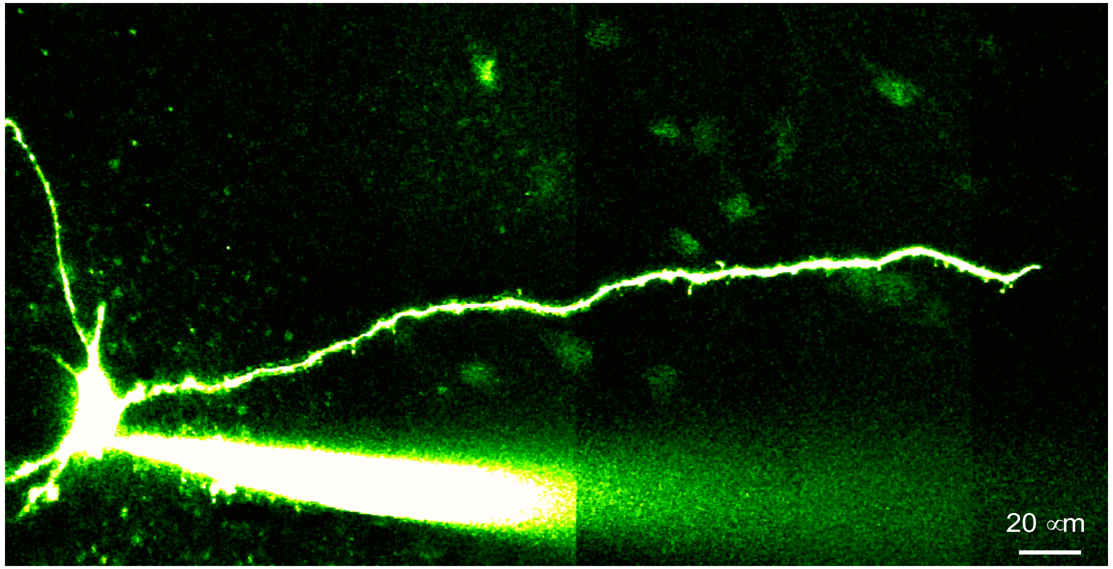
Synaptic integration in single neurons



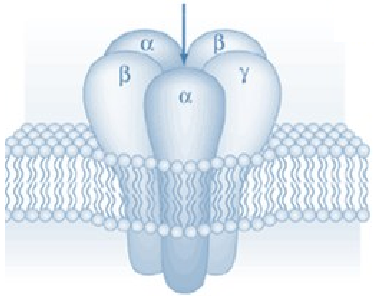
Tiago Branco

Model

$$\tau \frac{dV_i}{dt} = -(V_i - V_{rest}) + \Sigma_j w_{ij} g_j(t)$$

Neuron

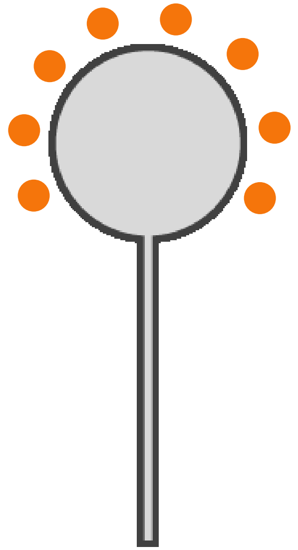
Molecules



Why do we care?

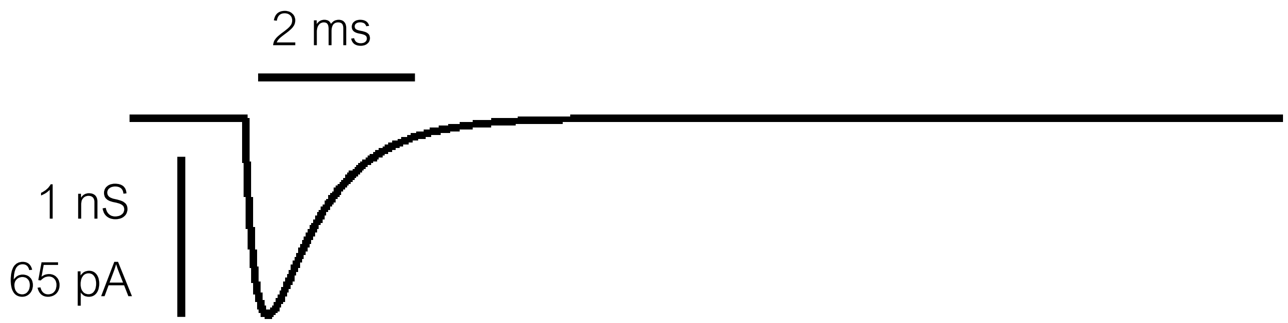
Input-output function of single neurons

$$C \frac{dV}{dt} = g_{syn}(V_{syn} - V_{rest})$$



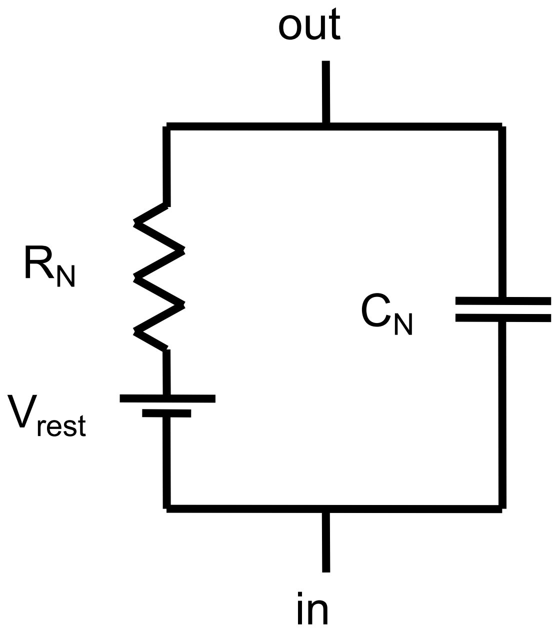
Synaptic conductance and currents

Single synapses are weak and brief



$$I_{ion} = G_{ion} \cdot (V_m - E_{ion})$$

Equivalent electrical circuit of the membrane



$$\tau_m = R_N C_N$$

Ohm's law: **V = IR** voltage equals current times resistance (only at steady state)

At rest, the cell membrane is electrically equivalent to a parallel RC circuit

Membrane potential in response to step current

Growin

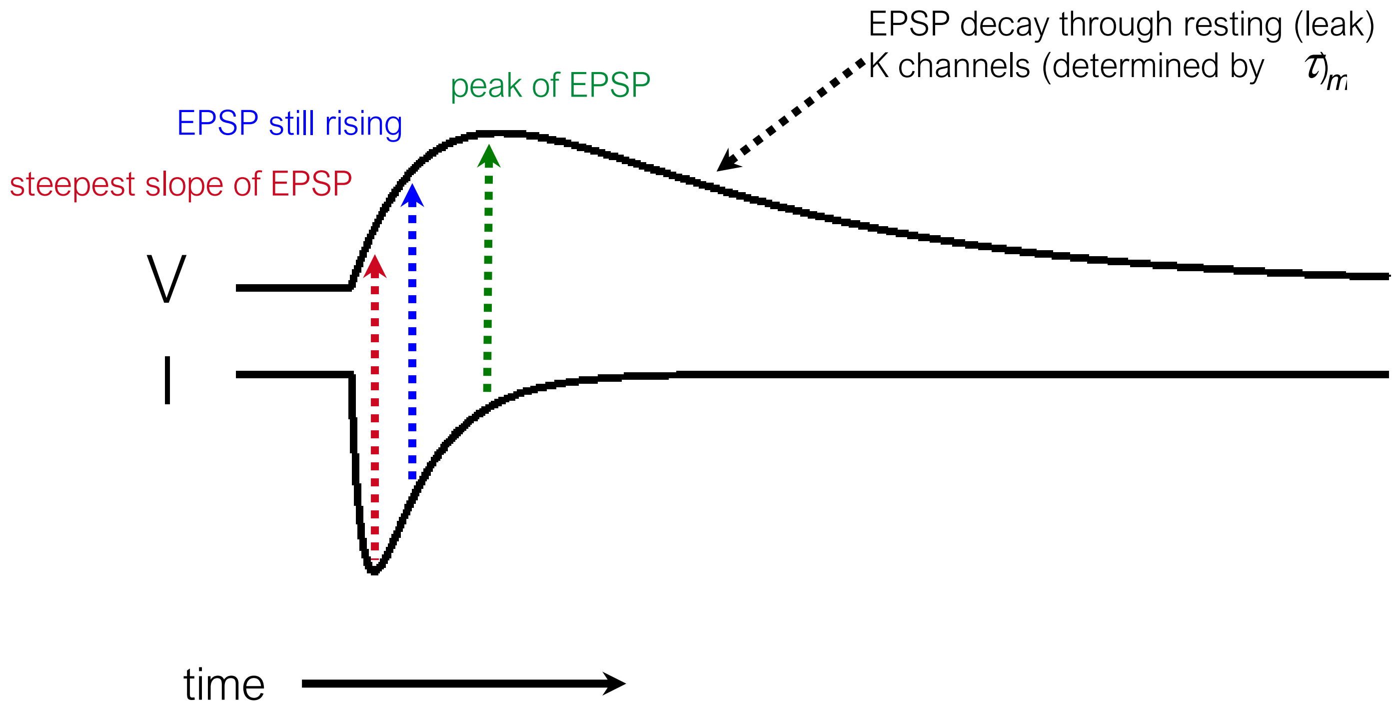
Growing phase: $$\Delta V = \Delta V_{ss} \cdot (1 - e^{-t/\tau_m})$$

Decaying phase: $$\Delta V = \Delta V_{ss} \cdot e^{-t/\tau_m}$$

$$\tau_m = R_m C_m$$

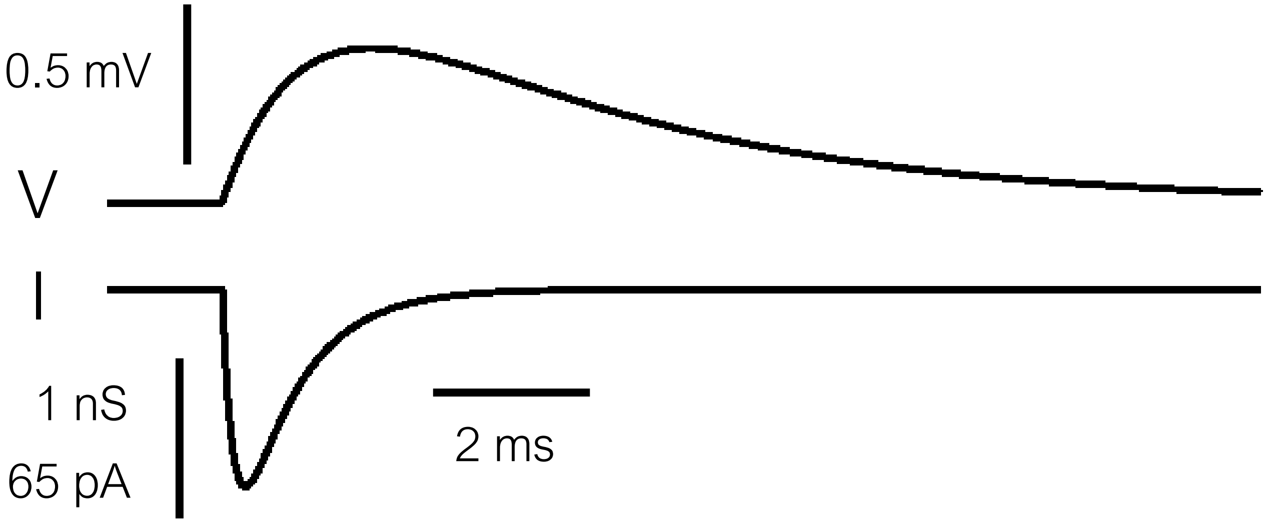
Membrane potential responds to a step current with exponential rise and decay, governed by the membrane time constant, τ_m

Membrane potential in response to synaptic current

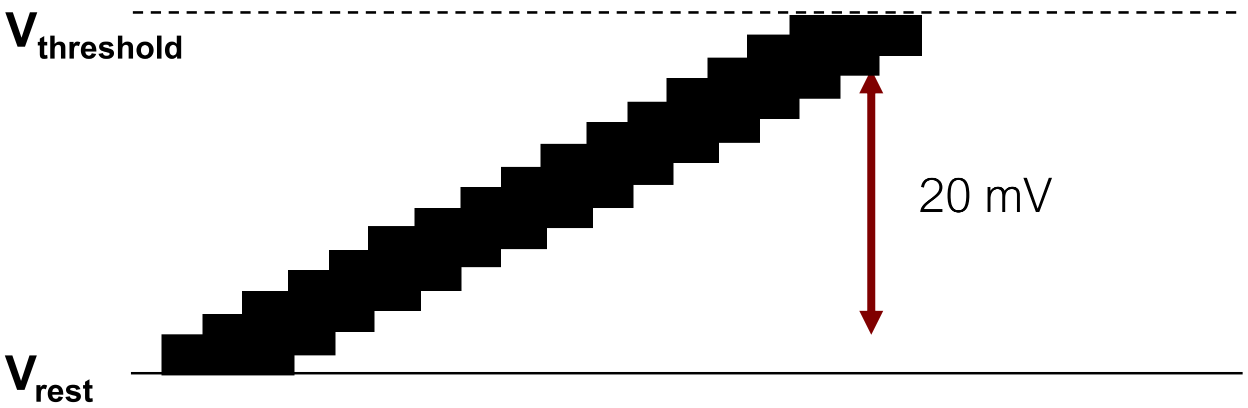


A PSP is slower than a PSC, and its decay is governed by the membrane time constant, τ_m.

Membrane potential in response to synaptic current



Basic problem

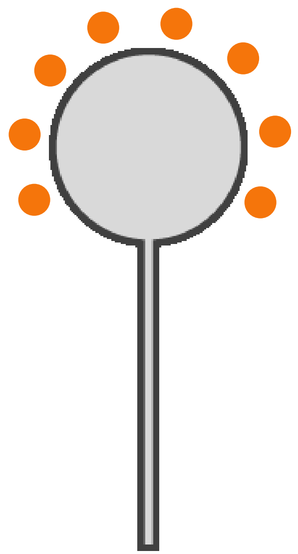


Most neurons need to **integrate** synaptic input to generate action potential output

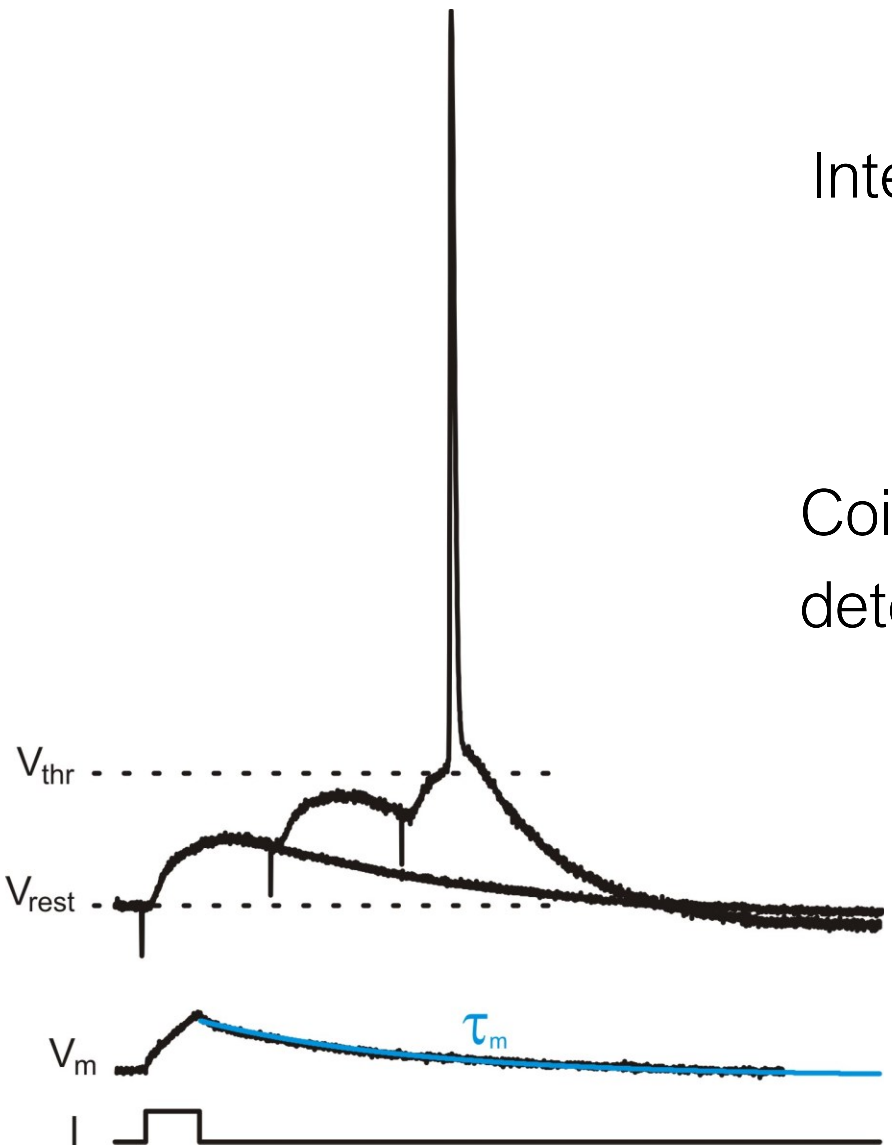
Integration allows for **Computation**

How is synaptic input integrated ?

Timing



Membrane time constant sets summation time window



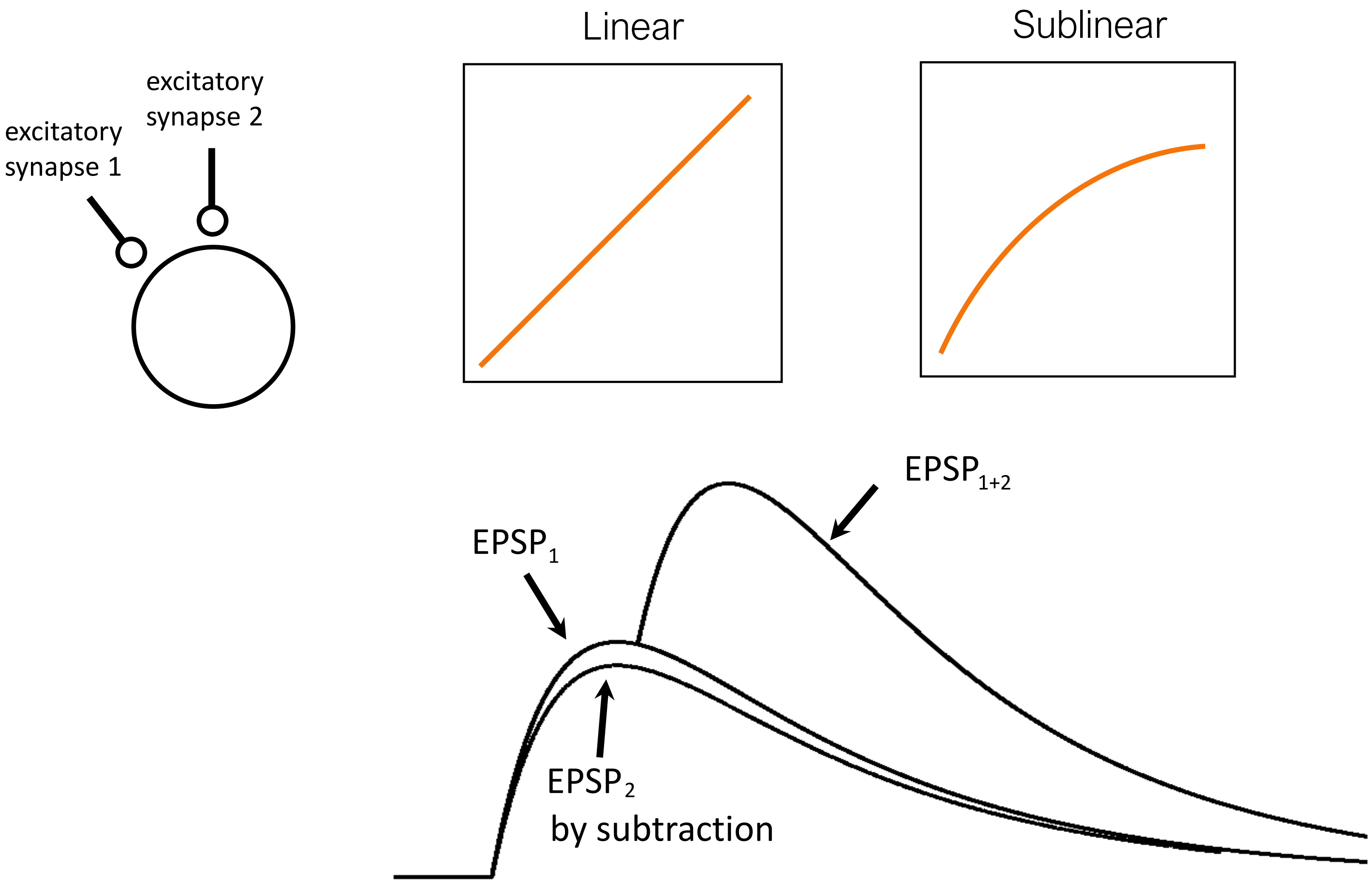
Integration

↓

Coincidence detection

M. Scanziani

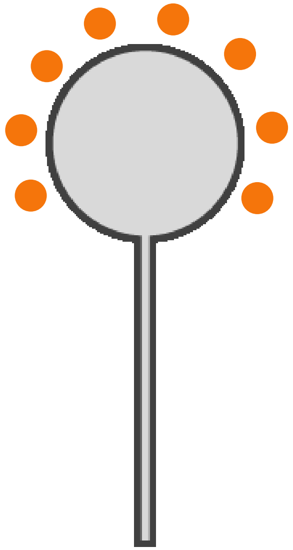
Basic Input-Output function



Voltage-gated conductances change IO function

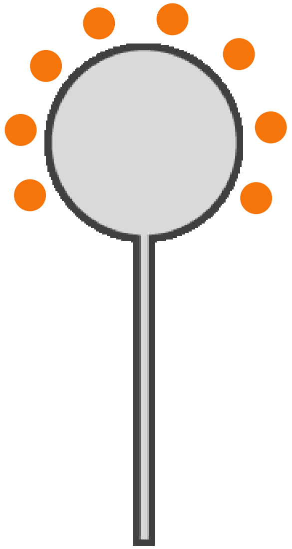
$$C\frac{dV}{dt} + g_{Nav}(V_{Nav} - V_{rest}) + g_{Cav}(V_{Cav} - V_{rest}) + g_{Kv}(V_{kv} - V_{rest})$$

$$g_{syn}(V_{syn} - V_{rest})$$

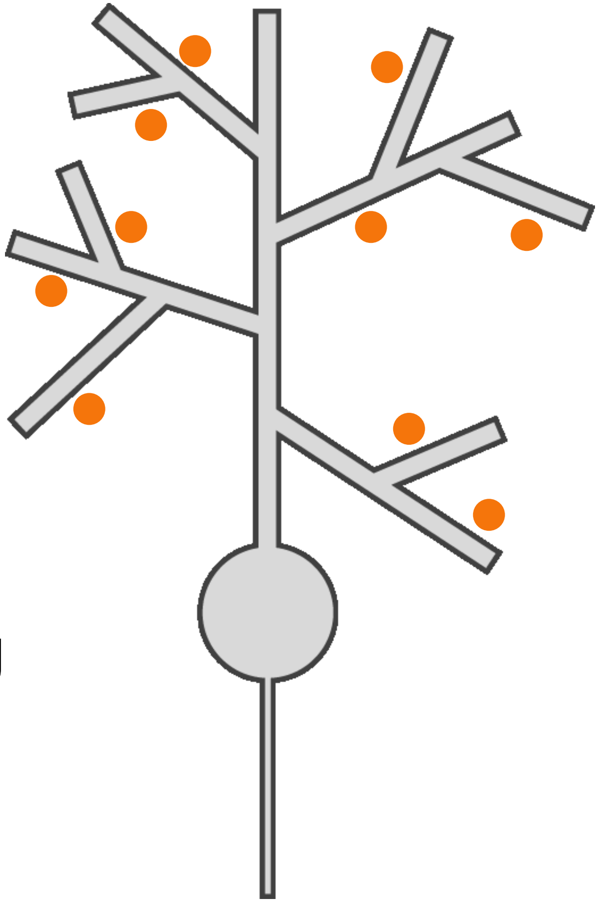


Dendritic trees add a spatial dimension to integration

Timing



Location



Timing

Current flow in neuron with dendrites

FIG. 1. Diagram illustrating the flow of electric current from a microelectrode whose tip penetrates the cell body (soma) of a neuron. The full extent of the dendrites is not shown. The external electrode to which the current flows is at a distance far beyond the limits of this diagram.

Wilfrid Rall

Voltage attenuation in cables

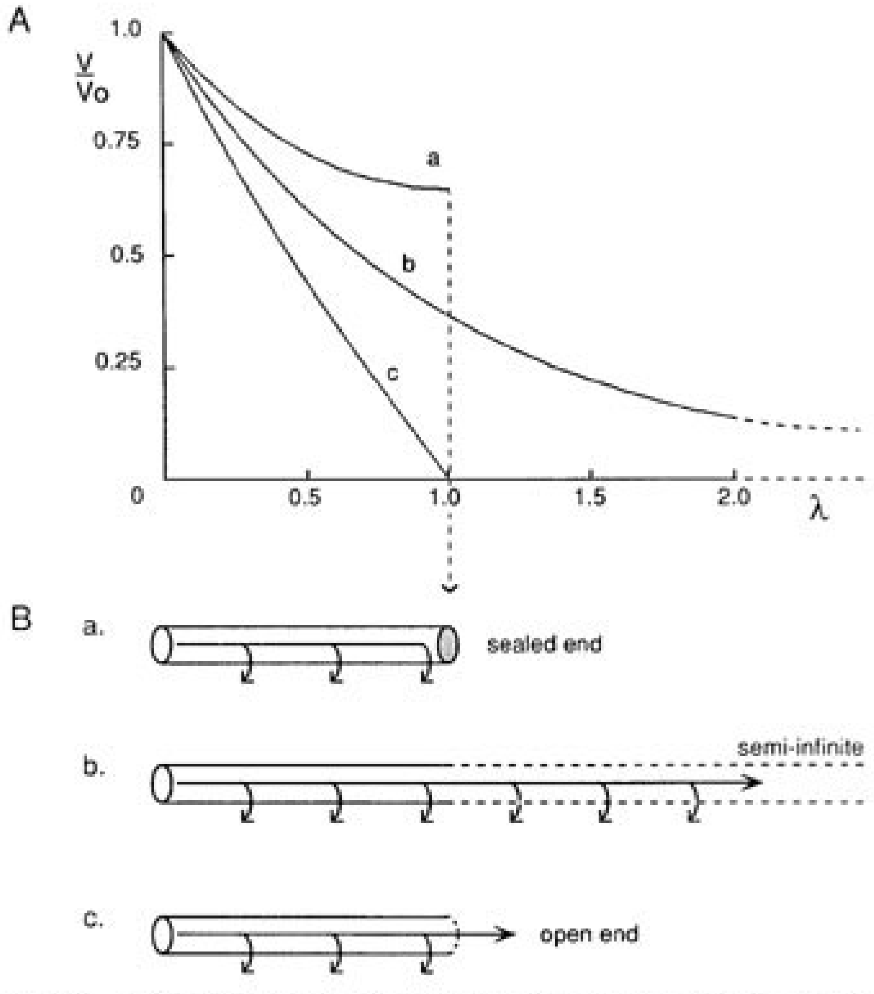


FIG. 13.6. Effect of different modes of termination on the spread of electrotonic potential. **A.** Graph of steady-state potential spread for the case of a sealed end at λ = 1 (a), an infinite extension of the cable (b), and an open end (short-circuit) at λ = 1 (c). **B.** Diagrams illustrating each of the boundary conditions in A. (Modified from Rall, 1958.)

Space constant

$$\lambda = \sqrt{\frac{R_m \cdot d}{R_i \cdot 4}}$$

Voltage attenuation

$$V = V_0 \, e^{-x/\lambda}$$

Electrotonic distance

$$X = x / \lambda$$

Compartmental modeling of neurons

The **NEURON** simulation environment

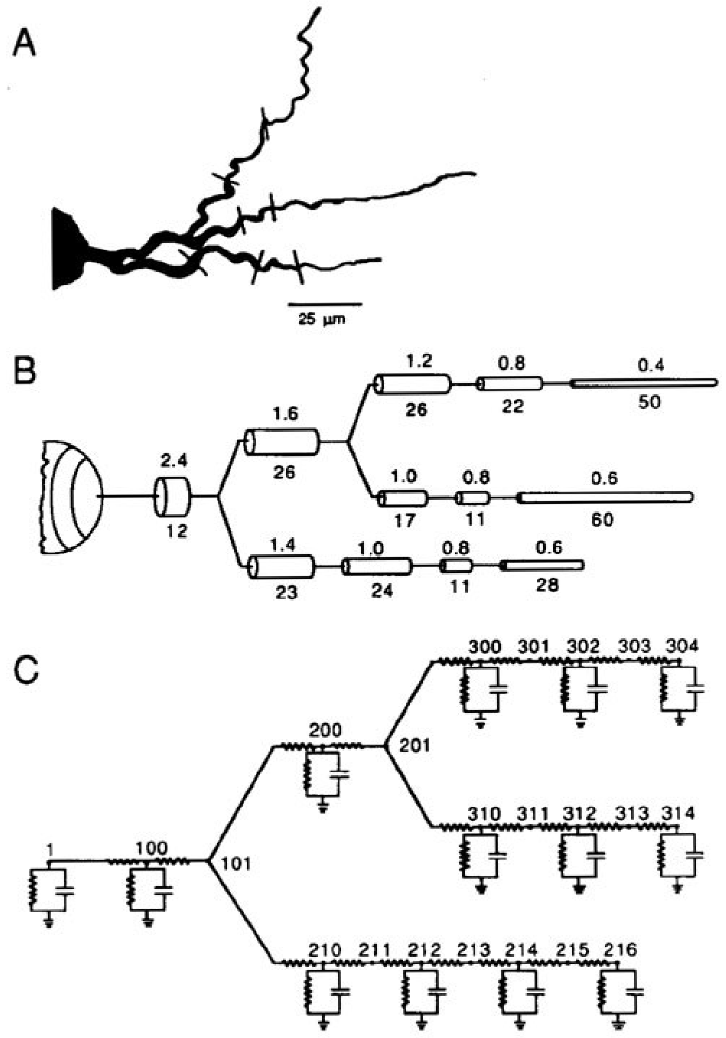
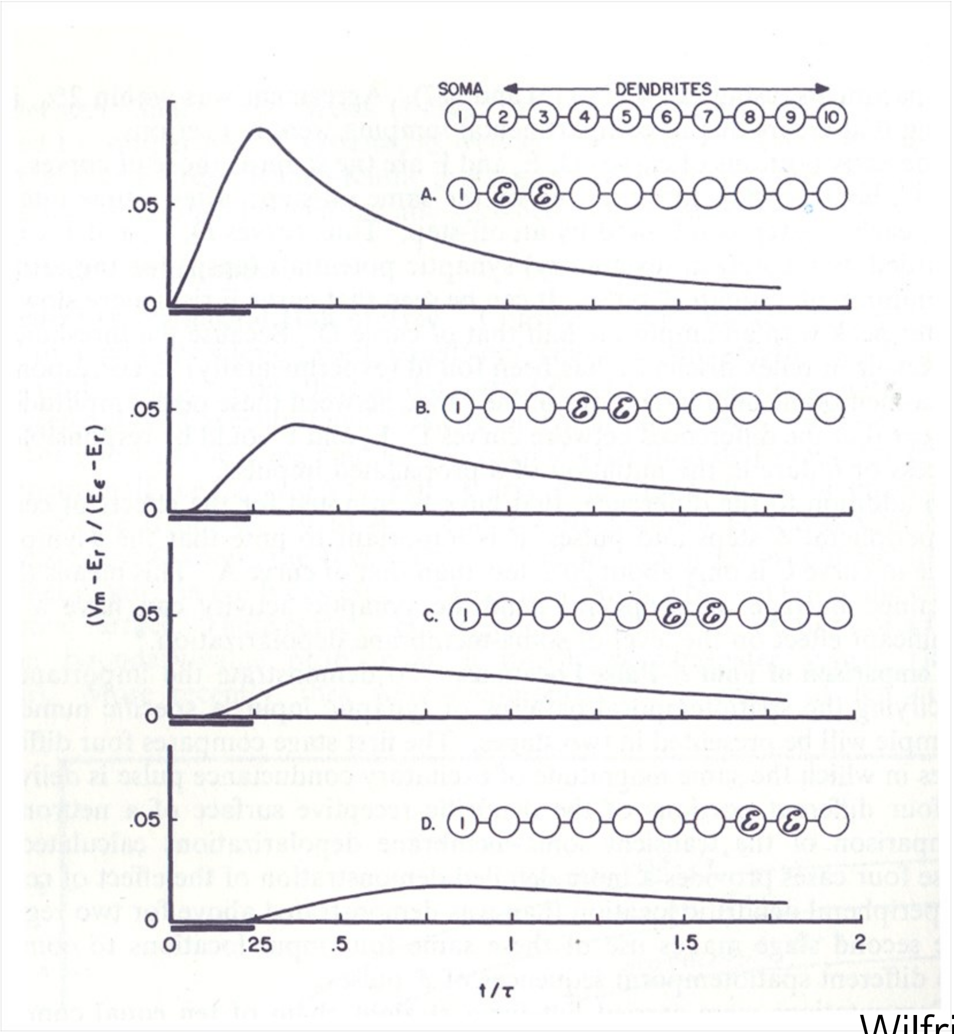


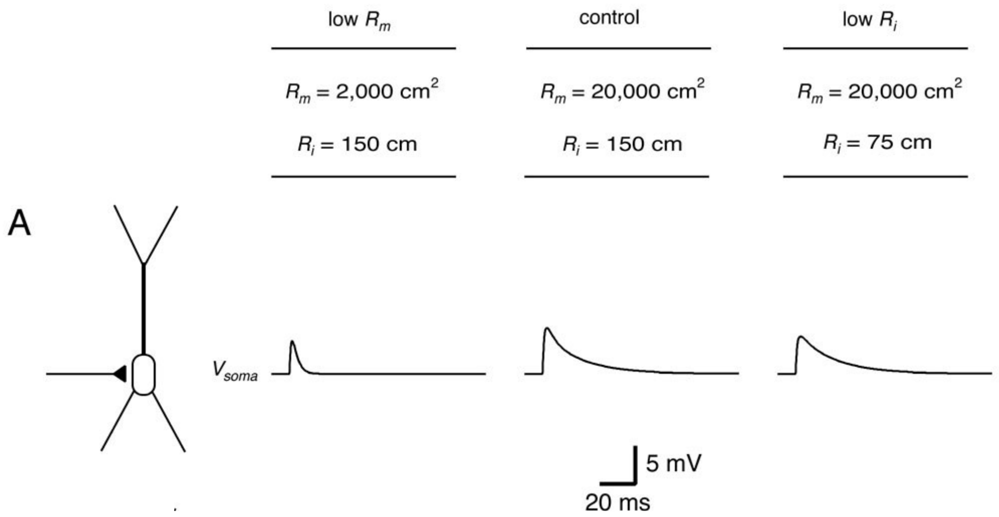
Figure 3.3
Stages in abstraction from an anatomical dendritic tree to an electrical circuit analog. (A) Two-dimensional projection of part of the soma and one dendrite of a vagus motoneuron in the guinea pig. Points at which unbranched dendrites were broken into successive cylindrical segments are indicated by lines. (B) Representation of the same dendrite as a branched system of cylindrical segments, indicating the length (below) and diameter (above) of each dendritic segment (in μm). Diameters are not drawn to the same scale as the lengths, but both are in the correct proportions. The motoneuron soma (shown partially) had a maximum diameter of 20 μm and minimum diameter of 15 μm. (C) Circuit analog of B (see fig. 3.1) showing the pattern of connections at branch points and the numbers assigned to circuit nodes within (even numbers) and between (odd numbers) successive segments.

EPSP attenuation by dendrites



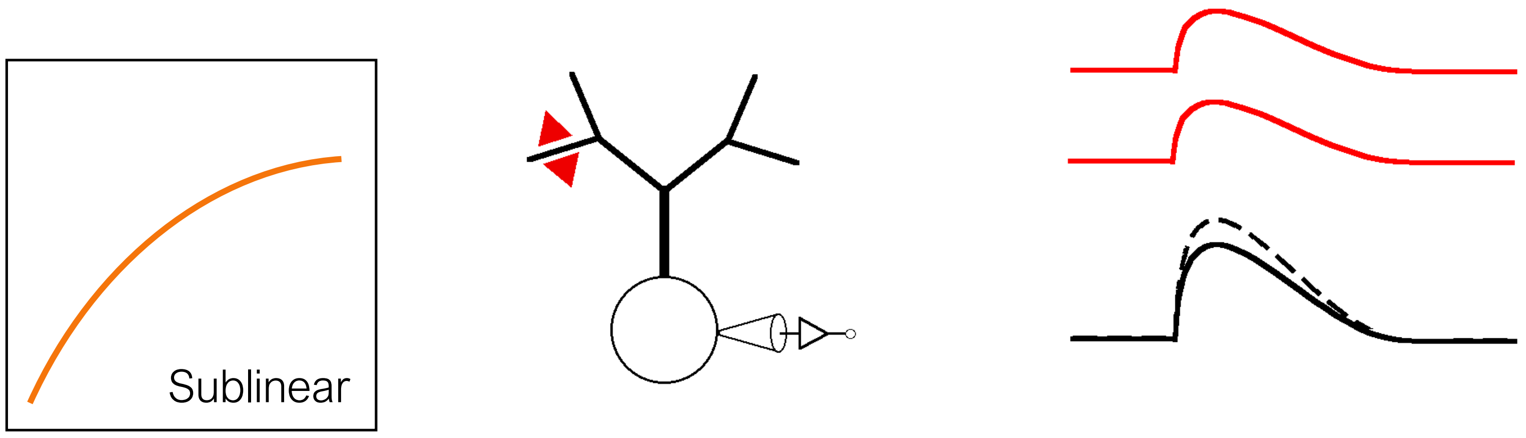
Wilfrid Rall, 1964

Effects of location, R_m and R_i on EPSP attenuation

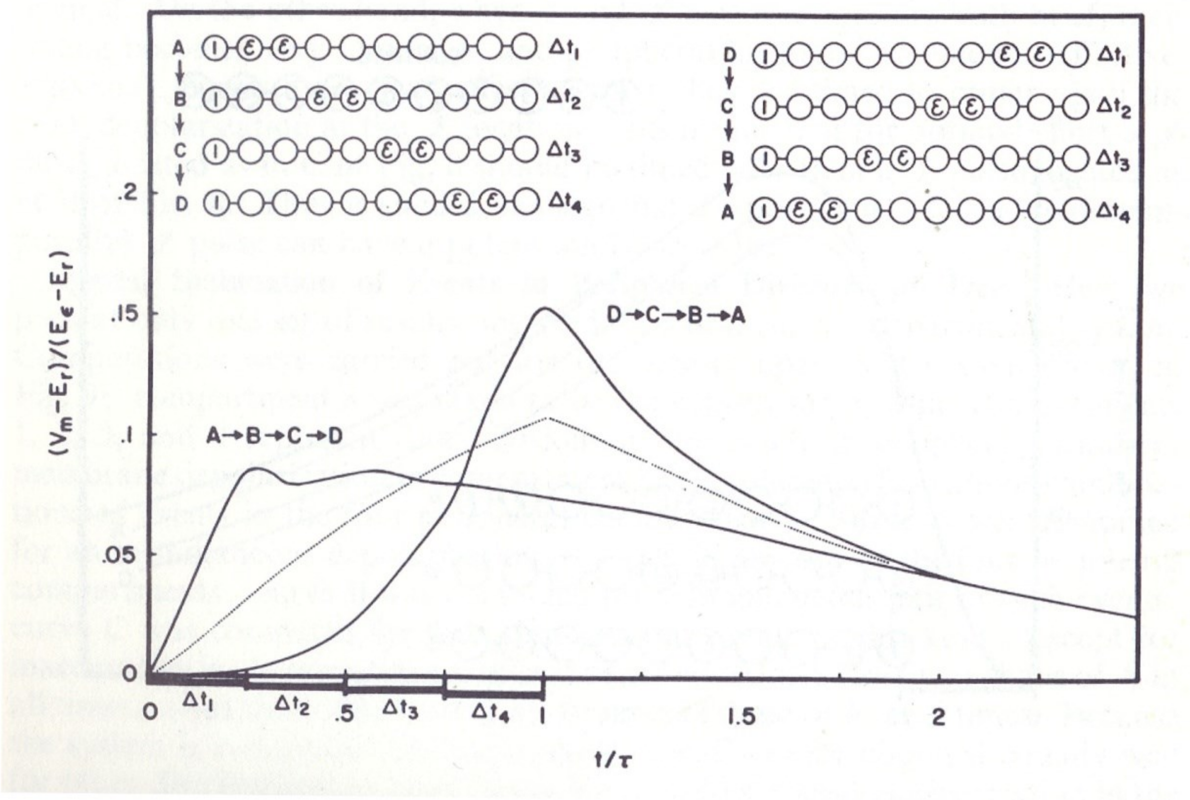


Input-Output function in dendrites

2. Two excitatory inputs onto the same dendrite



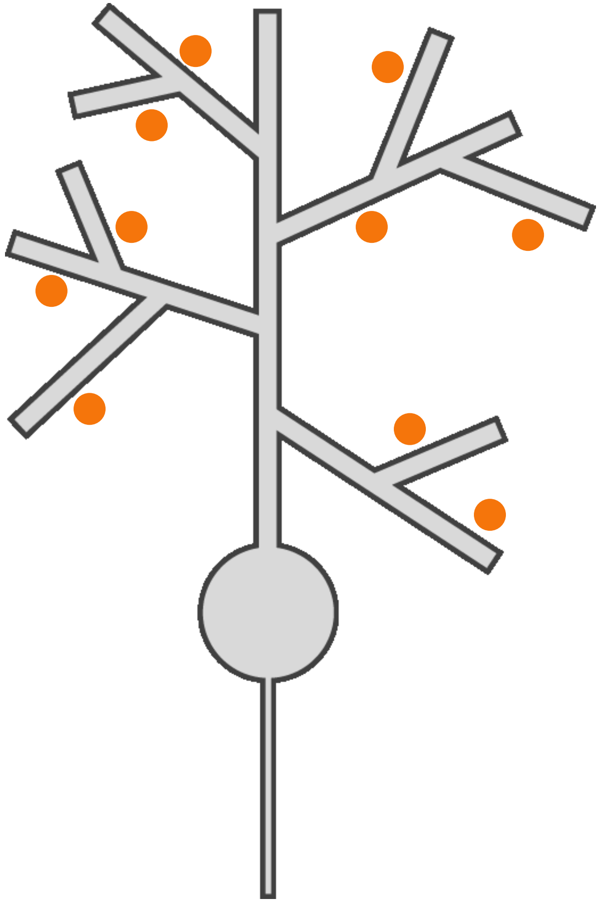
Computation of input direction



Rall, W. 1964

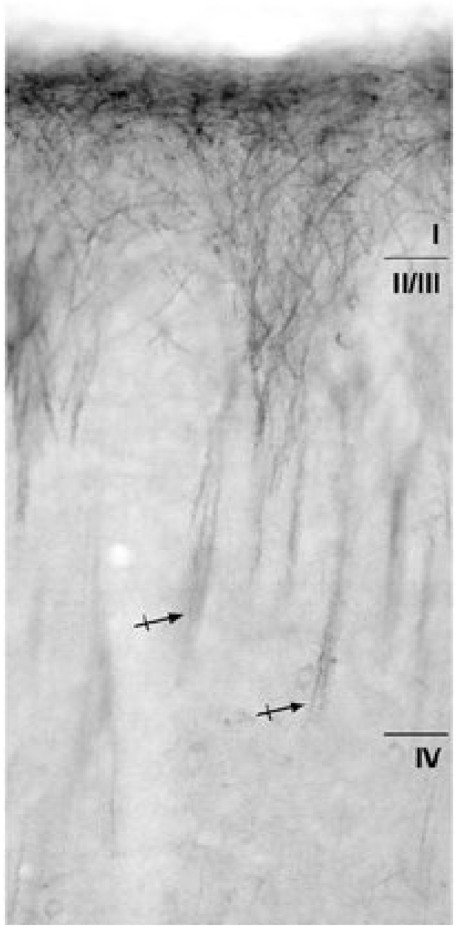
Voltage-gated conductances change IO function

$$C \frac{dV}{dt} = g_{syn}(V_{syn} - V_{rest}) + g_{Nav}(V_{Nav} - V_{rest}) + g_{Cav}(V_{Cav} - V_{rest}) + g_{Kv}(V_{kv} - V_{rest})$$



Voltage-gated conductances change IO function

I_h channels



Lorincz, A. et al. 2002

Dendritic Spikes

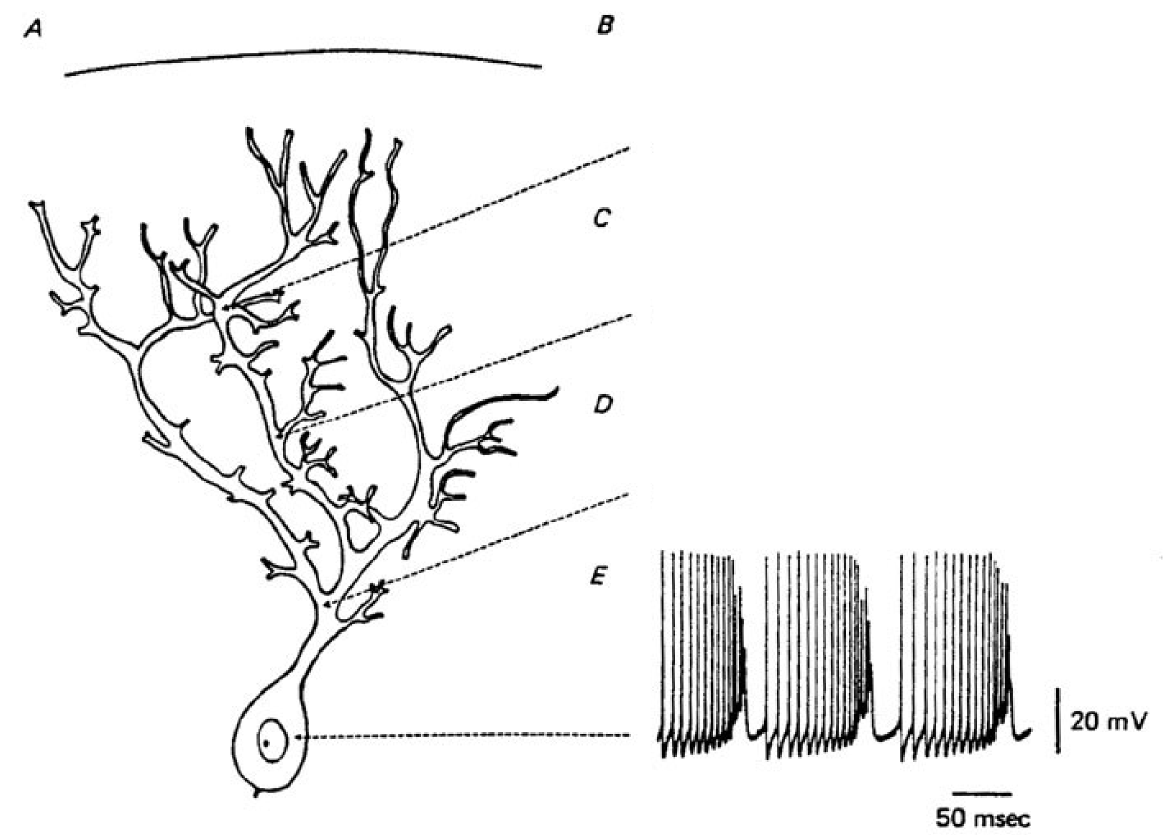
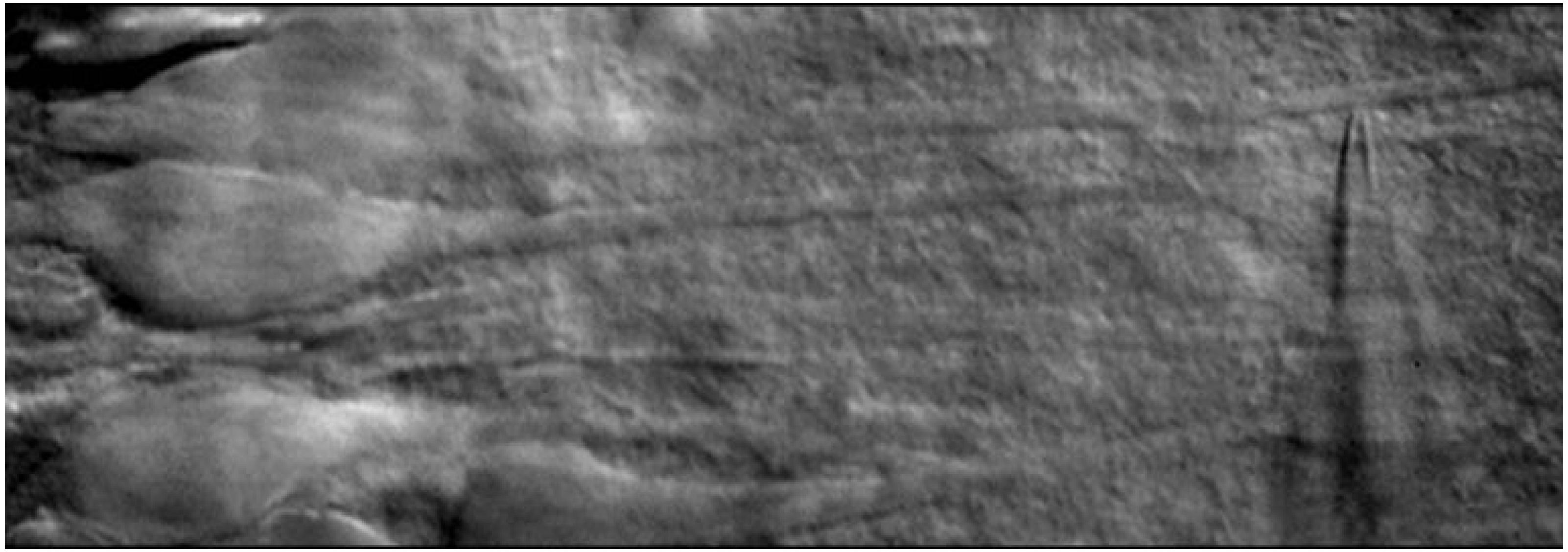


Fig. 4. Composite picture showing the relationship between somatic and dendritic action potentials following DC depolarization through the recording electrode. A clear shift in amplitude of the s.s. against the dendritic Ca-dependent potentials is seen when comparing the more superficial recording in *B* with the somatic recording in *E*. Note that at increasing distances from the soma the fast spikes are reduced in amplitude and are barely noticeable in the more peripheral recordings. However, the prolonged and slow-rising burst spikes are more prominent at dendritic level.

Na^+ spikes

from Llinas & Sugimori 1980

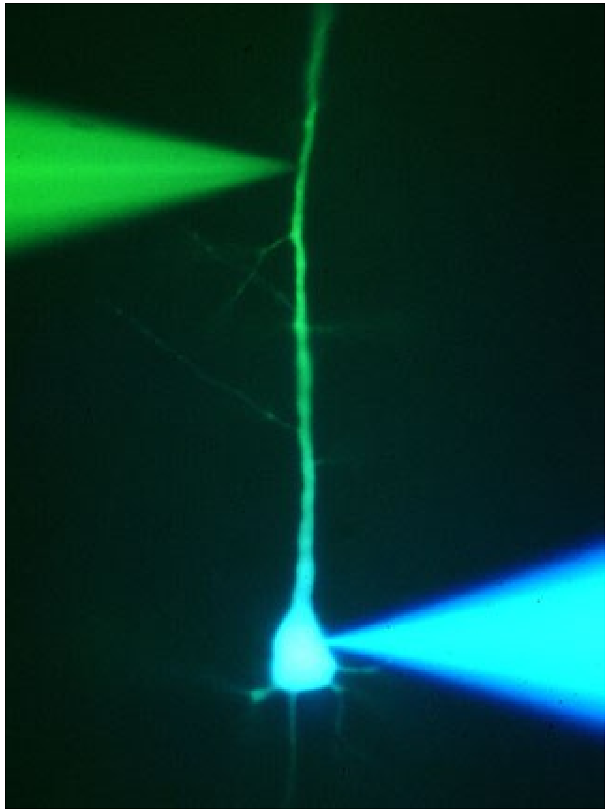
Dendritic patch-clamp recording



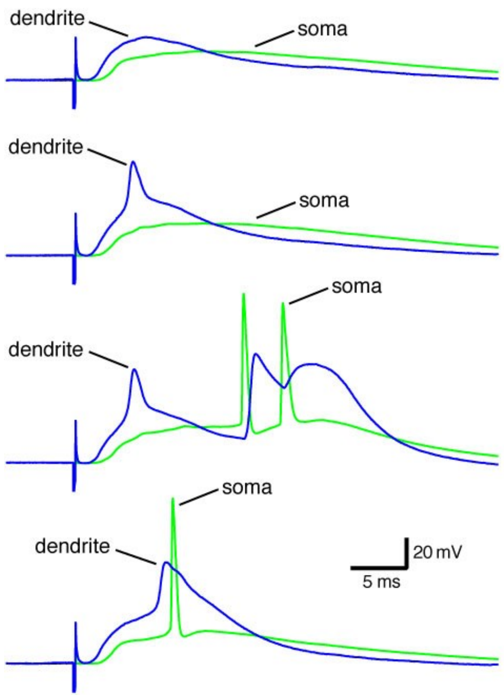
Stuart et al.,
Pflüger's Archiv, 1993

Dendritic Spikes

Neocortical layer 5 pyramidal neurons

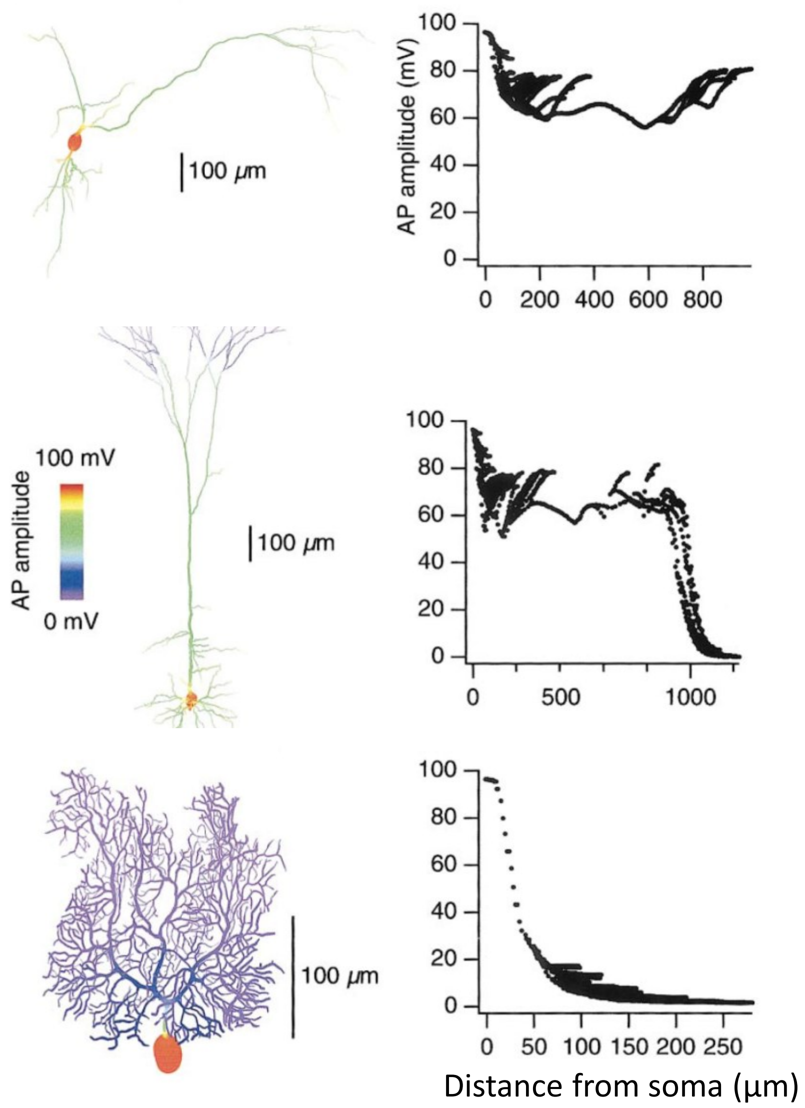


Stuart and Sakmann, Nature 1994



Stuart et al, J. Physiol. 1997

Backpropagating action potentials



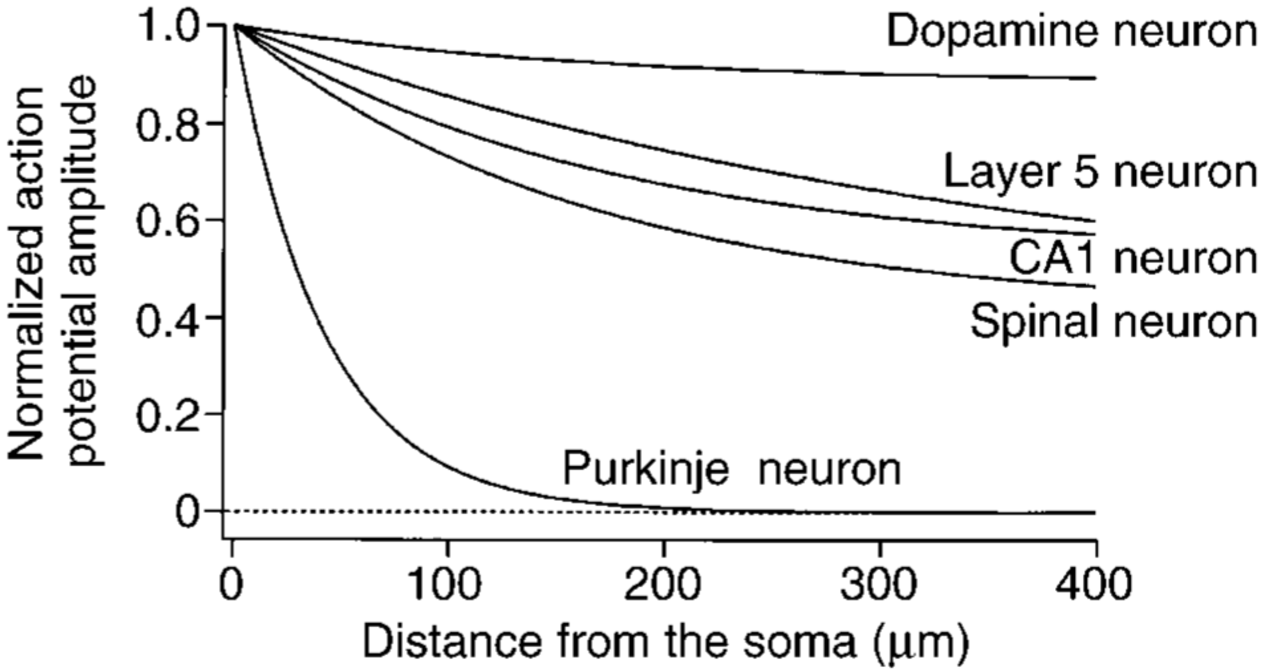
Dopamine neurons: high Na channel density and little branching.

Layer 5 pyramidal neurons: moderate Na channel density and moderate branching; more branching in the tuft.

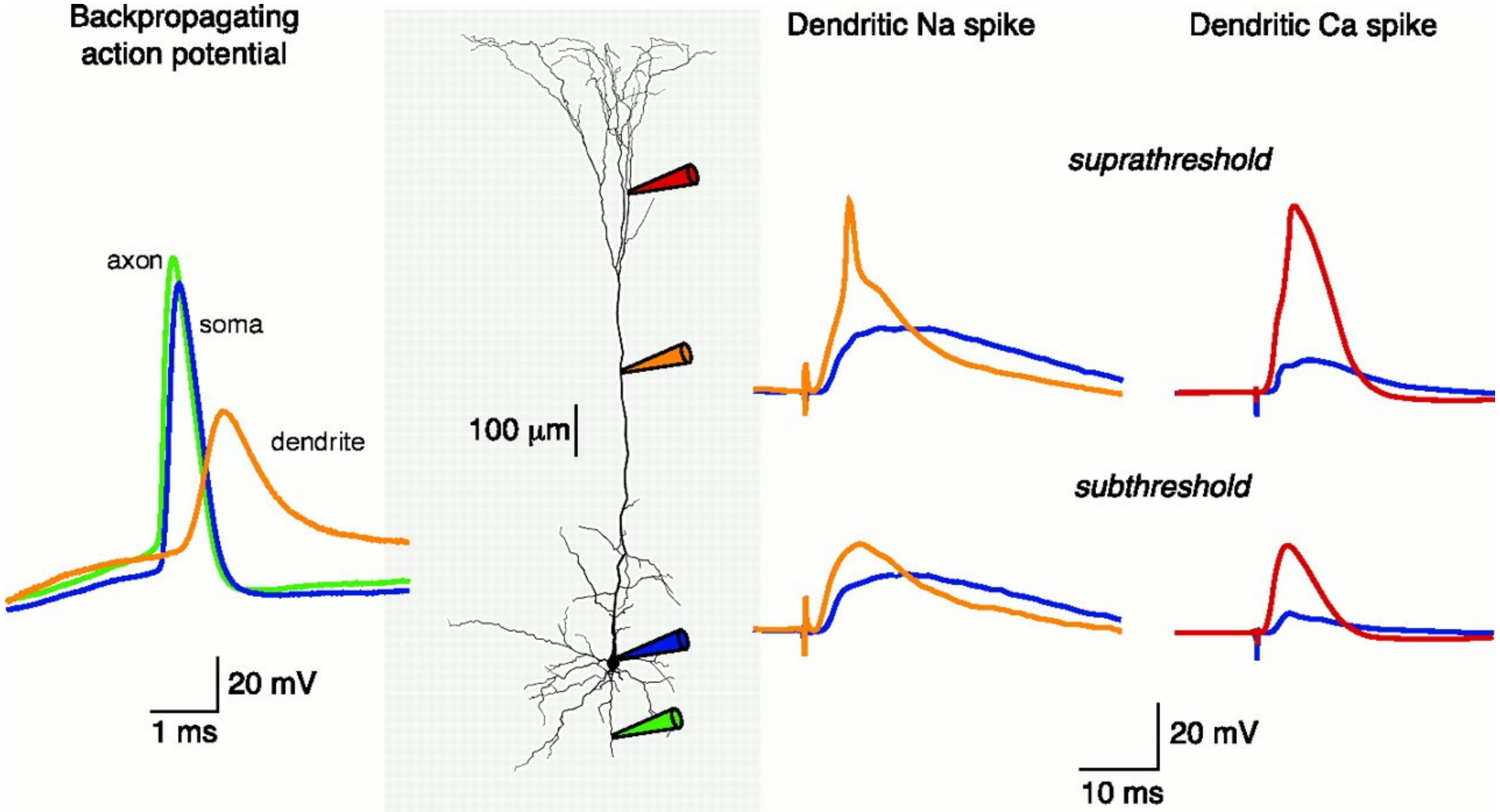
Purkinje neurons: low Na channel density (none in dendrites) and extensive branching.

Vetter et al, J. Neurophysiology, 2001

Backpropagating action potentials



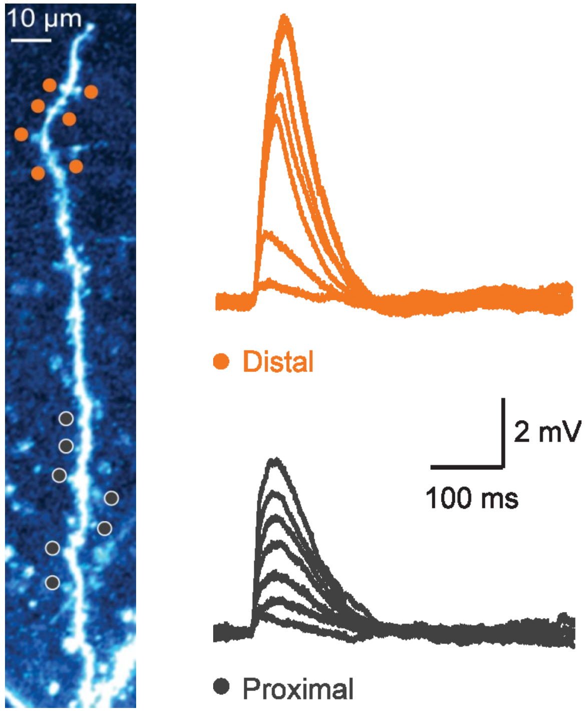
Active properties in dendrites



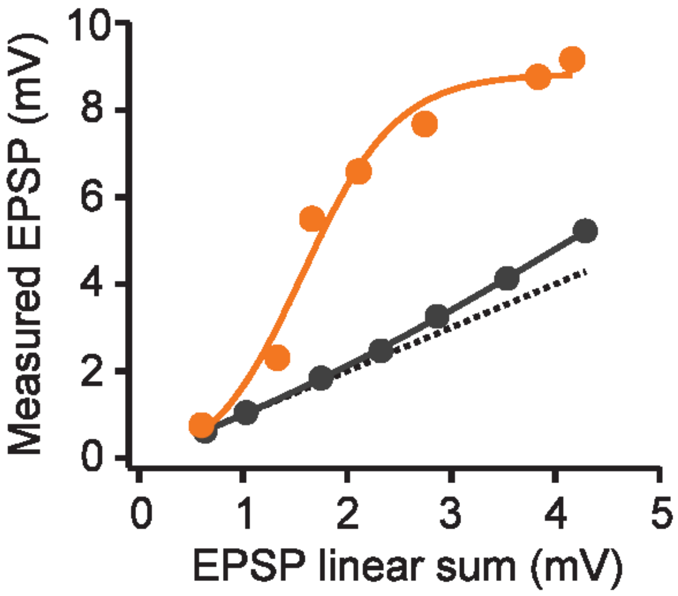
Hausser, M., Spruston, N. and Stuart, G. 2000

Input-output function varies with dendritic location

Basal dendrite



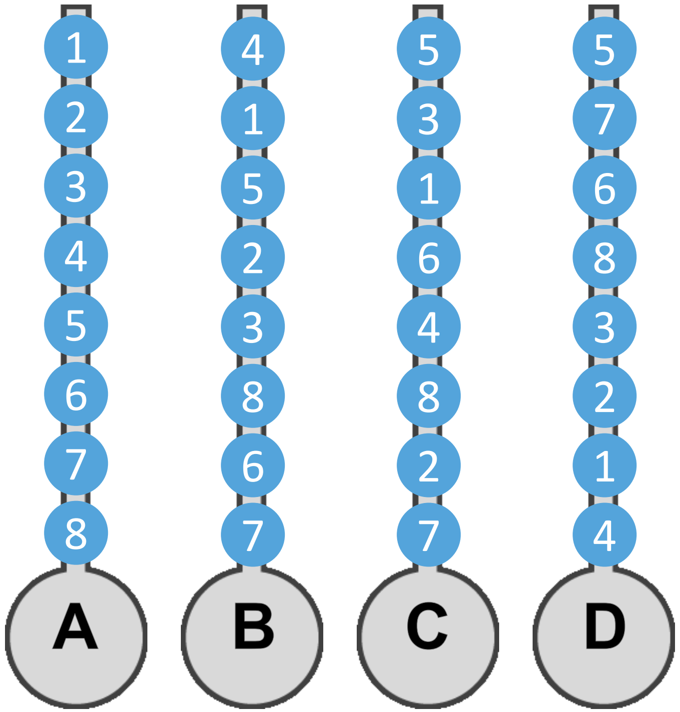
Input-output function



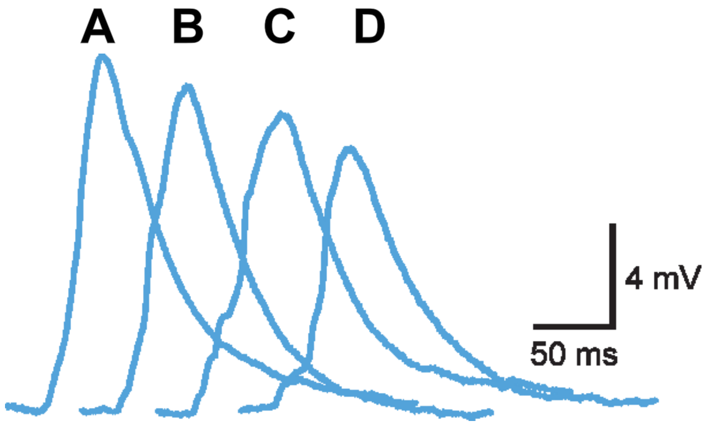
Branco & Hausser 2011

Dendritic computation of input sequences

Patterns



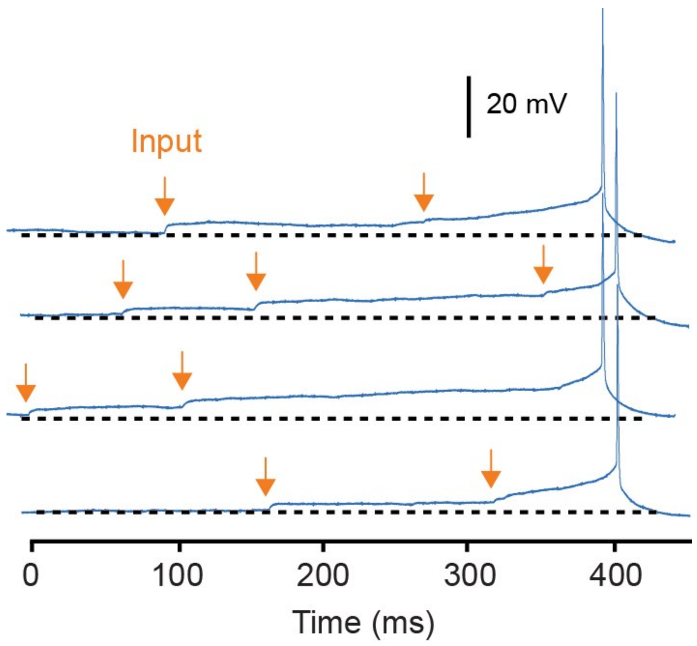
Soma voltage



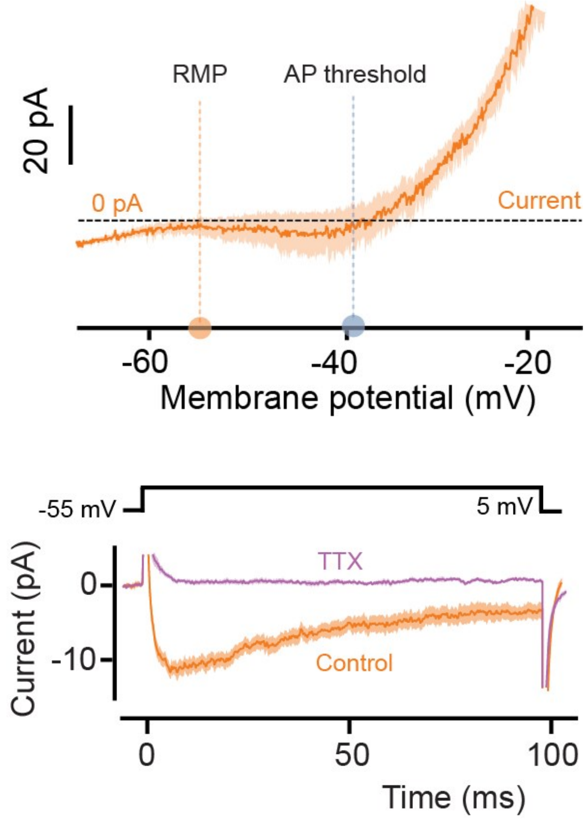
Branco, Clark & Hausser 2011

Near-perfect integration

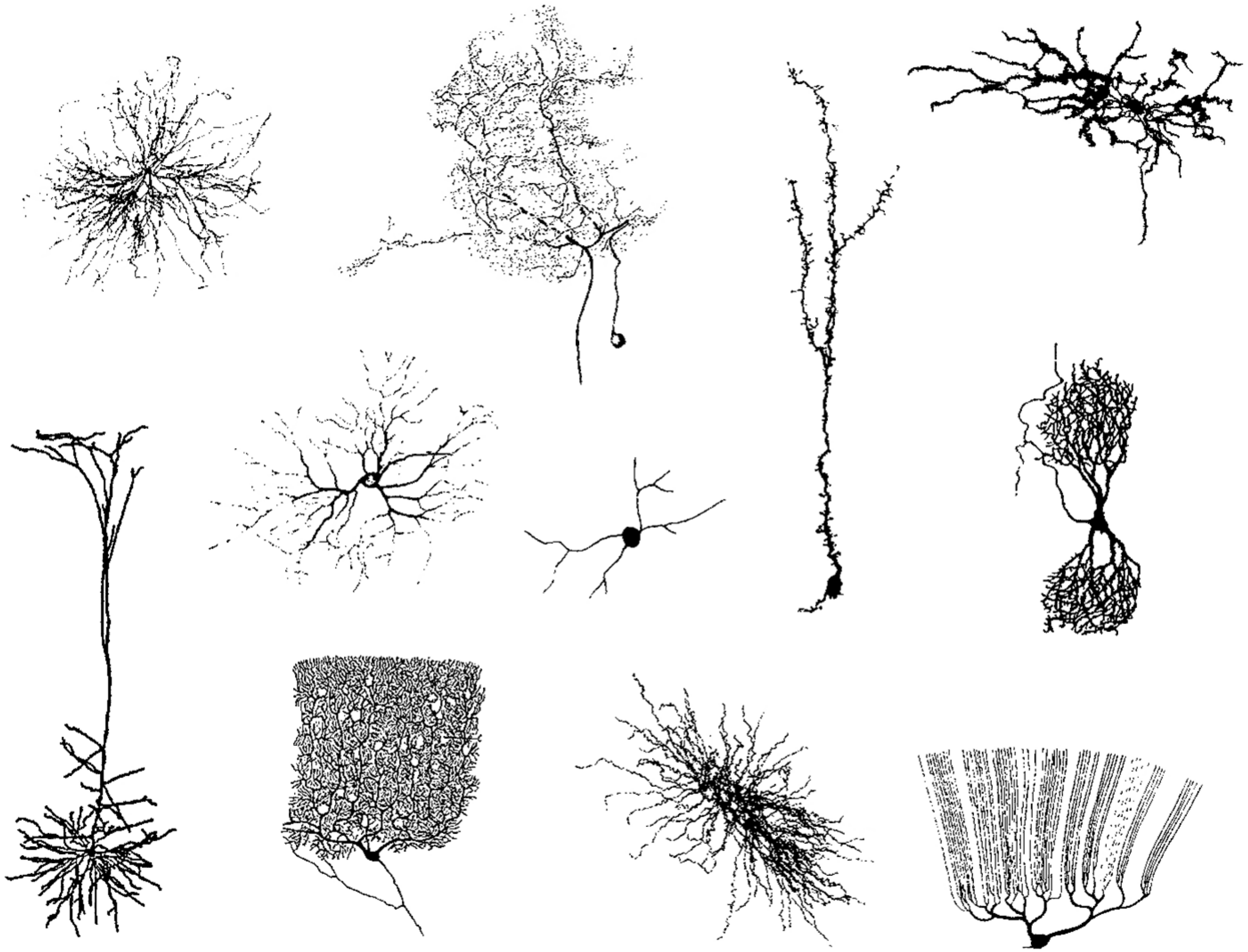
AGRP neurons

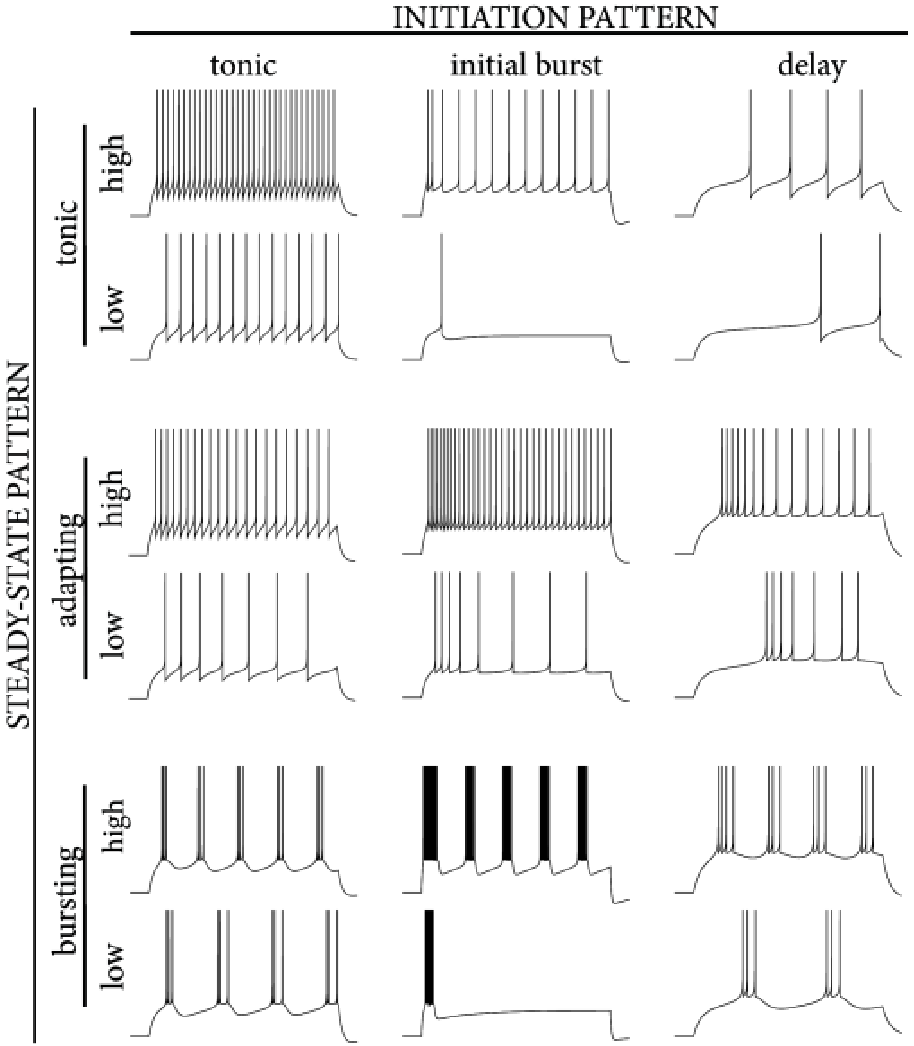


Persistent Na current



Branco et al. 2016




INITIATION PATTERN
tonic
initial burst
delay
STEADY-STATE PATTERN
tonic
high
low
adapting
high
low
bursting
high
low

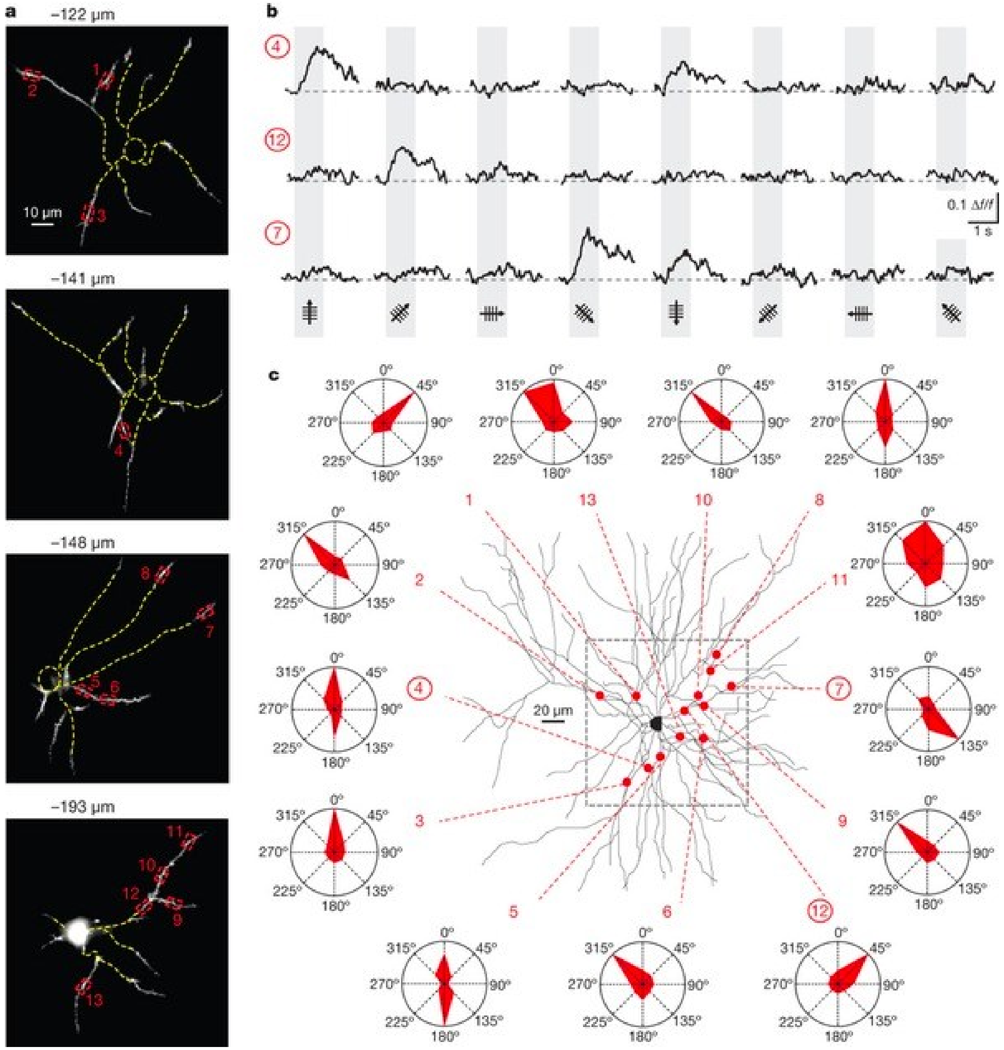
How do we move forward?

Critical step missing

Measure the actual input-output function of a single neuron *in vivo*

while performing a known computation

Measuring input-output subsets in the sensory cortex



Jia et al, *Nature* 2010

Roadmap

Measure input activity in **all** synapses

Measure sub and supra-threshold output

Formalise the transformation

Identify key ion channels (*molecular biology*)

Make models and generate predictions about integration

Test predictions and generalise models

Incorporate in network models and tell PEL how the brain works