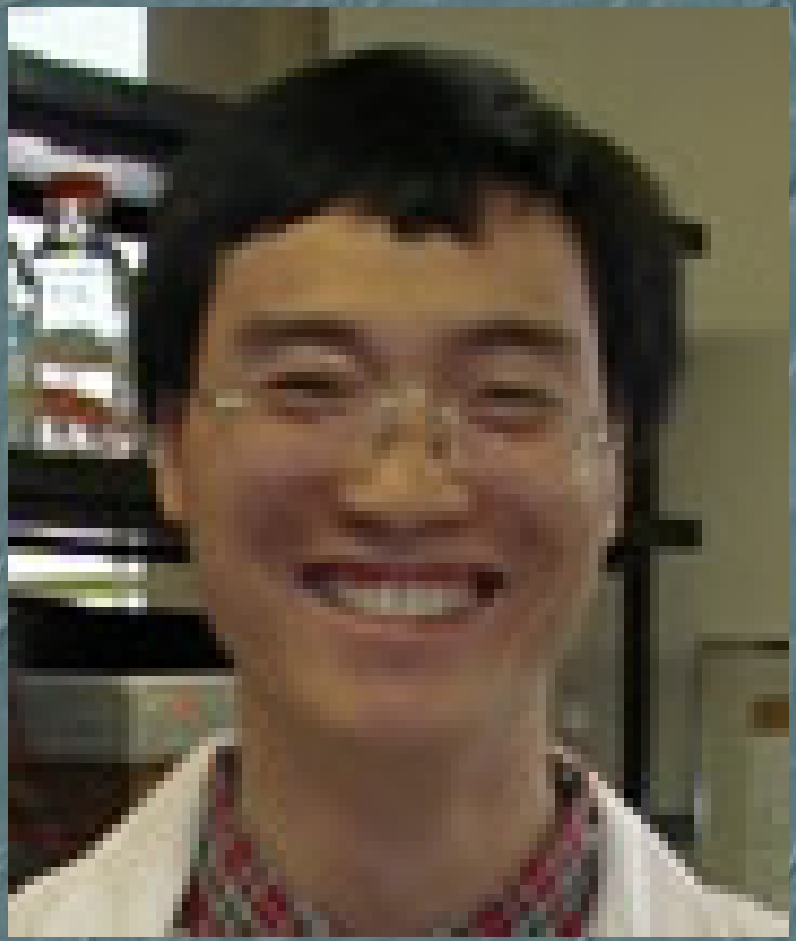
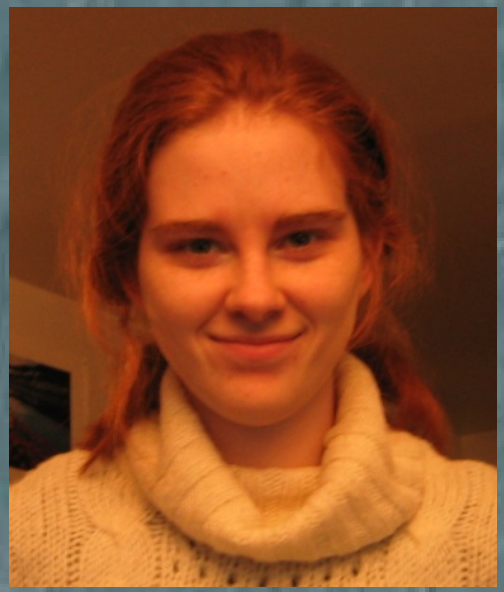
Combined Analog/digital signaling in local cortical networks

YouSheng Shu

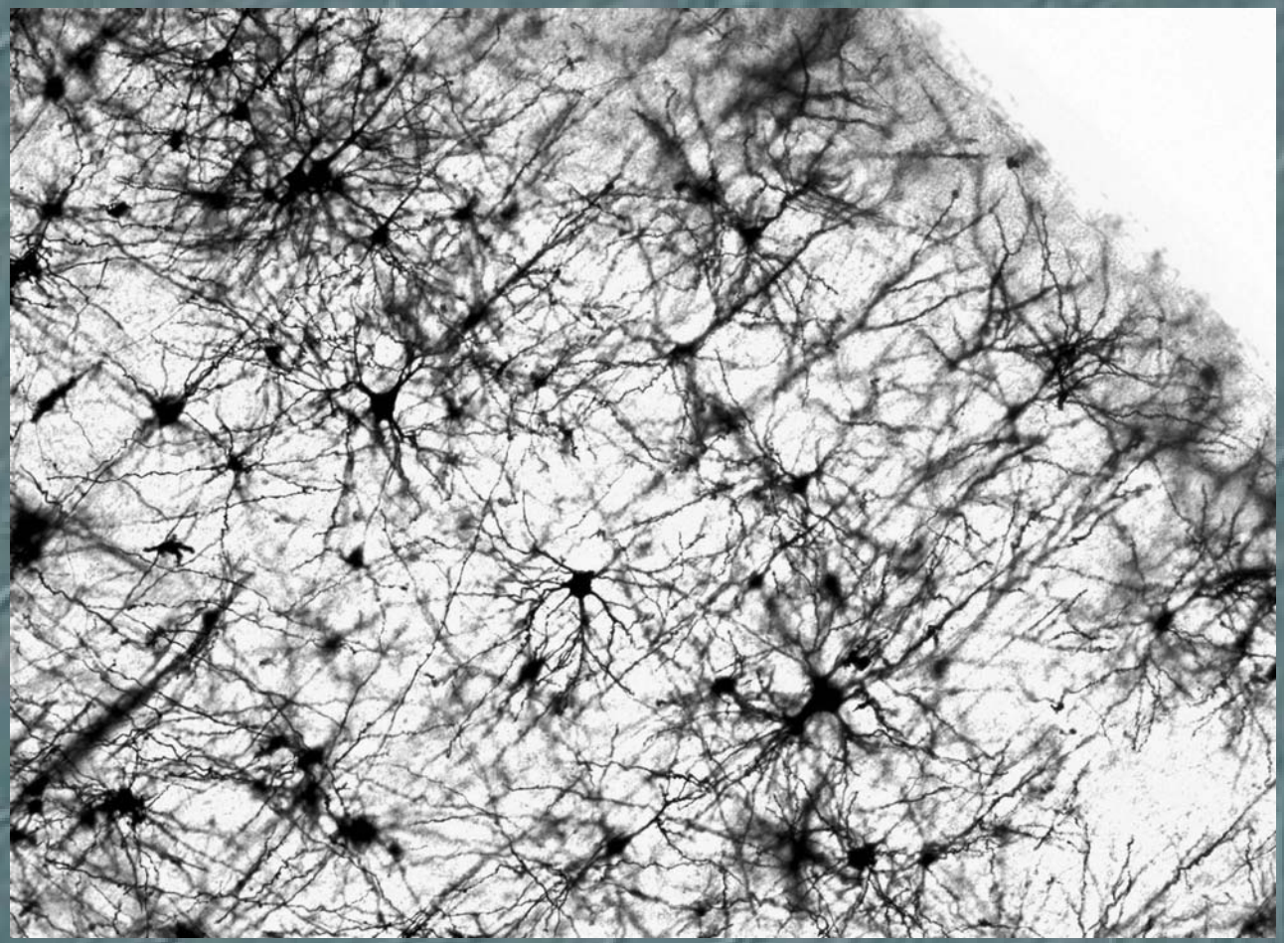


Andrea Hasenstaub



Yuguo Yu

Action Potentials and Triggered Transmitter Release: The Workhorse of Information Communication in the Brain



Membrane Potential of Cortical Neurons Varies Widely During Slow Wave Sleep and Even During Waking

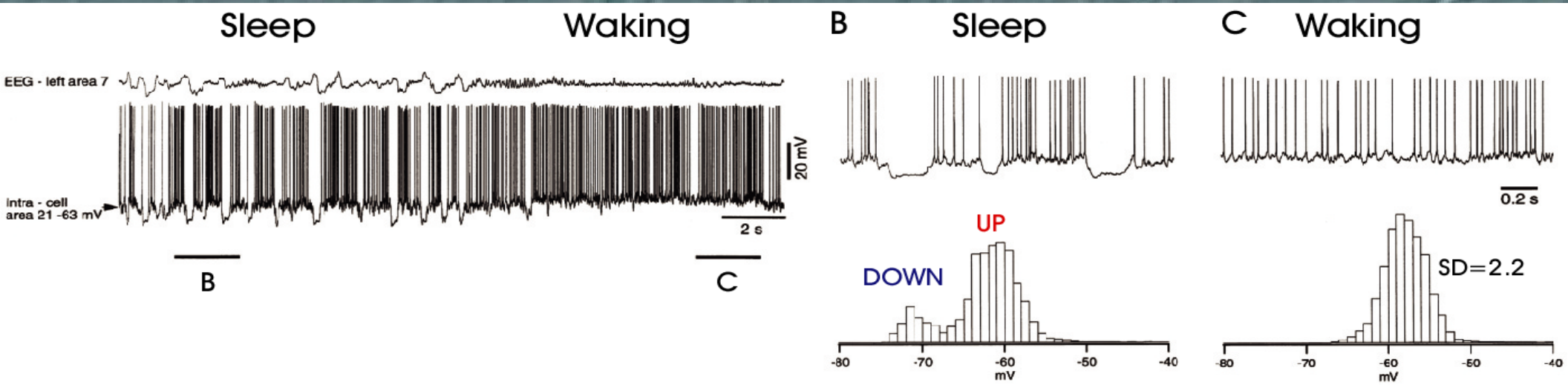
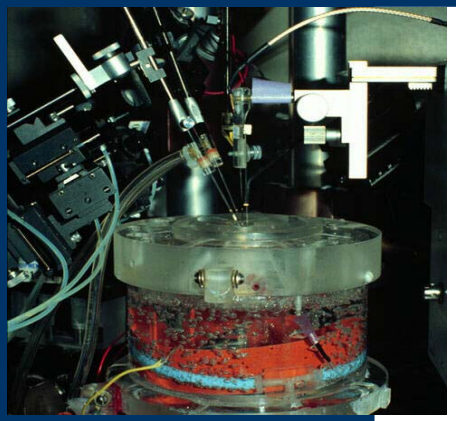
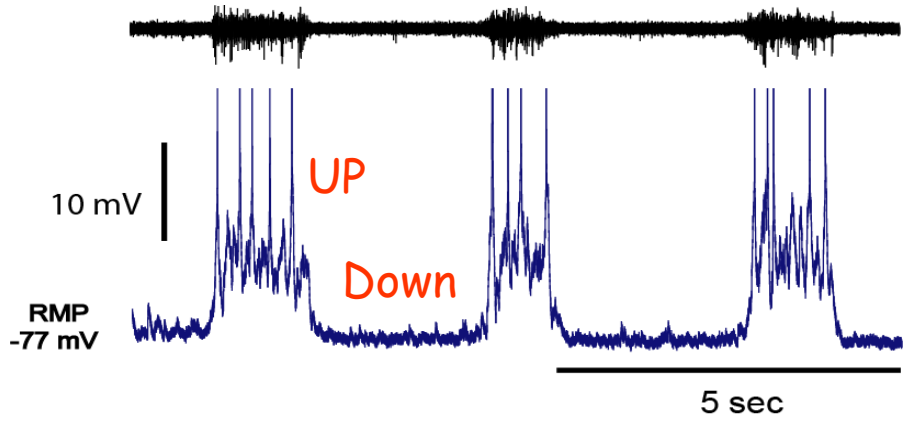


Figure adapted from Steriade et al, J. Neurophysiol 85:1969, 2001

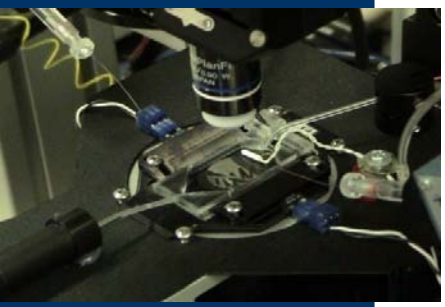
Spontaneous recurrent cortical activity occurs *in vitro*

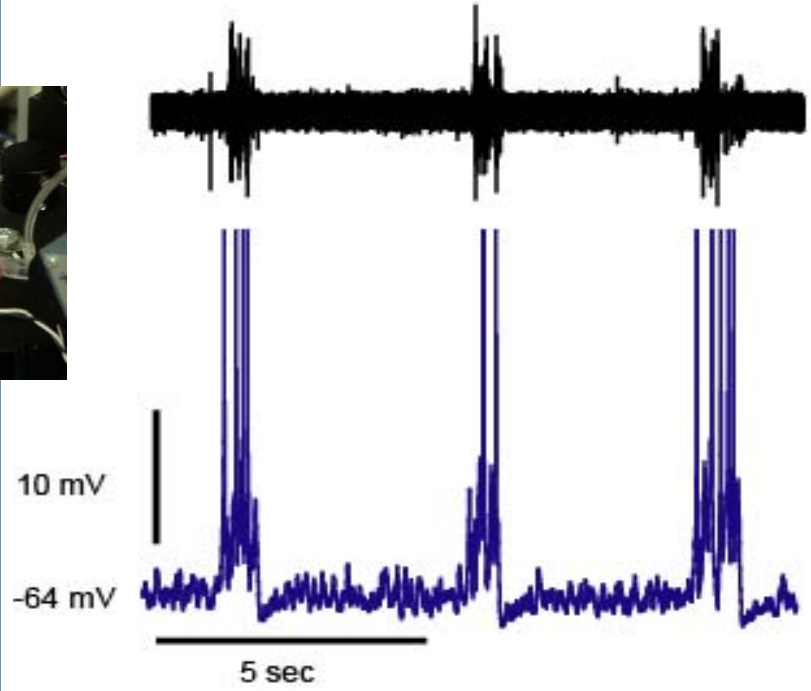


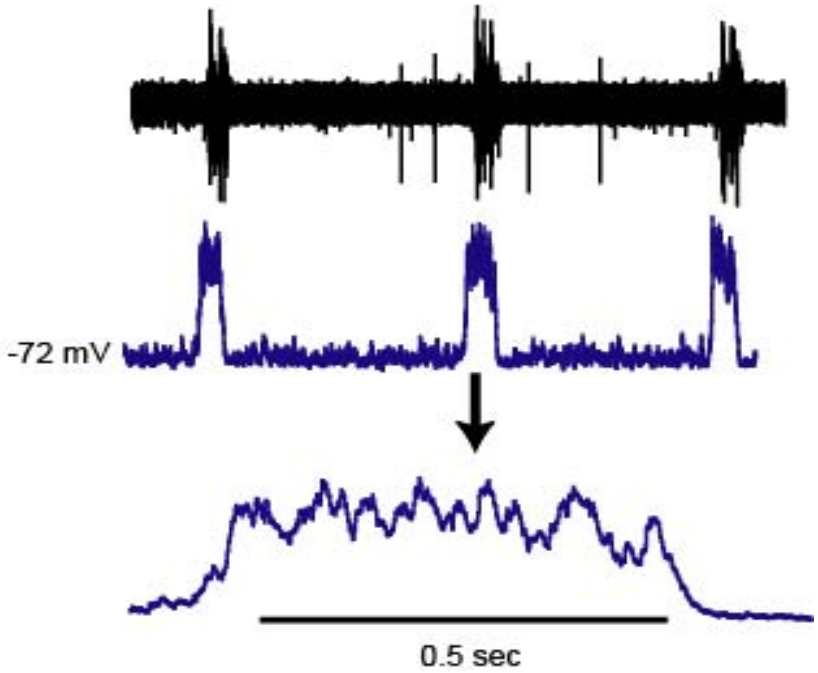
Interface



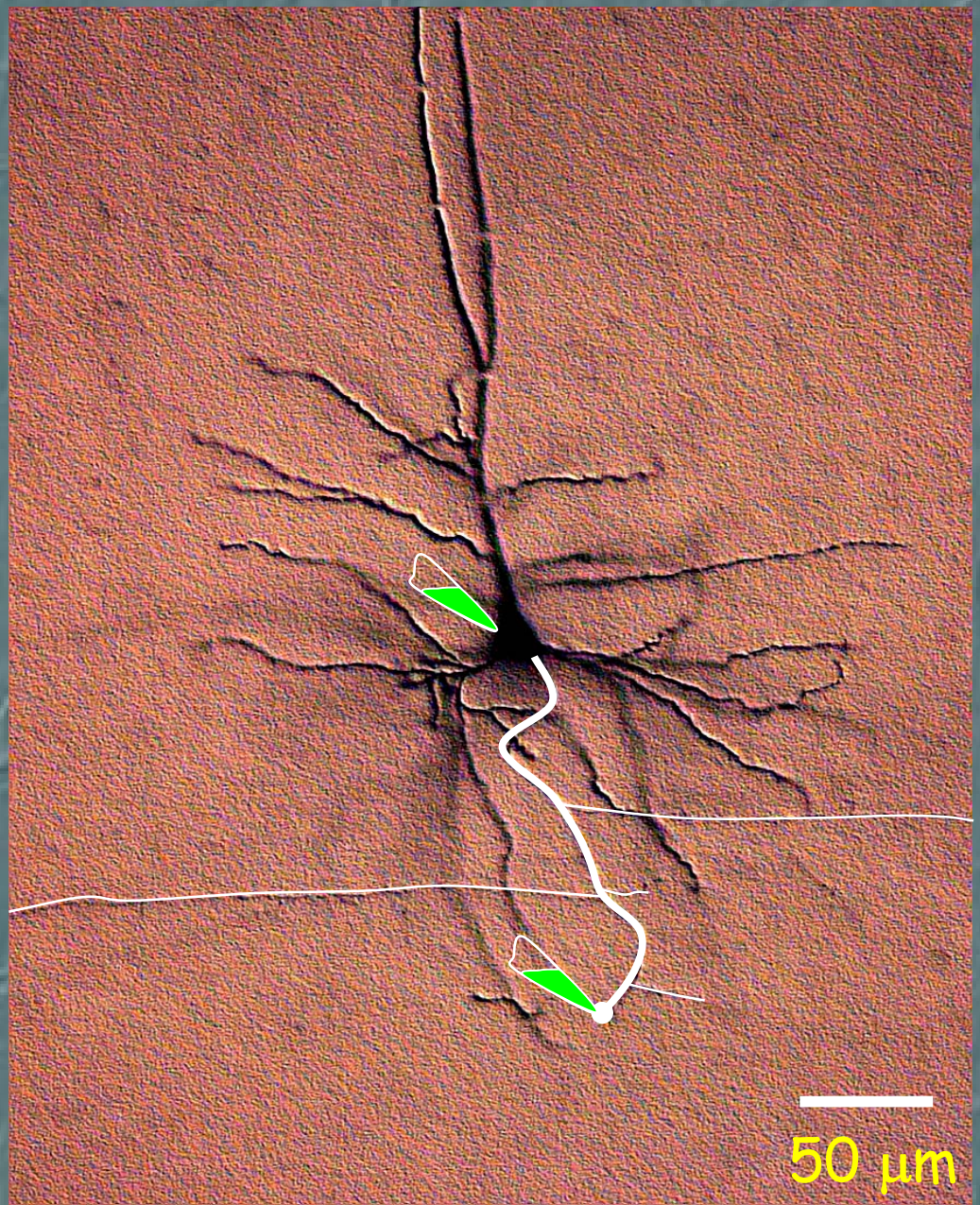
Submerged







Subthreshold synaptic potentials travel down axon



dendrites

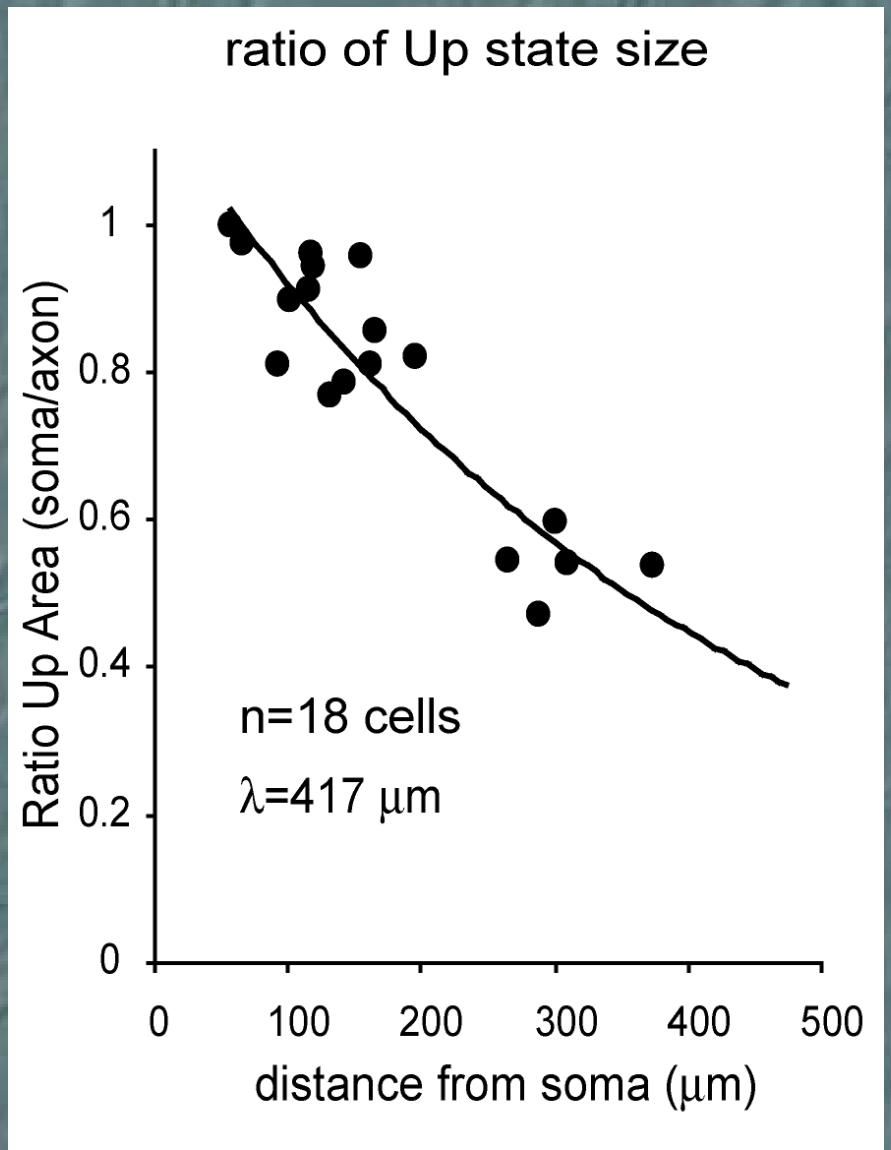
5 mV

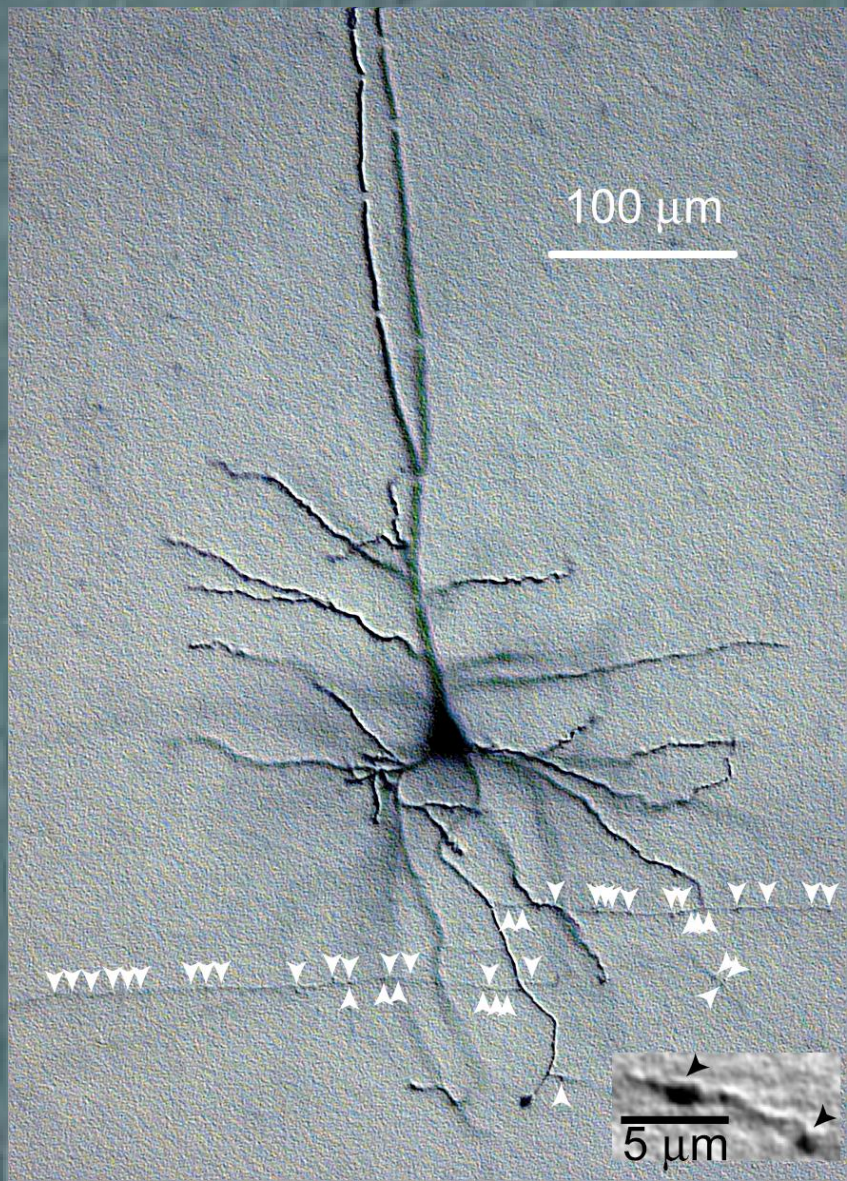
500 ms

soma

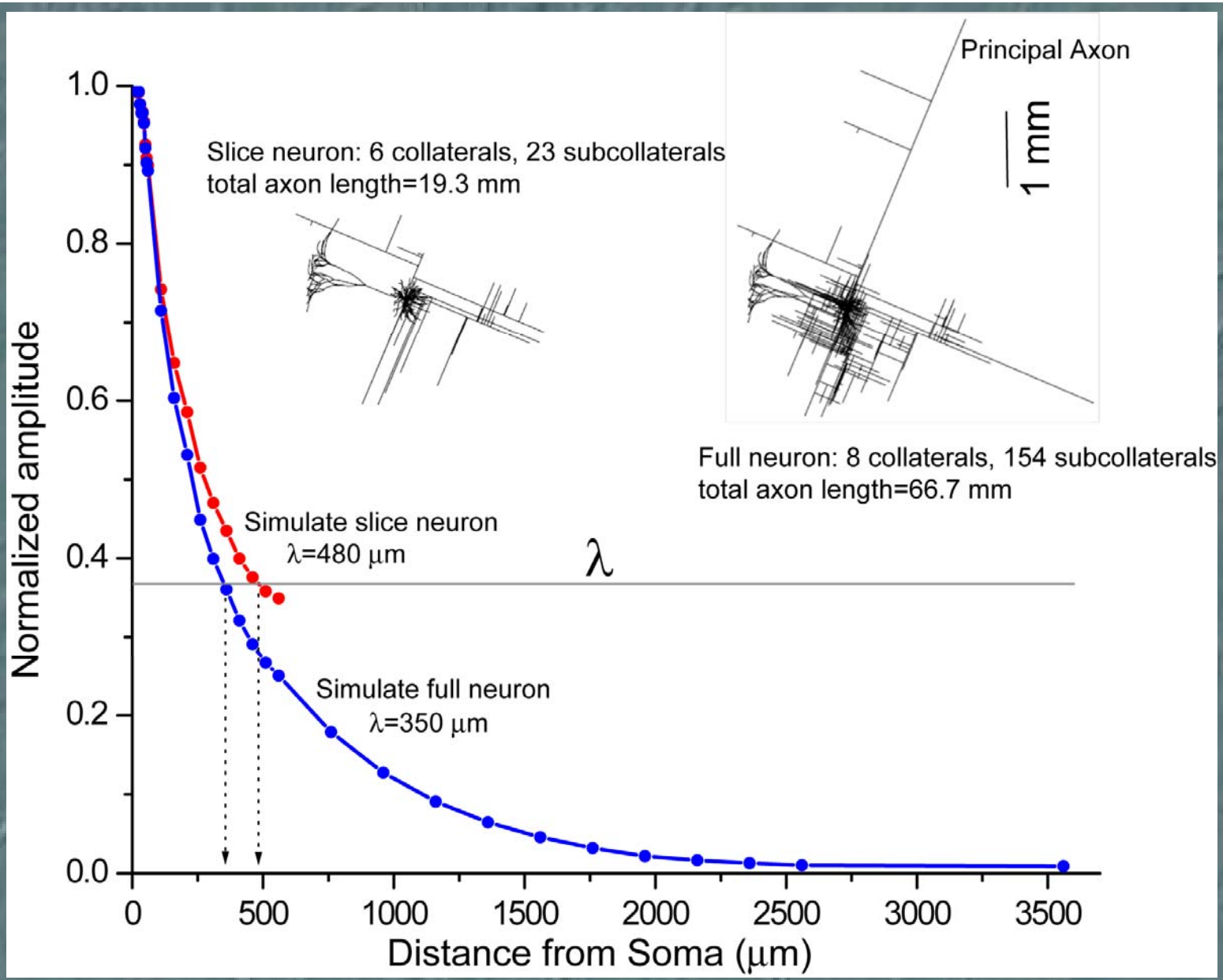
axon

The Axon Exhibits a Long Length Constant During Synaptic Activity

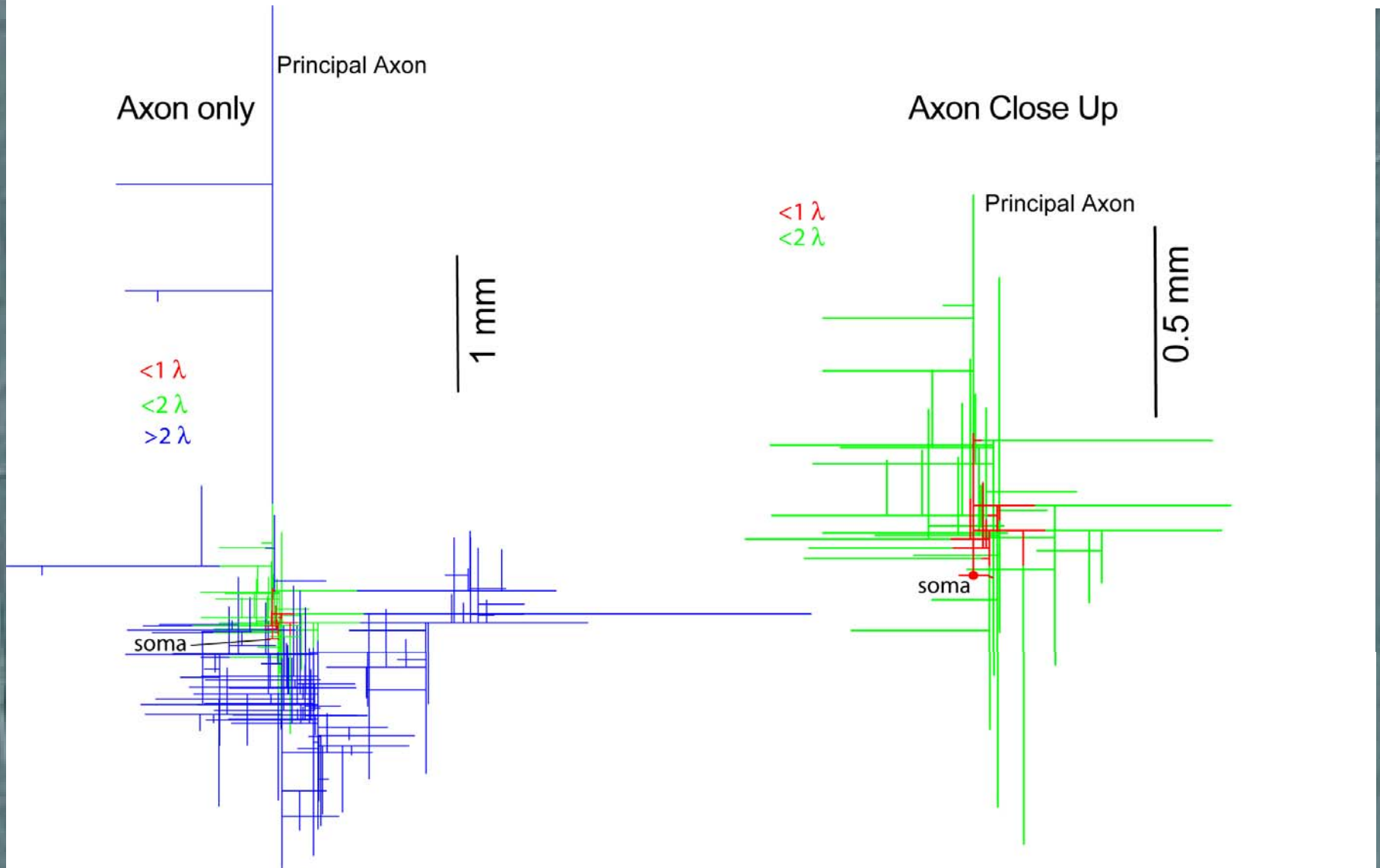




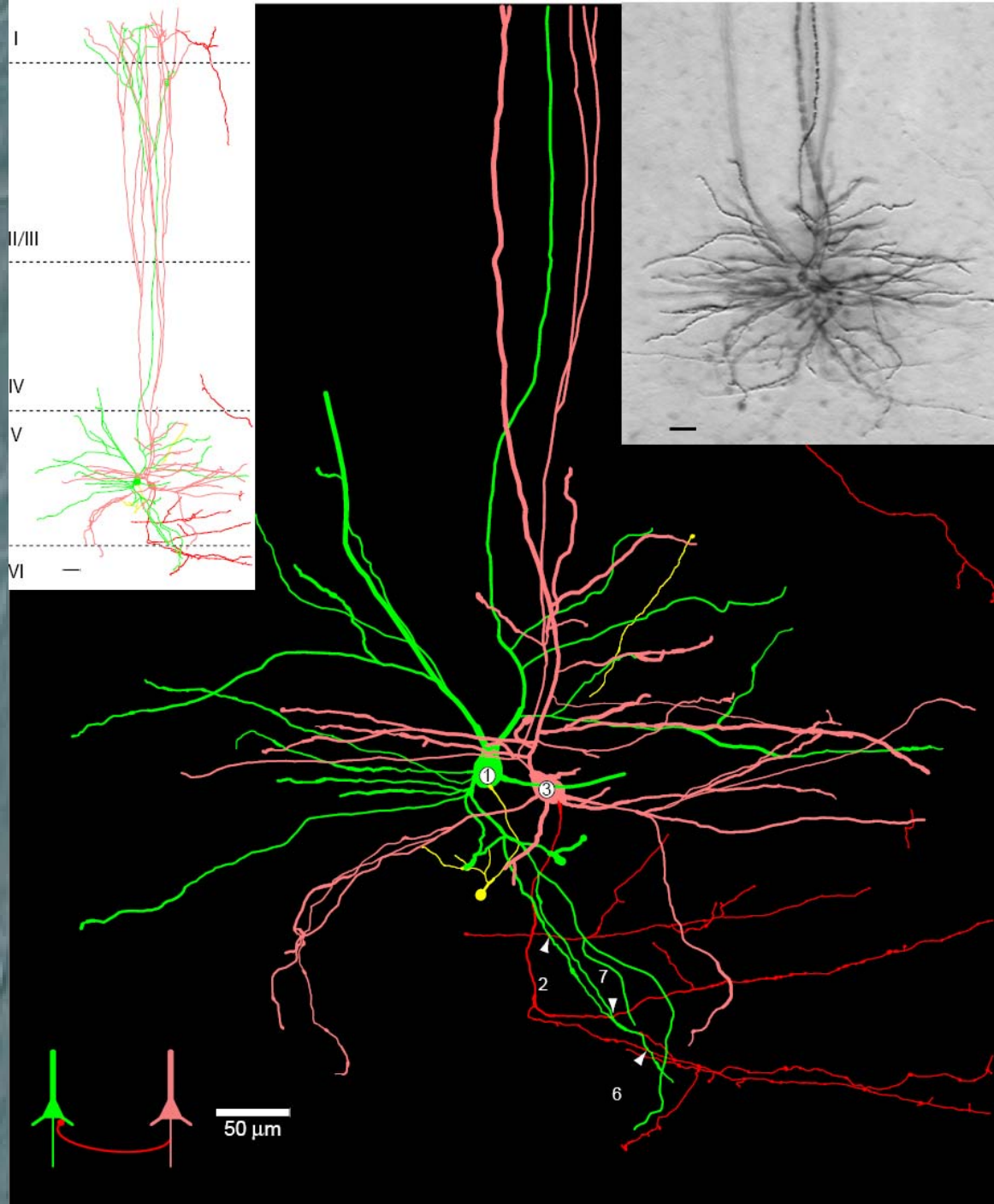
Models of Complete Axonal Tree Indicate that the Length Constant of Axons if in the Hundreds of Microns



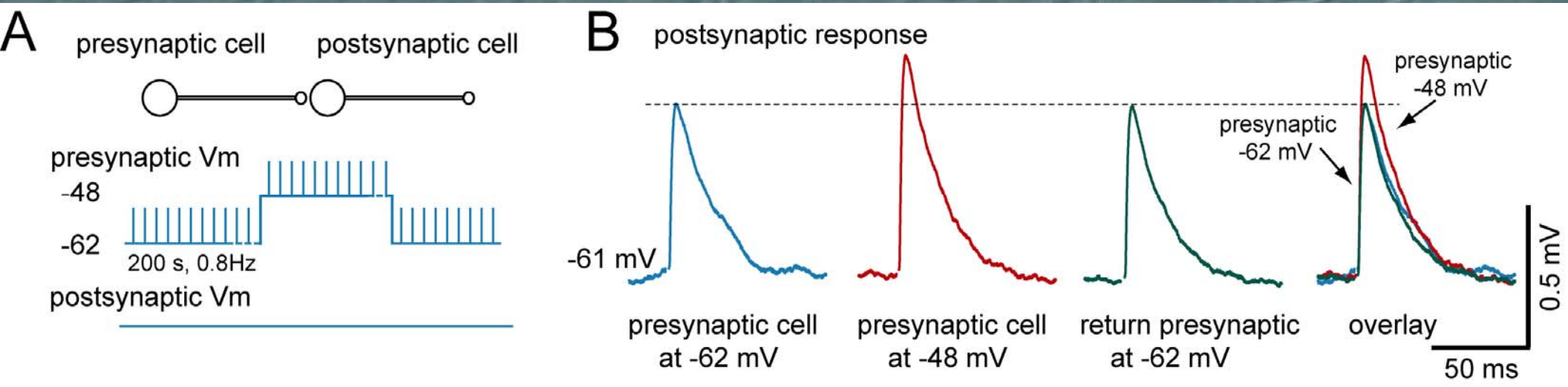
A Significant Portion of the Axonal Tree is within 1 and 2 Length Constants (approximately 200 synapses in 1 and 2000 in 2 length constants)



Morphology of the Two Pyramidal Cells for Which the Synaptic Physiology was Examined in the Next Slide



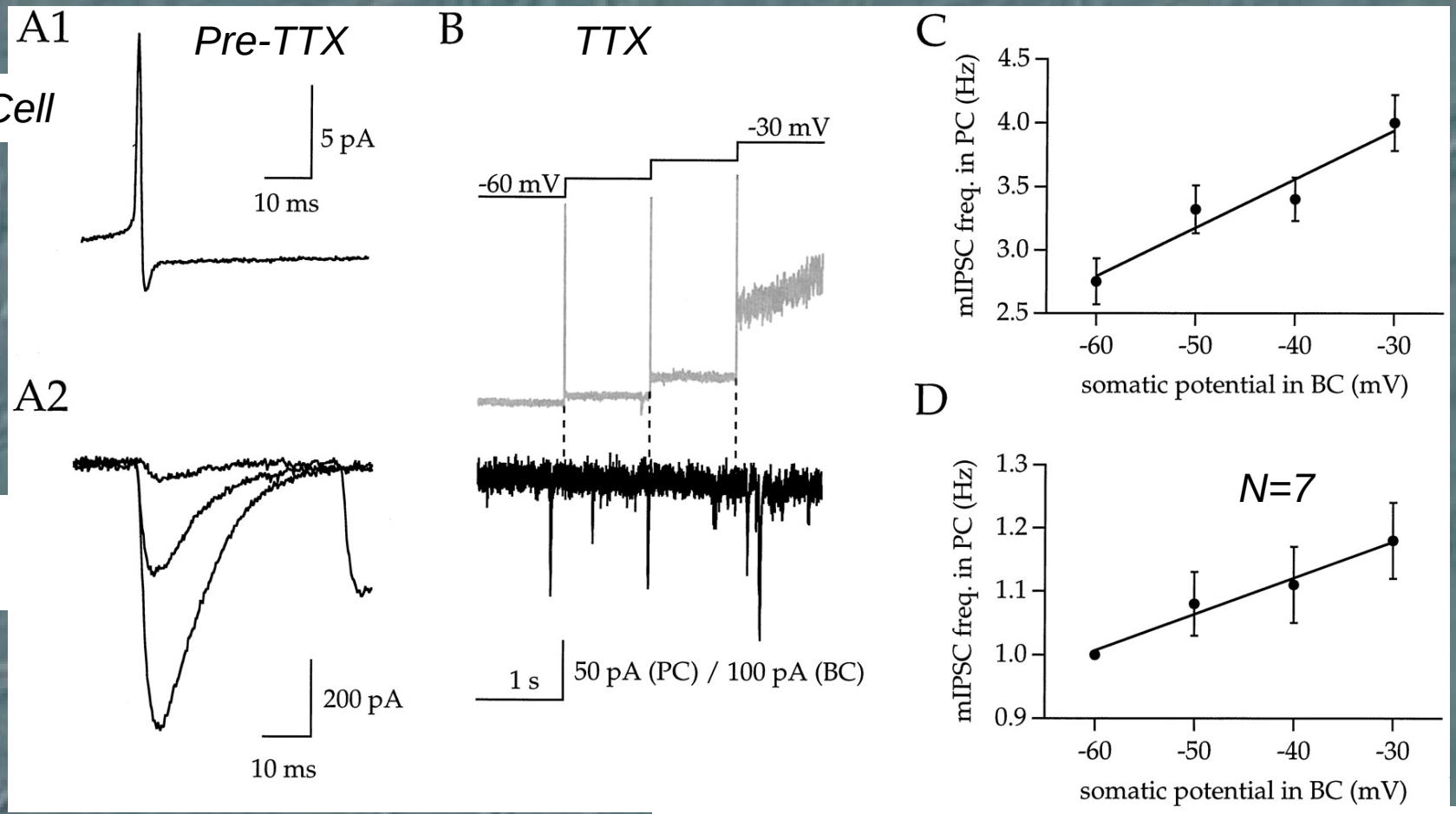
Membrane Potential of the Presynaptic Soma Affects the Amplitude of the Average Postsynaptic Potential!



Action-potential free Synaptic Transmission in the Brain

Basket Cell

Purkinje Cell

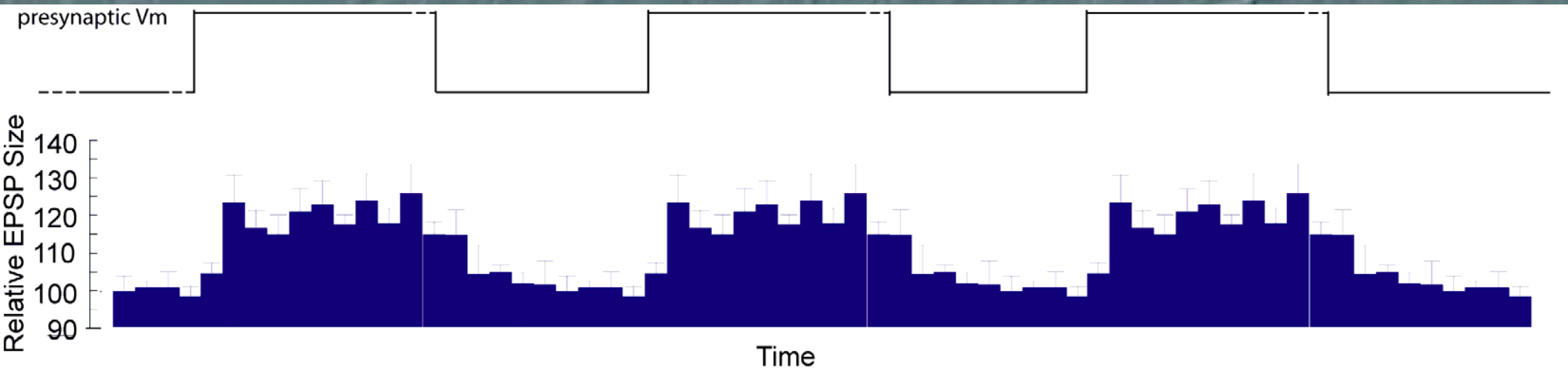


Glitsch and Marty, J. Neurosci. 19: 511 (1999)

These Results Indicate That the Amplitude of the EPSP Encodes the Membrane Potential of the Presynaptic Cell.

This Indicates that Information is NOT Encoded Only Through the Pattern of Action Potentials.

Rather, Information is Encoded as a Mixture of Spike Pattern and Membrane Potential of the Presynaptic Cell and Network



Critical Points to be determined:

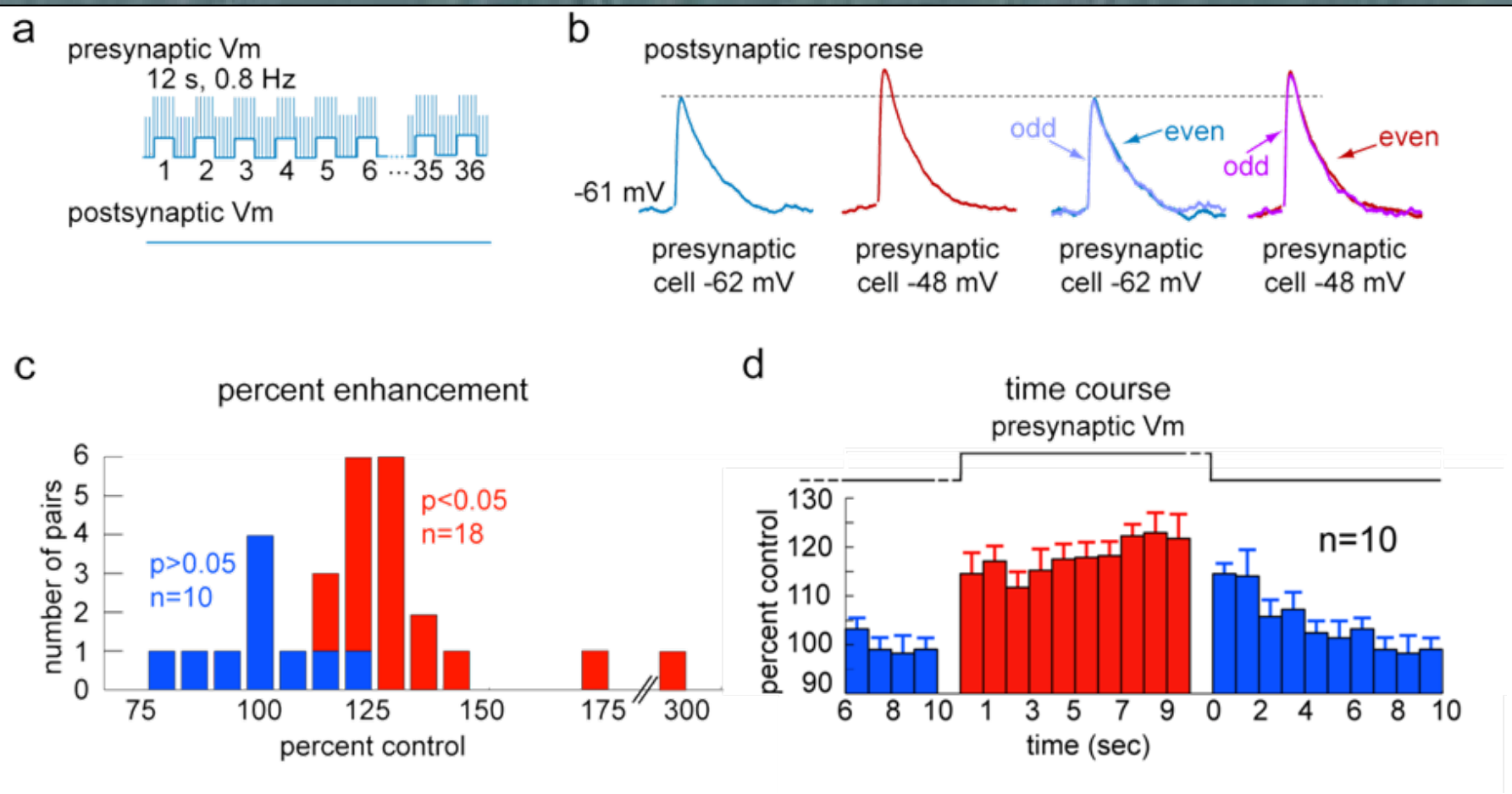
1) ***Mechanism*** (change in basal or triggered presynaptic Ca2+, change in axonal action potential duration, or voltage-dependent changes in synaptic transmission)

2) ***Kinetics*** (evidence for slow and fast components)

3) ***Voltage Dependence*** (appears to be linear in the range of rest to firing threshold)

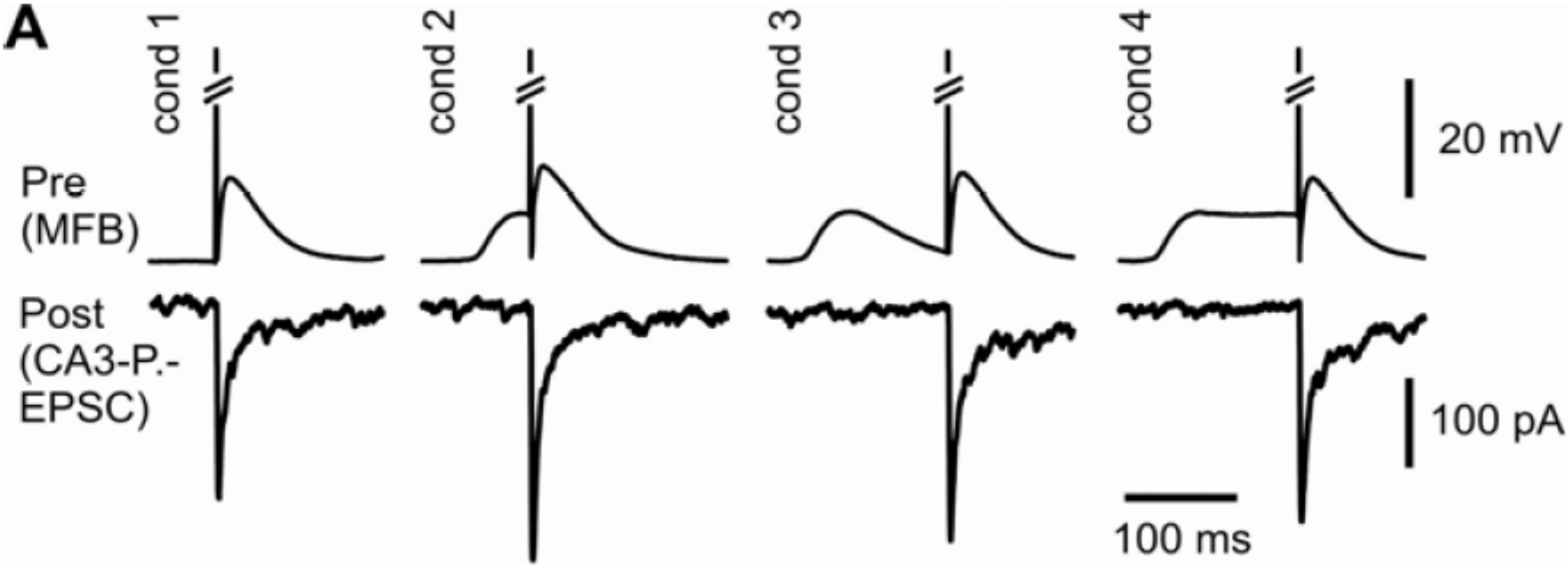
Goal: Understand the Functional (Computational) Consequences of Mixed Transmission on Cortical and Brain Function

The Modulation of EPSP Amplitude by Presynaptic Somatic Vm Requires > 1 Second to Fully Develop and Dissipate. Are there faster components?



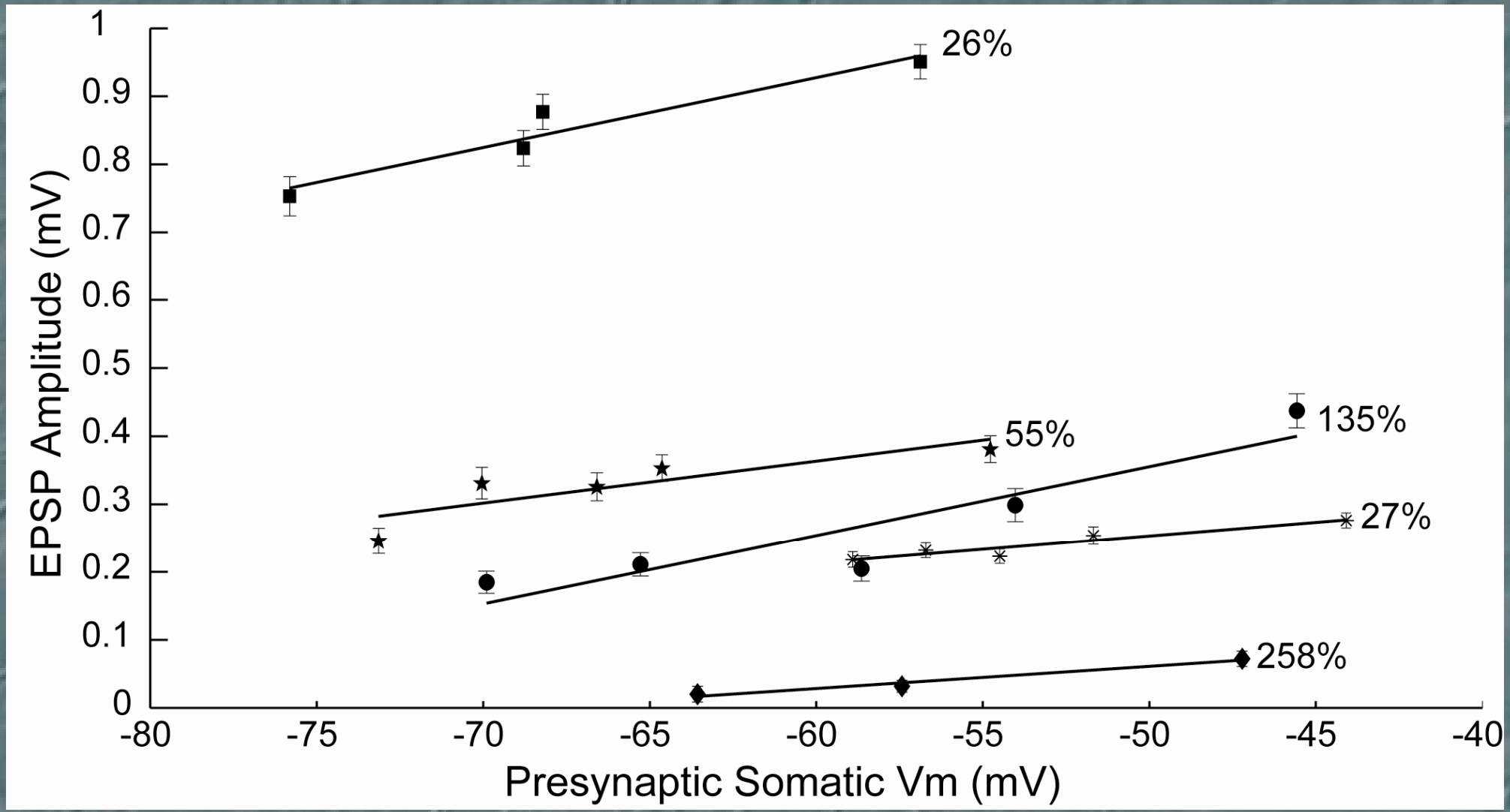
Note lack of adaptation with maintained membrane potential

Depolarization-induced facilitation at mossy fiber synapses shows rapid kinetics

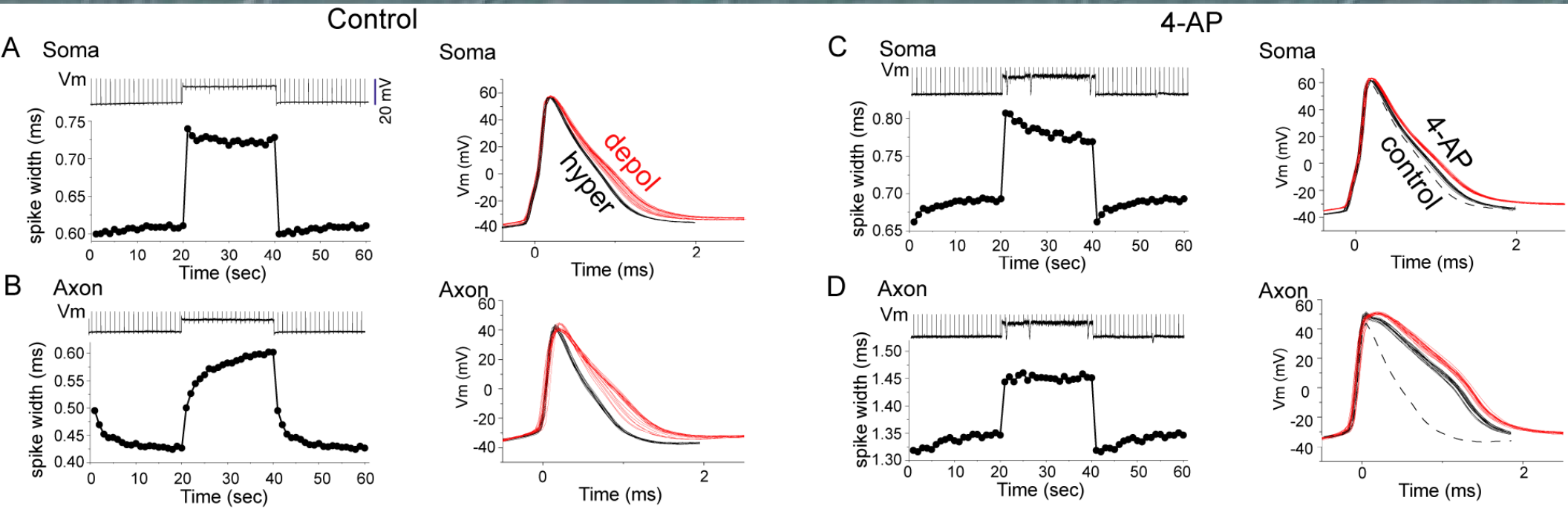


Alle and Geiger, Science (2006)

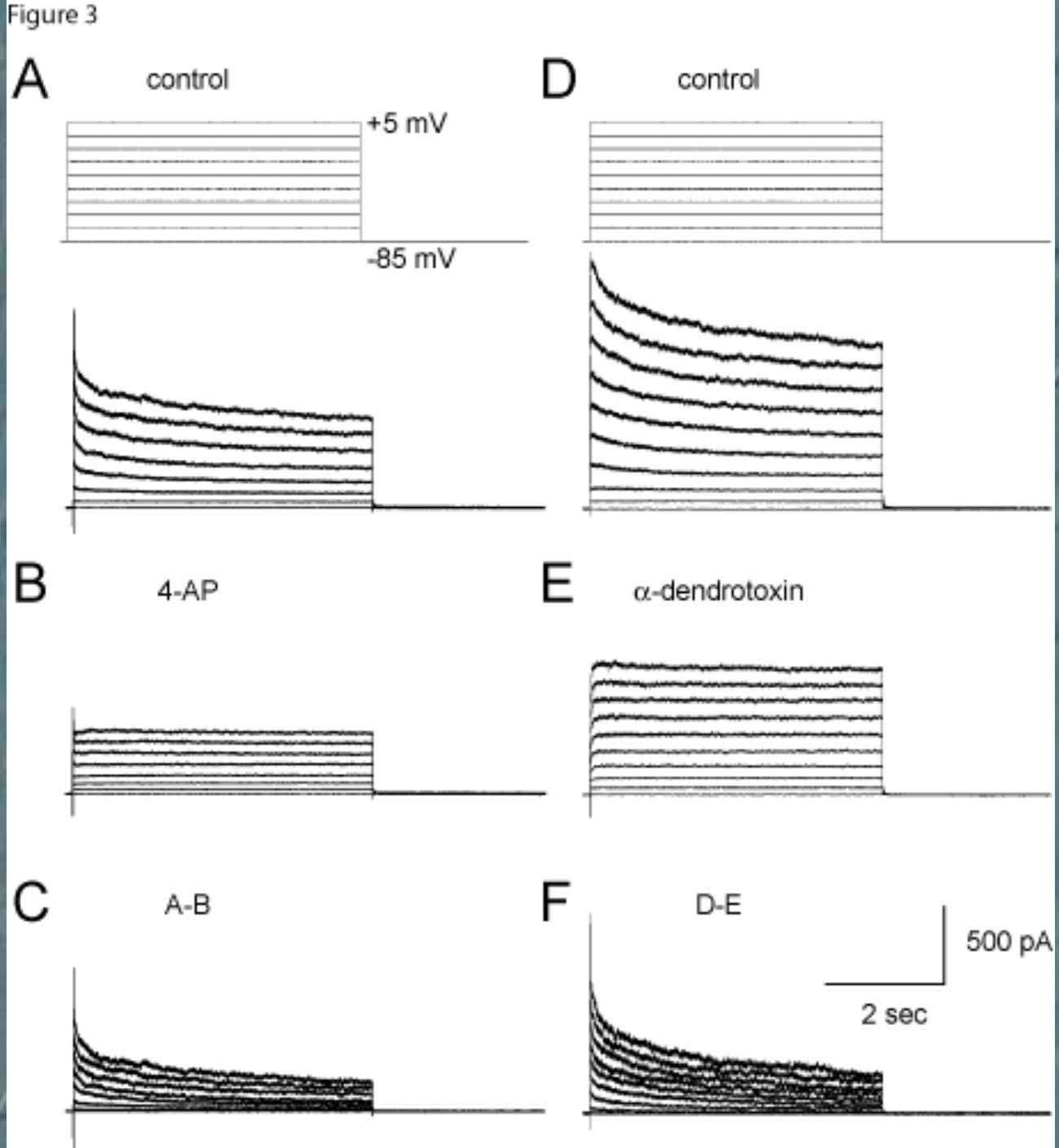
The Presynaptic Facilitatory Effect of Somatic Vm is a Continuous Function of Voltage



Possible Mechanism 1: Changes in AP duration with membrane potential. Depolarization slowly increases spike duration in the axon and this is blocked by 4AP

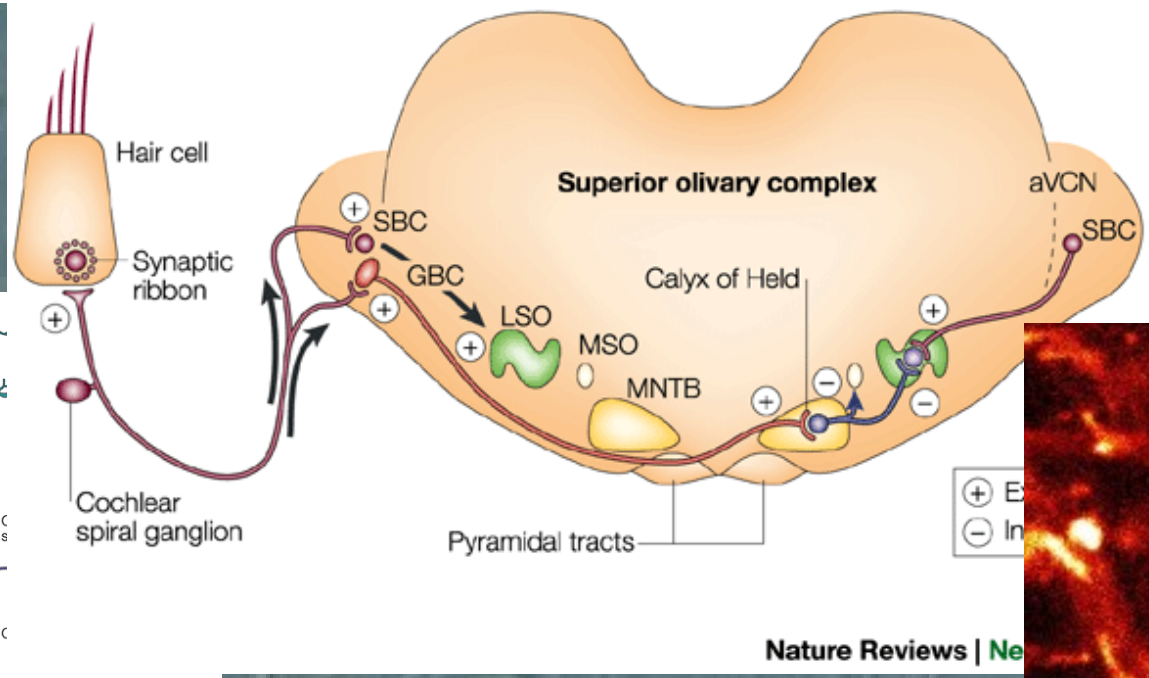


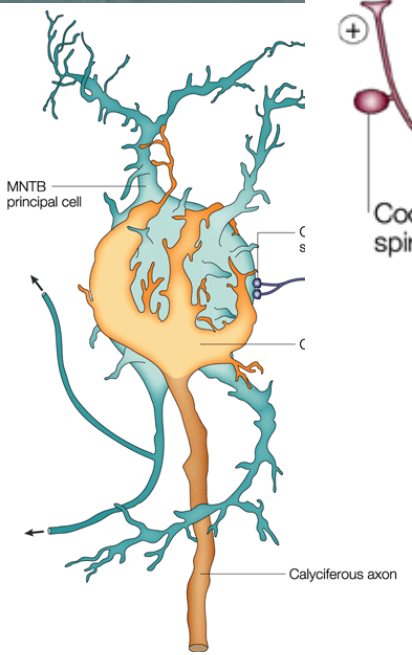
4AP and Dendrotoxin Block the Slowly Inactivating K+ current in the Axon

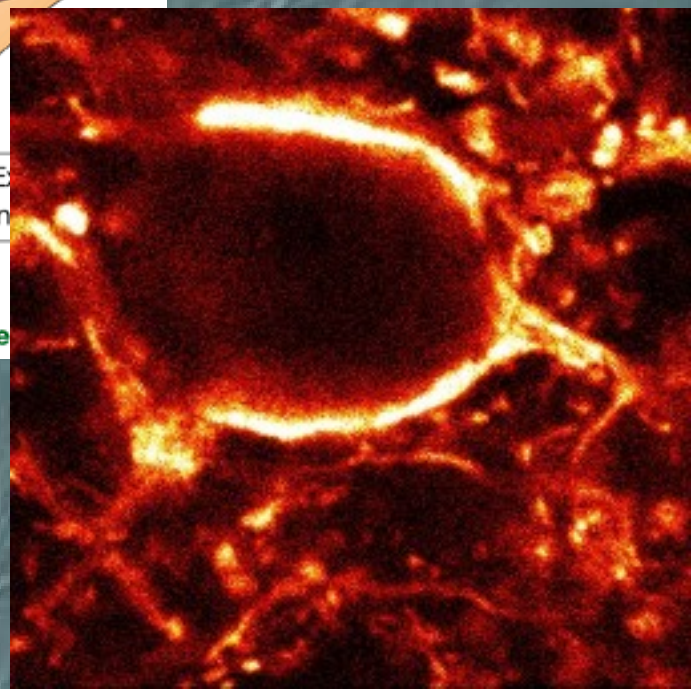


Possible Mechanism 2: Changes in probability of release by changes in synaptic Ca2+

Synaptic transmission at the Calyx of Held is Facilitated by depolarization though a Ca2+ dependent mechanism

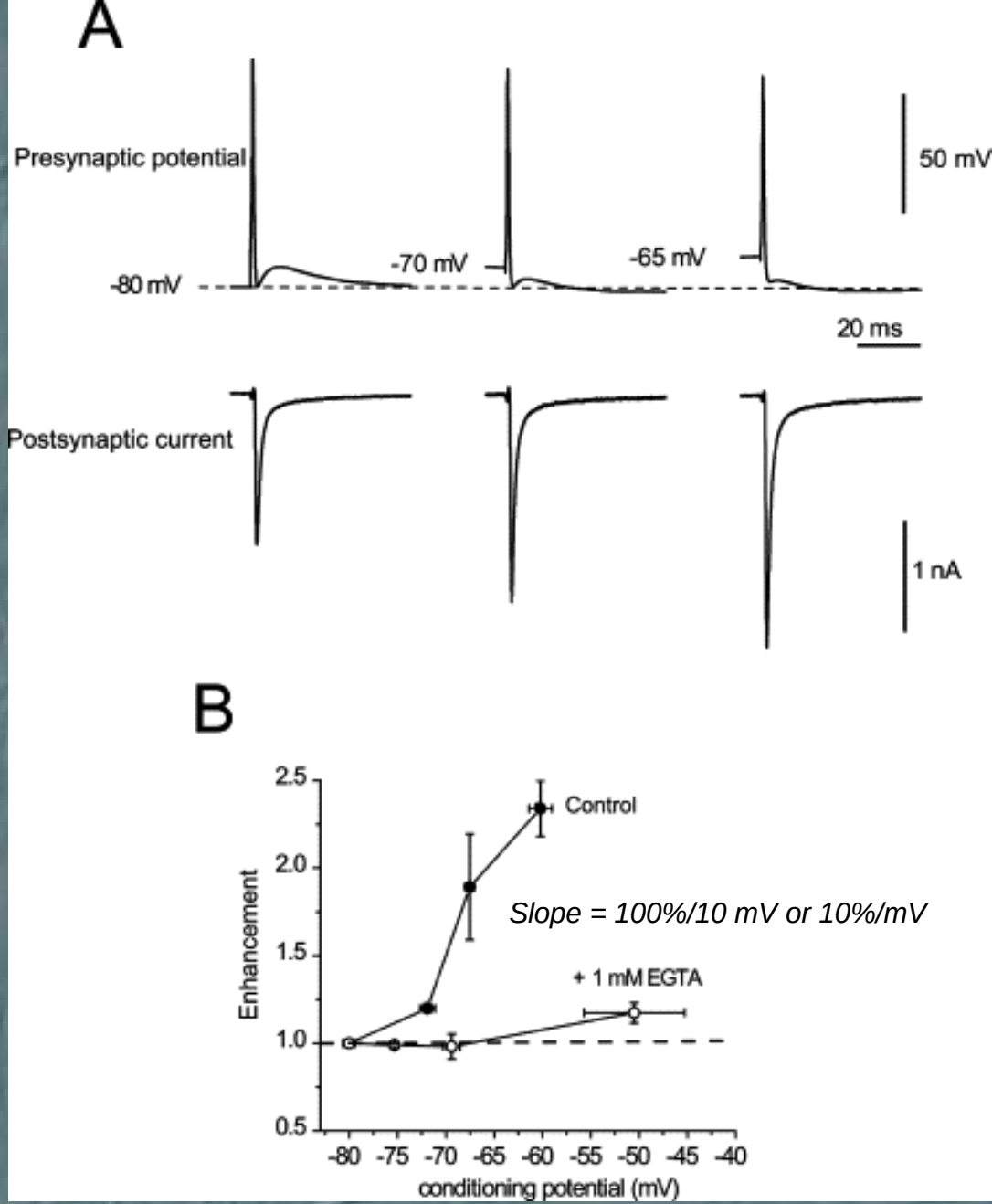






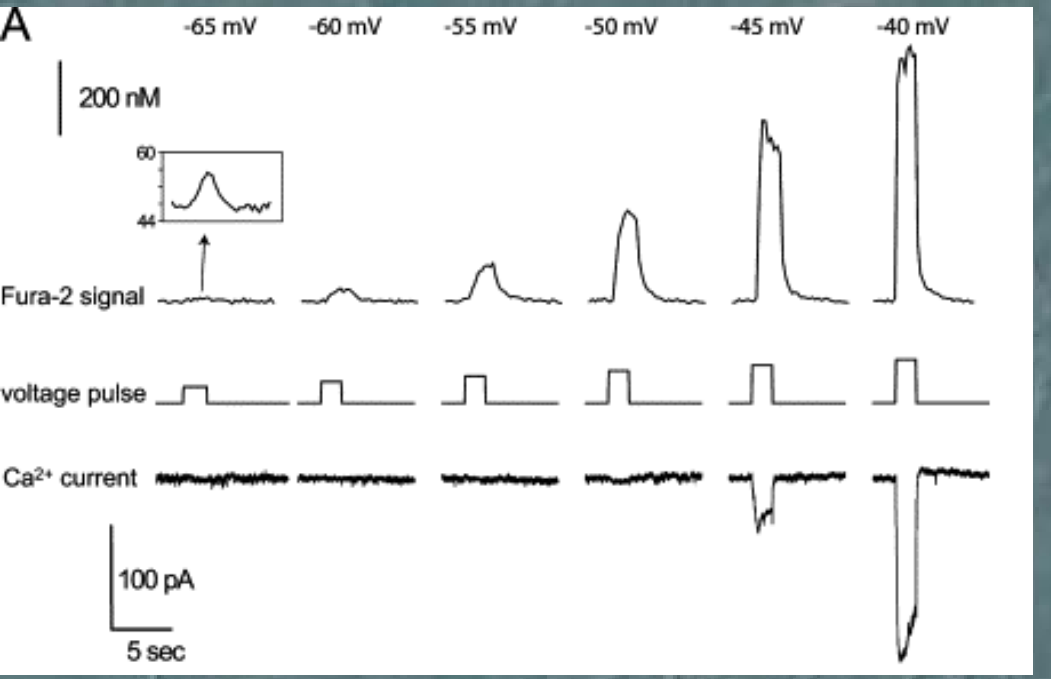
Nature Reviews Neuroscience ***3****, 53-64 (2002)*

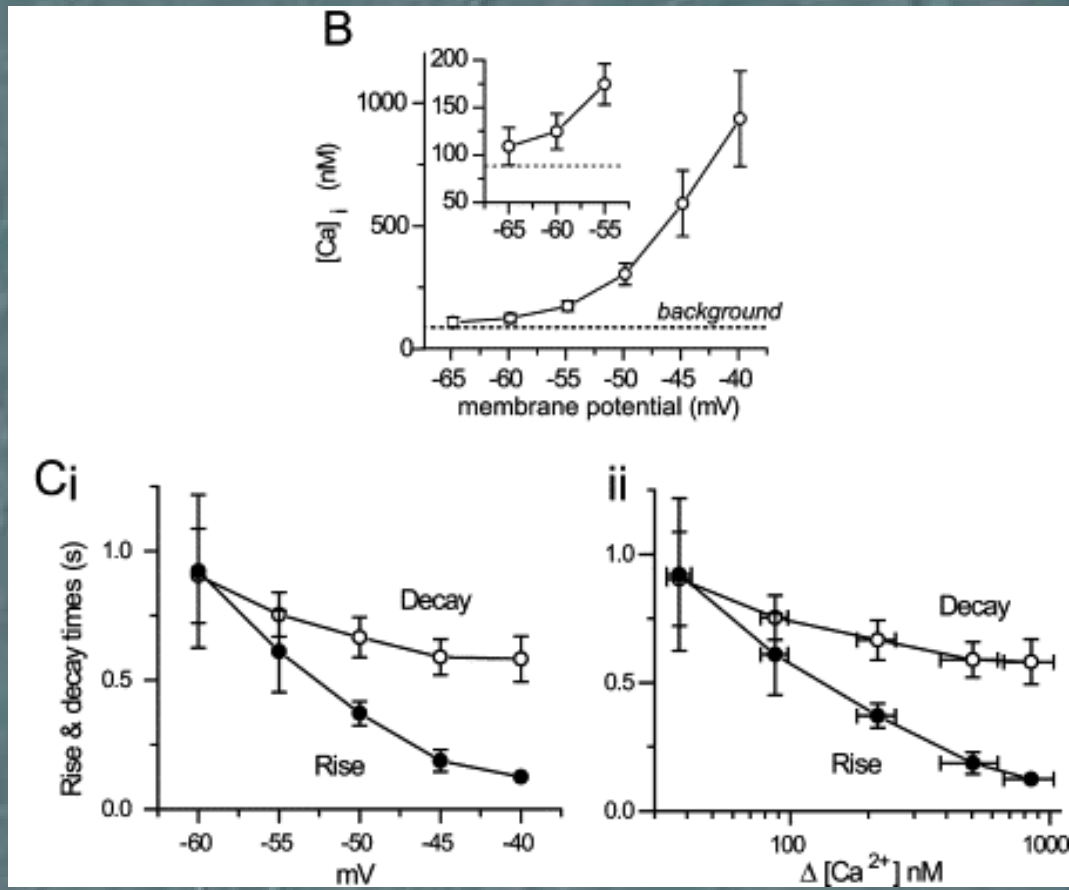
Membrane Potential of the Presynaptic Terminal in the Calyx of Held Determines the Amplitude of the EPSP Evoked



Awatramani, Price, Trussell Neuron 48: 109-121 (2005)

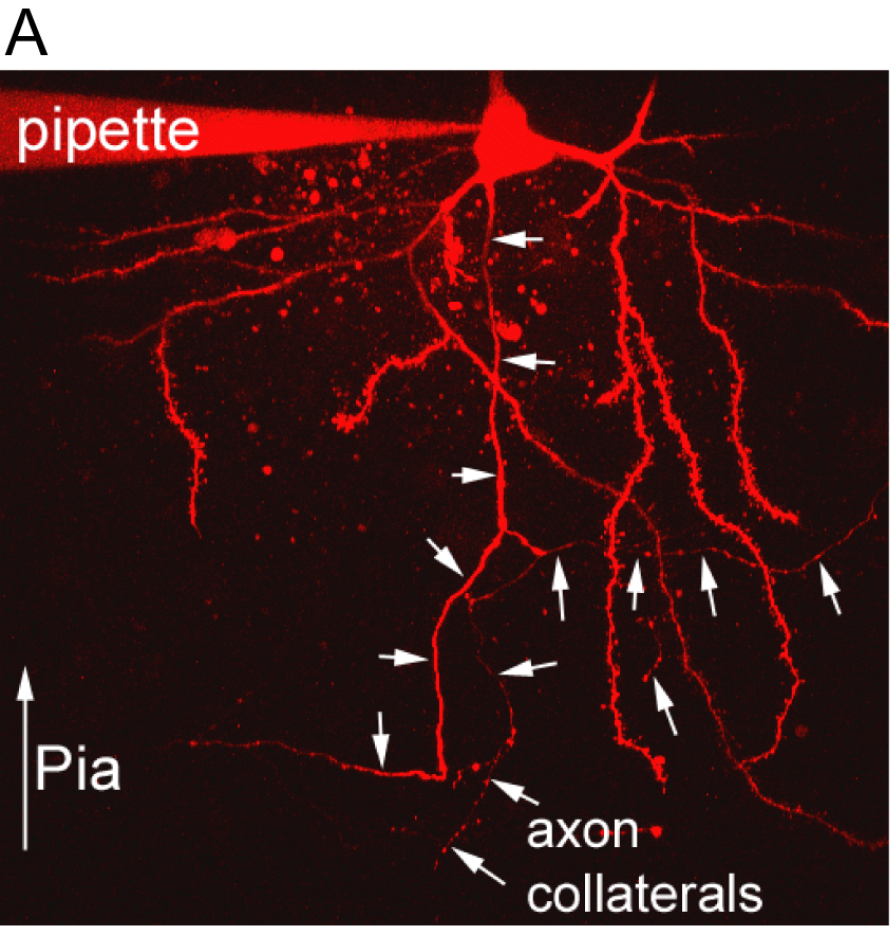
Small Voltage Steps at the Calyx of Held Result in Increases in Presynaptic Calcium Levels

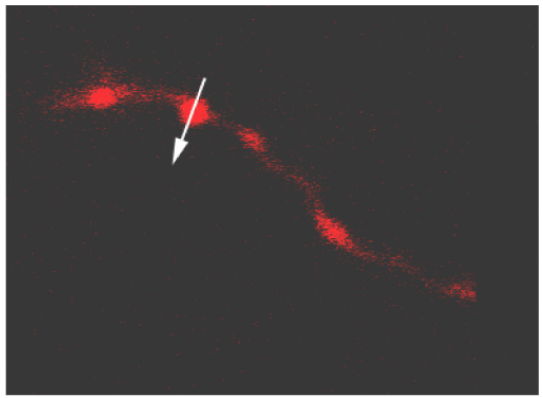


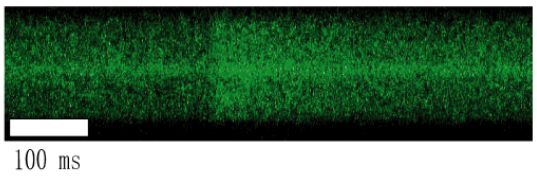


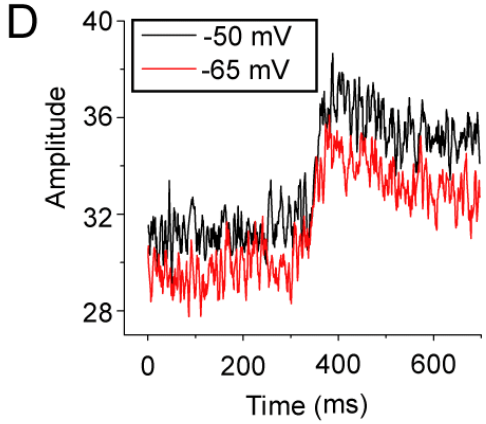
Awatramani, Price, Trussell Neuron 48: 109-121 (2005)

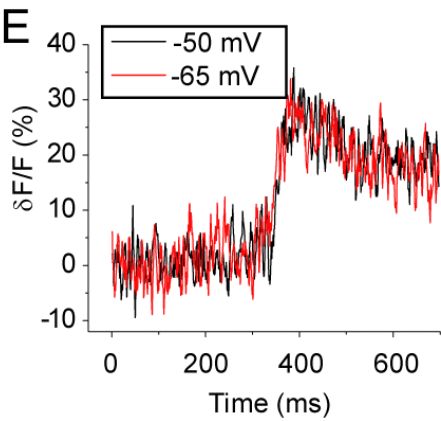
Two photon Imaging of Presynaptic Ca2+ in Axonal Terminals



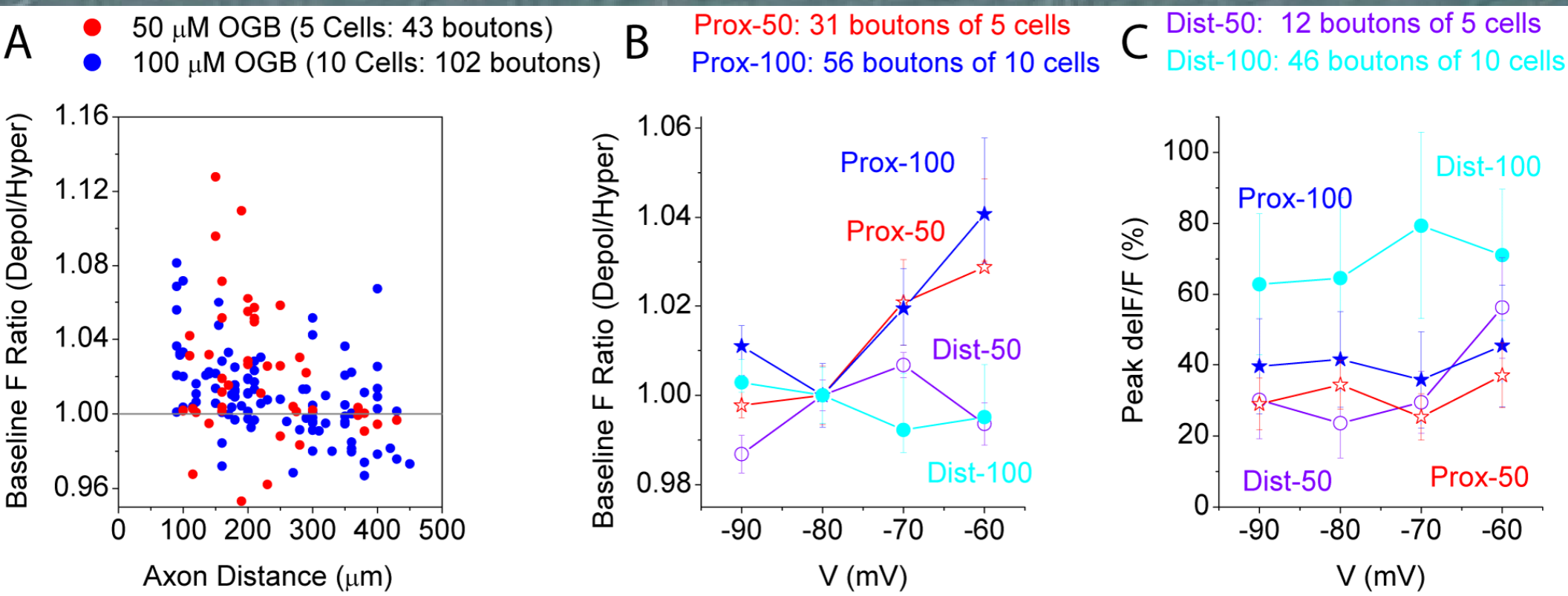








Group data illustrating the dependence of presynaptic Ca2+ levels on somatic membrane potential



The Facilitatory Effect of Presynaptic Somatic Depolarization on EPSP Amplitude Between Layer 5 Pyramidal Cells is Blocked by Buffering of Ca2+

Electrodes Containing 25 micromolar BAPTA: Facilitation in 17/26 pairs

Electrodes Containing 1 mM EGTA: Facilitation in 3/11 (p=0.01)

Electrodes Containing 10 mM EGTA: Facilitation in only 1/16 pairs (p<0.01)

Conclusions:

Local Information Transmission in the Cerebral Cortex (and other brain areas) may occur through a mix of "graded" and "triggered" or analog and digital modes.

The mechanisms of this mixed communication may involve:

Variations in axonal action potential duration

Variations in presynaptic Ca2+ levels

Voltage dependent changes in release probability

The use of a combined "analog/digital" mode of synaptic transmission may increase the efficiency of information coding in the brain and may be important in the operation of neuronal assemblies. The mechanisms and implications remain to be determined.