Outline of Dendrites Lecture

Basic Properties of Synaptic Currents

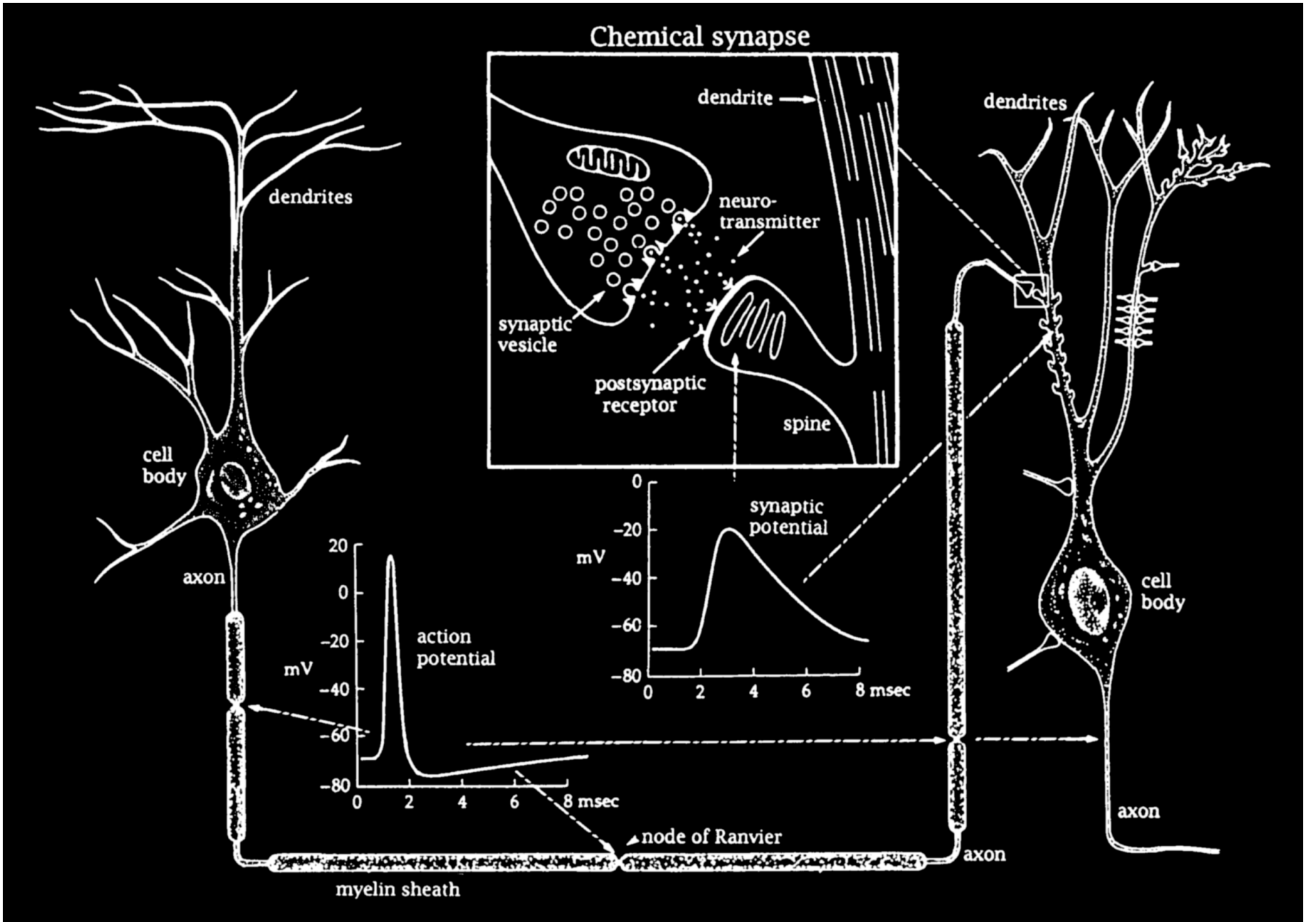
Morphology of Dendrites

Passive Cable Properties - Rall Model

Measuring and Modeling PSP Attenuation and Summation

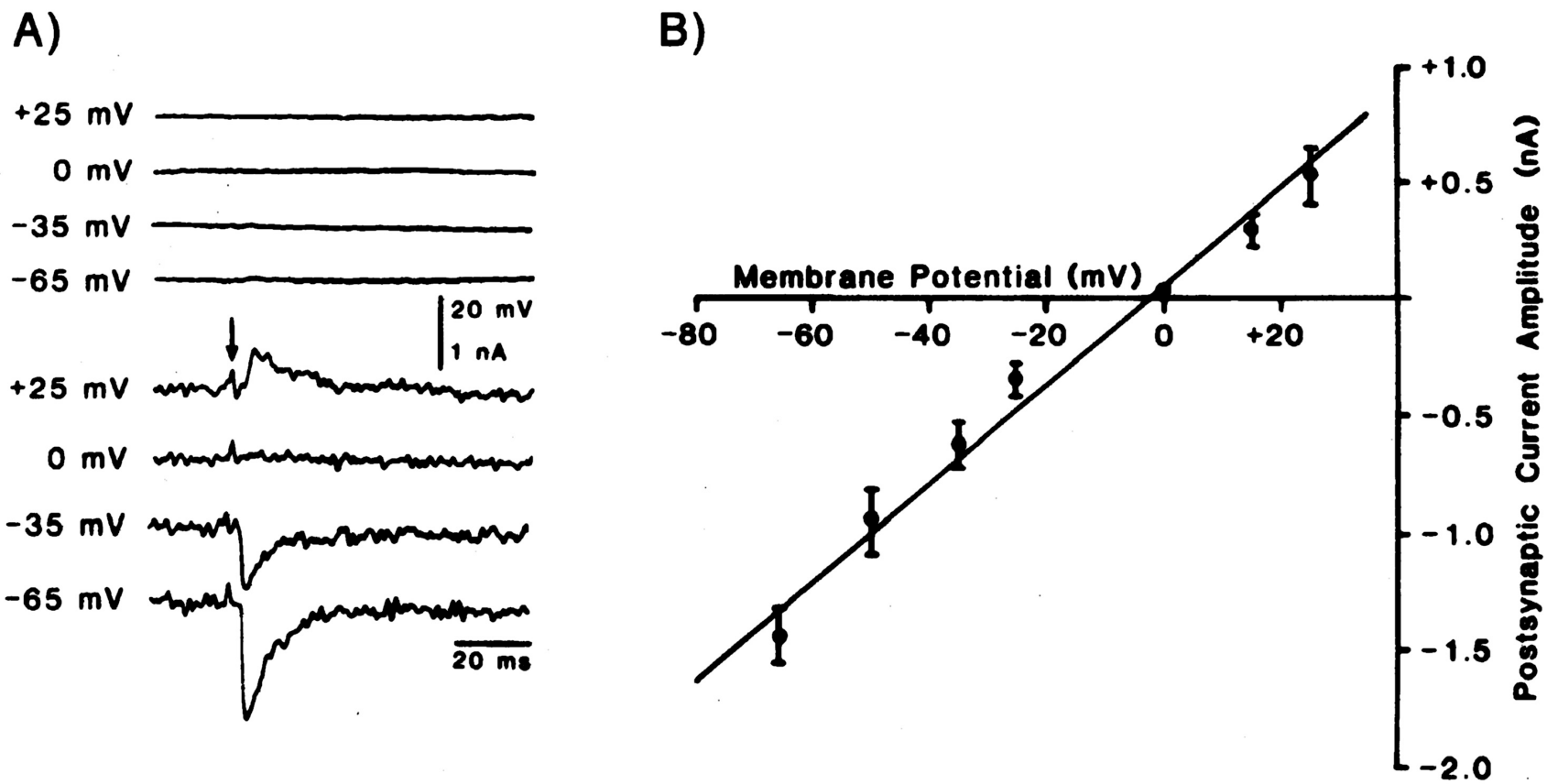
Active Dendrites

Computation in Dendrites


Chemical synapse
dendrite
neuro-
transmitter
synaptic
vesicle
postsynaptic
receptor
spine
dendrites
cell
body
axon
20
0
-20
-40
-60
-80
mV
action
potential
0
2
4
6
8 msec
0
-20
-40
-60
-80
mV
synaptic
potential
0
2
4
6
8 msec
node of Ranvier
myelin sheath
dendrites
cell
body
axon
axon

Membrane Conductance Change Underlying a Synaptic Potential

voltage clamp of synaptic current



Augment generalized H/H equations with synaptic conductance terms:

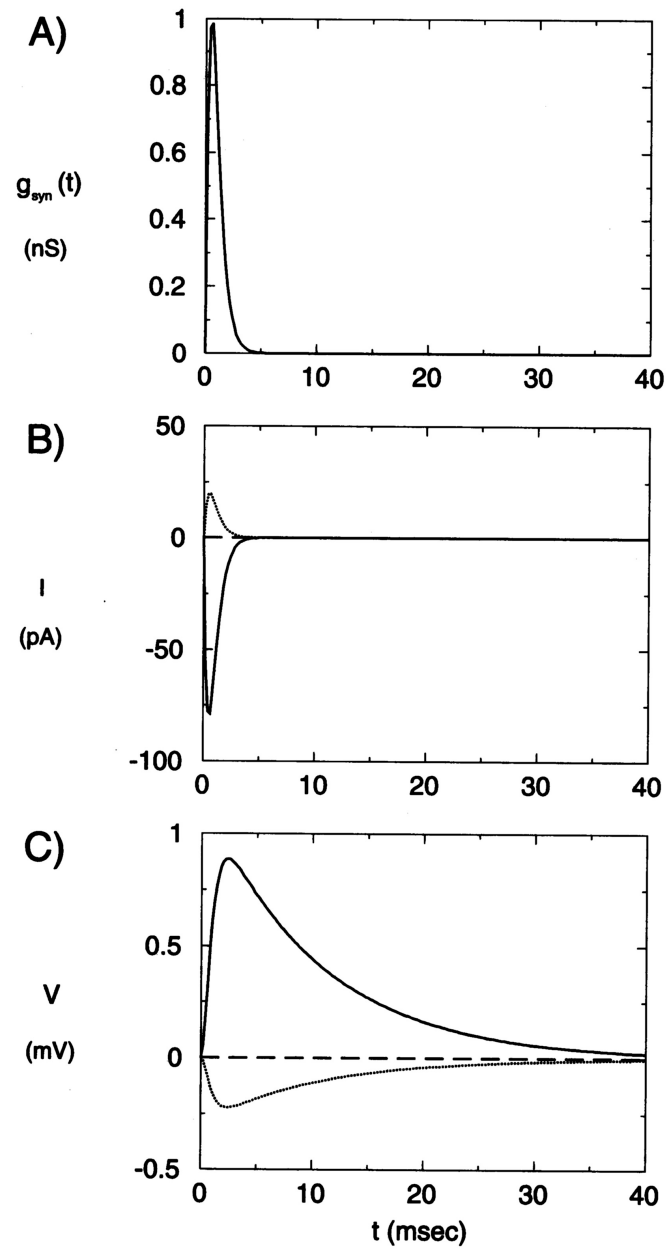
$$I_{syn} = g_{syn}(t)(V_m - V_{syn})$$

a function

$$g_{syn}(t) = \bar{g}_{syn} t e^{-t/t_{peak}}$$

or difference of two exponentials

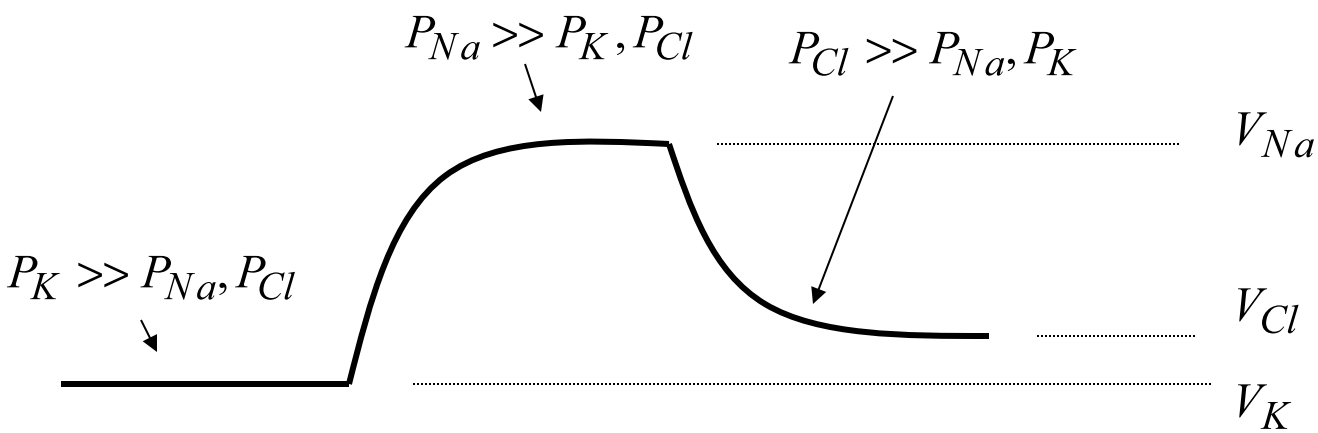
$$g_{syn}(t) = \bar{g}_{syn}(e^{-t/\tau_1} - e^{-t/\tau_2})$$



Goldman Hodgkin Katz Equation

$$V = 58 \log \frac{P_K[K]_{ext} + P_{Na}[Na]_{ext} + P_{Cl}[Cl]_{int}}{P_K[K]_{int} + P_{Na}[Na]_{int} + P_{Cl}[Cl]_{ext}}$$

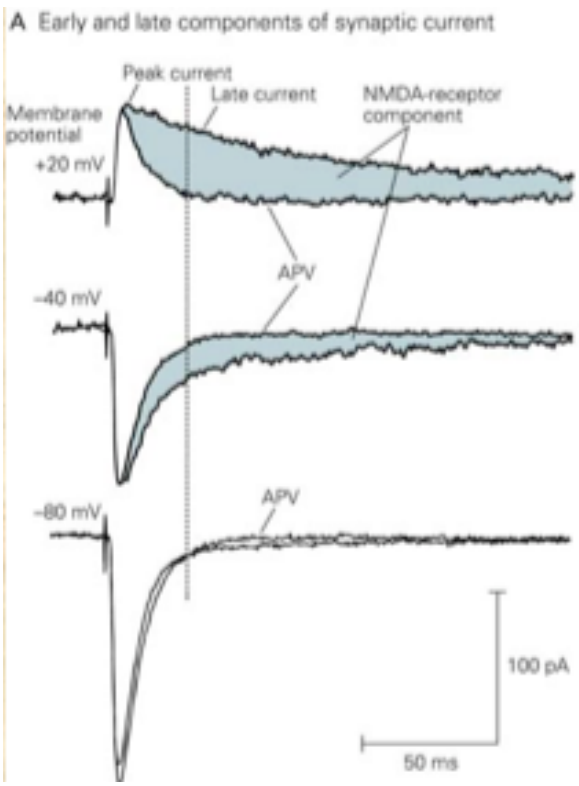
$$P_K : P_{Na} : P_{Cl}$$ relative permeabilities

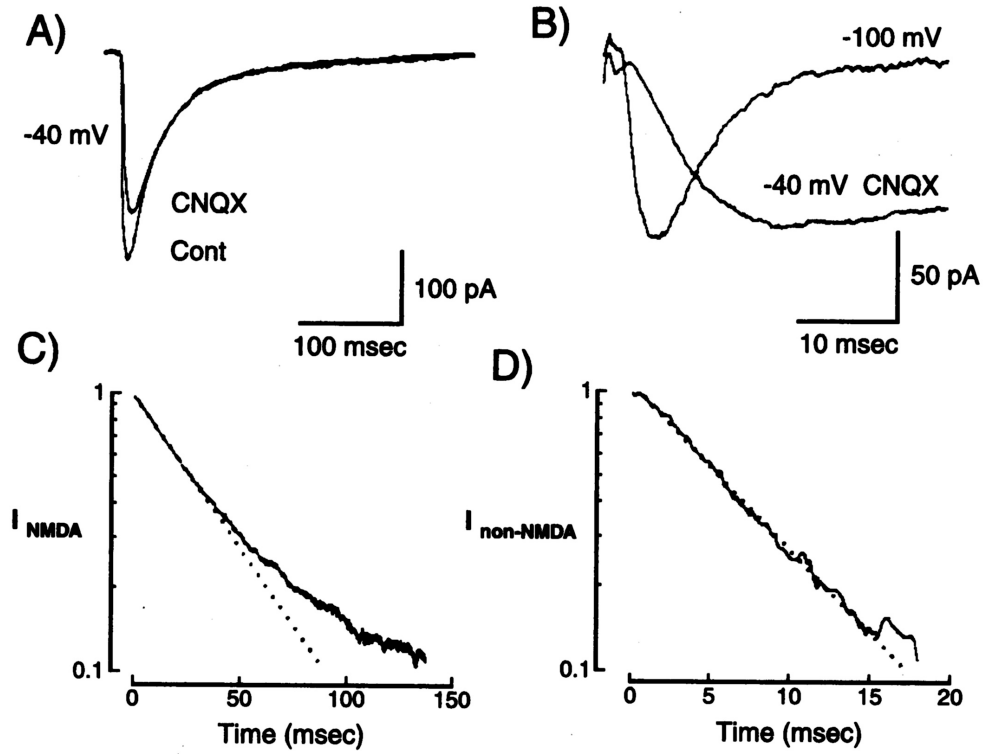


		[out]	[in]	E	P/PK	
		(mM)	(mM)	(mV)		
"inhibitory/hyperpolarizing"	K^+	5	100	-80	1	$GABA_BR$
"Excitatory/depolarizing"	Na^+	150	15	+62	0.025	
	Ca^{2+}	2	0.0002	+123	–	
"inhibitory/shunting"	Cl^-	150	13	-65	0.1	$GABA_AR$, GlyR

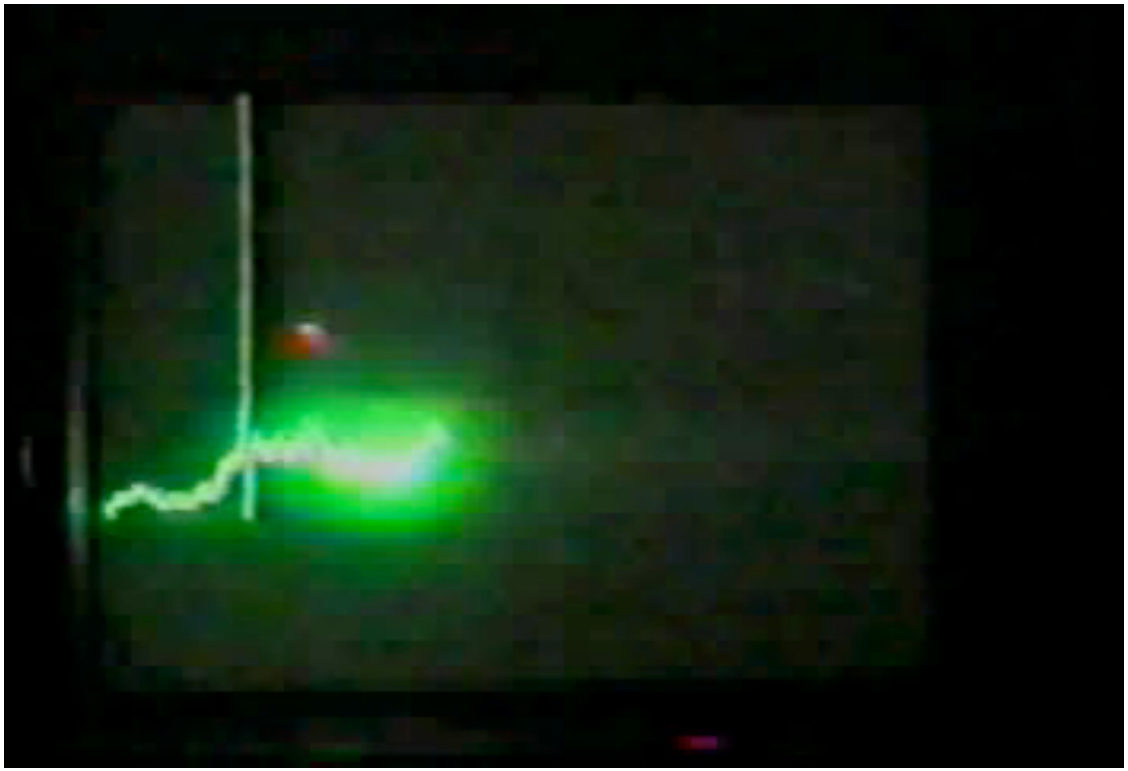
V_m = -65 mV

AMPA and NMDA currents





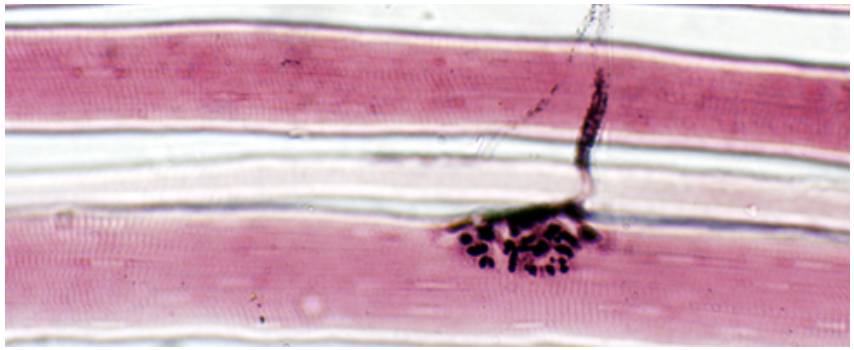
Voltage dependent activation of NMDA component



V_thr

V_rest

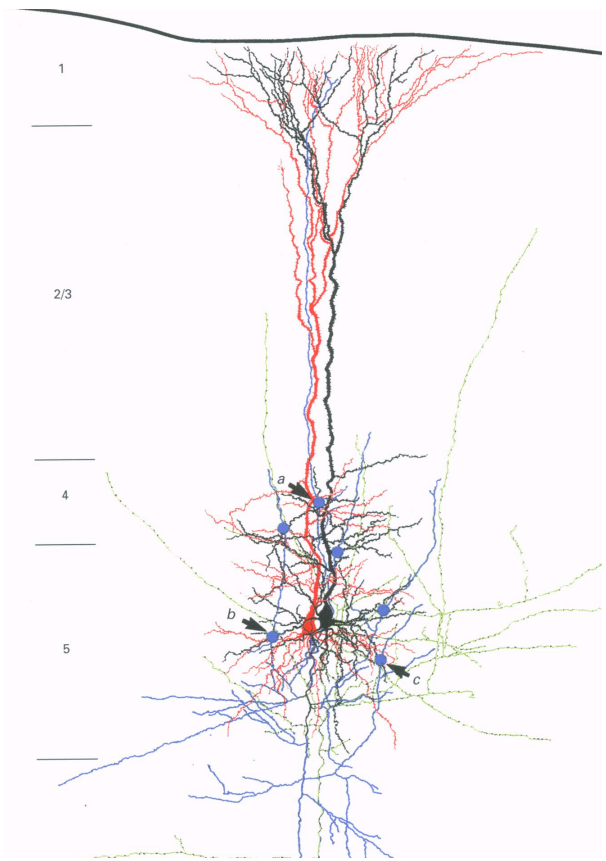
Synaptic input required to generate an AP



Neuromuscular Junction

- Many tens of synaptic boutons per axon
- Many release sites per bouton

EJPs from the input from a single motorneuron are large

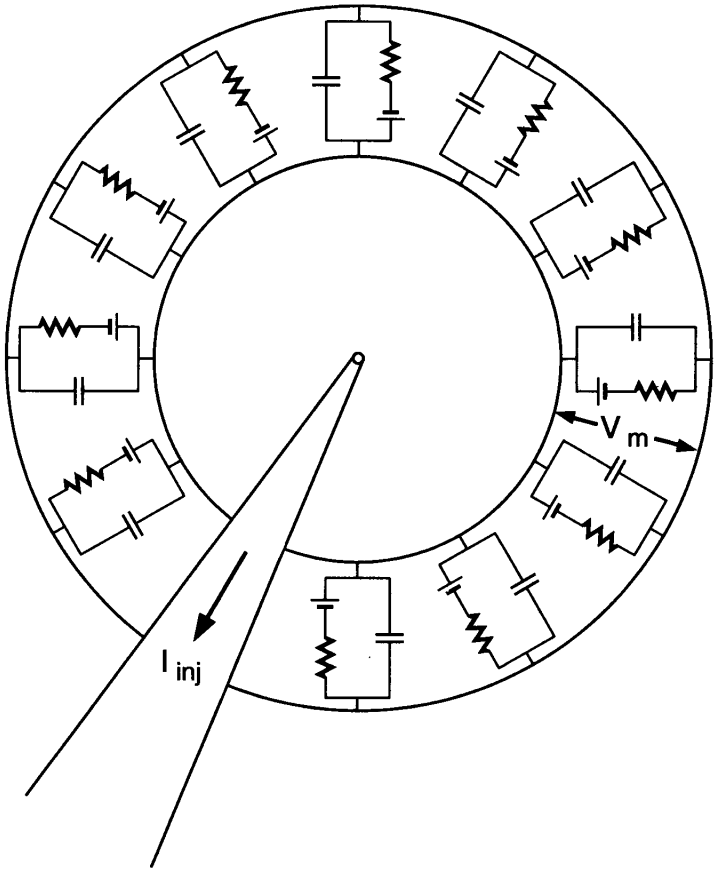


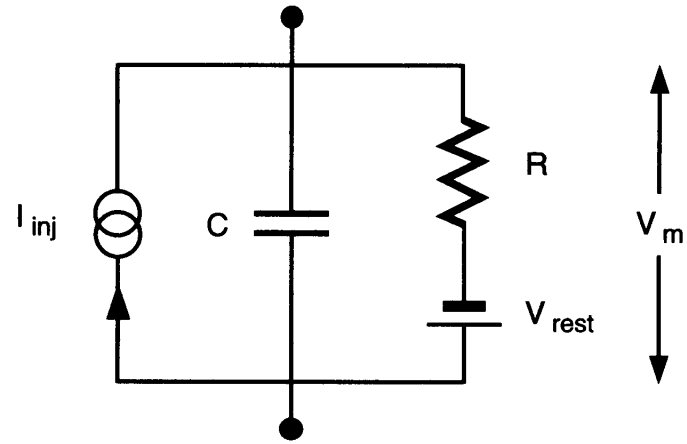
Markram et al., J. Physiol. (1997)

Central Synapses

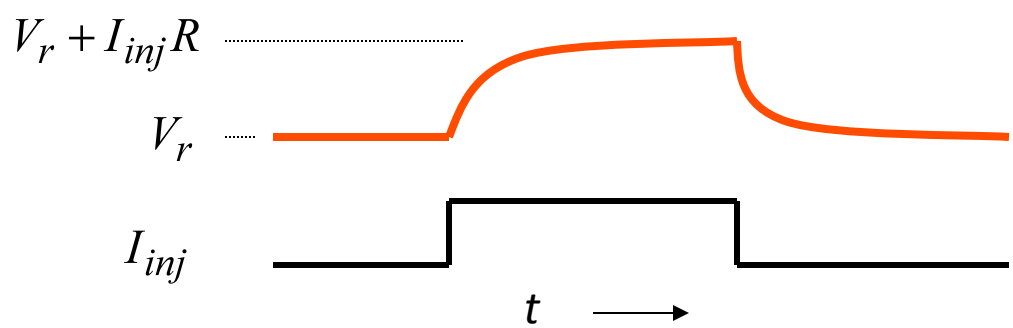
- The axon from a given presynaptic cell only has a few (1-5) synaptic boutons onto a given postsynaptic target cell
- Typically only one release site per bouton
- Very small quantal size

EPSPs from single presynaptic cells are small (0.1mV)
Summation of many presynaptic cells required for AP generation

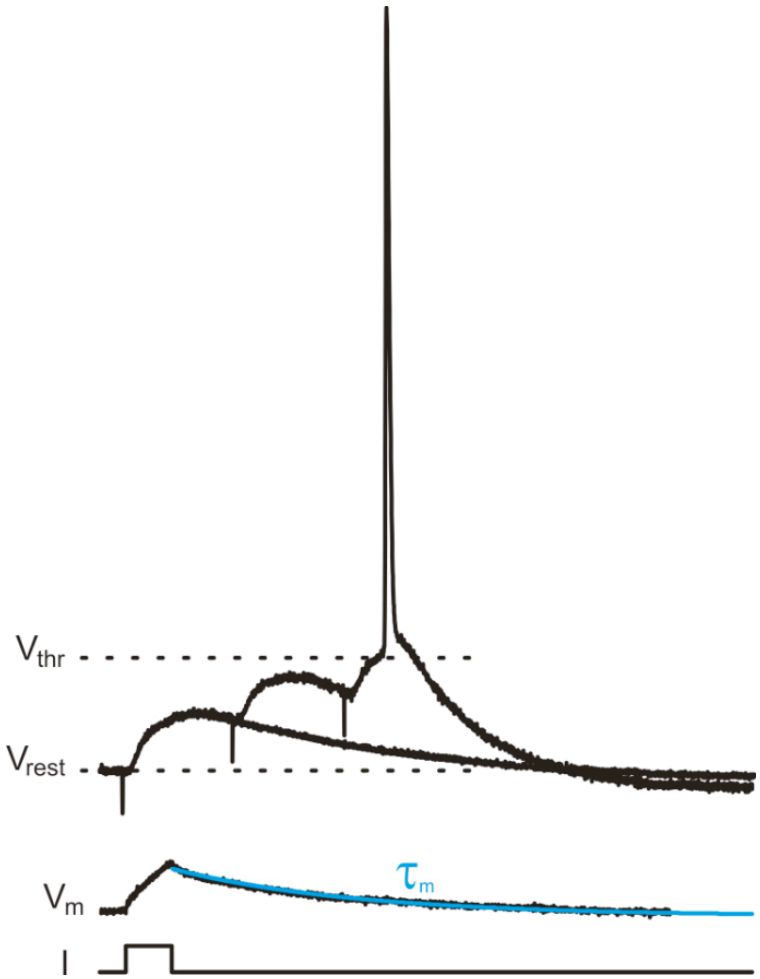




$$C\frac{dV_m}{dt} = I_{inj} + \frac{(V_m - V_r)}{R}$$

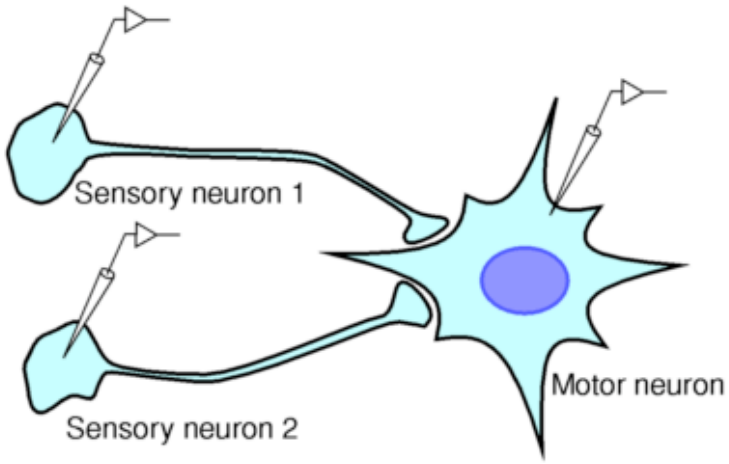


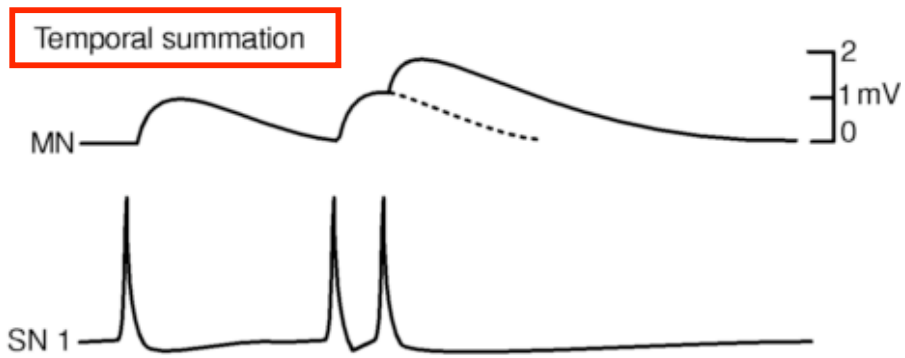
Membrane Time Constant Sets the Scale of Temporal Summation

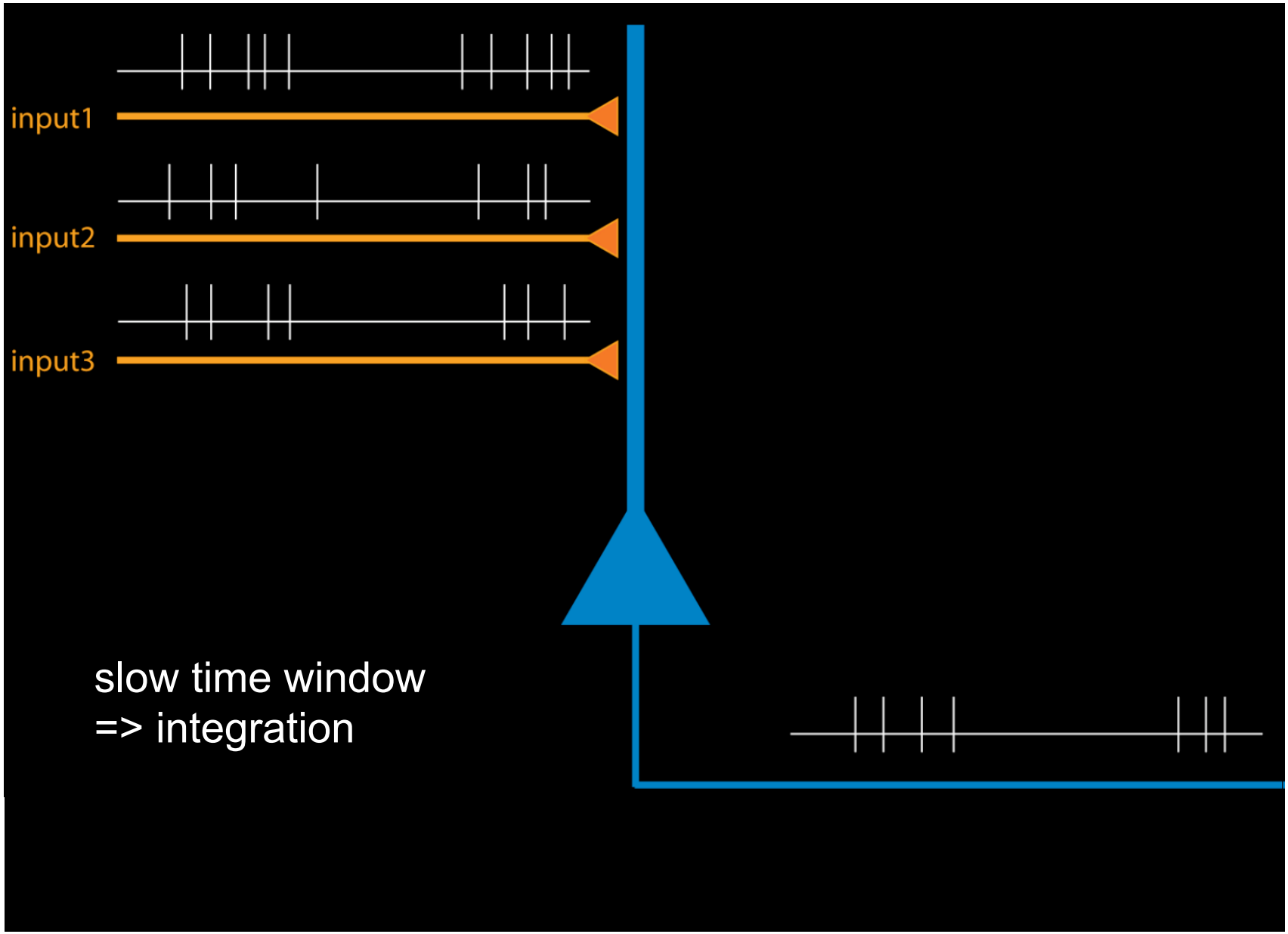


M. Scanziani

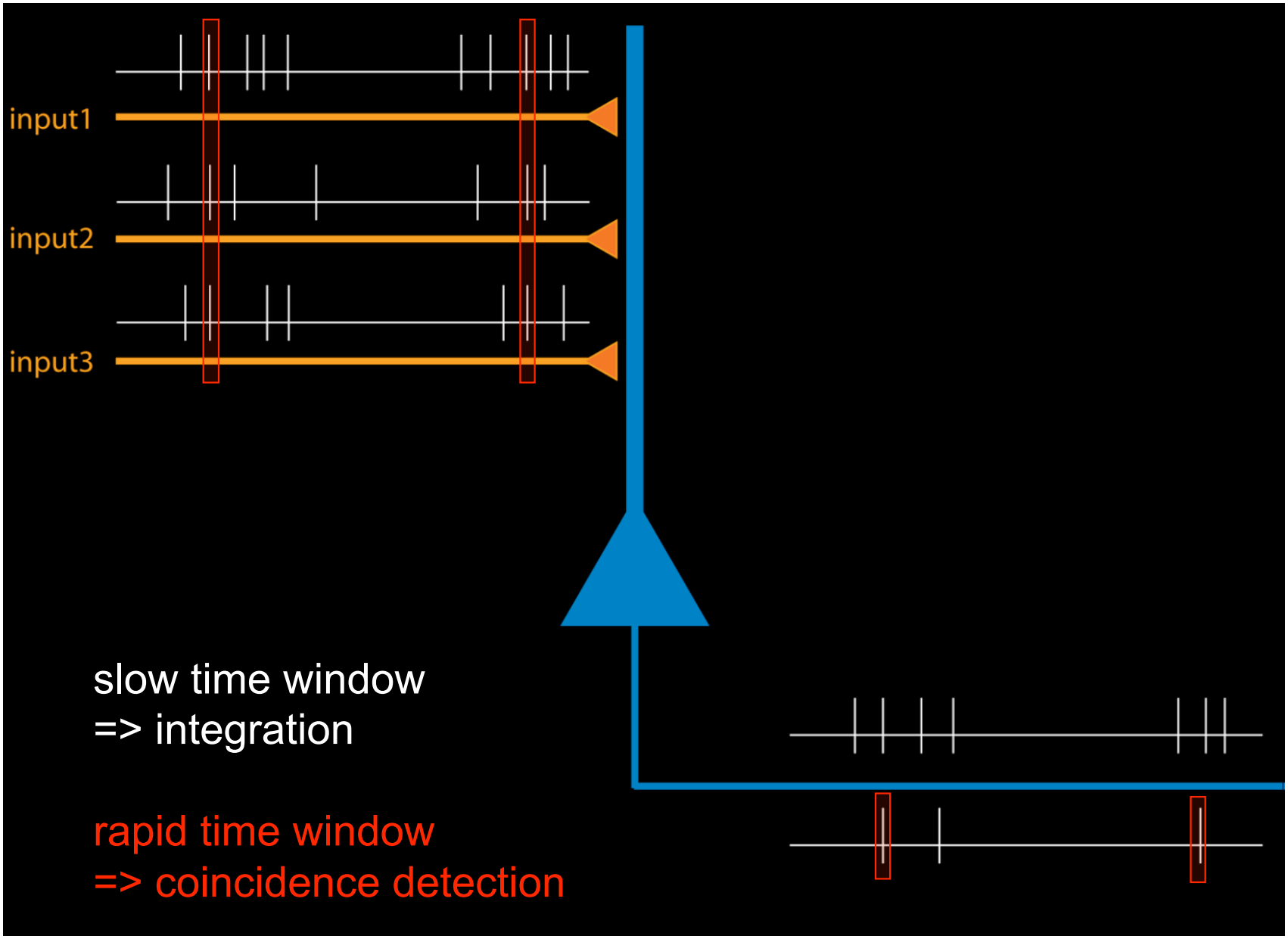
Temporal and Spatial Summation





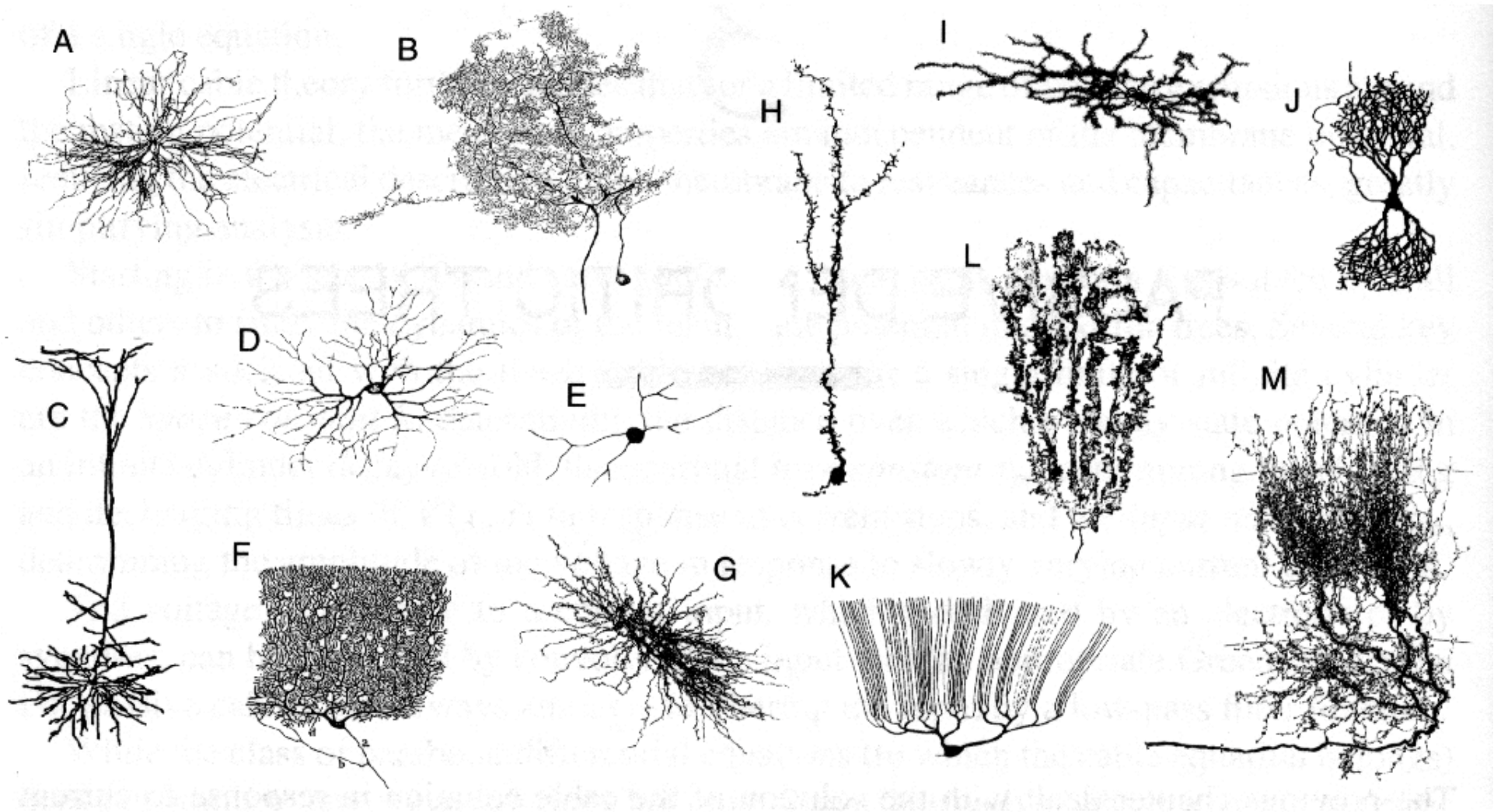


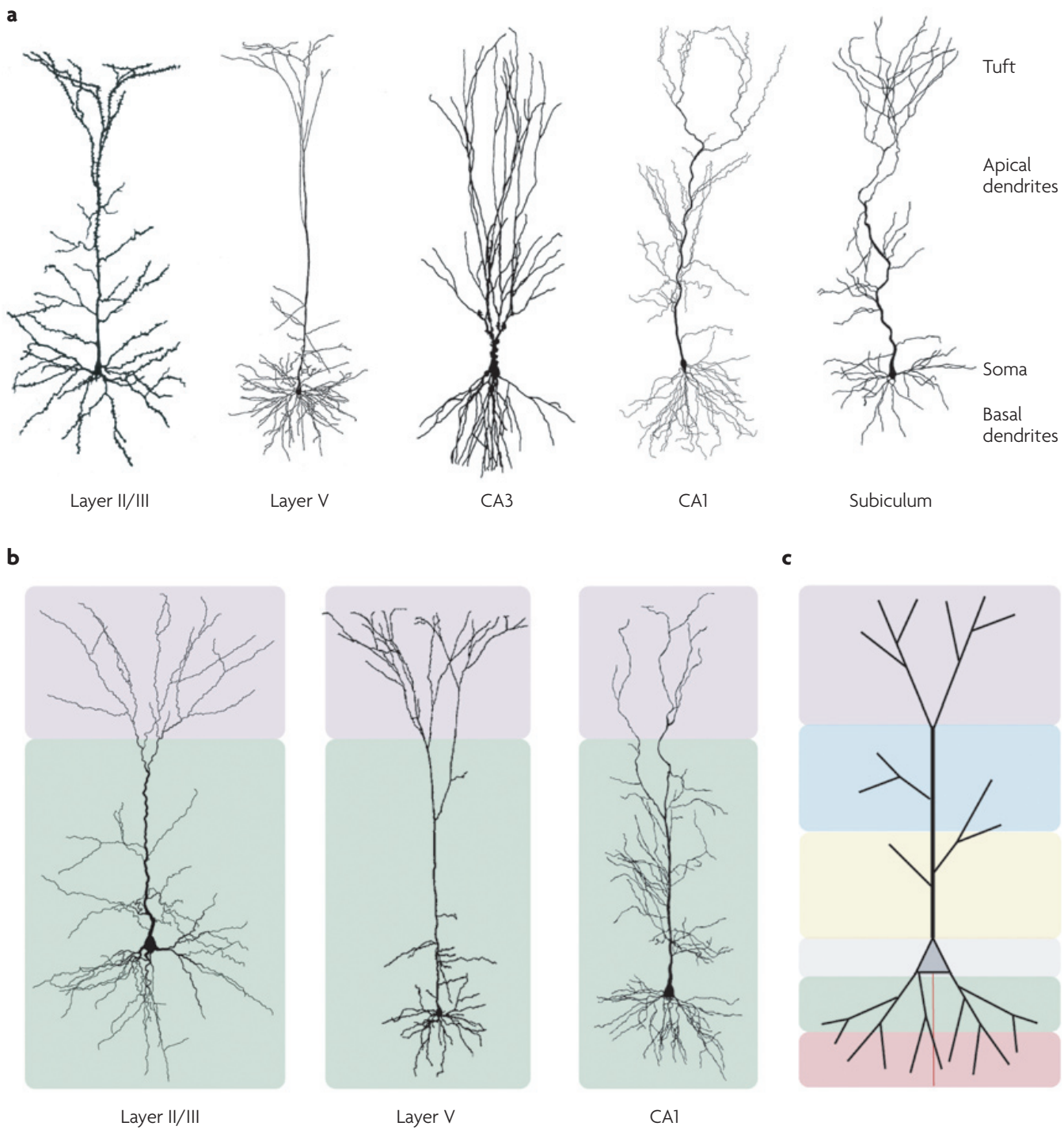
M. Hausser


input1
input2
input3
slow time window
=> integration
rapid time window
=> coincidence detection

M. Hausser

Spheres and Cables

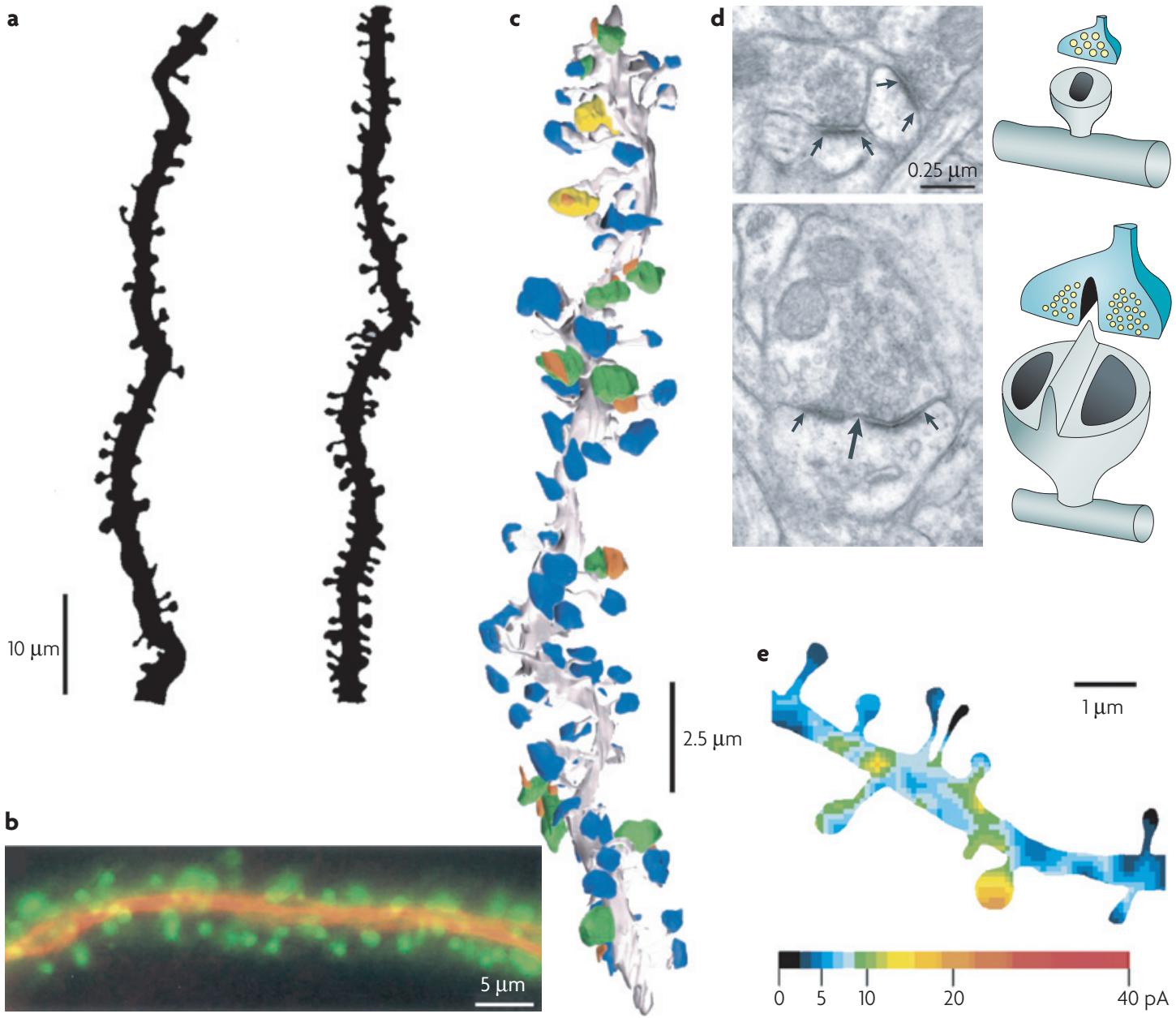




Pyramidal Cell Terminology

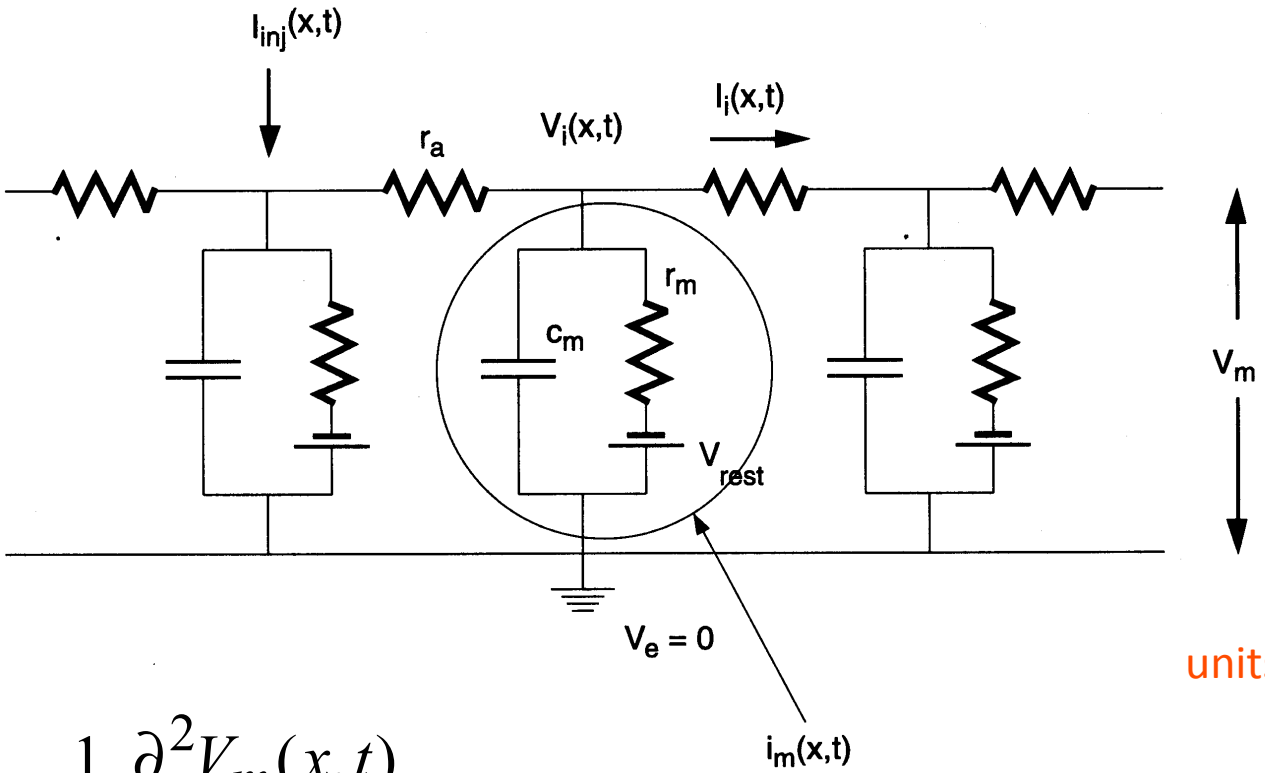
Apical
Basal
Oblique
Primary
Secondary
Tuft
Branch point

N. Spruston
Nature Reviews Neurosci. (2008)



Spruston (2008)

Modeling Dendritic Dynamics – Rall Model



units:

r_m: ohm-cm

r_a: ohm/cm

i_m: A/cm

c_m: F/cm

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

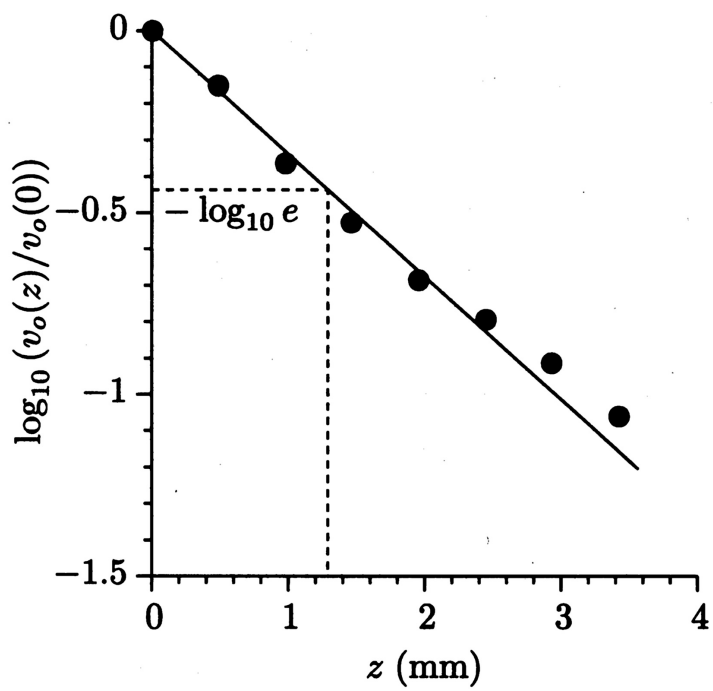
$$i_m(x,t) = \frac{V_m(x,t) - V_{rest}}{r_m} + c_m \frac{\partial V_m}{\partial t} - I_{inj}(x,t)$$

$$\tau_m = r_m c_m$$

$$\lambda = \sqrt{\frac{r_m}{r_a}}$$

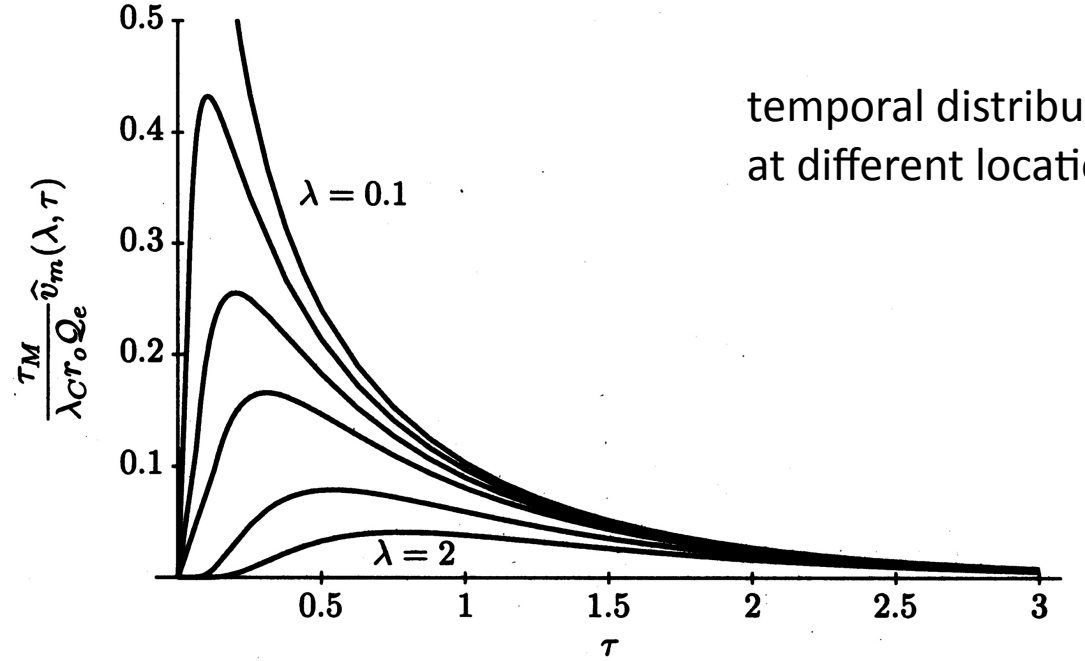
$$\lambda^2 \frac{\partial^2 V_m(x,t)}{\partial x^2} = \tau_m \frac{\partial V_m(x,t)}{\partial t} + (V_m(x,t) - V_{rest}) - r_m I_{inj}(x,t)$$

$$V(x) = V_0 \exp(-|x| / \lambda)$$

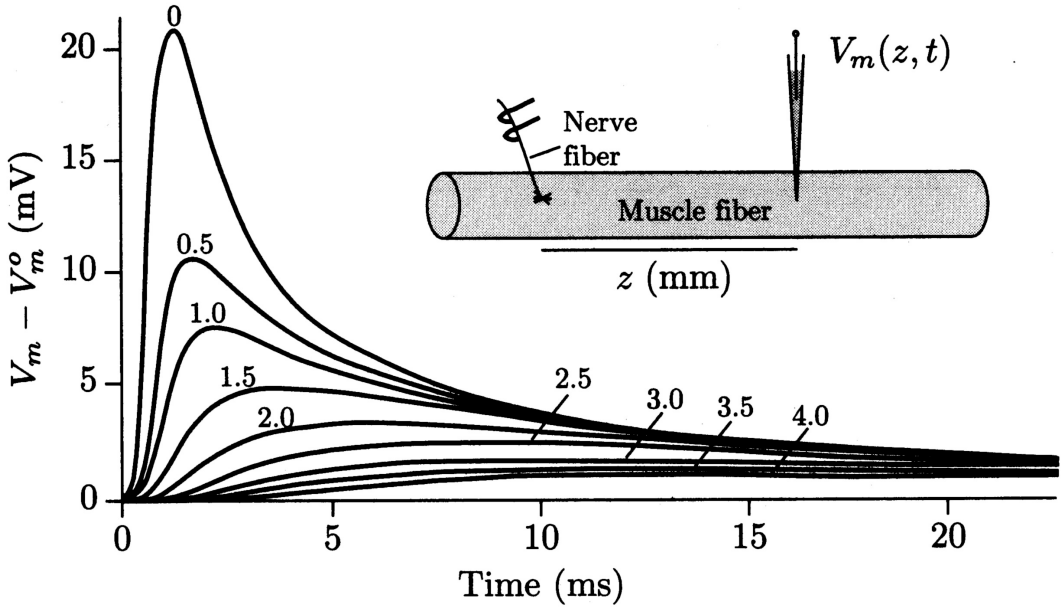


temporal distribution
at different locations

theory



experiment



Voltage attenuation in branching cables

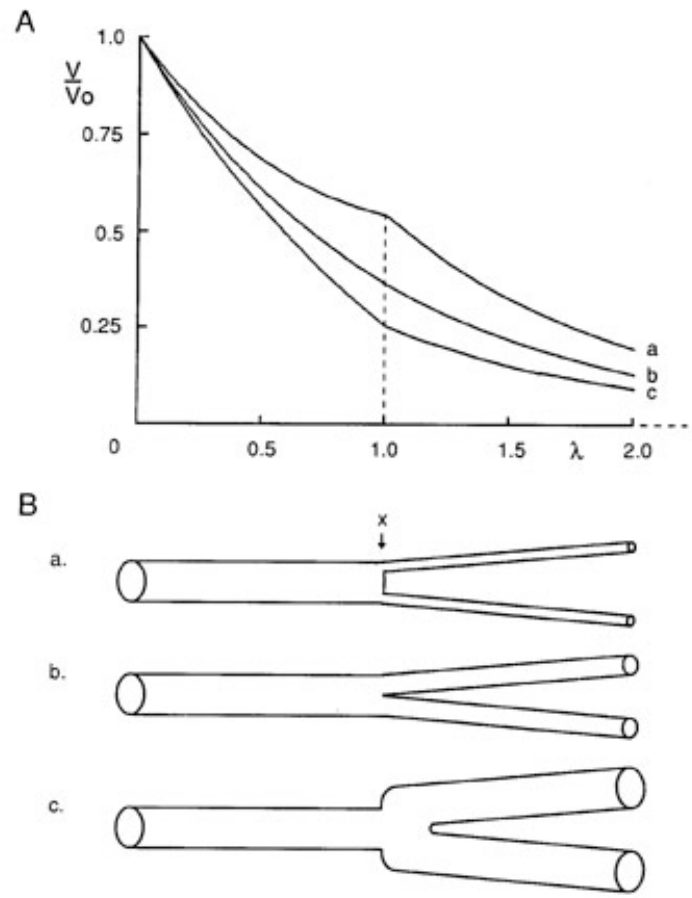
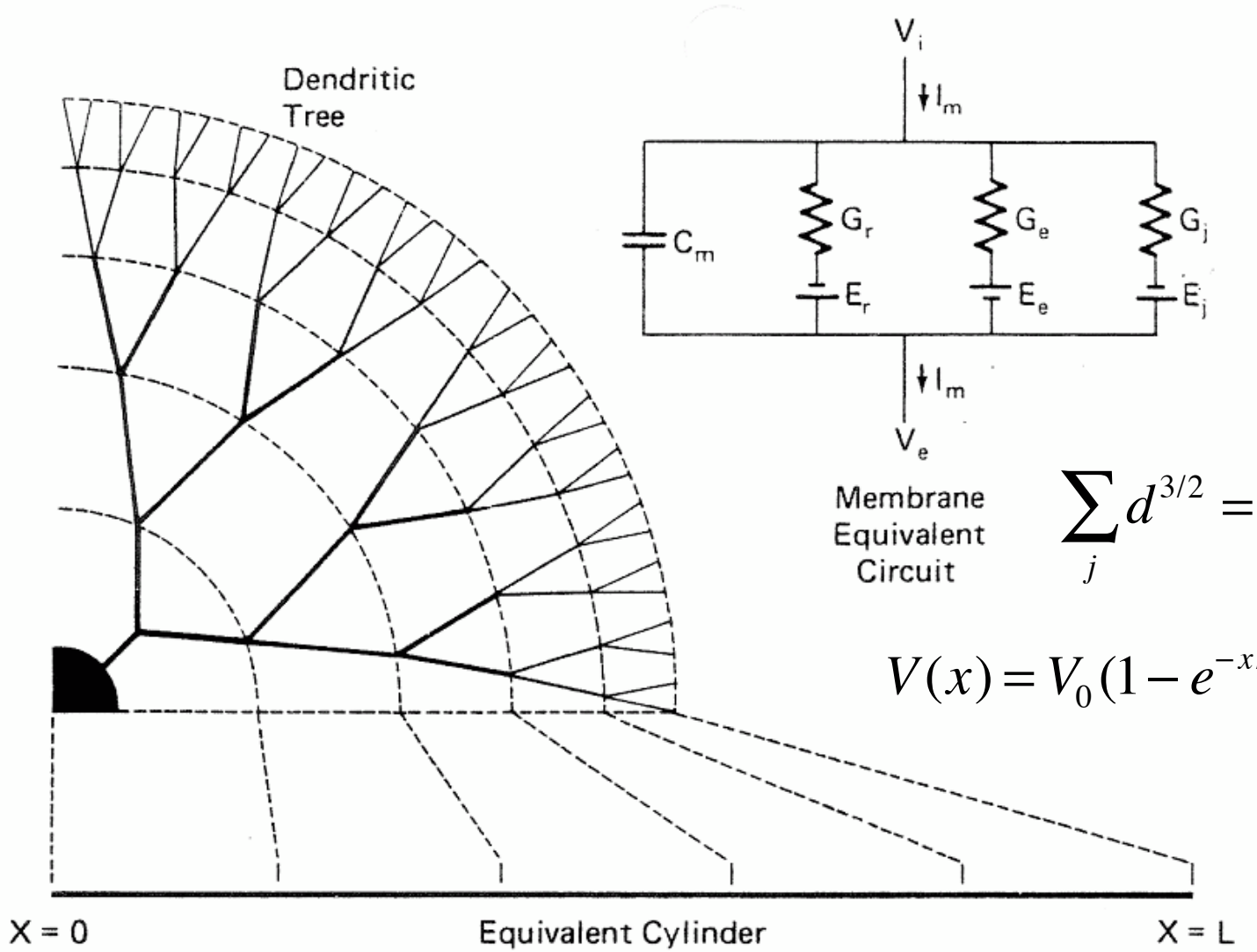


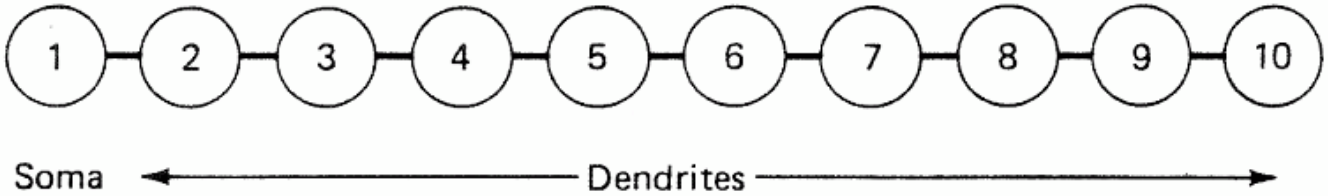
FIG. 13.7. Effect of different modes of dendritic branching on the spread of electrotonic potential. **A.** Graph of steady-state potential spread for the three cases illustrated in B. **B.** Diagrams illustrating three basic modes of branching; in each case the stem diameter is 4 μm : (a) Each daughter branch is 1 μm in diameter; (b) each daughter branch is approximately 2.5 μm, so that sum of $d^{3/2}$ equals $d^{3/2}$ of the stem; (c) each daughter branch has the same diameter as the stem. (Modified from Rall, 1958.)

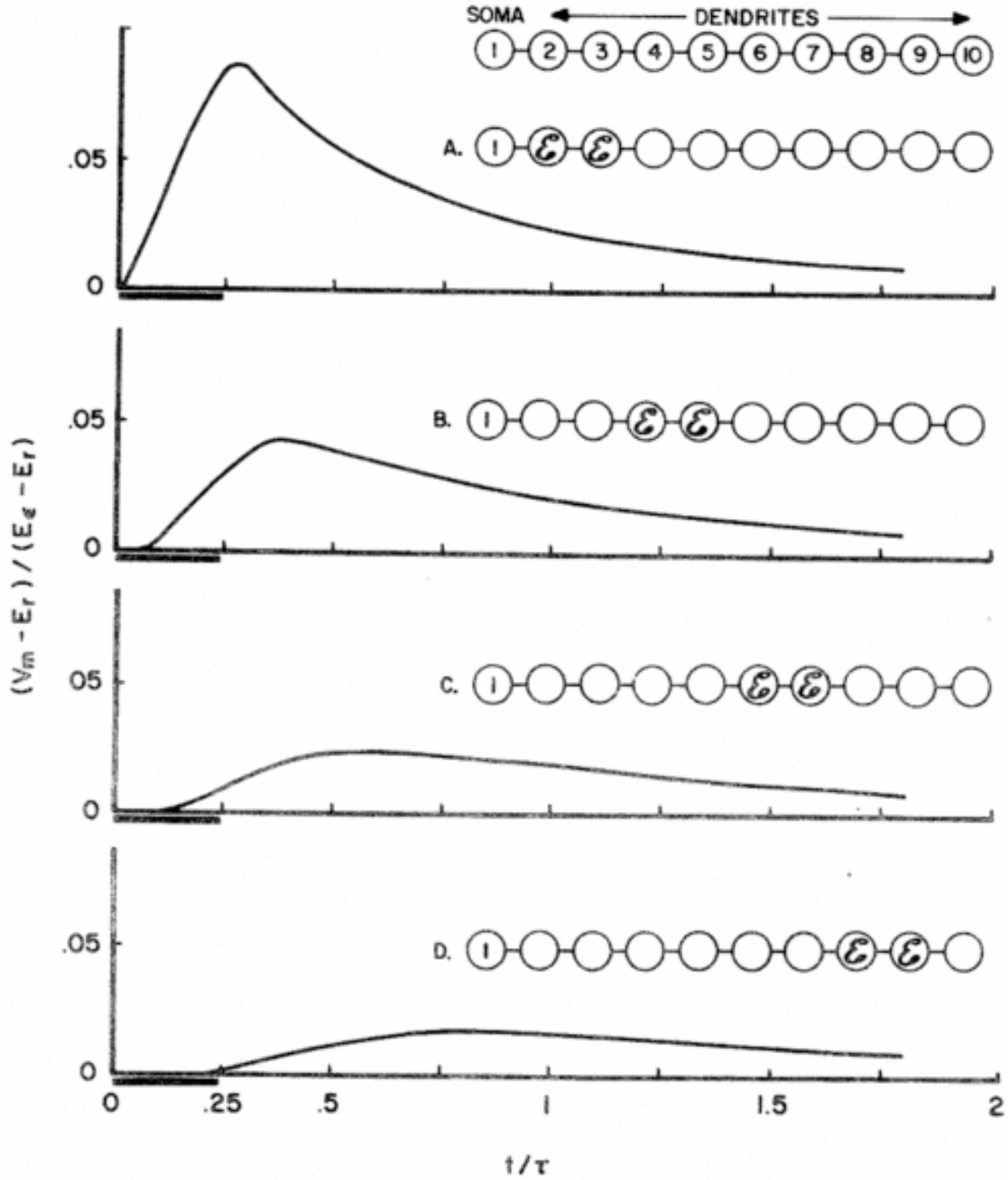
$$d_1^{3/2} = d_{21}^{3/2} + d_{22}^{3/2}$$



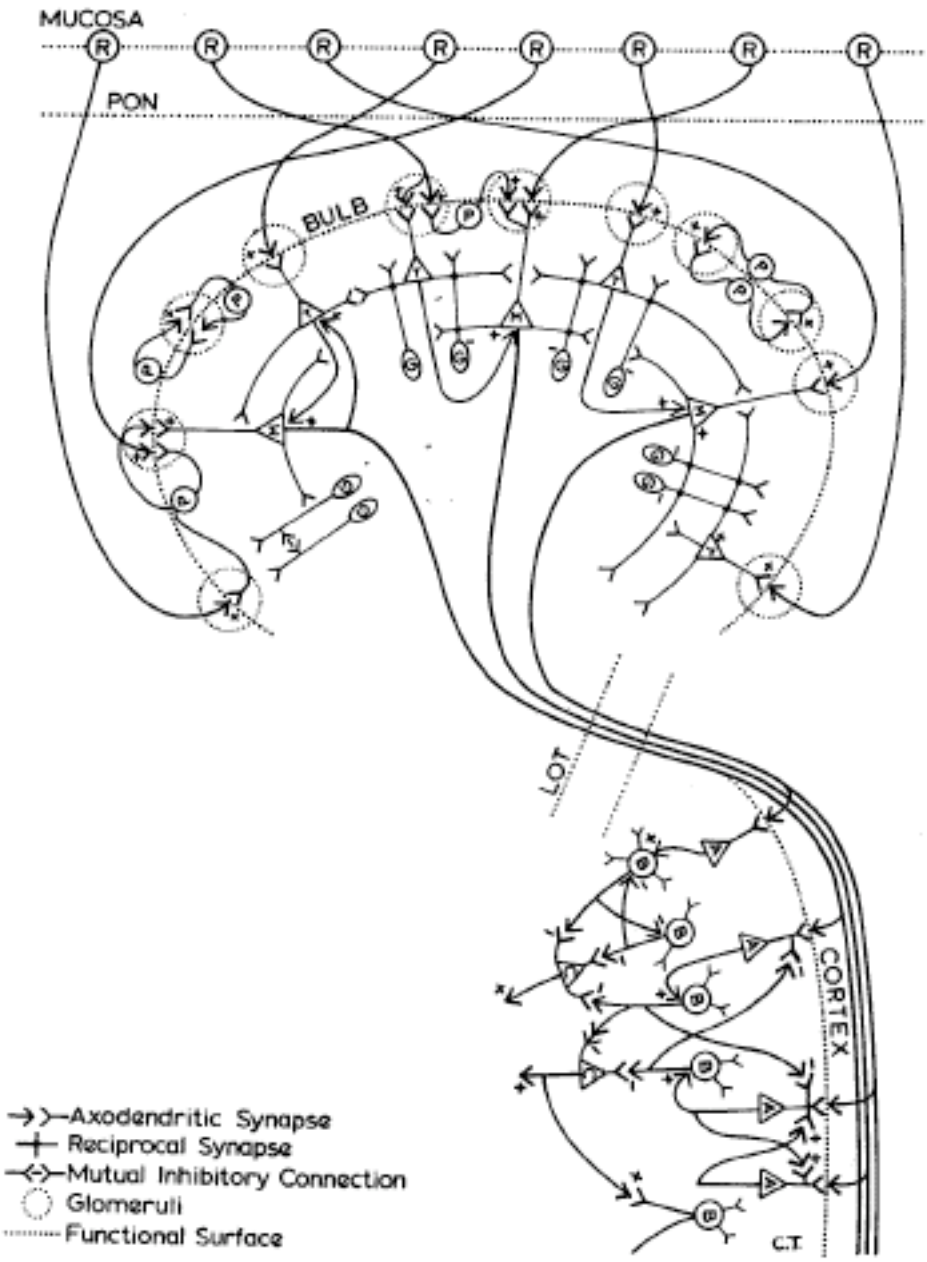
$$\sum_j d^{3/2} = \text{constant}$$

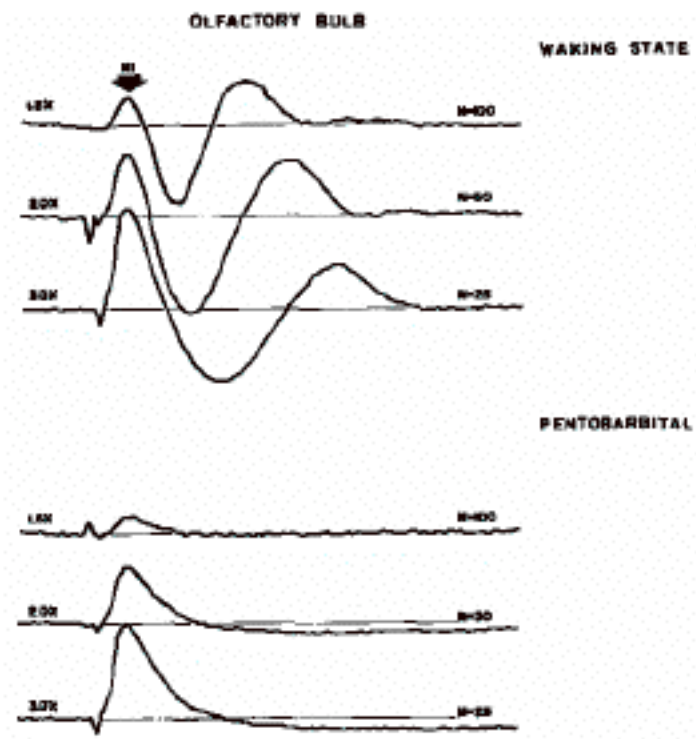
$$V(x) = V_0(1 - e^{-x/\lambda})$$



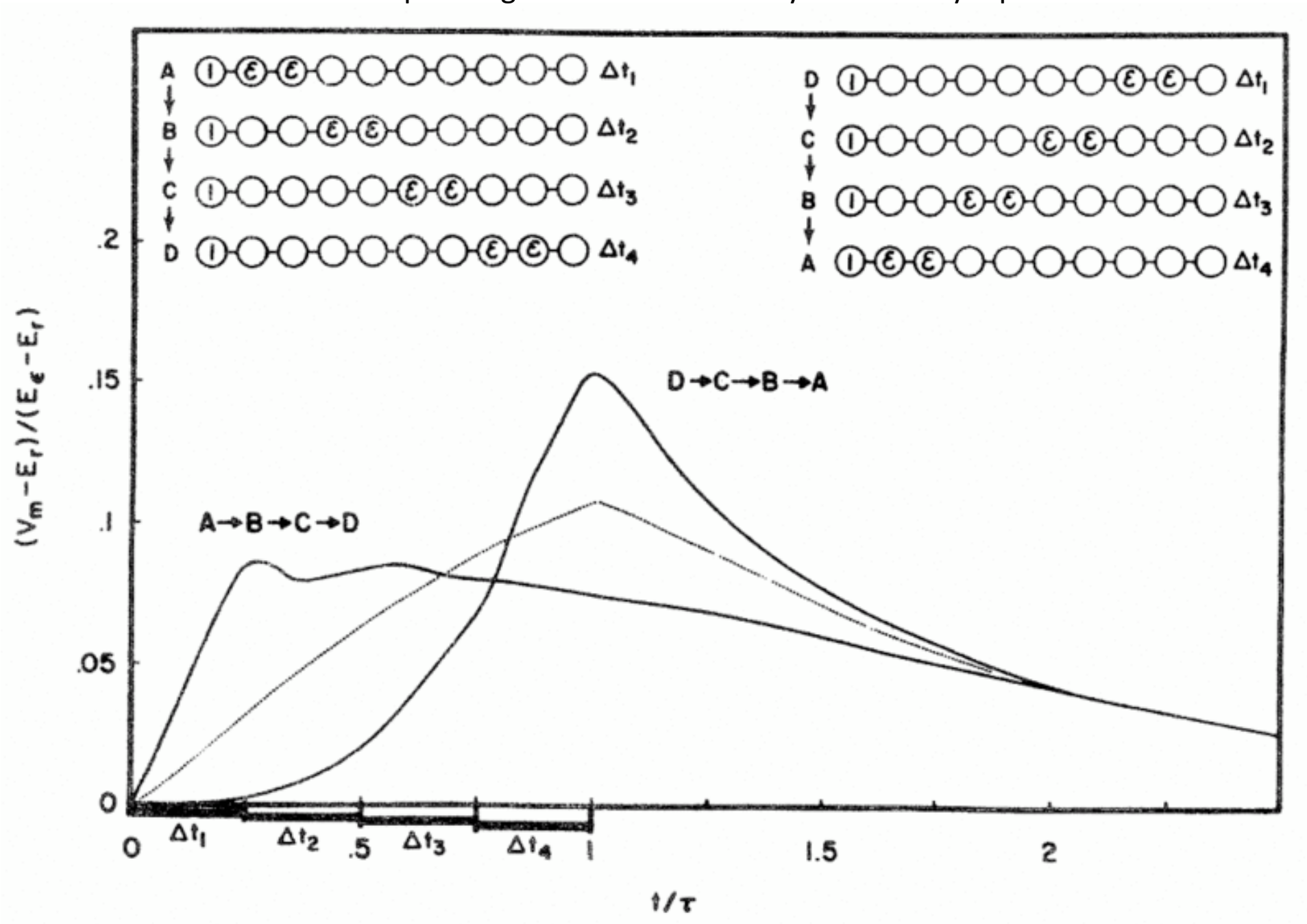

SOMA
DENDRITES
1 2 3 4 5 6 7 8 9 10
A.
B.
C.
D.
.05
0
$(V_m - E_r) / (E_e - E_r)$
0 .25 .5 1 1.5 2
t/τ

Rall & Shepherd – Evoked potential in OB

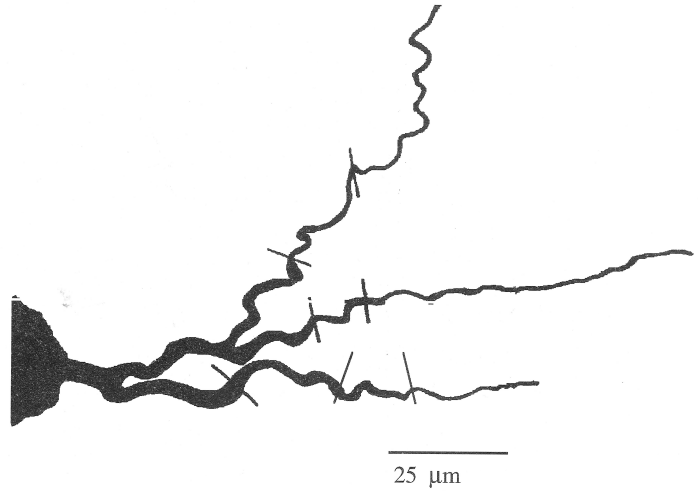




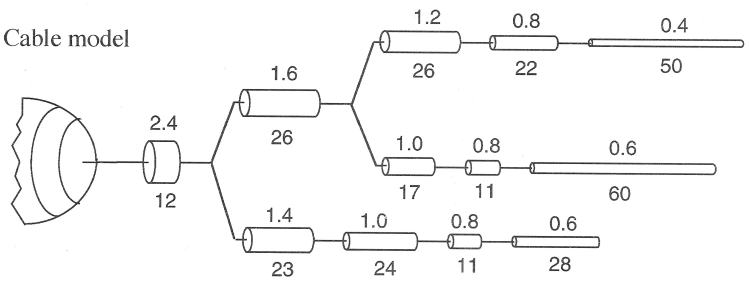
Sequencing Effects of Time Delay for Distal Synapses



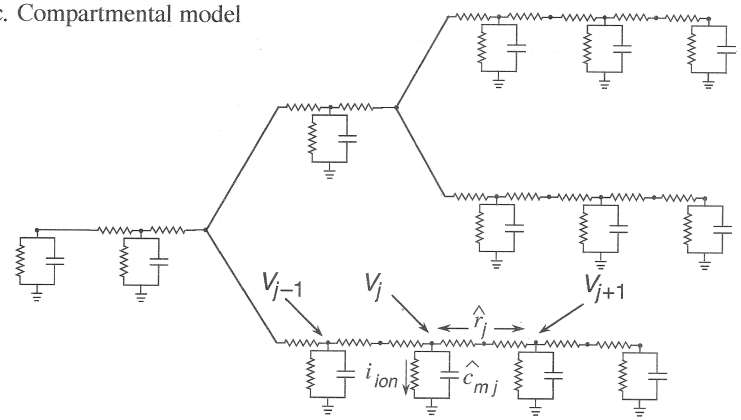
a. Physiologically and morphologically characterized neuron



b. Cable model



c. Compartmental model



Documentation | NEURON

http://www.neuron.yale.edu/neuron/docs

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NEURON

for empirically-based simulations of neurons and networks of neurons

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Documentation

FAQ
Programmer's Reference
Get a pkzip archive of the Programmer's Reference
The mercurial repository change log and sources

Tutorials

Construction and Use of Models: Part 1. Elementary Tools
A good place to start. Introduces some of NEURON's basic GUI tools.
Import3D tutorial
A convenient GUI tool for converting Eutectic, Neurolucida, and swc morphometric data into NEURON models. This used to be ../docs/import3d/main.html
CellBuilder tutorial

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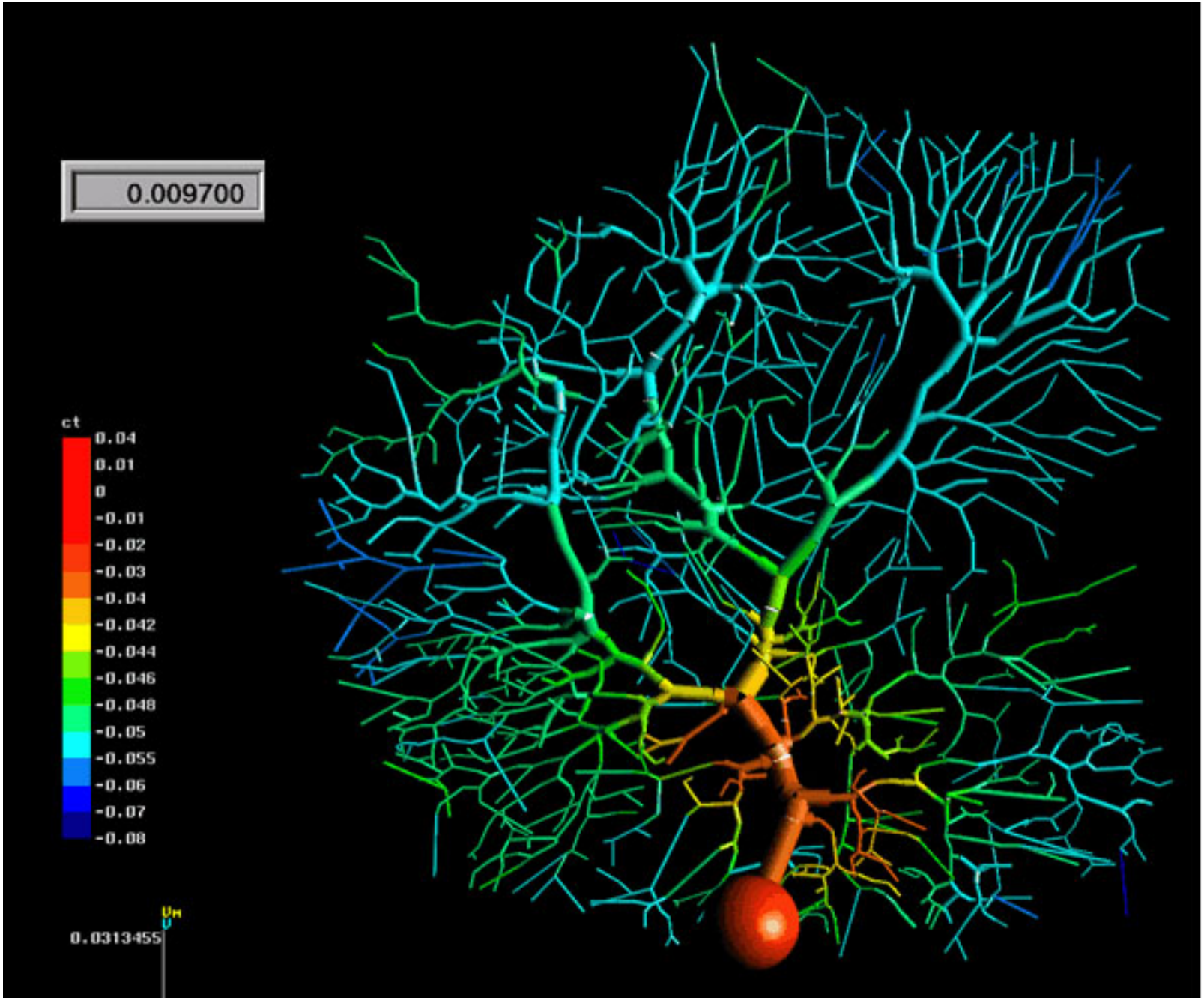
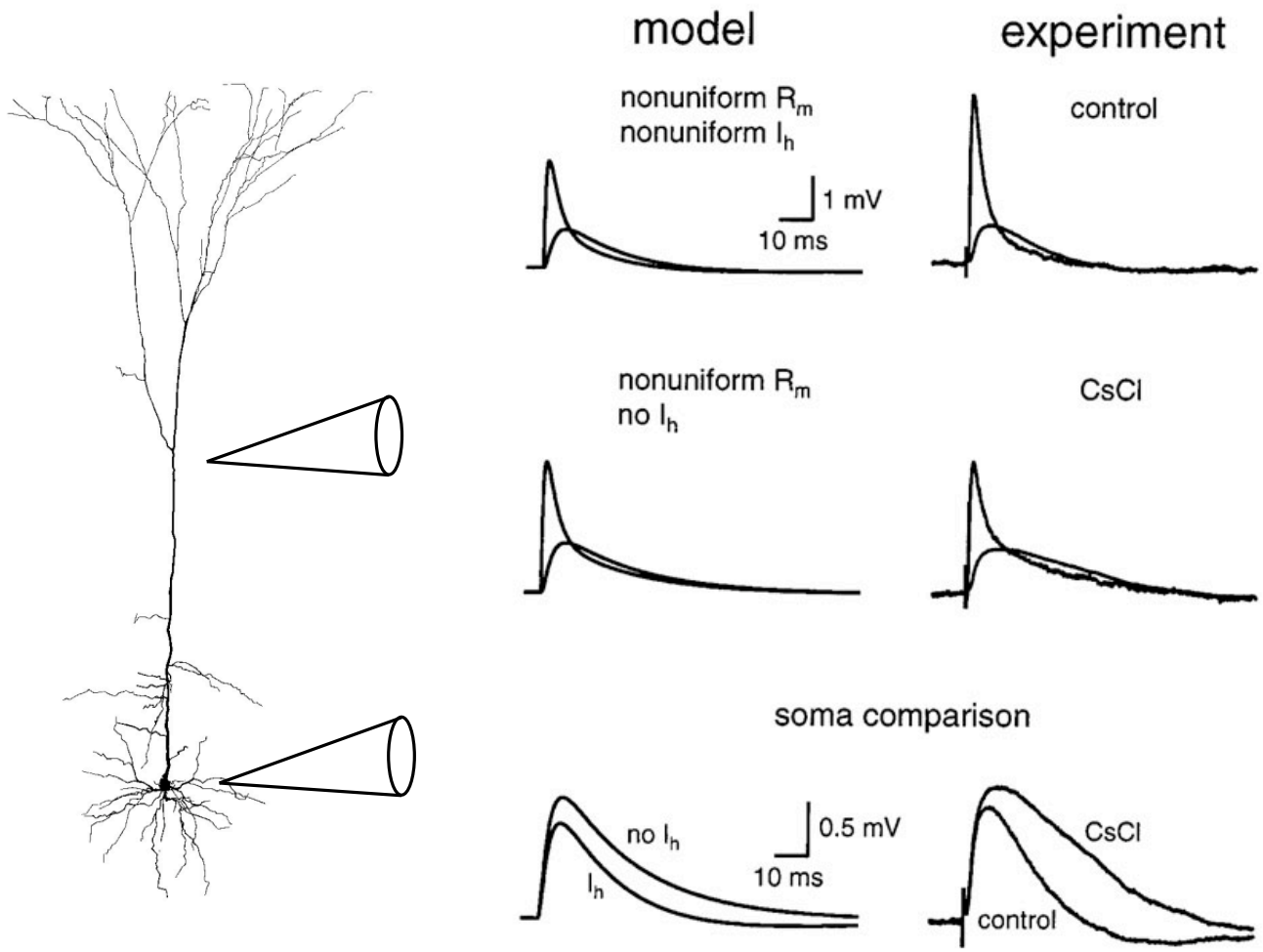
- Previous news and milestones

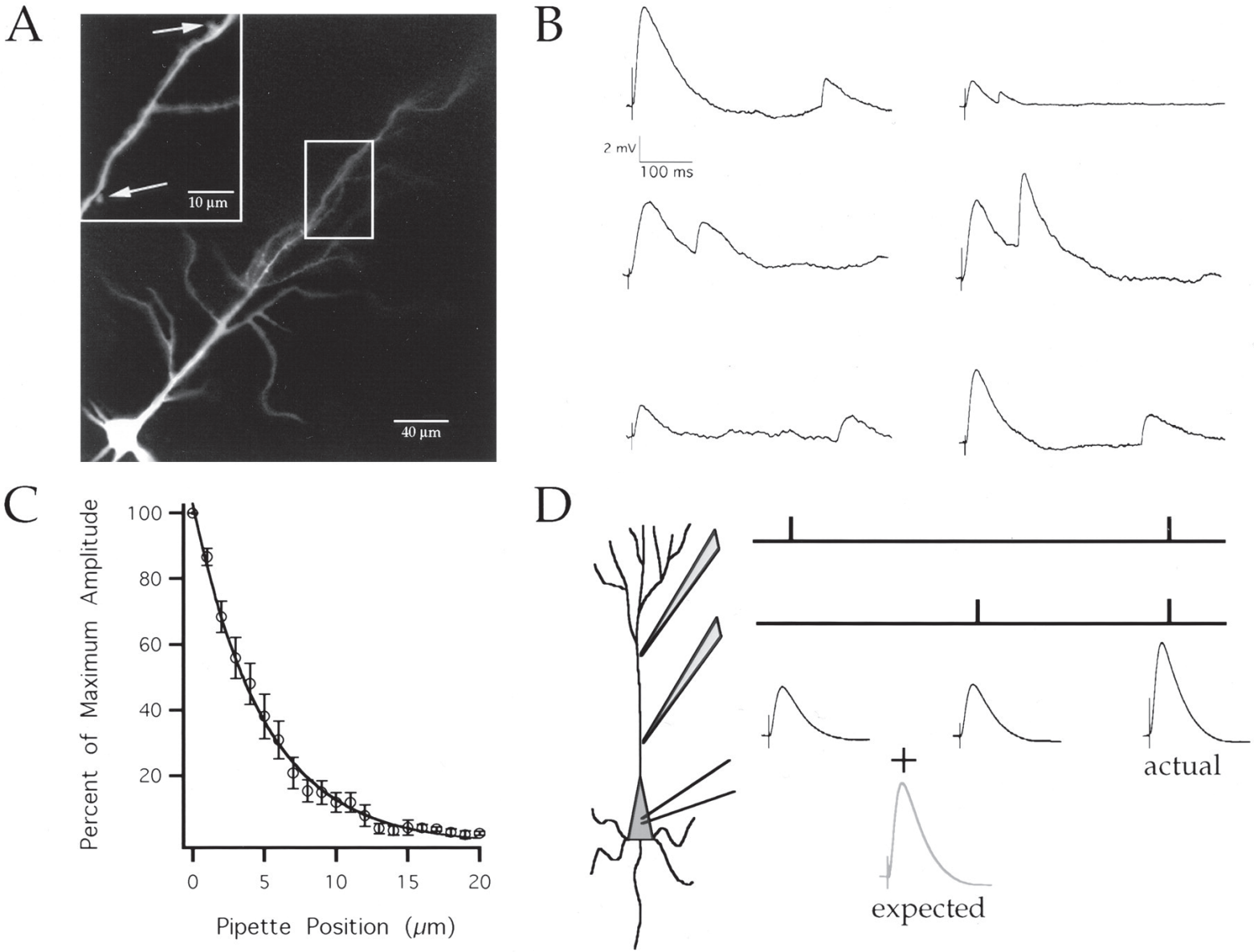

0.009700
ct
0.04
0.01
0
-0.01
-0.02
-0.03
-0.04
-0.042
-0.044
-0.046
-0.048
-0.05
-0.055
-0.06
-0.07
-0.08
Vm
0.0313455

EPSP attenuation in dendrites of pyramidal neurons



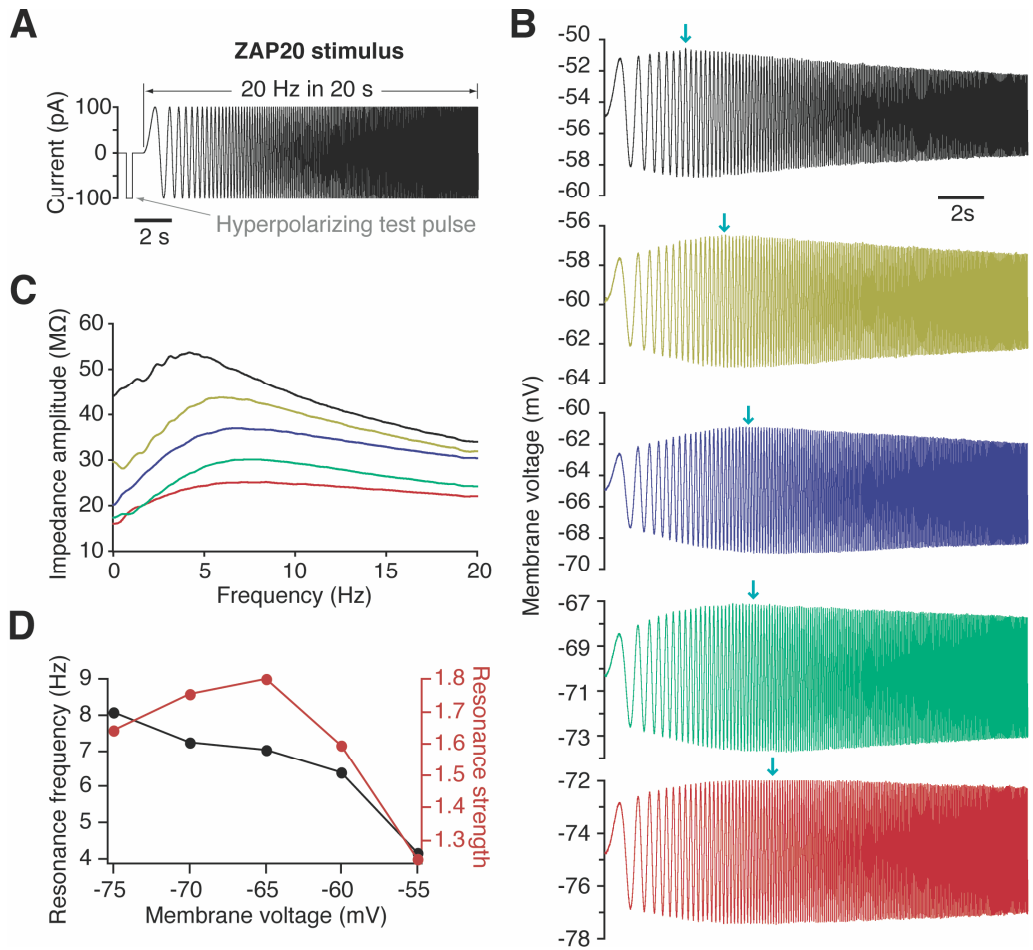
Stuart & Spruston, 1998

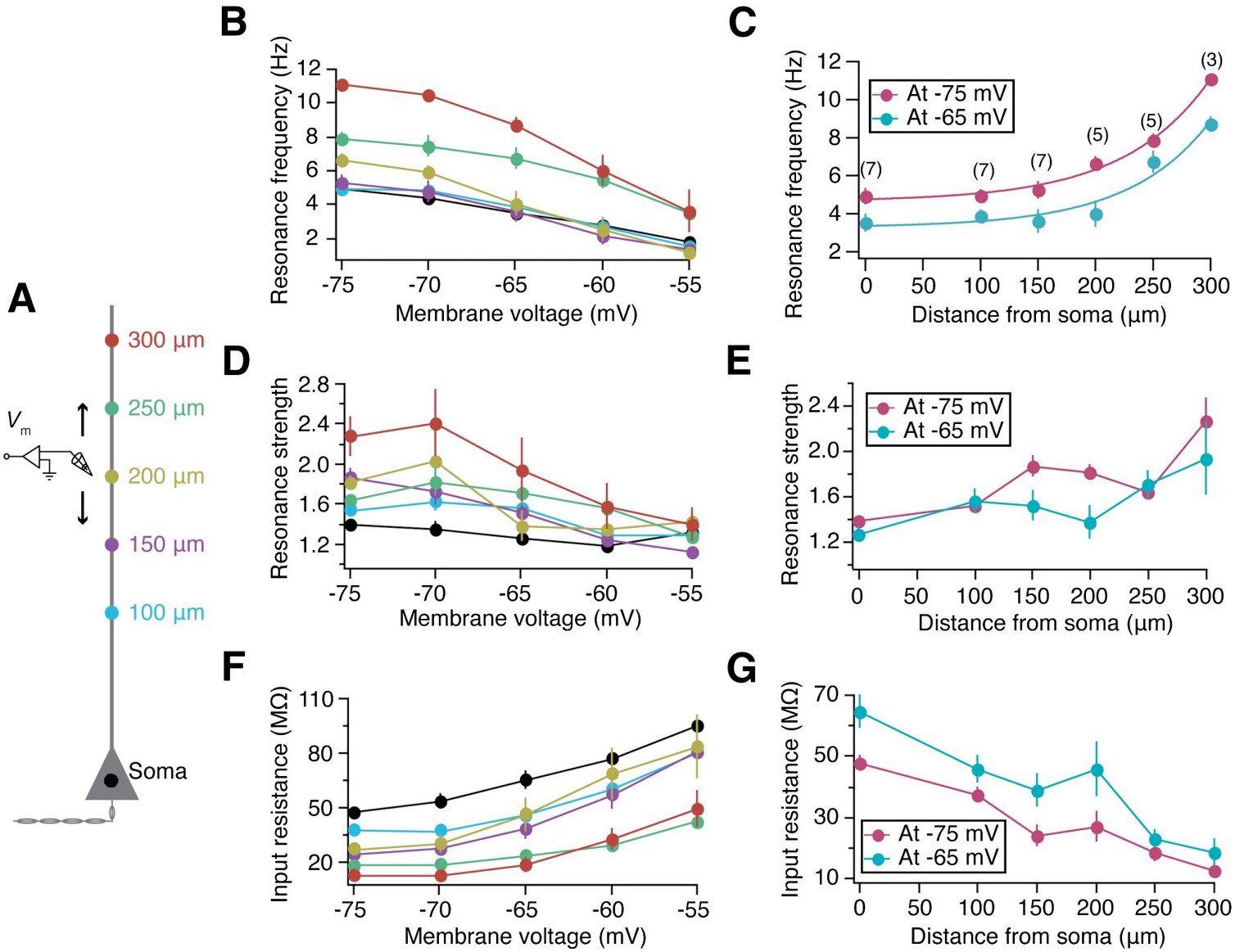
Spatial Summation in Dendrites: Evidence for Linearity



Cash and Yuste, Neuron (1999)

Voltage dependent channels (h current)
Resonance Properties in Dendrites

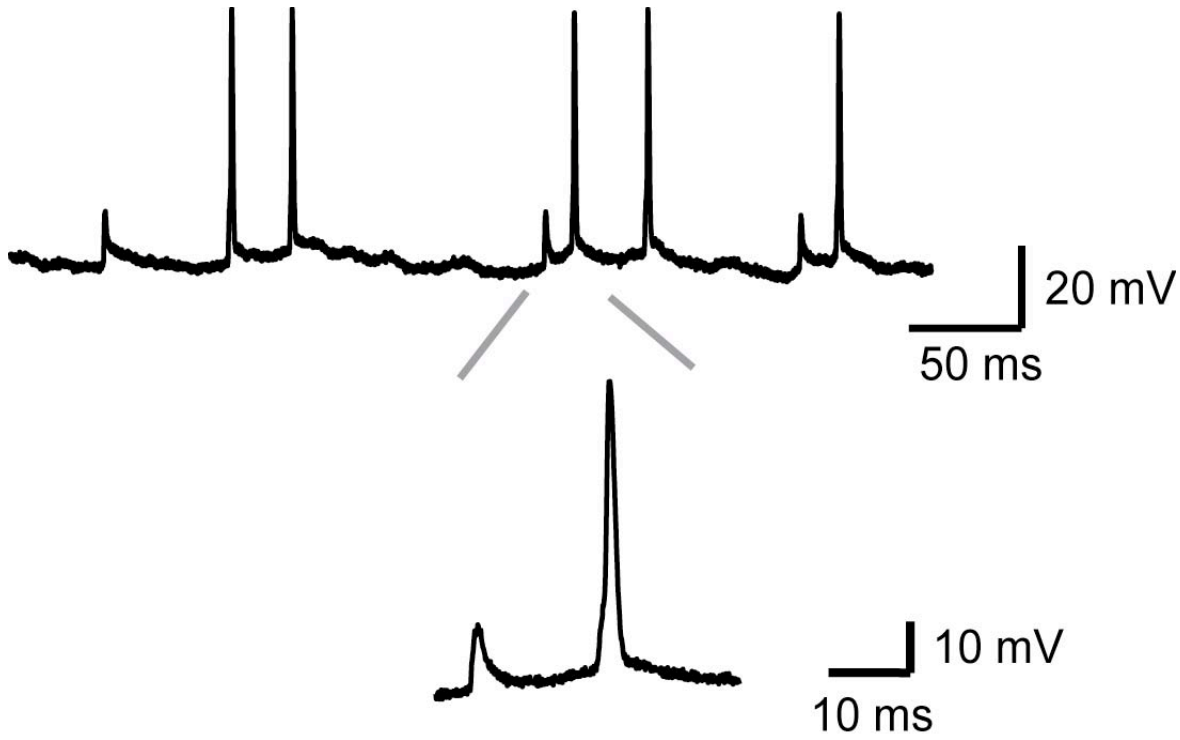


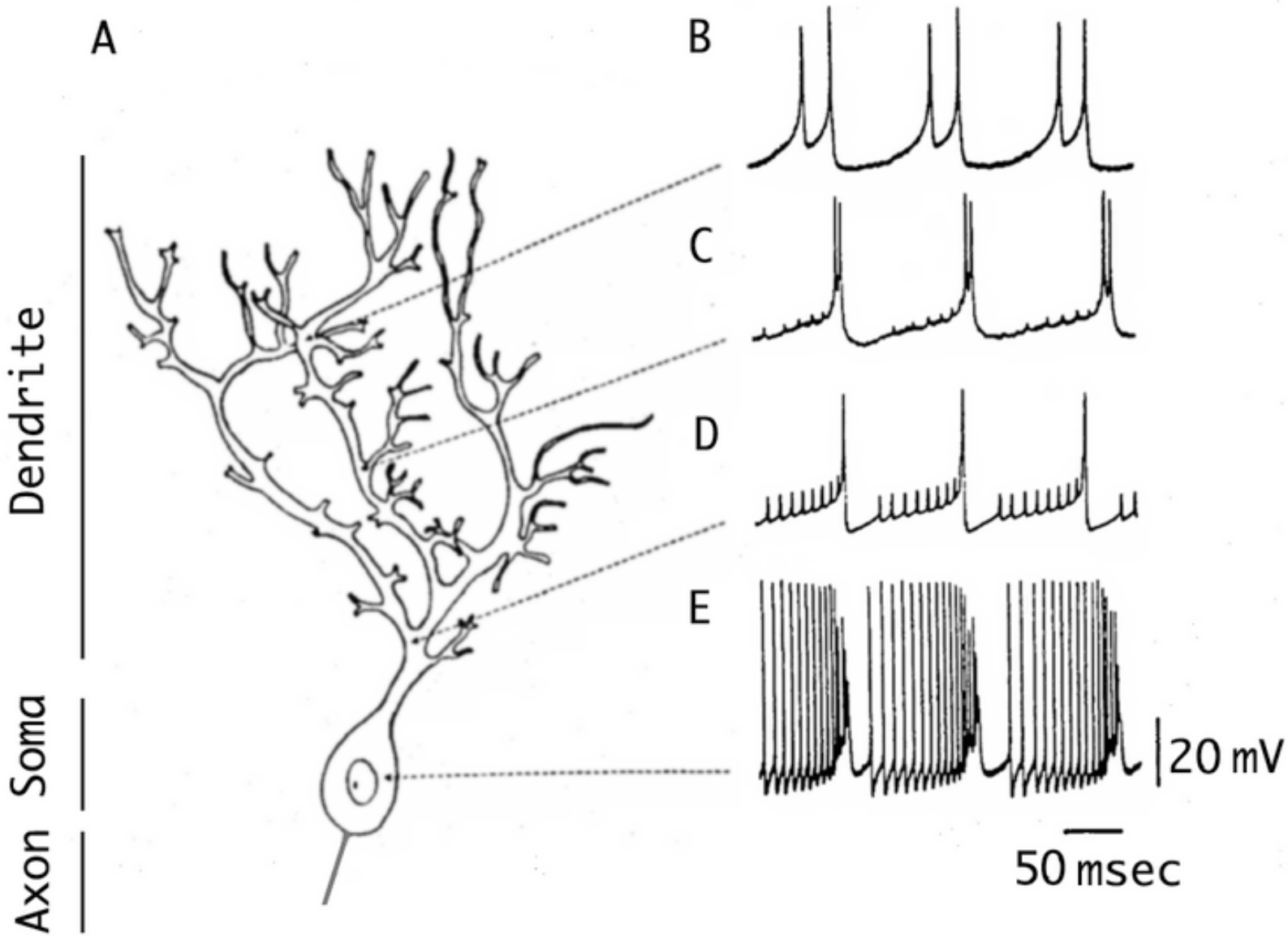

A
300 µm
250 µm
200 µm
150 µm
100 µm
V_m
Soma
B
Resonance frequency (Hz)
Membrane voltage (mV)
C
Resonance frequency (Hz)
Distance from soma (µm)
At -75 mV
At -65 mV
(7)
(7)
(7)
(5)
(5)
(3)
D
Resonance strength
Membrane voltage (mV)
E
Resonance strength
Distance from soma (µm)
At -75 mV
At -65 mV
F
Input resistance (MΩ)
Membrane voltage (mV)
G
Input resistance (MΩ)
Distance from soma (µm)
At -75 mV
At -65 mV

Active Dendrites

Spencer and Kandel

“prepotentials”



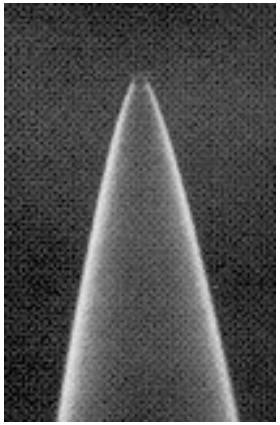


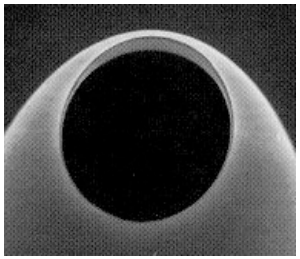
Llinas & Sugimori

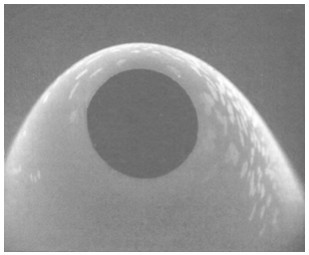
New Techniques to Study Dendrites

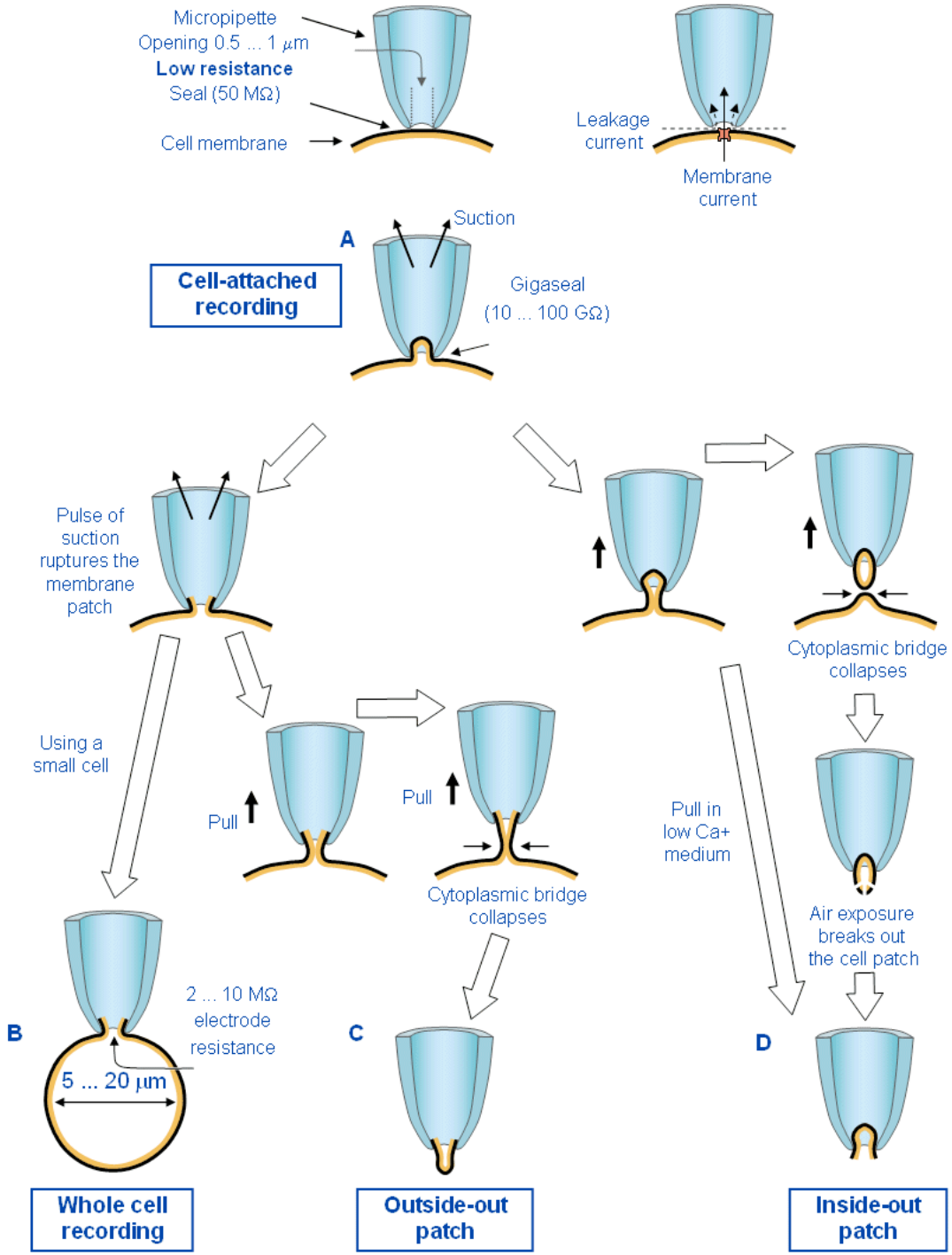
Visualization (IR and Fluorescence)
Patch recording from dendrites
Two photon laser scanning microscopy
Calcium concentration dynamics
Caged transmitters and two photon uncaging

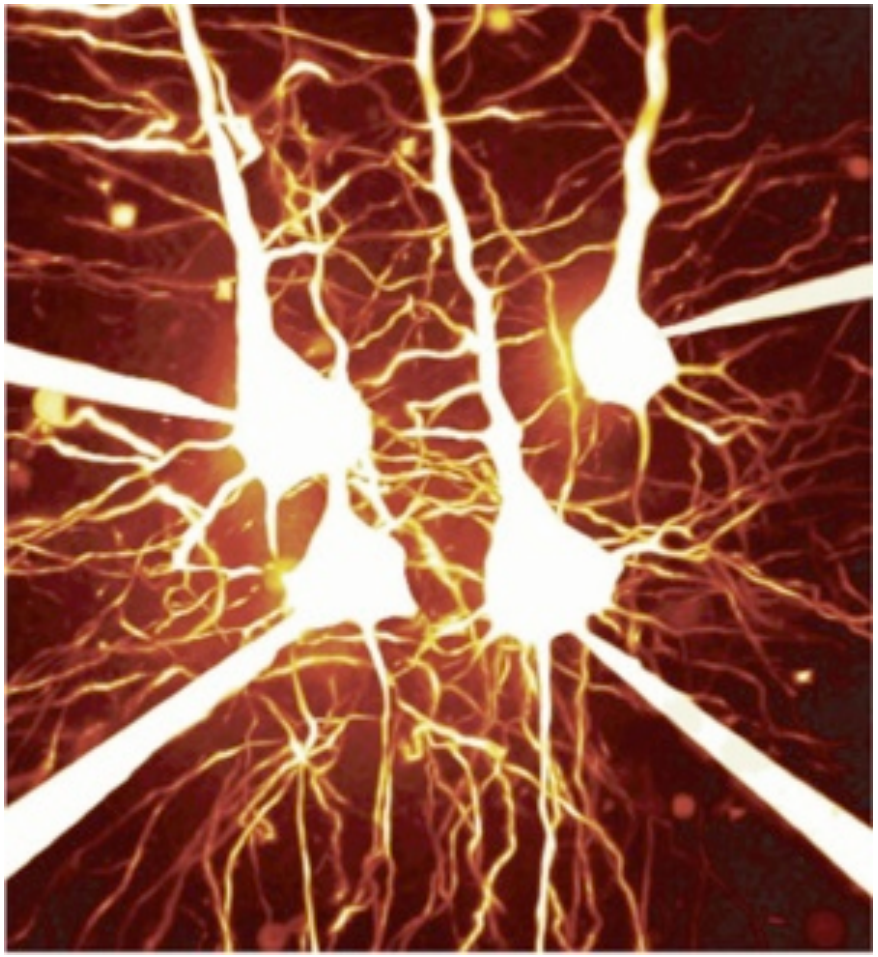
Patch Recording



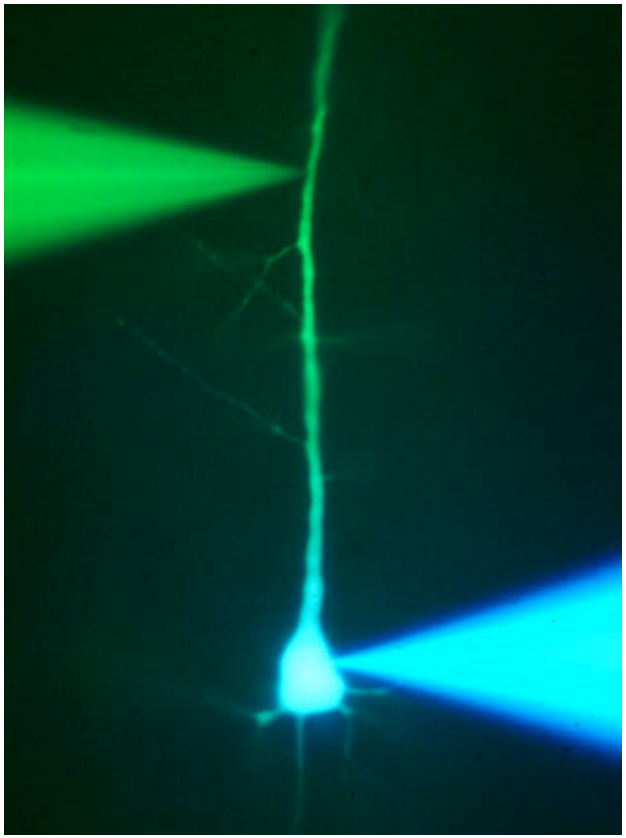




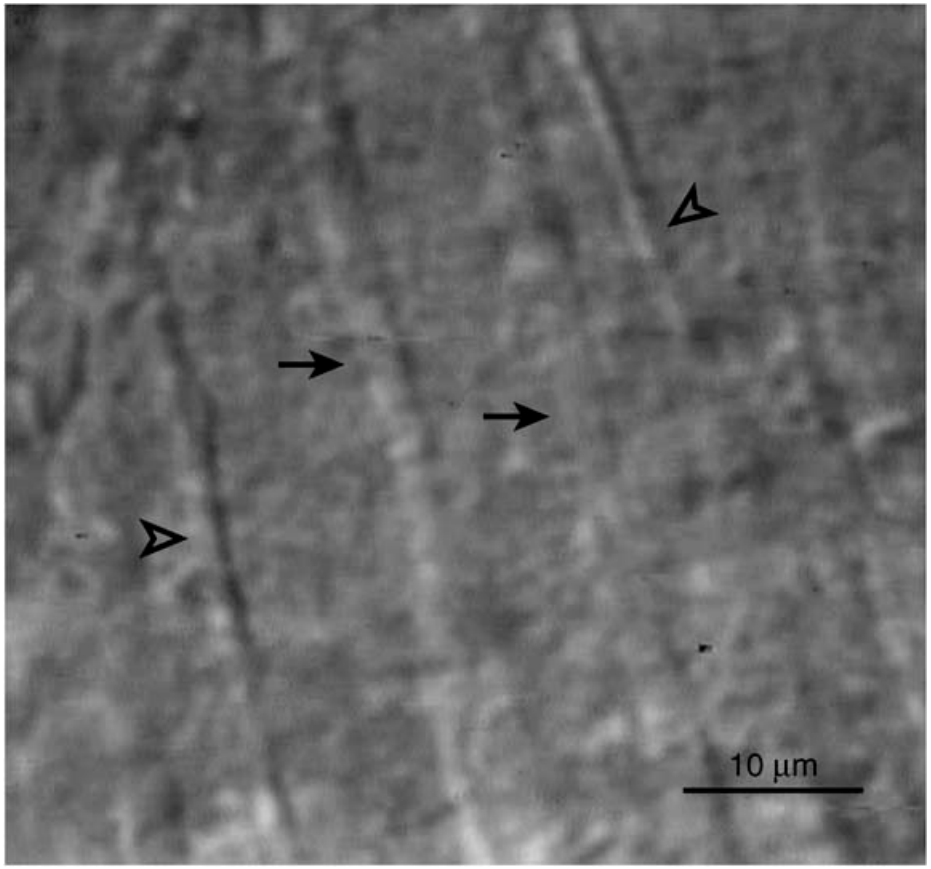


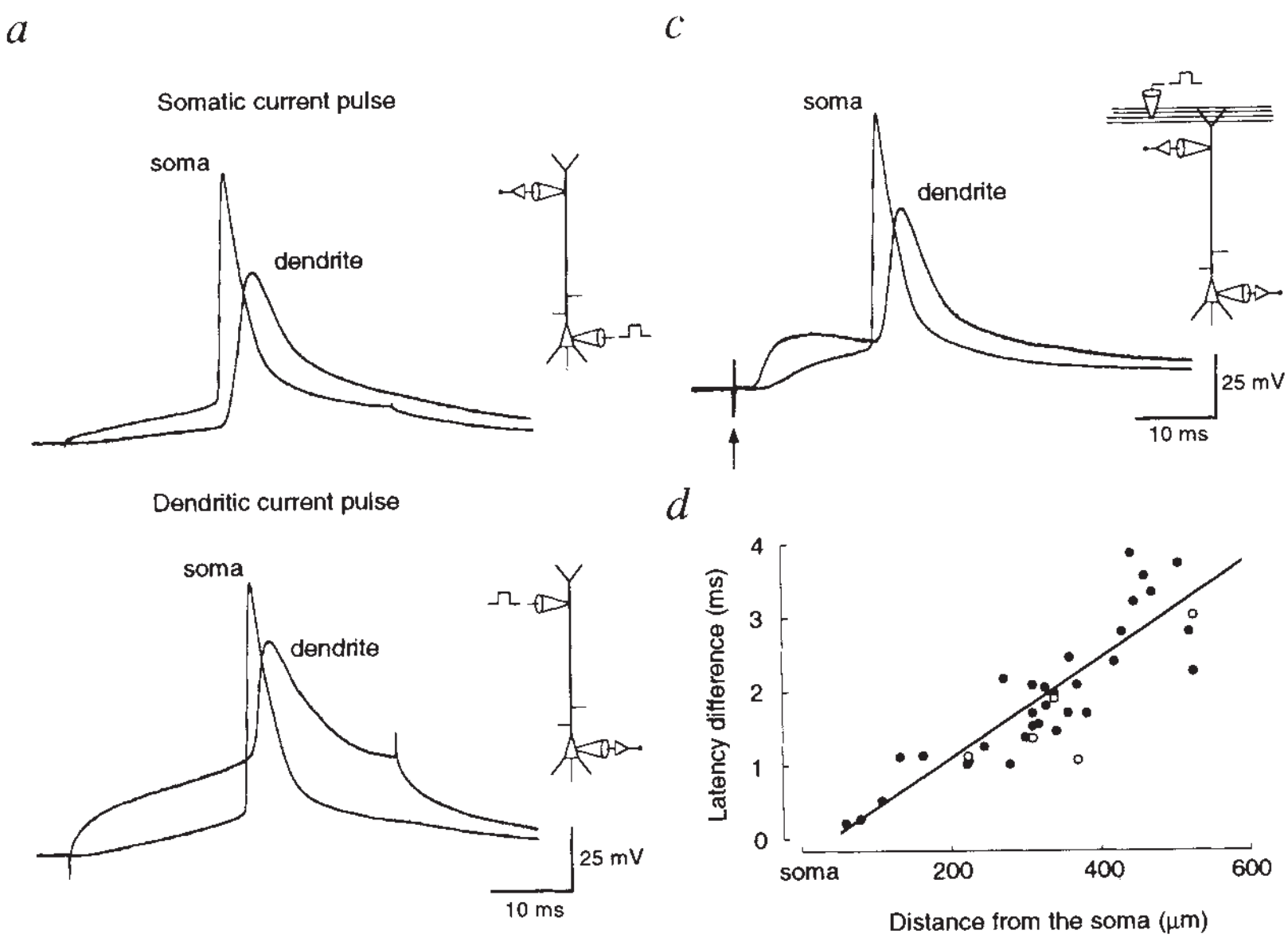


M. Hausser

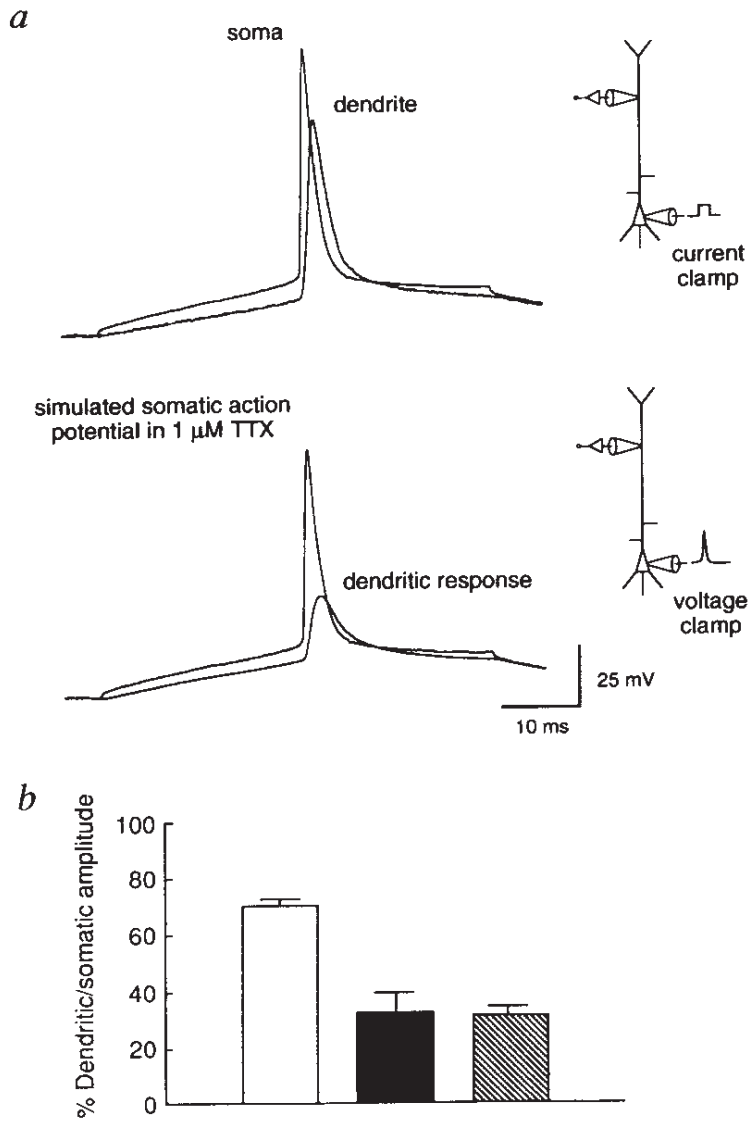


Diffusion, Visualization, and Dialysis

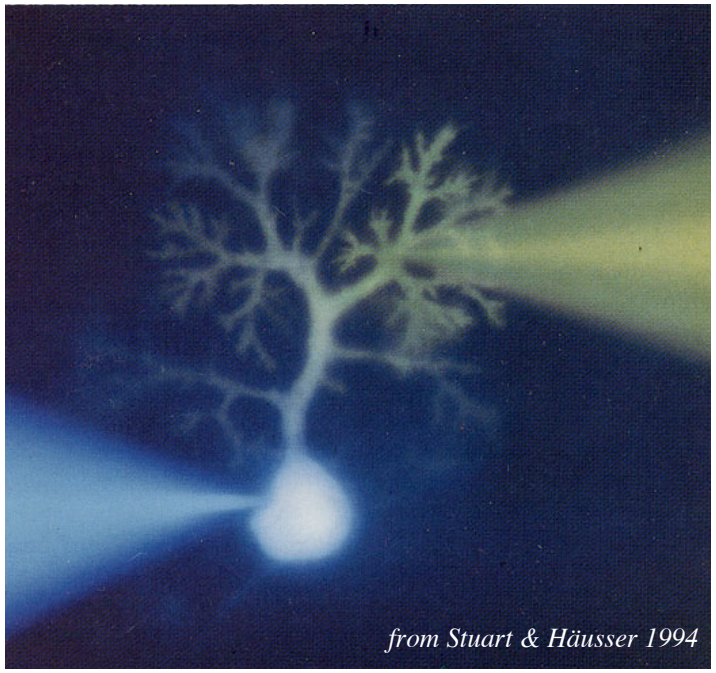

10 µm

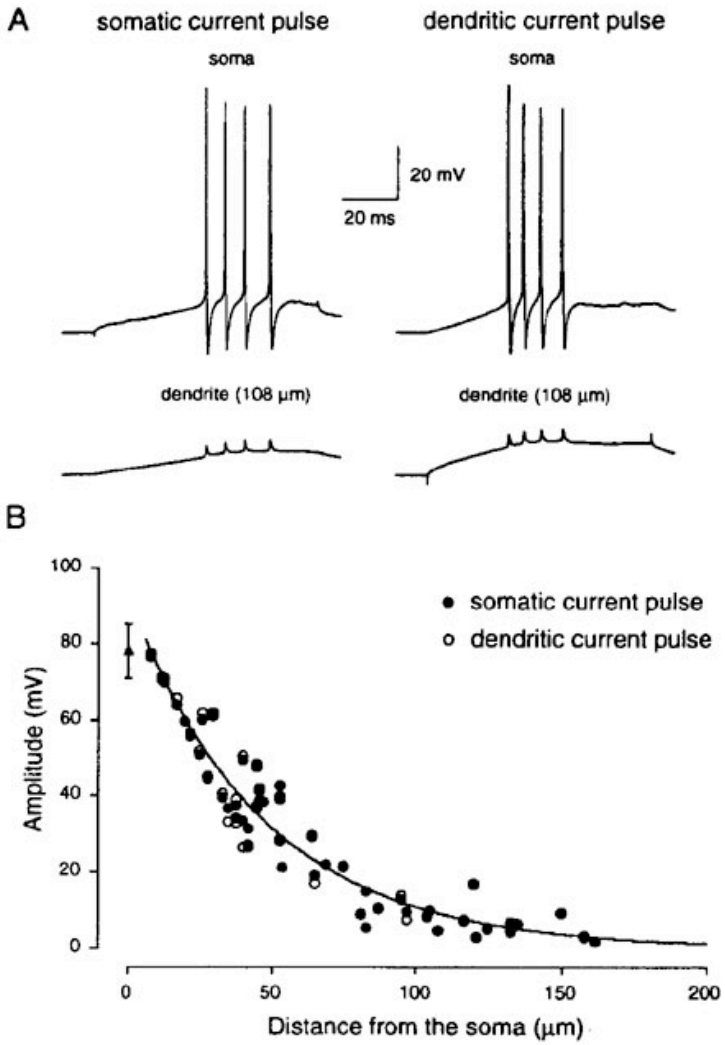


Stuart & Sakmann, Nature (1994)

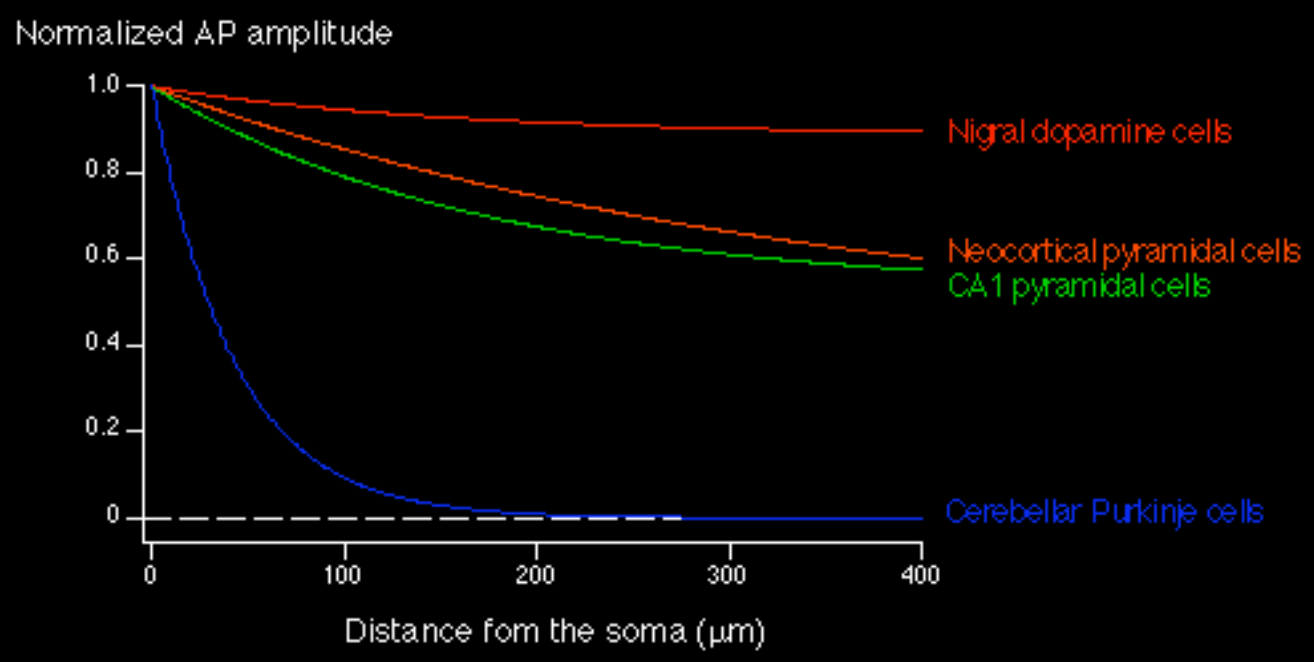

a
soma
dendrite
current
clamp
simulated somatic action
potential in 1 μM TTX
dendritic response
voltage
clamp
25 mV
10 ms
b
% Dendritic/somatic amplitude
100
80
60
40
20
0

Backpropagation is not present in all neurons (e.g. Purkinje cells)

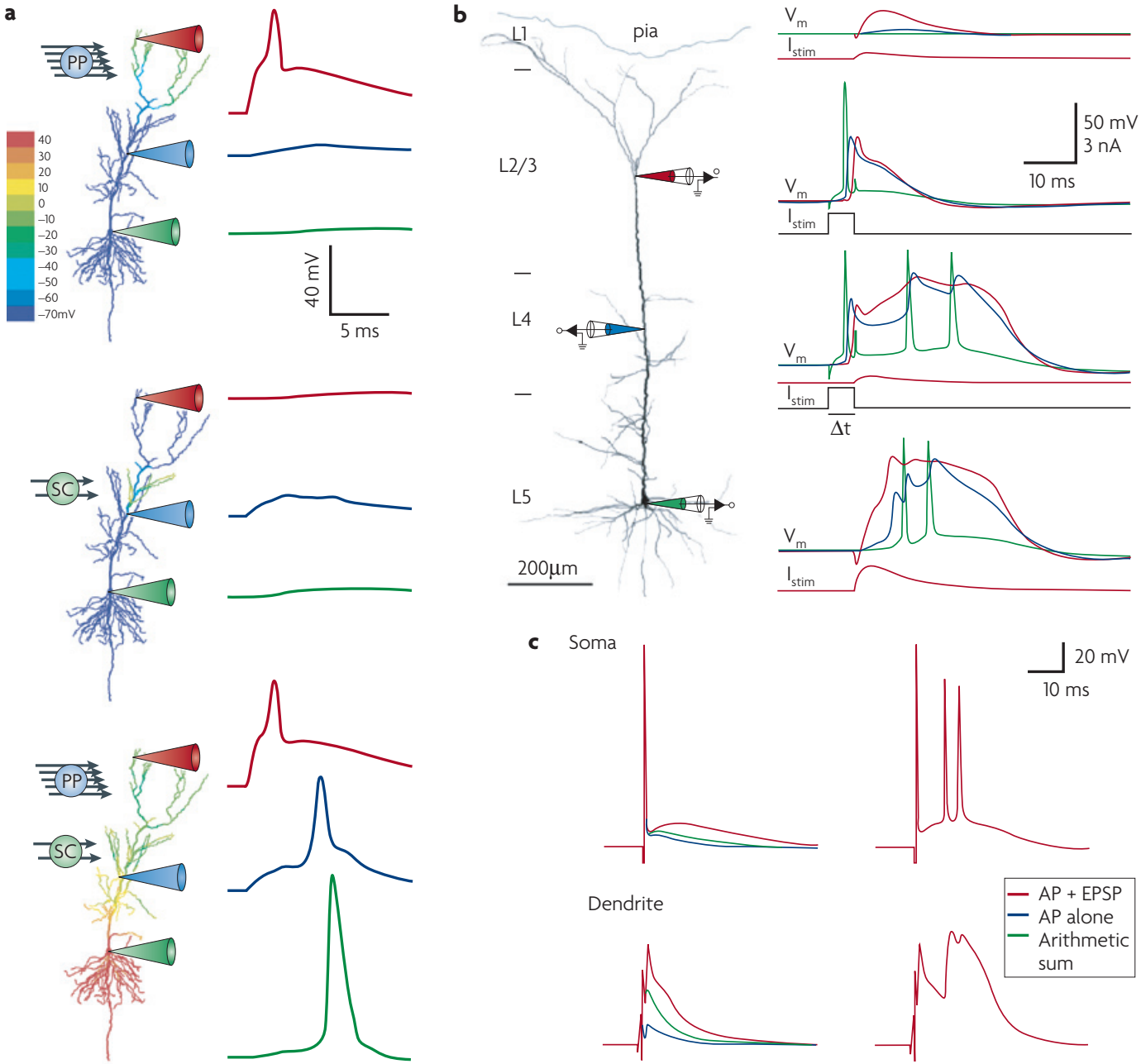




Backpropagation is cell-type specific



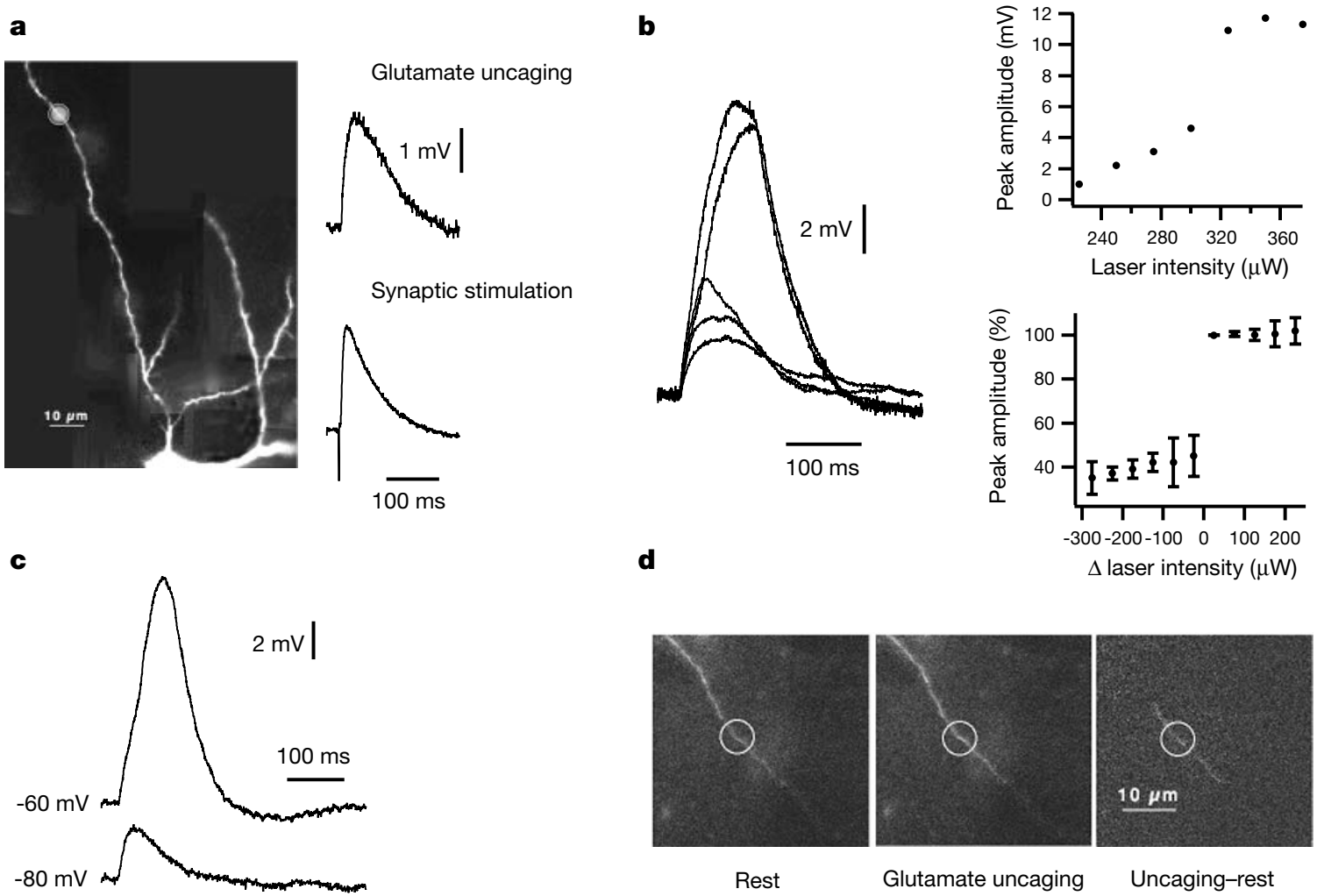
Nonlinear effects of mixed PSPs and Spikes



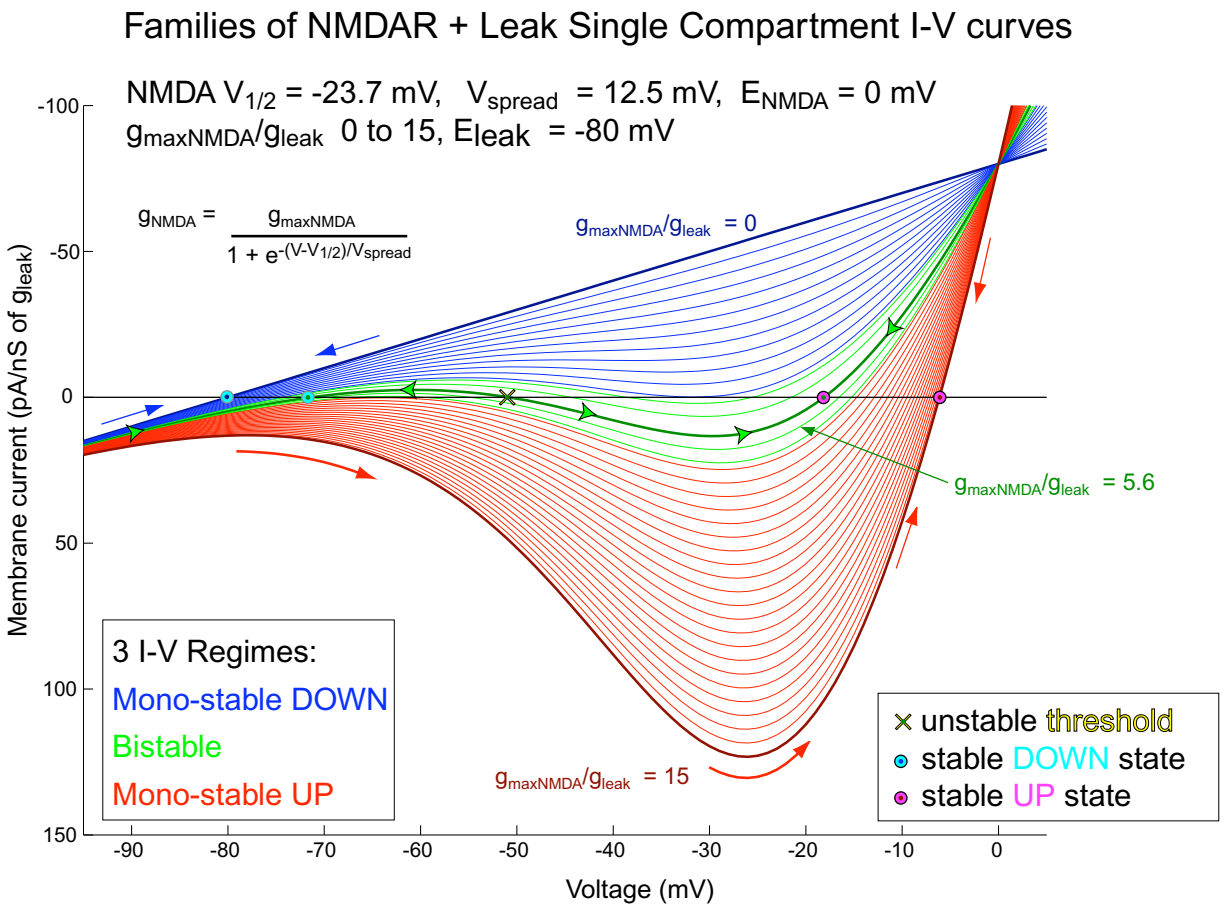
BAC: backprop. activated calcium spike

Stuart & Hausser Nat. Neurosci. 4:63 (2001)

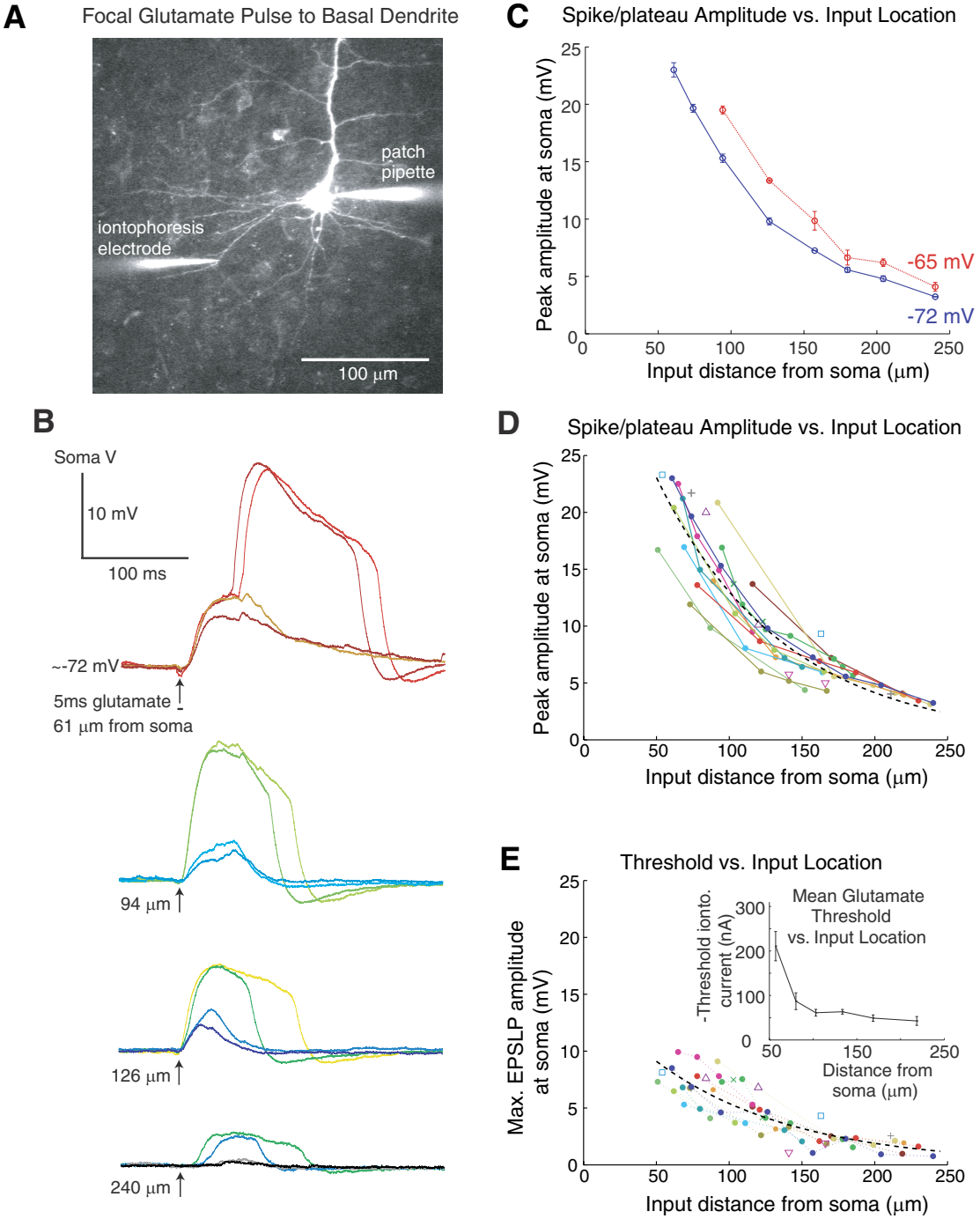
NMDA Spikes

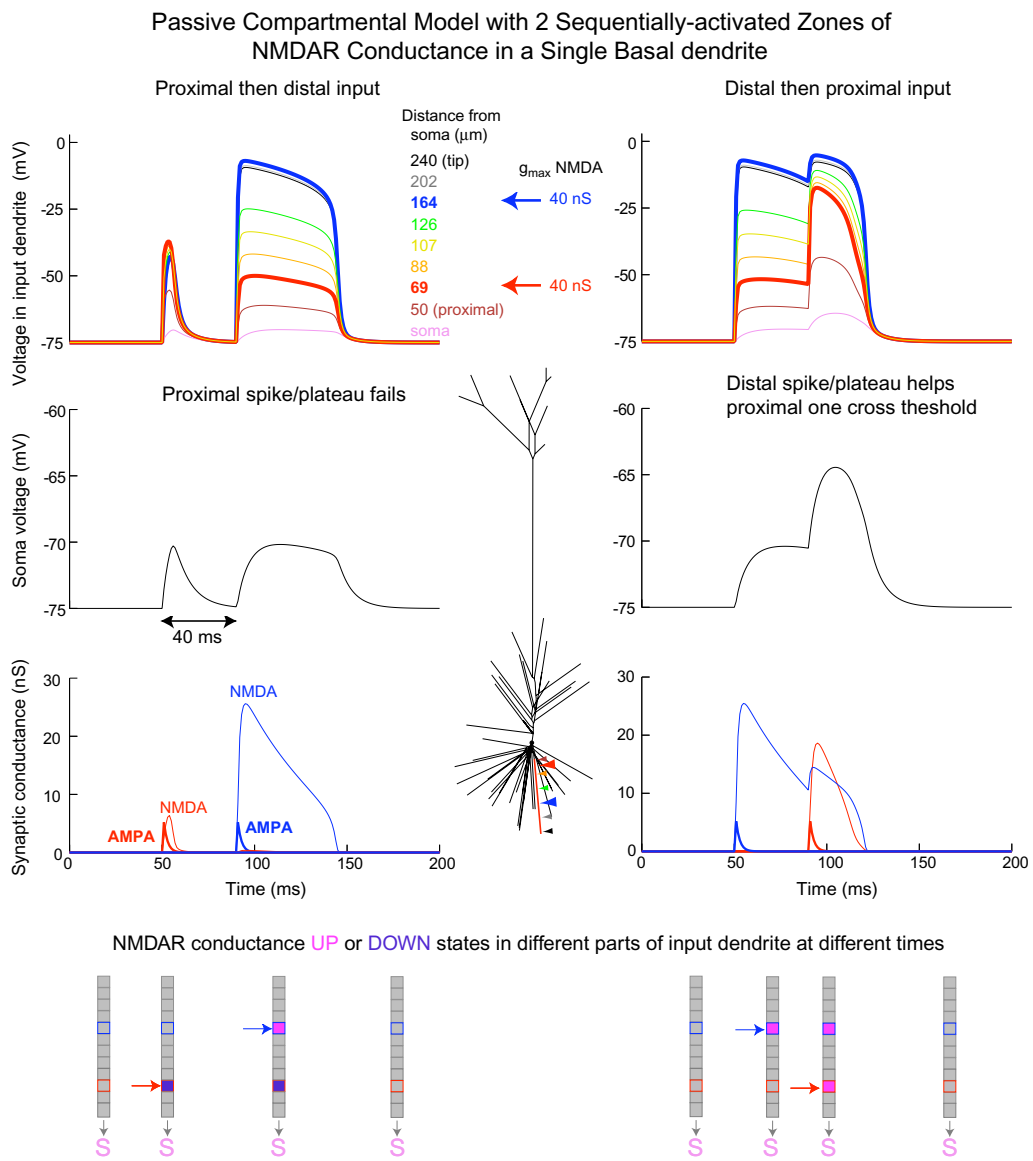


Schiller et al., Nature (2000)



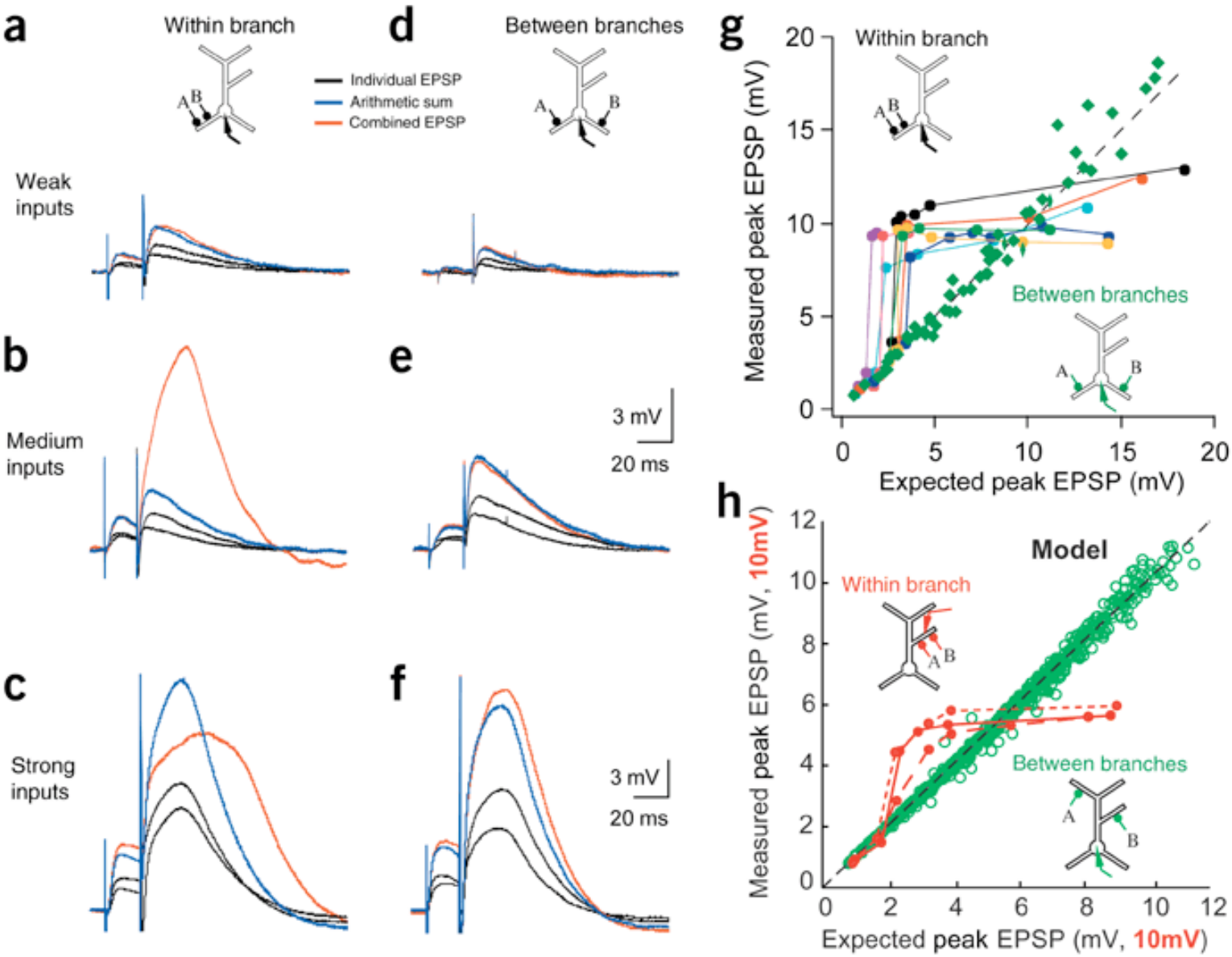
Supplementary Figure 4. Voltage-dependent NMDA conductance + passive leak can generate current-voltage (I-V) relations exhibiting 3 stability regimes. Theoretical illustration based on single compartment model with parameters indicated (Lisman et al. 1998). As the maximum (fully-depolarized) NMDA conductance $g_{maxNMDA}$ increases, the I-V relation sweeps successively through three regimes: mono-stable DOWN ('boosting', blue lines), bistable (green lines), and mono-stable UP ('self-triggering', red lines), depending on the number and positions of the fixed points (zero current axis crossings). Stable fixed points on an exemplar I-V relation (thicker darker lines) for each regime indicated by concentric targets, unstable threshold fixed point on bistable exemplar marked by X. Neighboring I-V curves separated by increments in $g_{maxNMDA}/g_{leak}$ ratio of 0.2 (near regime boundaries), 0.4 (default) or 0.6 (just above bistable exemplar curve). Note negative currents are upwards (voltage clamp convention). System flow is indicated by arrows. For example, in the case of the thick dark green bistable curve, small negative voltage perturbations away from threshold result in negative currents through the membrane, hyperpolarizing the system progressively towards the stable DOWN state (cyan target). Small positive perturbations from threshold lead to positive currents, forcing the system to flow towards the UP-state (magenta target). Note that the DOWN and UP-states move to more depolarized levels as the NMDAR conductance increases, but the threshold is reduced. Pyramidal neurons typically exhibit inward rectification (see Supplementary Figure 2D3). The first segment of the I-V curve can be made steeper by including an inward rectification conductance in the membrane (not shown); this can make the N-shape more symmetrical as well as increasing the breadth (in parameter space) of the bistable regime.


A
Focal Glutamate Pulse to Basal Dendrite
patch pipette
iontophoresis electrode
100 μm
B
Soma V
10 mV
100 ms
~-72 mV
5ms glutamate
61 μm from soma
94 μm
126 μm
240 μm
C
Spike/plateau Amplitude vs. Input Location
Peak amplitude at soma (mV)
Input distance from soma (μm)
-65 mV
-72 mV
D
Spike/plateau Amplitude vs. Input Location
Peak amplitude at soma (mV)
Input distance from soma (μm)
E
Threshold vs. Input Location
Max. EPSLP amplitude at soma (mV)
Input distance from soma (μm)
Mean Glutamate Threshold vs. Input Location
-Threshold iontophoresis current (nA)
Distance from soma (μm)



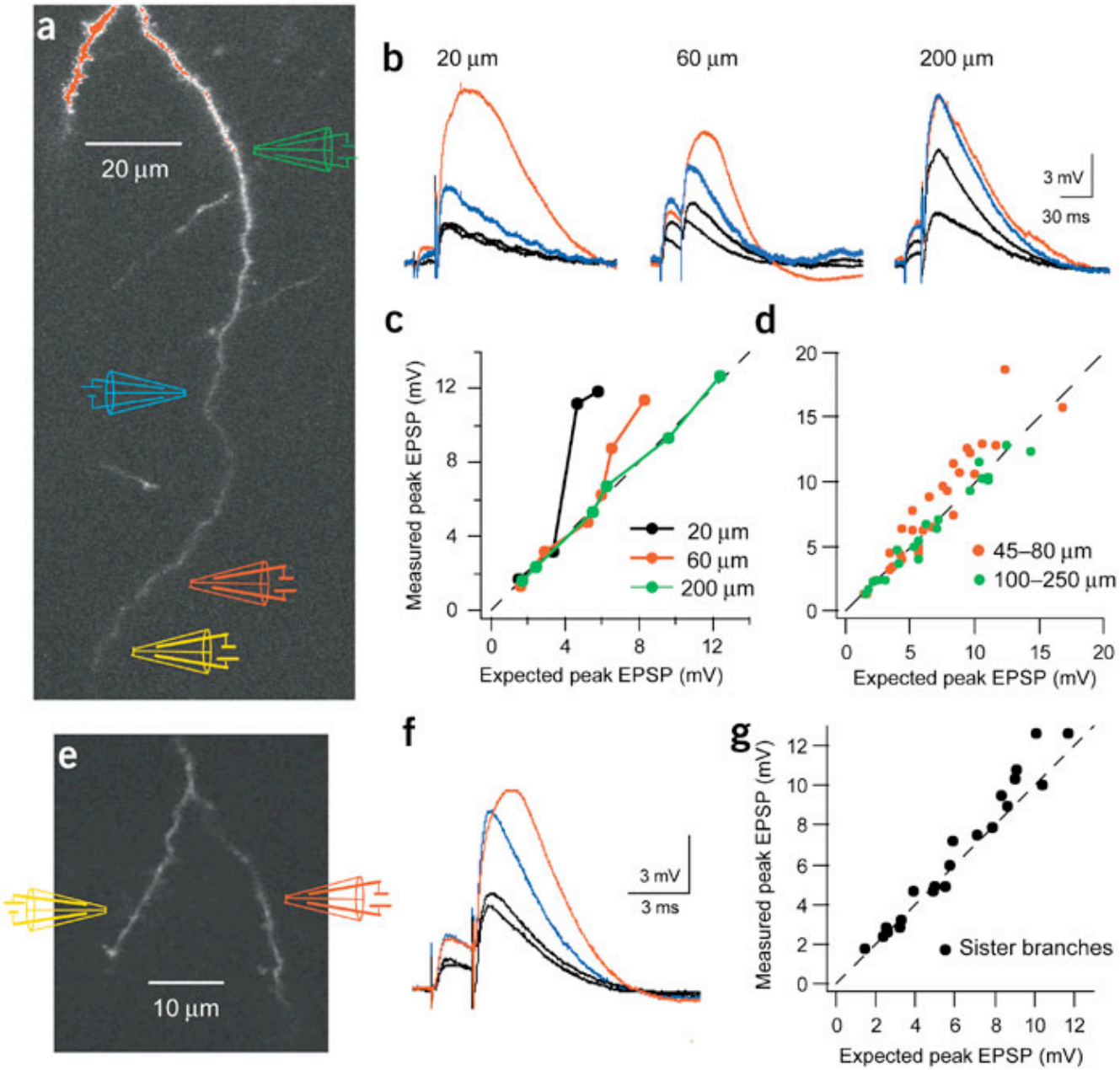
Supplementary Figure 6. Stimulating two different functional subunits in a single basal dendrite in a different temporal order can give dramatically different output. Same model as in Supplementary Figure 3, R_m 10000 Ωcm^2, but with a 40 nS g_{max} NMDAR input at 164 µm and 69 µm at the indicated times. AMPAR component g_{max} is 6 nS at both sites. *Left*: proximal input followed after 40 ms by distal input. The proximal input fails to trigger an NMDA spike. The distal input then triggers a distal NMDA spike, but by then the proximal NMDAR conductance has decayed below the level at which it can produce an NMDA spike. *Right*: distal input followed by proximal input after 40 ms. The distal input is big enough to trigger a distal NMDA spike, in the subunit centered on 164 µm. The resulting depolarization propagates in attenuated form proximally, and lasts long enough to help the subsequent proximal input across threshold. The result is a proximal NMDA spike with a large somatic amplitude. *Lower panel*: schematic indicating which subunits are in high (UP) or low (DOWN) NMDAR conductance states at various times (magenta and dark purple, respectively).

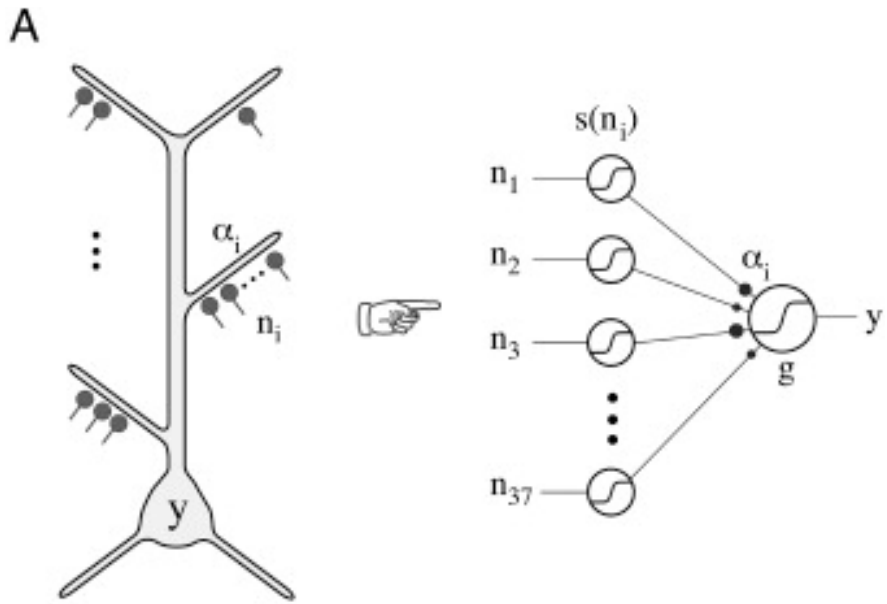
Nonlinear Interactions and Functional Compartments



Polsky, Mel, Schiller, Nat. Neuro (2004)

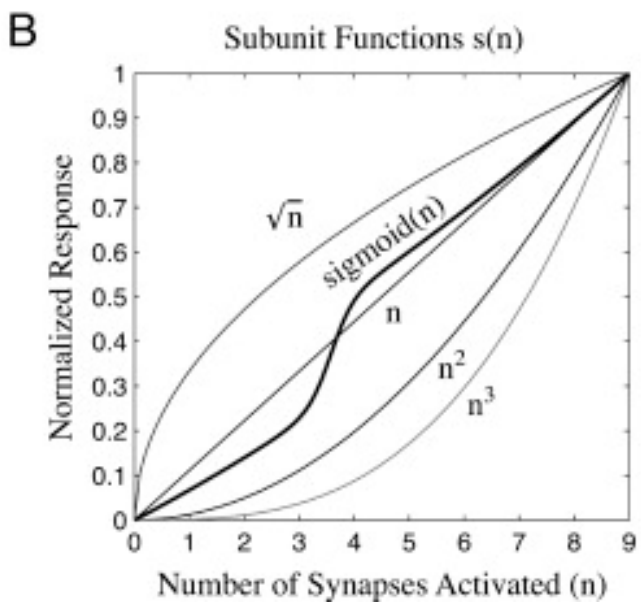
Estimating the Size of the Functional Unit





B. Mel

Two layer network model of a pyramidal cell



Other Examples of Computation in Dendrites

Directional selectivity in starburst amacrine cell dendrites

Hausselt SE, Euler T, Detwiler PB, Denk W,
A dendrite-autonomous mechanism for direction selectivity in retinal starburst amacrine cells. PLoS Biol. 2007 Jul;5(7):e185. Epub 2007 Jul 10.

Using nonlinear dendrites to build robustness into network models of persistent activity

Goldman MS, Levine JH, Major G, Tank DW, Seung HS,
Robust persistent neural activity in a model integrator with multiple hysteretic dendrites per neuron. Cereb Cortex. 2003 Nov;13(11):1185-95.