Synapses & Dendritic Computation

Lecture 8

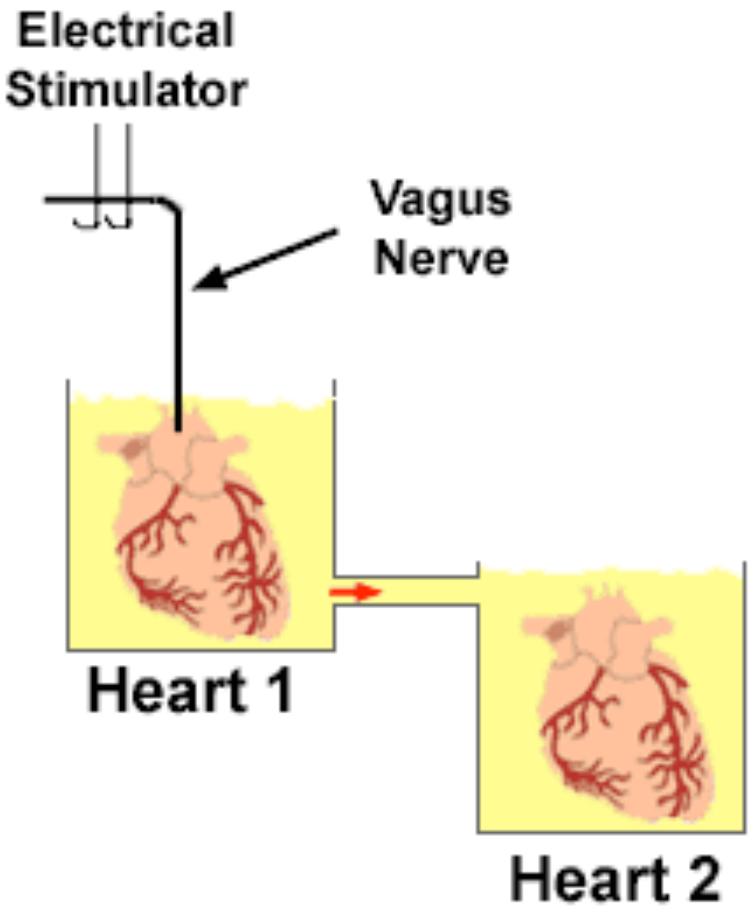
Neural Communication

- **Synapse**
  - Communication of information between neurons is accomplished by movement of chemicals across a small gap called the **synapse**
  - Synapses play a role in all the operations of the nervous system

- **Flavors of synaptic transmission**
  - Electrical Synapses or Gap Junctions
  - Chemical Synapses

Loewi's Experiment - 1921

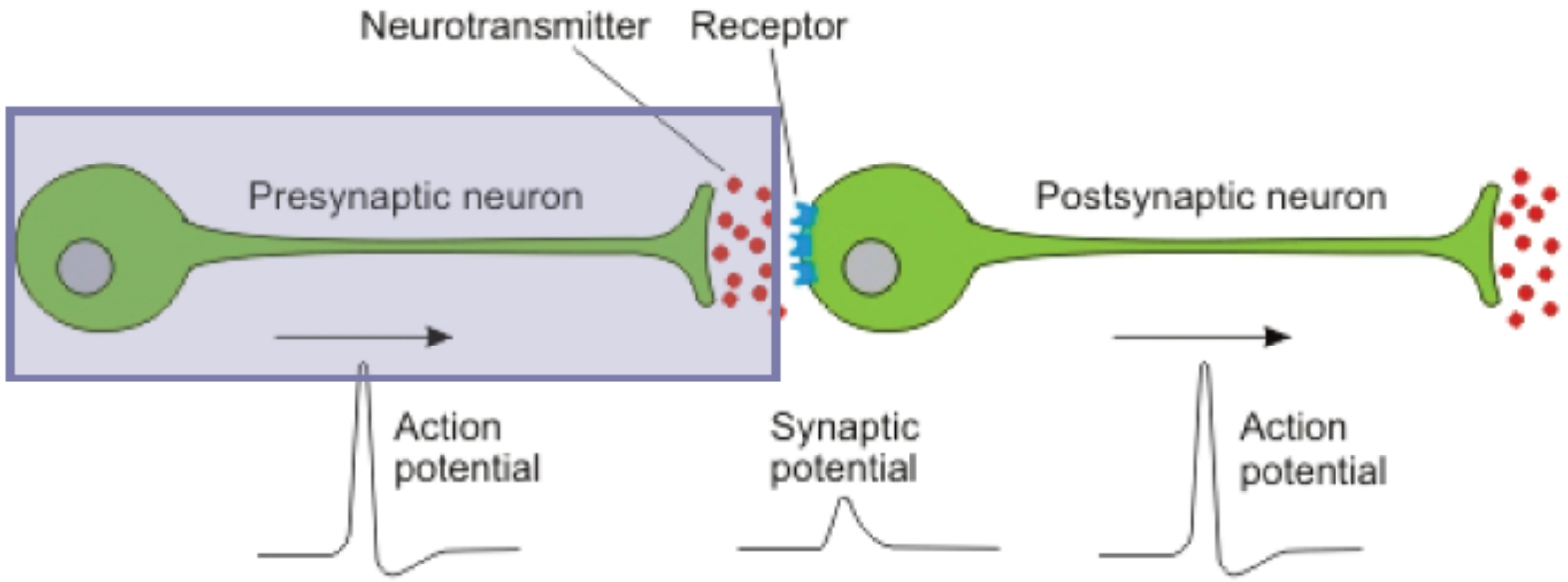
- **Chemical transmission at synapses**
  - Vagus nerve stimulation slowed heart1
  - Allowing fluid flow from chamber #1 into chamber #2 also slowed heart2 with some delay
  - Loewi hypothesized that electrical stimulation of the vagus nerve released a chemical "Vagusstoff" into the fluid of chamber #1 that flowed into chamber #2



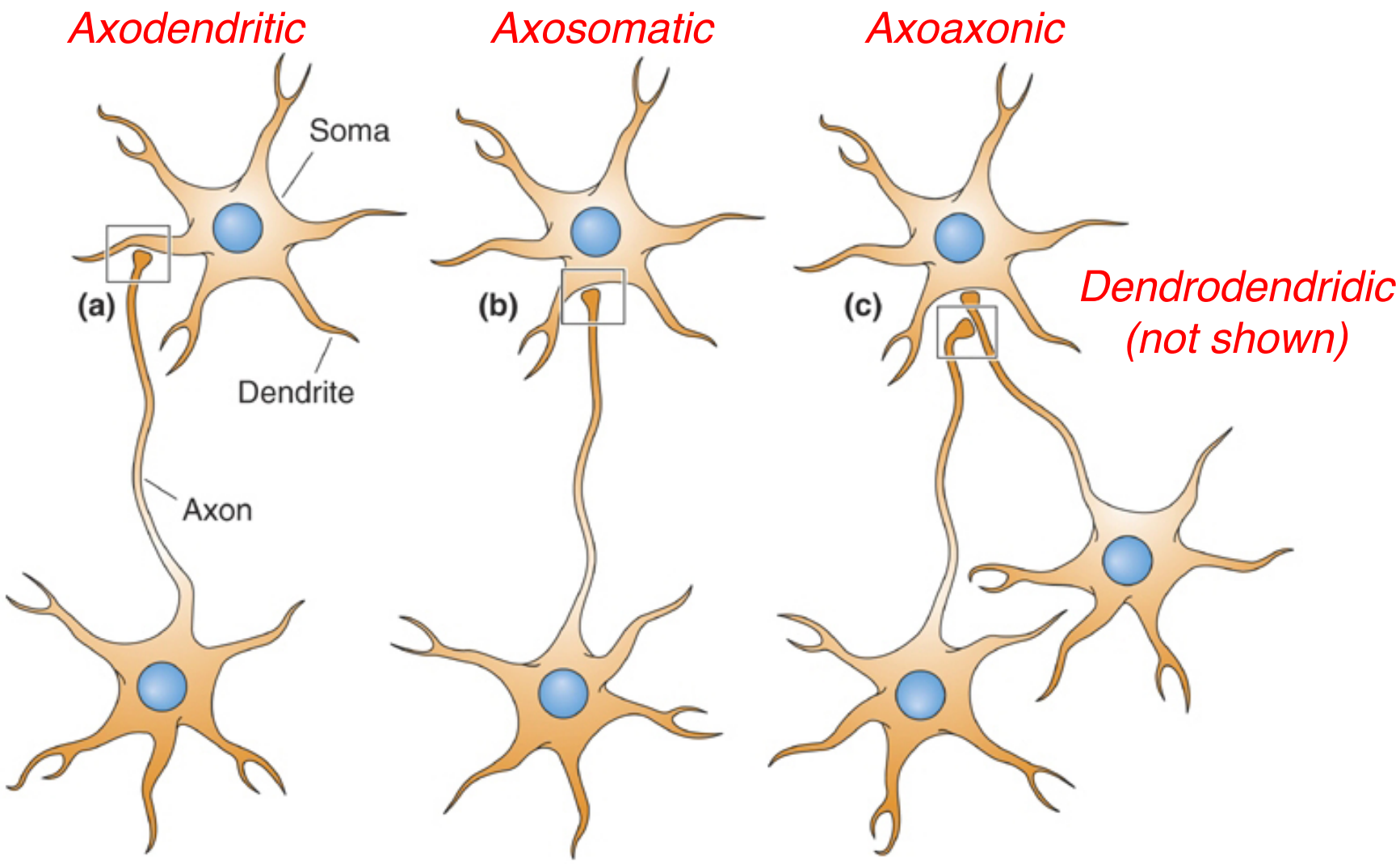
Chemical Synapses

Direction of Information Flow

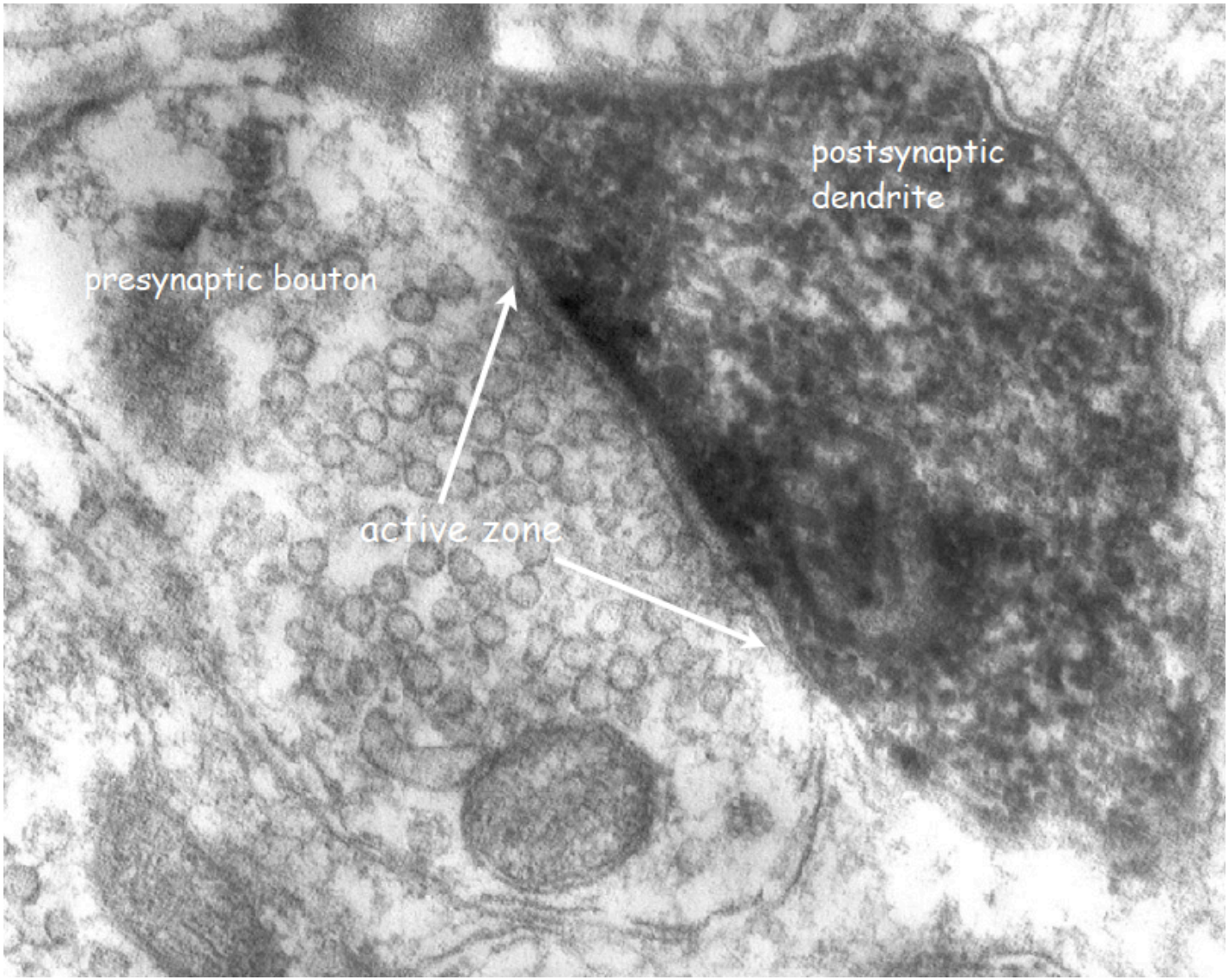
- In one direction: Neuron to target cell
- First neuron = Presynaptic neuron
- Target cell = Postsynaptic neuron



Types of Synapses



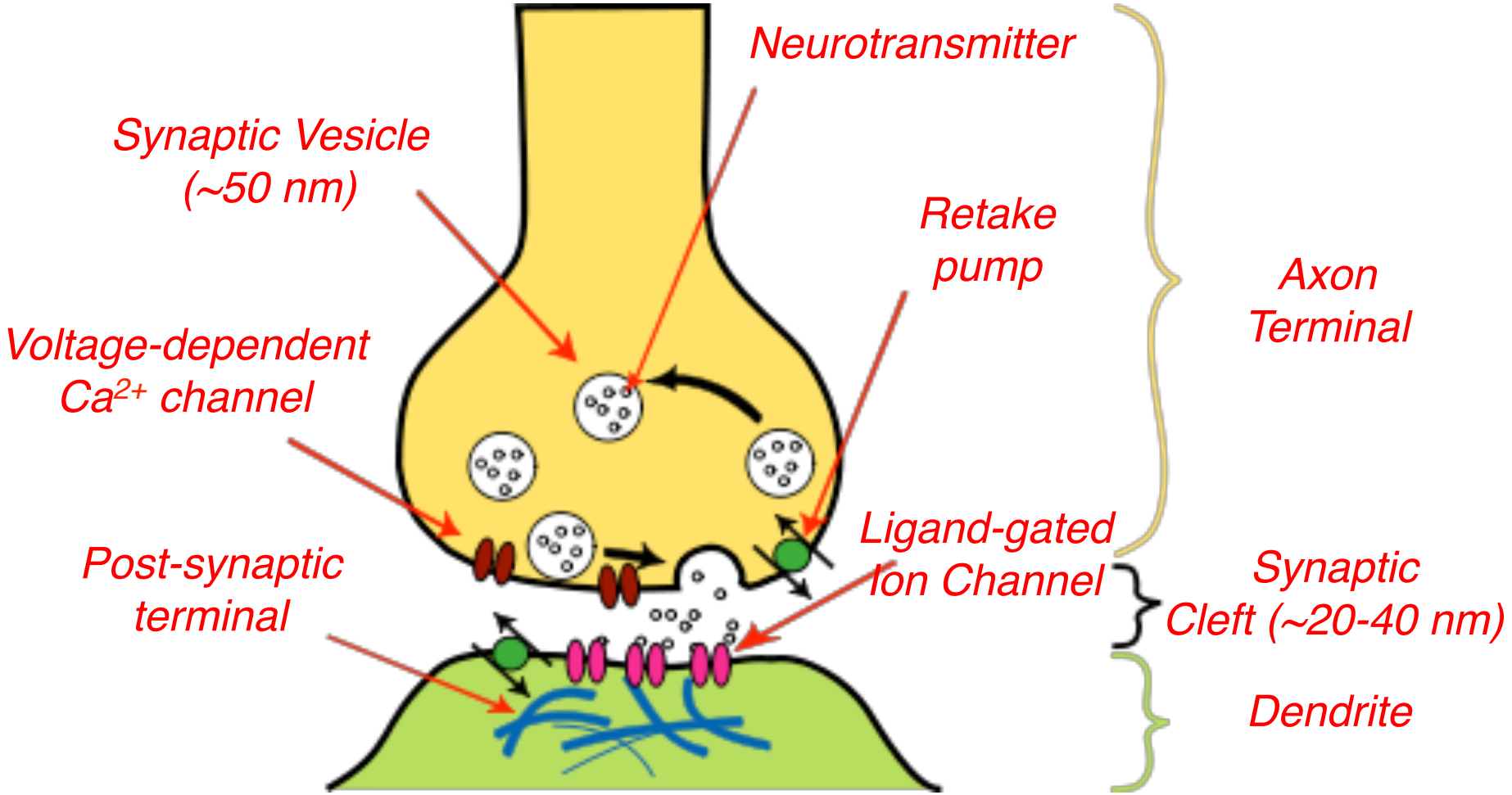
A Chemical Synapse



Principles of Chemical Synaptic Transmission

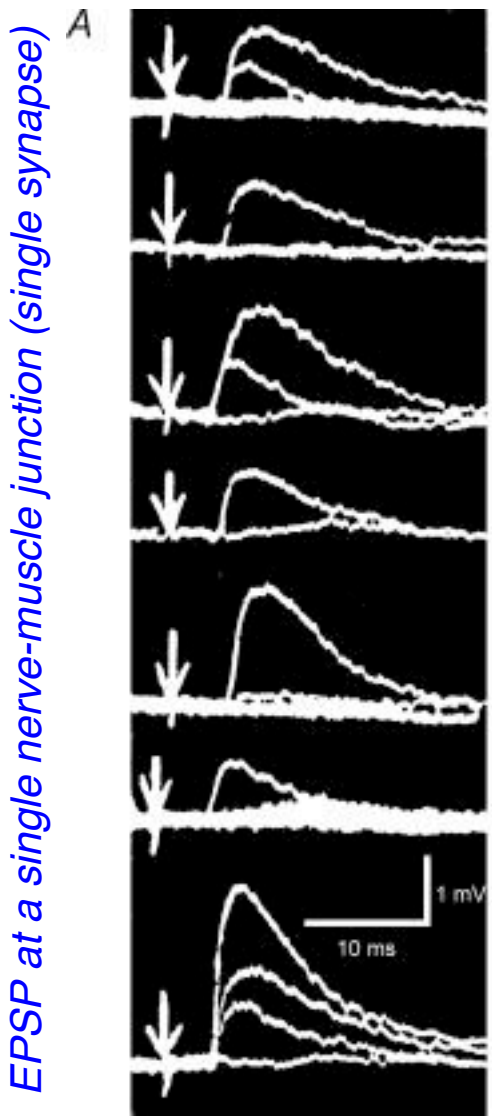
- **Sequence of events in chemical transmission (duration 0.5 – 2 ms)**
  - action potential conducted down the axon
  - action potential invades terminal, opening of Ca^{2+} channels
  - fusion of vesicle to membrane, exocytotic release of vesicle contents (time between influx of Ca2+ and transmitter release: 100 - 200 µs)
  - diffusion of transmitter (~30 nm in 0.6 µs)
  - gating of ion channels
  - recycling of vesicles

Principles of Chemical Synaptic Transmission



Wikipedia, Synapses

Quantal Release of Neurotransmitters

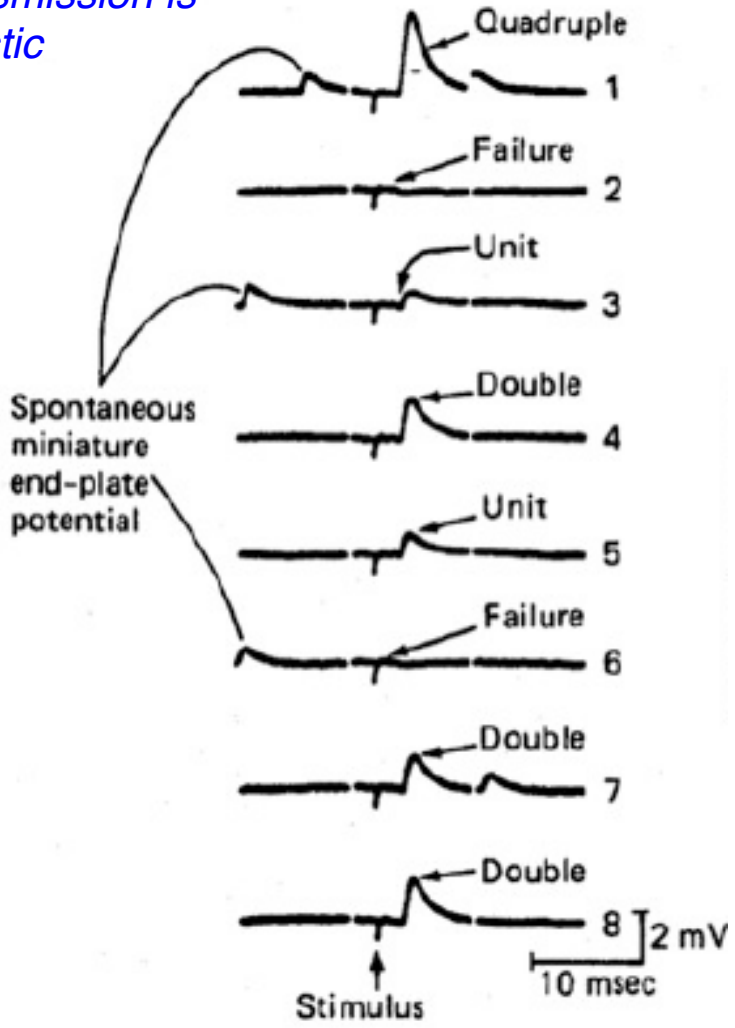


EPSP at a single nerve-muscle junction (single synapse)

Time

1. Synaptic transmission is Stochastic

Del Castillo and Katz; 1954



2. Each successful event is some product of a some unit event (or quanta)

Quantal Release of Neurotransmitters

- If the probability of a single unit responding is *'p'*, and if each unit has an independent and equal *'p'*, then the mean number of units responding to each stimulus is given by: *'np'*
  n is the total number of available

- Probability that x-units successfully contributing is given by the binomial distribution:

$$P(success = x) = \binom{n}{x} p^x (1-p)^x$$

Problem: n and p are not known

Quantal Release of Neurotransmitters

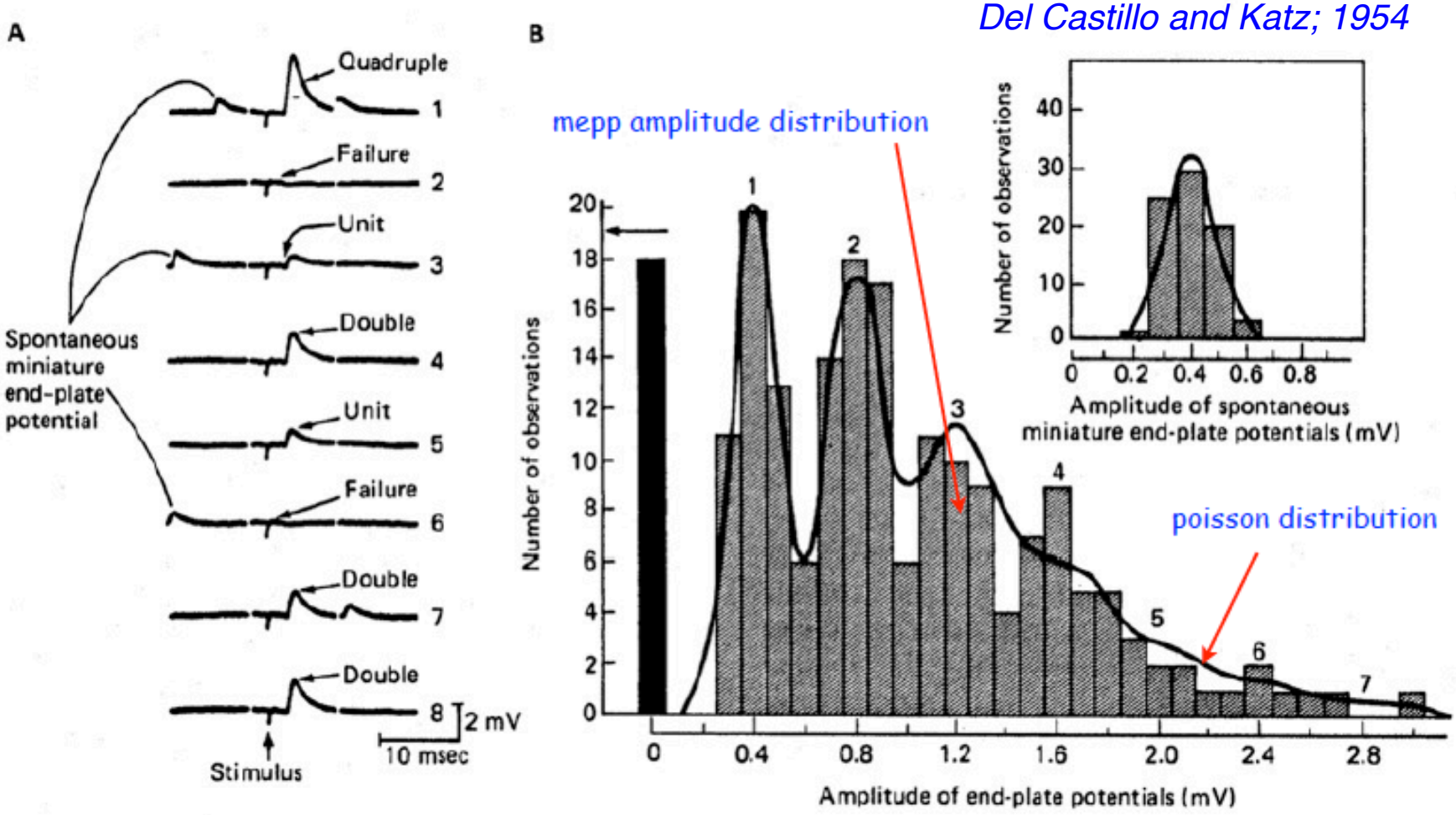
- **If n is large (or p is small), then approximate the binomial distribution with Poisson distribution**

$$P(success = x) = \frac{\lambda^x e^{-\lambda}}{x!} [\lambda = np]$$

- **λ can be estimated as follows:**
  - mean amplitude of synaptic potential/mean amplitude of minimal synaptic potential, or,
  - Count for failures (x=0)

$$\lambda = \ln \frac{N}{P(success = 0; trials = N)}$$

Quantal Release of Neurotransmitters



Del Castillo and Katz; 1954

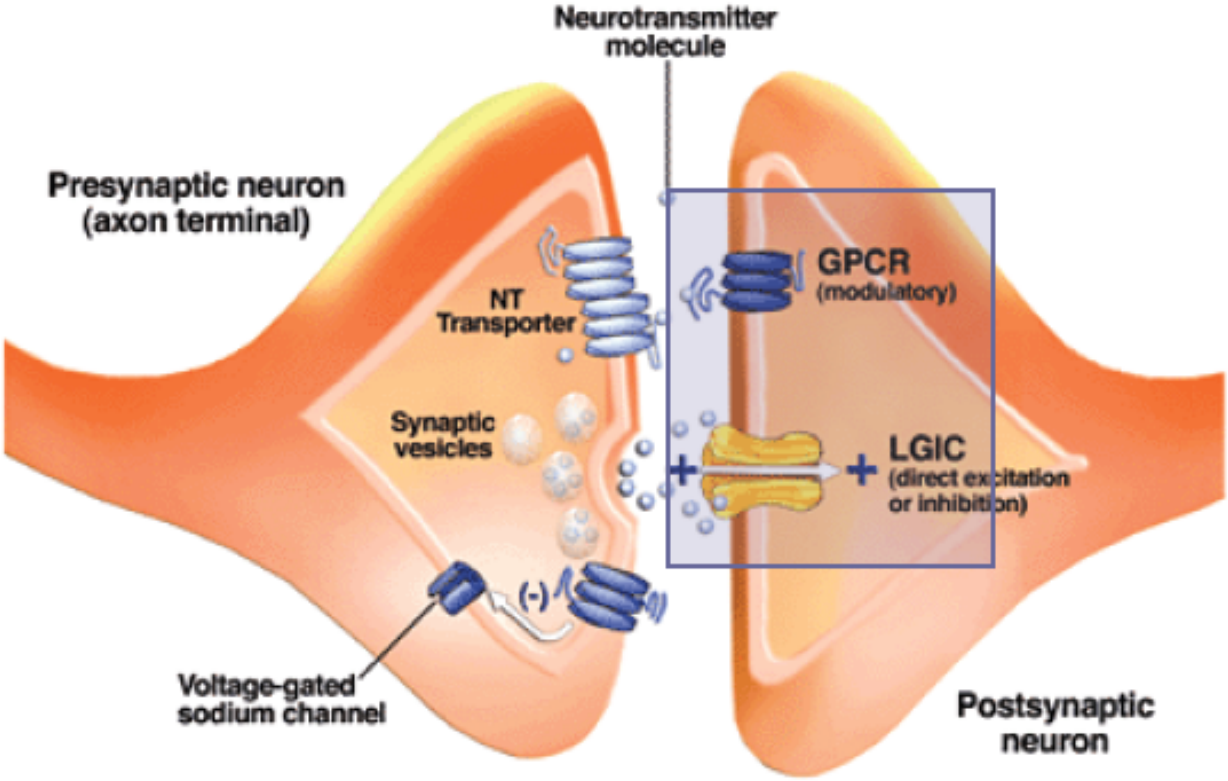
Neurotransmitters are released in small pockets called vesicles.

Neurotransmitters

- **Amino acids: Small organic molecules**
  - e.g., Glutamate, Glycine, GABA
- **Amines: Small organic molecules**
  - e.g., Dopamine, Acetylcholine, Histamine
- **Peptides: Short amino acid chains (i.e. proteins) stored in and released from secretory granules**
  - e.g., Dynorphin, Enkephalins

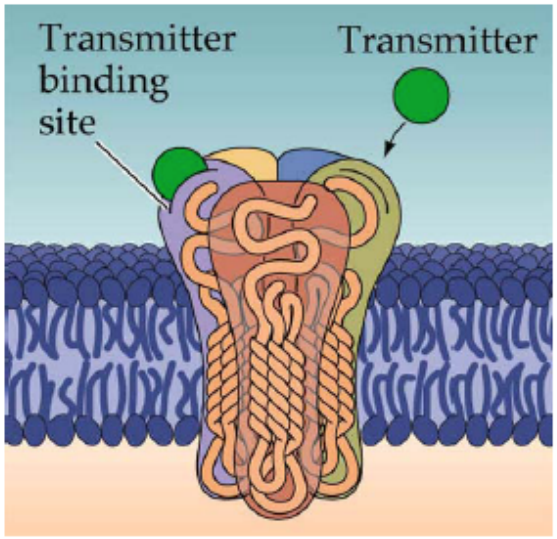
Post-synaptic Receptors

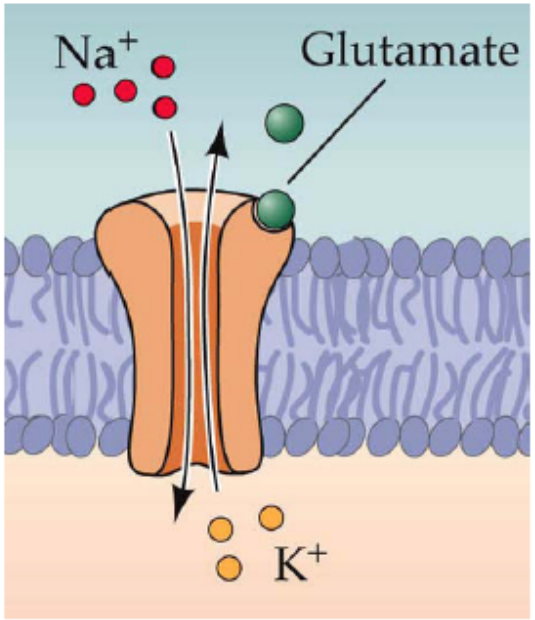
- **Neurotransmitters cross synaptic-cleft and can bind to two types of receptors:**
  - Ionotropic (Ligand-gated ion channels; LGIC)
  - Metabotropic (G-protein coupled receptors; GPCR)



Post-synaptic Receptors

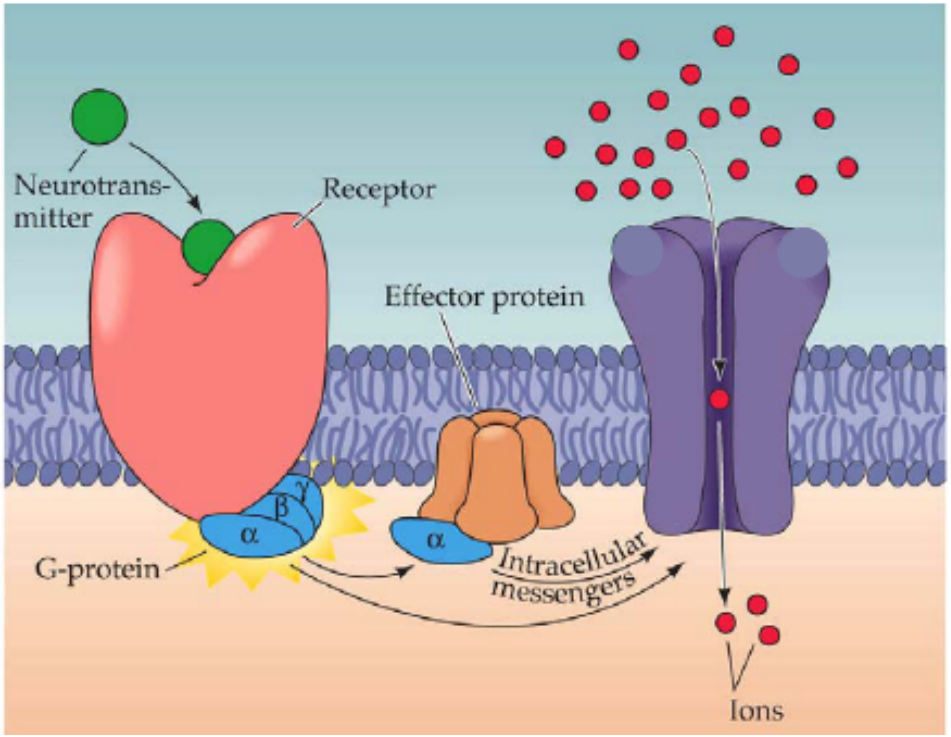
- **Ionotropic**
  - Contains a ligand-binding site
  - A normally-closed ion channel that opens after binding with the neurotransmitter
  - Contribute to fast changes in the membrane potential



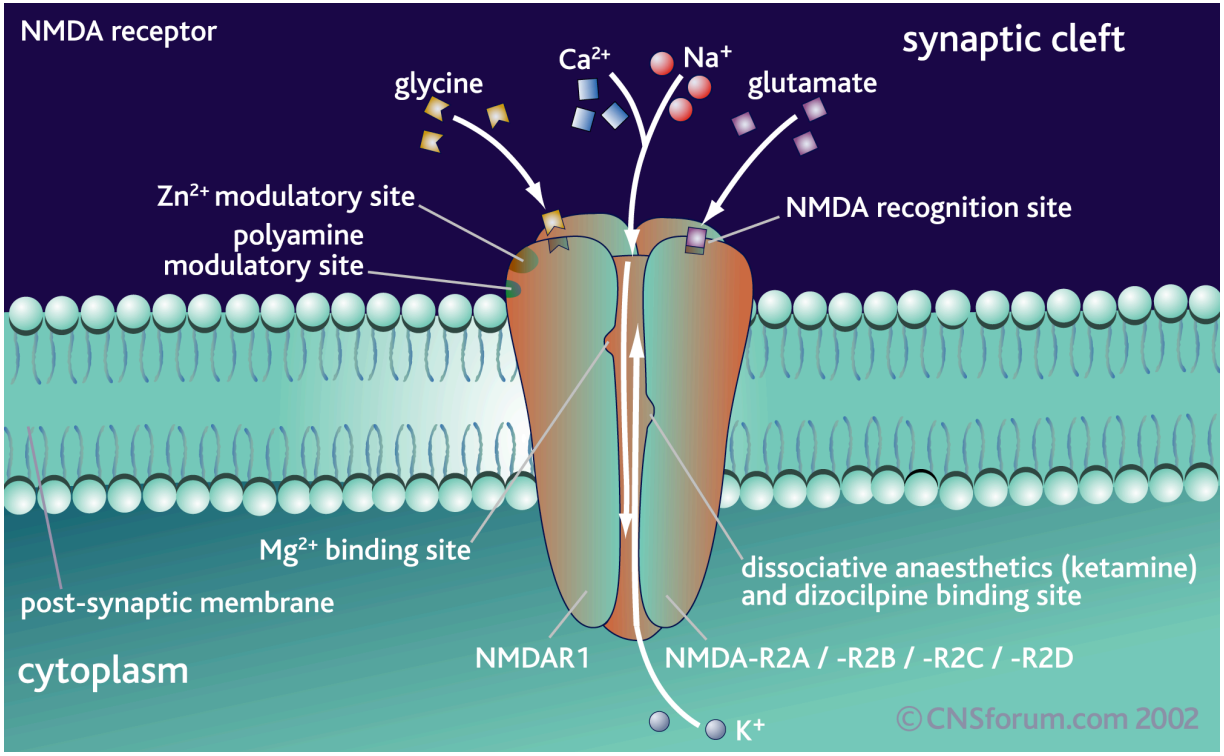


Post-synaptic Receptors

- **Metabotropic**
  - G-protein coupled receptor
  - Secondary messenger involved
  - Slow postsynaptic processes (plays a role in synaptic plasticity)

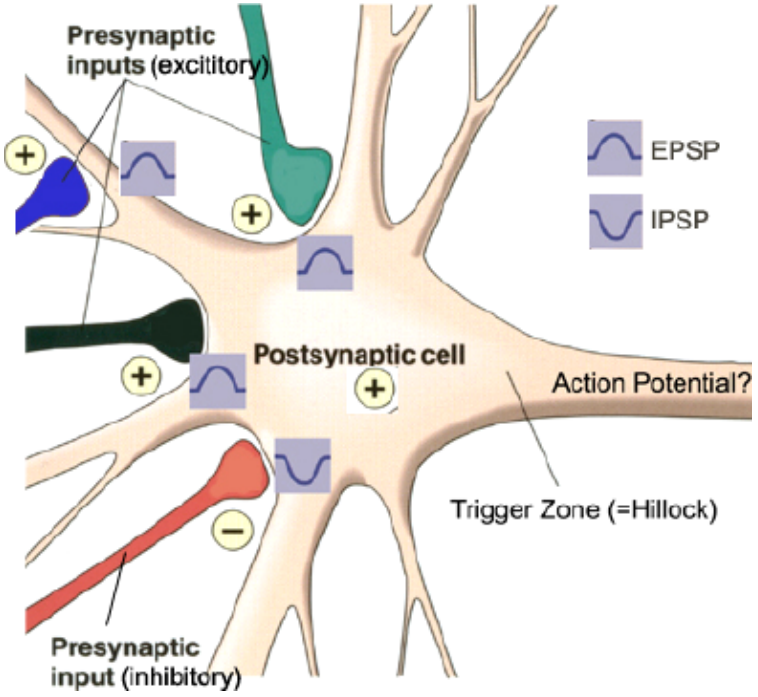


NMDA Receptor

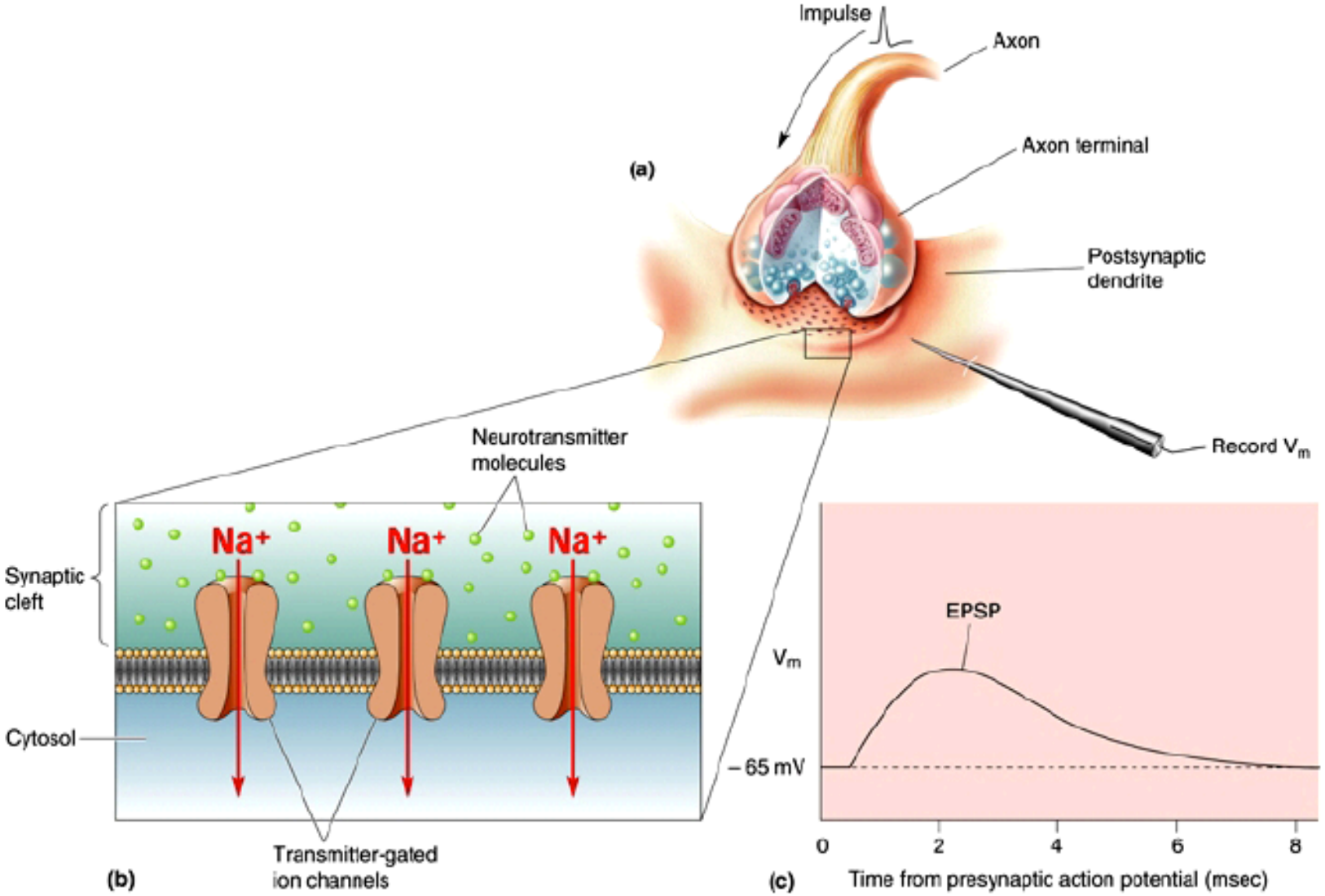


Synapses types

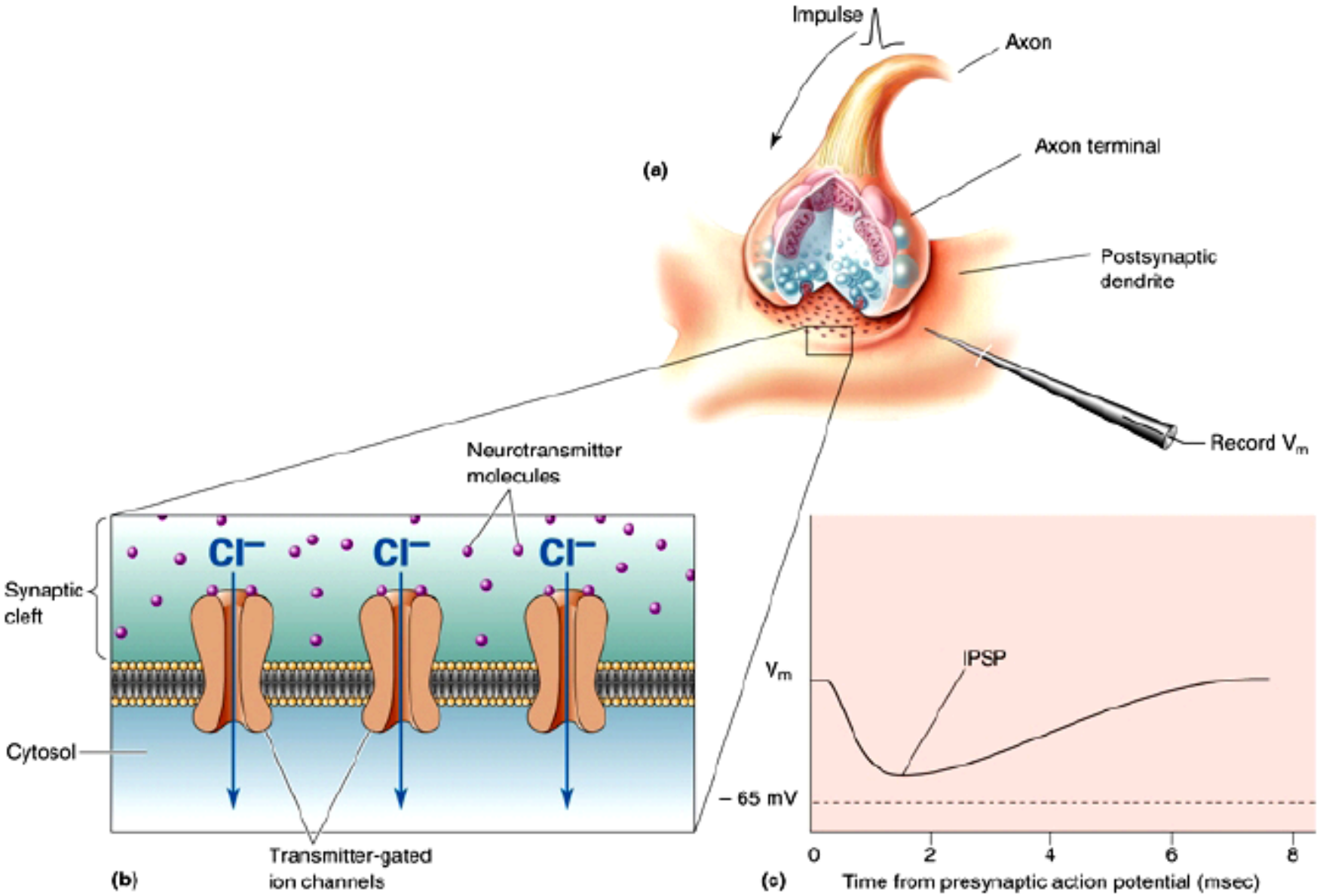
- **The potential change produced in the post-synaptic cell is called a "Post-Synaptic Potential" (PSP)**
  - when the influence of this potential is to increase firing, it is called an "Excitatory Post-Synaptic Potential" (EPSP)
  - when the influence of this potential is to decrease firing, it is called an "Inhibitory Post-Synaptic Potential" (IPSP)



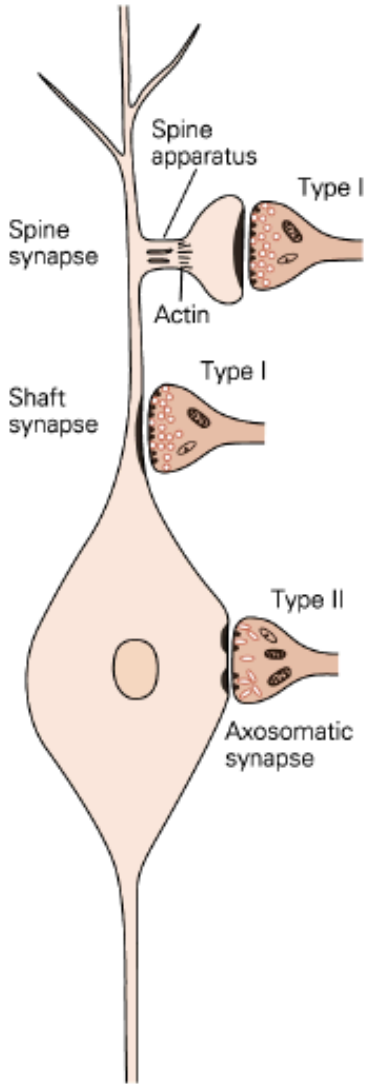
Excitatory Synapse

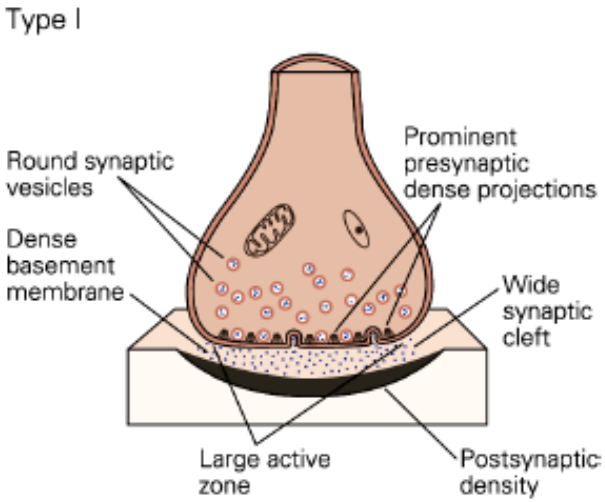


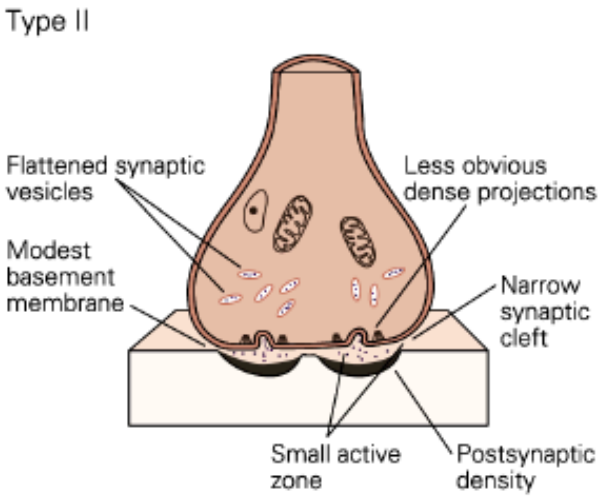
Inhibitory Synapse



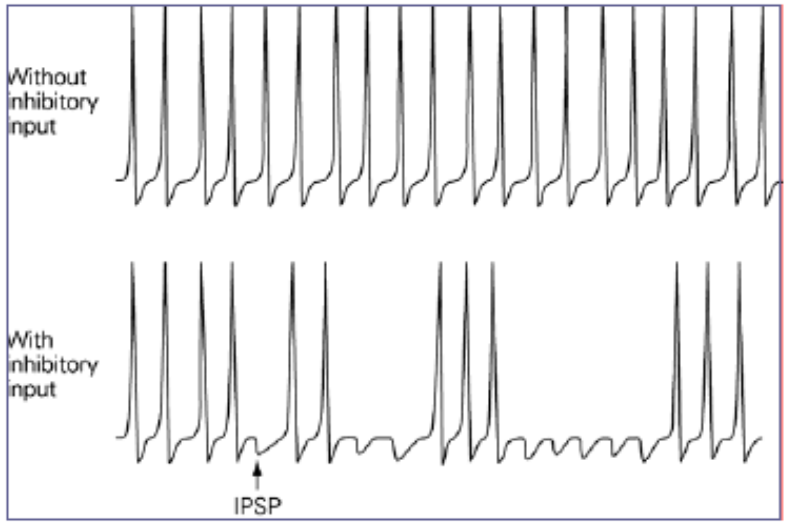
Synapses types





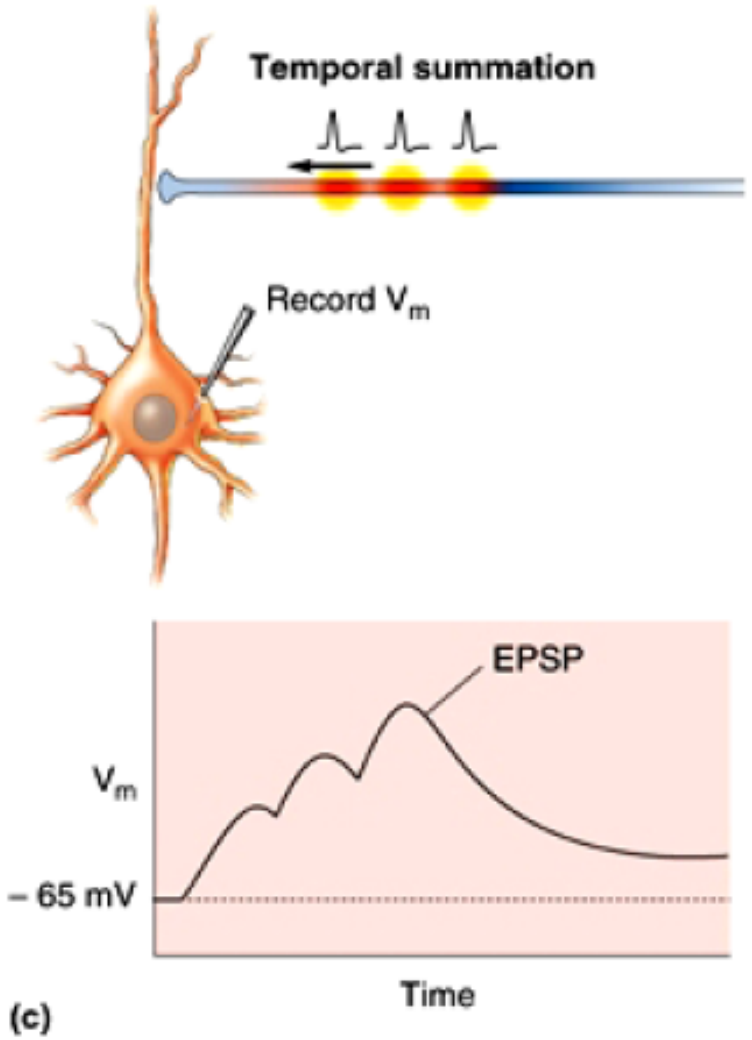


- **Type I** – glutamergic synapses – usually on dendrites
- **Type II** – GABAergic synapses – usually on cell bodies



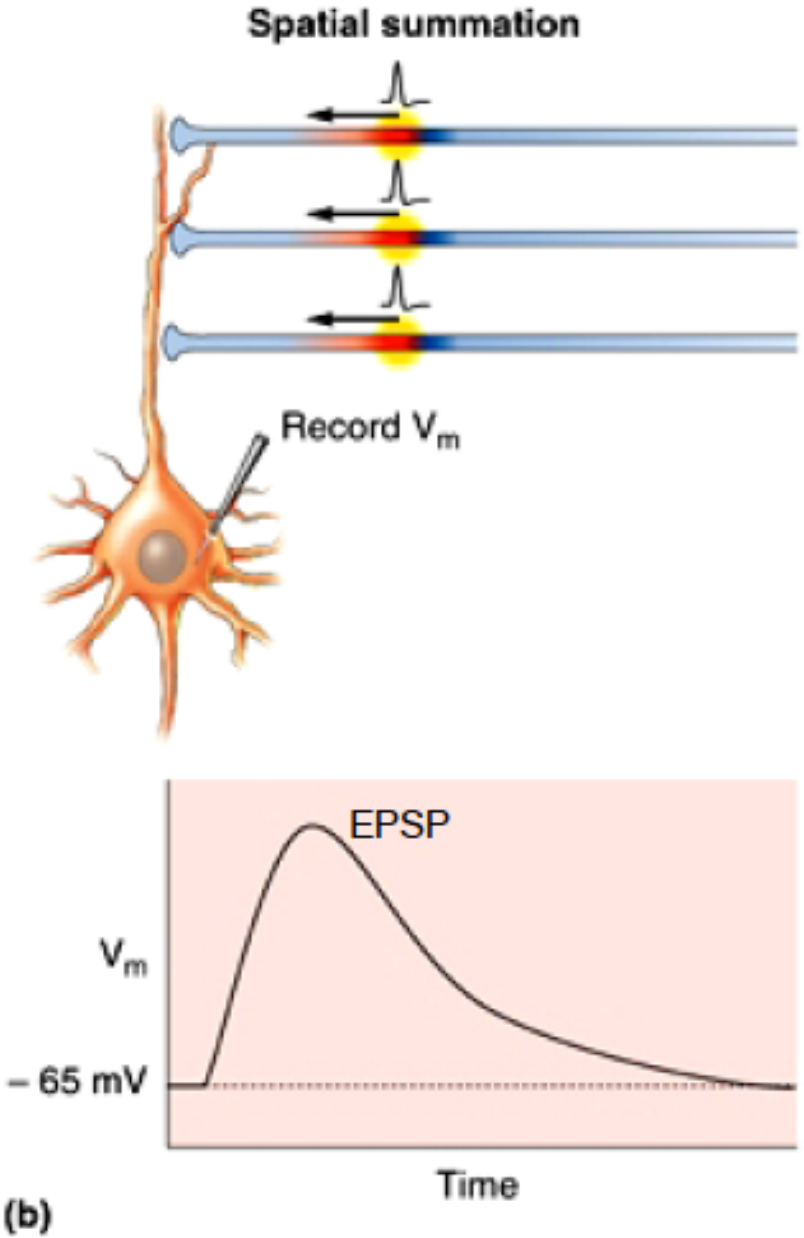
Temporal Summation

- **A single nerve cell may receive up to 100,000 synapses**
  - some of excitatory
  - some inhibitory
- **Summation**
  - the process whereby these inputs are added up by the cell body
- **Temporal -summation of input from a single synapse over time**



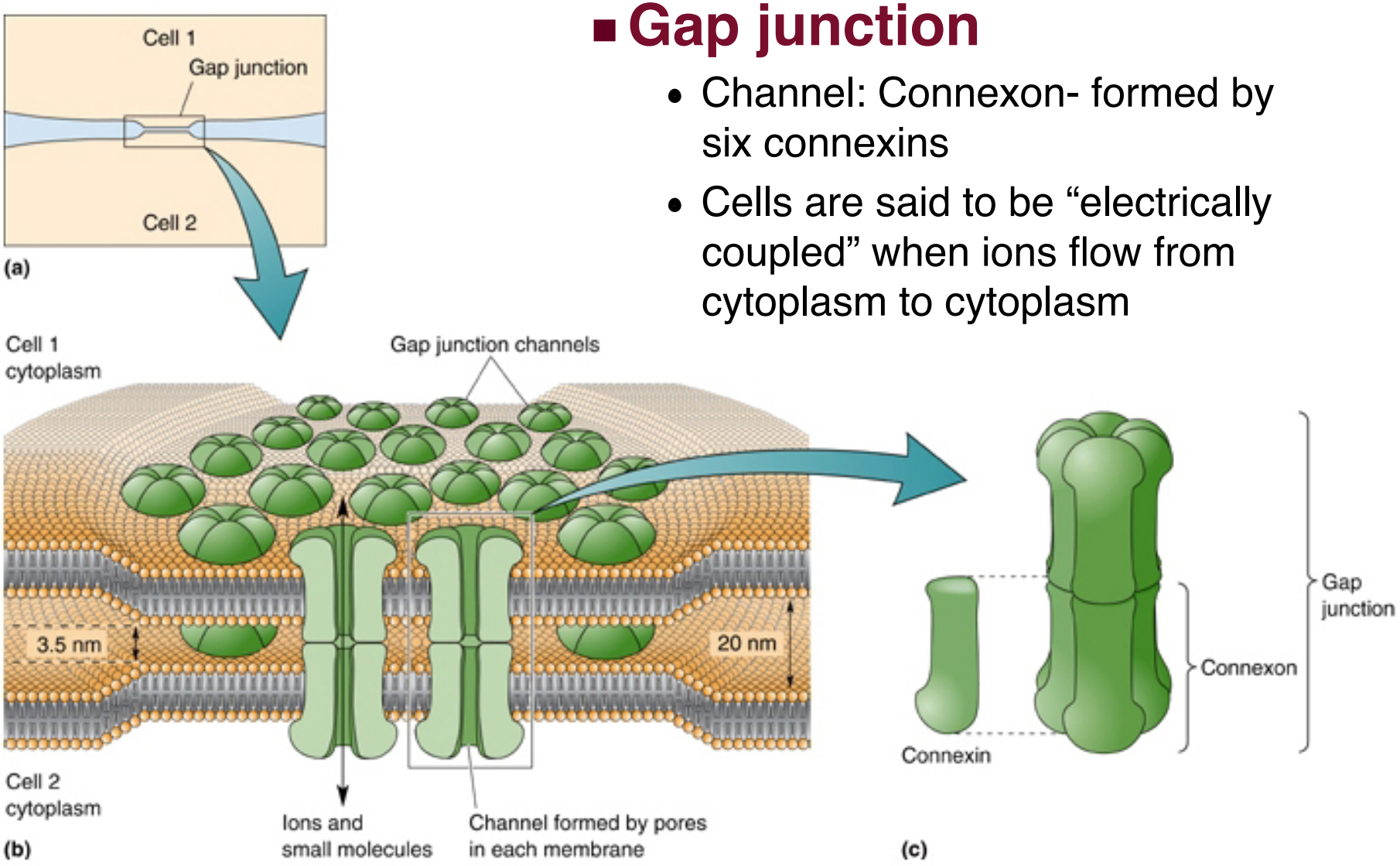
Spatial Summation

- **A single nerve cell may receive up to 100,000 synapses**
  - some of excitatory
  - some inhibitory
- **Summation**
  - the process whereby these inputs are added up by the cell body
- **Spatial -summation of input from multiple synapses**

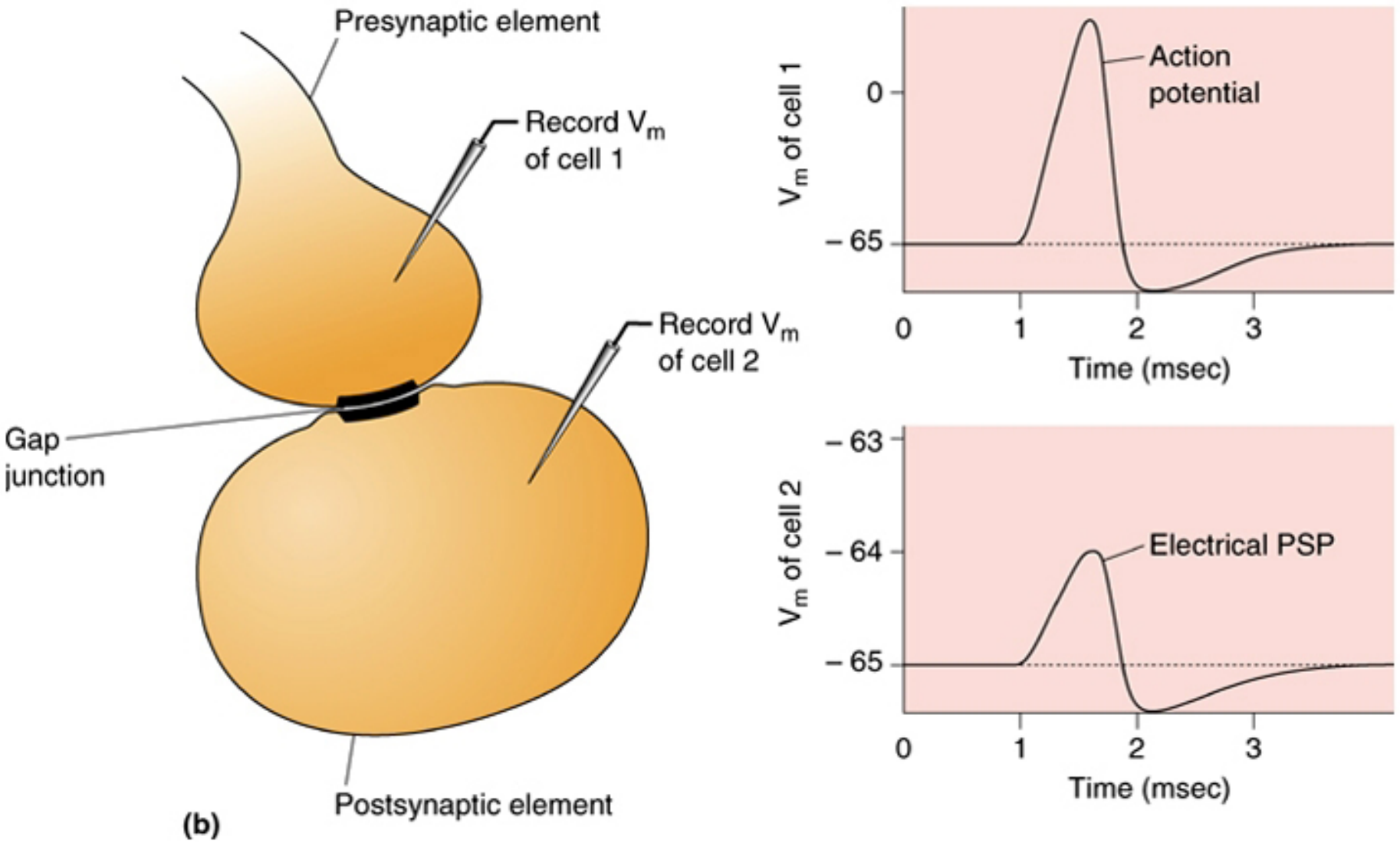


Electrical Synapses

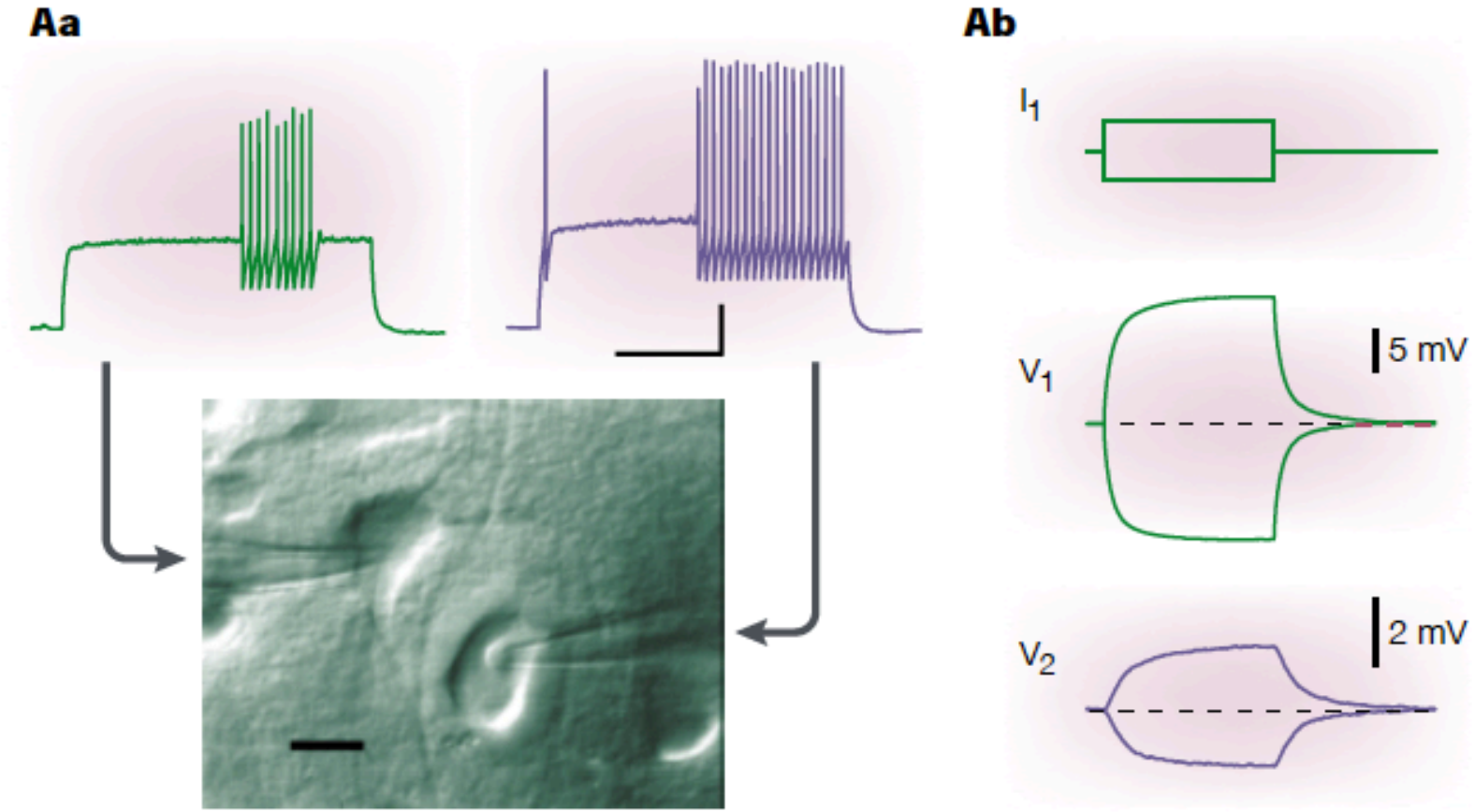
- **Gap junction**
  - Channel: Connexon- formed by six connexins
  - Cells are said to be “electrically coupled” when ions flow from cytoplasm to cytoplasm



Electrical Synapses



Electrical Synapse



Galarreta & Hestrin, 2001

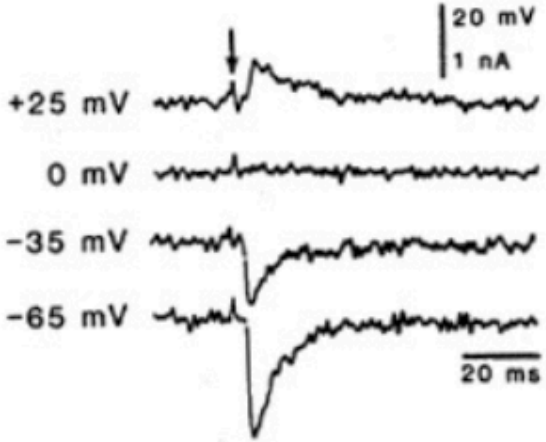
Electrical vs. Chemical Synapse

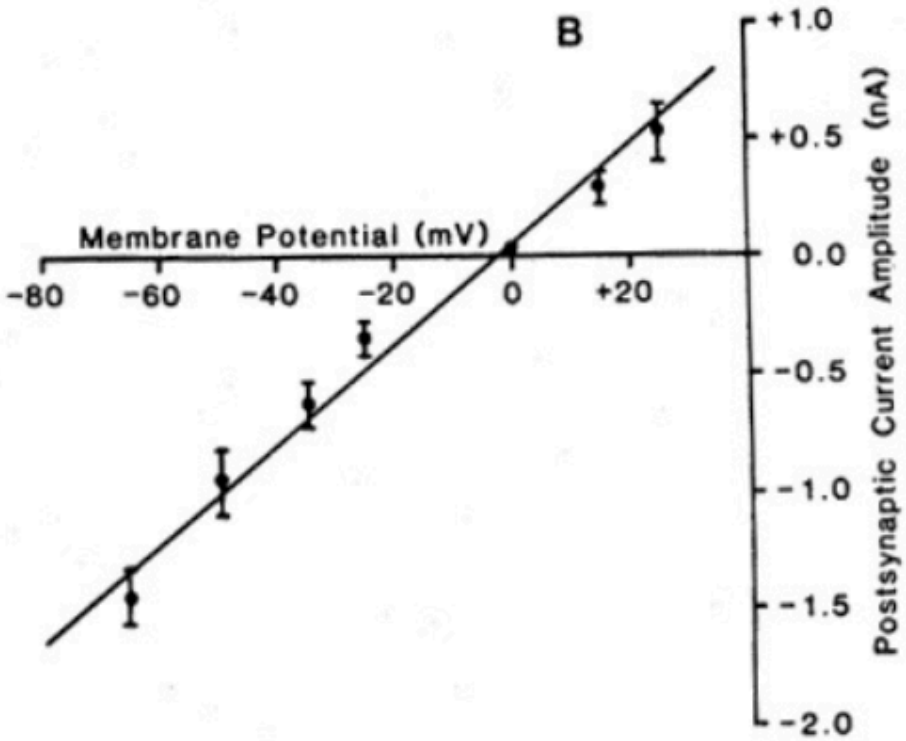
Electrical Synapse	Chemical Synapse
simple primitive system	highly developed structure
often symmetrical, bidirectional	polarized, structurally and functionally
gap junction (connexins)	pre: active zone post: postsynaptic density
very fast, no synaptic delay	slower, synaptic delay (~ 0.5 ms)
Ca2+-independent	transmitter release requires Ca2+ influx
temperature-insensitive	temperature-sensitive
large synapse	thousands of small synapses
limited functions, usually excitatory	versatile: excitatory and Inhibitory
synchronized activity	specificity: point to point communication

Modeling Synapses

I-V curve

Voltage clamp data



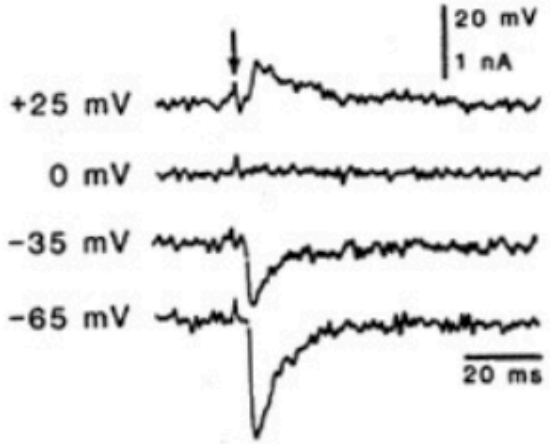


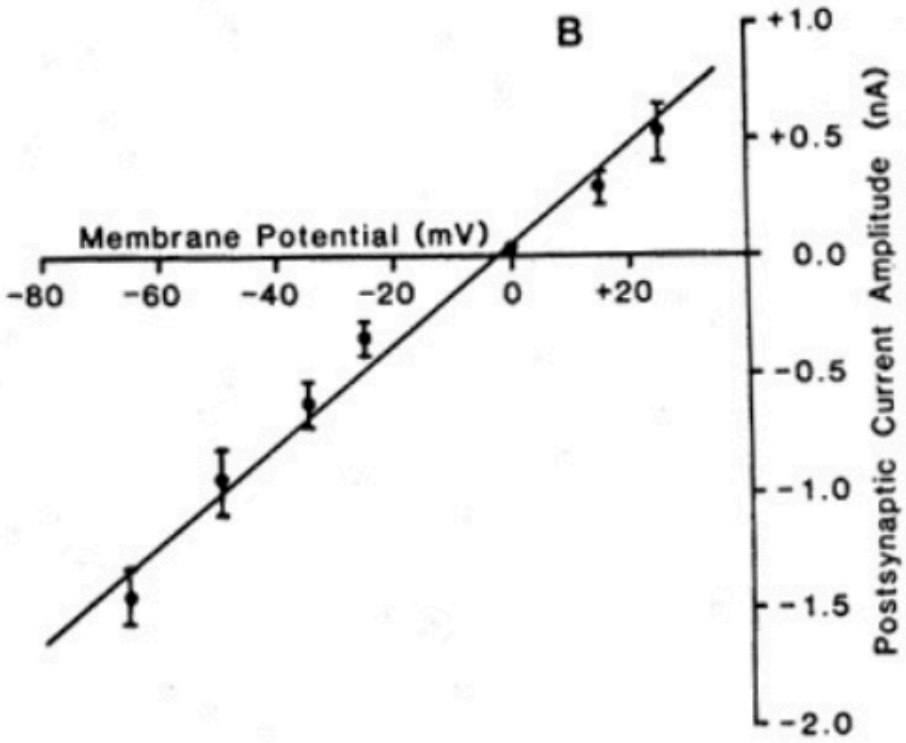
What do these plots tell you?

Modeling Synapses

I-V curve

Voltage clamp data (Excitatory Synapse)





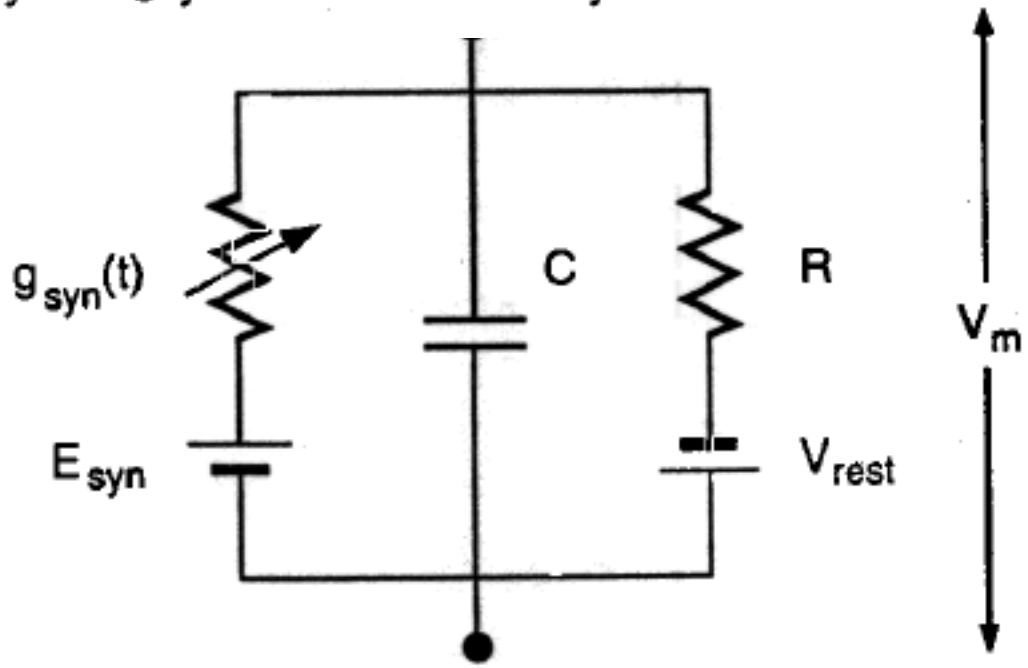
What do these plots tell you?

Synaptic input well capture by Ohm's law

Equivalent circuit of a fast chemical synapse

Koch, Biophysics of Computation, Chapter 1

$$I_{syn} = g_{syn}(t)(V_m(t) - E_{syn})$$

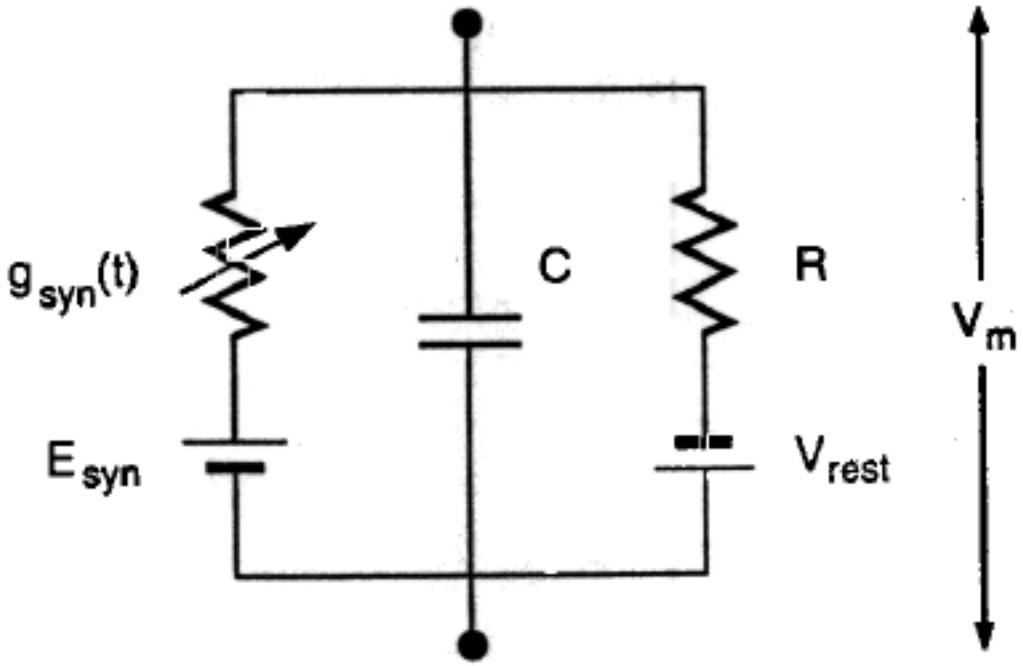


Modified membrane patch equation with a synapse:

$$C\frac{dV_m}{dt} + g_{syn}(t)(V_m - E_{syn}) + \frac{V_m - V_{rest}}{R} = 0$$

Equivalent circuit of a fast chemical synapse

Koch, Biophysics of Computation, Chapter 1



Rewriting, we get:

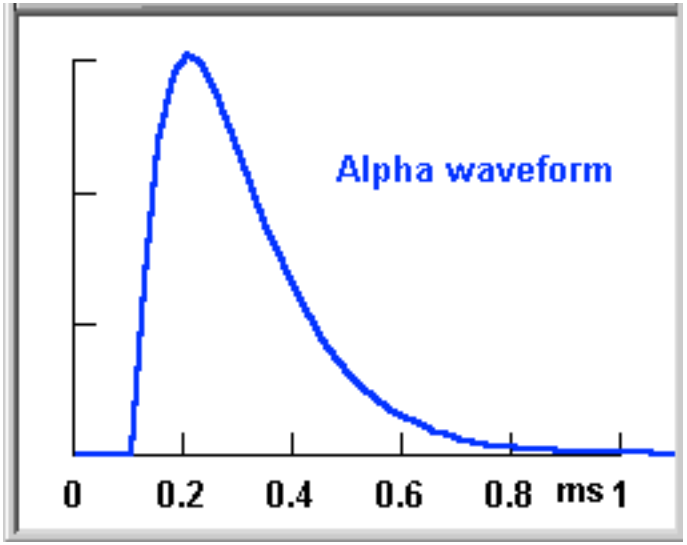
$$\tau \frac{dV_m}{dt} = -(1 + Rg_{syn}(t))V_m + Rg_{syn}(t)E_{syn} + V_{rest}$$

$$[\tau = RC]$$

Alpha Function

- **Synaptic input is usually approximated by an 'alpha function' of the form**

$$g_{syn}(t) = g_{peak} \cdot t \cdot \exp\left(-t / t_{peak}\right)$$



Multiple Synaptic Input

- You will need to add synapses in parallel with the RC circuit to created additional synaptic components.

- Since current add:

$$C\frac{dV_m}{dt} = \sum_{i=0}^{n} g_{syn,i}(t)(E_{syn,i} - V_m) + \frac{V_{\text{rest}} - V_m}{R}$$

Synaptic input is non-linear

- If we consider synaptic input to be slowly varying, we can approximate $g_{syn}(t) \sim = g_{syn}$;
- Further, if $V_m << E_{syn}$, we can approximate synaptic input as a const current source ($g_{syn} * E_{syn}$)

Original:

$$\tau \frac{dV_m}{dt} = -(1 + Rg_{syn}(t))V_m + Rg_{syn}(t)E_{syn} + V_{rest}$$

New (slightly re-written):

$$\tau' \frac{dV}{dt} = -V + \frac{g_{syn}E_{syn}}{G_{in}}$$

$$\begin{bmatrix} G_{in} = g_{syn} + \frac{1}{R} \\ \tau' = \frac{C}{G_{in}} \end{bmatrix}$$

Synaptic input is non-linear

Solving ODE: $$\tau' \frac{dV}{dt} = -V + \frac{g_{syn} E_{syn}}{G_{in}}$$

$$V_\infty = \frac{R g_{syn} E_{syn}}{1 + R g_{syn}}.$$

Case 1: Small synaptic input

$$Rg_{syn} << 1$$

$$V_\infty = Rg_{syn} E_{syn}$$

Scales linearly with synaptic input

Case 2: Large synaptic input

$$Rg_{syn} >> 1$$

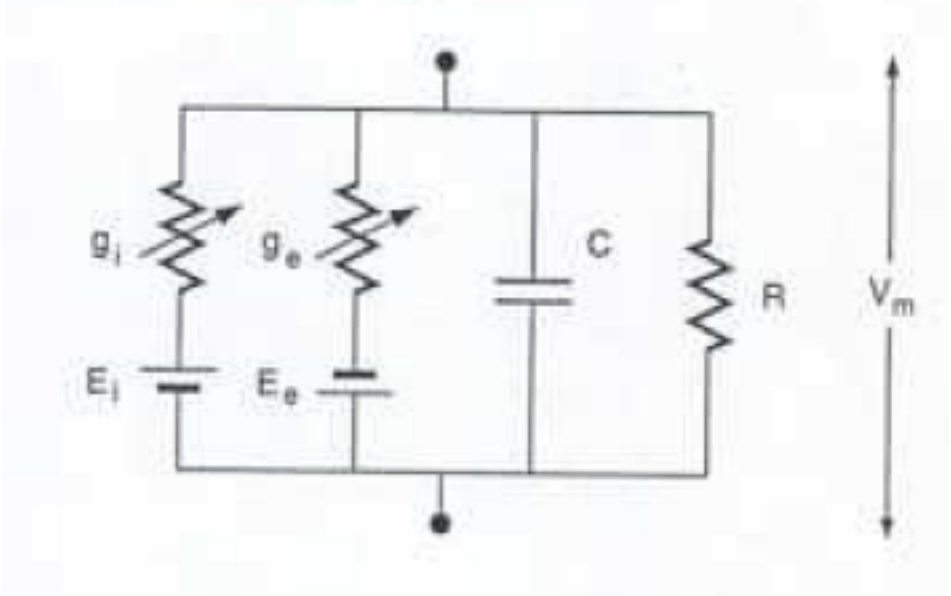
$$V_\infty = E_{syn}$$

Saturates at Synaptic reversal potential

Shunting Inhibition

- **Special case, when the synaptic reversal potential is equivalent to the resting membrane potential**

$$C\frac{dV}{dt} = g_e(E_e - V) - g_i V - \frac{V}{R}$$



Rewrite this to:

$$\tau' \frac{dV}{dt} = -V + \frac{g_e E_{syn}}{G_{in}}$$

$$G_{in} = g_e + g_i + \frac{1}{R}$$

$$\tau' = \frac{C}{G_{in}}$$

Shunting Inhibition

Solving ODE:

$$\tau' \frac{dV}{dt} = -V + \frac{g_e E_{syn}}{G_{in}}$$

$$V(t) = \frac{g_e E_e}{G_{in}}(1 - e^{-t/\tau'})$$

$$V\infty = \frac{g_e E_e}{g_e + \frac{1}{R} + g_i}$$

Notice g_i only appears in the denominator

This is reason why shunting inhibition is often referred to as 'divisive inhibition'

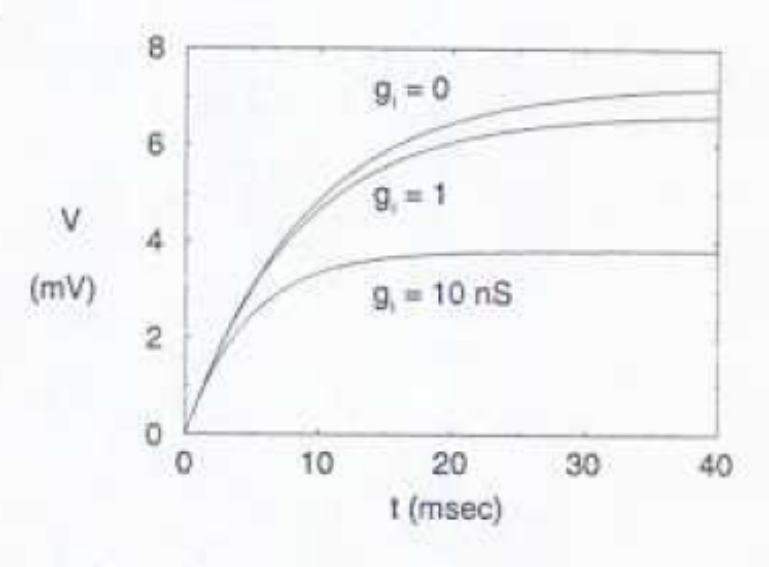
Shunting Inhibition

Solving ODE:

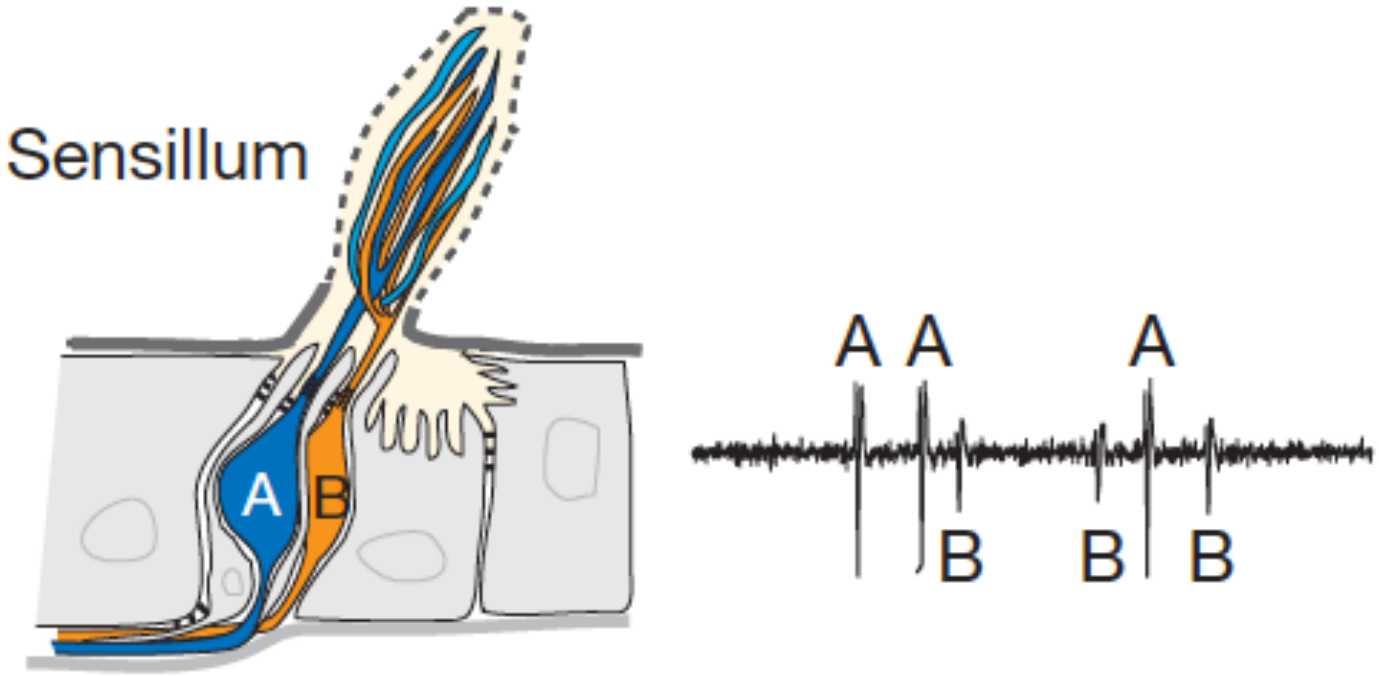
$$\tau' \frac{dV}{dt} = -V + \frac{g_e E_{syn}}{G_{in}}$$

$$V(t) = \frac{g_e E_e}{G_{in}} (1 - e^{-t/\tau'})$$

$$V\infty = \frac{g_e E_e}{g_e + \frac{1}{R} + g_i}$$

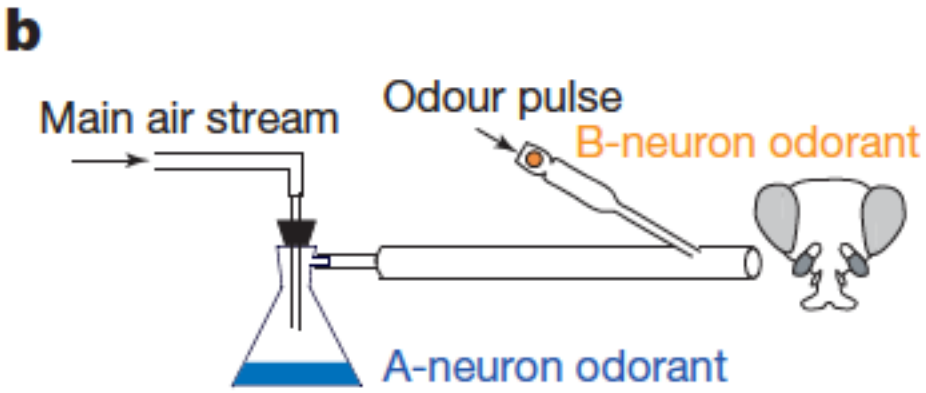


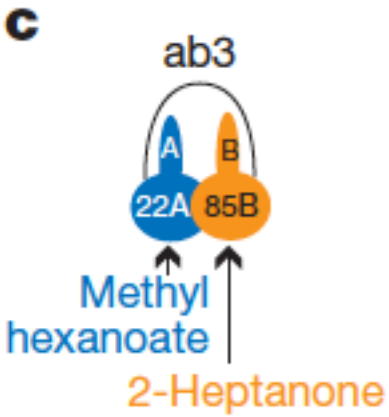
Non-synaptic interactions



Su et al, 2012

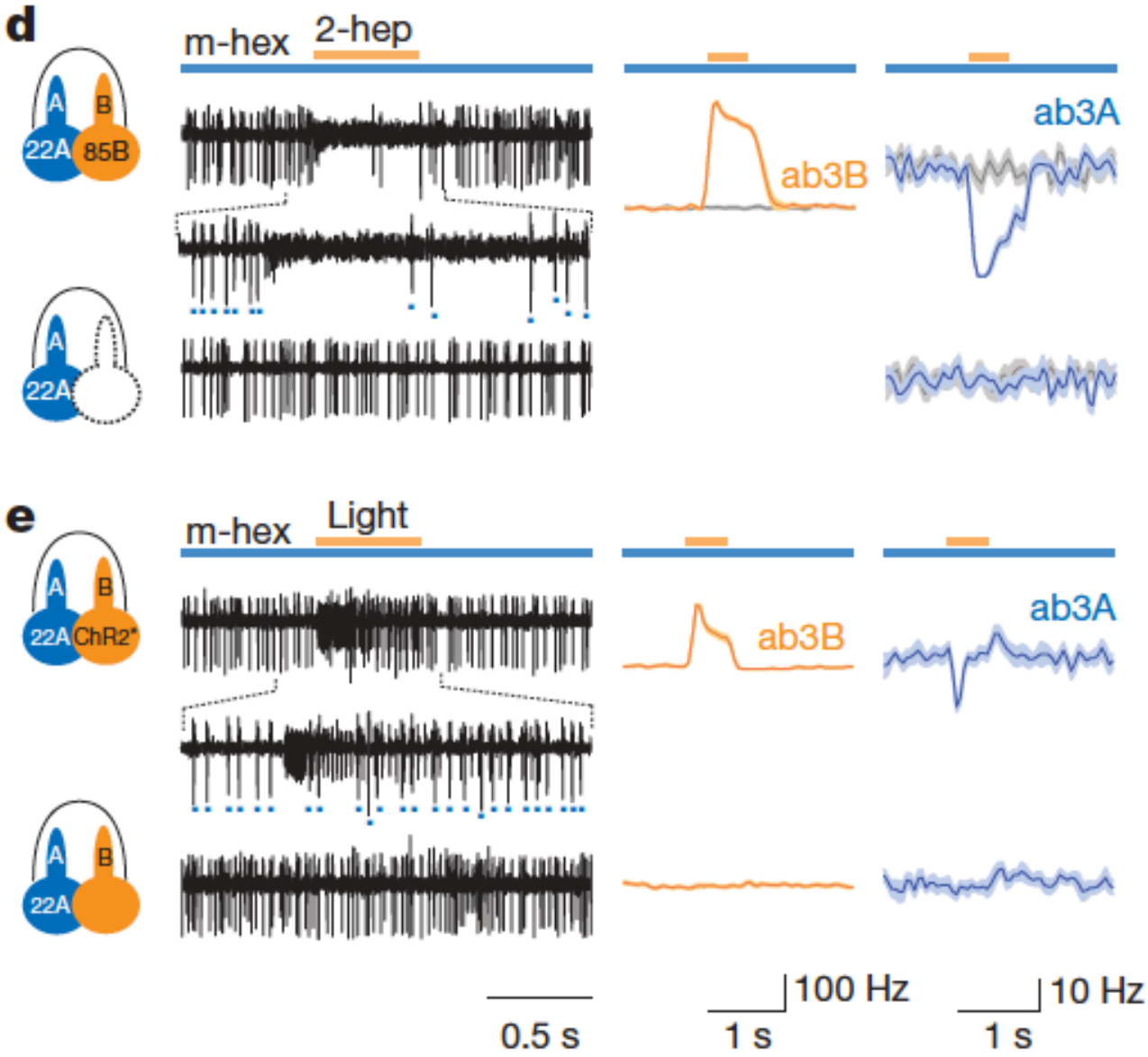
Ephaptic Coupling





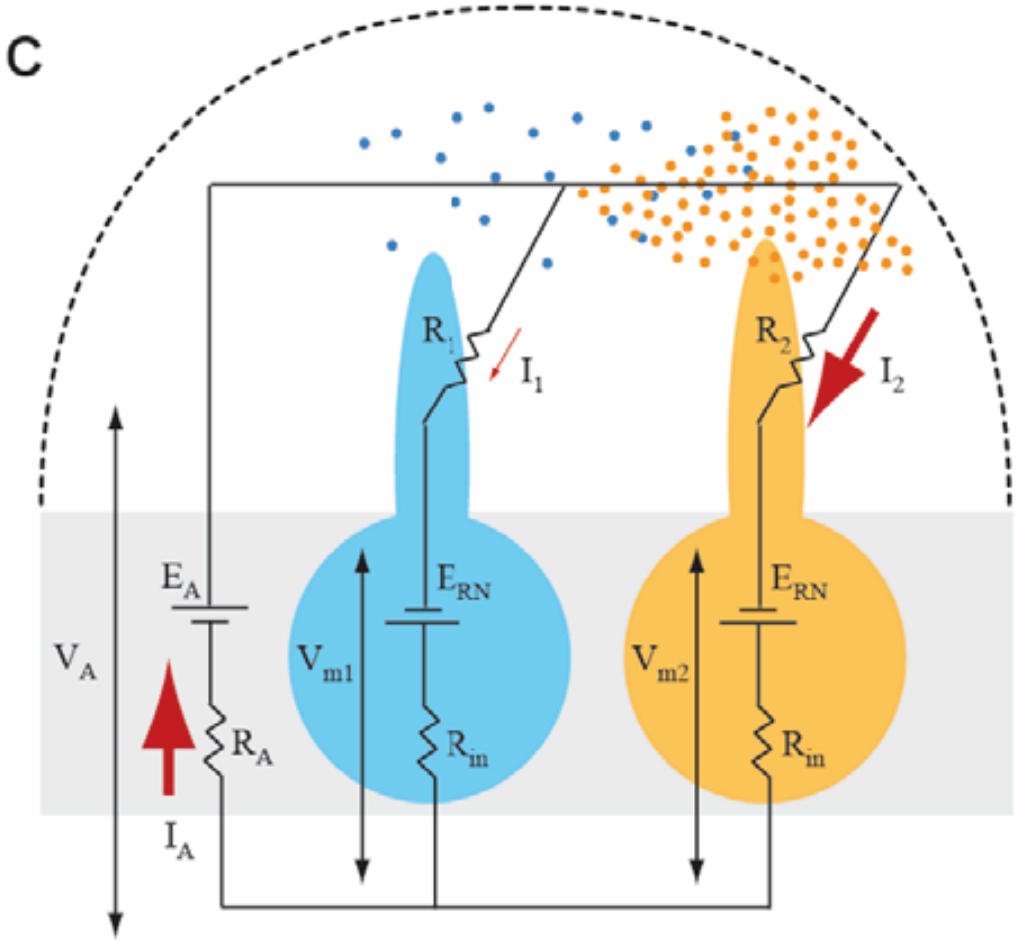
Su et al, 2012

Ephaptic Coupling



Su et al, 2012

Ephaptic Coupling

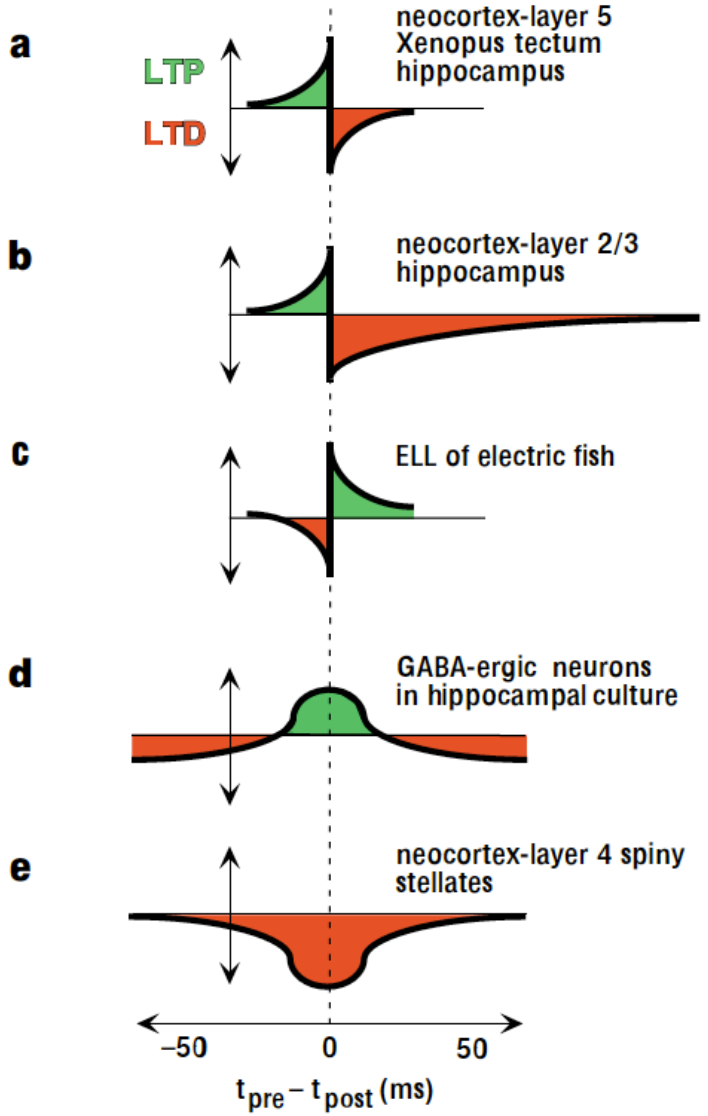


Plasticity

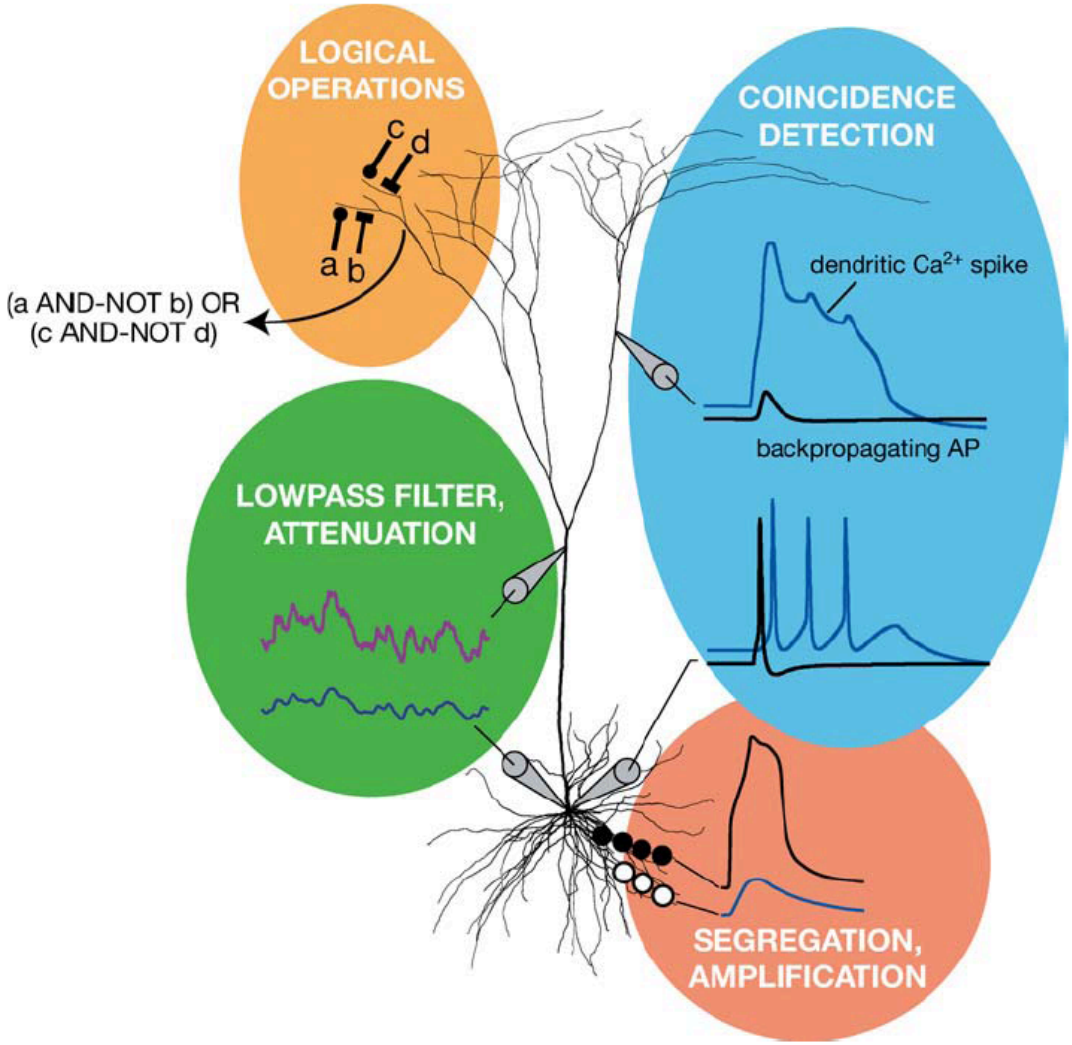
- **Hebb's law:**
  - Neurons that fire together wire together

Spike-time Dependent Plasticity

- LTP



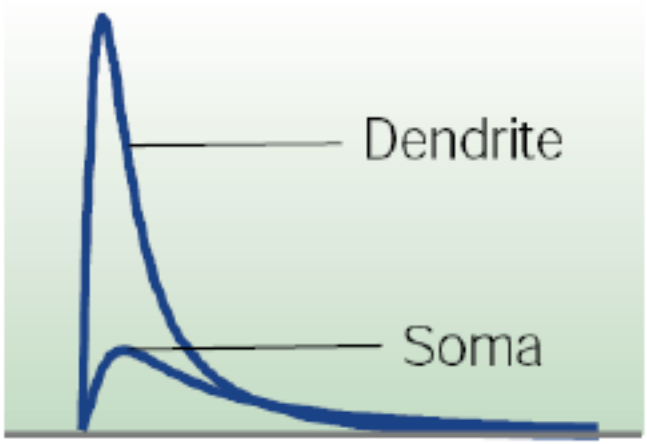
Dendritic Computational Toolkit



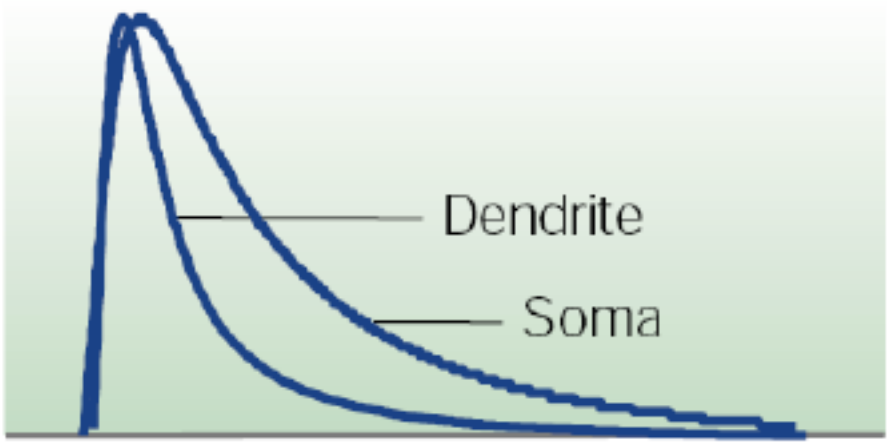
London and Hausser, Dendritic Computation, 2005

Passive Properties of Dendrites

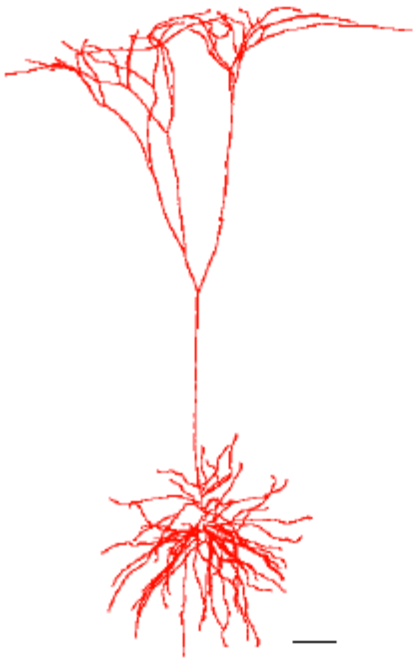
- Amplitude



Time course



Passive Properties of Dendrites



Linear filtering:

→ Inputs from dendrites are broadened and delayed

→ Alters summation properties..
coincidence detection to temporal integration

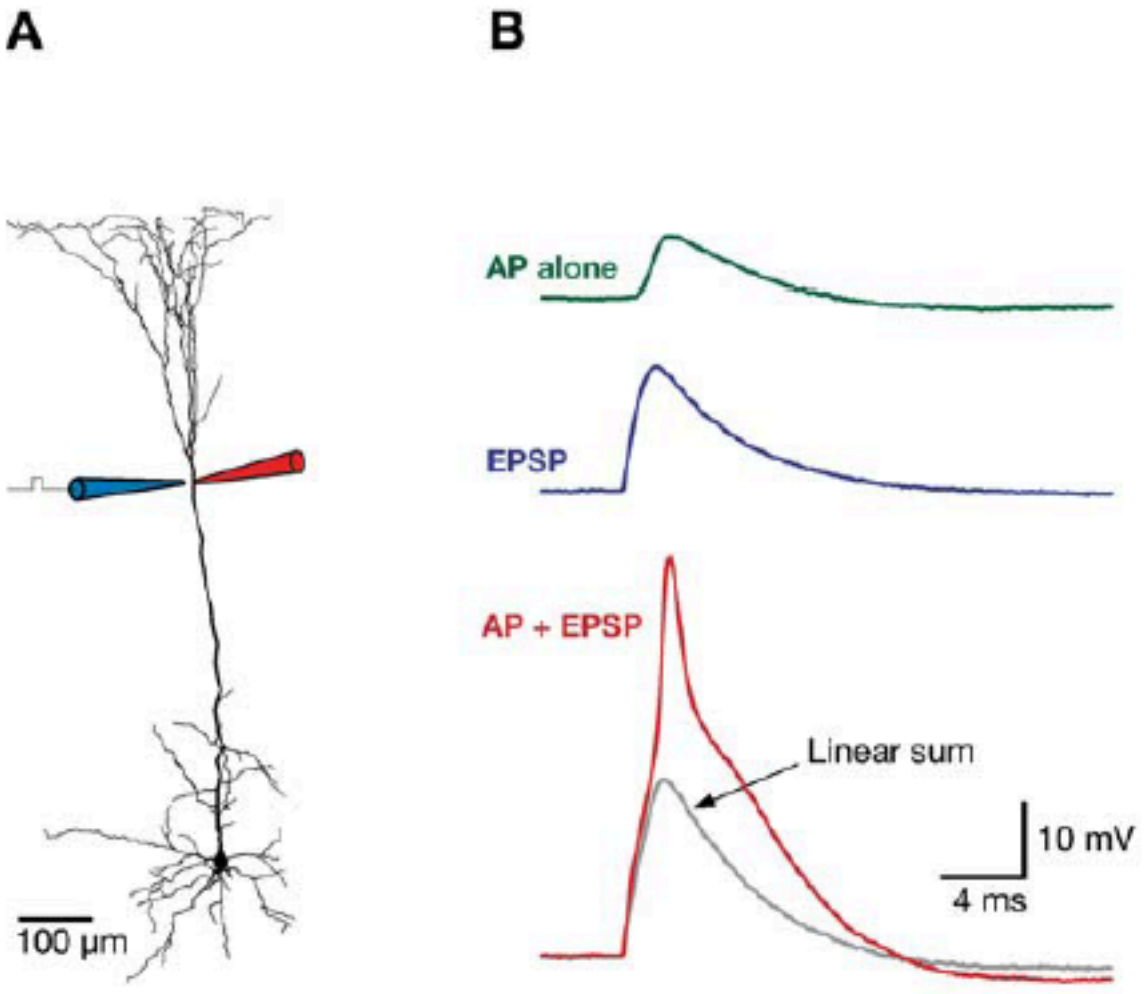
→ Delay lines

→ Segregation of inputs

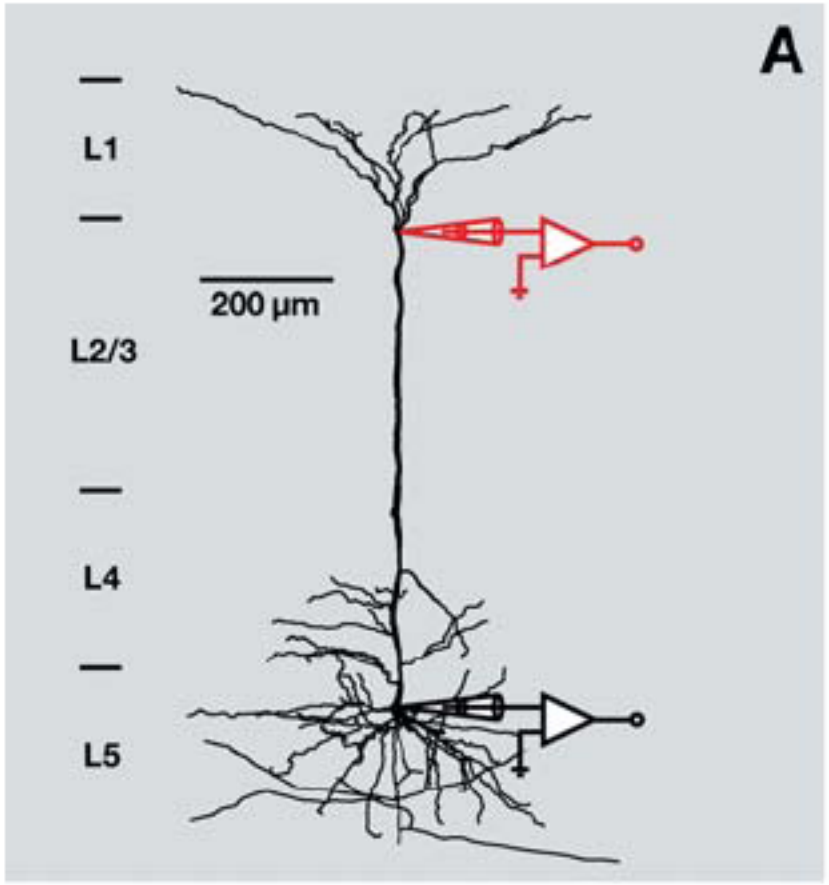
→ Nonlinear interactions within a dendrite
-- sublinear summation
-- shunting inhibition

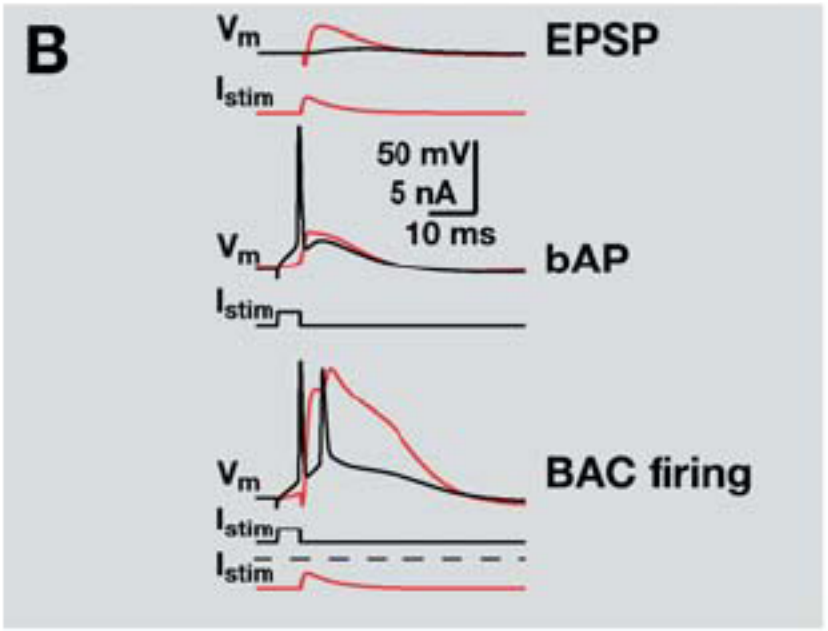
→ Dendritic inputs “labelled”

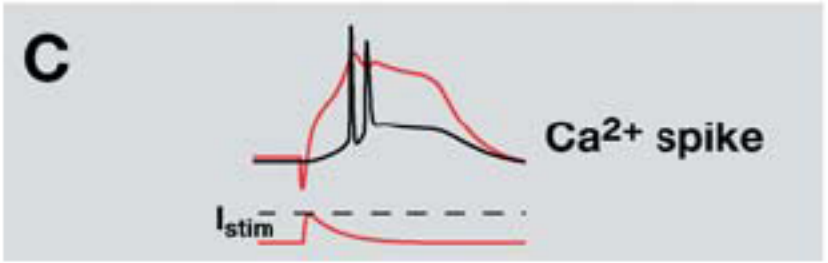
Coincidence Detection – Backpropagating APs



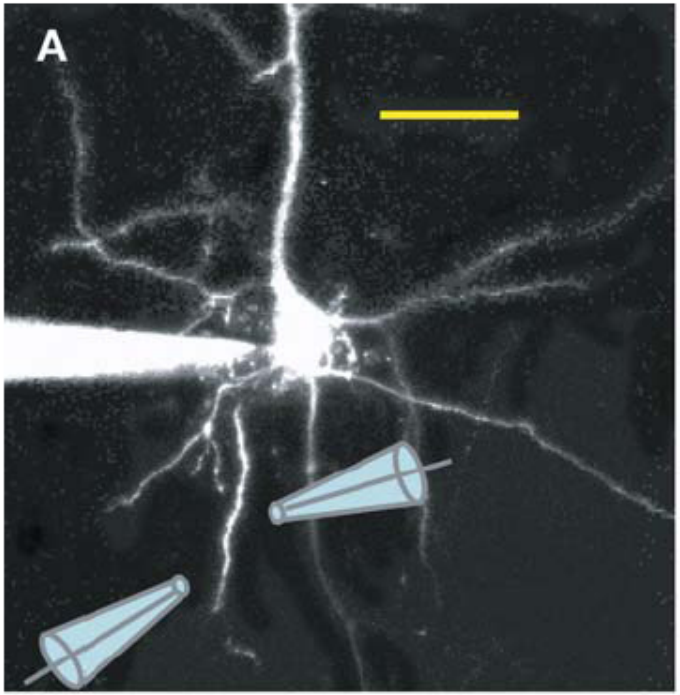
Coincidence Detection – Backpropagating APs

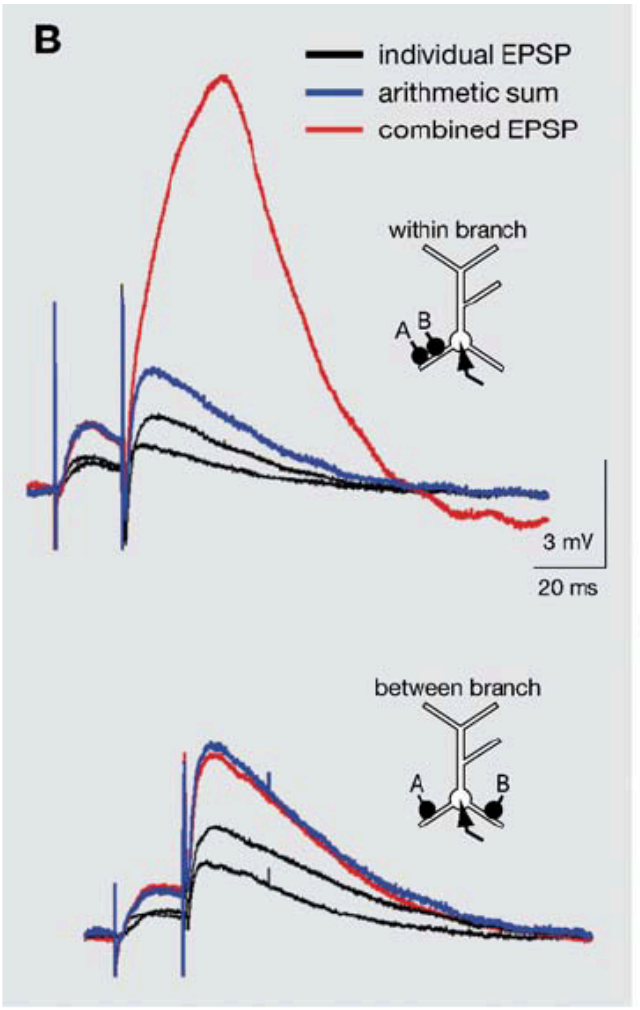




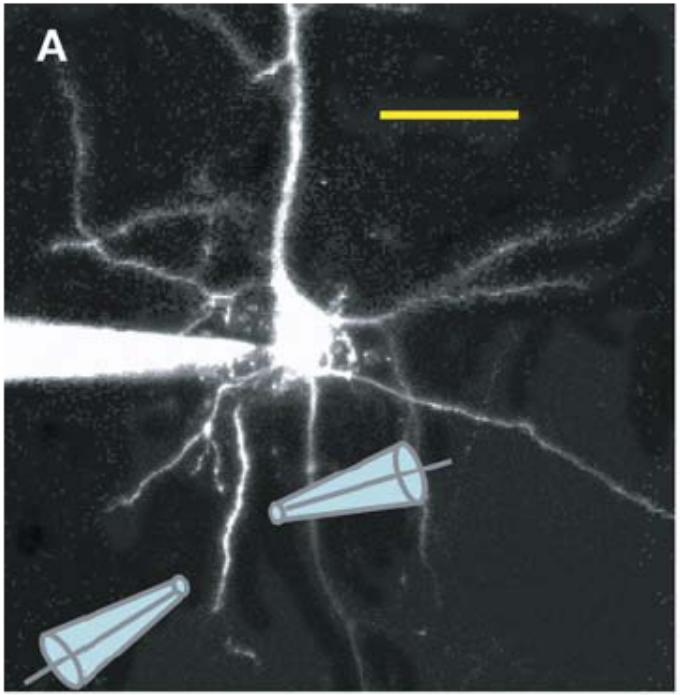


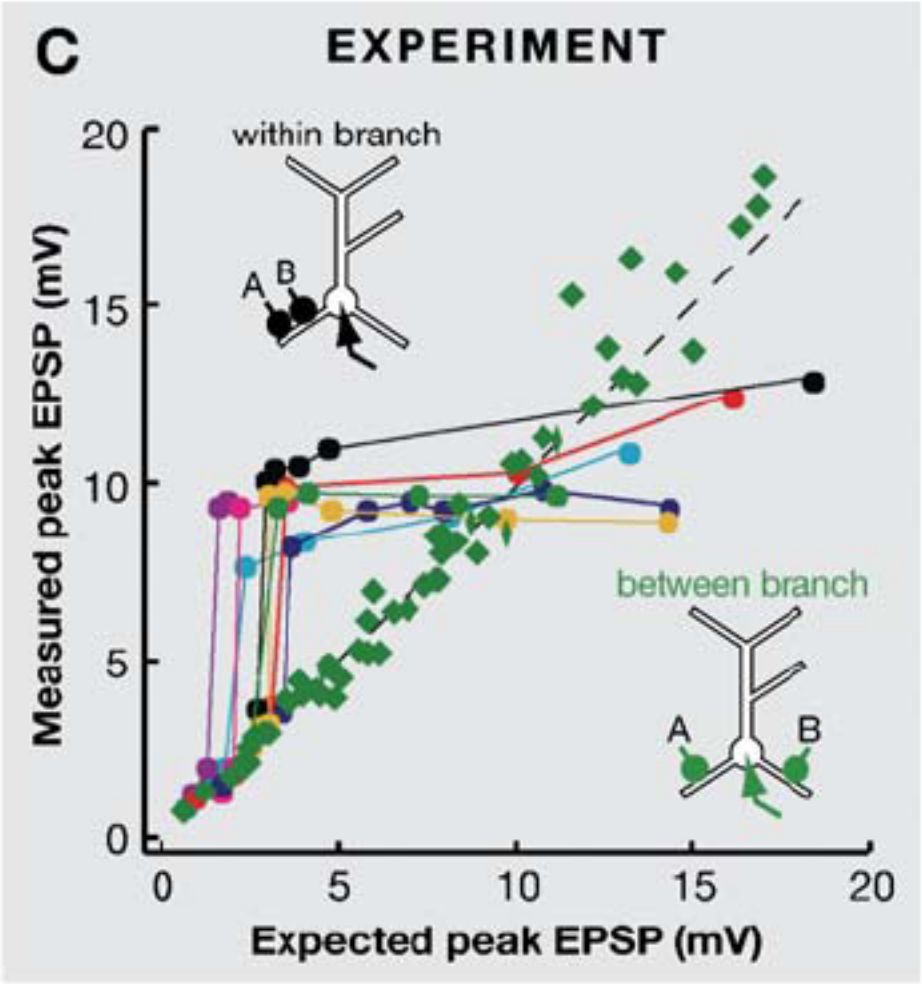
Dendritic Multiplication





Dendritic Multiplication





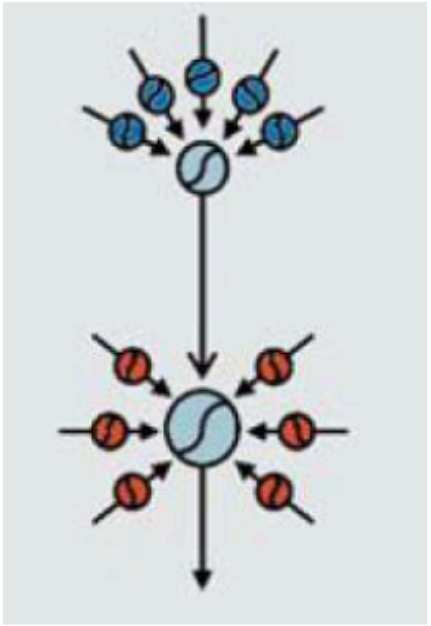
Active Properties of Dendrites

Mechanisms to deal with the distance dependence of PSP size

→ Subthreshold boosting: inward currents with reversal near rest
Eg persistent Na^+

→ Synaptic scaling

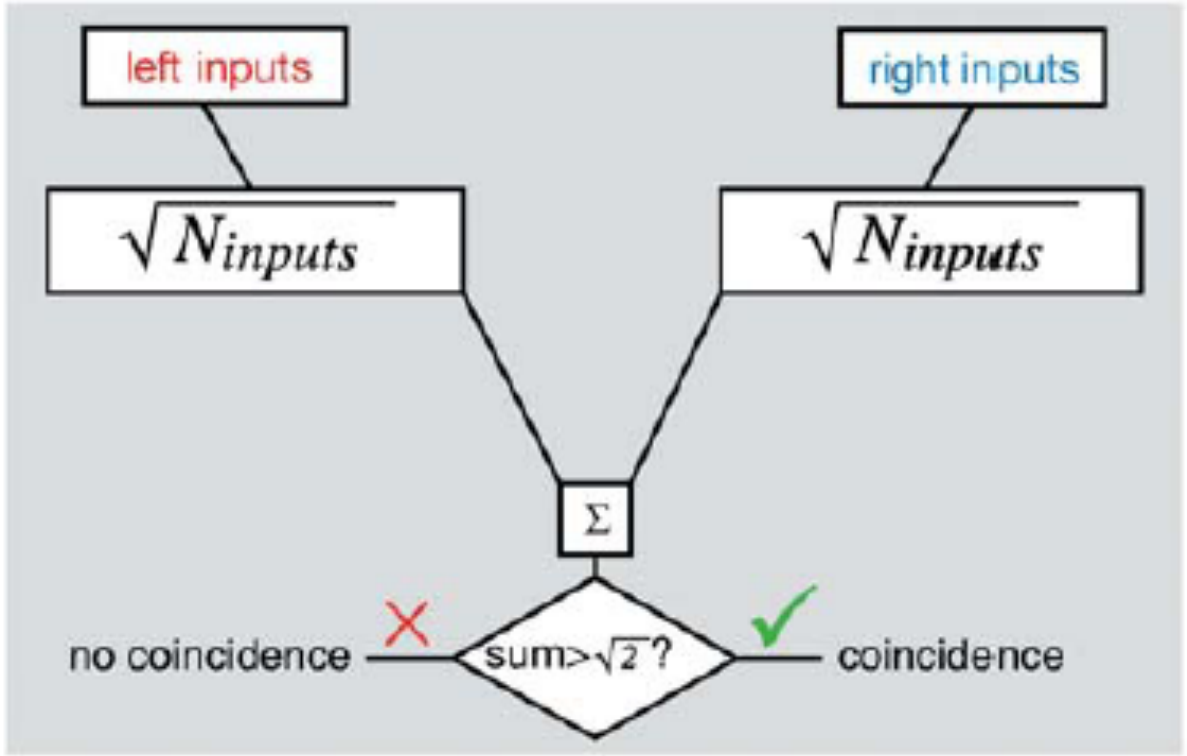
→ Dendritic spikes
Na^+, Ca^{2+} and NMDA
Dendritic branches as
mini computational units



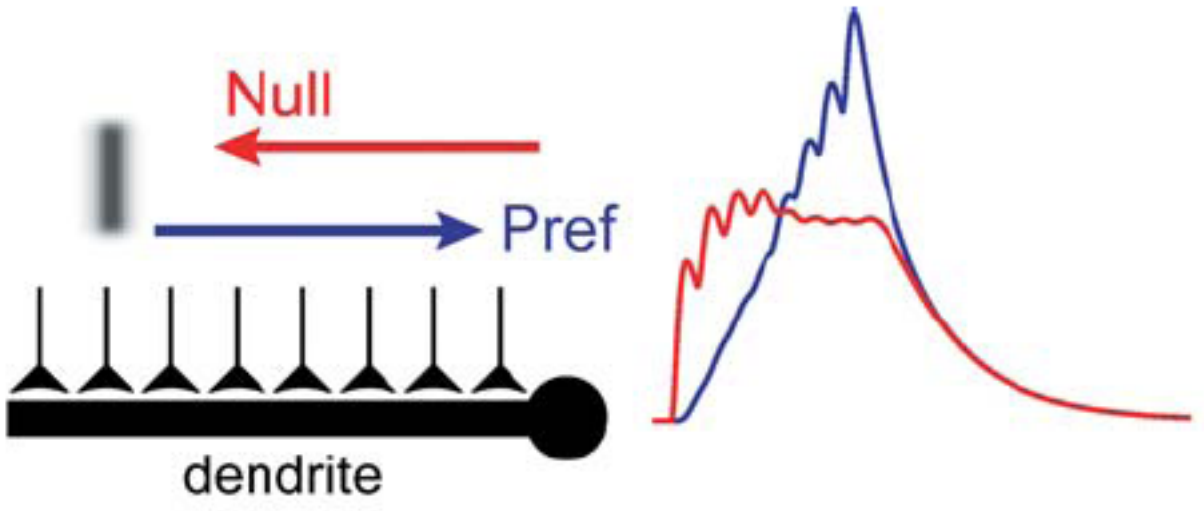
→ backpropagation:
feedback circuit
Hebbian learning through
supralinear interaction of backprop spikes with inputs

Sound Localization

Computation: Do the inputs from both ears arrive together?



Direction Selectivity



Direction Selectivity

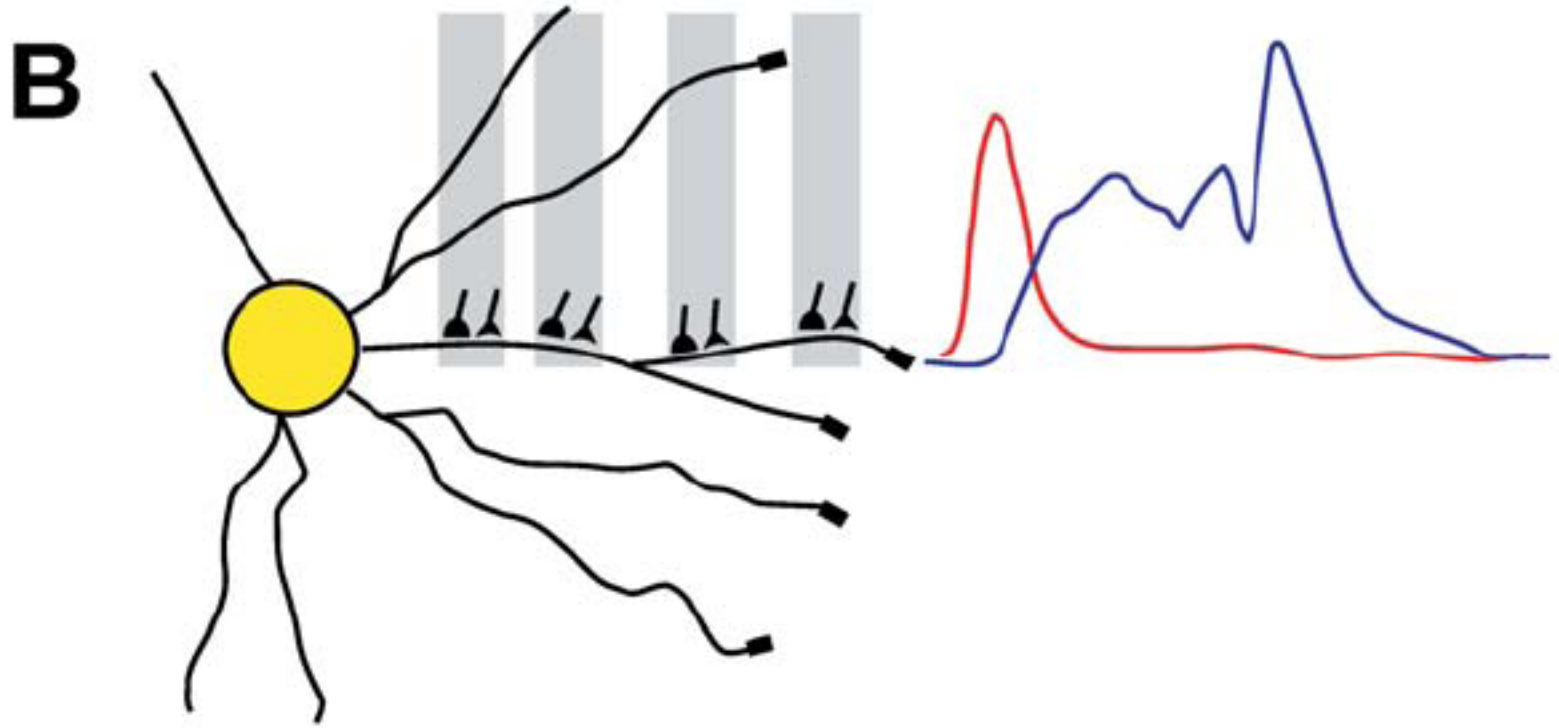
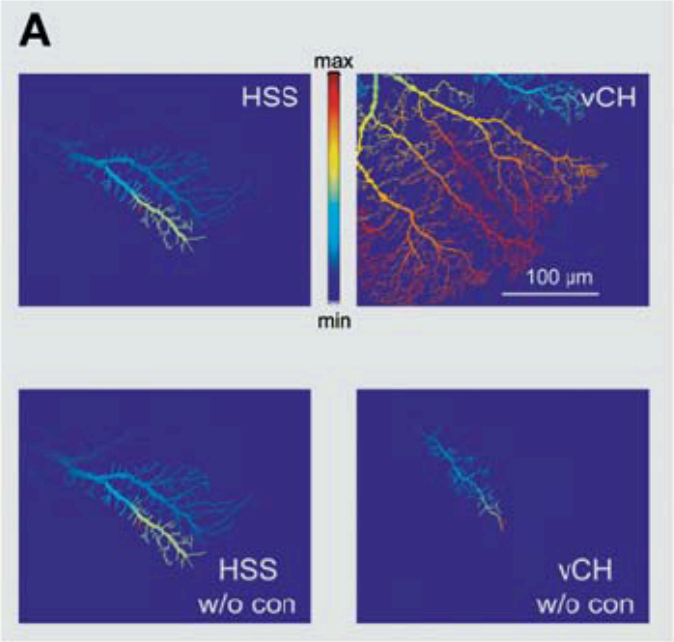
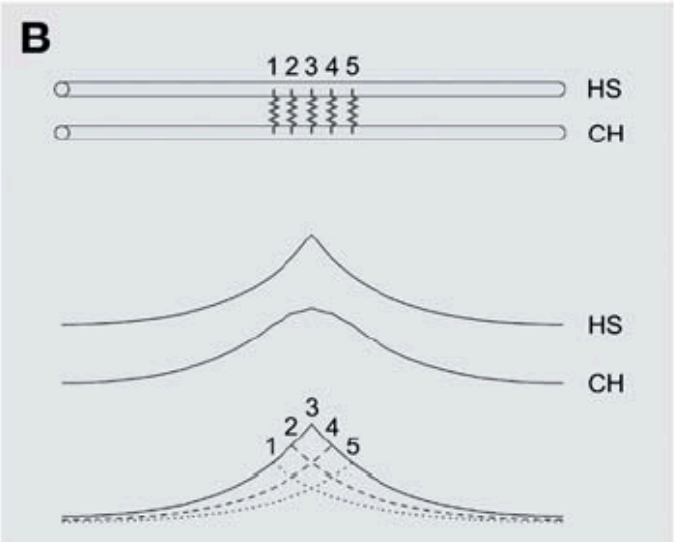
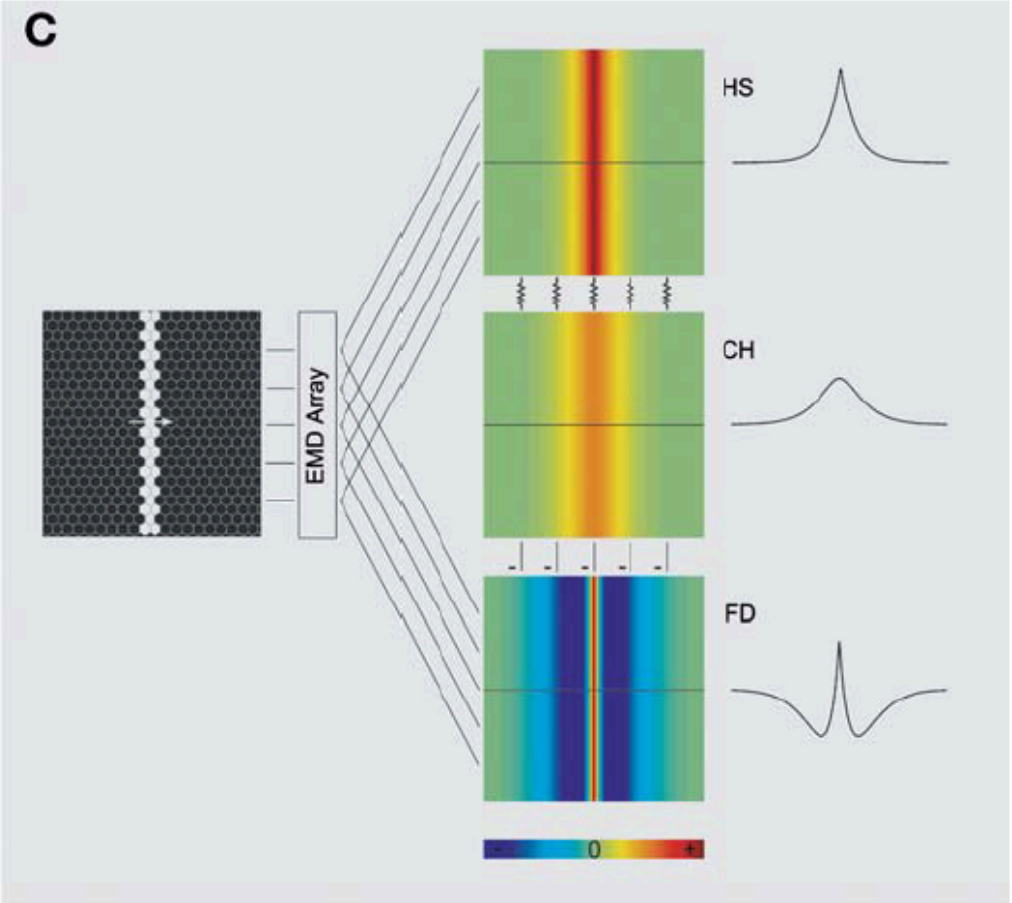


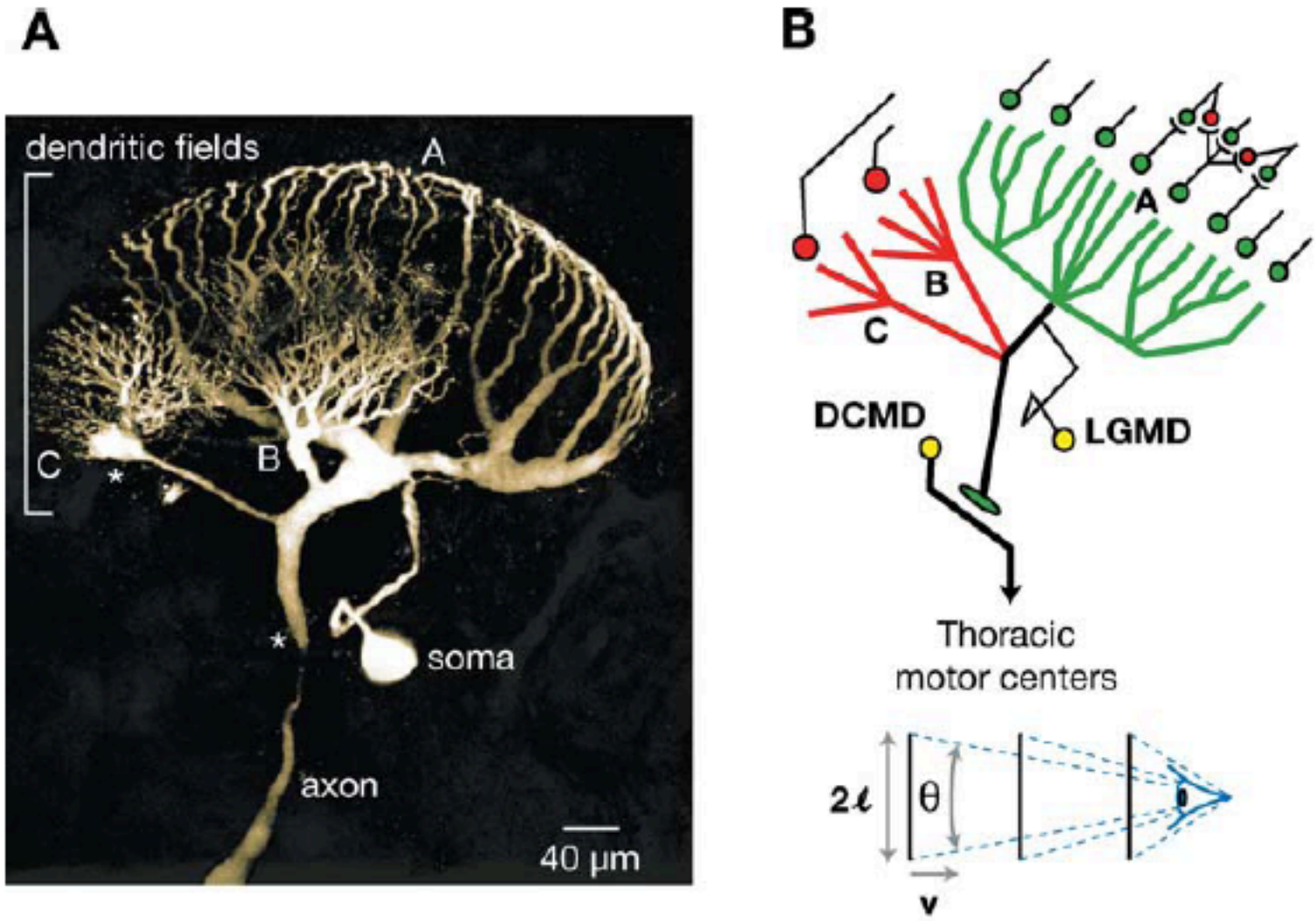
Image Processing







Looming object recognition



Looming object recognition