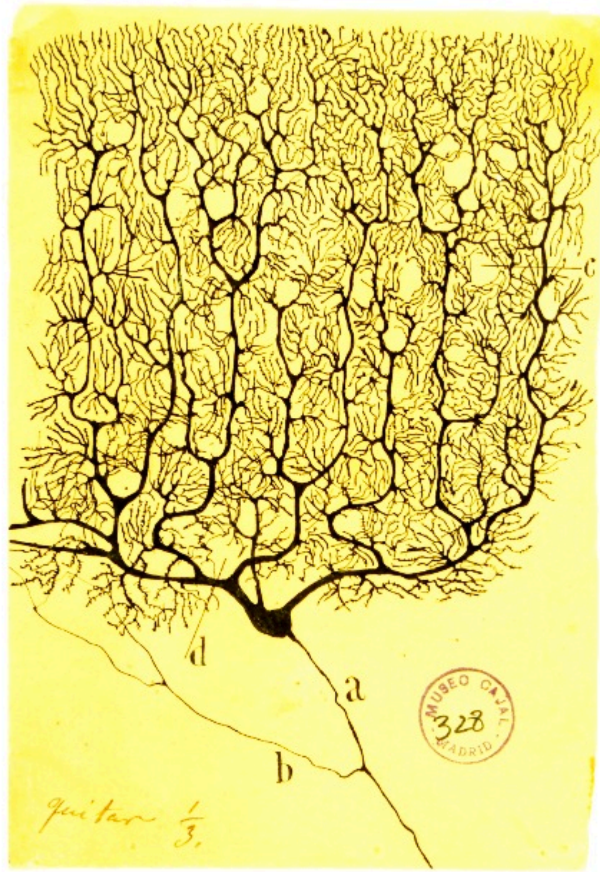
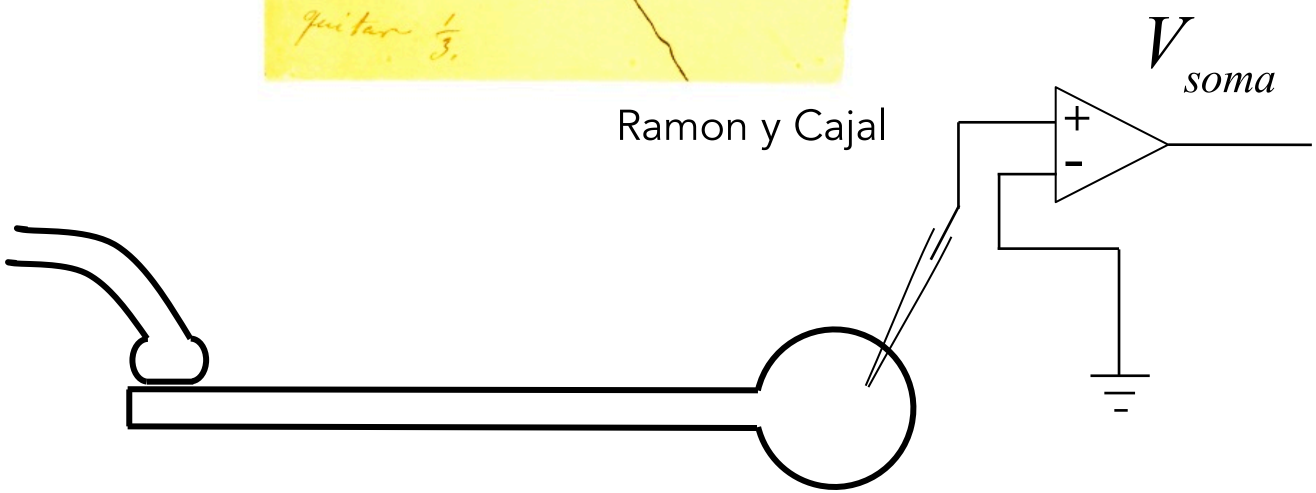
Introduction to Neural Computation

Prof. Michale Fee
MIT BCS 9.40 — 2018
Lecture 7



Ramon y Cajal

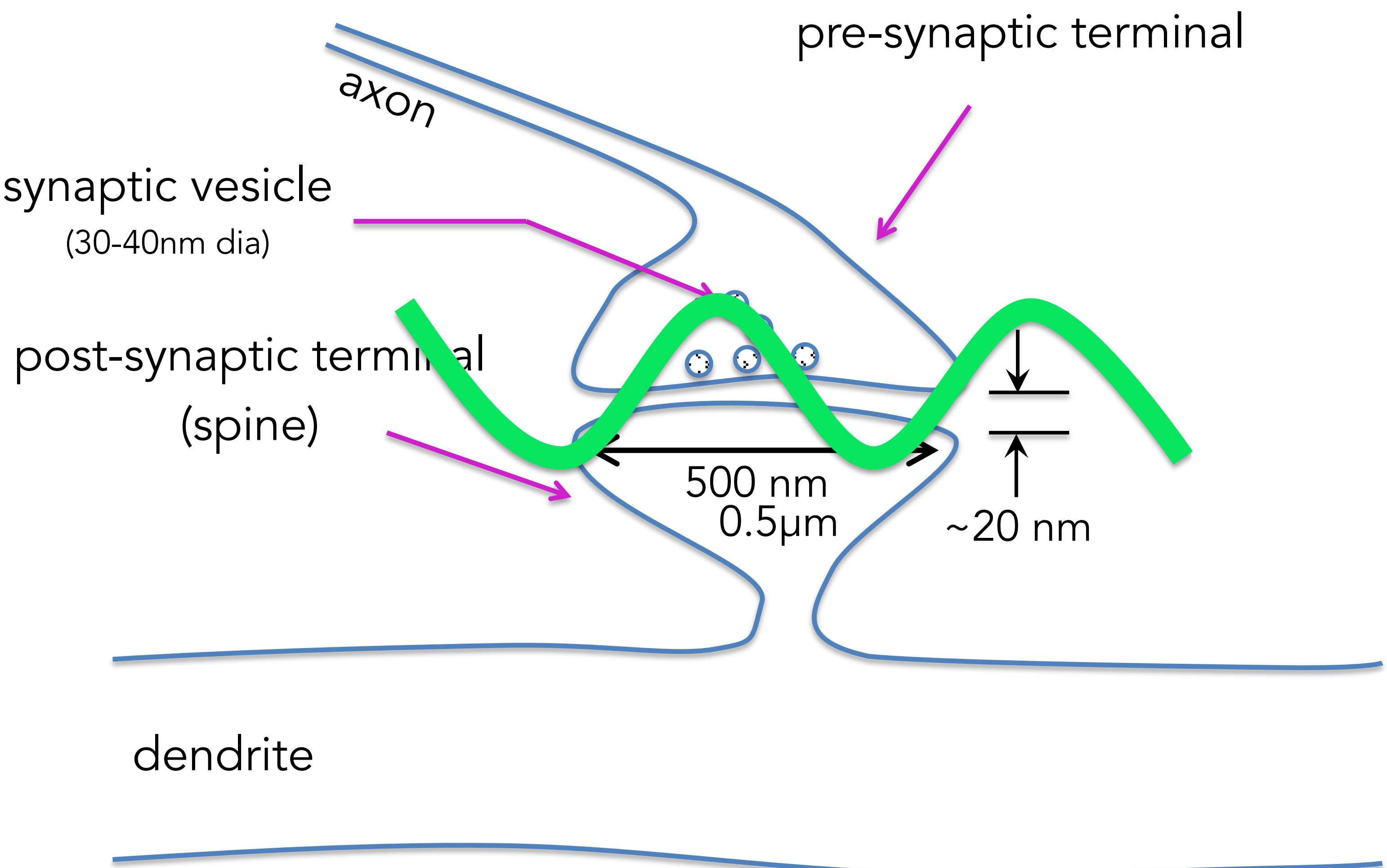


Learning objectives for Lecture 7

- 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

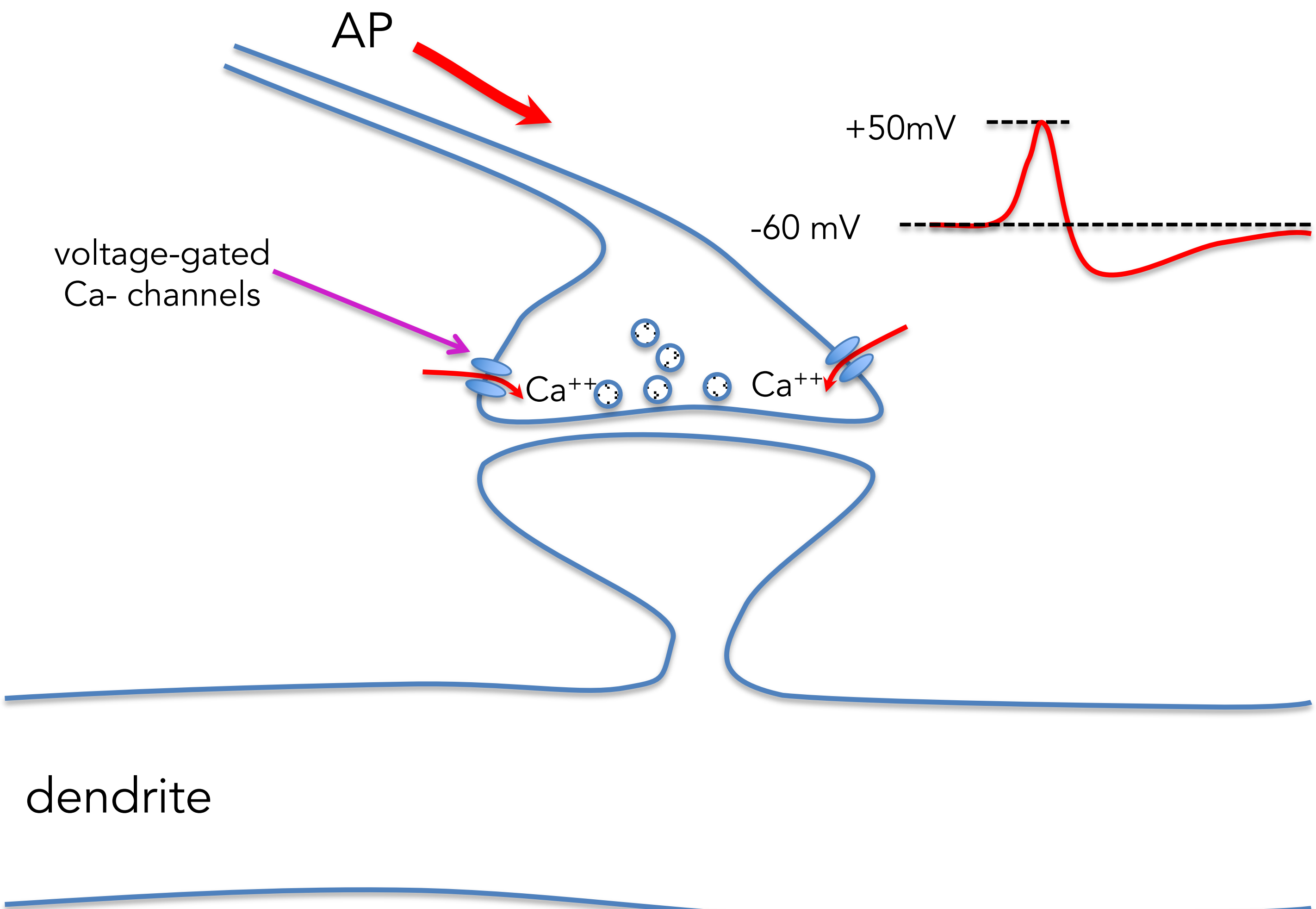
Chemical synapse

- Structure of typical excitatory synapse



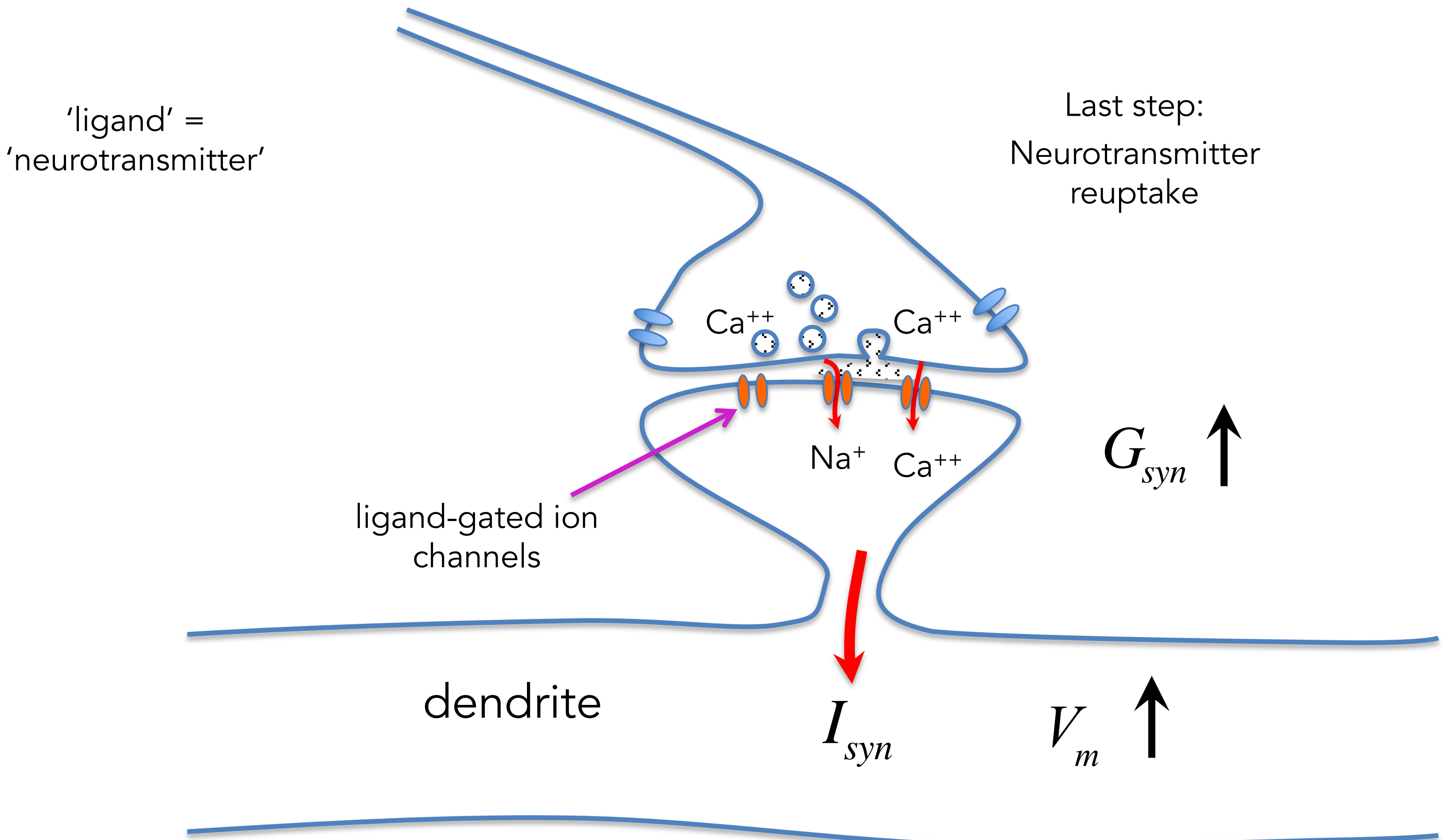
Chemical synapse

- 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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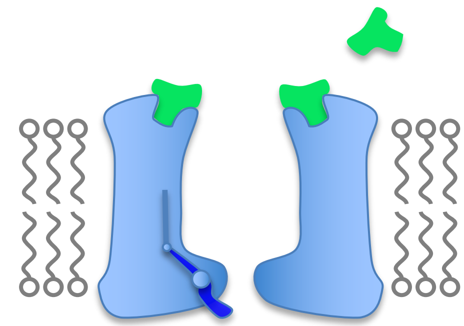
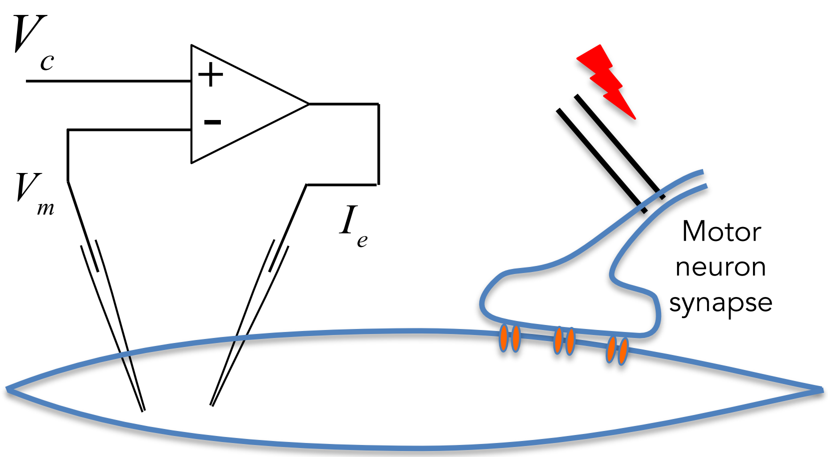
How does a synapse respond?

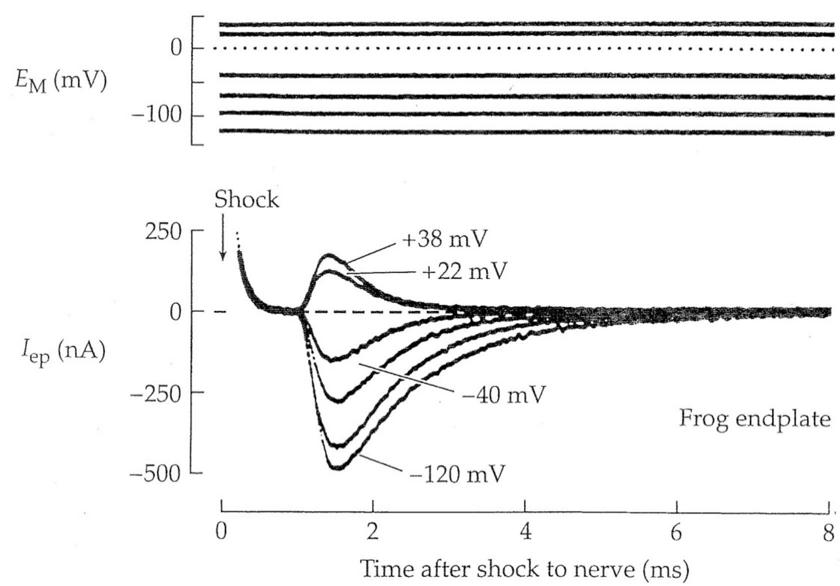
- Ionotropic receptors



Two electrode voltage-clamp experiment



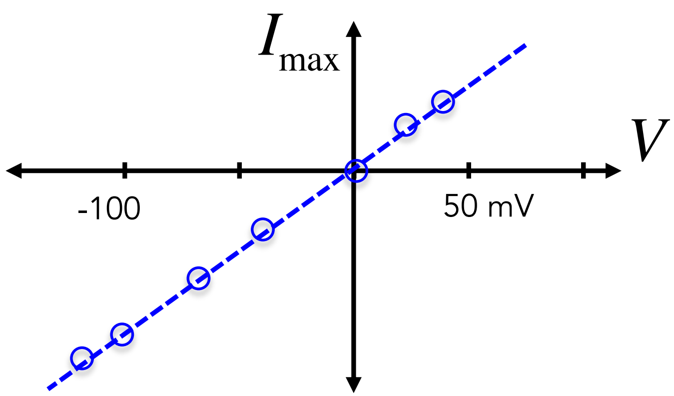
Frog sartorius muscle fiber

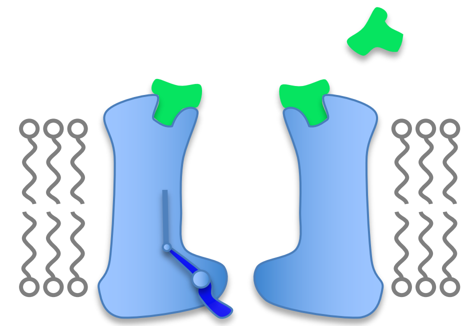


Magleby and Stevens, 1972

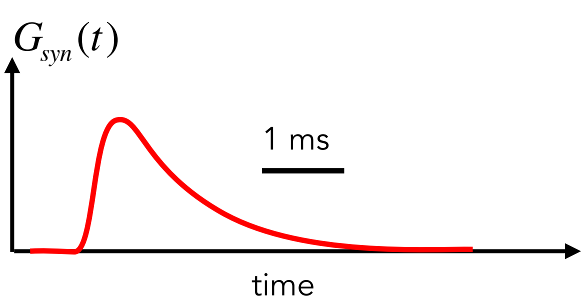
How does a synapse respond?

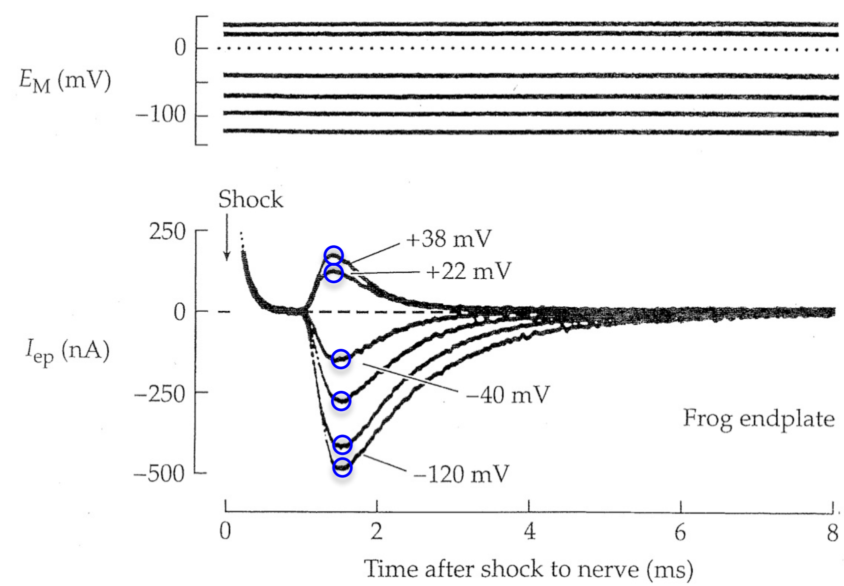
- Ionotropic receptors





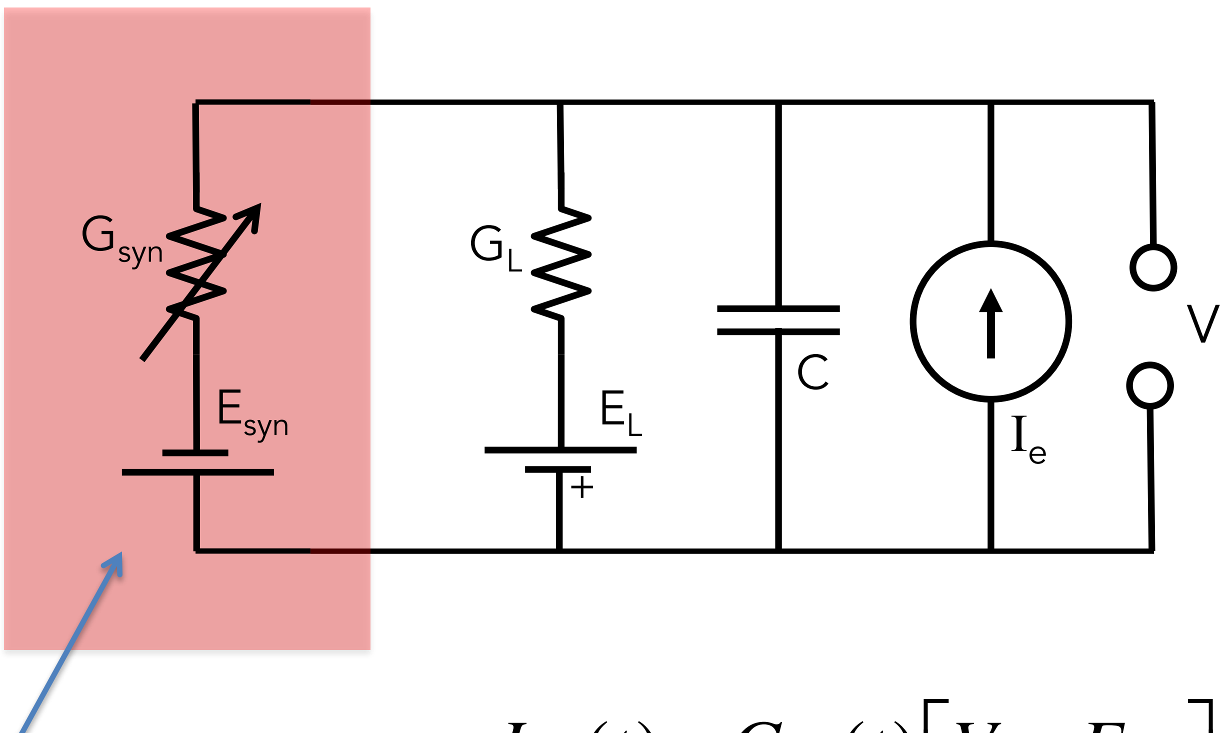
$$I_{syn}(t) = G_{syn}(t)\left[V - E_{syn}\right]$$





Equivalent circuit model of a synapse

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



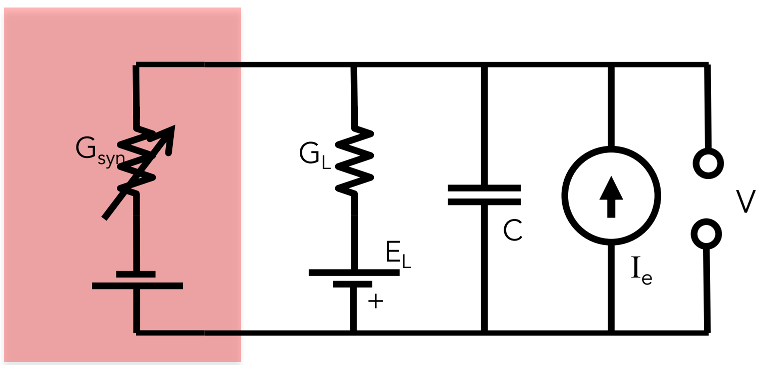
Equivalent circuit of a synapse

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

Excitatory synapses

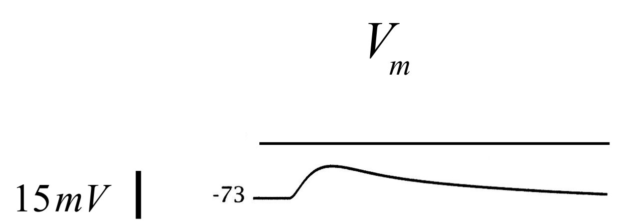
- Increased synaptic conductance causes the membrane potential to approach the reversal potential for that synapse.

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



$E_{syn} = 0\, mV$

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

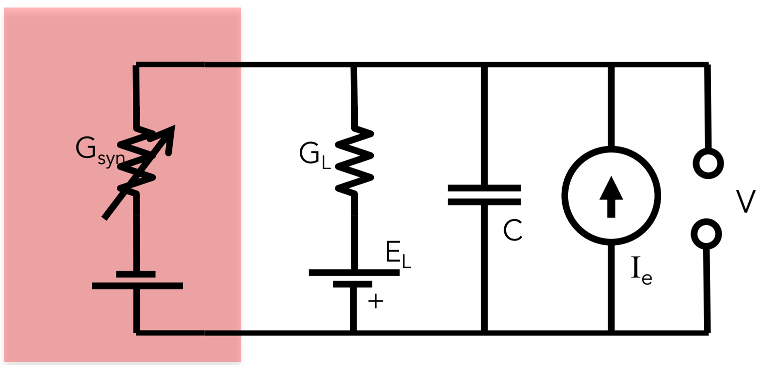


Excitatory postsynaptic potential (EPSP)

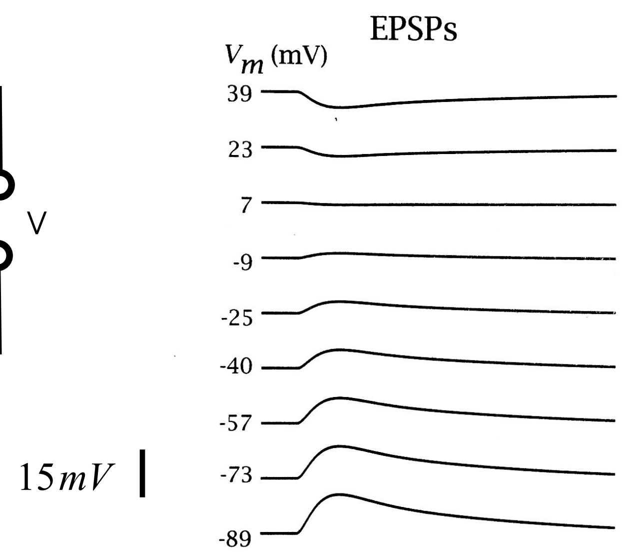
Excitatory and inhibitory synapses

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

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



$E_{syn} = 0\,mV$



Excitatory synapse if

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

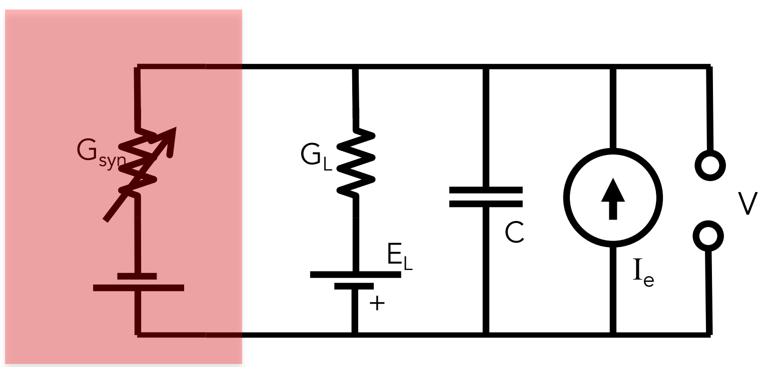
Excitatory postsynaptic potential (EPSP)

Excitatory and inhibitory synapses

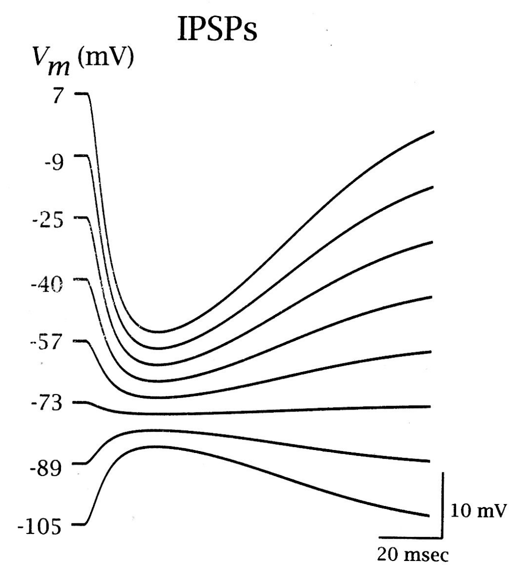
- Increased synaptic conductance causes the membrane potential to approach the reversal potential for that synapse.

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

GABAergic synapse



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



Inhibitory synapse if

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

Inhibitory postsynaptic potential (IPSP)

Equivalent circuit model of a synapse

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

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

- 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'.

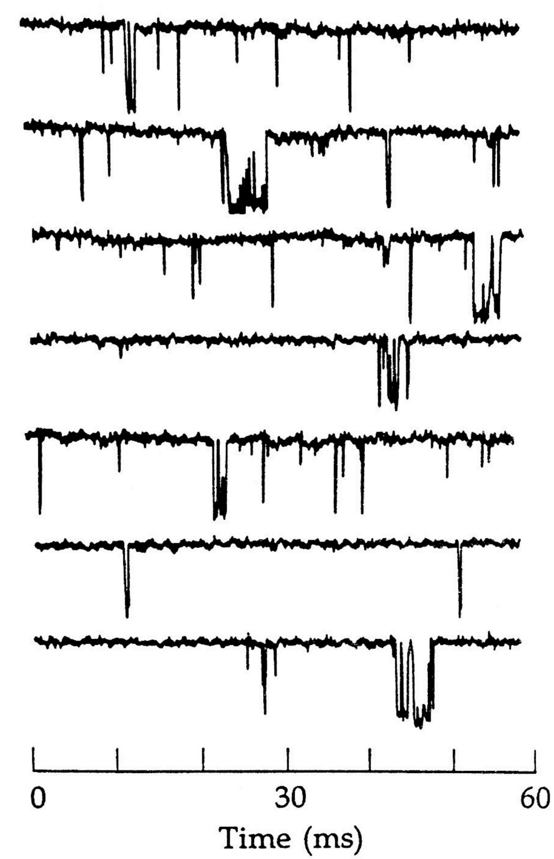
$$G_{syn}(t) = \hat{g}_R \, N_R \, P_R(t)$$

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

N_R =number of receptors

Single-channel patch recording

GABA$_A$ receptor



Kinetic model of synapse gating

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

$$\underset{1-P_R}{\text{'closed'}} \underset{\beta}{\overset{\alpha}{\rightleftharpoons}} \underset{P_R}{\text{'open'}}$$

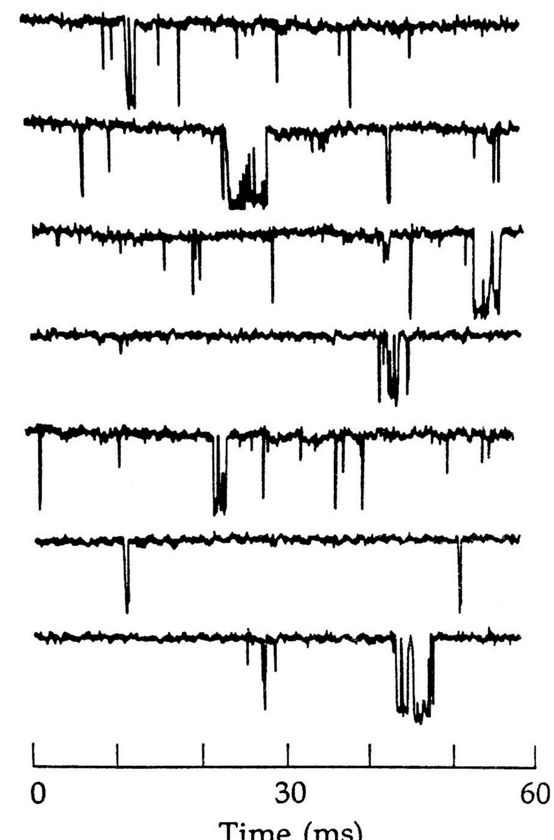
α, β are transition rate constants

Probability per unit time;

units are 1/s

Single-channel patch recording

$GABA_A$ receptor



- What controls the rate at which channels open ?

Neurotransmitter!

Equivalent circuit model of a synapse

- Simplified version of Magleby-Stevens model

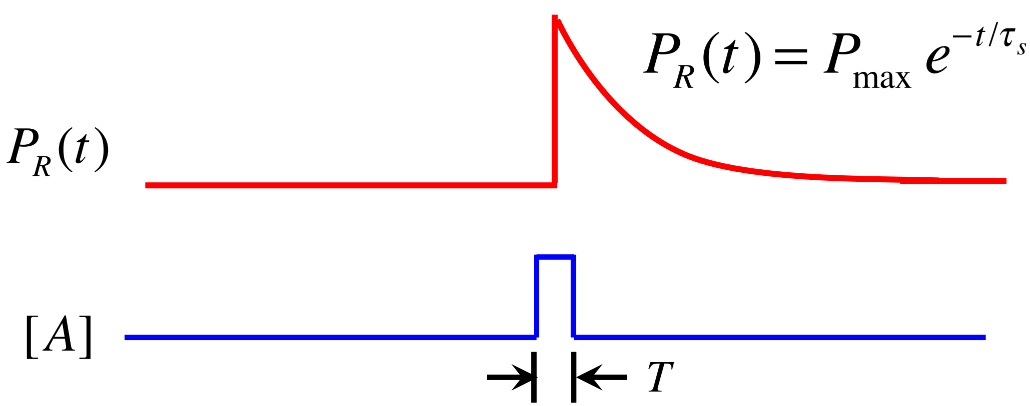
unbound NT

$$R \xrightleftharpoons[\beta]{A,\ \alpha} AR^*$$

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

(closed)
unbound receptor
$1-P_R$

(open)
bound receptor complex
P_R



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

Learning objectives for Lecture 7

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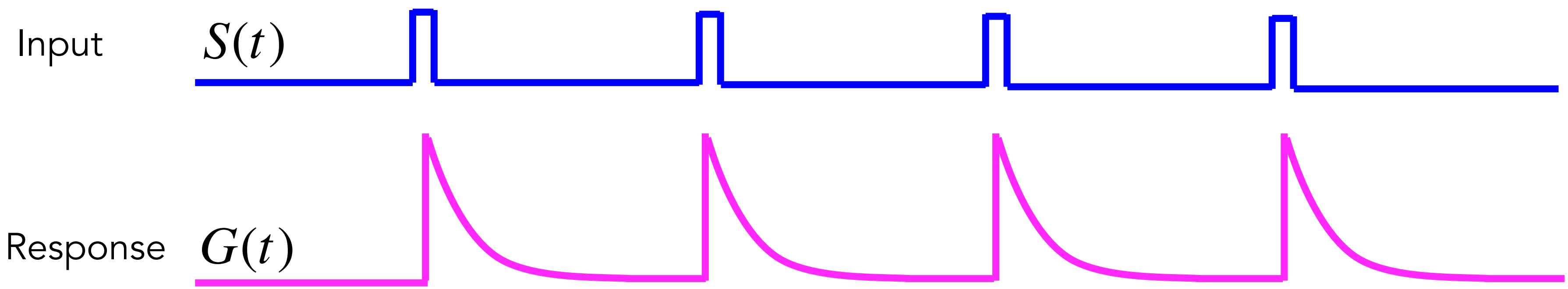
Response of a synapse to a spike train input

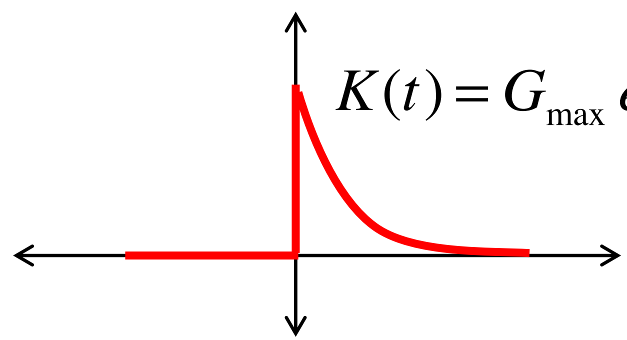
- This simple model makes it very easy to describe the response of a synapse to a train of spikes!



Impulse response or Linear Kernel

Convolution

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

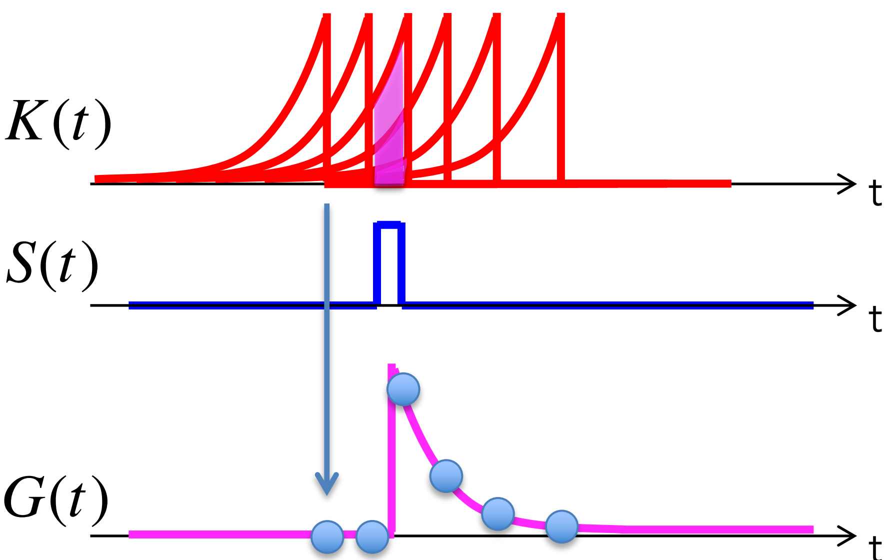


$$K(t) = G_{\max}\, e^{-t/\tau_s}$$

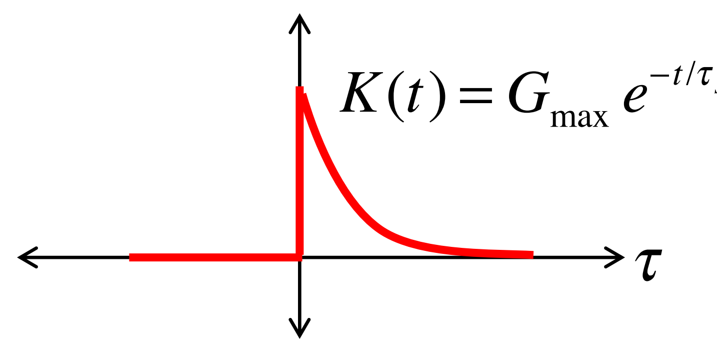
Response of a synapse to a spike train input

- 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

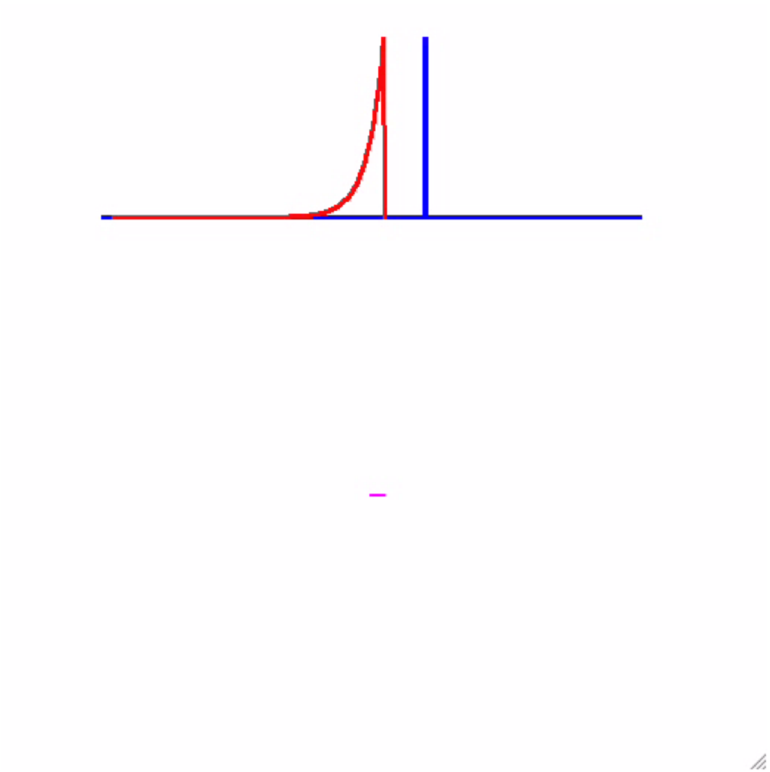


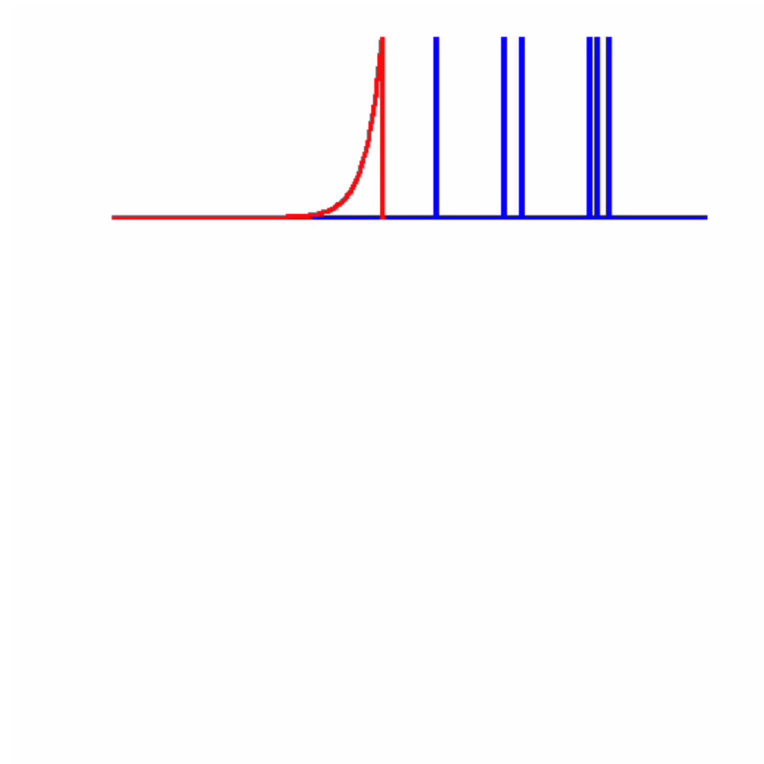
Response of a synapse to a spike train input

- 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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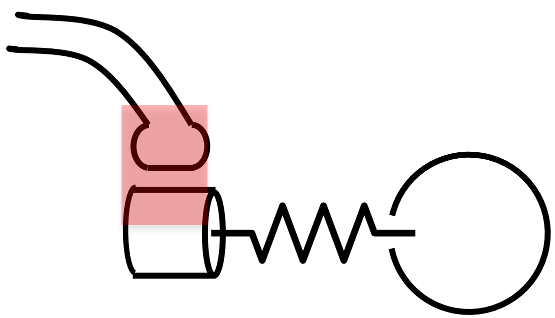
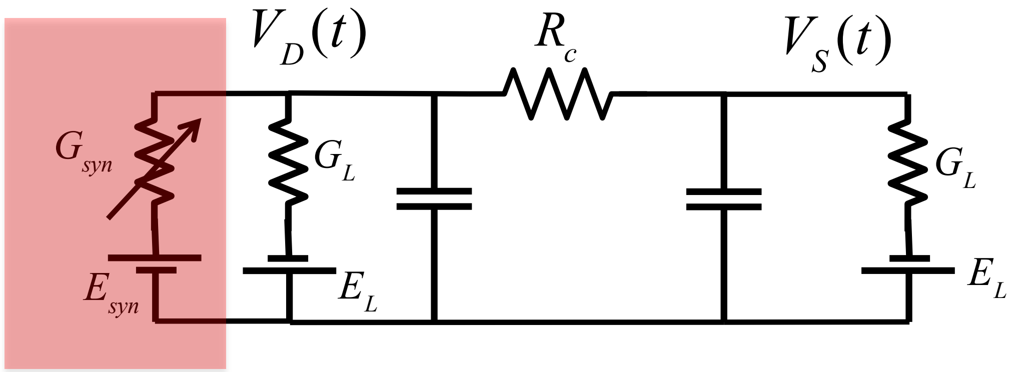
Synaptic saturation

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



dendritic compartment

somatic compartment



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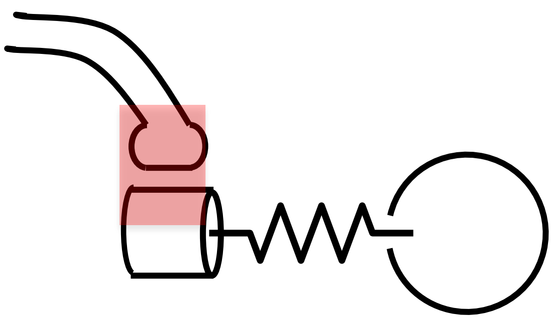
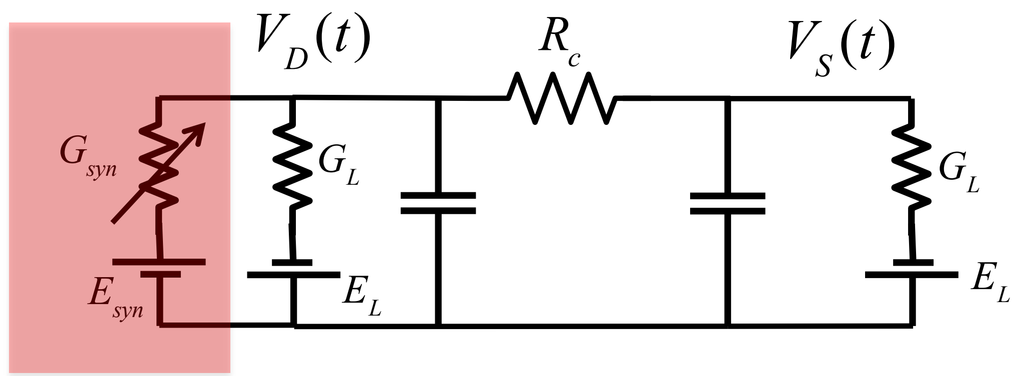


dendritic compartment

somatic compartment



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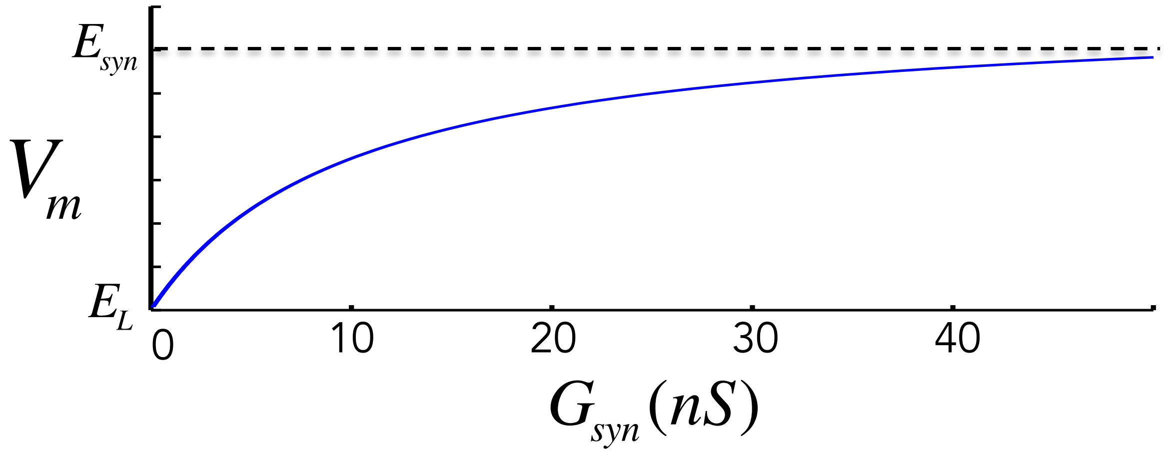
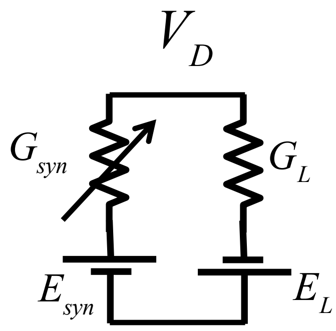




dendritic compartment

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…

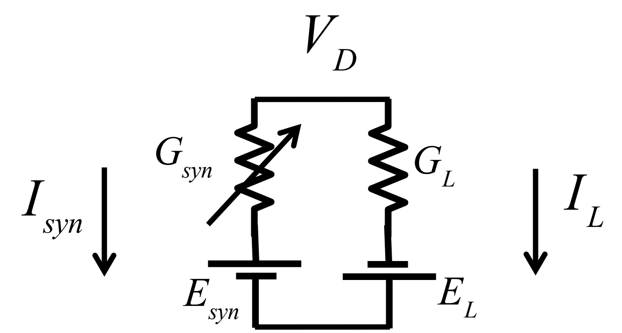
Kirchoff's current law says:

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

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

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

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



dendritic compartment

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

Synaptic saturation

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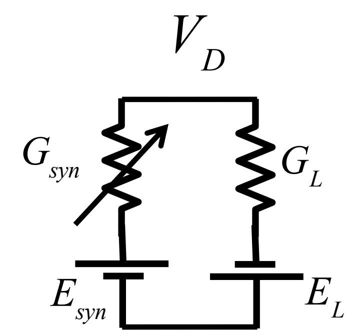


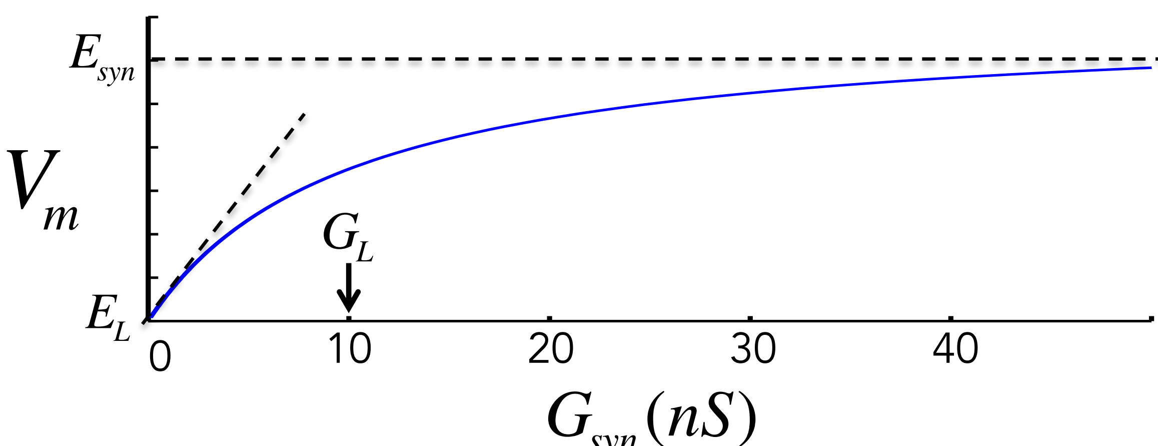
dendritic compartment

$$\text{For} \quad G_L >> G_{syn}$$

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

$$\text{For} \quad G_{syn} >> G_L$$

$$V \rightarrow E_{syn}$$



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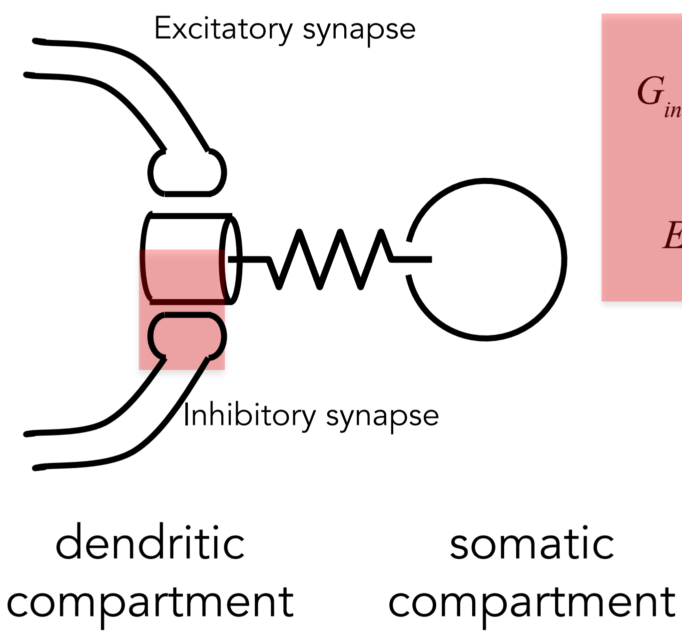
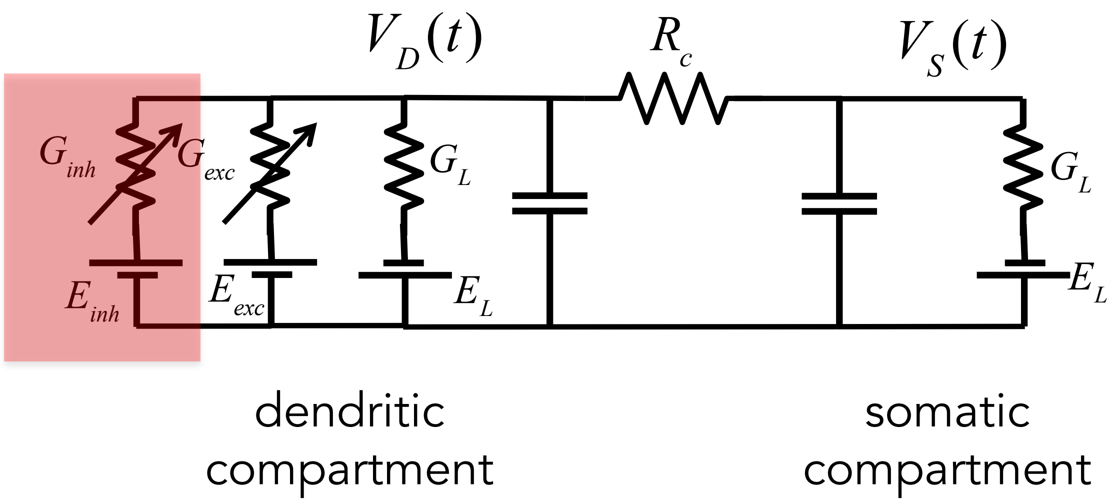
Inhibitory inputs

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





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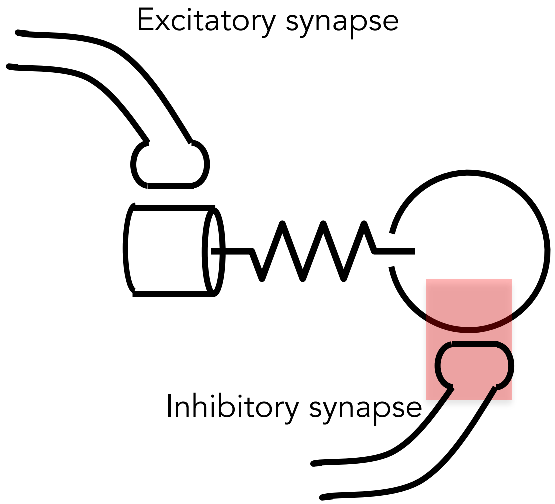
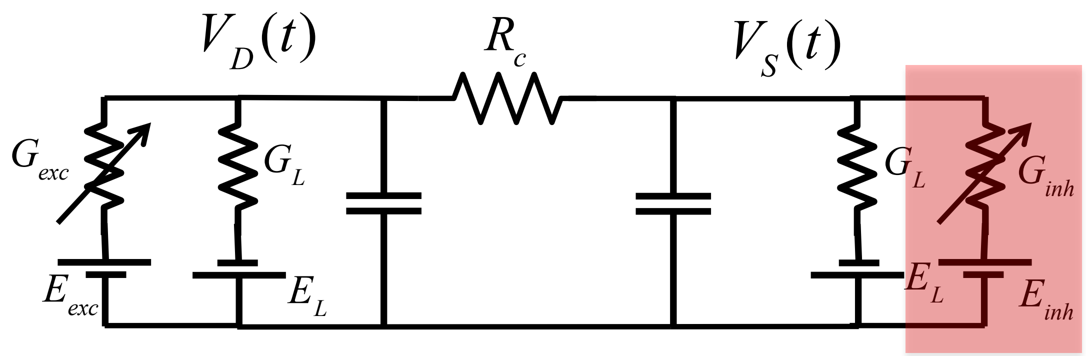


dendritic compartment

somatic compartment

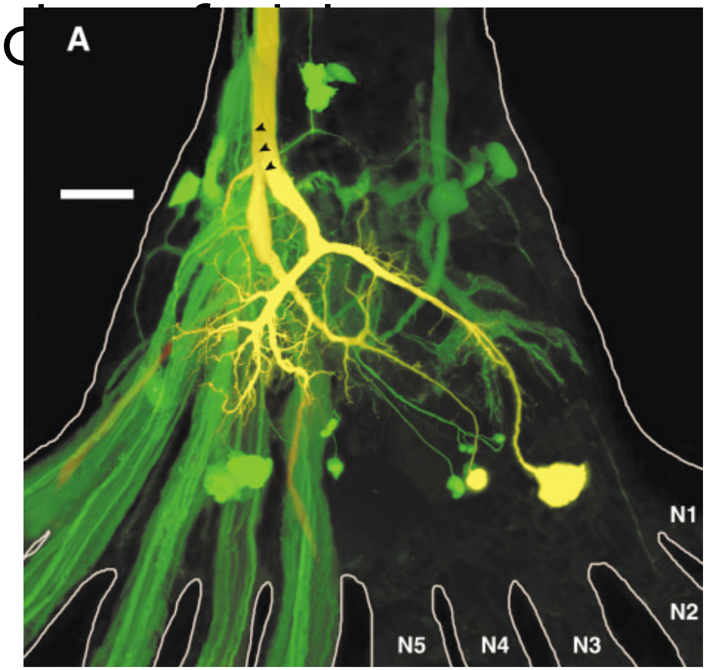


dendritic compartment

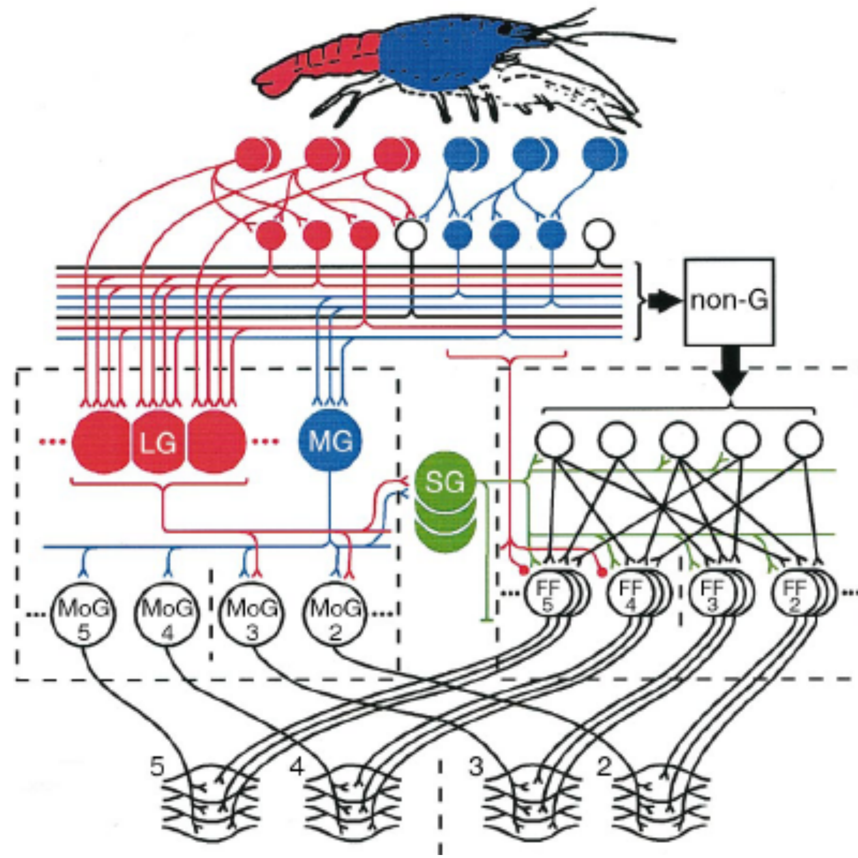
somatic compartment

Crayfish as a model system

- Stereotypic behavior
- Identifiable neurons
- Id



Yellow: LG neuron
(Antonsen & Edwards, 2003)



Edwards et al. (Trends Neurosci, 1999)

Escape behavior in crayfish

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

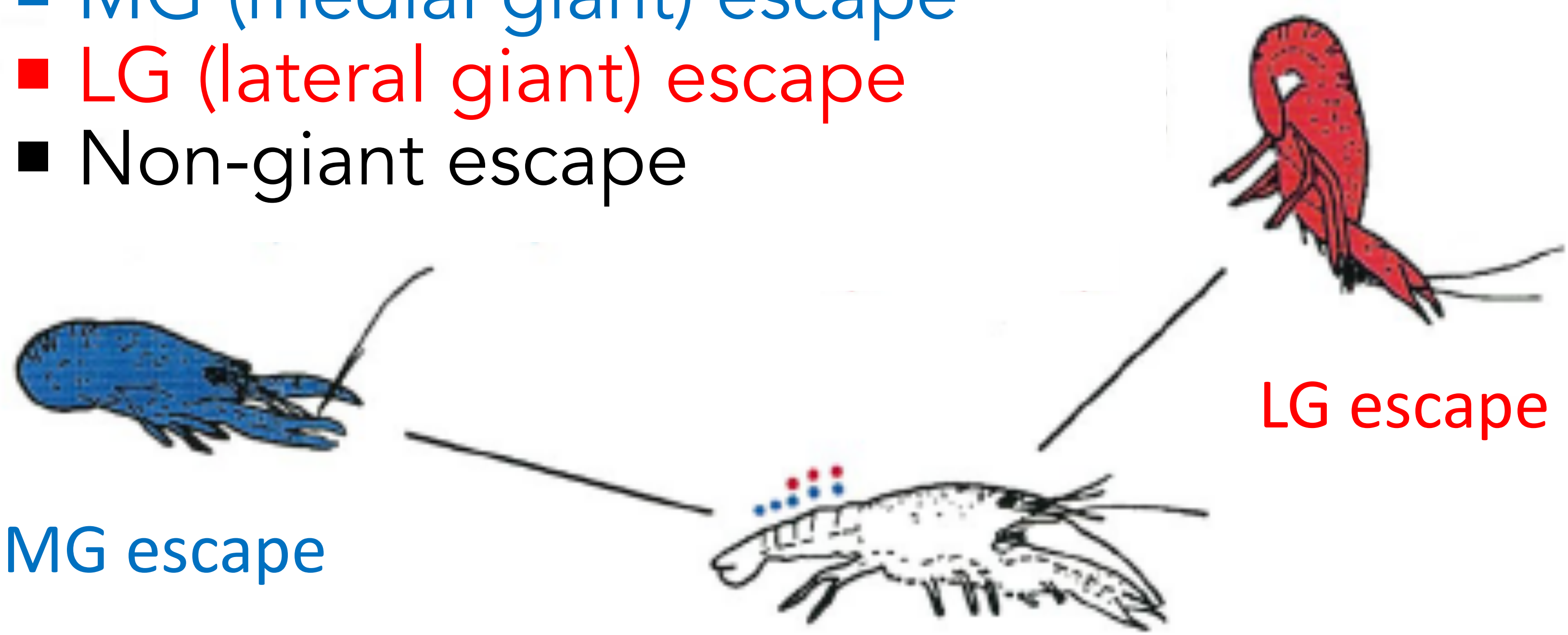
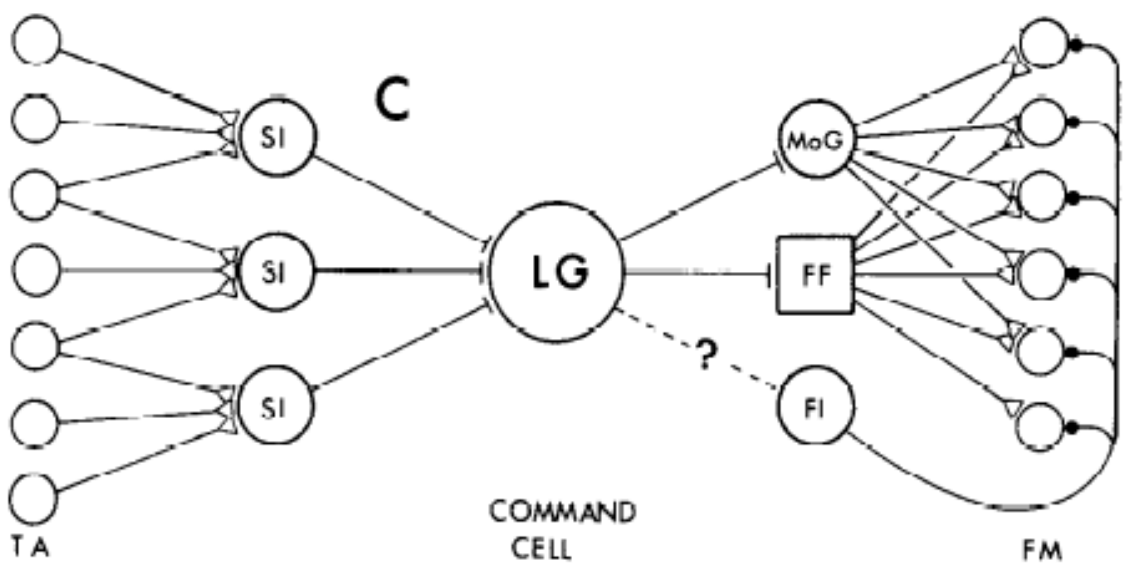


Figure: Edwards et al. (Trends Neurosci, 1999)

LG is a ‘command neuron’

- LG neuron is <u>sufficient</u> for LG escape.
  - Electrical stimulation of LG neuron produces tail flip.

- LG neuron is <u>necessary</u> for LG escape.
  - Tail flip is not elicited if the LG neuron is hyperpolarized.



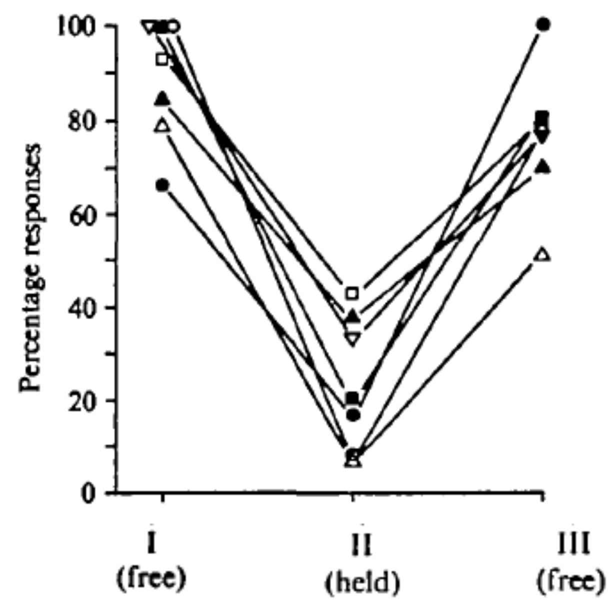
Wine & Mistick (1977)

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?

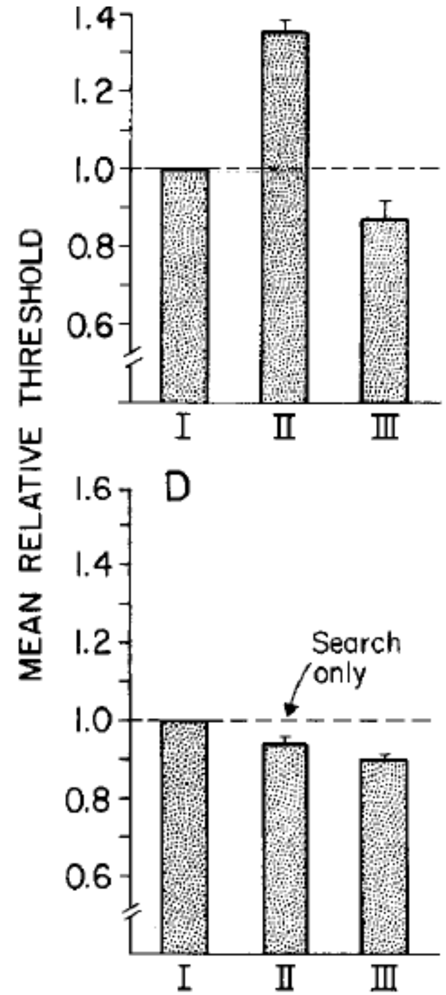


Krasne & Wine (1975)

Escape behaviors are strongly modulated by inhibition

- Escape response is suppressed while the animal is eating

- 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.

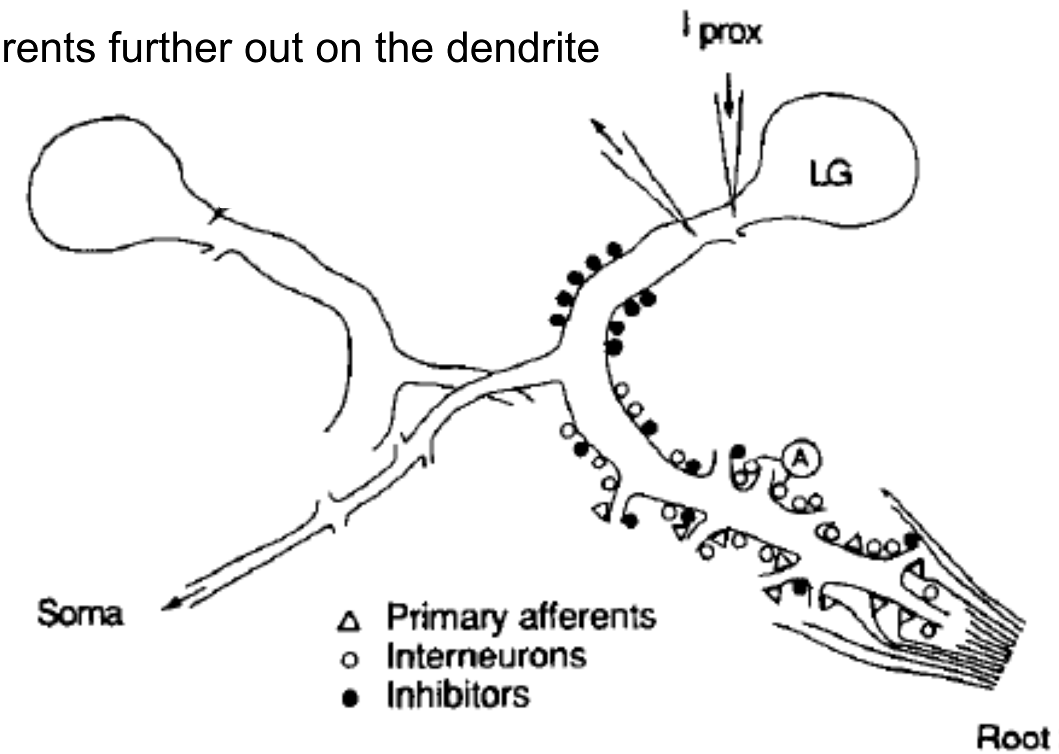
Location of inhibitory synapses

- 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'**

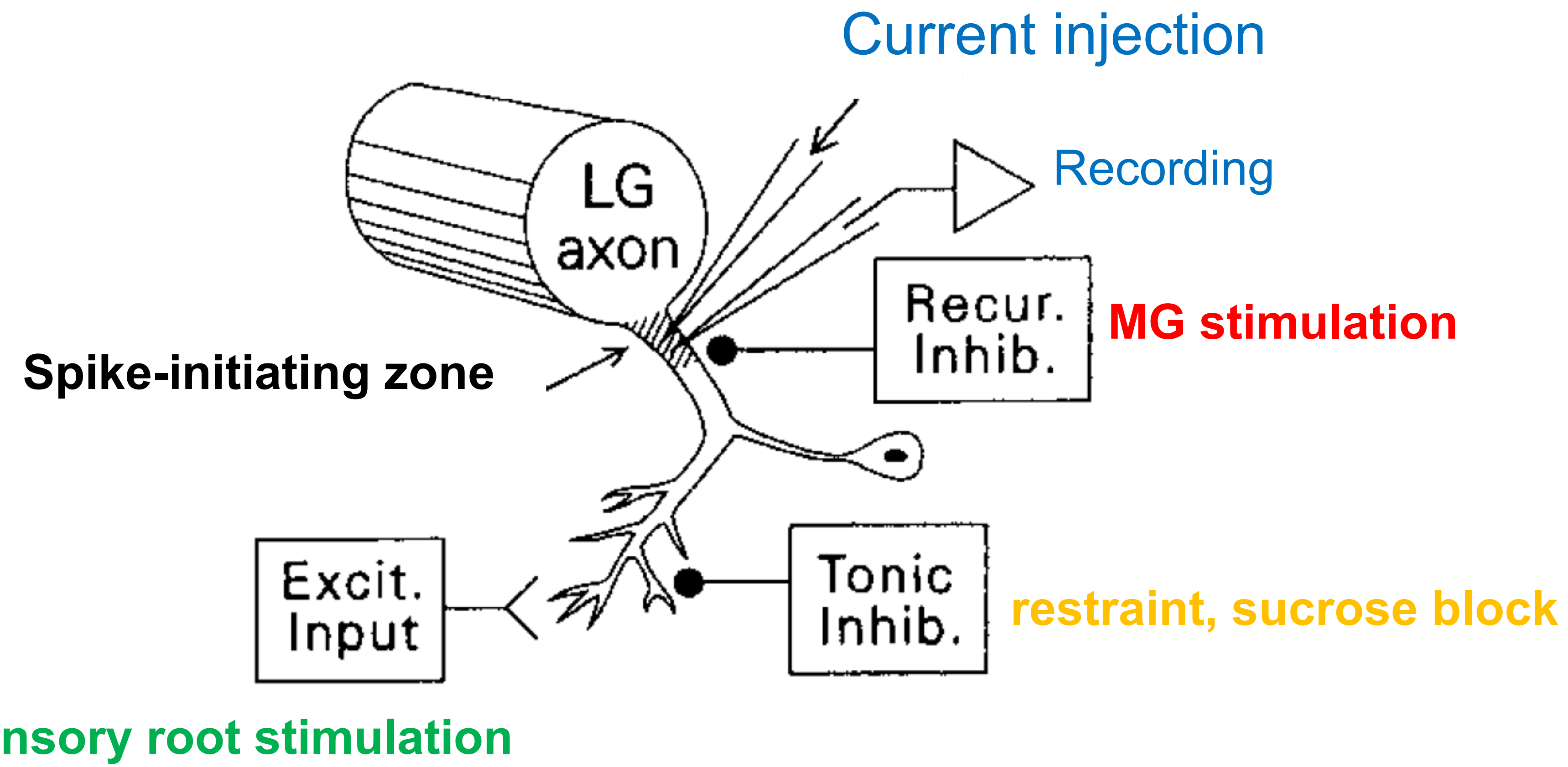
Previous hypothesis:

Distal inhibition allows selective inhibition for particular dendritic branches



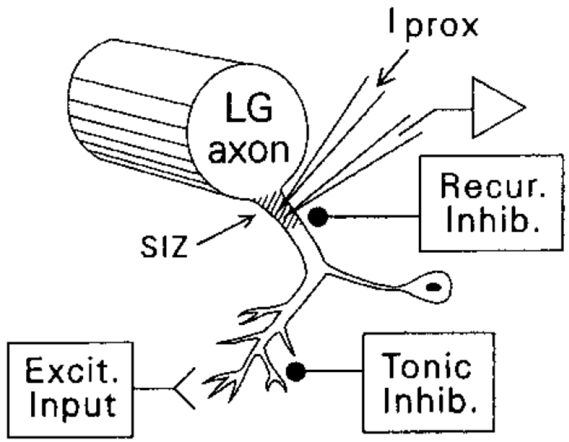
Vu et al. (JNS, 1993)

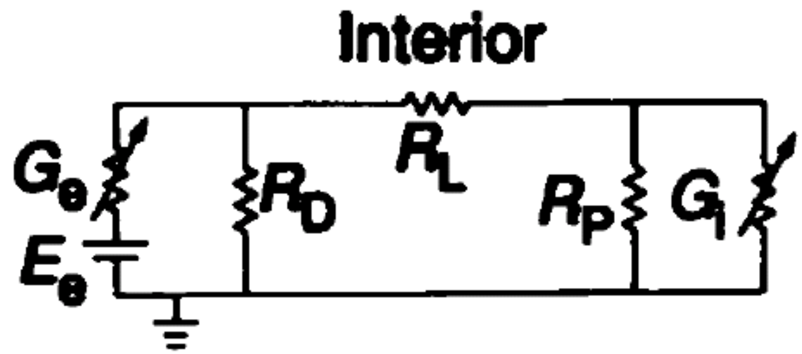
Measuring the effect of different types of inhibition



Vu and Krasne, 1992

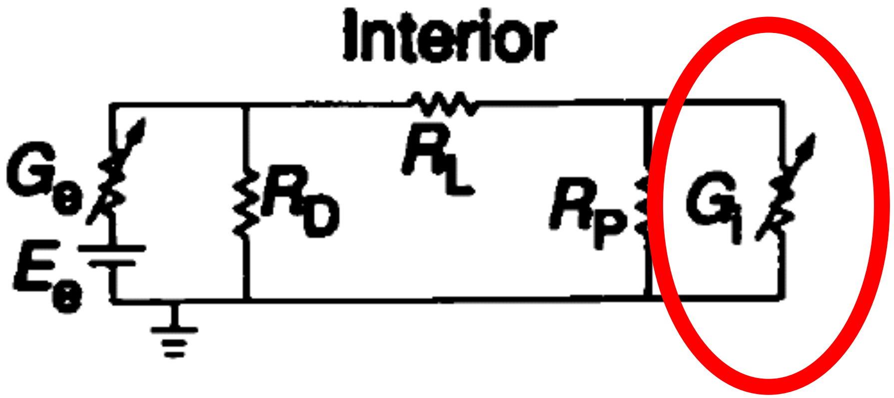
Equivalent circuit model



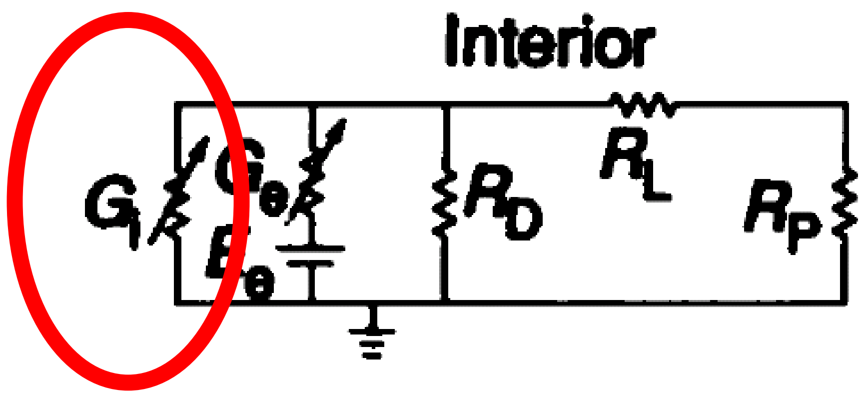


- R_L: longitudinal resistance
- R_P: proximal resistance
- R_D: distal resistance
- Ee: reversal potential for excitatory synapse (100 mV)
- Ge: excitatory conductance
- Gi: inhibitory conductance

Proximal versus Distal inhibition

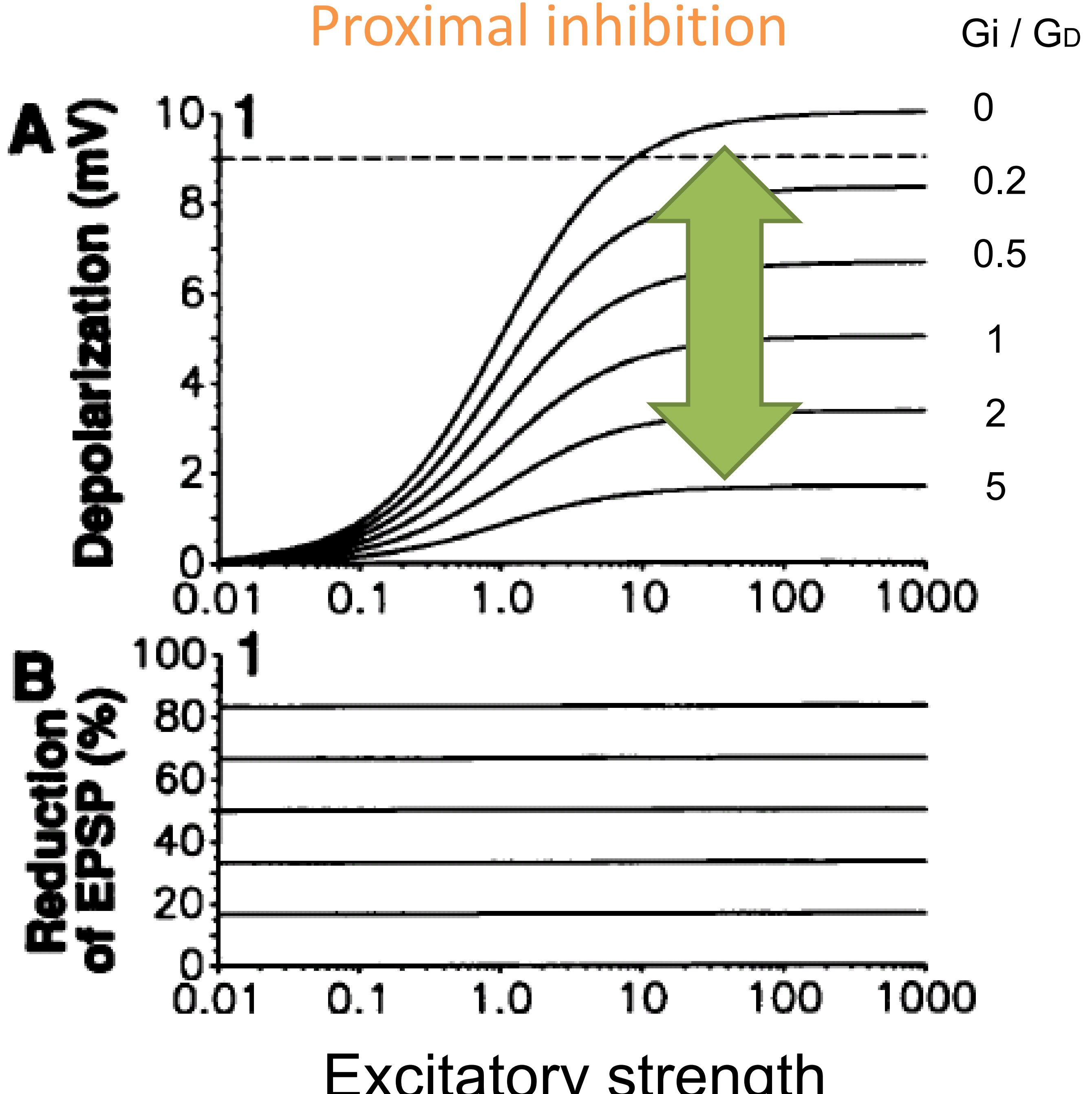


Proximal inhibition

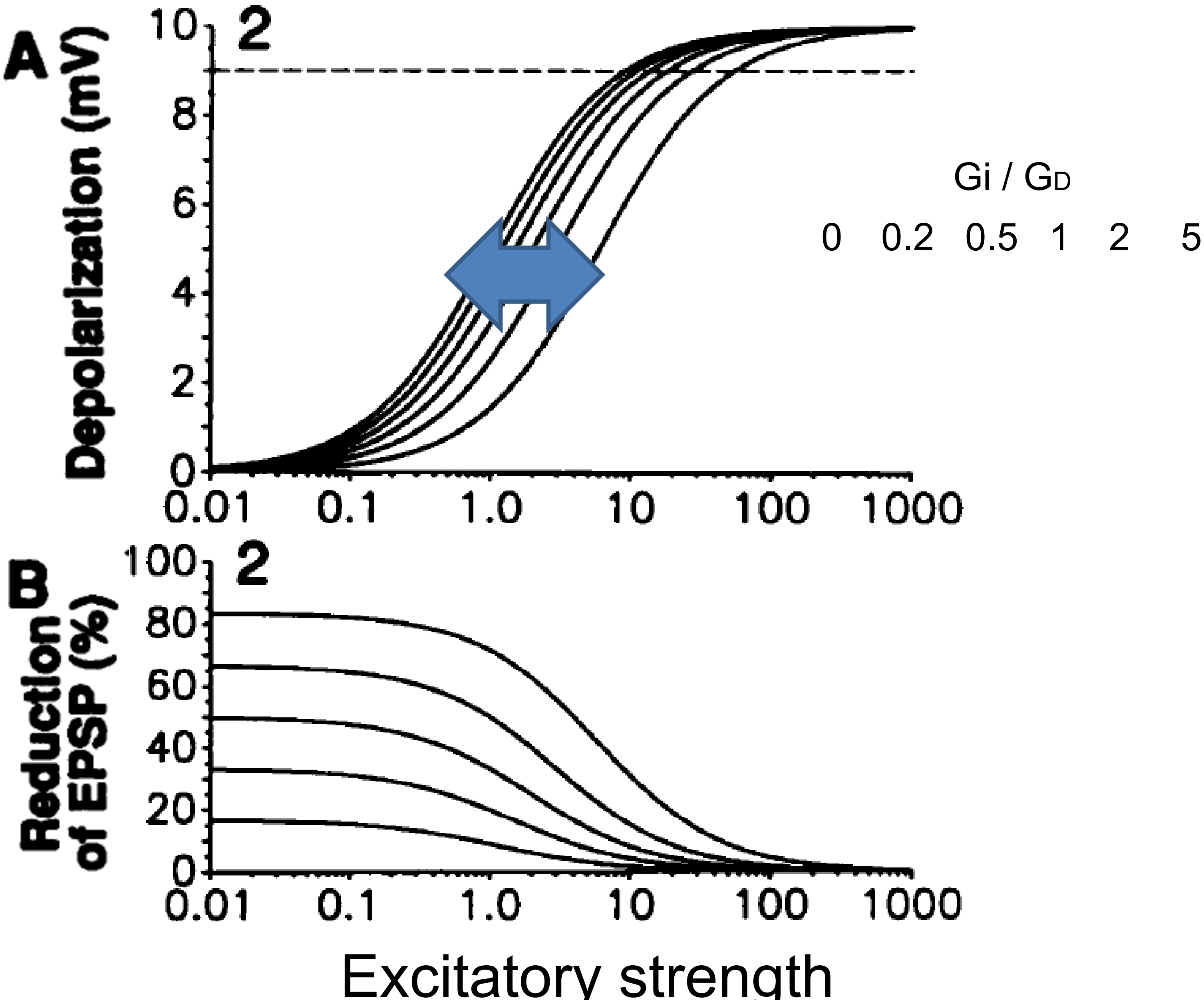


Distal inhibition

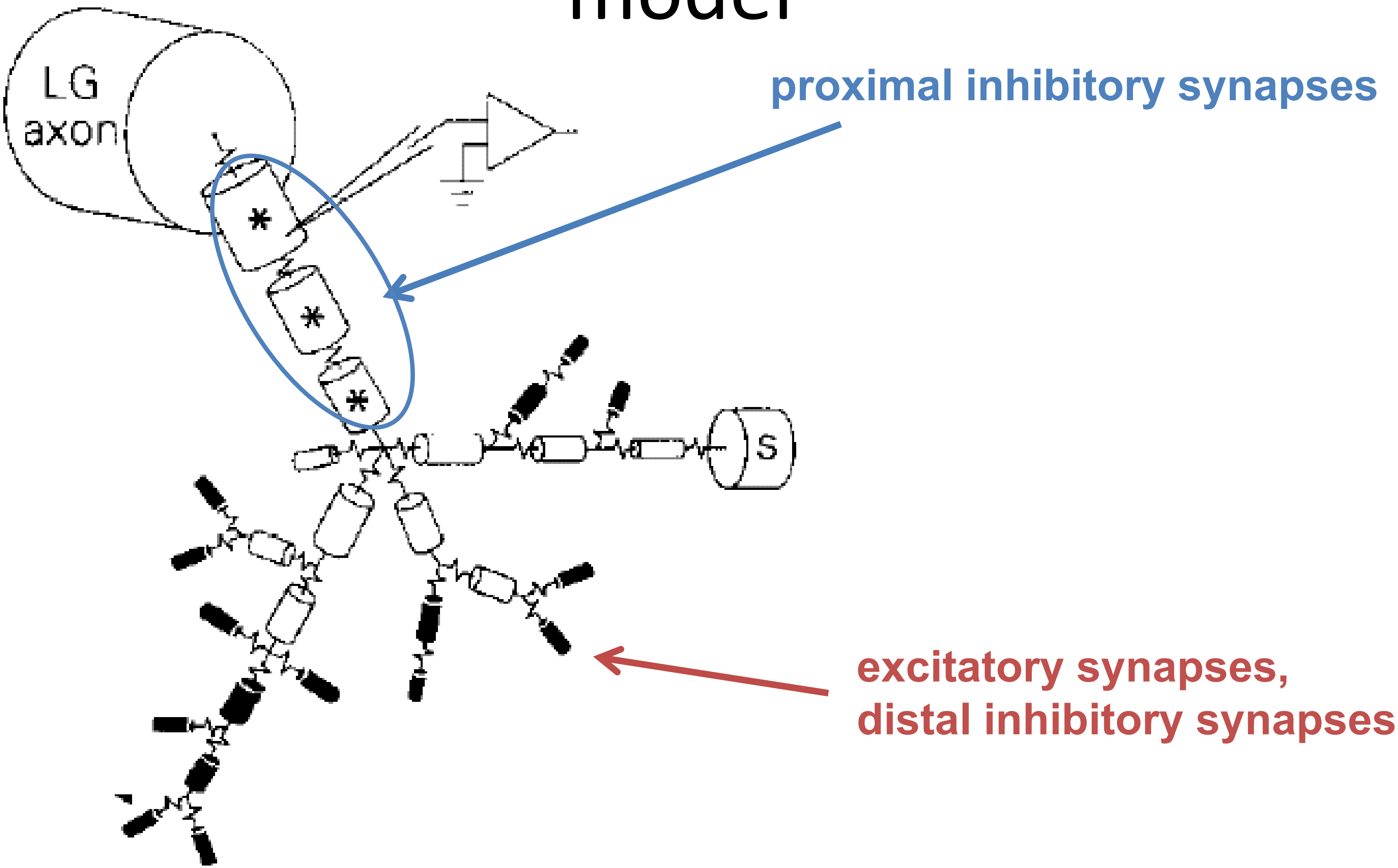
Proximal inhibition



Distal inhibition

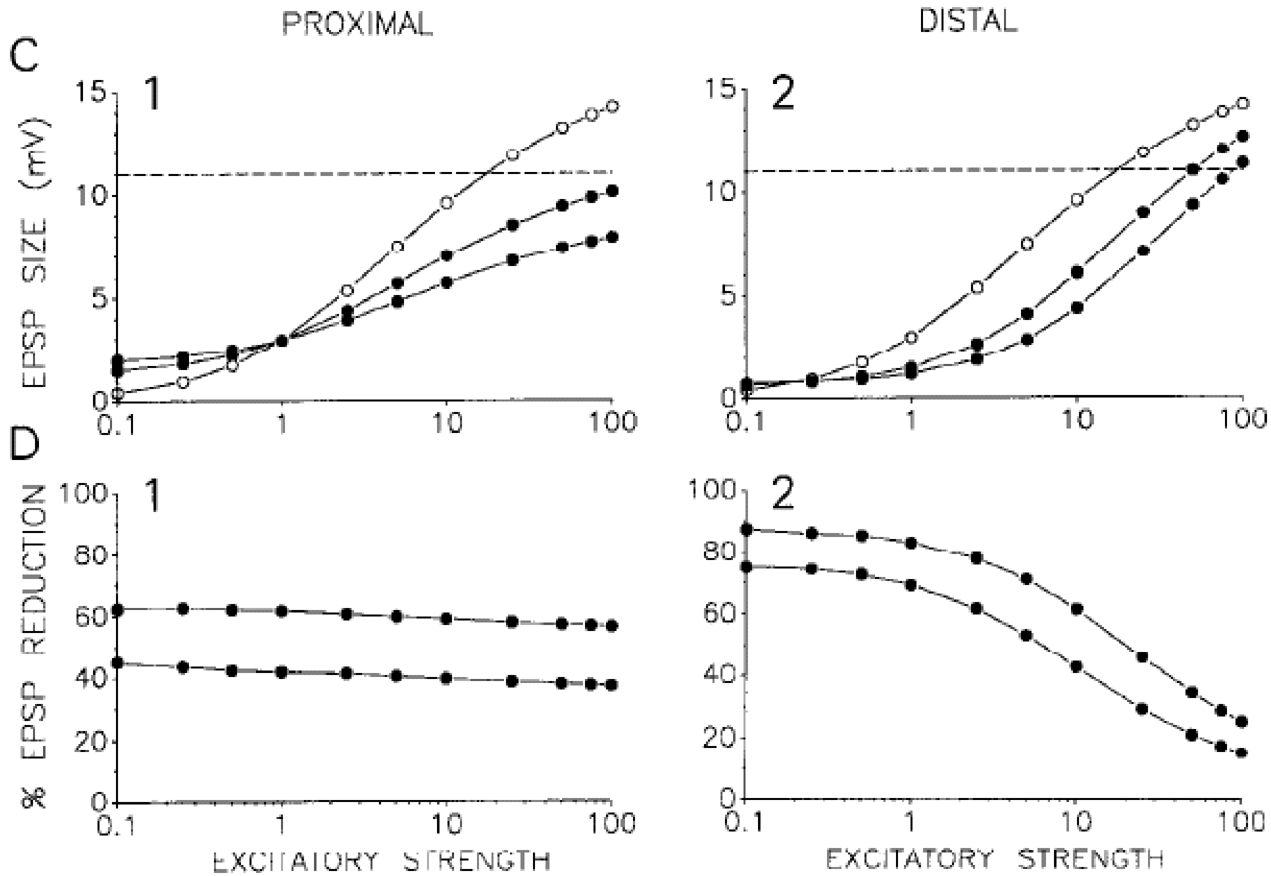


More 'realistic' multi-compartment model



Vu et al. (JNS, 1993)

Multi-compartment model results



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