DONDERS
INSTITUTE
for Brain, Cognition and Behaviour

DENDRITES

Alessio Quaresima

Institut de l’Audition, Institut Pasteur

alessio.quaresima@pasteur.fr

Structure of the lecture

1. Dendritic physiology and integration

- 1.1 Dendritic morphologies
- 1.2 Voltage and current transmission
- 1.3 Biophysical computations in segregated dendrites
- 1.4 Dendritic spikes

2. Dendrites in computation

- 2.1 NMDA favors clustered vs sparse inputs
- 2.2 Minimal dendritic reductions
- 2.3 Memory consolidation in the dendrites
- 2.4 Dendritic information processing
- 2.5 ANN with dendrites

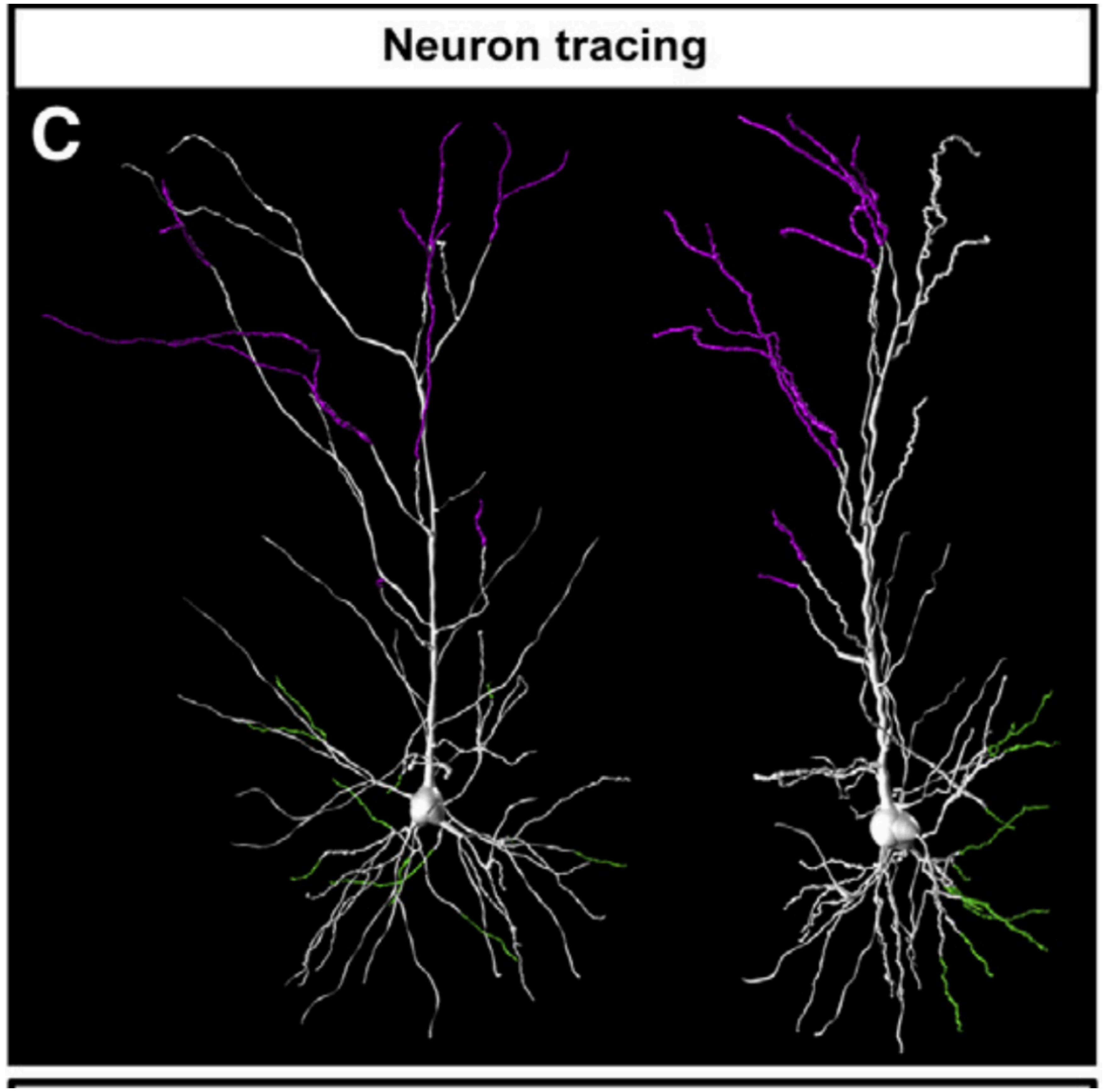
What are the dendrites?

Dendrites are the **branched extensions of neurons** that receive electrical signals from other neurons and convey this information toward the cell body.

Dendrites play a crucial role in neural communication by **increasing the surface area** available for synaptic connections.

The changes in dendritic membrane potential following a synaptic input, and the consequent flow of electrochemical currents from the dendrites to the cell's soma, are called **dendritic integration**.

C. Koch, The Biophysics of Computation 1999



Iascone 2020

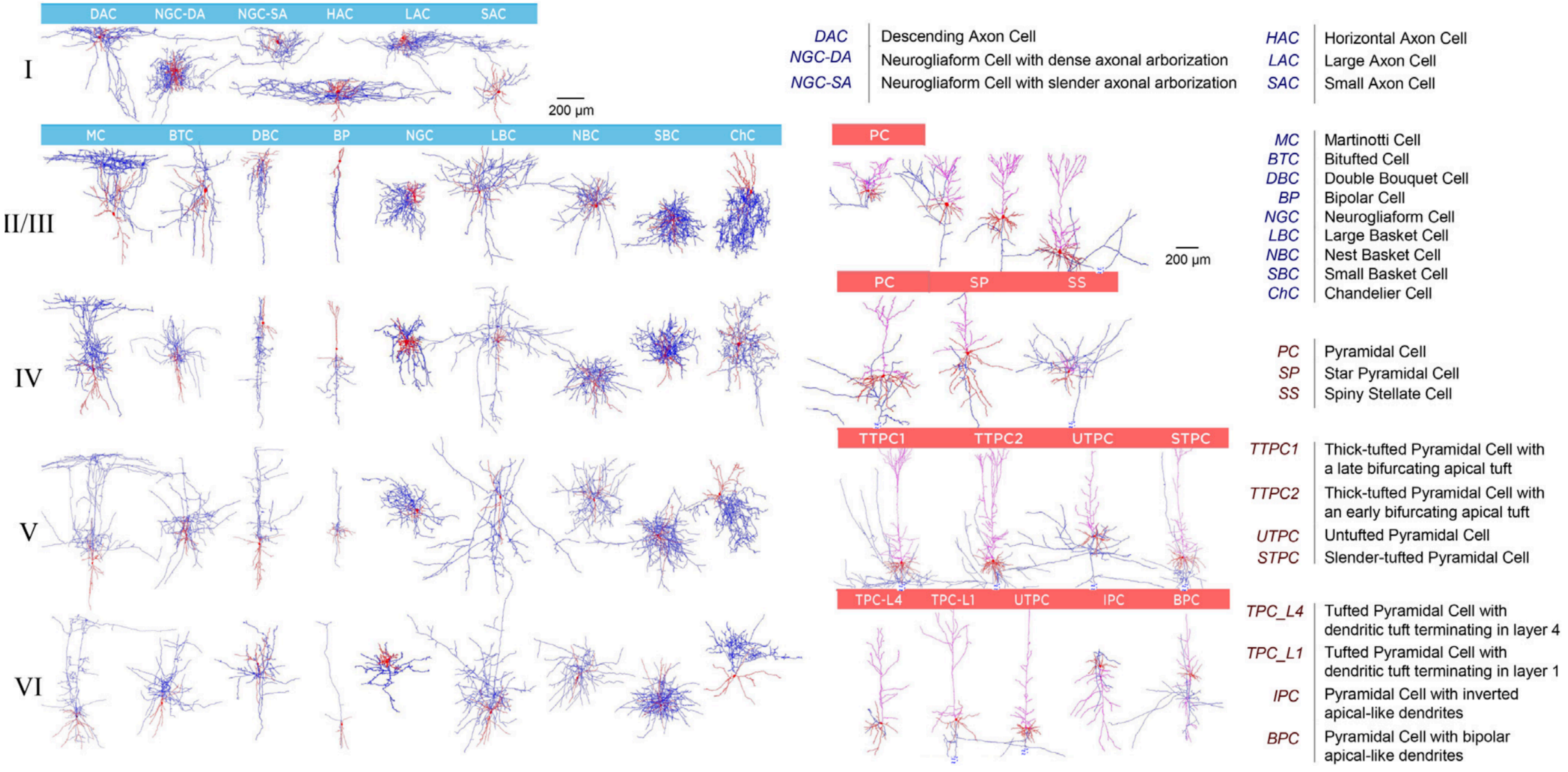
Dendritic morphologies

Dendritic structure changes with cell type

Cortical cells can be organized for their electrical, genetic, and morphological properties.

The morphology concerns the shape of the dendritic processes that extend from the cell body.

Does the dendritic structure impact how the cells integrate signals?

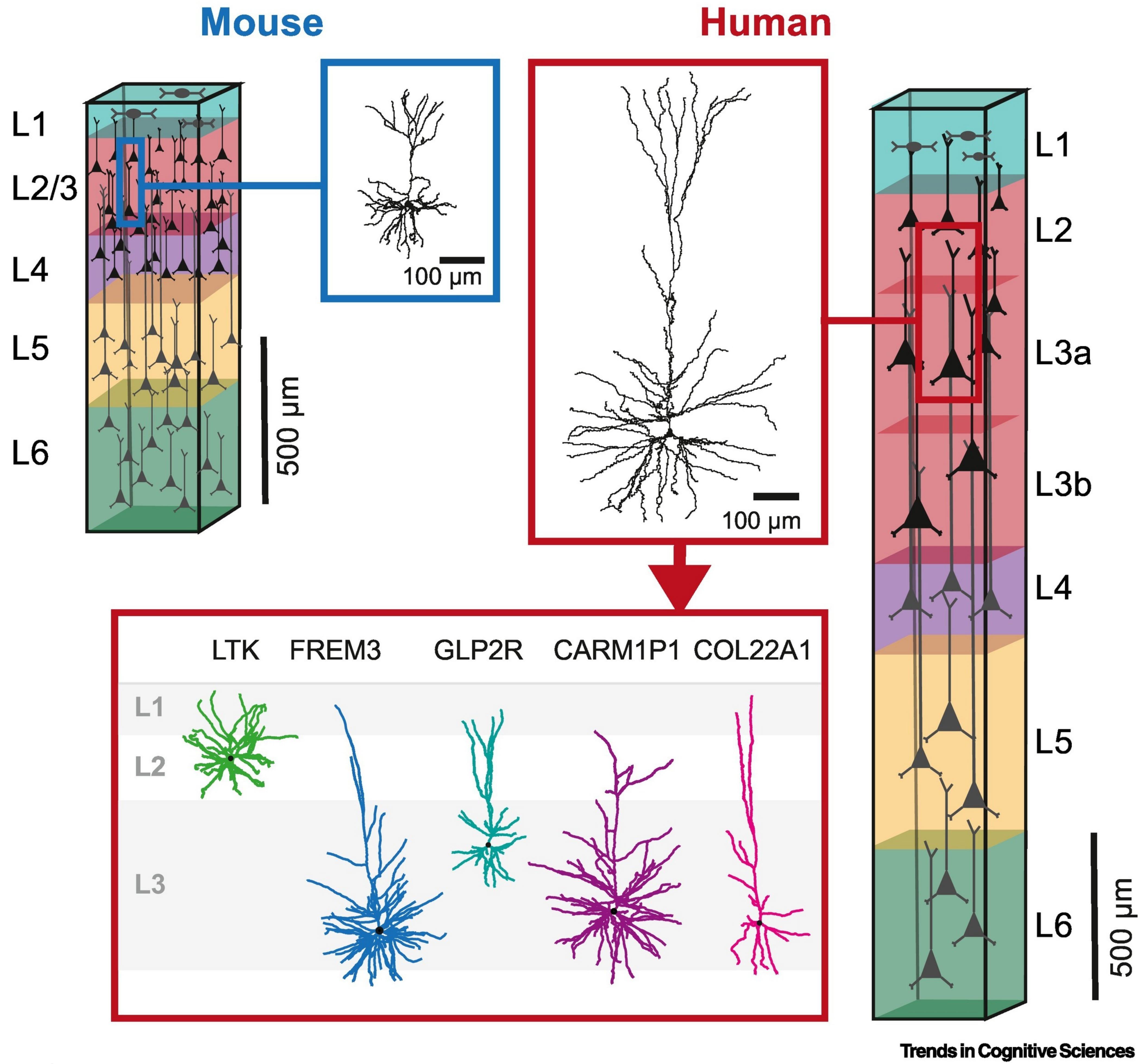


DAC	Descending Axon Cell
NGC-DA	Neurogliaform Cell with dense axonal arborization
NGC-SA	Neurogliaform Cell with slender axonal arborization
HAC	Horizontal Axon Cell
LAC	Large Axon Cell
SAC	Small Axon Cell
MC	Martinotti Cell
BTC	Bitufted Cell
DBC	Double Bouquet Cell
BP	Bipolar Cell
NGC	Neurogliaform Cell
LBC	Large Basket Cell
NBC	Nest Basket Cell
SBC	Small Basket Cell
ChC	Chandelier Cell
PC	Pyramidal Cell
SP	Star Pyramidal Cell
SS	Spiny Stellate Cell
TTPC1	Thick-tufted Pyramidal Cell with a late bifurcating apical tuft
TTPC2	Thick-tufted Pyramidal Cell with an early bifurcating apical tuft
UTPC	Untufted Pyramidal Cell
STPC	Slender-tufted Pyramidal Cell
TPC_L4	Tufted Pyramidal Cell with dendritic tuft terminating in layer 4
TPC_L1	Tufted Pyramidal Cell with dendritic tuft terminating in layer 1
IPC	Pyramidal Cell with inverted apical-like dendrites
BPC	Pyramidal Cell with bipolar apical-like dendrites

Markram et al. 2015

Dendritic morphologies

The backbone of cortical computation: the pyramidal cell

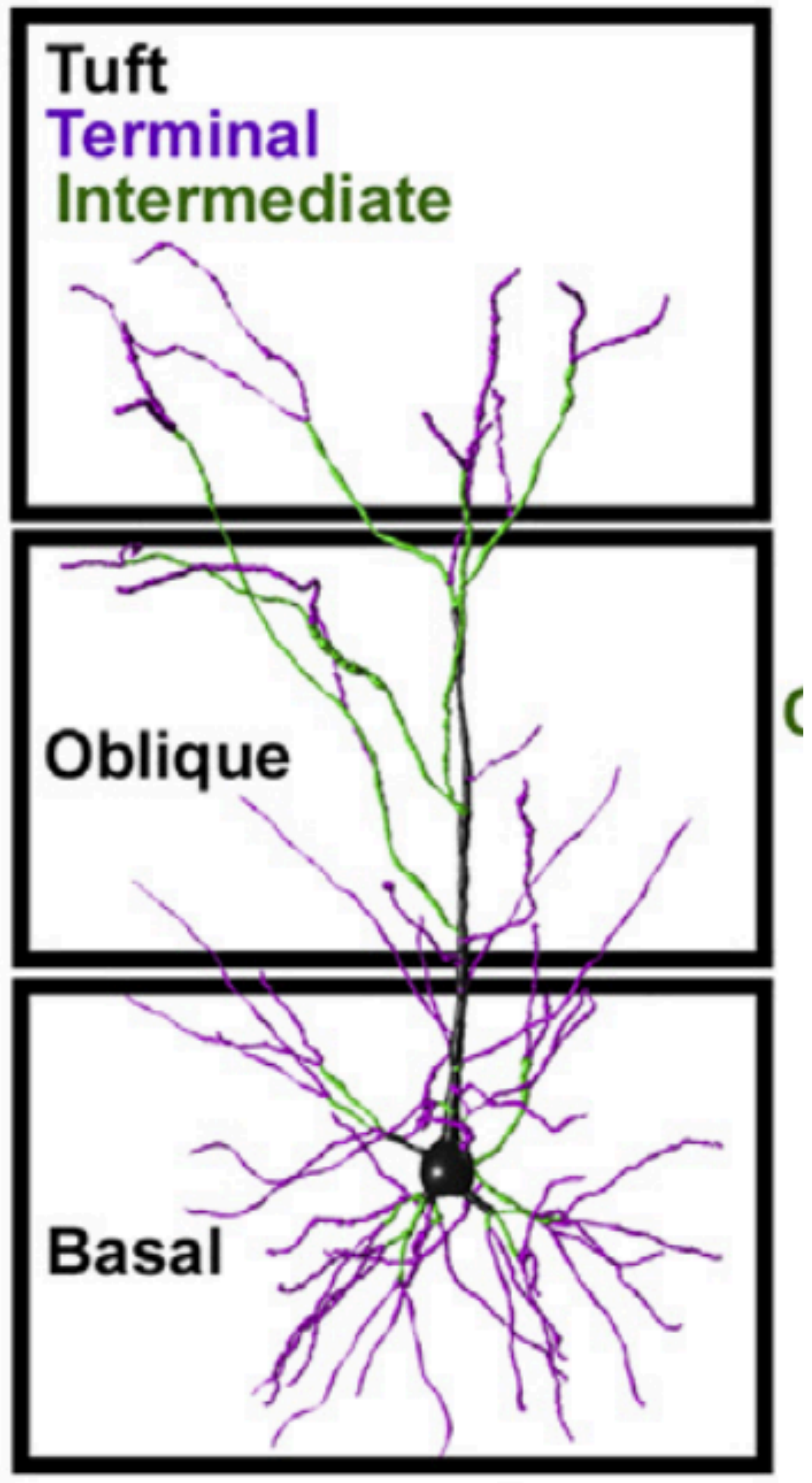


Galakhova 2023

The pyramidal cells are the most abundant in the neocortex, about 70-80%.

Pyramidal cells' dendrites can be categorised according to their distance from the soma and their orientation in:

- Basal
- Oblique
- Apical tuft



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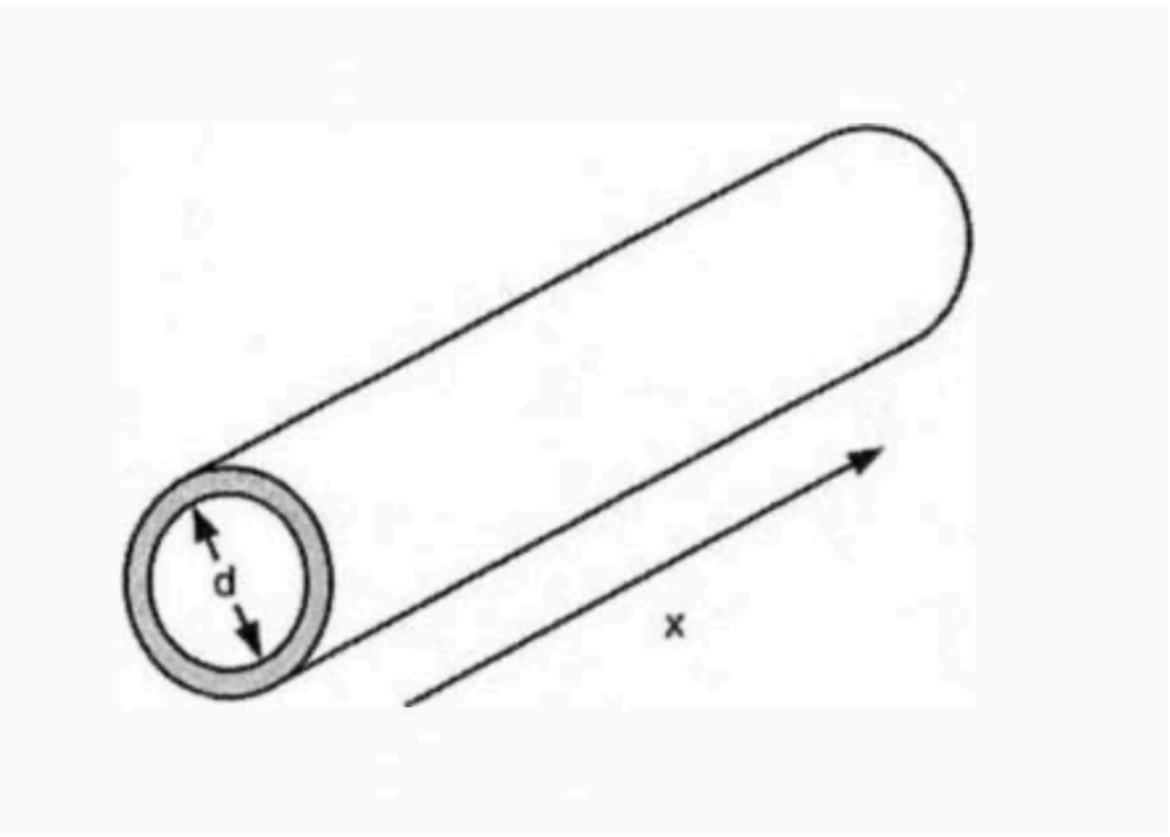
Integration of electrical activity in the dendrites

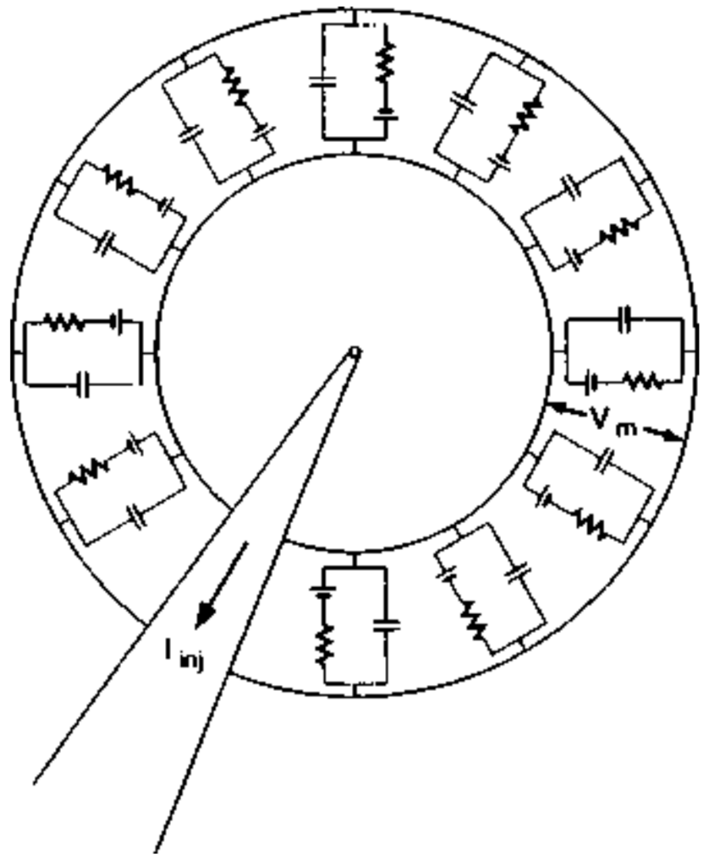
Current flowing in one dimensional cable

The membrane potential in *x* at time *t* depends on:

$$V_i(x,t) - V_i(x+\Delta x,t) = R I_i(x,t)$$

$$\frac{\partial V_m}{\partial x}(x,t) = -r_a \cdot I_i(x,t) \qquad r_a = R/\Delta x$$

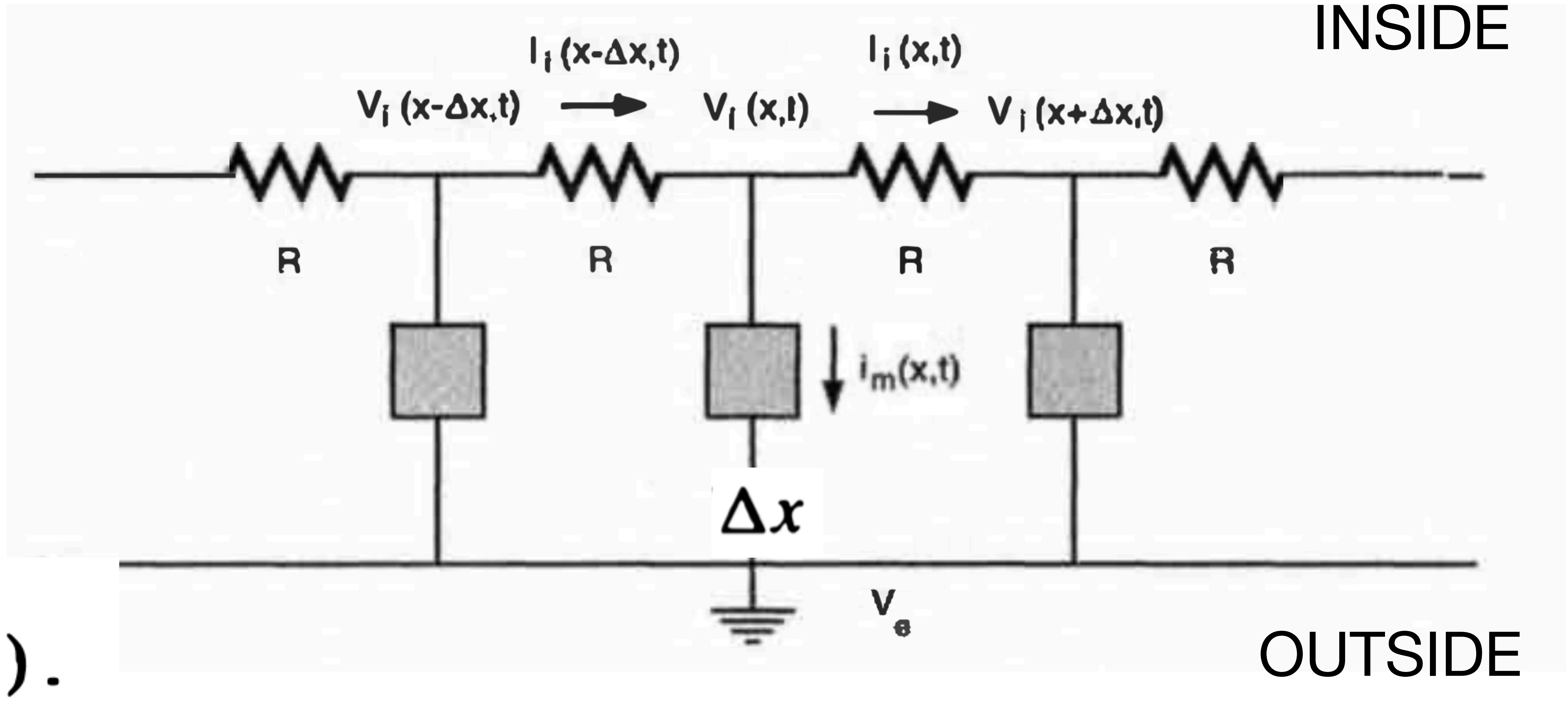




The density of current i_m is the current flowing *through* the membrane

$$i_m(x,t)\Delta x + I_i(x,t) - I_i(x-\Delta x,t) = 0$$

$$i_m(x,t) = -\frac{\partial I_i}{\partial x}(x,t)\,.$$



Combining, we obtain

$$\frac{1}{r_a}\frac{\partial^2 V_m}{\partial x^2}(x,t) = i_m(x,t)\,.$$

C. Koch, The Biophysics of Computation 1999

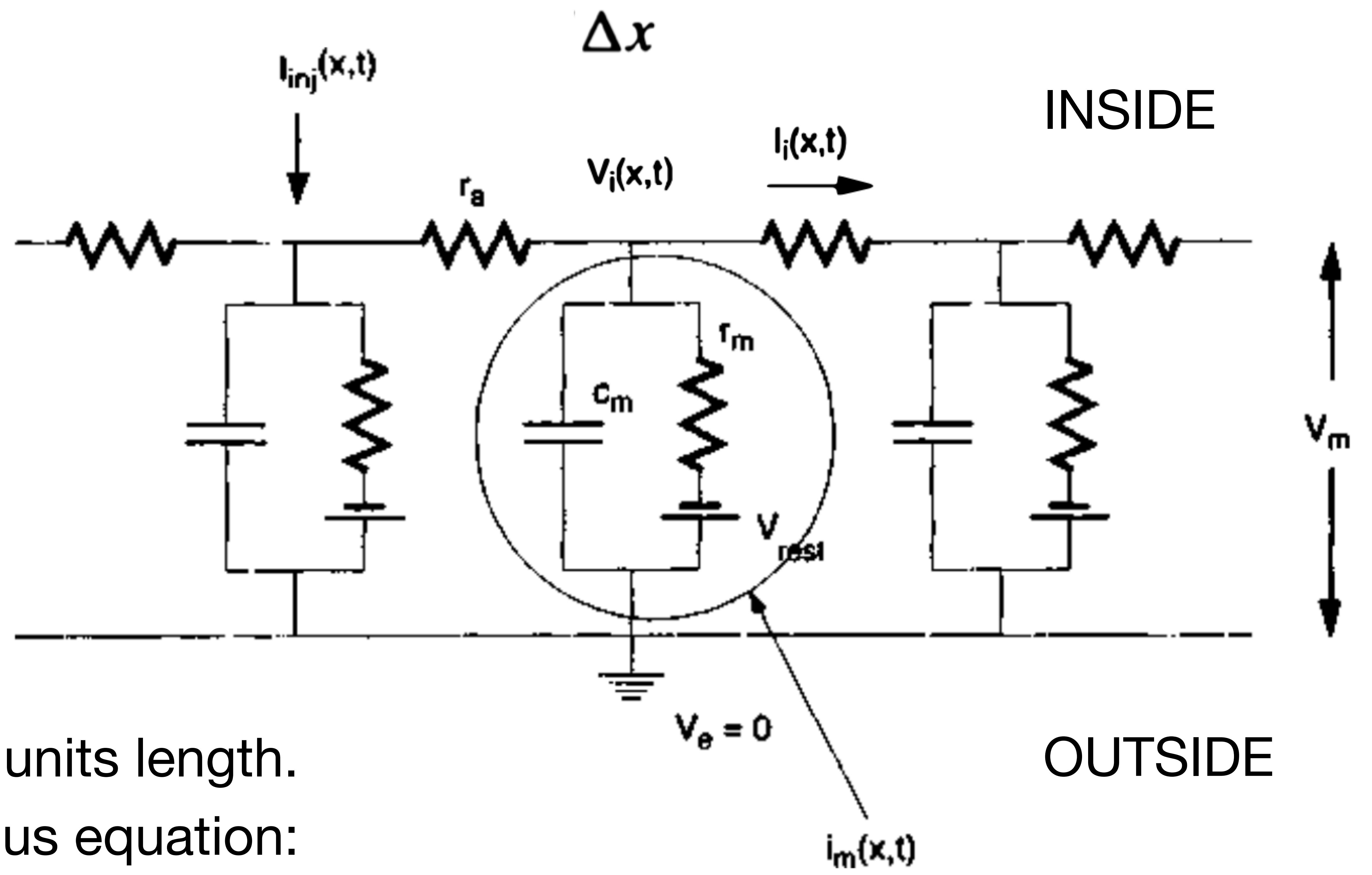
Integration of electrical activity in the dendrites

The infinitesimal membrane patch

Each segment is a membrane patch. The current flowing through is the HH membrane patch model.

$$i_m(x,t) = \frac{V_m(x,t) - V_{\text{rest}}}{r_m} + c_m \frac{\partial V_m(x,t)}{\partial t} - I_{\text{inj}}(x,t),$$

$$r_a = \frac{4R_i}{\pi d^2} \qquad r_m = \frac{R_m}{\pi d} \qquad c_m = C_m \cdot \pi d$$



The cable equation components are defined as quantity per units length.

The density of current i_m is the current substituted in previous equation:

$$\lambda^2 \frac{\partial^2 V_m(x,t)}{\partial x^2} = \tau_m \frac{\partial V_m(x,t)}{\partial t} + (V_m(x,t) - V_{\text{rest}}) - r_m I_{\text{inj}}(x,t),$$

$$\tau_m = r_m c_m \qquad \lambda = (r_m/r_a)^{1/2}.$$

C. Koch, The Biophysics of Computation 1999

Integration of electrical activity in the dendrites

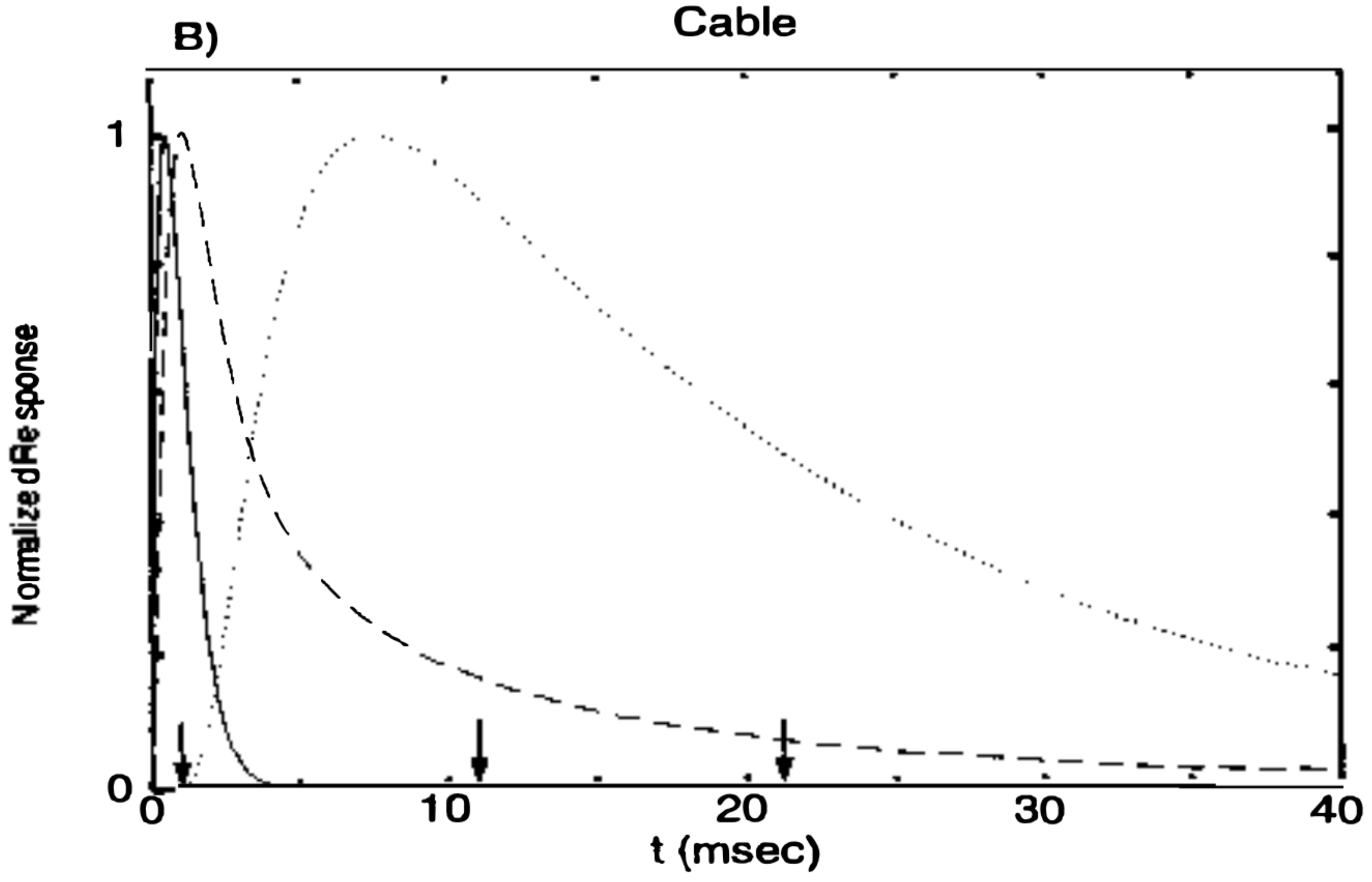
Segregated activity

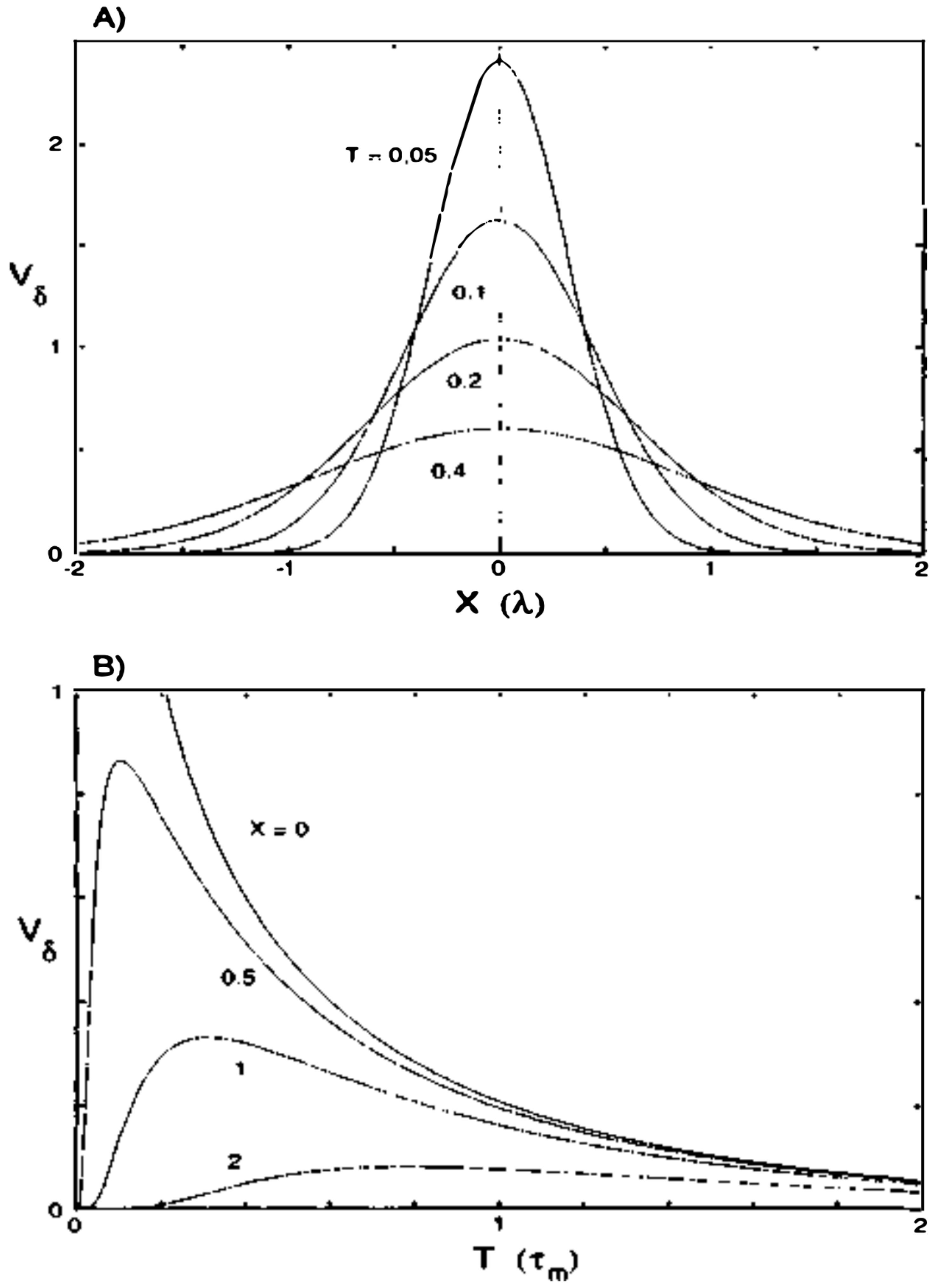
$$\lambda^2 \frac{\partial^2 V_m(x,t)}{\partial x^2} = \tau_m \frac{\partial V_m(x,t)}{\partial t} + (V_m(x,t) - V_{\text{rest}}) - r_m I_{\text{inj}}(x,t)\,,$$

The direct consequences of the cable equation are:

1. the variation in membrane potential are transmitted with a delay. To define the signal propagation speed we use measure the centroid of the time (see book, eqs. 2.43), and this result in a pseudovelocity:

$$v = 2\frac{\lambda}{\tau_m} = \left(\frac{d}{R_m R_i C_m^2}\right)^{1/2}.$$





C. Koch, The Biophysics of Computation 1999

Integration of electrical activity in the dendrites

Segregated activity

2. When a synaptic event leads to an inflow of current in the dendrites, the current is attenuated over time and space.

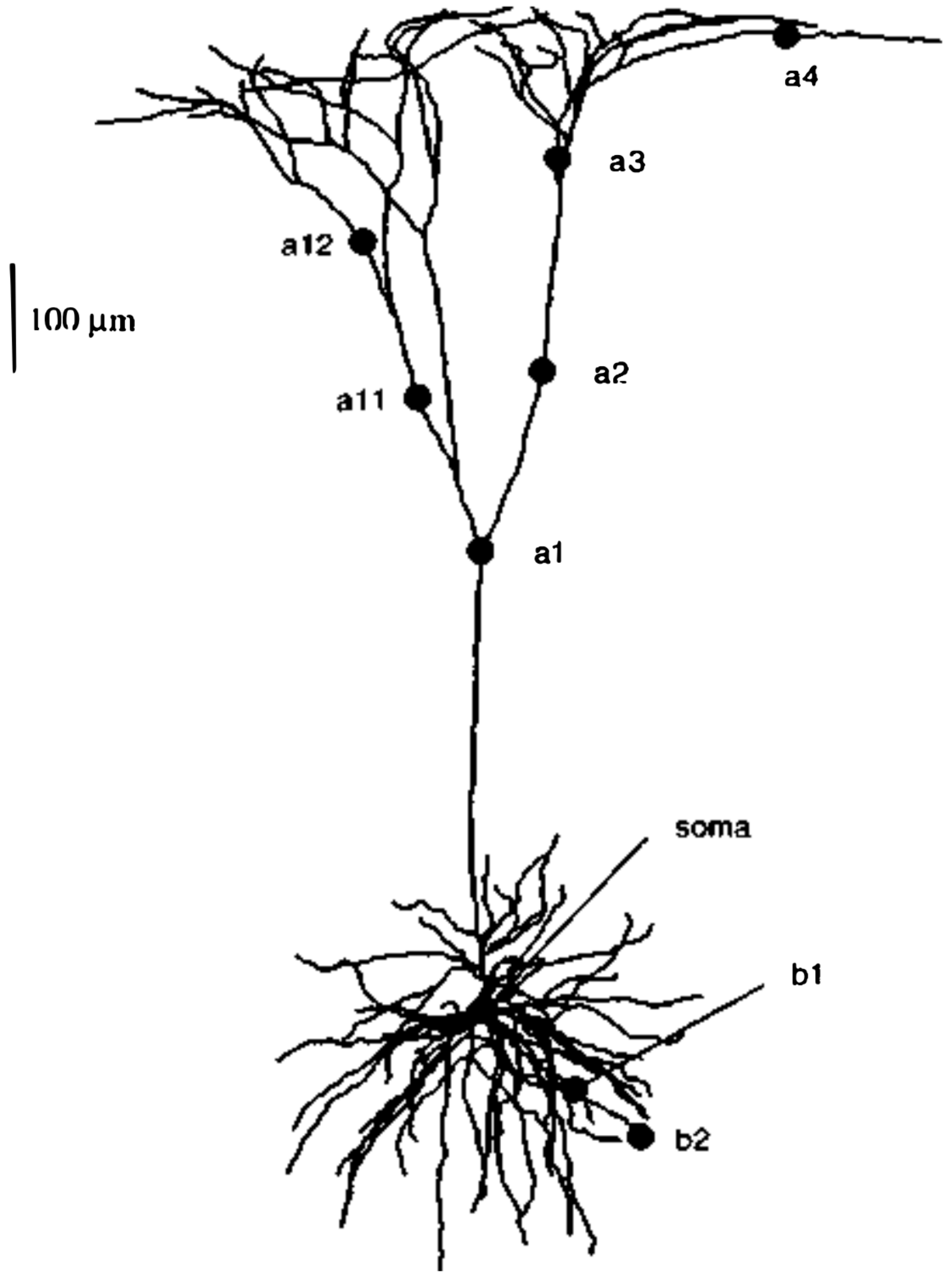
Same site - delayed

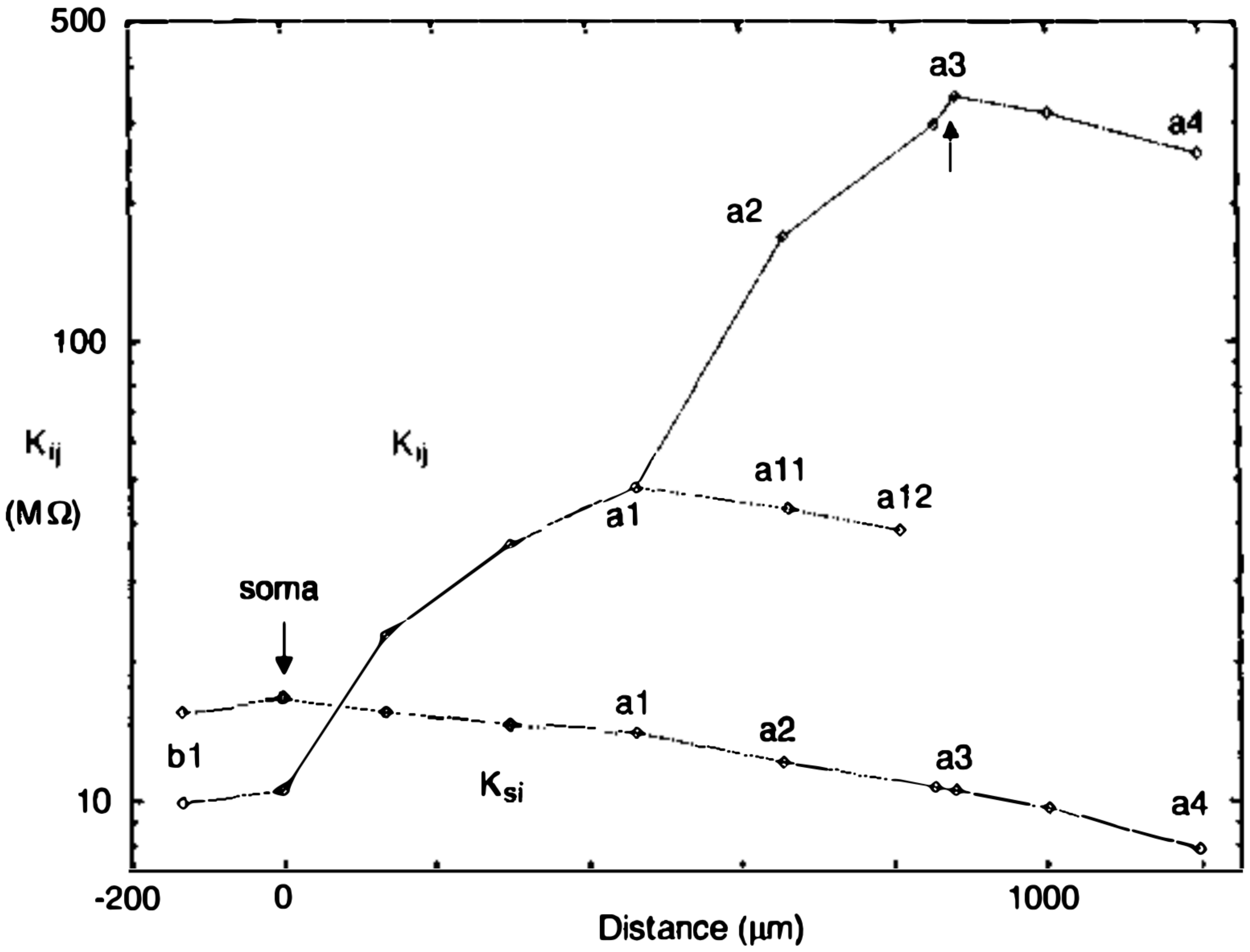
$$K_{ii}(T) = \frac{R_m}{2\pi d\lambda(\pi T)^{1/2}} e^{-T} .$$

Different site - stationary input

$$\tilde{K}_{ij} = \frac{R_\infty}{2} e^{-|i-j|/\lambda}$$

$$R_{\infty,0} = \left(\frac{R_m \cdot R_i}{\pi^2}\right)^{1/2} \frac{2}{d_0^{3/2}} .$$





C. Koch, The Biophysics of Computation 1999

Biophysical computations in segregated dendrites

Passive dendrites

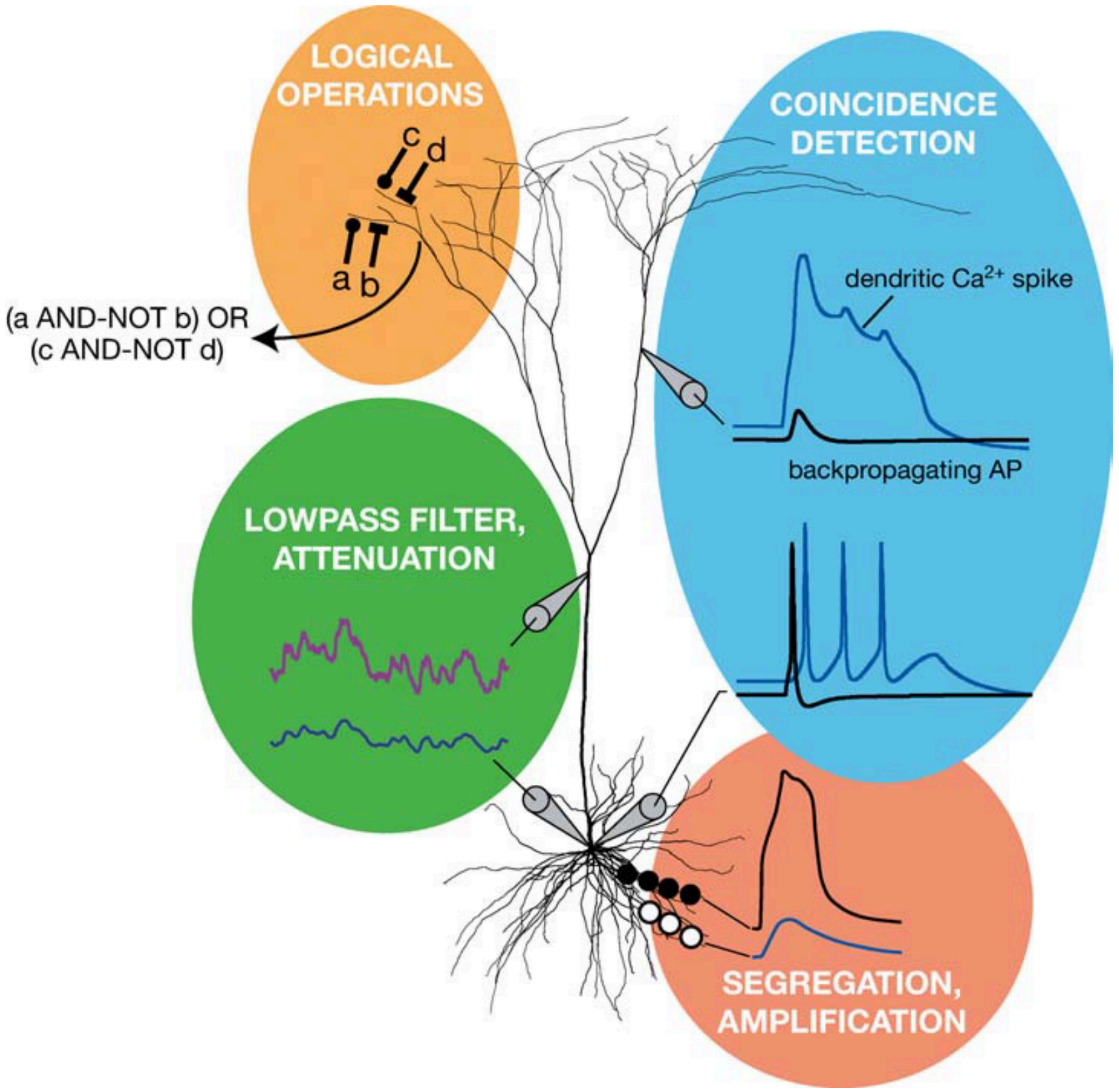
The passive properties of the dendritic tree are the backbone of dendritic computation.

- **Delay lines via dendritic filtering**

  This filtering tends to attenuate the dendritic signal as a function of the distance it travels and the frequency of the original signal.

- **Parallel processing and local computations**

  Spatial proximity leads to a nonlinear interaction between multiple synaptic inputs if they colocalize in time and space.De Dendrites enable the spatial separation of inputs to minimize their interaction.

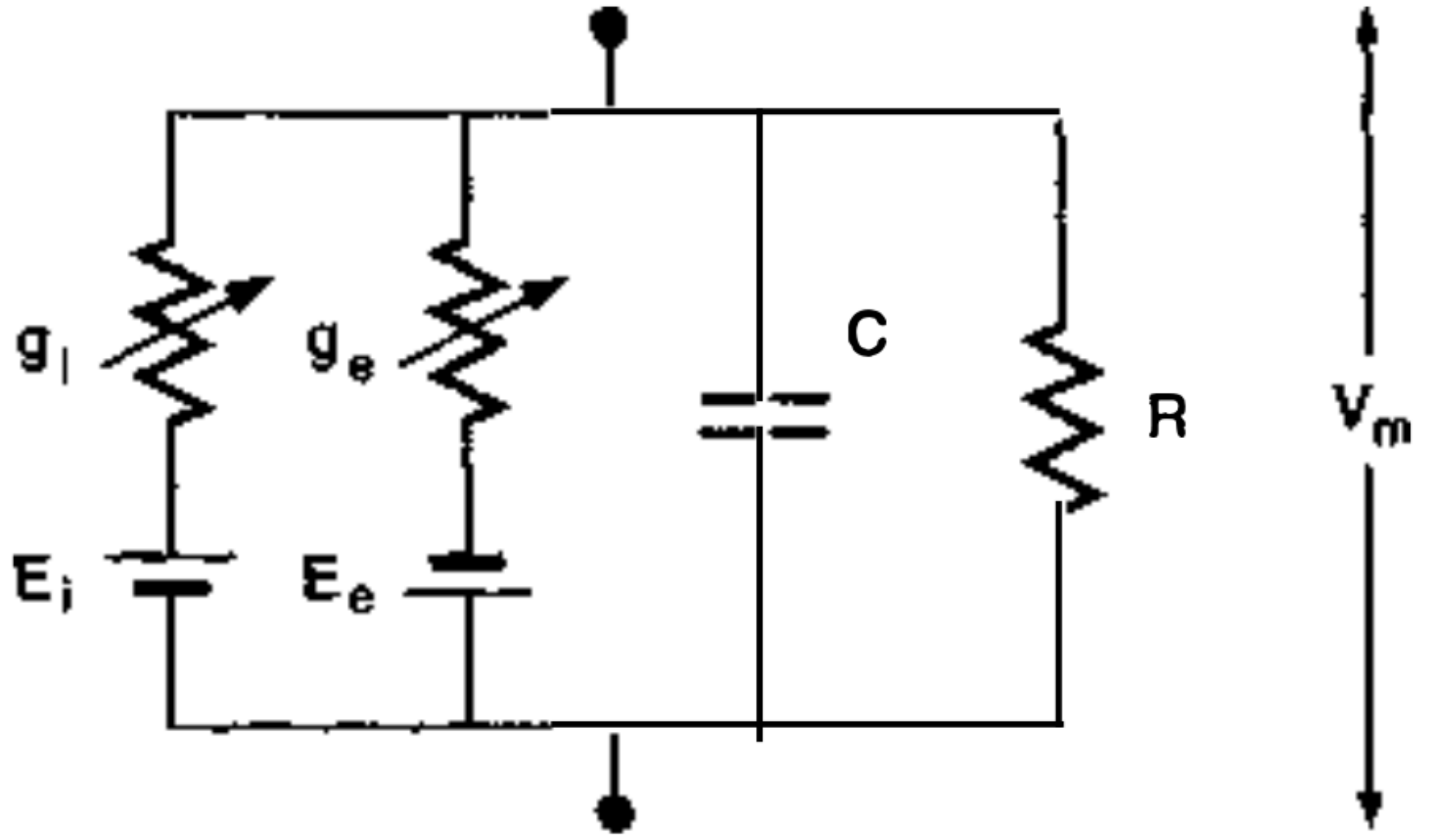


London & Hausser 2005

Synaptic interaction in a passive tree

Shunting inhibition - recall from previous class

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



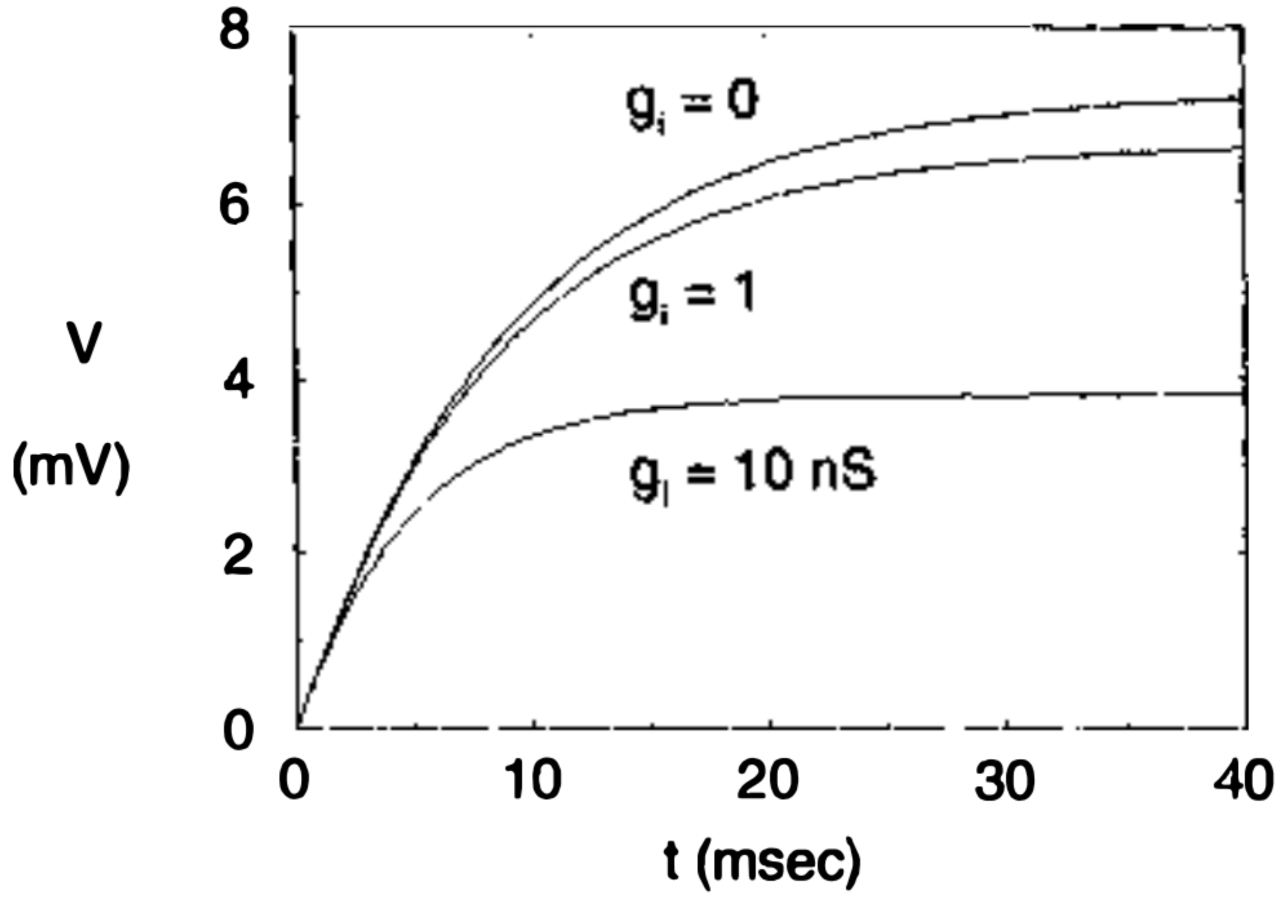
Synaptic input acts to change the membrane conductance.

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

The change in membrane voltage caused by two or more synaptic inputs is not the sum of the voltages induced by the individual synaptic inputs.

A classical effect of this interaction is **shunting inhibition**, where inhibition has a divisive effect on the total input current

$$V_\infty = \frac{g_e R E_e}{1 + g_e R + g_i R} \approx \frac{g_e E_e}{g_i}.$$



C. Koch, The Biophysics of Computation 1999

Synaptic interaction in a passive tree

Shunting inhibition in the dendritic tree

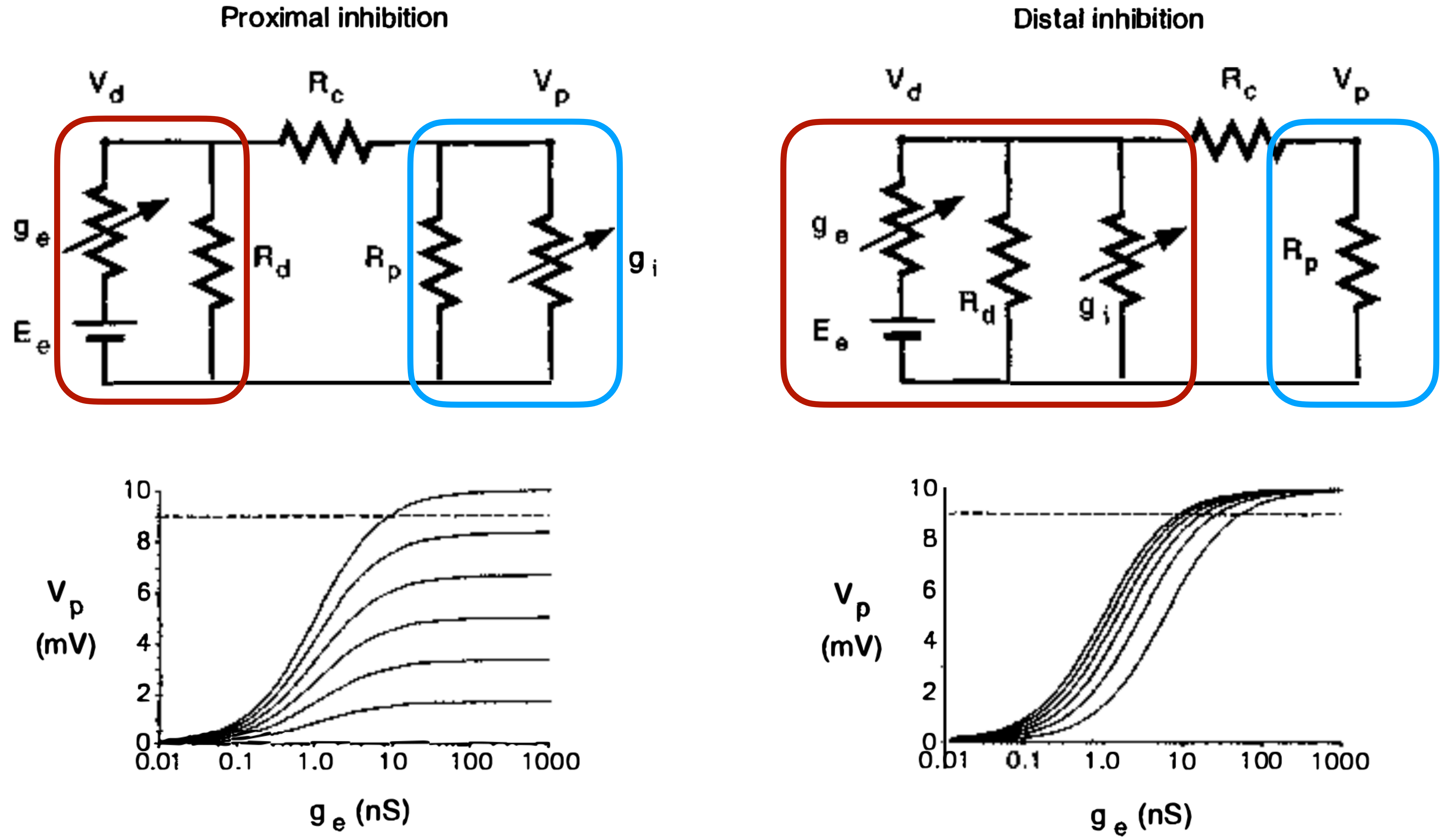
Let’s now consider the case in which the dendrite is a single compartment, attached to the soma.

If excitation is distal and inhibition is proximal, inhibition acts as **absolute suppression.** Independent of the strength of the input:

$$\lim_{g_e \to \infty} V_p = \frac{E_e R_p}{R_p + R_c + g_i R_c R_p} .$$

If excitation and inhibition are both distal, excitation can overcome inhibition, that acts as **relative suppression**

$$\lim_{g_e \to \infty} V_p = \frac{E_e R_p}{R_p + R_c}$$



C. Koch, The Biophysics of Computation 1999

Synaptic interaction in a passive tree

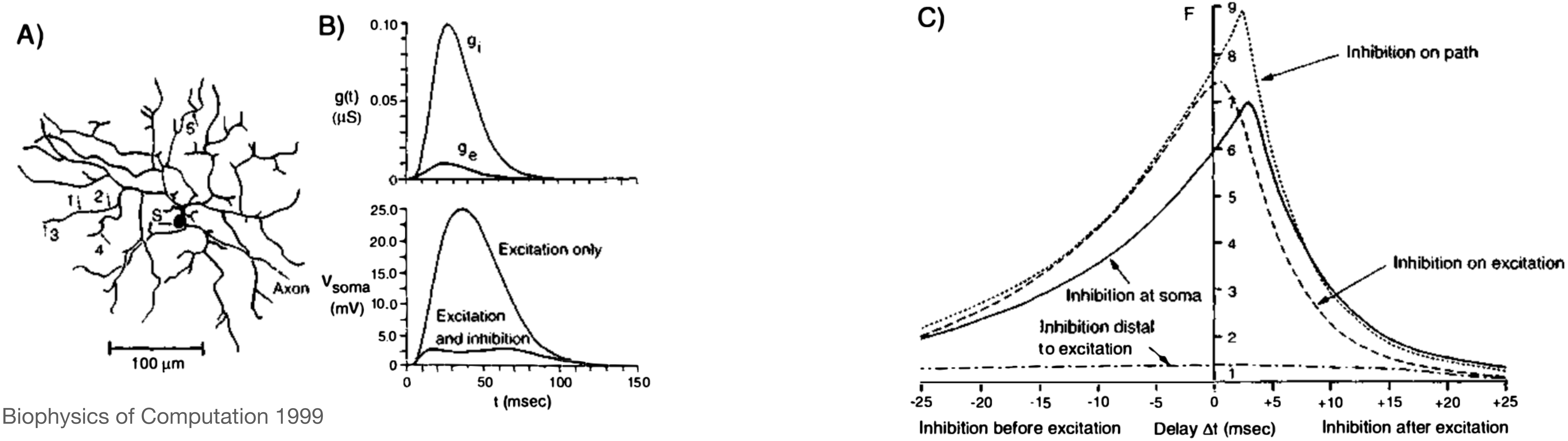
Shunting inhibition in the dendritic tree

This interaction can be generalized to any two points, introducing the F factor as the depolarization diffence inpresence of pure excitation or excitation and inhibition

$$F = \frac{g_e \tilde{K}_{es}}{1 + g_e \tilde{K}_{ee}} \cdot \frac{1 + g_e \tilde{K}_{ee} + g_i \tilde{K}_{ii} + g_e g_i \tilde{K}^*}{g_e \tilde{K}_{es} + g_e g_i \tilde{K}_e^+}$$

$$\tilde{K}_e^+ = \tilde{K}_{es} \tilde{K}_{ii} - \tilde{K}_{is} \tilde{K}_{ie}$$

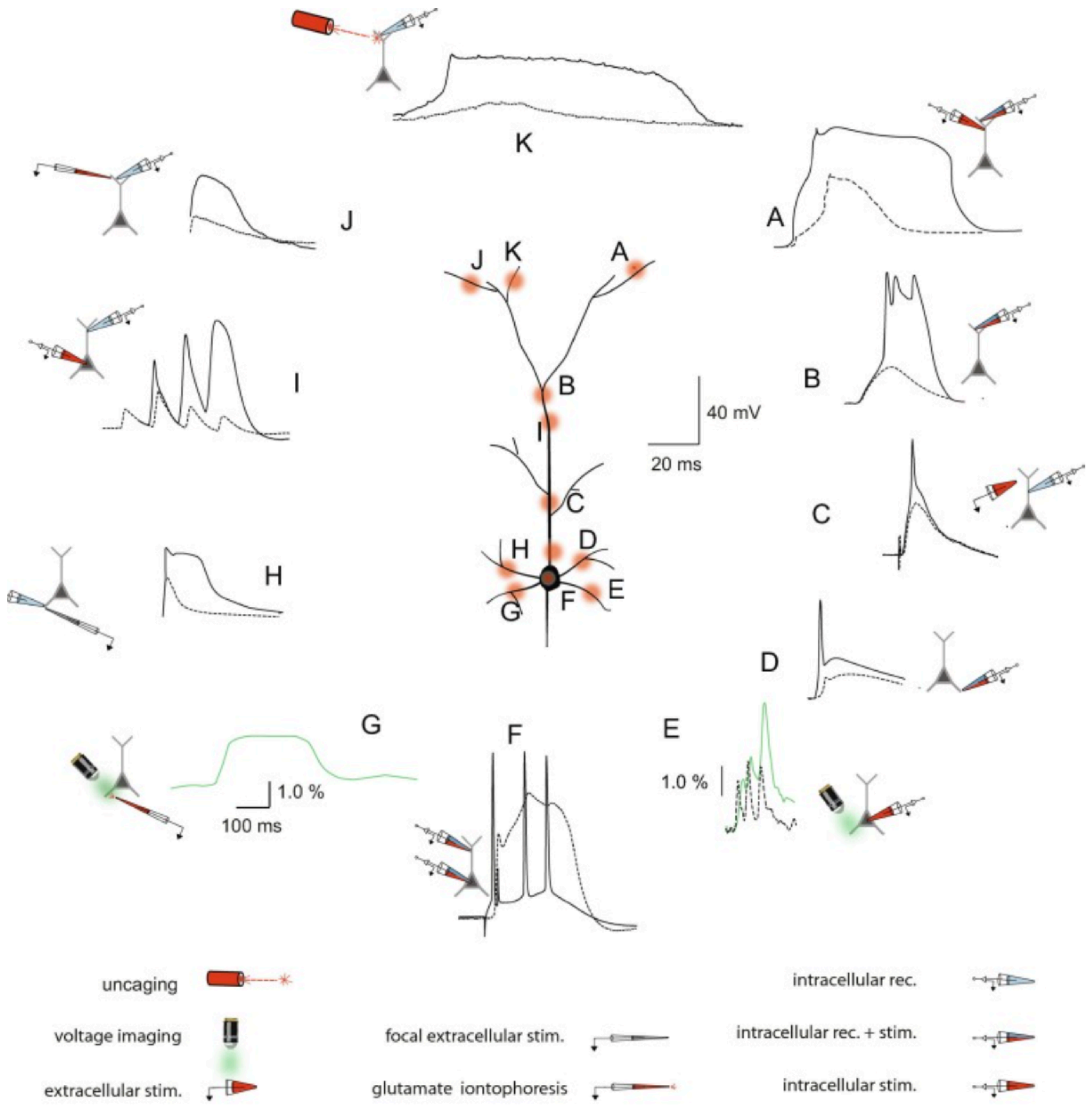
$$\tilde{K}^* = \tilde{K}_{ee} \tilde{K}_{ii} - \tilde{K}_{ie}^2$$



C. Koch, The Biophysics of Computation 1999

Non linear integration and dendritic spikes

Dendritic spikes in pyramidal cells



Dendrites exhibits voltage-dependent non-linear responses

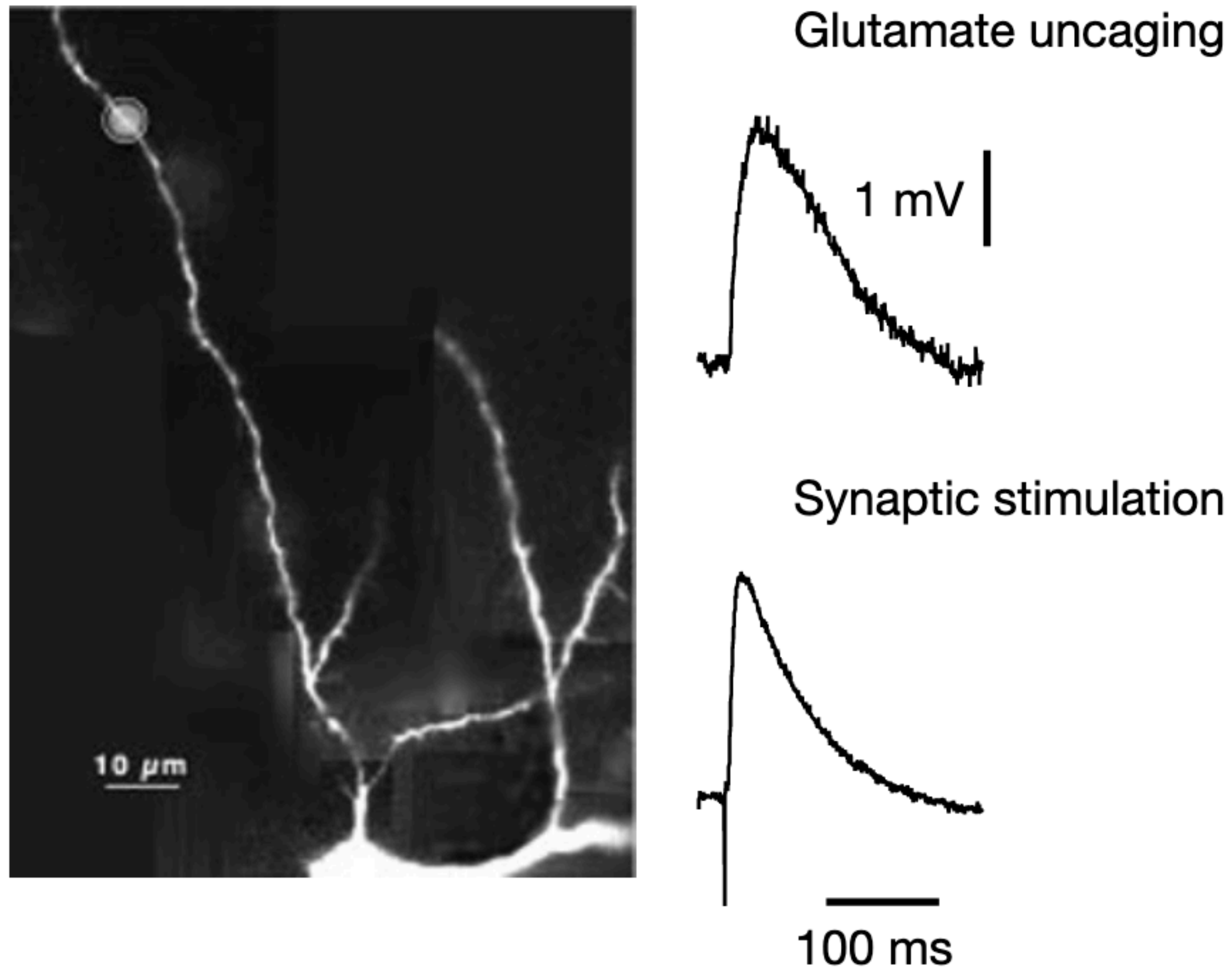
The different classes of dendritic spikes vary significantly in duration, lasting between about a millisecond and hundreds of milliseconds:

- **Intrinsic spikes** are triggered when the dendritic membrane crosses a voltage threshold. These include: Na+ spikes/ spikelets, Ca2+ spikes, low–threshold spikes (LTS), and Ca2+ plateau-potentials.
- **Synaptic spikes** consist of NMDA spikes and plateau potentials, and NMDAR-dependent Ca2+ spikes.

Larkum et al. 2002

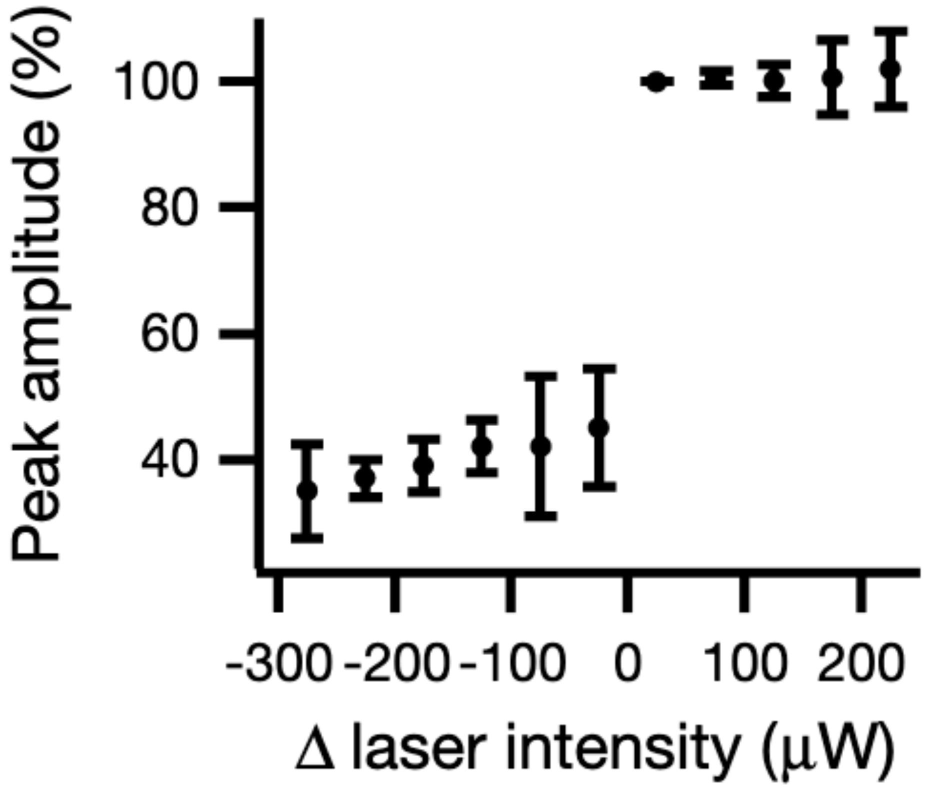
Non linear integration and dendritic spikes

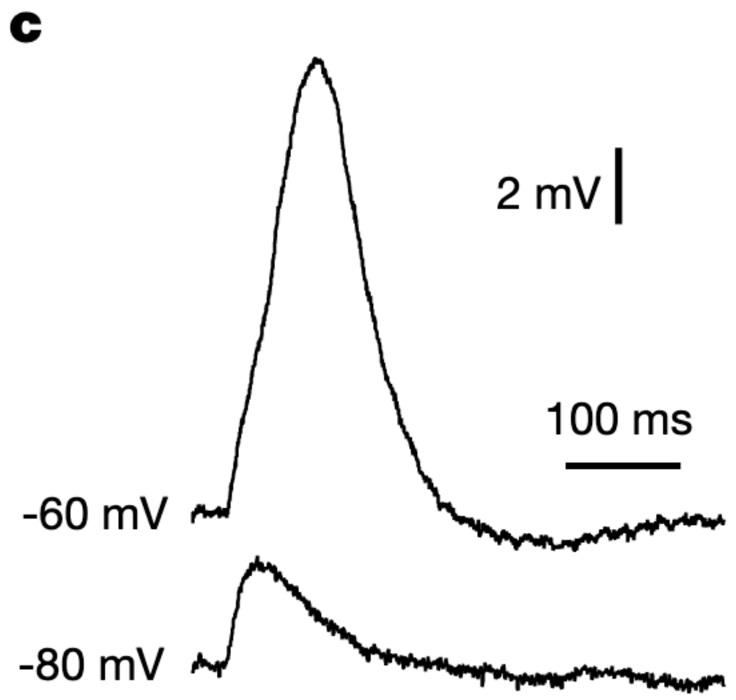
Voltage-dependent NMDA receptors lead to dendritic Calcium spikes



Experiment with glutamate uncaging and laser stimulation shows:

- Coactivation of clustered neighbouring basal inputs initiated local dendritic spikes;
- Results in ~6 mV (peak) and ~70 ms (half-width) voltage change at the soma, amplifying the somatic voltage response by 226%;
- The voltage threshold and all-or-none nature of the response indicated the initiation of local dendritic spikes;



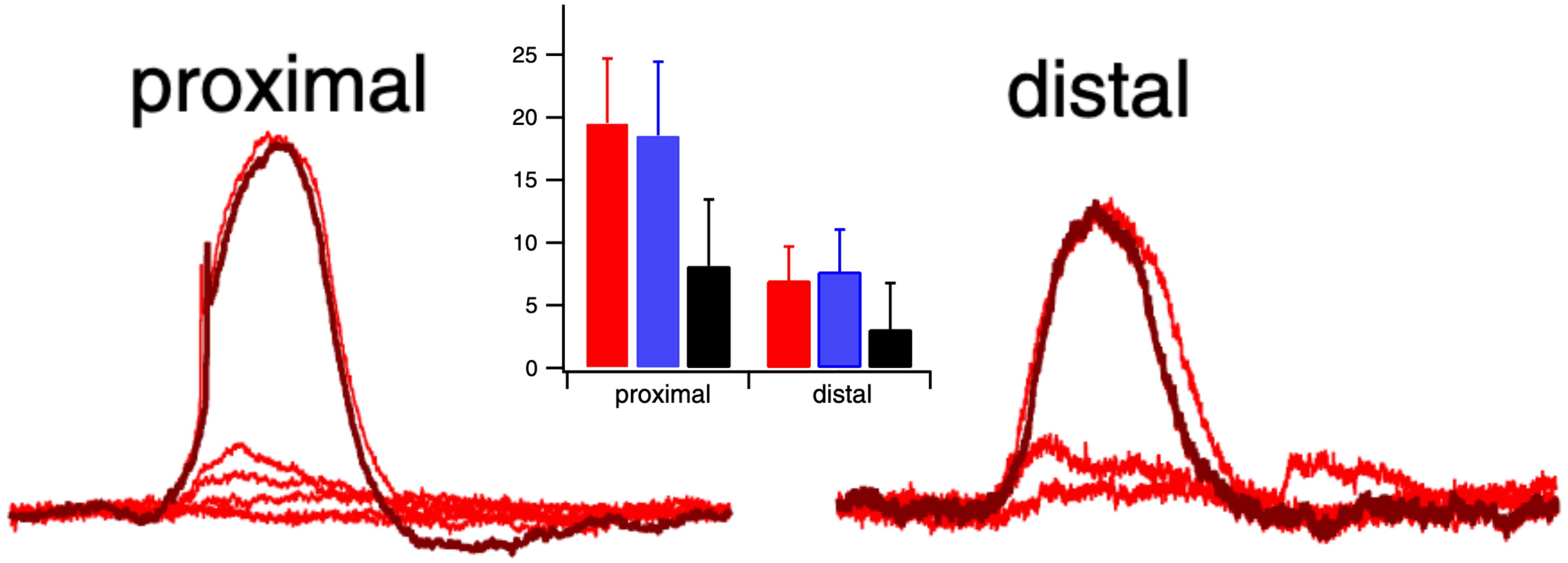


These spikes were mediated mostly by **NMDA (N-methyl-D-aspartate)** receptor channels, which contributed at least 80% of the total charge.

Schiller et al. 2000

Spatiotemporally Graded NMDA Spike/Plateau

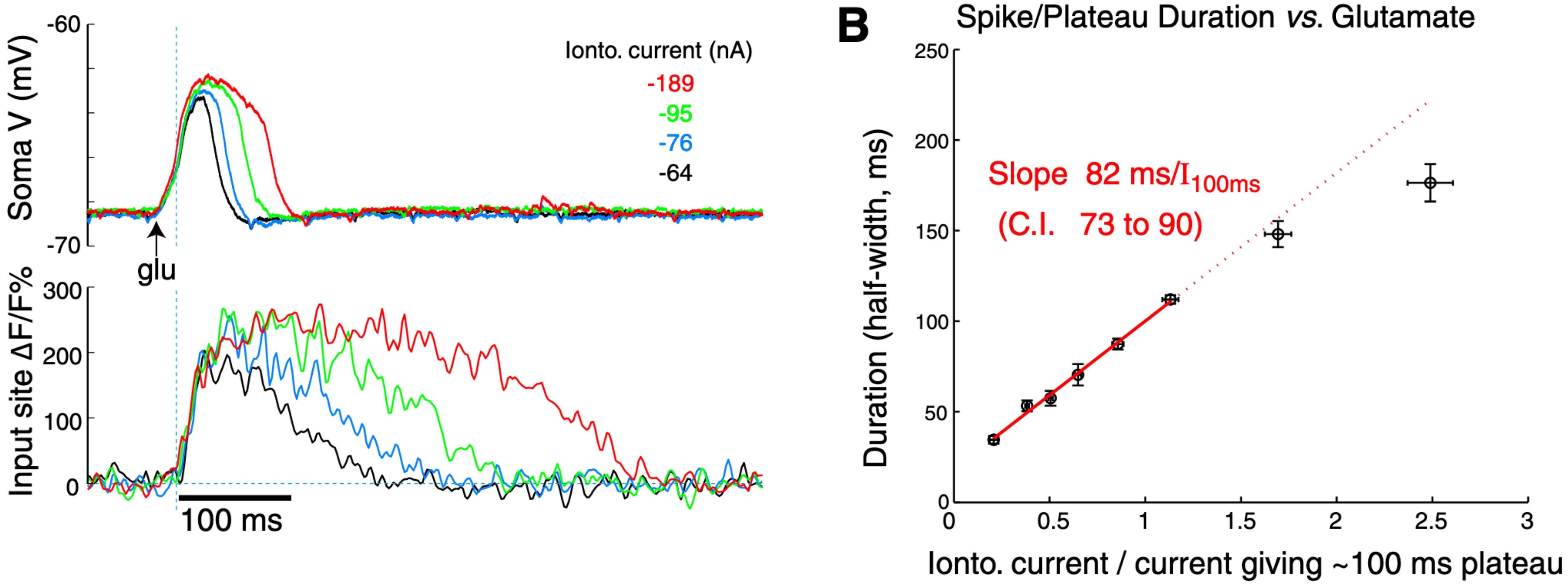
NMDA amplitude and duration depends on input location and strength



There is an 7x spatial gradient in average spike/plateau amplitude measured at the soma.

The threshold for NMDA spike grows from distal to proximal.

Spike/plateau duration grew with increasing glutamate and depolarization; high Ca2 zone size grew with spike/plateau duration.



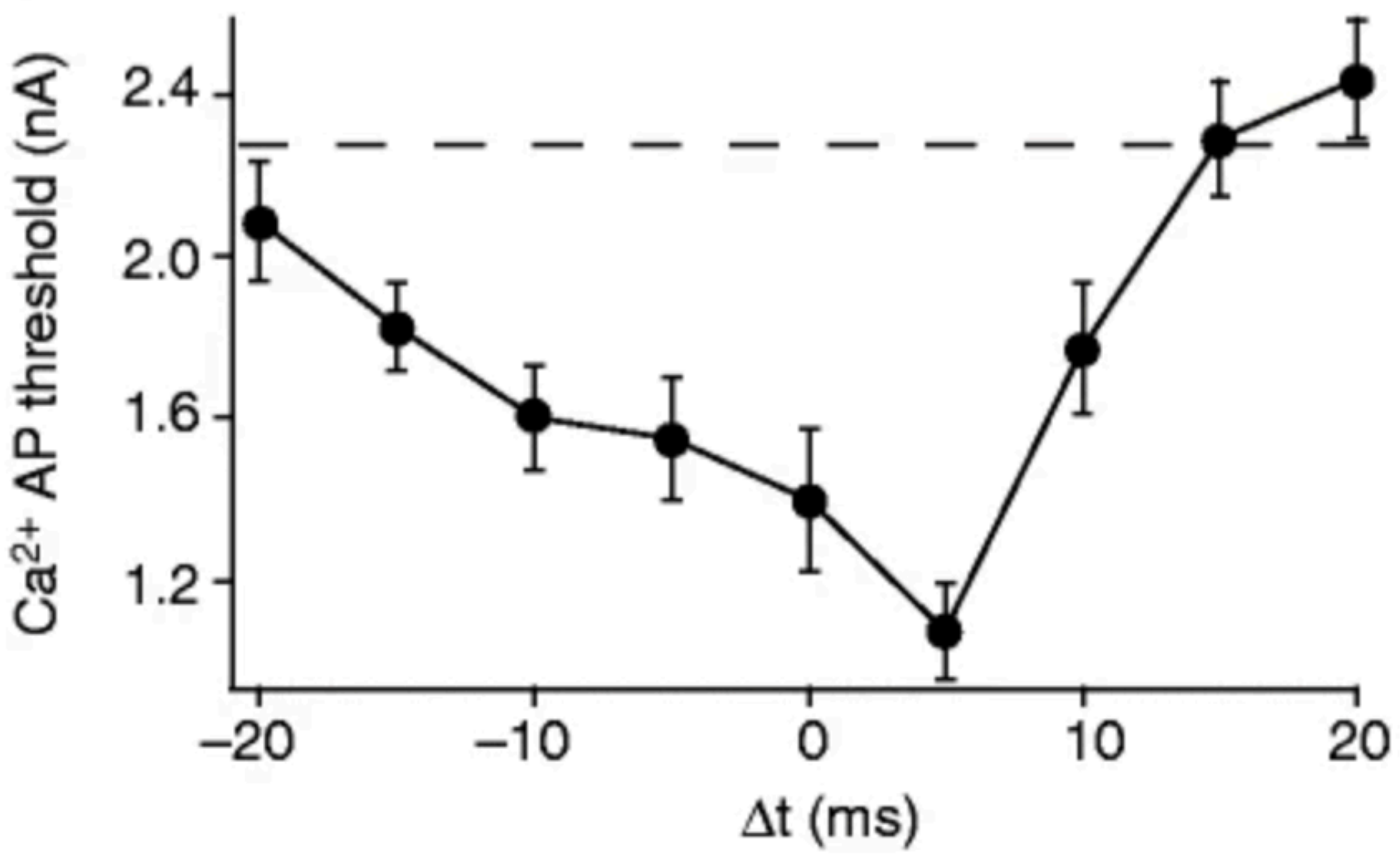
Major et al. 2008

Back-propagating action potential

A cellular mechanism for coupling inputs arriving at different cortical layers

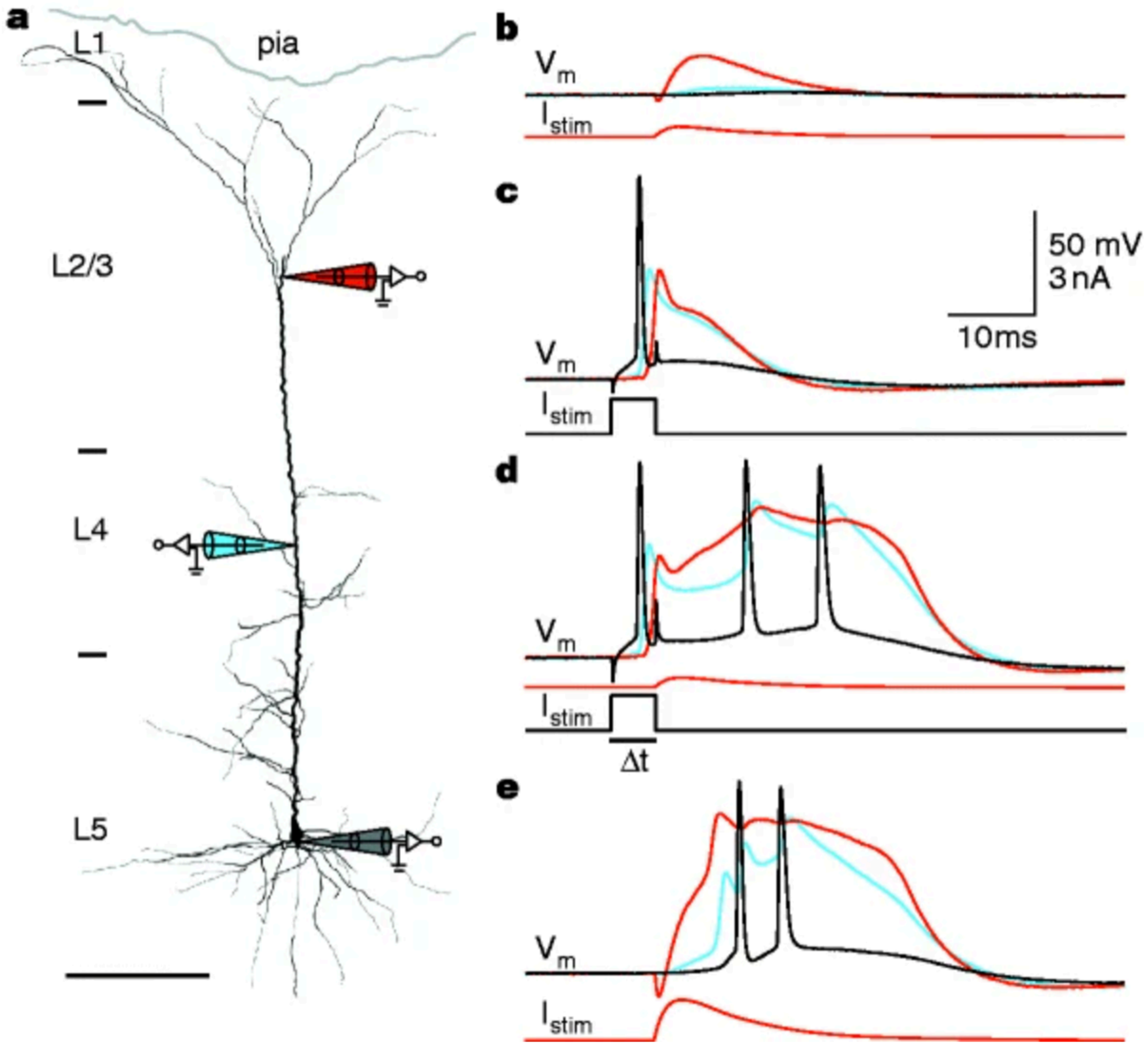
Distal dendritic inputs must cross a high threshold at the dendritic initiation zone to evoke calcium action potentials

They can then generate bursts of axonal action potential when they coincide with back-propagating sodium action potential generated in the axon.



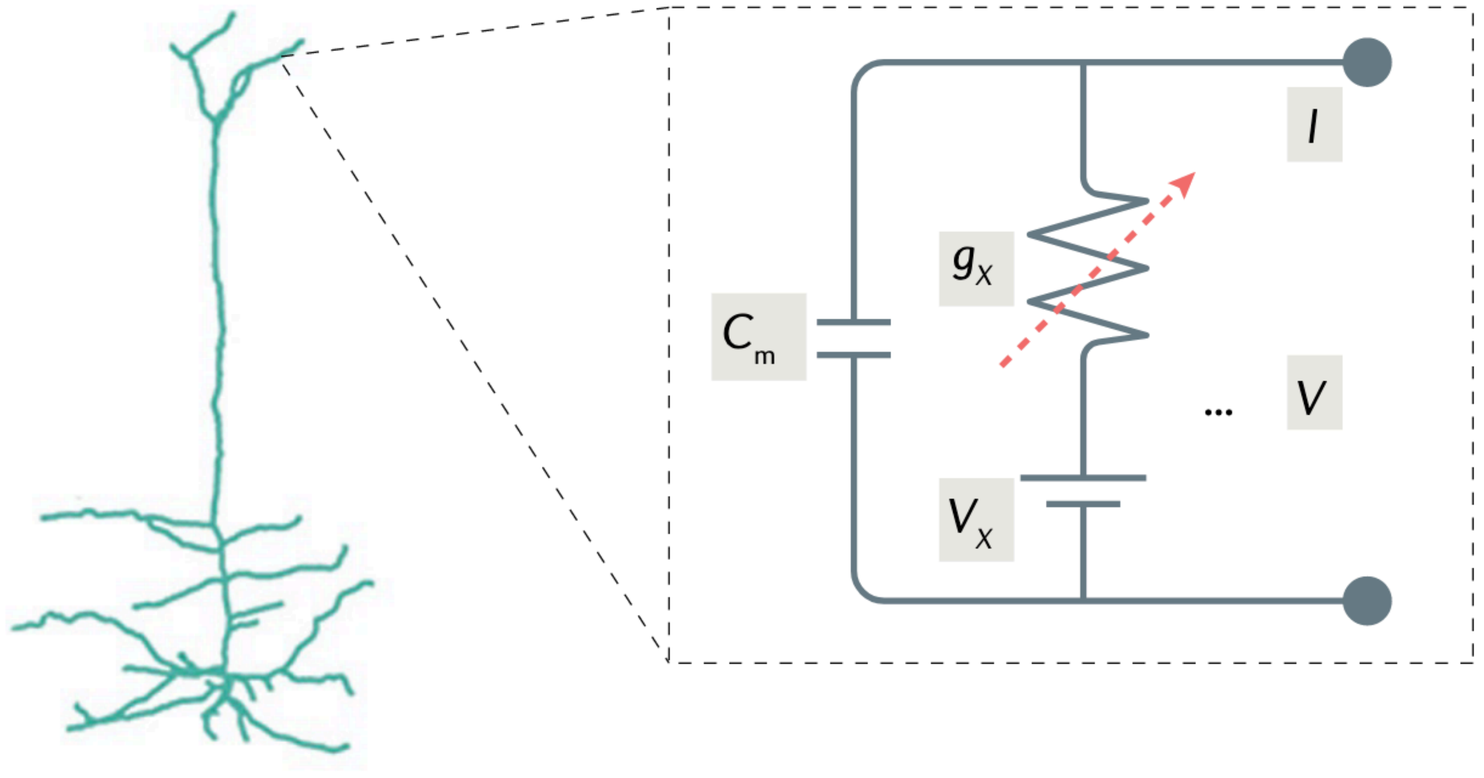
Larkum 1999

Precision of timing is required, the distal Ca+ spikes and the bAP must occur within ~10-30ms



Computational models of dendrites

Illumination dendritic function with simulations



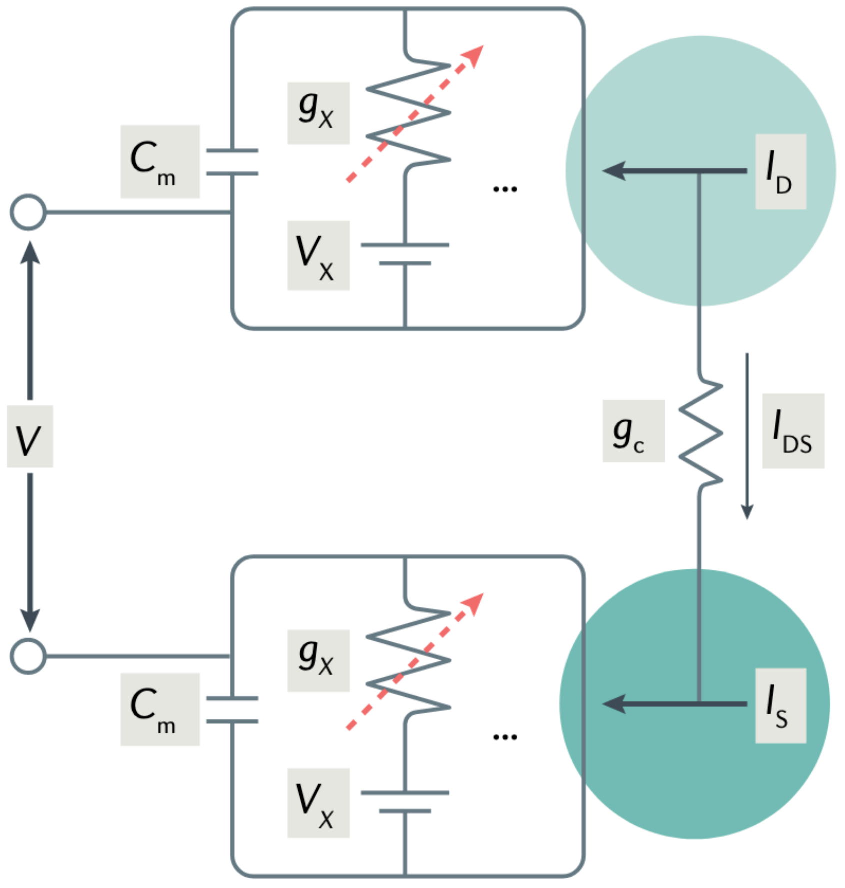
Multi-compartmental model

Reduced models allow for embedding the neuron in **neuronal microcircuits** and testing their **computational properties**

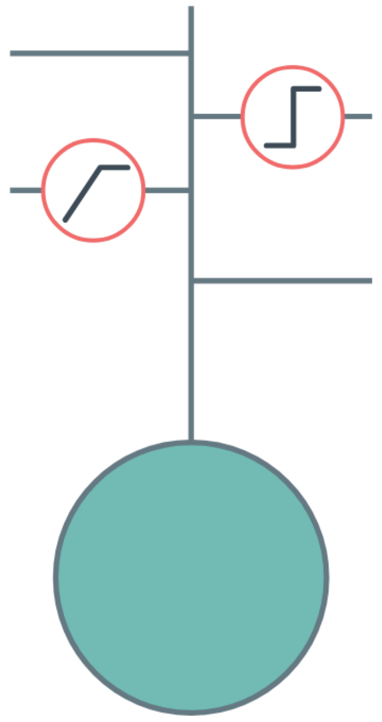
SST+ interneurons inhibit the apical dendrites of pyramidal neurons.
PV+ interneurons target the perisomatic regions of pyramidal neurons

There is no single answer to the quest of finding the ‘best model’.

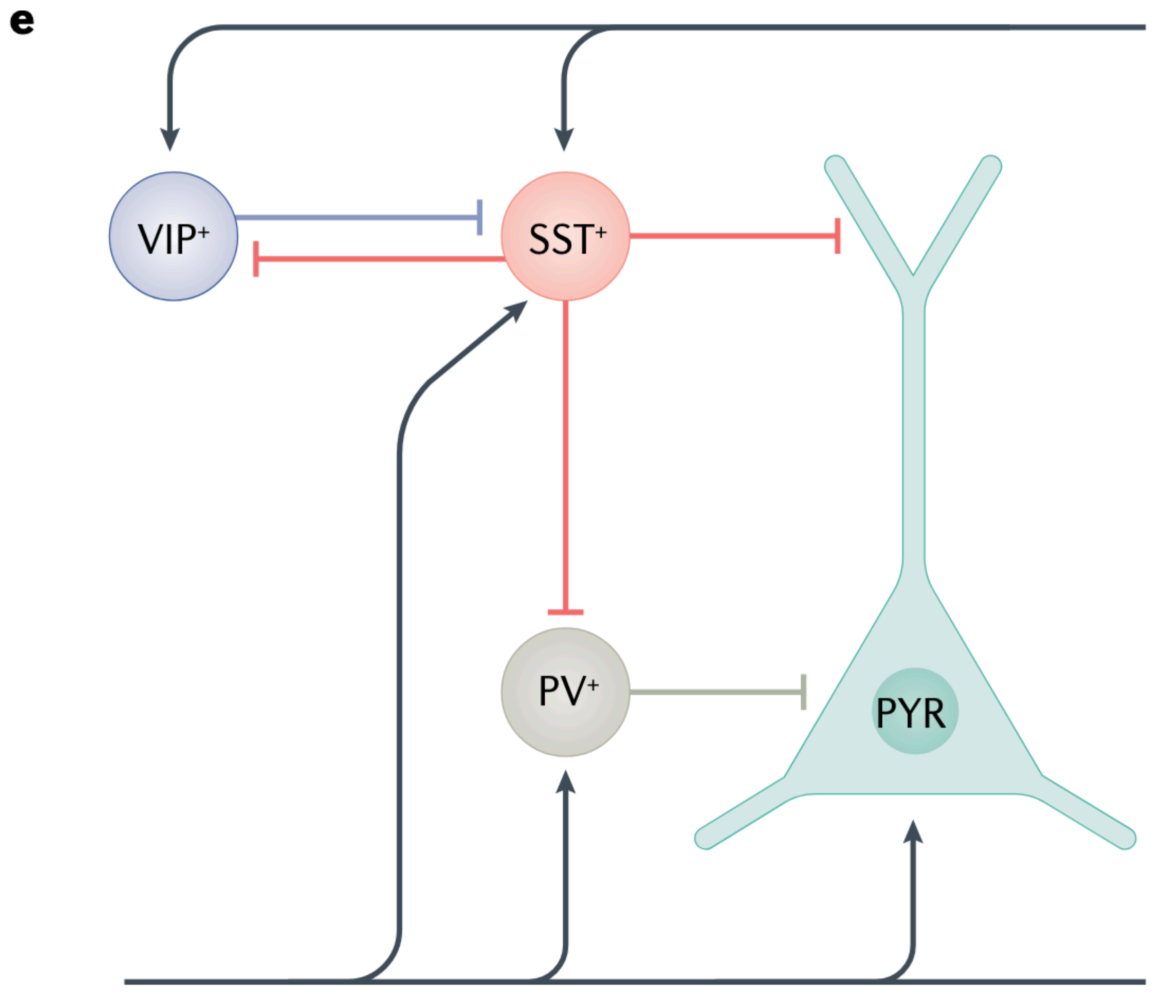
Single-neuron models with multiple-compartment dendrites can be used to assess **the effects of dendritic morphology, biophysics, and plasticity on neuronal output.**



Two-compartment model



Two-stage integrate-and-fire model

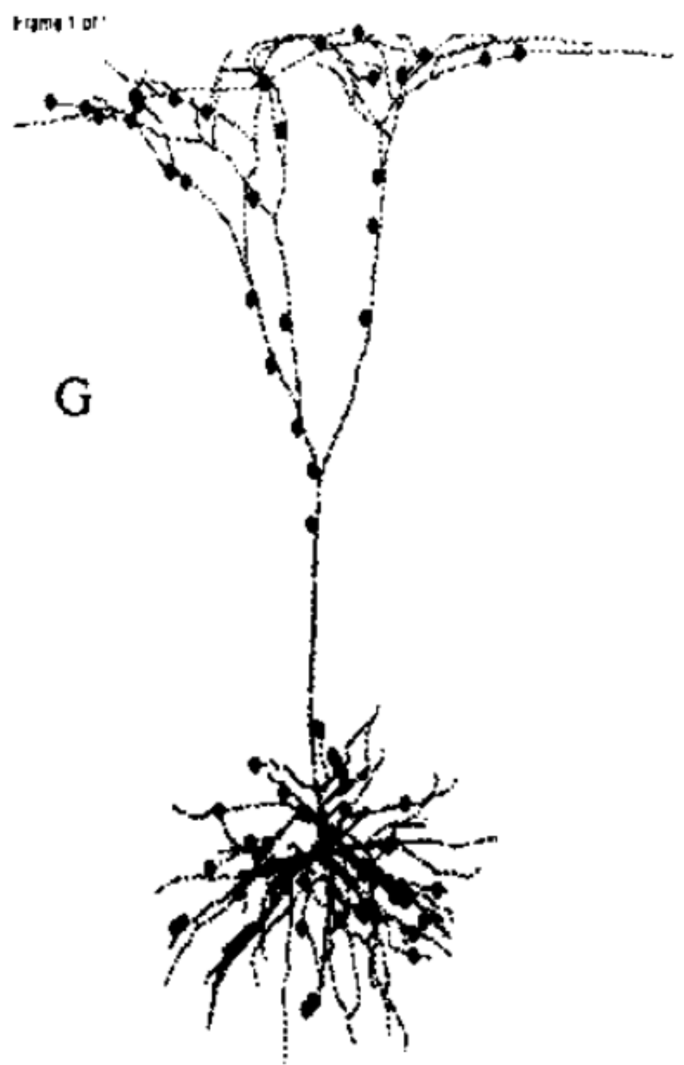


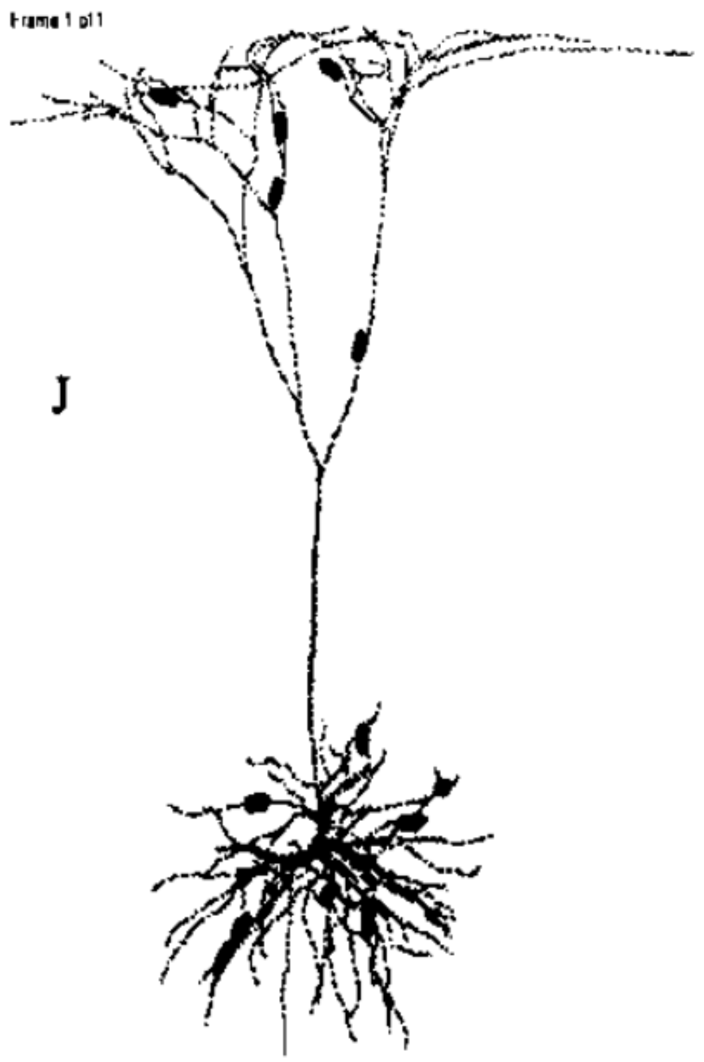
Few-compartment model

Poirazi & Papoutsi 2020

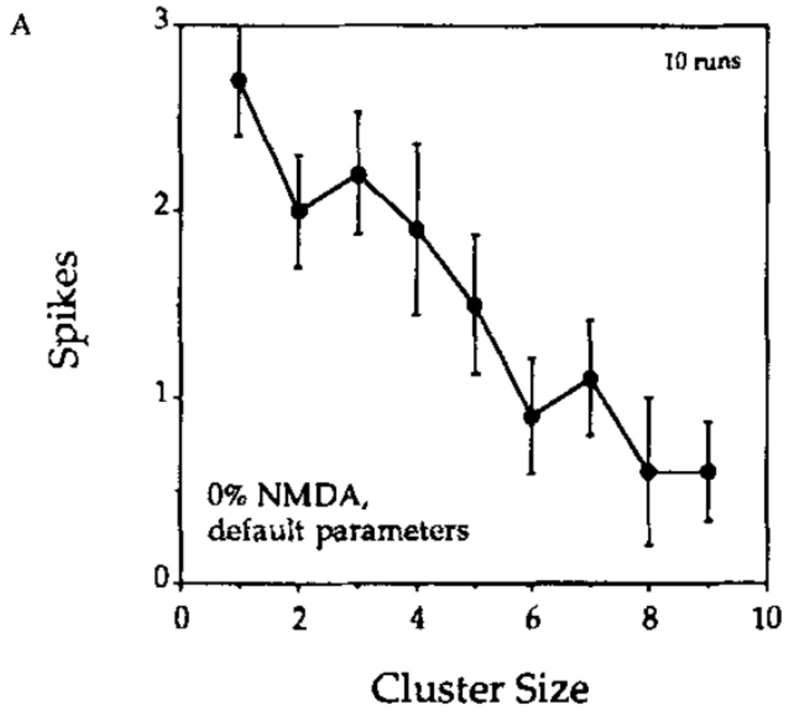
Realistic models of the dendritic tree

Precise synaptic locations and clustering predict NMDA *advantage*

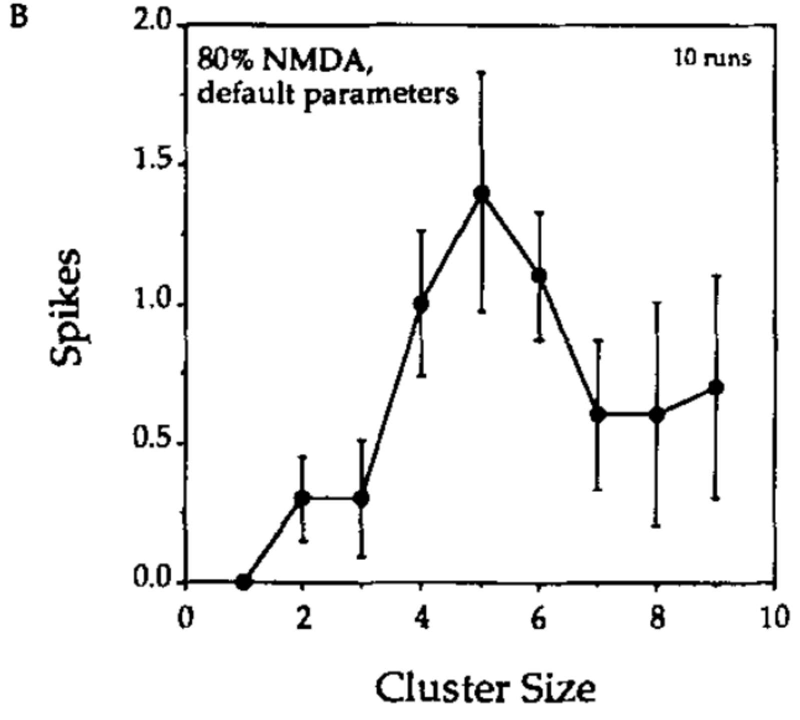




AMPA



NMDA



Multiplicative interactions among groups of neighboring synapses greatly enhance the processing power of a neuron.

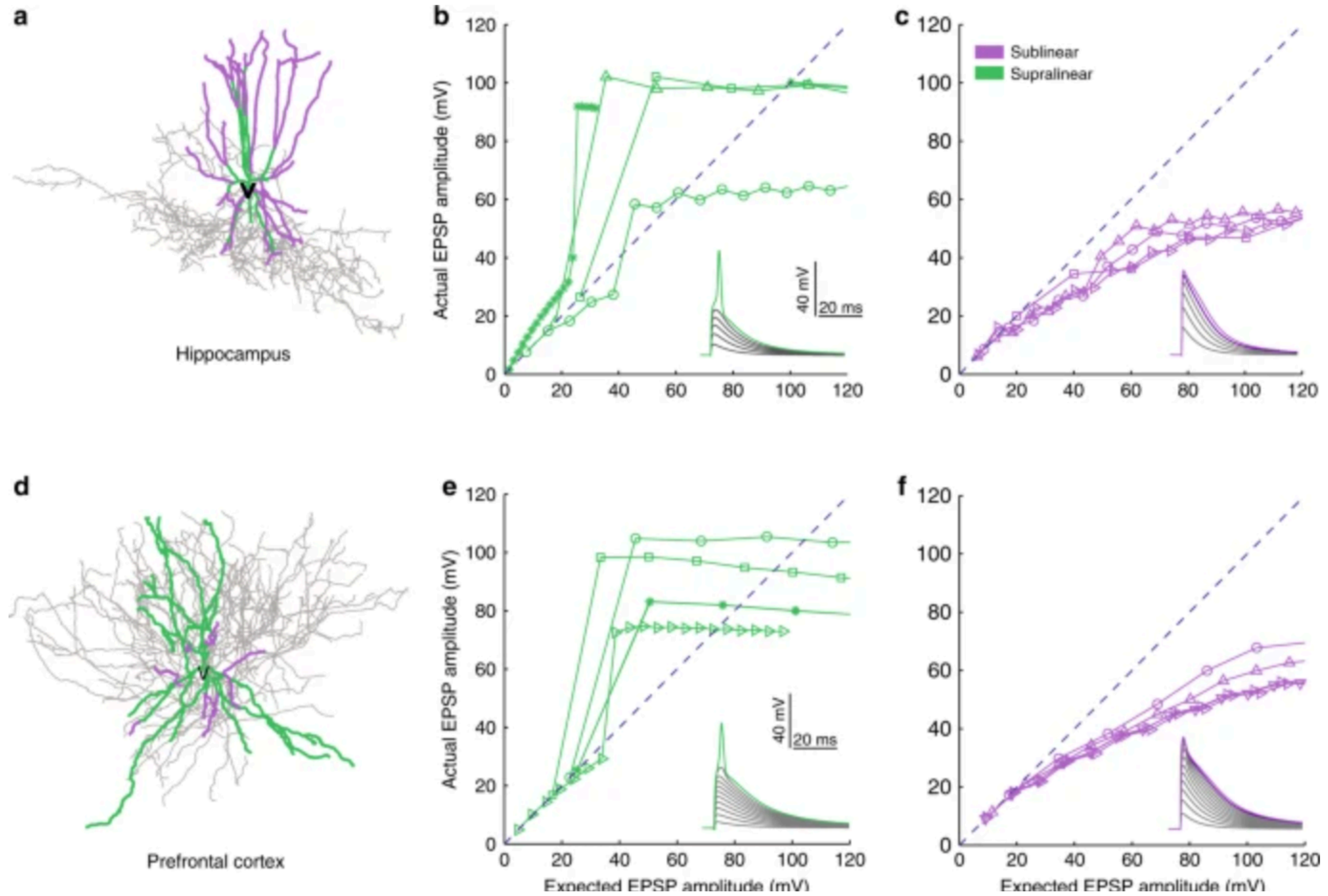
1. Large proportion of the excitatory synaptic input to dendritic spines is carried by NMDA channels
2. the pyramidal cell responds preferentially to spatially clustered, rather than random, distributions of activated synapses.
3. Second, based on this mechanism, the NMDA-rich neuron is shown to be capable of solving a nonlinear pattern discrimination task.

The spatial ordering of afferent synaptic connections onto the dendritic arbor is a possible biological strategy for pattern information storage during learning.

Mel & Poirazi 1992

Realistic models of the dendritic tree

Non-linear integration in interneurons

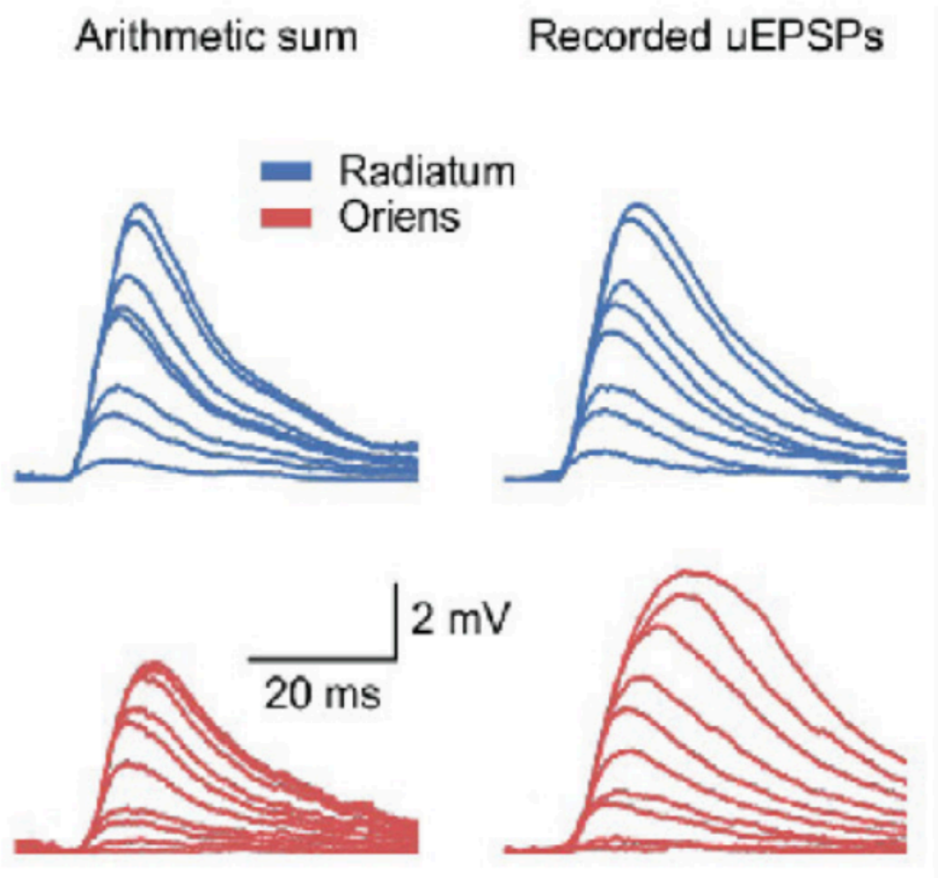


Experimental results:

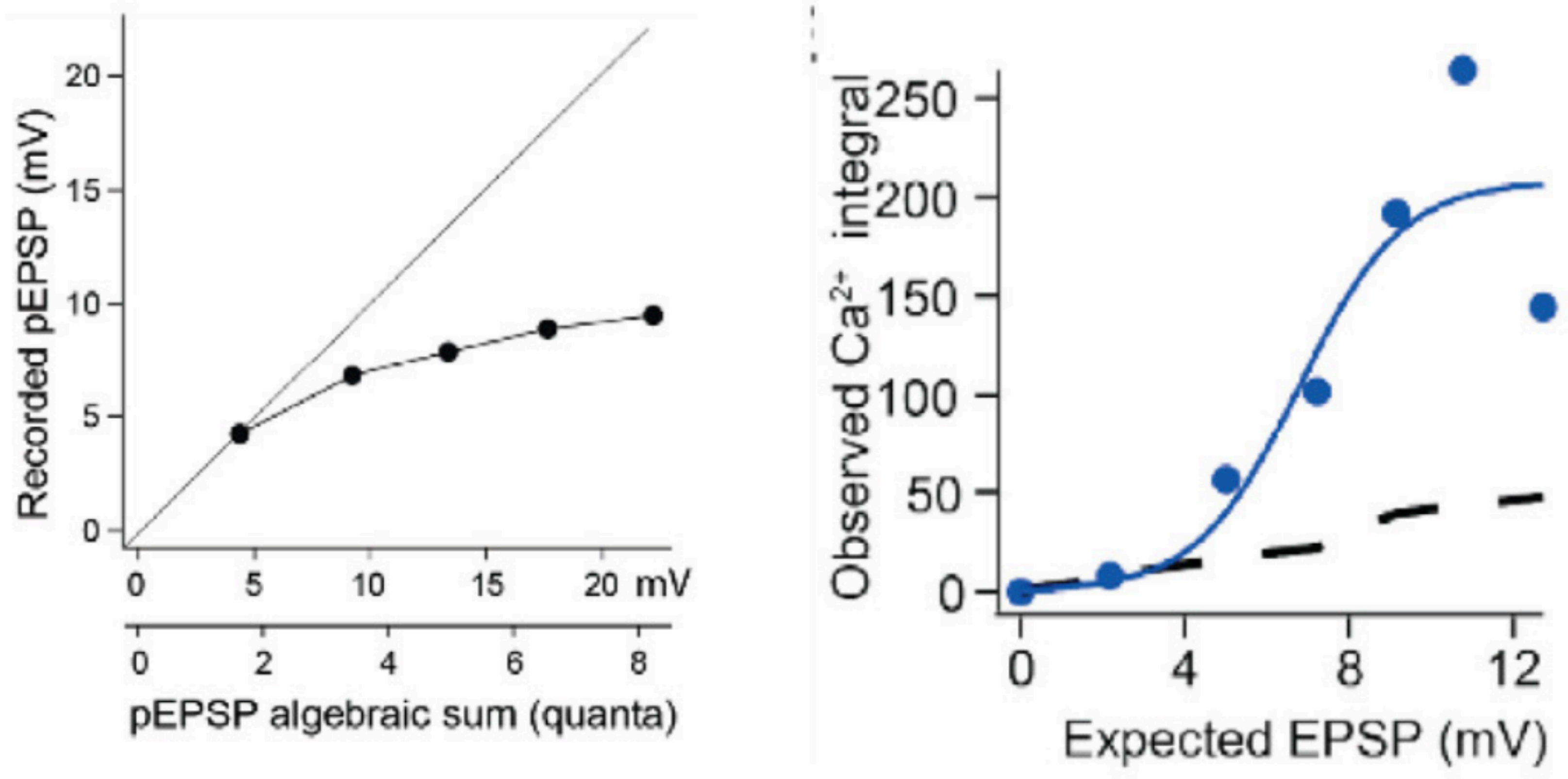
- *CA1 PV+ INs have two types of dendrites: supralinear and linear.*
- *Cerebellar have sublinear EPSP summation but supralinear calcium accumulation.*

Different modes of synaptic integration can also coexist within the same dendritic tree.

Computational modelling predicts that dendrites of both cortical and hippocampal Fast Spiking Basket Cells operate in one of two modes: supralinear or sublinear.



CA1 str. radiatum and oriens PV



Cerebellar Interneurons (Stellate Cells)

Tzilivaki et al. 2022

How many compartments?

A few non-linear compartments are enough

Synaptic bombardment smooths the effect of dendritic non-linearity

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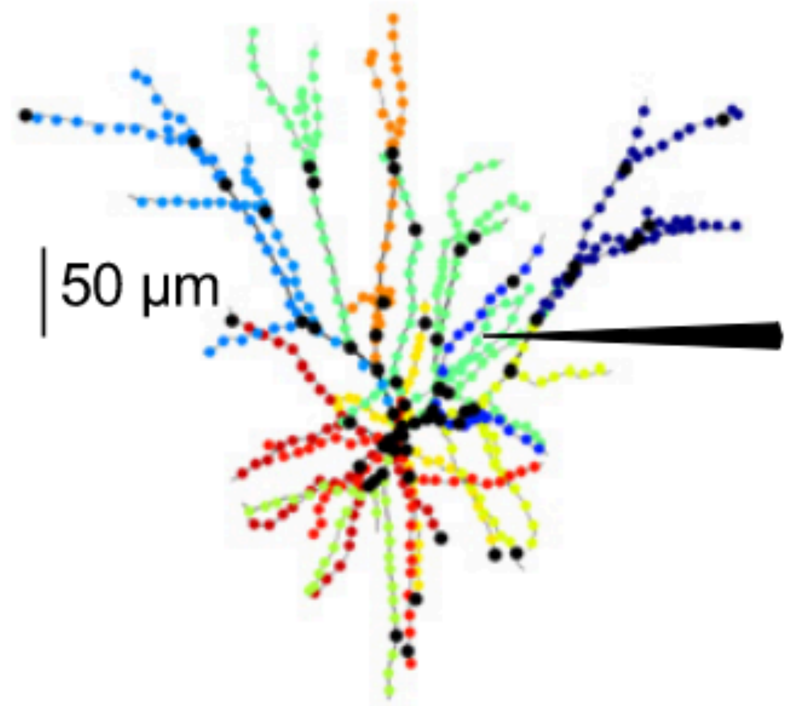

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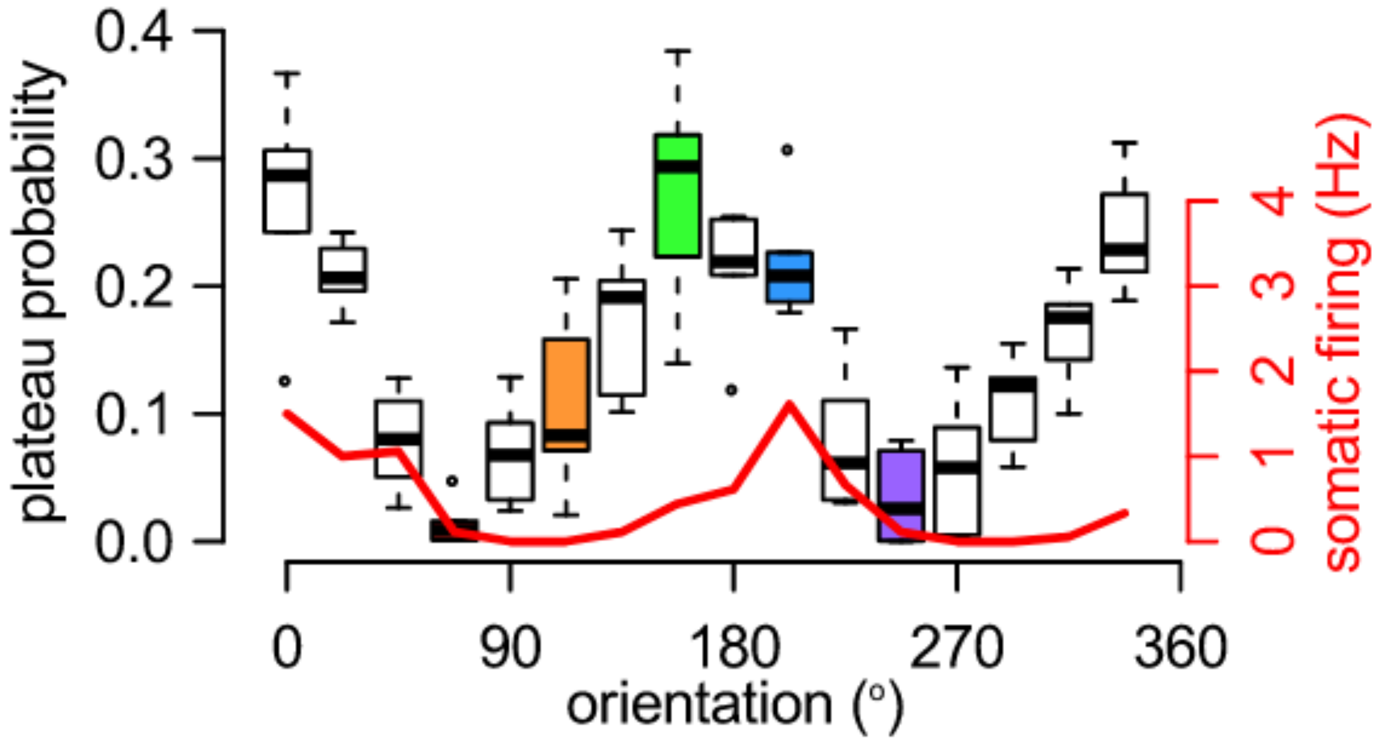
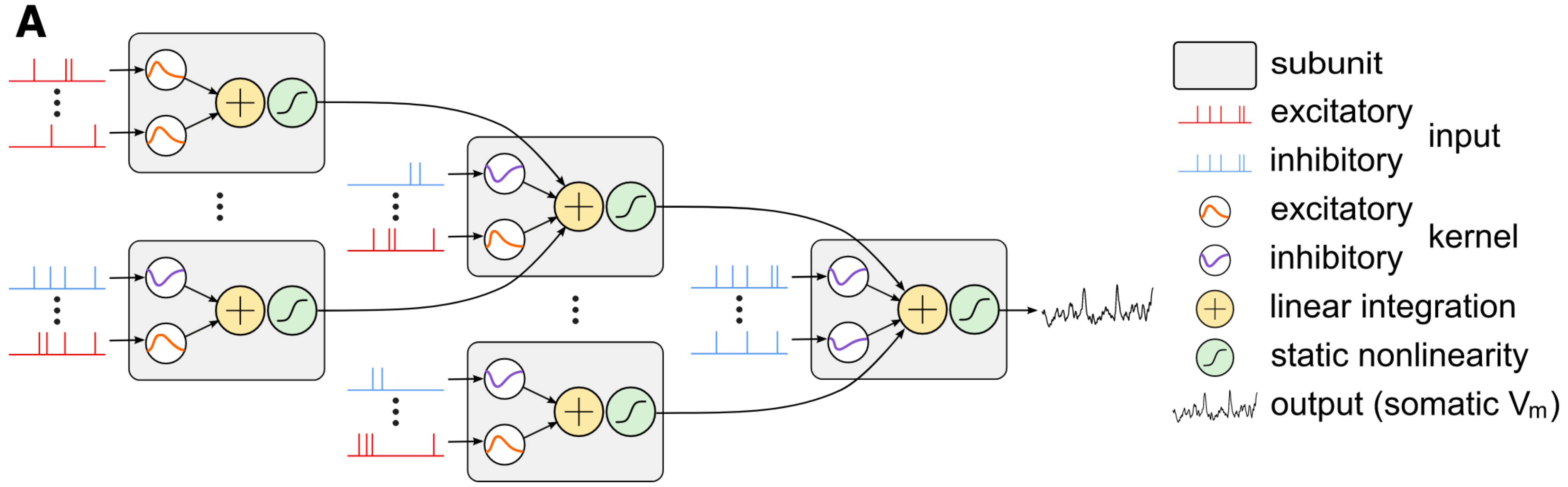
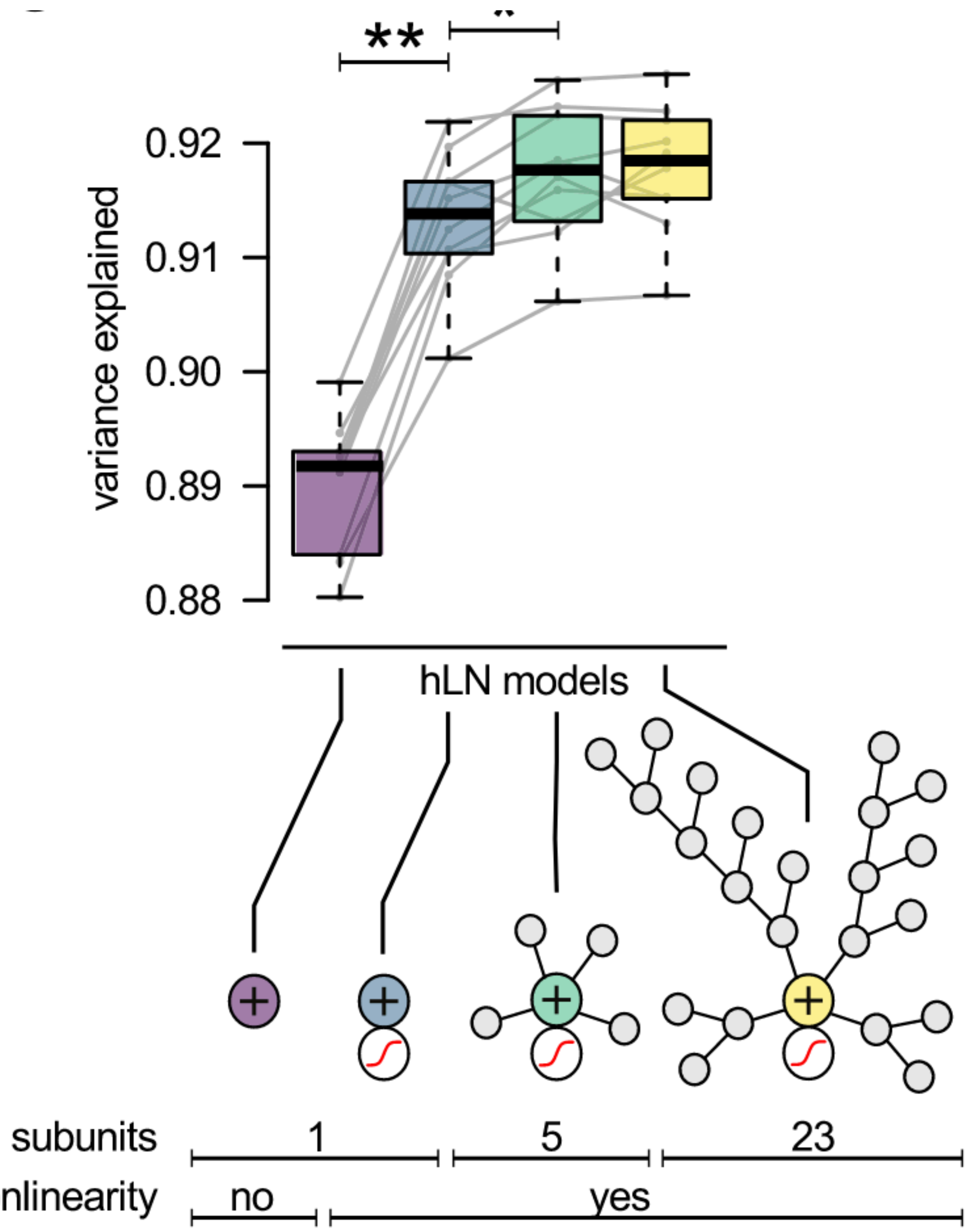


- Fit realistic neuron models to realistic inputs.
- Systematic reduction with hierarchical Linear-NonLinear units.
- Comparison of models with many or few units.

A

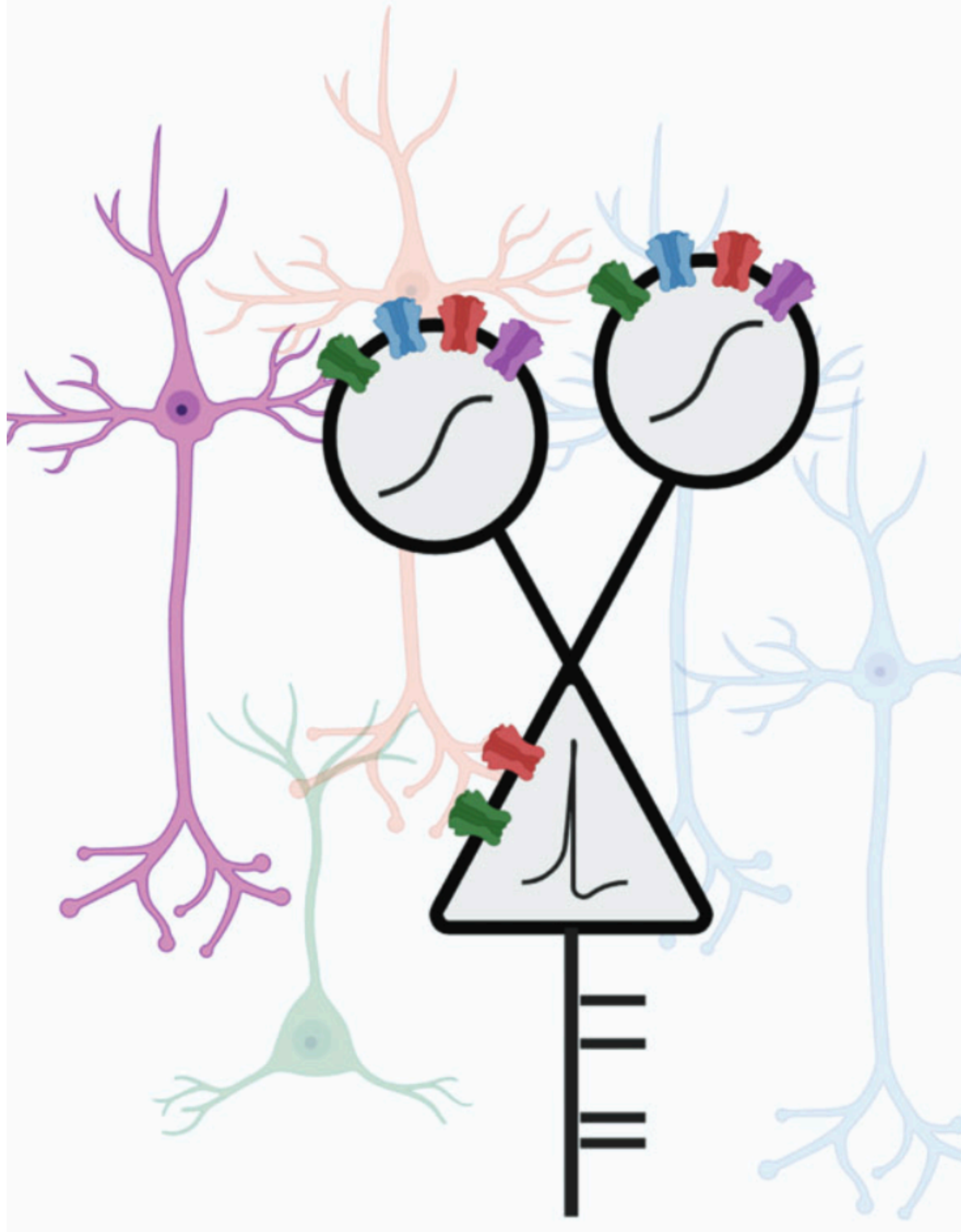




Ujfalussy et al 2018

Reduced models of the dendritic tree

Few compartment models are composed of small sets of equations



The Tripod neuron

Segregated dendrites with realistic physiology and geometries from human cells

Gabaergic (GABA$_A$, GABA$_B$) and glutamatergic (AMPA, NMDA) receptors

Adaptive exponential axosomatic compartment

Quaresima, Fitz, et al. 2022

Soma compartment

$$\tau_m \frac{d}{dt} V_i(t) = -(V_i - V_r) + \Delta_T \exp\left(\frac{V_i - \theta}{\Delta_T}\right) + R\, I_\mathrm{d}$$

Dendrite compartments

$$C_\mathrm{m}^\mathrm{d} \frac{dV^\mathrm{d}}{dt} = -g_\mathrm{m}^\mathrm{d}(V^\mathrm{d} - V_\mathrm{r}) - \sum_k g_k(t)(V^\mathrm{d} - E_k) - I_\mathrm{d} \tag{3}$$

$$I_\mathrm{d} = g_\mathrm{ax}^\mathrm{d}(V^\mathrm{d} - V^s) \tag{4}$$

Synaptic conductance

$$g_k(t) = \bar{g}_k^\mathrm{syn} \mathcal{N}_k \left(\exp\left(-\frac{t - t_0}{\tau_k^r}\right) - \exp\left(-\frac{t - t_0}{\tau_k^\mathrm{d}}\right) \right)$$

$$g_\mathrm{NMDA} = \bar{g}_\mathrm{NMDA}^\mathrm{syn} G(v)$$

$$G(v) = \left(1 + \frac{C}{3.57\,\mu\mathrm{mol/L}} \cdot e^{-\gamma v}\right)^{-1}$$

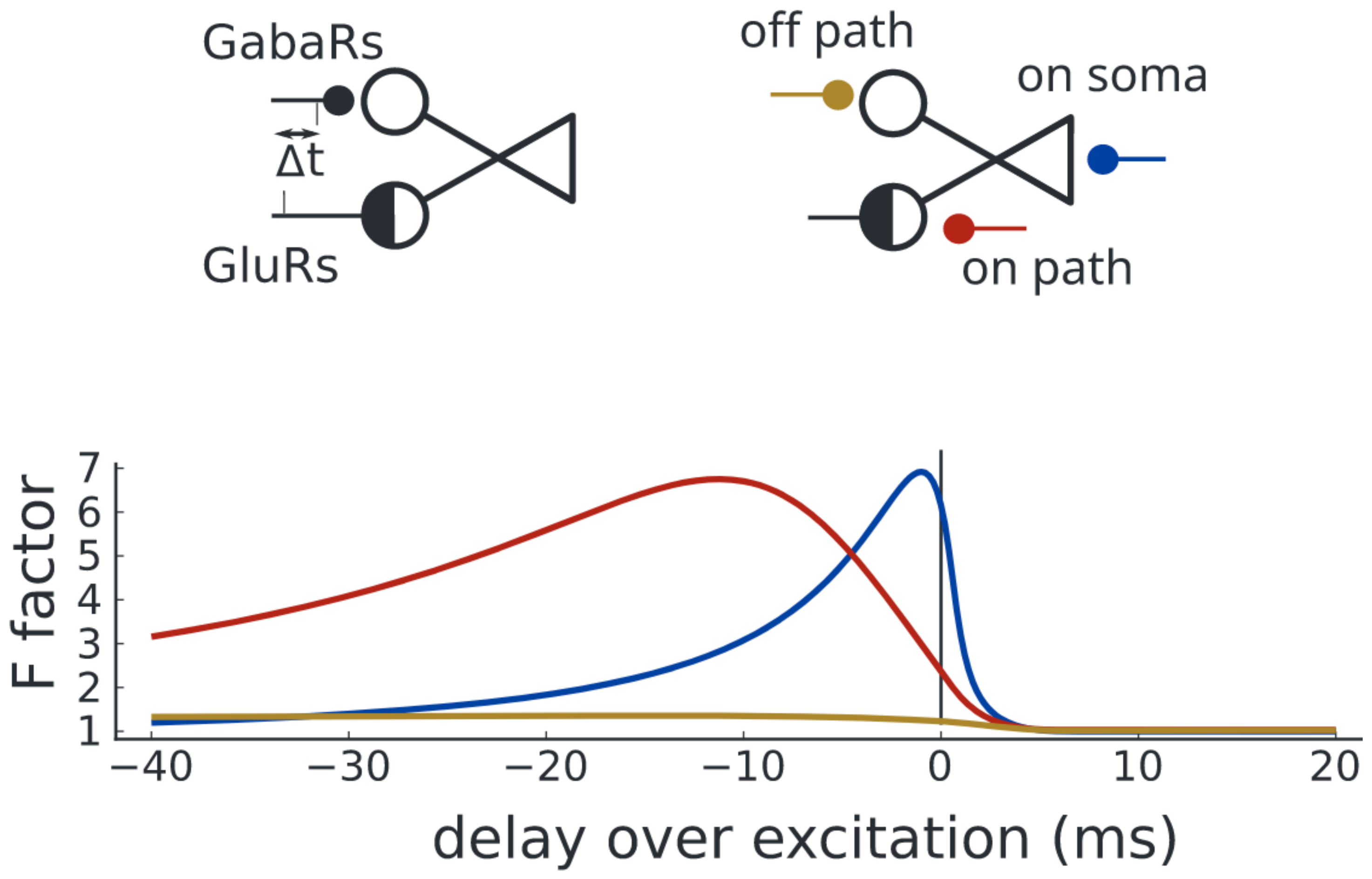
Reduced models of the dendritic tree

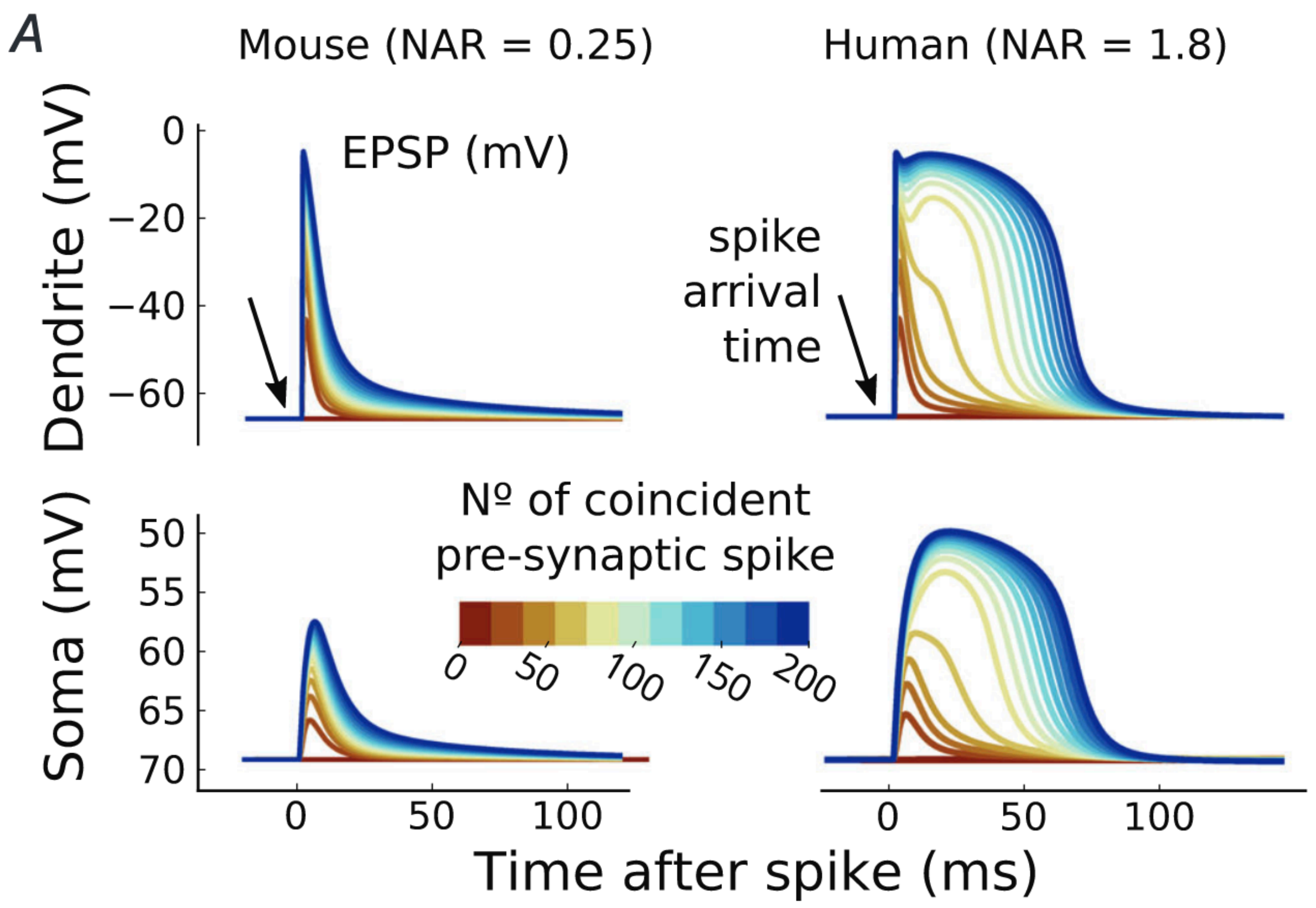
The Tripod neuron reproduces dendritic integration and computations

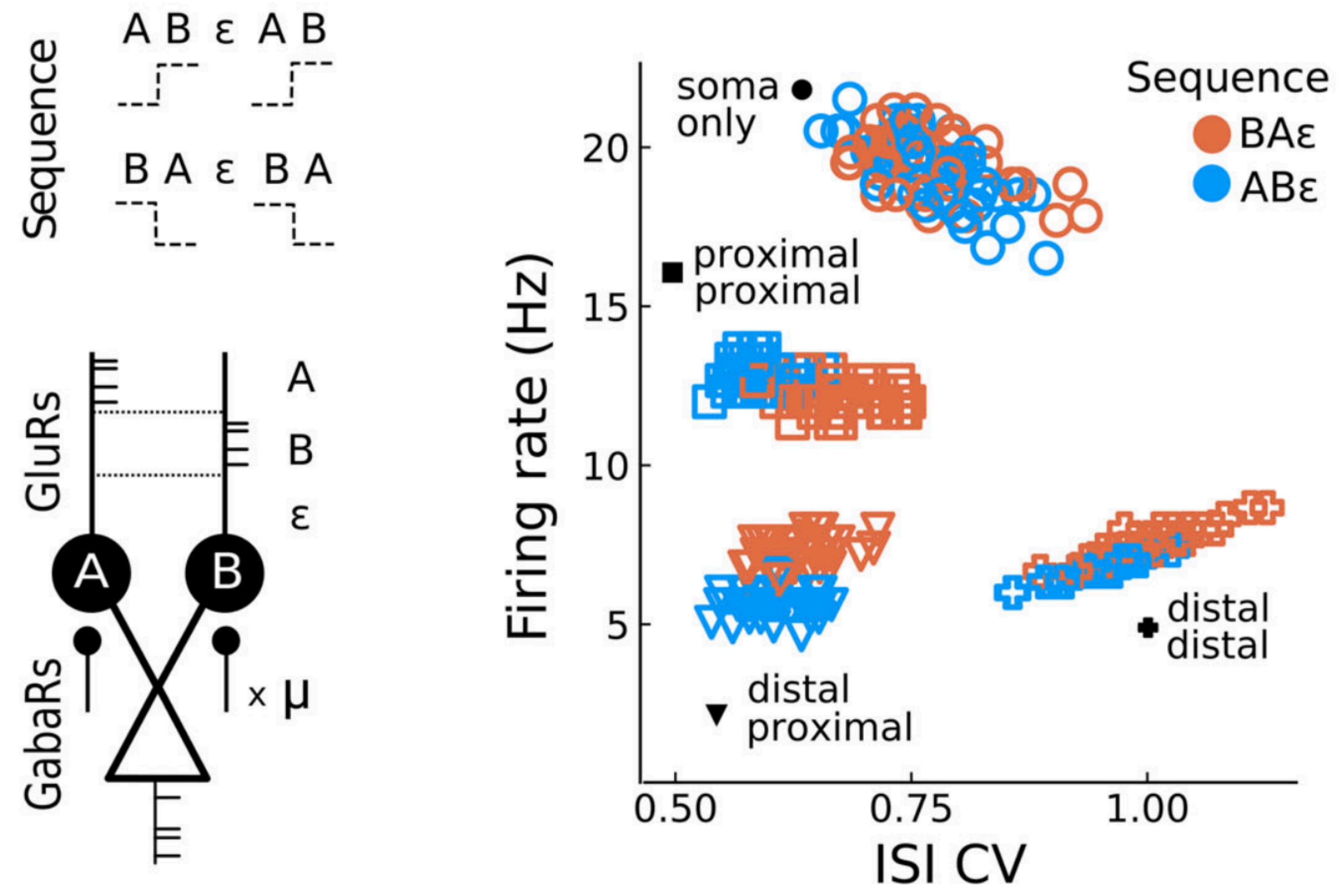
Passive cable effect
Inhibition over the same or different dendrite from excitation changes the somatic response.

Dendritic non-linearities
The Intensity and duration of NMDA spikes depend on geometry and the concentration of NMDA receptors.

Dendritic computations
The model increases the computational capabilities of single-cells. It introduces a spike-silent dendritic memory







The impact of dendrites on memory and learning

Dendritic engram

Dendrites integrate synaptic inputs in non-linear ways, affecting the formation and retrieval of memories.

Voltage-dependent plasticity

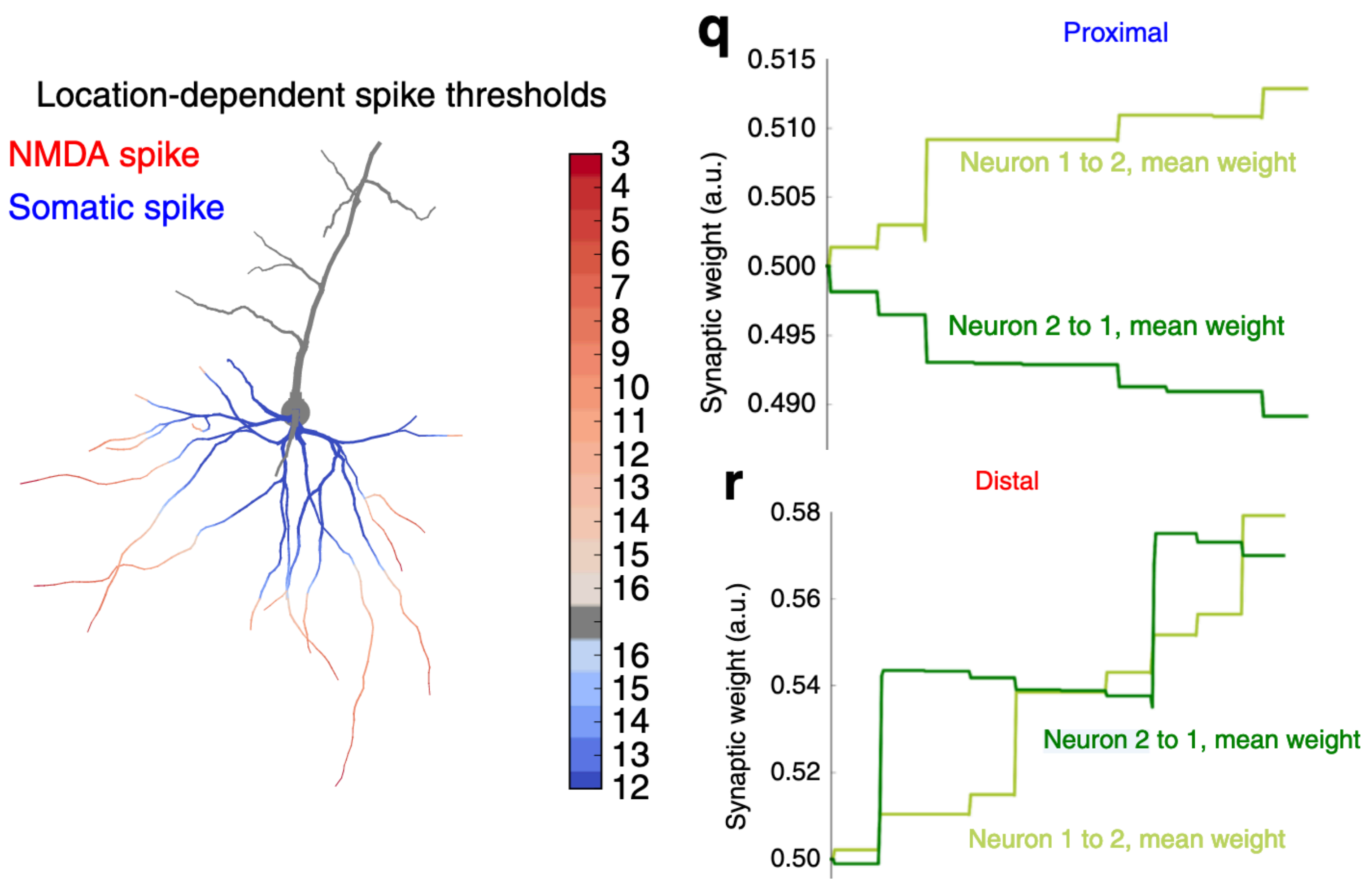
Potentiation/Depression depends on synaptic location and dendritic depolarization.

Memory clustering

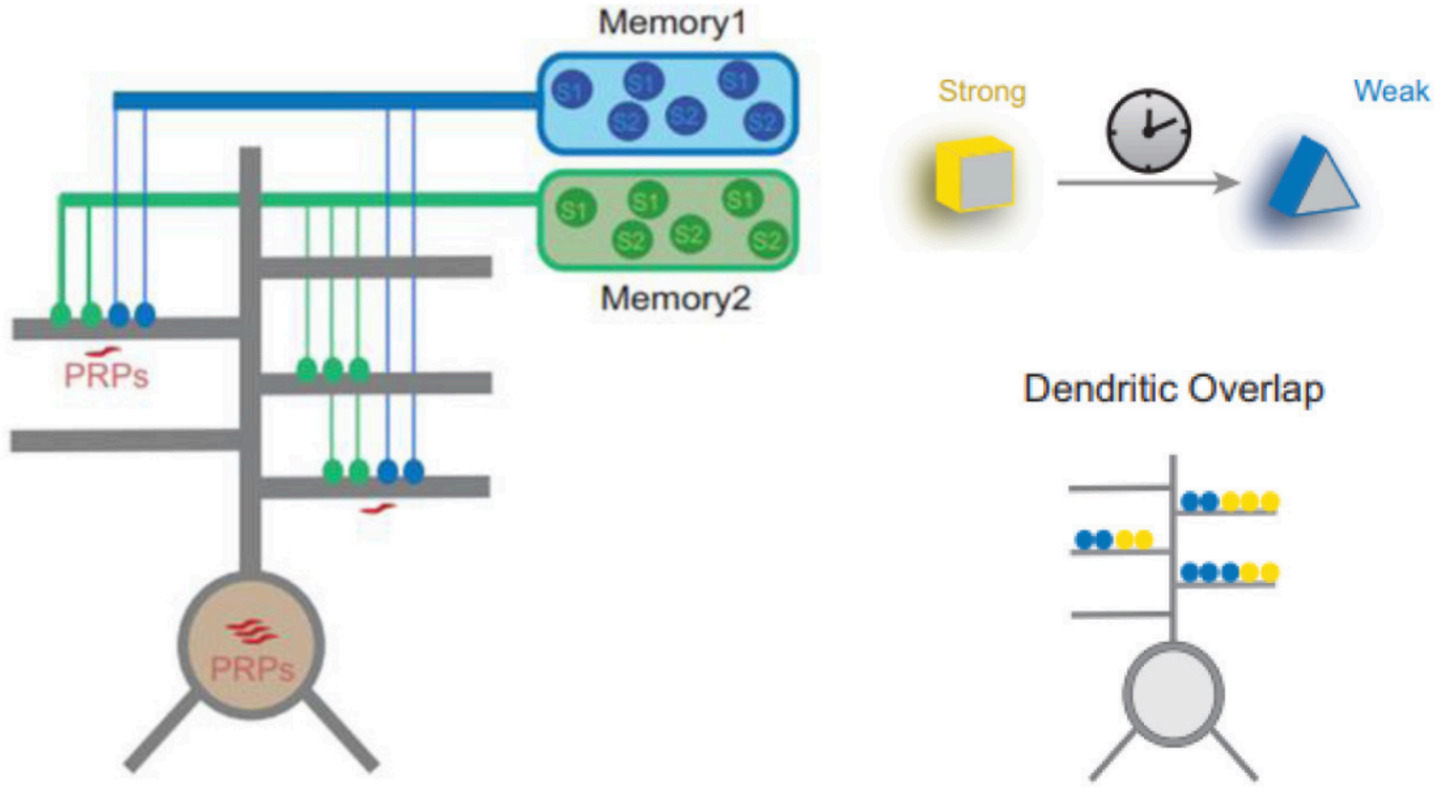
Different memories can be associated by clustering on the same branch.

Sequence learning and retrieval

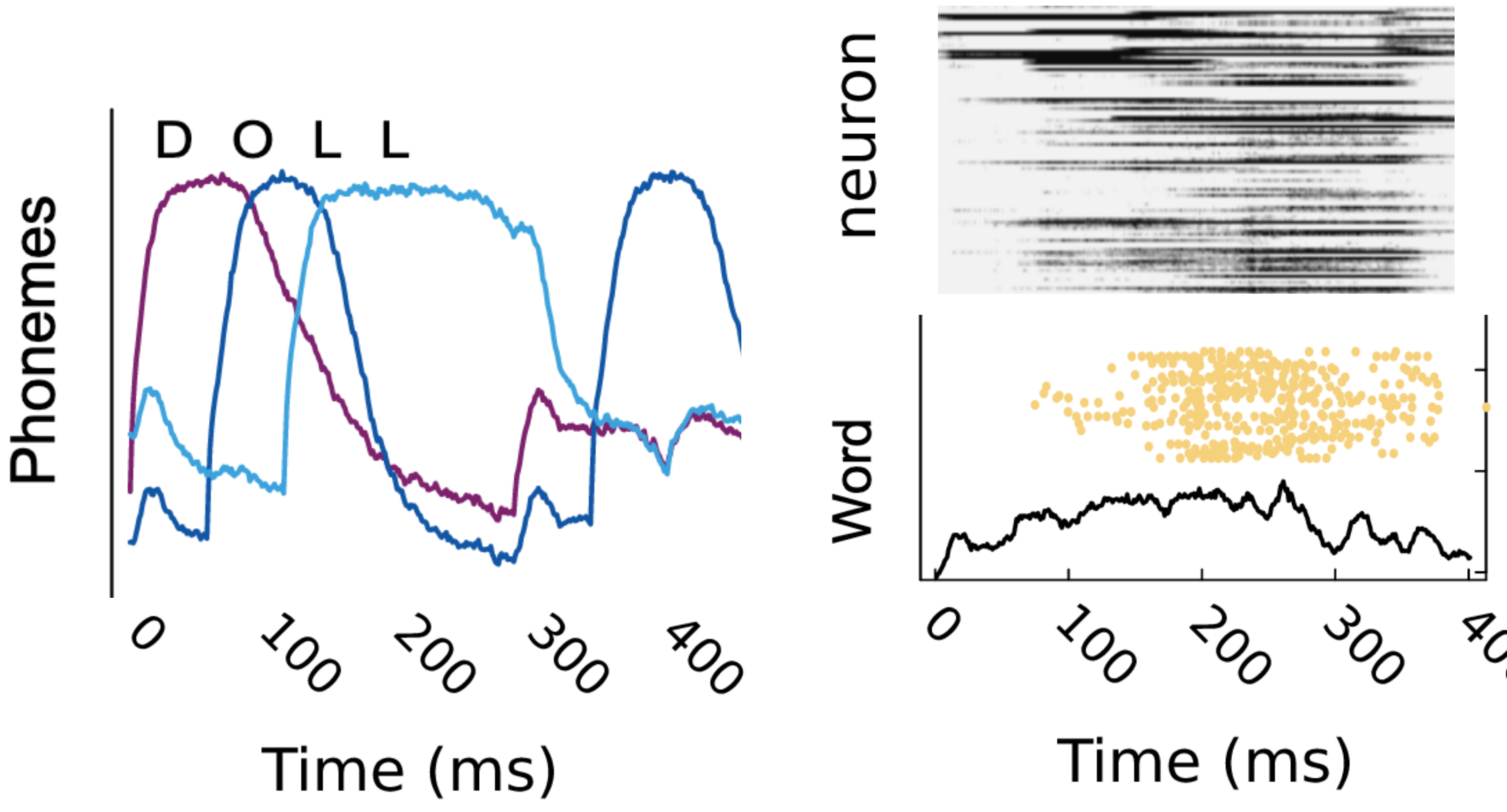
Dendritic engrams support the retrieval of overlapping memories via dendritic memory



Bono & Clopath (2019)



Kastellakis & Poirazi (2015)



Quaresima, Fitz et al. (2023)

Information processing in dendrites

Dendritic arborization makes up the many aisles of the Telegrapher's building.

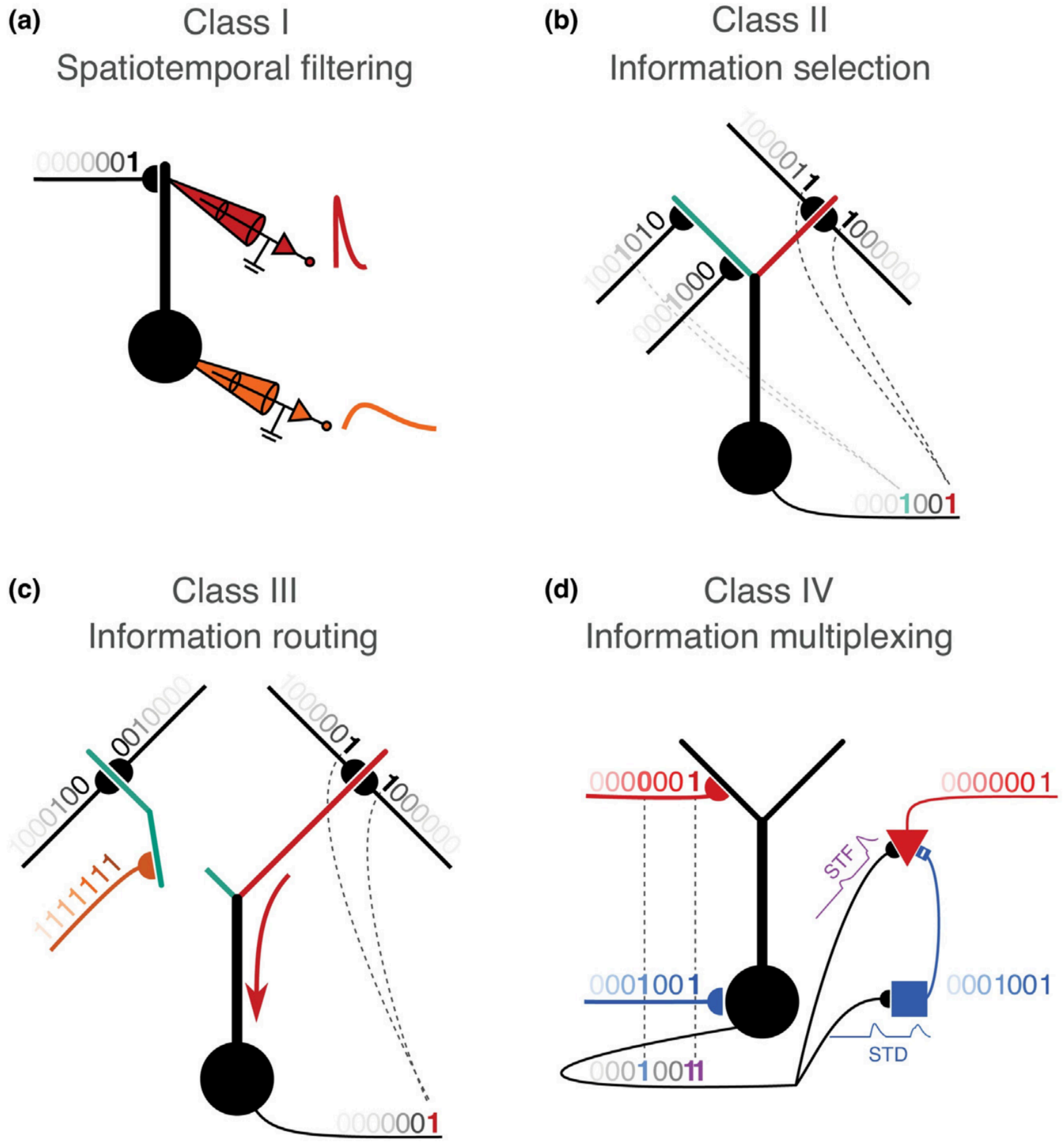
A coherent view of their algorithmic power and how they may contribute to neural network models.

Spatio-temporal filtering: Location-dependent attenuation and filtering combined with linear summation.

Information selection: Nonlinear amplification mechanisms select the information that determines the cell's output.

Information routing: Spatial distribution of excitation and inhibition selects which input pathway is active.

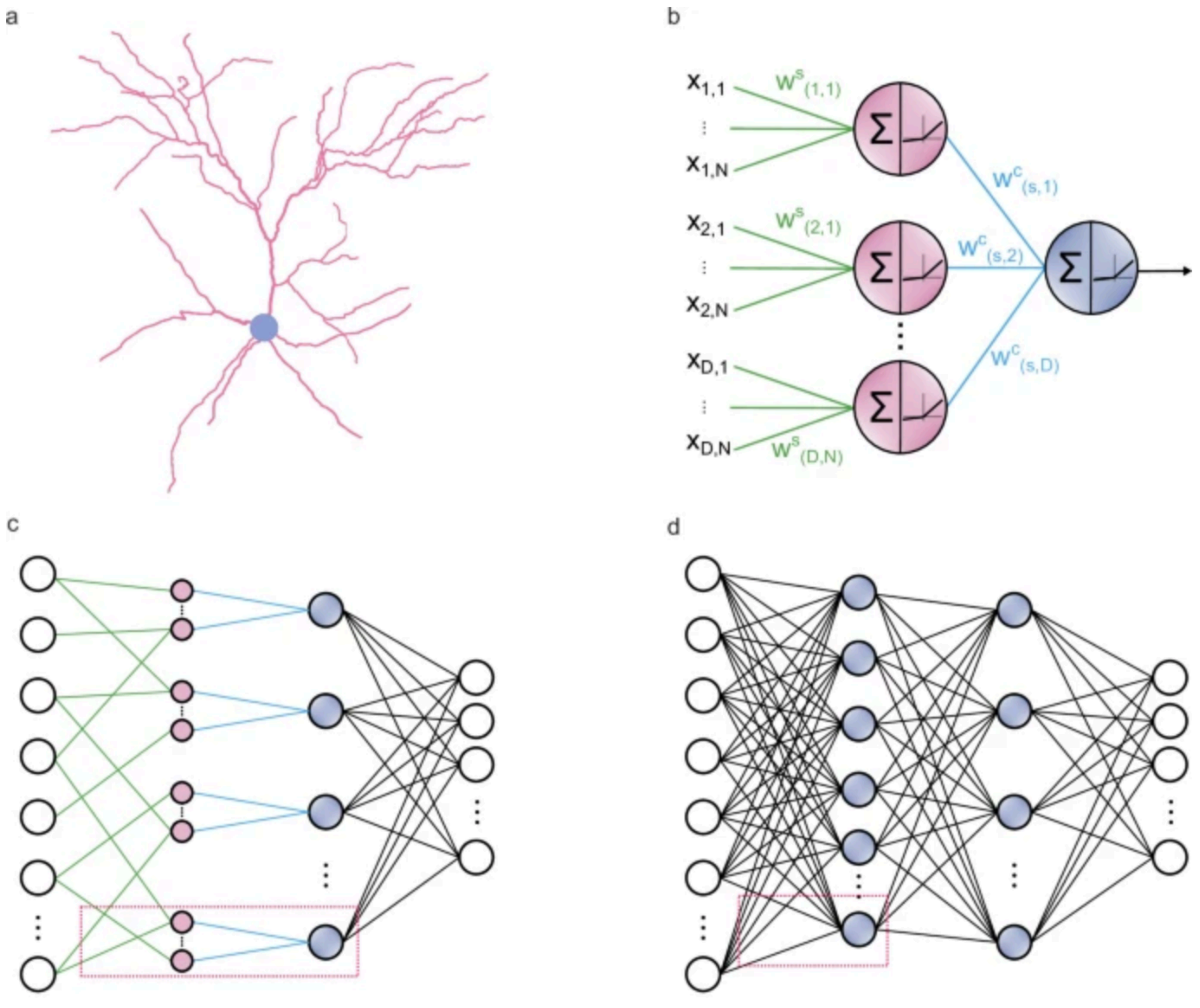
Information multiplexing: Dendritic-driven bursts represent multiple inputs into one spiking output,



Payeur et al. 2019

Dendrites in Deep Neural Networks

Dendrites lead to accurate, robust and parameter efficient learning



Chavlis & Poirazi (2019)

Dendrites as an additional layer that provides weighted inputs to the somatic nodes.

dANNs are constructed as typical ANNs with two hidden layers, in which the first (dendritic) layer is connected in a sparse and structured manner to the second (somatic).

Boolean mask: $\mathbf{W}_k \rightarrow \mathbf{W}_k \odot \mathbf{M}_k$

ANN architectures that incorporate the structured connectivity limit the number of trainable parameters, and counteract overfitting.

Two reasons:

- dANN models form primarily **mixed-selective nodes.**
- Define a scheme for **weight sparseness.**

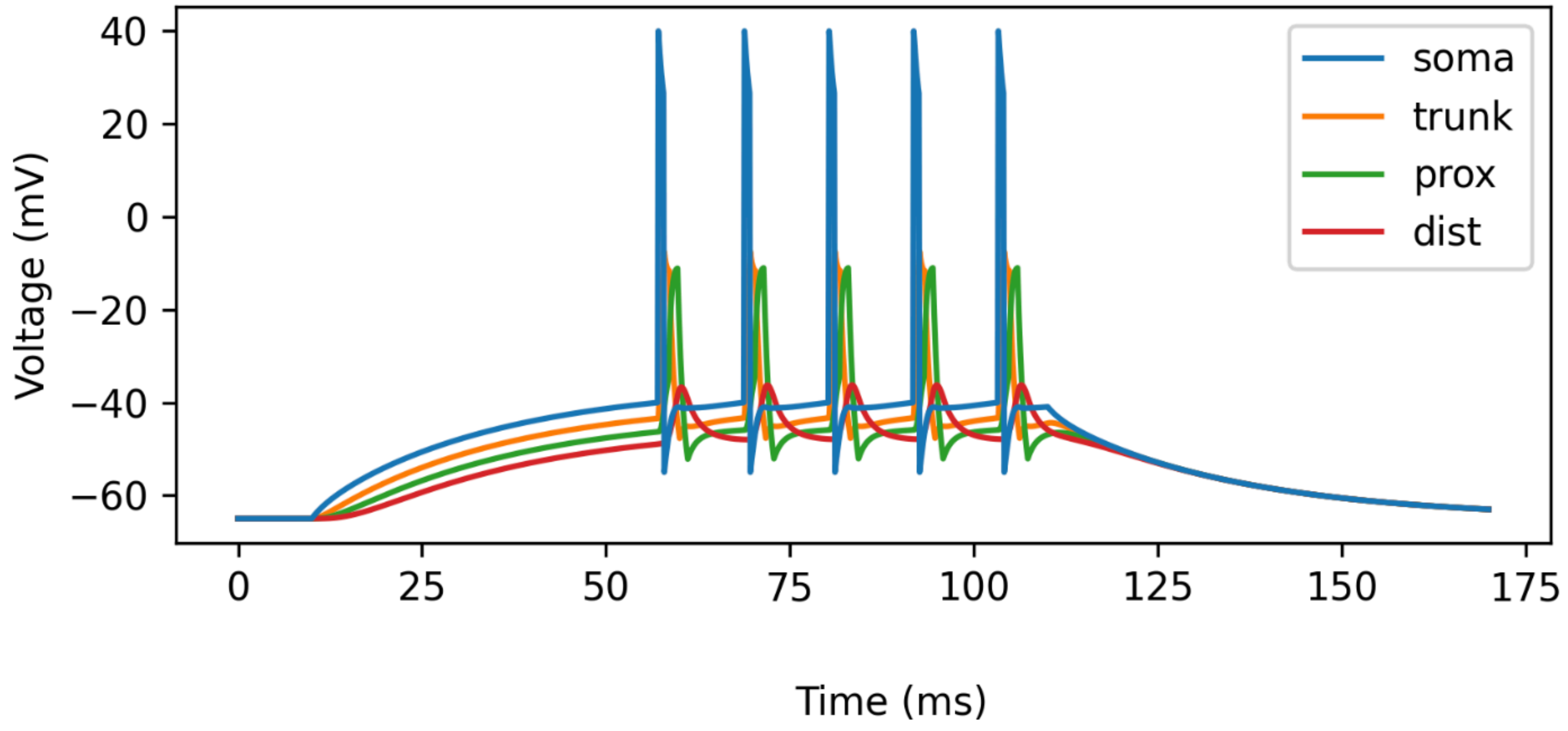
Computational models of dendrites

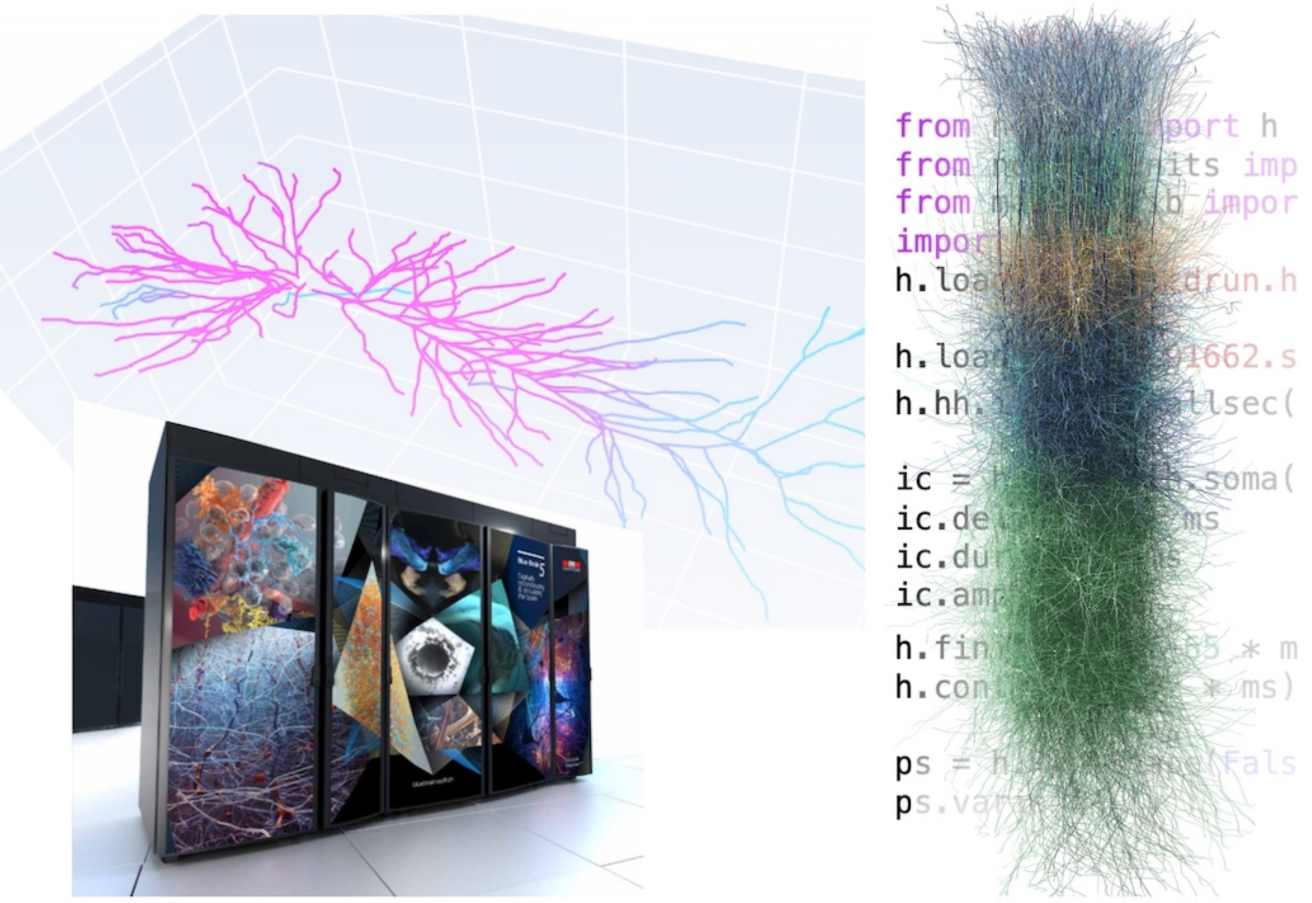
Tools to simulate multi-compartment neurons.

Dendrify allows for the integration of dendrites in Brian2 simulations. It focuses on neurons with few compartments

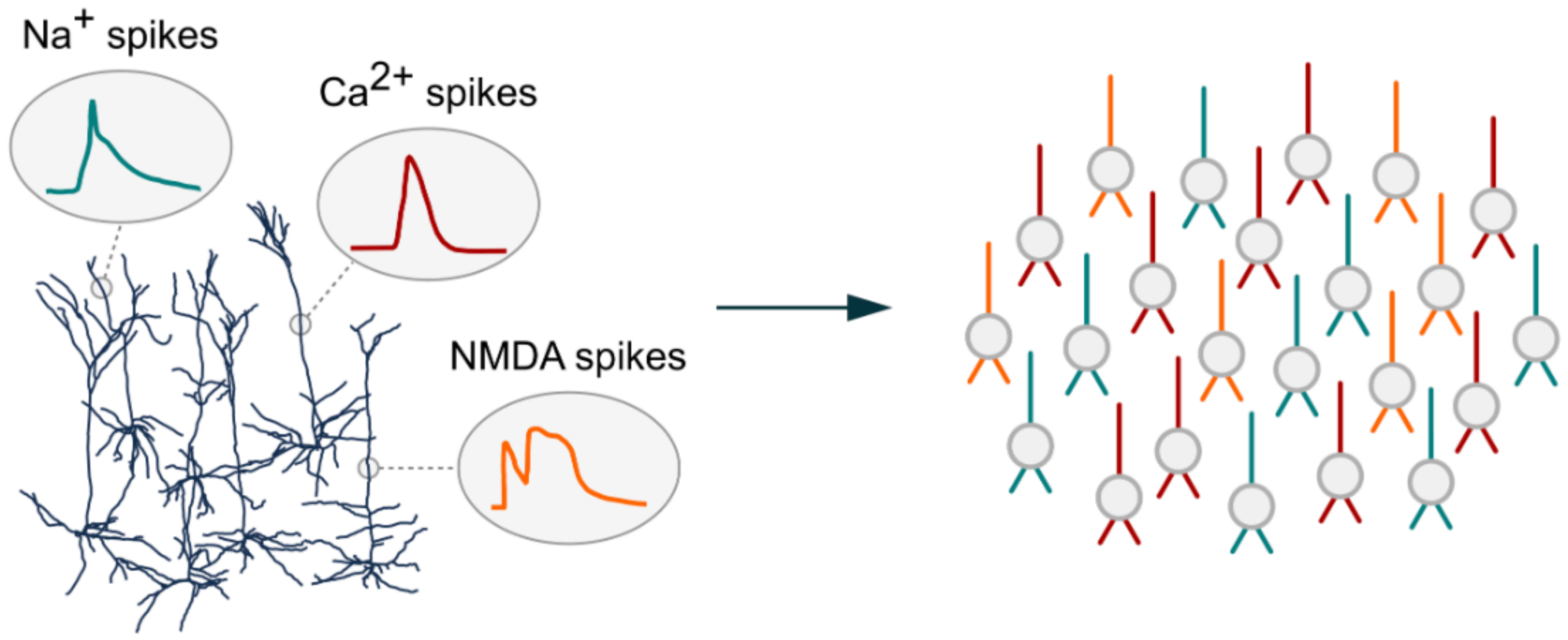
Neuron supports simulations of detailed multicompartment models. The construction of a neuron is fairly complex.

SpikingNeuralNetwork.jl allows for custom-definition of multi-compartment neurons, and it includes the Tripod in the model library.





SNN.jl



Microcircuit of detailed biophysical neurons

SNN comprising active dendritic mechanisms