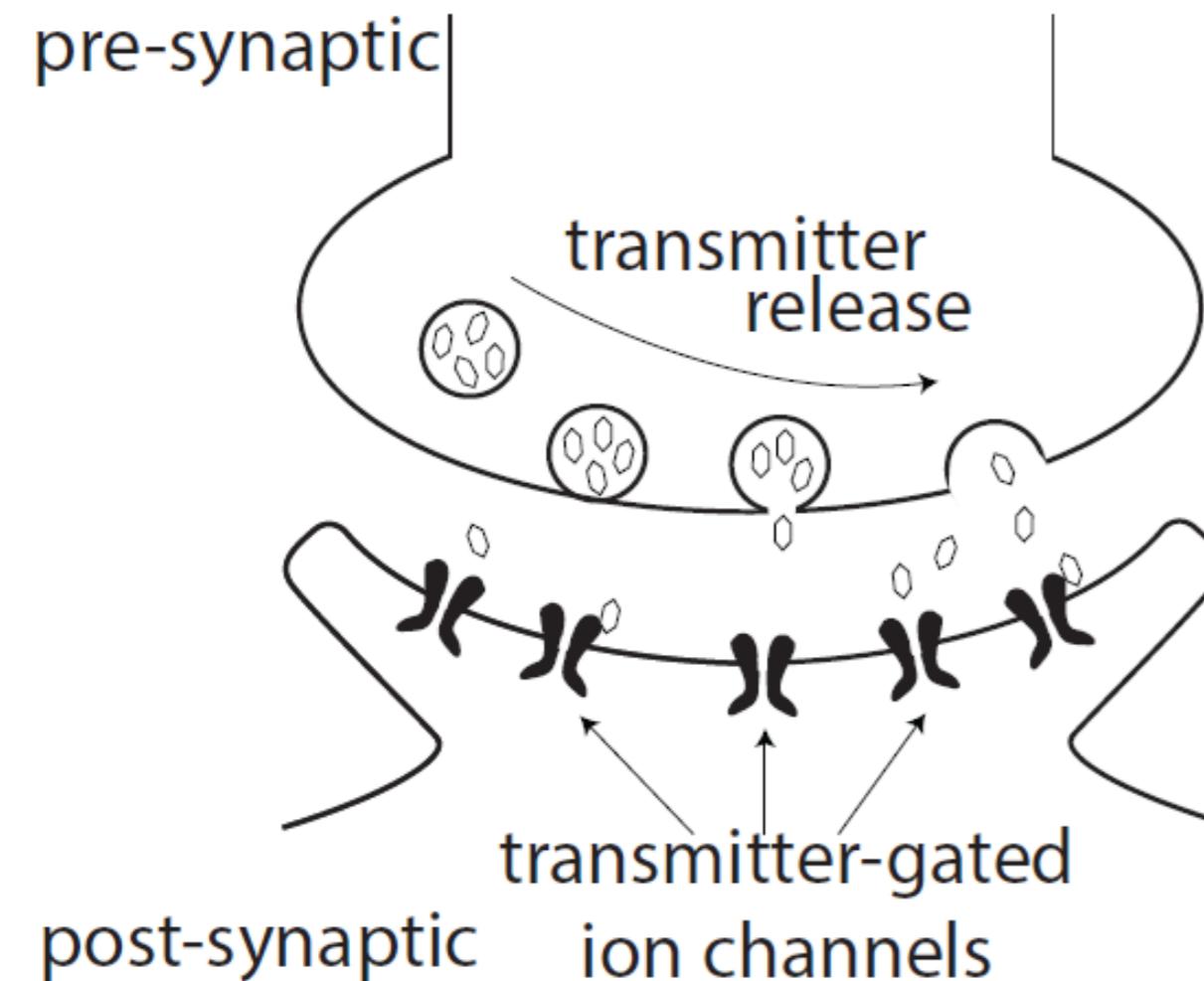
## Changes

- induced over 0.5 sec
- recover over 1 sec

Courtesy M.J.E Richardson  
Data: G. Silberberg, H. Markram  
Fit: M.J.E. Richardson (Tsodyks-Pawelzik-Markram model)

# Neuronal Dynamics – 3.2 Model of Short-Term Plasticity

*Dayan and Abbott, Fraction of filled release sites  
2001*



*image: Neuronal Dynamics,  
Cambridge Univ. Press*

$$\frac{dP_{rel}}{dt} = -\frac{P_{rel} - P_0}{\tau_P} - f_D P_{rel} \sum_k \delta(t - t^k)$$

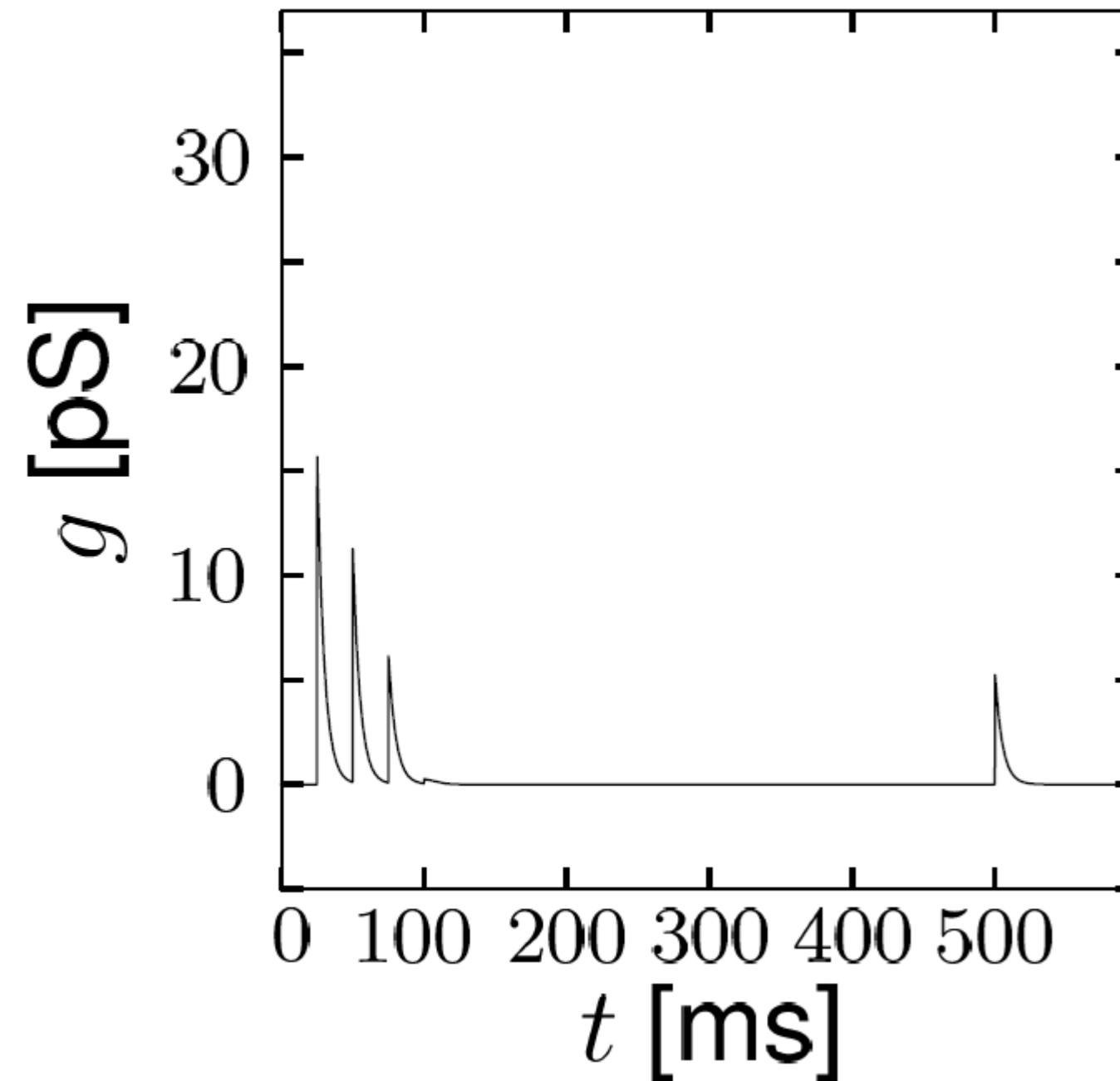
Synaptic conductance

$$g_{syn}(t) = \bar{g}_{syn} e^{-(t-t_k)/\tau} \Theta(t - t_k)$$

# Neuronal Dynamics – 3.2 Model of synaptic depression

4 + 1 pulses

$\tau_P = 400ms$



*image: Neuronal Dynamics,  
Cambridge Univ. Press*

Fraction of filled release sites

$$\frac{dP_{rel}}{dt} = -\frac{P_{rel} - P_0}{\tau_P} - f_D P_{rel} \sum_k \delta(t - t^k)$$

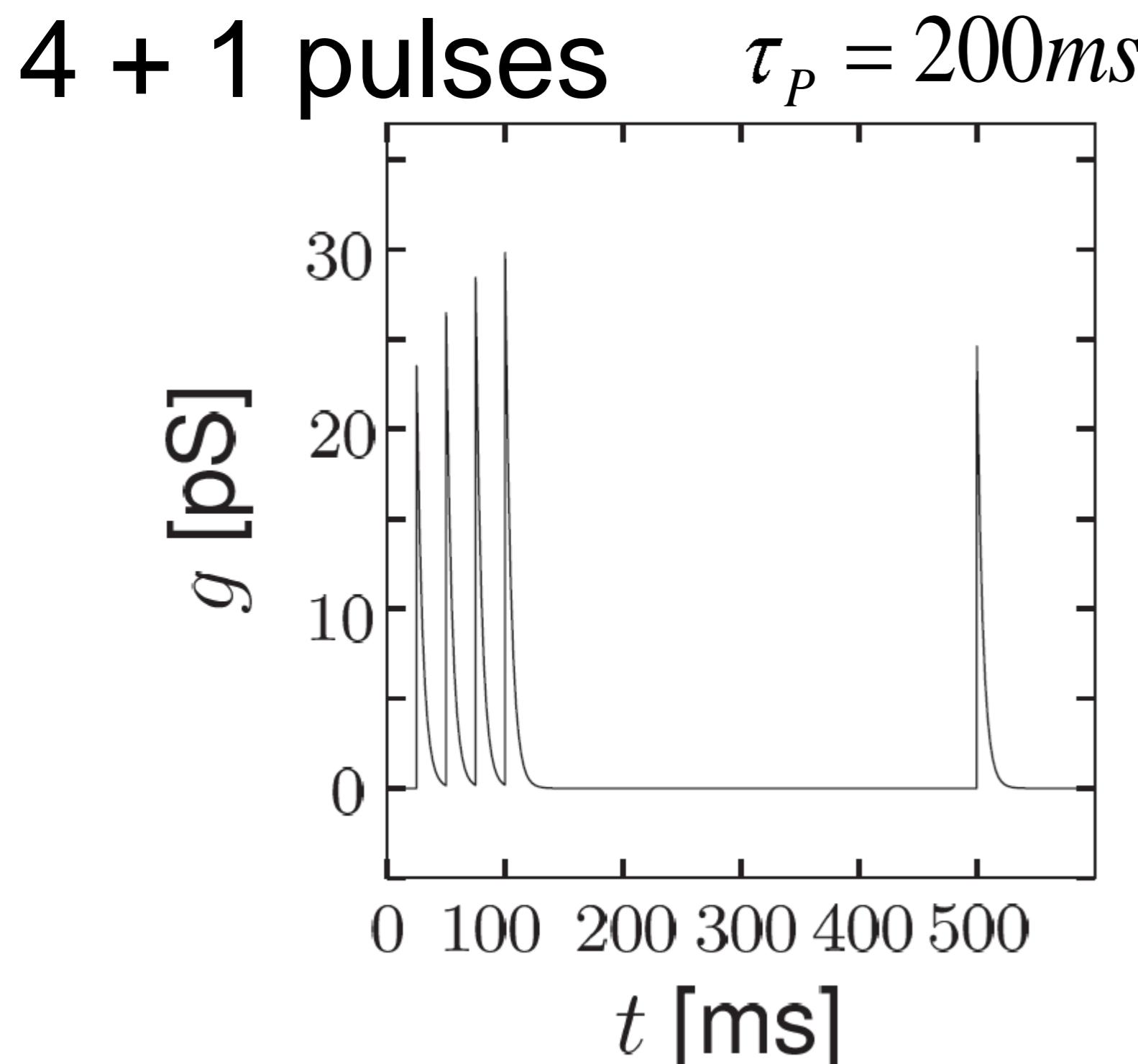
Synaptic conductance

$$\bar{g}_{syn} = c P_{rel}$$

$$g_{syn}(t) = \bar{g}_{syn} e^{-(t-t_k)/\tau} \Theta(t - t_k)$$

*Dayan and Abbott, 2001*

# Neuronal Dynamics – 3.2 Model of synaptic facilitation



*image: Neuronal Dynamics,  
Cambridge Univ. Press*

Fraction of filled release sites

$$\frac{dP_{rel}}{dt} = -\frac{P_{rel} - P_0}{\tau_P} + f_F (1 - P_{rel}) \sum_k \delta(t - t^k)$$

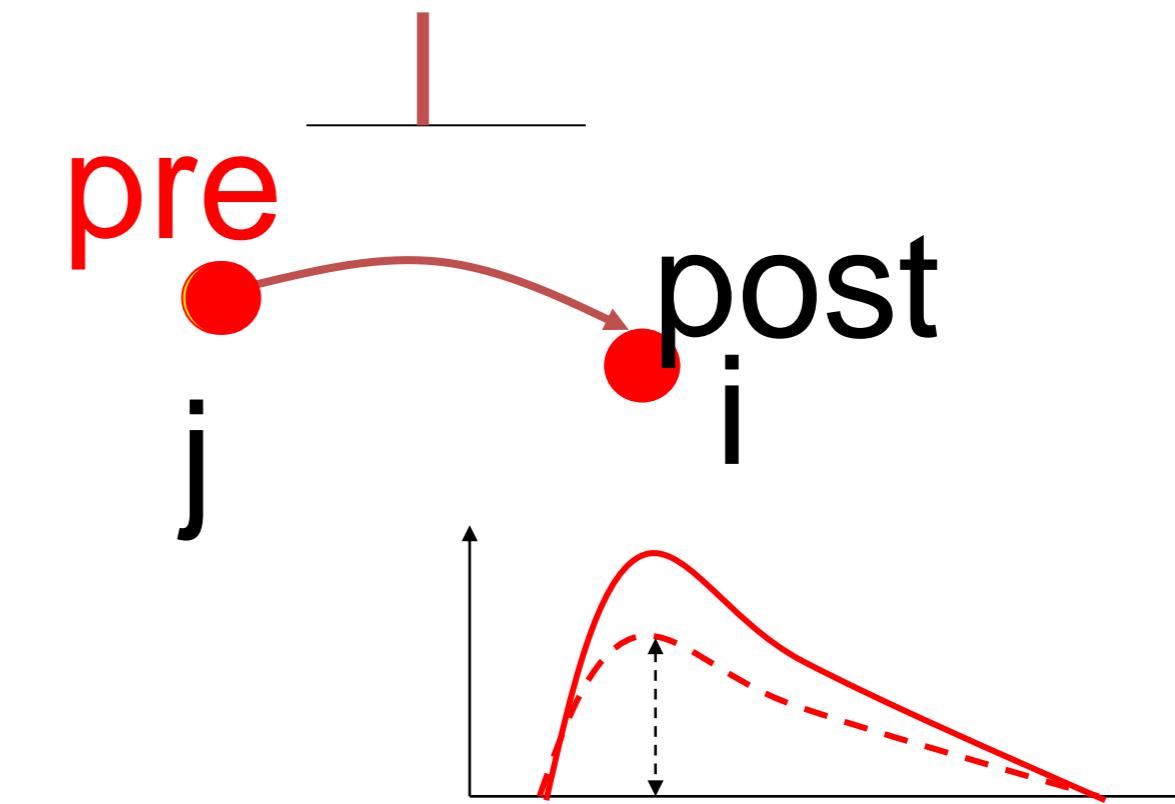
Synaptic conductance

$$\bar{g}_{syn} = c P_{rel}$$

$$g_{syn}(t) = \bar{g}_{syn} e^{-(t-t_k)/\tau} \Theta(t - t_k)$$

*Dayan and Abbott, 2001*

# Neuronal Dynamics – 3.2 Summary



**Synapses are not constant**

- Depression
- Facilitation

Models are available

- Tsodyks-Pawelzik-Markram 1997
- Dayan-Abbott 2001

# Neuronal Dynamics – Quiz 3.2

*Multiple answers possible!*

## Time scales of Synaptic dynamics

- [ ] The rise time of a synapse can be in the range of a few ms.
- [ ] The decay time of a synapse can be in the range of few ms.
- [ ] The decay time of a synapse can be in the range of few hundred ms.
- [ ] The depression time of a synapse can be in the range of a few hundred ms.
- [ ] The facilitation time of a synapse can be in the range of a few hundred ms.

## Synaptic dynamics and membrane dynamics.

Consider the equation

$$(*) \quad \frac{dx}{dt} = -\frac{x}{\tau} + c \sum_k \delta(t - t^k)$$

With a suitable interpretation of the variable  $x$  and the constant  $c$

- [ ] Eq. (\*) describes a passive membrane voltage  $u(t)$  driven by spike arrivals.
- [ ] Eq. (\*) describes the conductance  $g(t)$  of a simple synapse model.
- [ ] Eq. (\*) describes the maximum conductance  $\bar{g}_{syn}$  of a facilitating synapse

# Neuronal Dynamics – 3.2 Literature/short-term plasticity

Dayan, P. and Abbott, L. F. (2001). Theoretical Neuroscience. MIT Press, Cambridge.

Abbott, L. F., Varela, J. A., Sen, K., and Nelson, S. B. (1997). Synaptic depression and cortical gain control. *Science* 275, 220–224.

Markram, H., and Tsodyks, M. (1996a). Redistribution of synaptic efficacy between neocortical pyramidal neurons. *Nature* 382, 807–810.

A.M. Thomson, Facilitation, augmentation and potentiation at central synapses, *Trends in Neurosciences*, 23: 305–312 ,2001

Tsodyks, M., Pawelzik, K., and Markram, H. (1998). Neural networks with dynamic synapses. *Neural. Comput.* 10, 821–835.