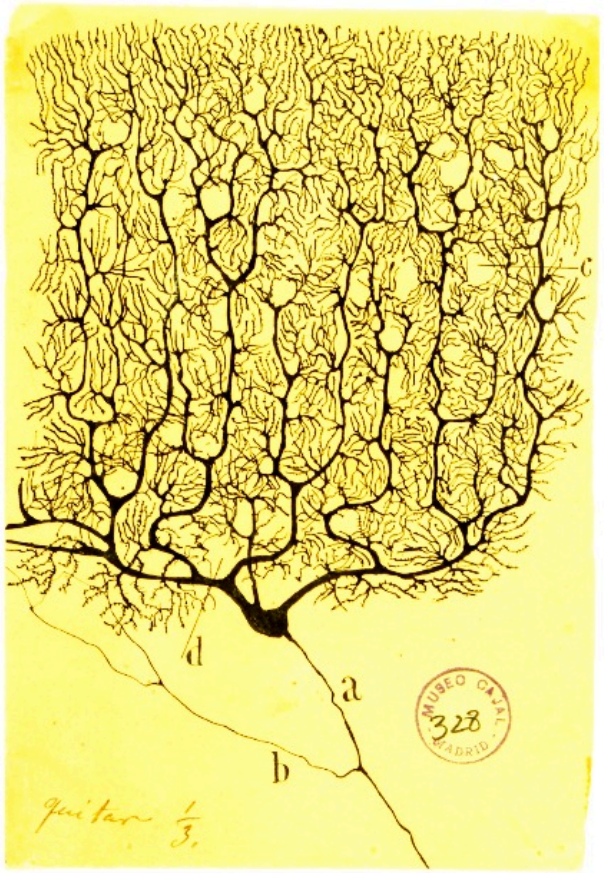
# Introduction to Neural Computation

Prof. Michale Fee

MIT BCS 9.40 — 2018

Lecture 7

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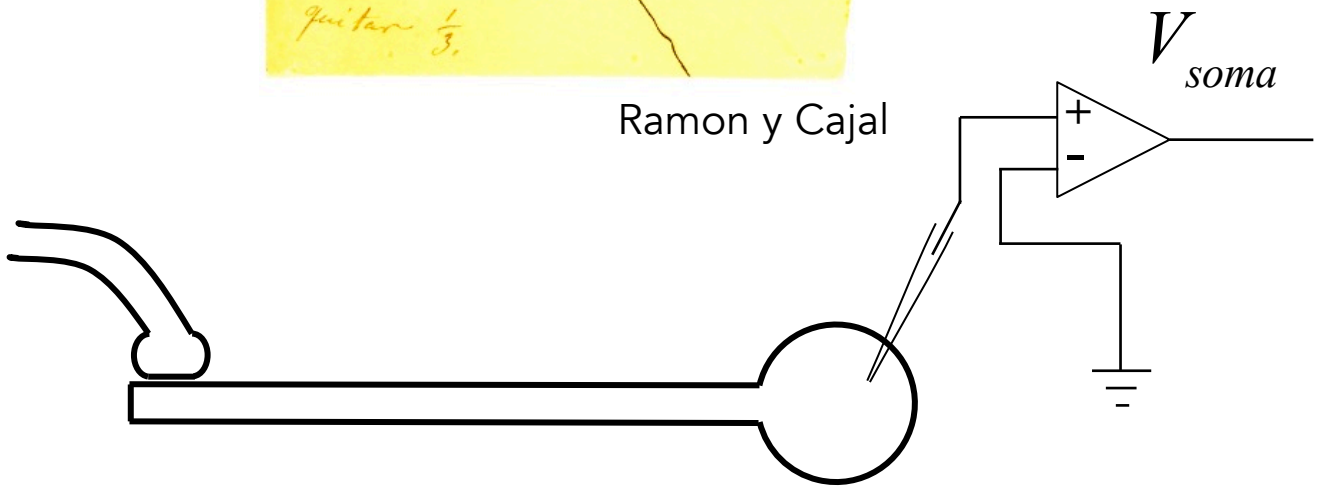
Ramon y Cajal

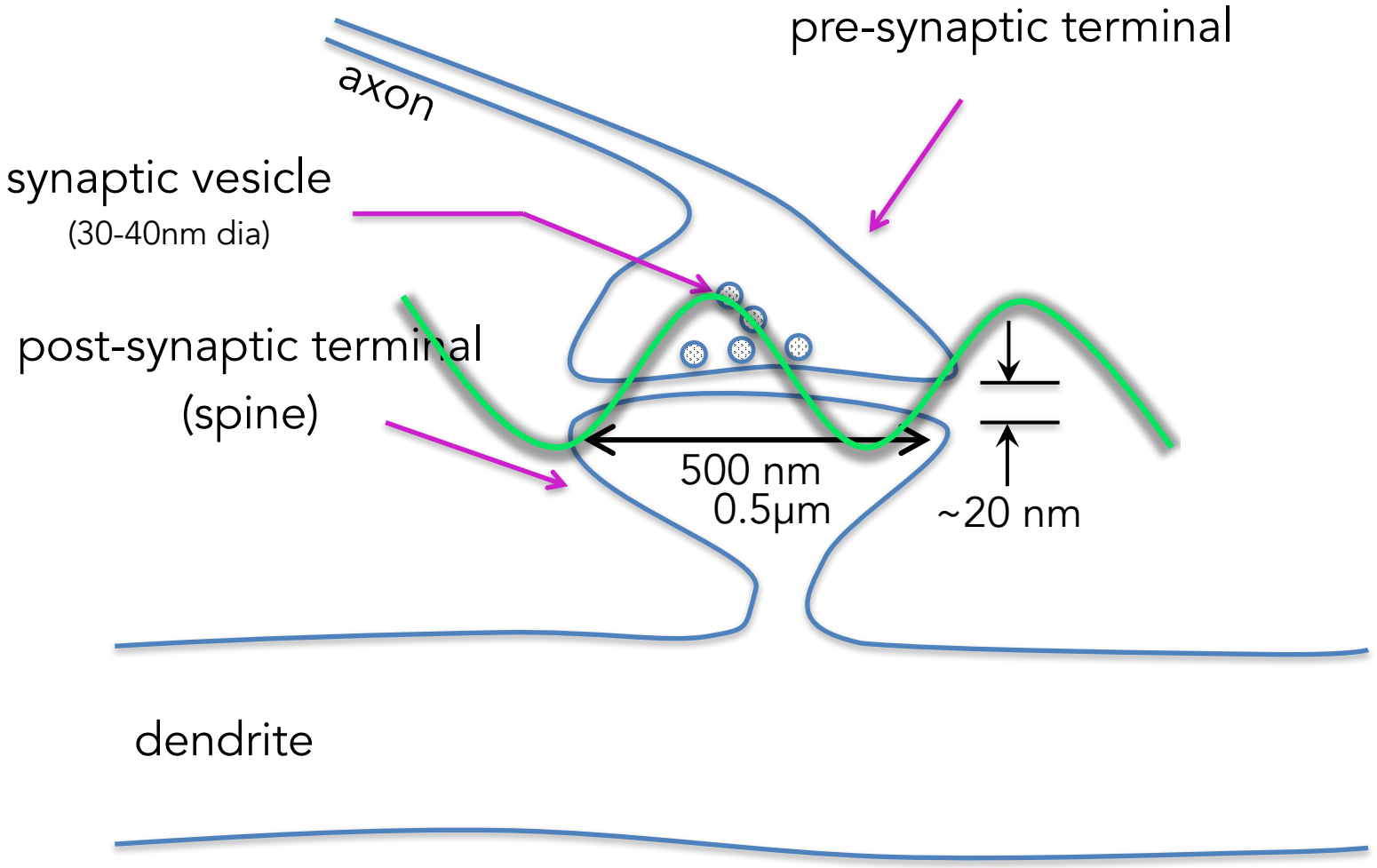


# Learning objectives for Lecture 7

- Be able to add a synapse in an equivalent circuit model
- To describe a simple model of synaptic transmission
- To be able to describe synaptic transmission as a convolution of a linear kernel with a spike train
- To understand synaptic saturation
- To understand the different functions of somatic and dendritic inhibition

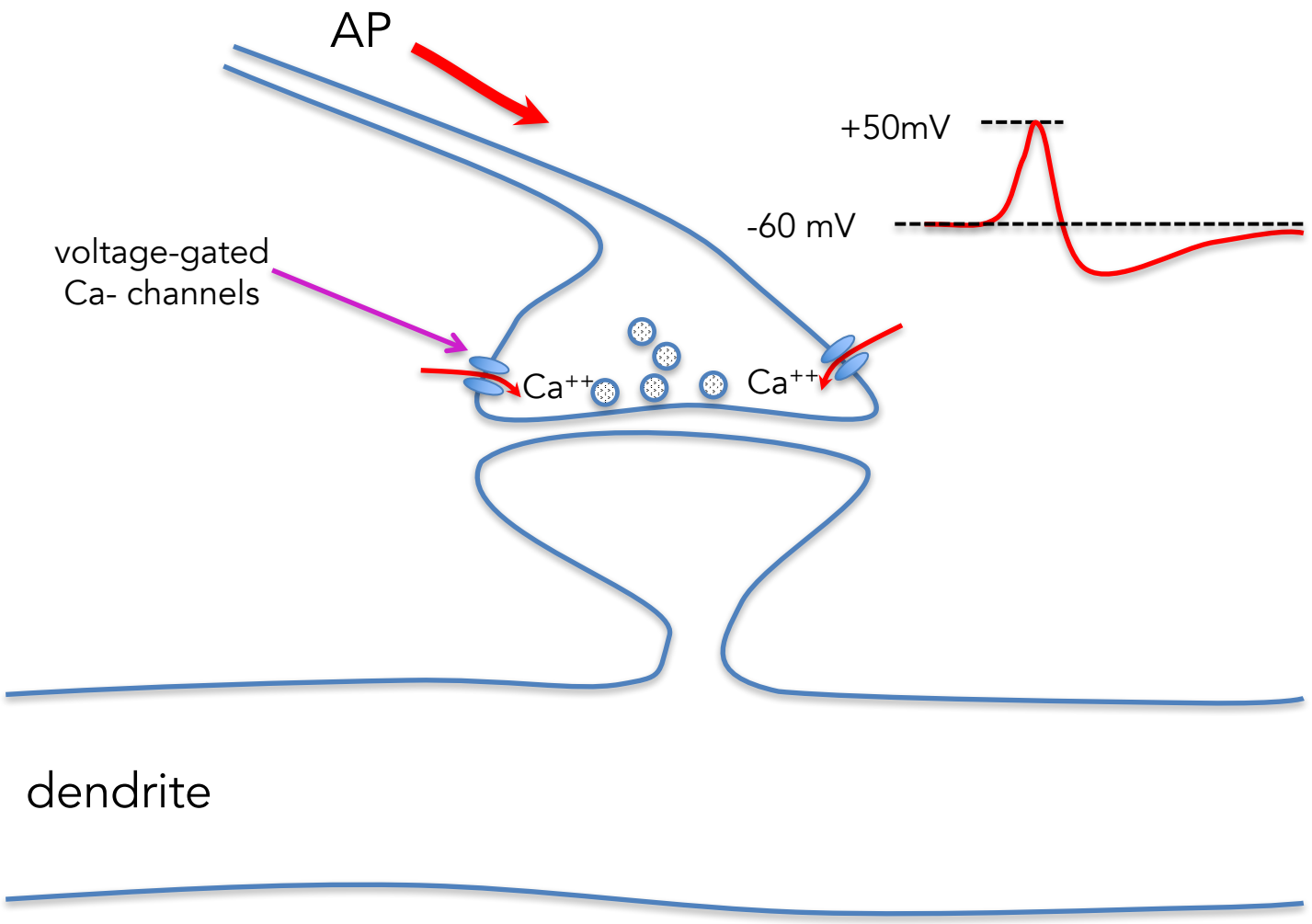
# Chemical synapse

- Structure of typical excitatory synapse



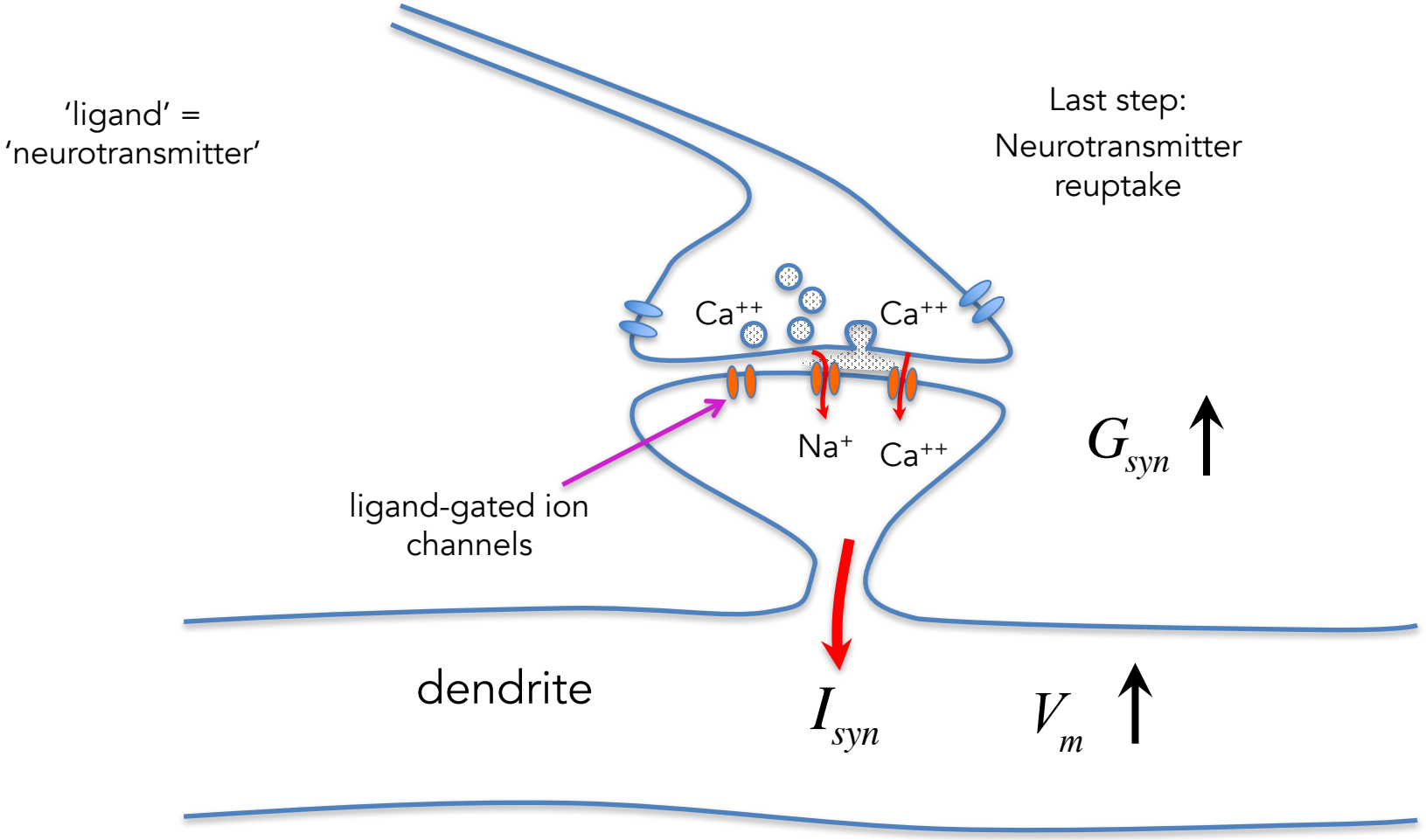
# Chemical synapse

- Sequence of events in synaptic transmission



# Chemical synapse

- Sequence of events in synaptic transmission



# Anatomy of synapses/axons/dendrites

- Synapses are small – contact area~0.5μm
- High packing density ~$10^9$ synapses/$mm^3$
  - 1.1um on a 3D lattice
  - 4.1km of axon (0.3μm dia)
  - 500m of dendrite
- A cell receives many synapses
  - 10000 synapses
  - on 4mm of dendrites (4 cm of axon)
  - $10^5$ neurons/$mm^3$ in mouse cortex

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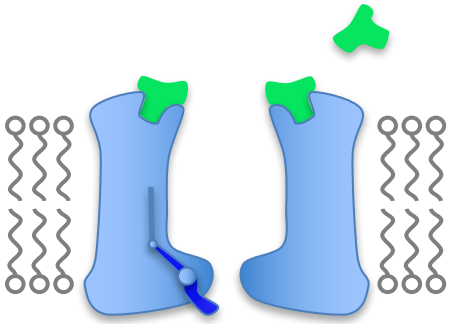
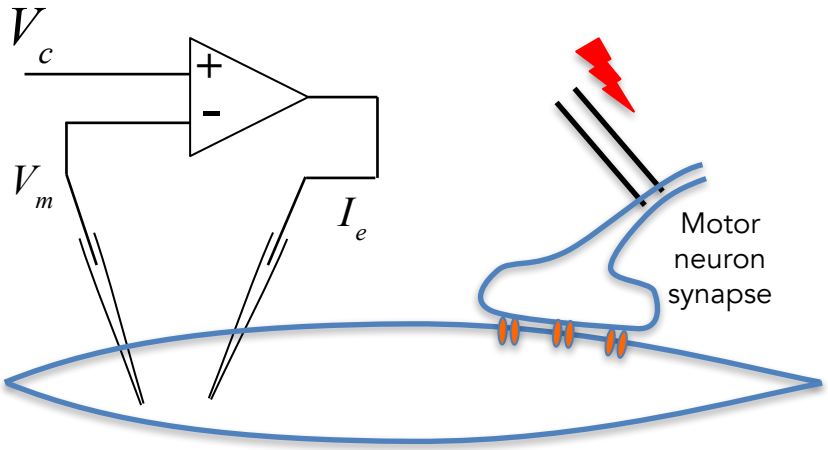
# How does a synapse respond?

- Ionotropic receptors



Two electrode voltage-clamp experiment

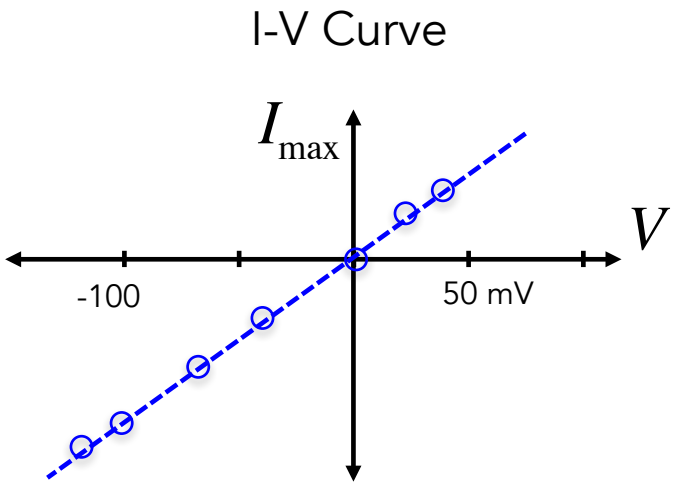


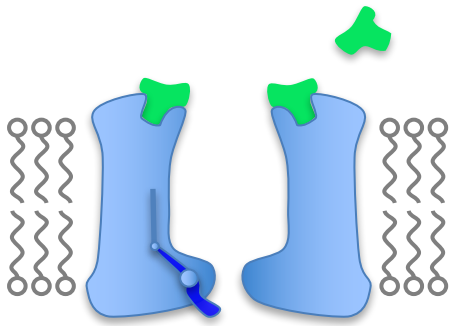

Frog sartorius muscle fiber

Magleby and Stevens, 1972

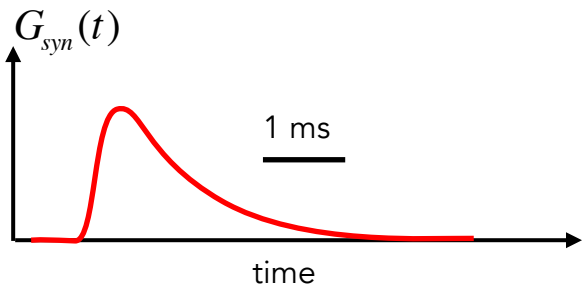
# How does a synapse respond?

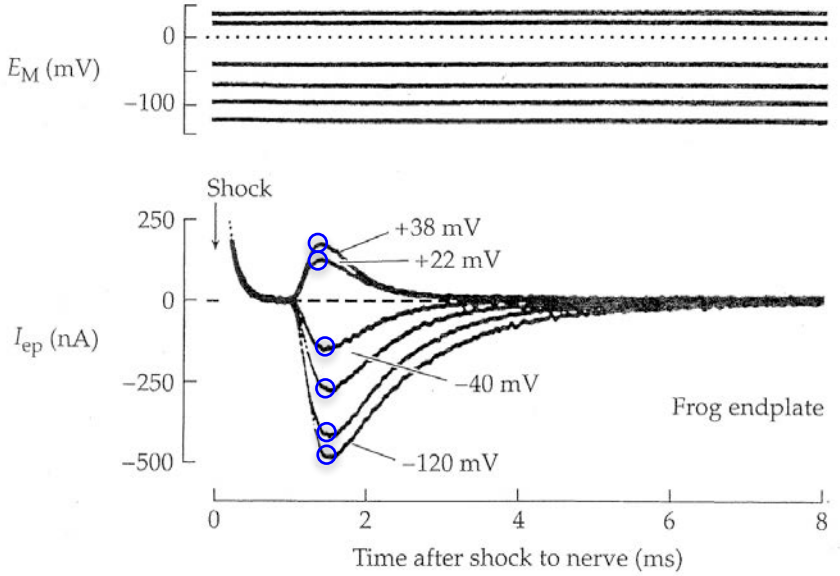
- Ionotropic receptors



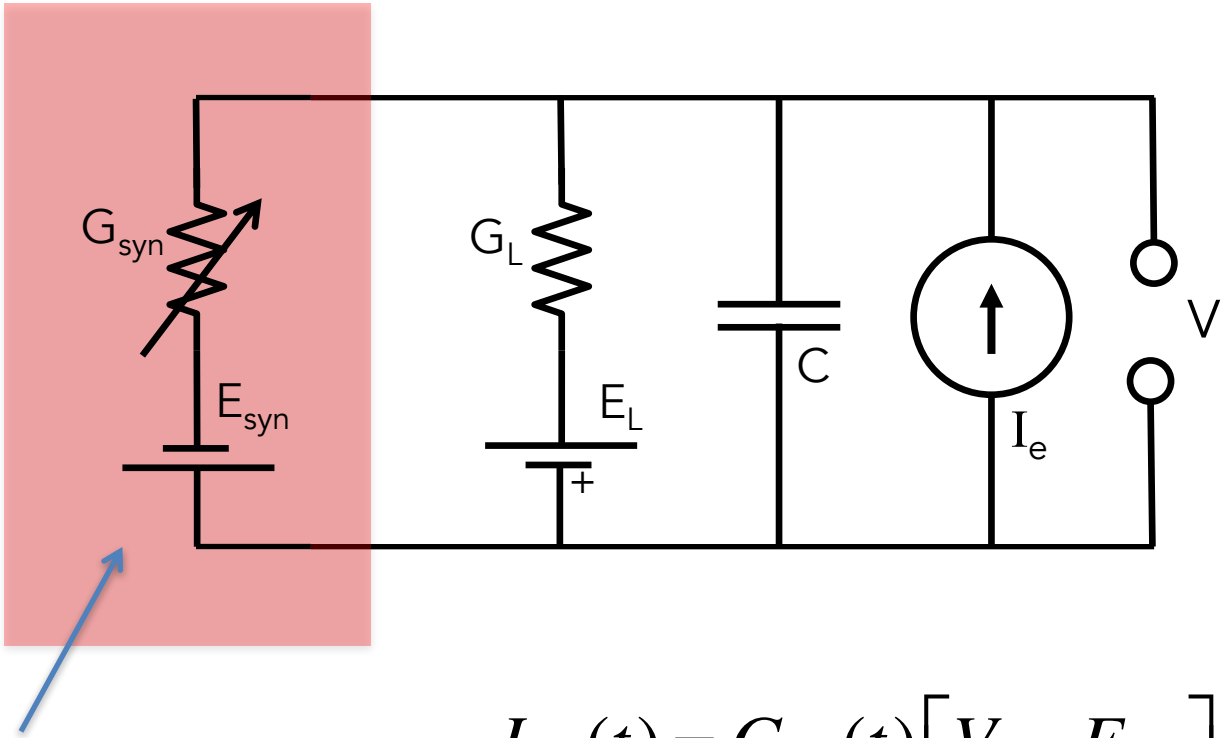
$$I_{syn}(t) = G_{syn}(t)\left[V - E_{syn}\right]$$



# Equivalent circuit model of a synapse

- Current flow through a synapse results from changes in synaptic conductance



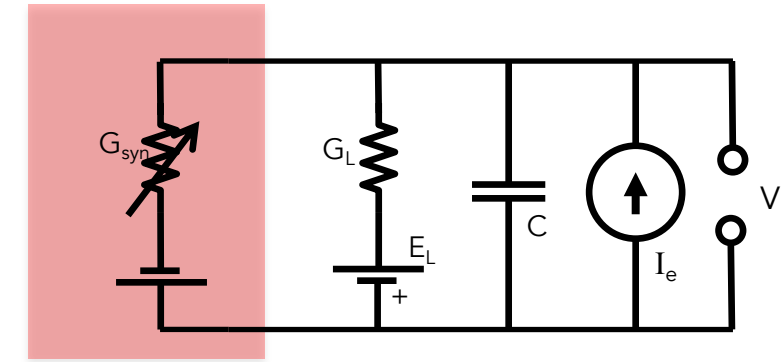

Equivalent circuit of a synapse

$$I_{syn}(t) = G_{syn}(t)\left[V - E_{syn}\right]$$

# Excitatory synapses

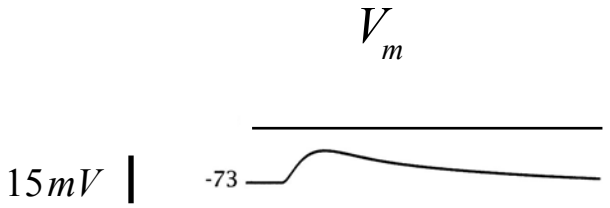
- Increased synaptic conductance causes the membrane potential to approach the reversal potential for that synapse.

$$I_{syn}(t) = G_{syn}(t)\left[V - E_{syn}\right]$$




$E_{syn} = 0\,mV$

Now we can change the 'holding potential of the cell by injecting a little current (current clamp experiment)

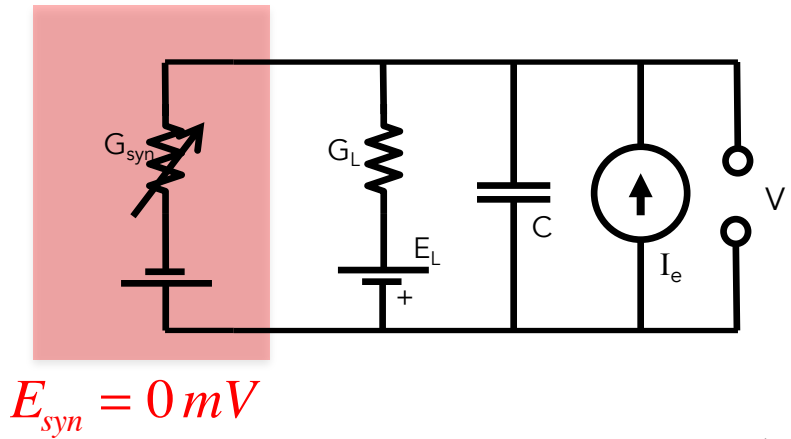


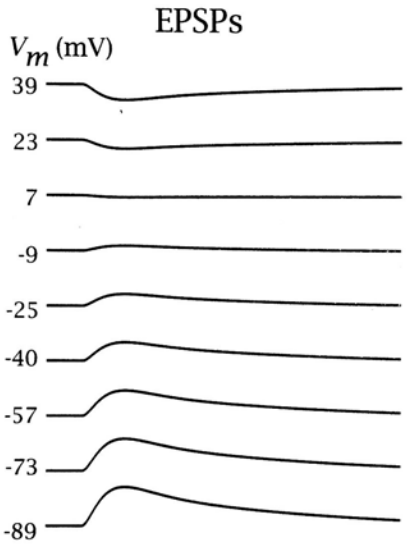

Excitatory postsynaptic potential (EPSP)

# Excitatory and inhibitory synapses

- Increased synaptic conductance causes the membrane potential to approach the reversal potential for that synapse.

$$I_{syn}(t) = G_{syn}(t)\left[V - E_{syn}\right]$$




Excitatory postsynaptic potential (EPSP)

Excitatory synapse if

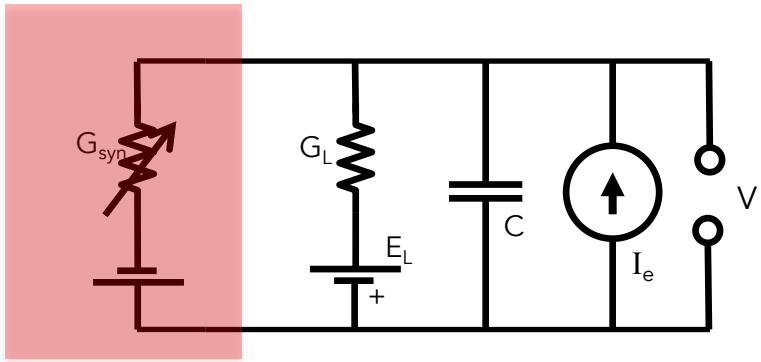
$$E_{syn} > V_{th}$$

Figure from Johnston, D. and M.-S. Wu. *Foundations of Cellular Neurophysiology*. 1995. Courtesy of MIT Press.

# Excitatory and inhibitory synapses

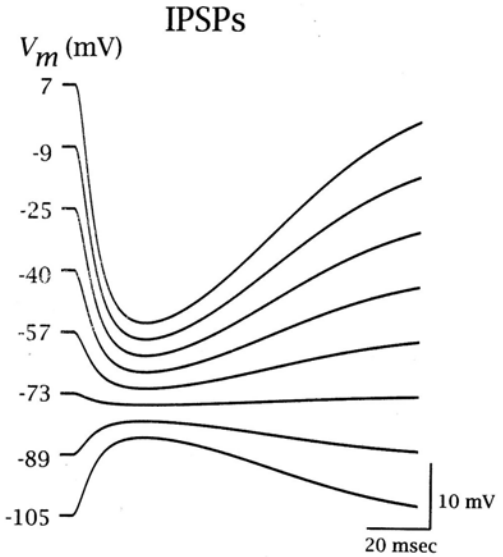
- Increased synaptic conductance causes the membrane potential to approach the reversal potential for that synapse.

$$I_{syn}(t) = G_{syn}(t)\left[V - E_{syn}\right]$$




$E_{syn} = -75\,mV$

GABAergic synapse




Inhibitory postsynaptic potential (IPSP)

Inhibitory synapse if

$$E_{syn} < V_{th}$$

Figure 13.4 from Johnston, D. and M.-S. Wu. *Foundations of Cellular Neurophysiology*. 1995. Courtesy of MIT Press.

# Equivalent circuit model of a synapse

- Current flow through a synapse results from changes in synaptic conductance

$$I_{syn}(t) = G_{syn}(t)\left[V_m(t) - E_{syn}\right]$$

Single-channel patch recording
$GABA_A$ receptor

Figure removed due to copyright restrictions. Single-channel patch recording, $GABA_A$ receptor. Figure 6.13 in: Hille, Bertil. *Ion Channels of Excitable Membranes* (3rd Ed.). 2001, Sinauer / Oxford University Press.

- Ligand gated ion channels 'flicker' between open and closed states.

- We can write the synaptic conductance in terms of the probability $P_R(t)$ that a receptor is 'open'.

$$G_{syn}(t) = \hat{g}_R \, N_R \, P_R(t)$$

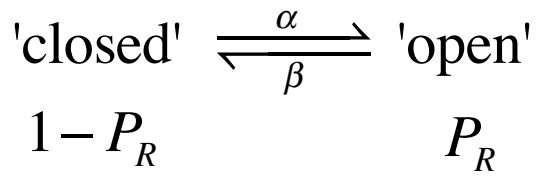
$\hat{g}_R$ =unitary 'open' conductance

$N_R$ =number of receptors

# Kinetic model of synapse gating

- We can describe the open probability using a 'kinetic' model.

Single-channel patch recording
$GABA_A$ receptor






$\alpha, \beta$ are transition rate constants

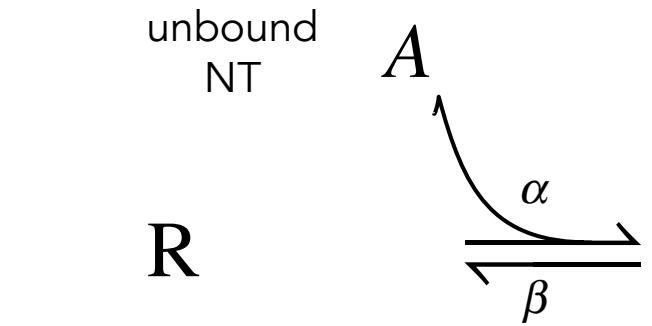
Probability per unit time;
units are 1/s

- What controls the rate at which channels open ?

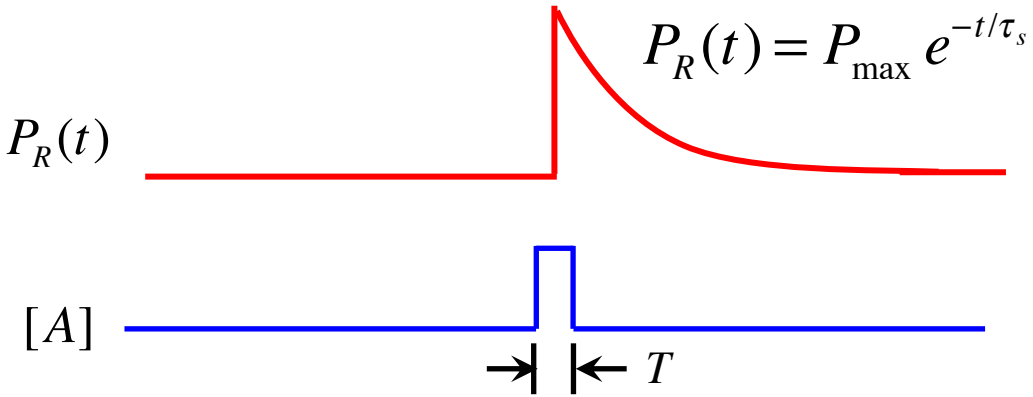
Neurotransmitter!

# Equivalent circuit model of a synapse

- Simplified version of Magleby-Stevens model




$$\frac{dP_R}{dt} = \alpha [A]^n (1 - P_R) - \beta P_R$$




$$G_{syn}(t) = \hat{g}_R N_R P_R(t)$$

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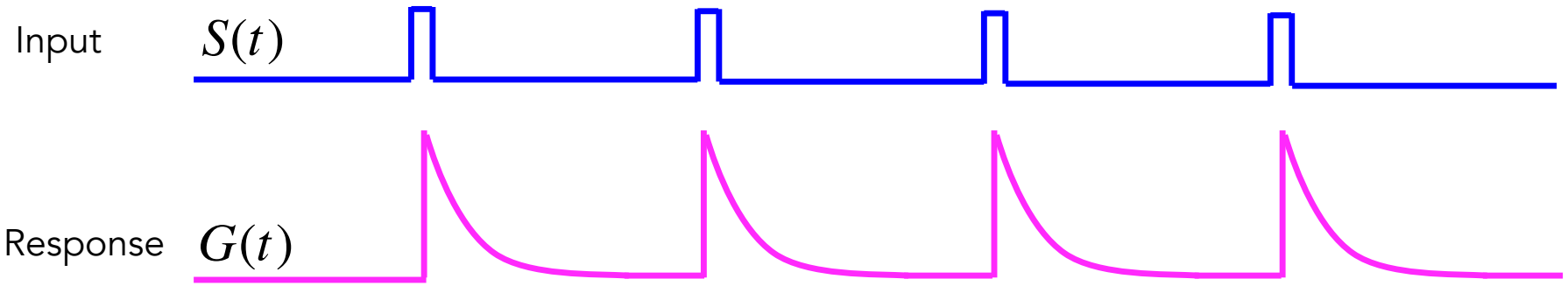
# Response of a synapse to a spike train input

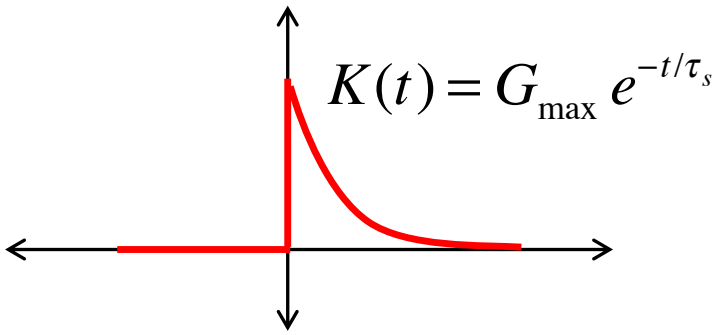
- This simple model makes it very easy to describe the response of a synapse to a train of spikes!




Convolution

$$G(t) = \int_{-\infty}^{\infty} K(\tau) S(t-\tau)\, d\tau$$

Impulse response or Linear Kernel



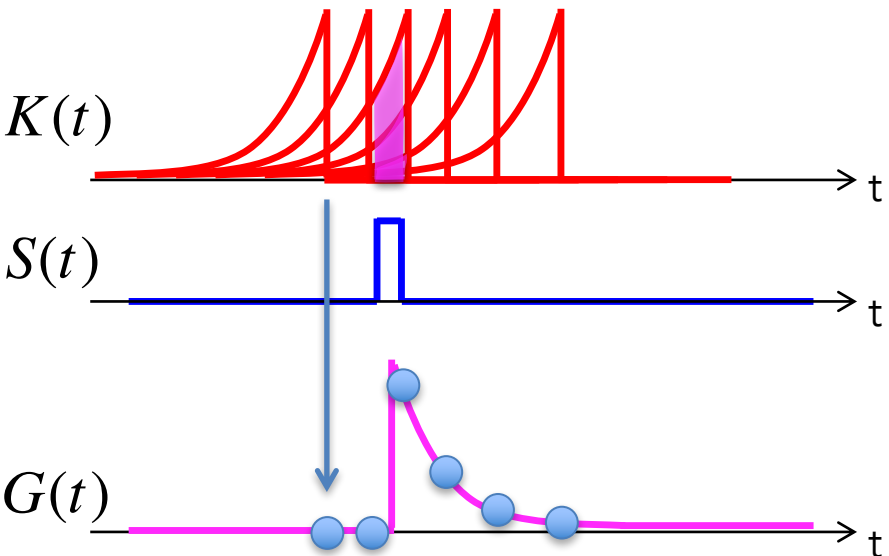
# Response of a synapse to a spike train input

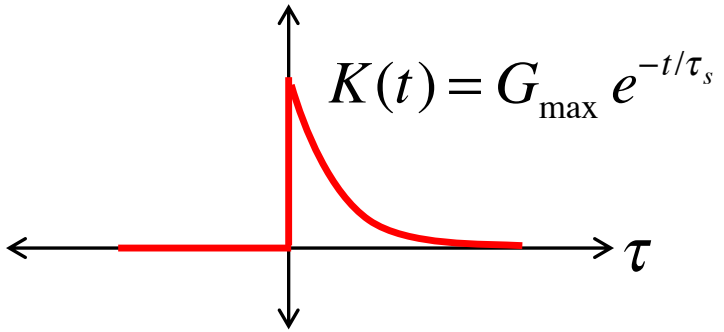
- This simple model makes it very easy to describe the response of a synapse to a train of spikes!
- We just ***convolve*** the spike train with the linear response of the synaptic conductance

$$G(t) = \int_{-\infty}^{\infty} K(\tau) S(t-\tau)\, d\tau$$

Impulse response

$$K(t) = G_{\max}\, e^{-t/\tau_s}$$



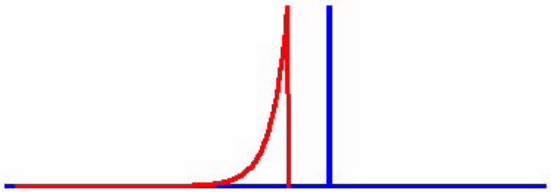



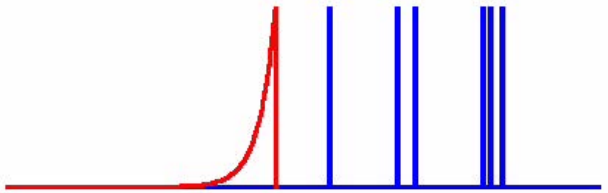
# Response of a synapse to a spike train input

- We just ***convolve*** the spike train with the linear response of the synaptic conductance

$$G(t) = \int_{-\infty}^{\infty} K(\tau) S(t-\tau)\, d\tau$$

- Easy to do in MATLAB®
  - use the **conv** function





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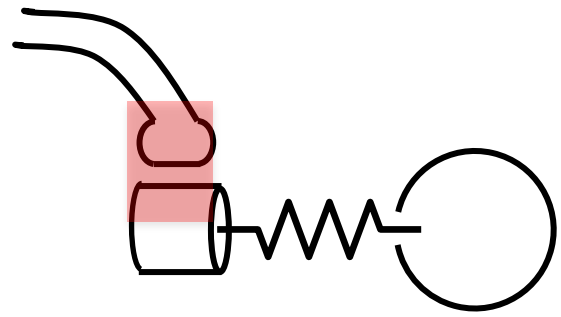
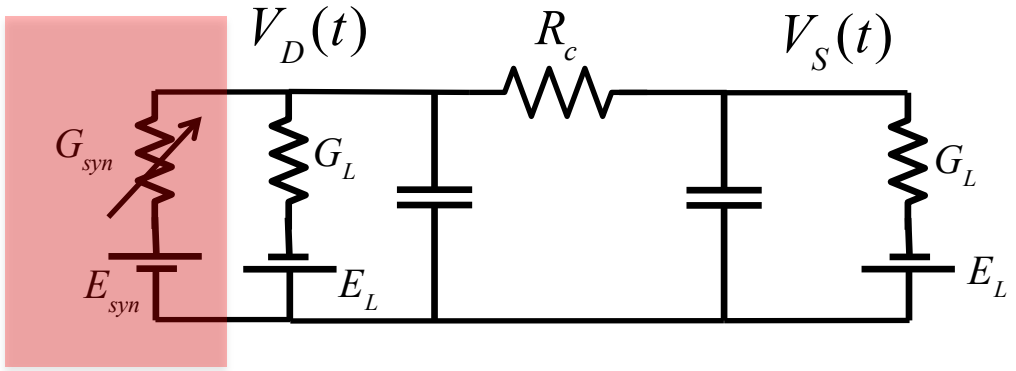
# Synaptic saturation

- Let's examine how the voltage in a dendrite changes as a function of the amount of excitatory conductance…



dendritic compartment

somatic compartment




dendritic compartment

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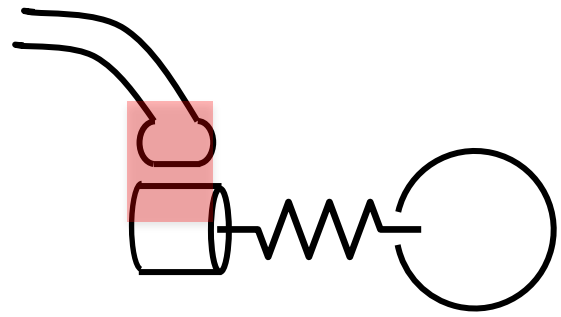
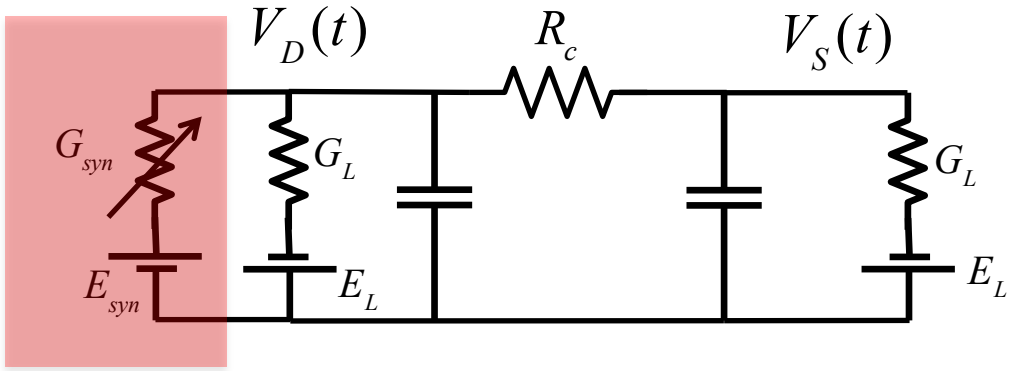


dendritic compartment

somatic compartment




dendritic compartment

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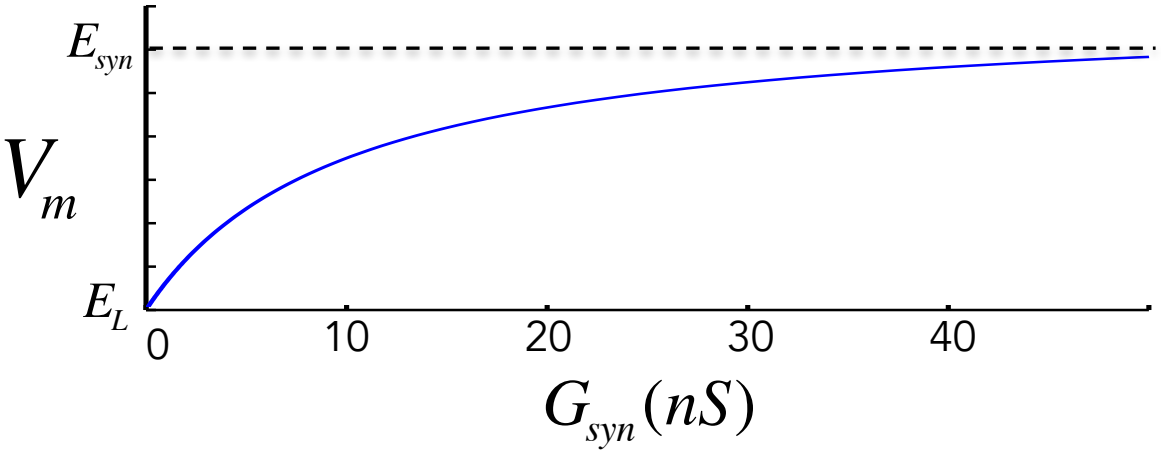
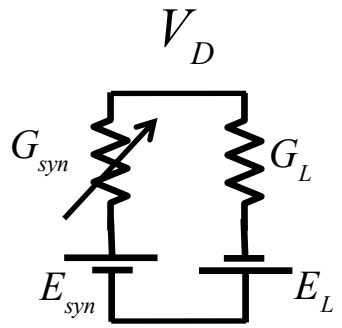



dendritic compartment

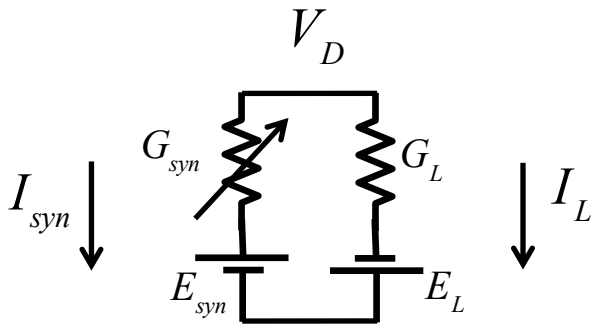
As synaptic input increases, the postsynaptic response saturates to a constant value

# Synaptic saturation

- Let's examine how the voltage in a dendrite changes as a function of the amount of excitatory conductance…

Kirchoff's current law says:

$$I_{syn} + I_L = 0$$




dendritic compartment

$$G_{syn}\left[V - E_{syn}\right] + G_L\left[V - E_L\right] = 0$$

$$G_{syn}V - G_{syn}E_{syn} + G_L V - G_L E_L = 0$$

$$V(G_{syn} + G_L) - (G_{syn}E_{syn} + G_L E_L) = 0$$

$$V = \frac{G_L E_L + G_{syn}E_{syn}}{G_L + G_{syn}}$$

# Synaptic saturation

- Let's examine how the voltage in a dendrite changes as a function of the amount of excitatory conductance…

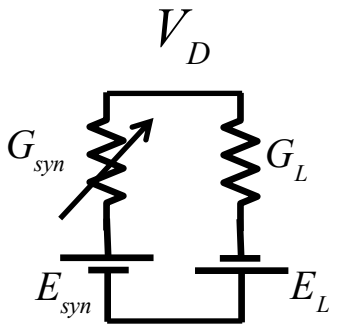
$$V = \frac{G_L E_L + G_{syn} E_{syn}}{G_L + G_{syn}}$$

For $G_L >> G_{syn}$

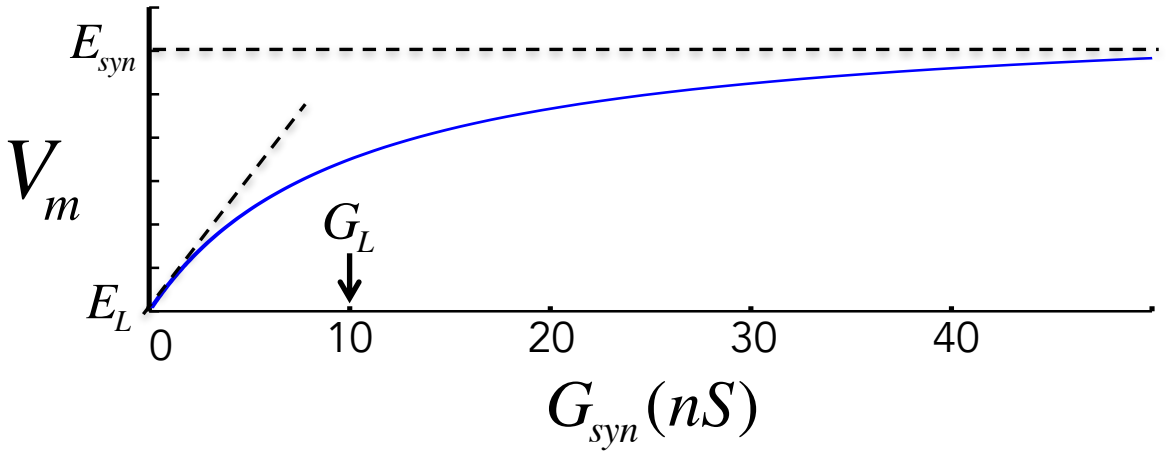
$$V \approx E_L + \left(\frac{E_{syn}}{G_L}\right) G_{syn}$$

For $G_{syn} >> G_L$

$$V \rightarrow E_{syn}$$




dendritic compartment



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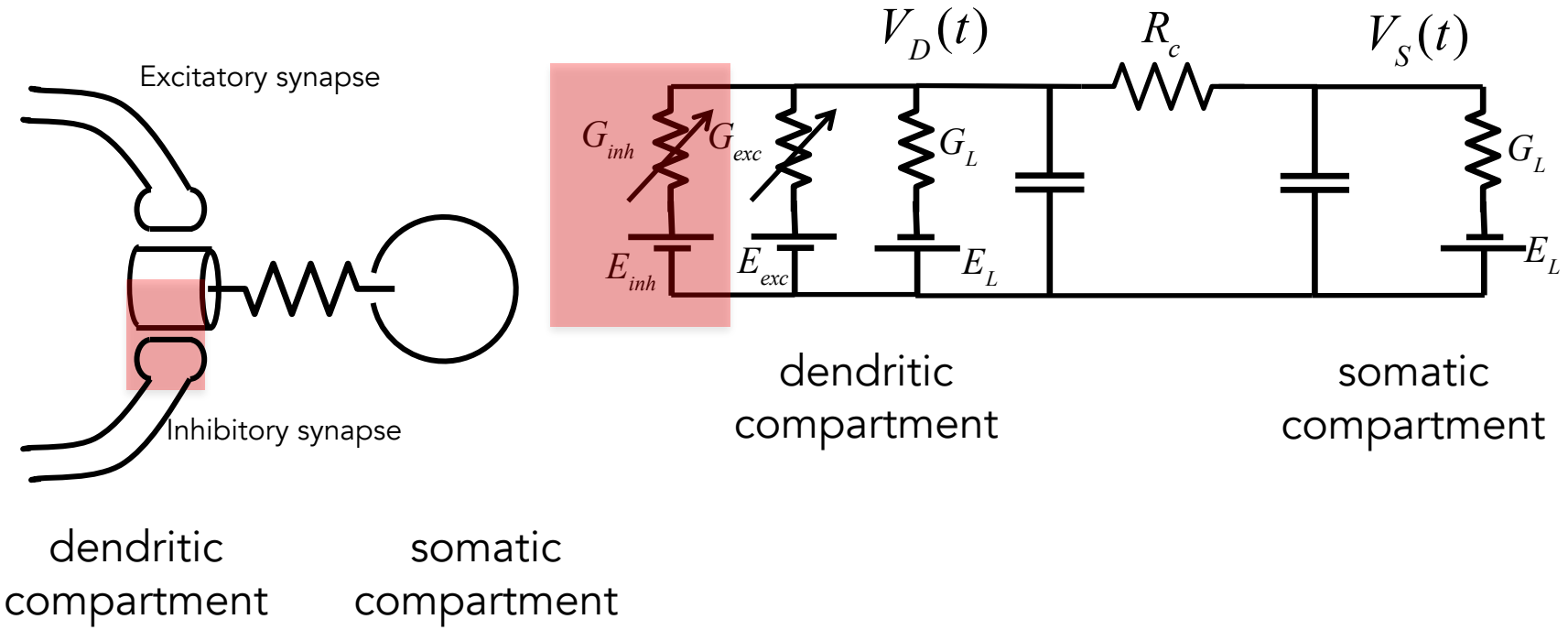
# Inhibitory inputs

- The effect of inhibitory input depends strongly on where the inhibitory synapse is.



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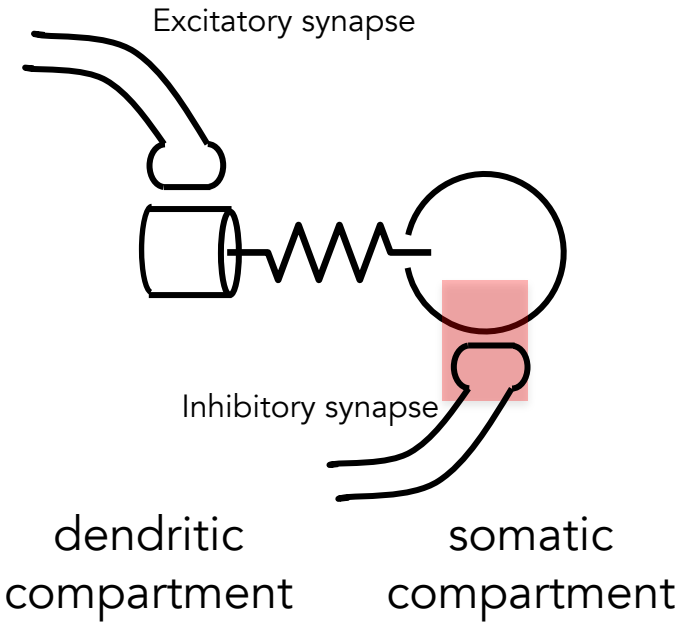
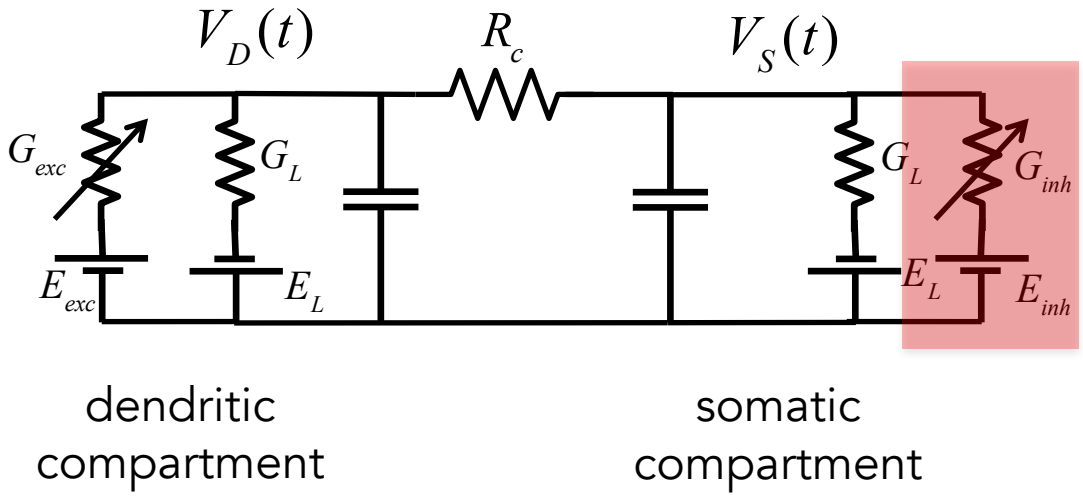
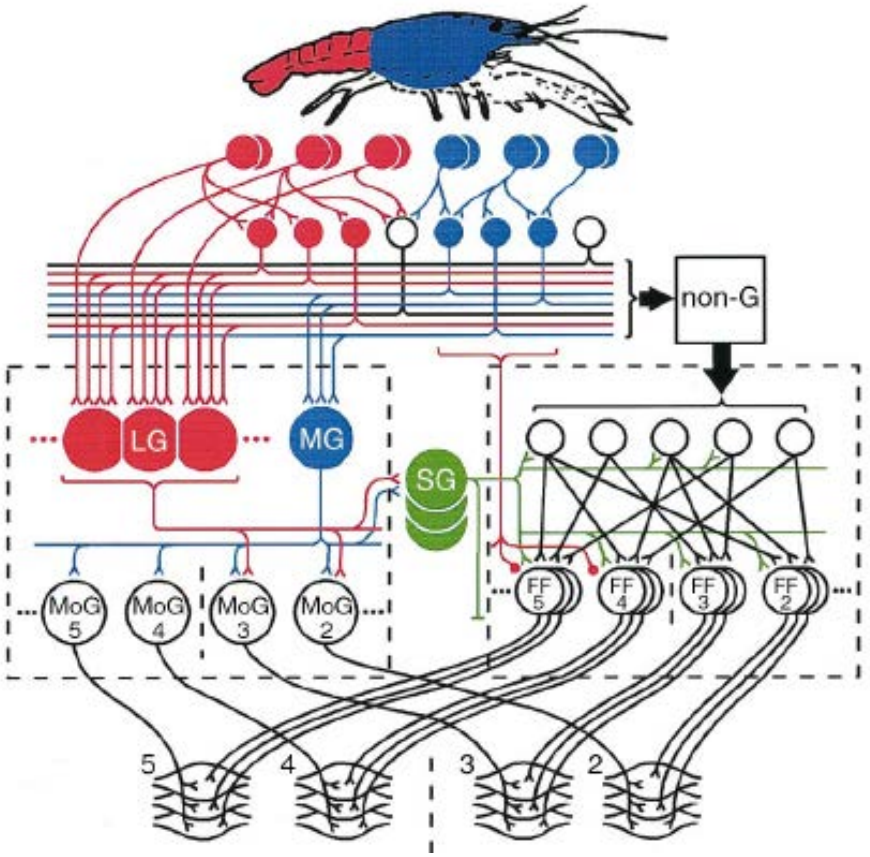


# Crayfish as a model system

- Stereotypic behavior
- Identifiable neurons
- Identifiable circuits

Figure removed due to copyright restrictions.
See Fig. 1 in Antonsen, B.L. and D.H. Edwards. "Differential Dye Coupling Reveals Lateral Giant Escape Circuit in Crayfish." *J. Comp. Neurol.* 466 no. 1 (2003):1-13.






Edwards et al. (Trends Neurosci, 1999)

Yellow: LG neuron
(Antonsen & Edwards, 2003)

# Escape behavior in crayfish

- MG (medial giant) escape
- LG (lateral giant) escape
- Non-giant escape

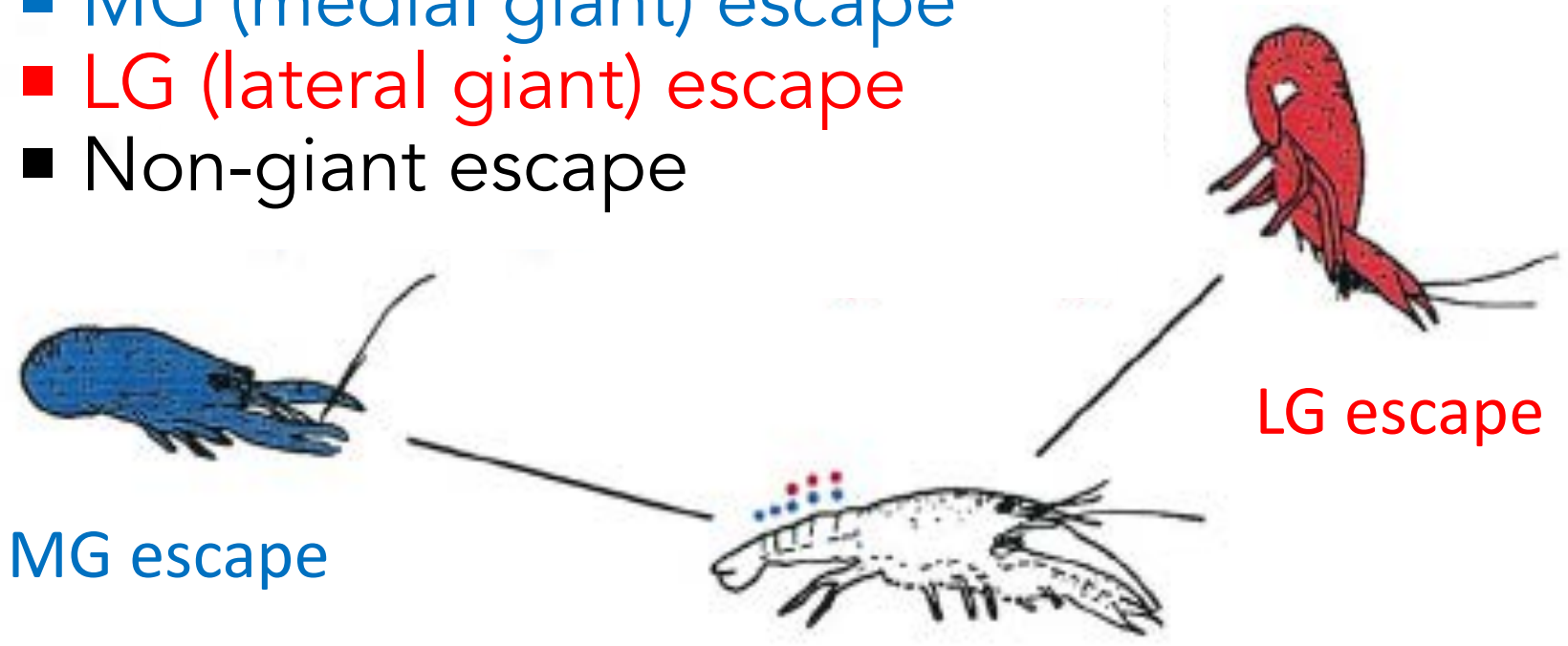





Figure: Edwards et al. (Trends Neurosci, 1999)

# LG is a 'command neuron'

- LG neuron is sufficient for LG escape.
  - Electrical stimulation of LG neuron produces tail flip.

- LG neuron is necessary for LG escape.
  - Tail flip is not elicited if the LG neuron is hyperpolarized.



Wine & Mistick (1977)

# Escape behaviors are strongly modulated by inhibition

- Escape response is suppressed while another escape response is in progress
  - Recurrent inhibition of LG neurons (and many other neurons) during escape behavior

- Escape response is suppressed when the animal is restrained

Hold off escape until timely moment?

Figure removed due to copyright restrictions. See Fig. 2 in Krasne, F.B. and J.J. Wine. "Extrinsic Modulation of Crayfish Escape Behaviour." *J. Experimental Biology* 63 (1975): 433-450.

Krasne & Wine (1975)

# Escape behaviors are strongly modulated by inhibition

- Escape response is suppressed while the animal is eating

Figure removed due to copyright restrictions. See Fig. 2 in Krasne, F.B. and S.C. Lee. "Response-dedicated Trigger Neurons as Control Points for Behavioral Actions." *J. Neuroscience* 8 no. 10 (1988): 3703-3712.

- But not while the animal is searching for food

Krasne & Lee (1988)

# Two types of modulation of LG escape reflex

- Absolute inhibition: The escape is inhibited no matter how strong the excitation is.

- Relative inhibition: The likelihood of escape is reduced, but it is still possible to override this kind of inhibition.

# Location of inhibitory synapses

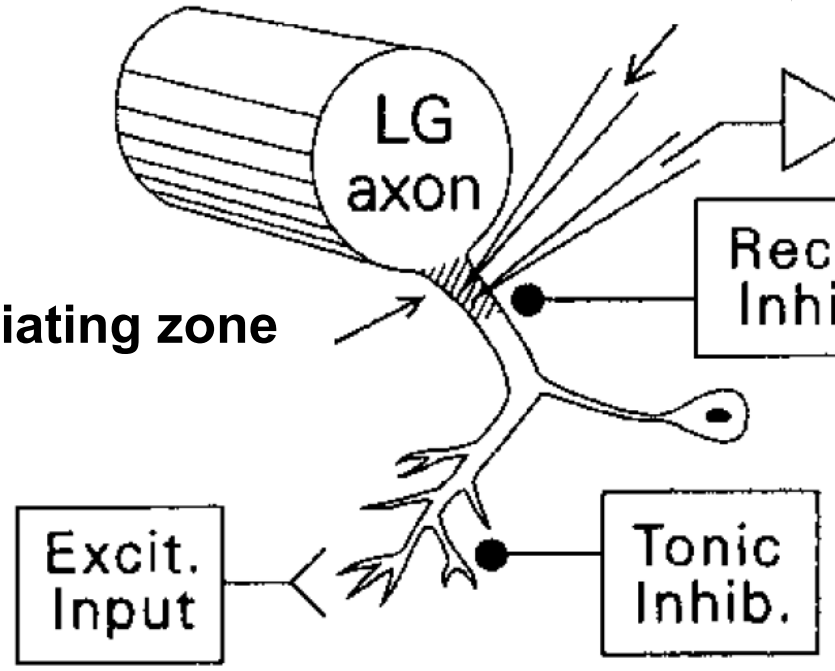
- Proximal inhibition:
  - Near the spike initiating zone
  - Arises from motor circuits that generate the MG escape
  - **Called 'recurrent inhibition'**

- Distal inhibition:
  - Intermixed with excitatory afferents further out on the dendrite
  - Arises from sensory areas
  - **Called 'tonic inhibition'**

Previous hypothesis:

Distal inhibition allows selective inhibition for particular dendritic branches

# Measuring the effect of different types of inhibition




Current injection

Recording

MG stimulation

Spike-initiating zone

restraint, sucrose block

Sensory root stimulation

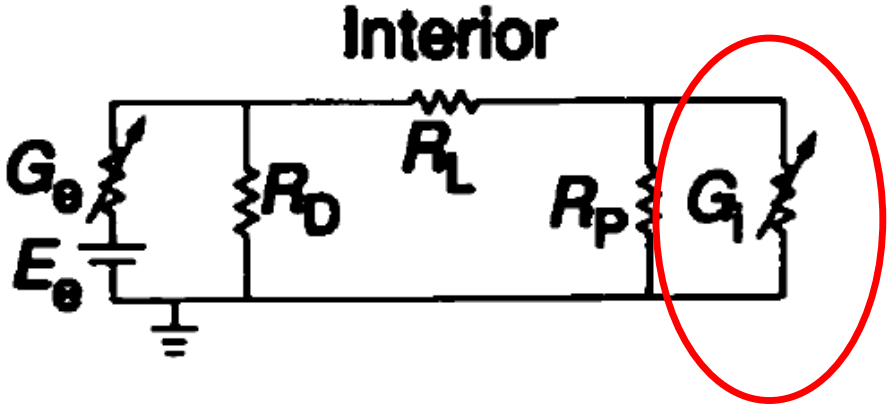


Vu and Krasne, 1992

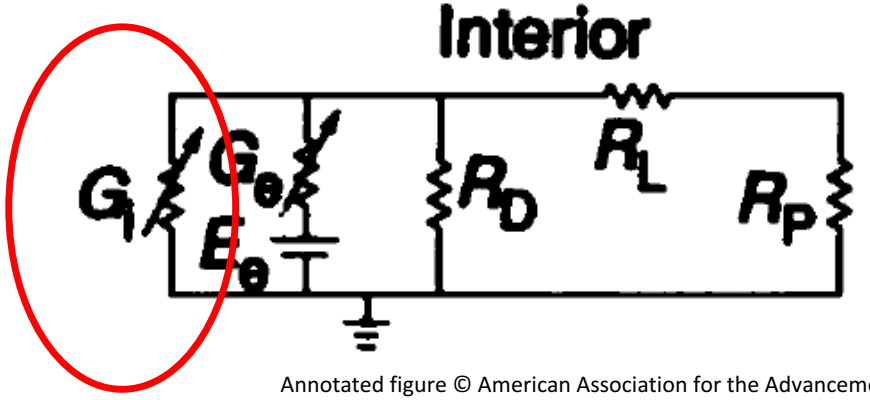
# Equivalent circuit model

- $R_L$: longitudinal resistance
- $R_P$: proximal resistance
- $R_D$: distal resistance
- Ee: reversal potential for excitatory synapse (100 mV)
- Ge: excitatory conductance
- Gi: inhibitory conductance

# Proximal versus Distal inhibition

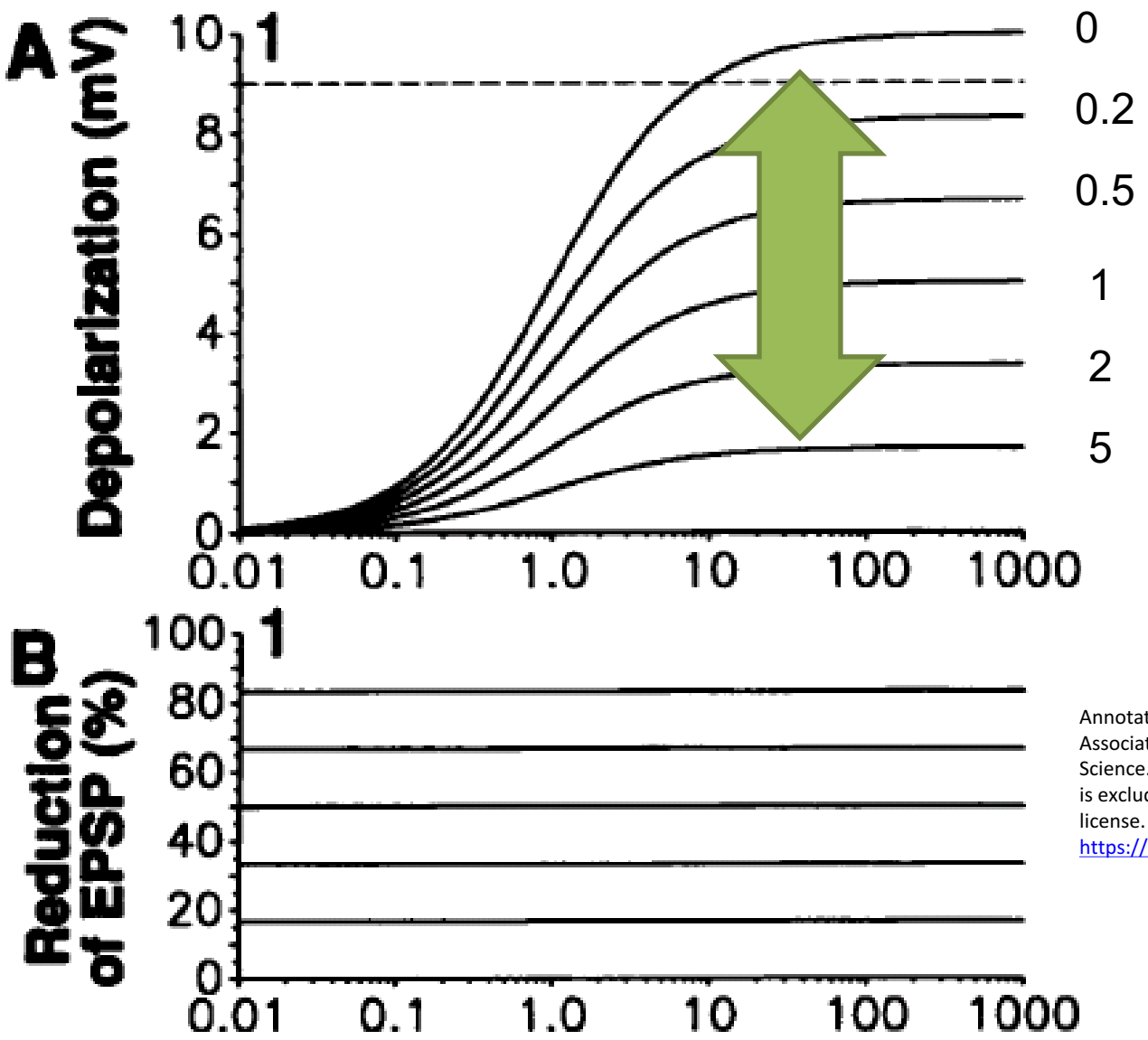



**Proximal inhibition**

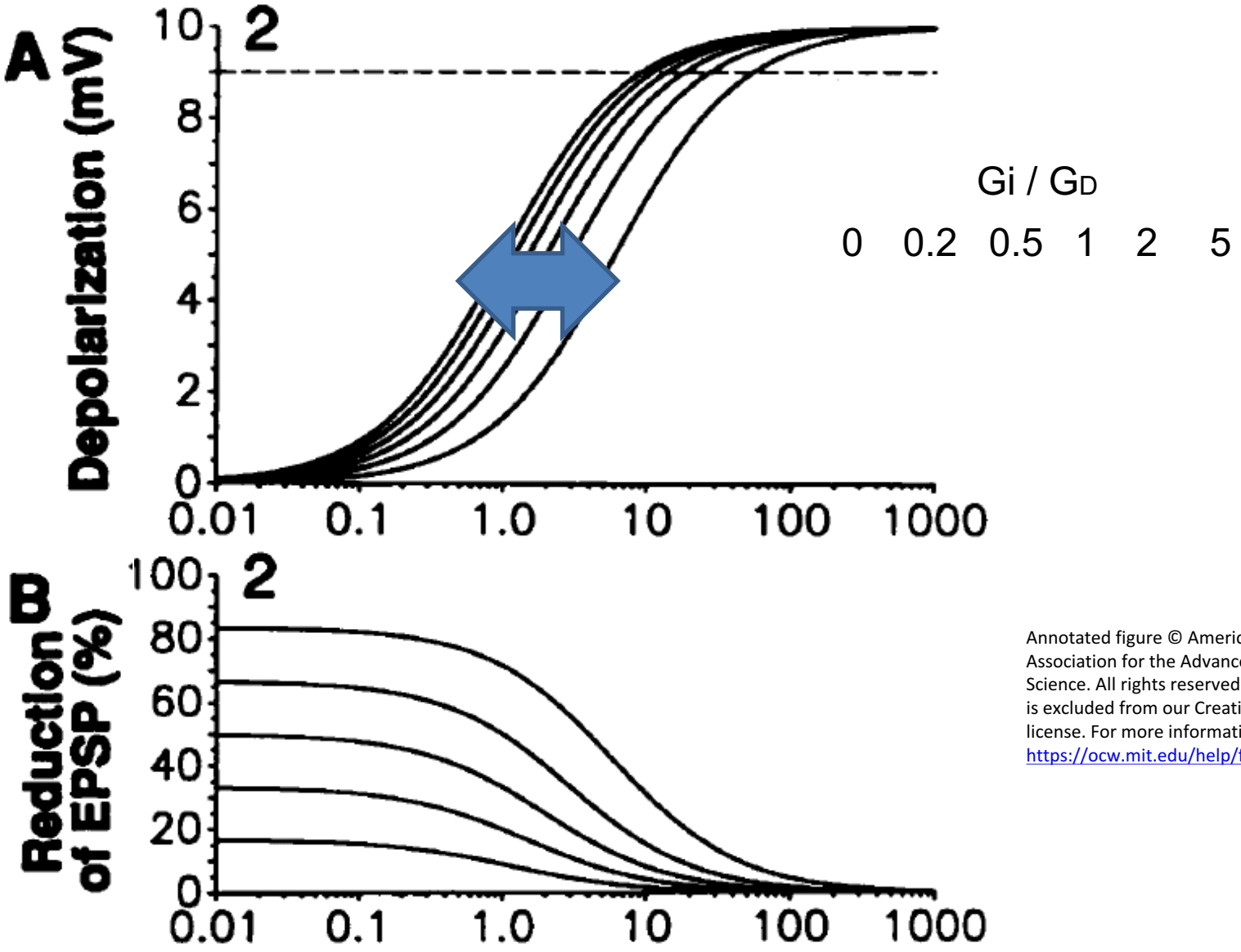



**Distal inhibition**

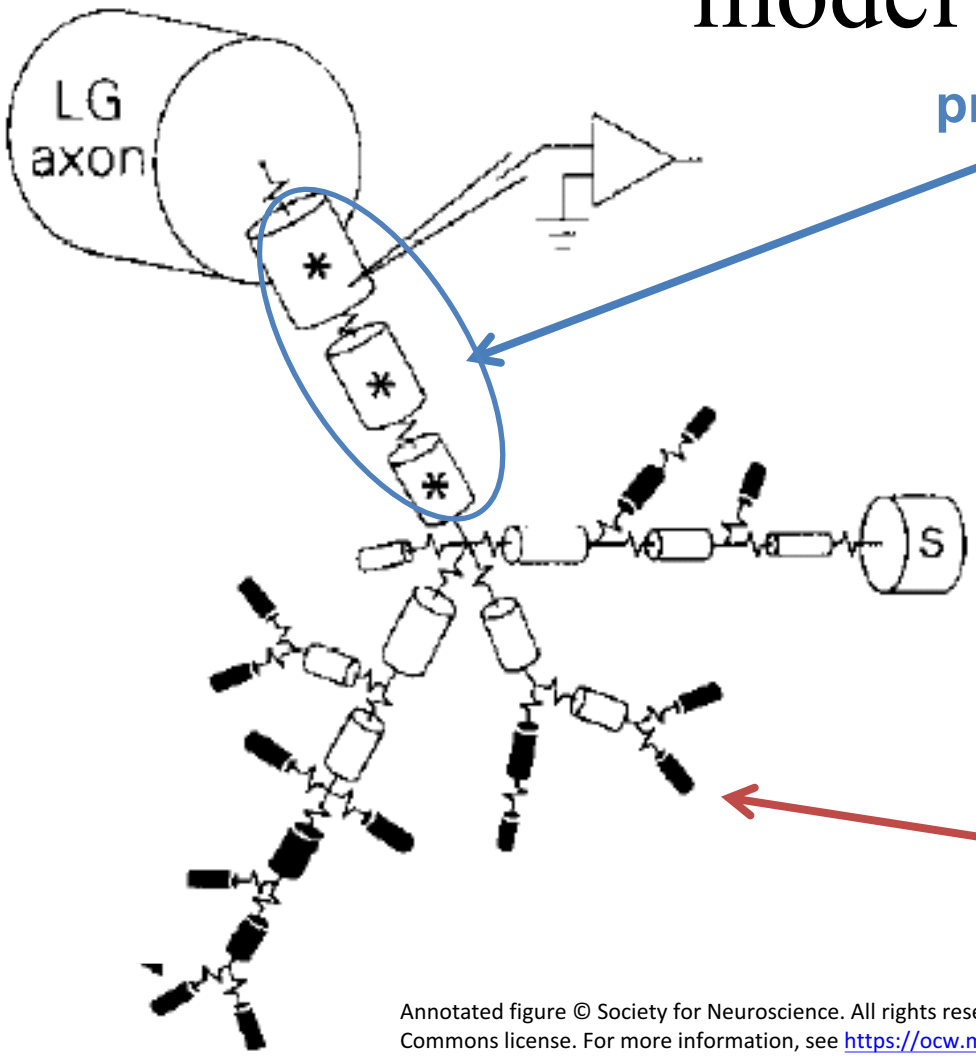
# Proximal inhibition



# Distal inhibition



# More ‘realistic’ multi-compartment model




**proximal inhibitory synapses**

**excitatory synapses,**
**distal inhibitory synapses**



Vu et al. (JNS, 1993)

# Different functions for proximal and distal inhibition

- Two-compartment model shows that the effect of proximal and distal inhibition are different.
  - Proximal inhibition: absolute
  - Distal inhibition: relative

- Qualitatively similar effects were seen when more complicated models were used.

# Learning objectives for Lecture 7

- Be able to add a synapse in an equivalent circuit model
- To describe a simple model of synaptic transmission
- To be able to describe synaptic transmission as a convolution of a linear kernel with a spike train
- To understand synaptic saturation
- To understand the different functions of somatic and dendritic inhibition

# 9.40 Introduction to Neural Computation
Spring 2018