Experiments and modeling of NMDA plateau potentials in cortical pyramidal neurons

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Introduction

Plateau potentials can be induced in the basal dendrites of cortical pyramidal neurons with either:

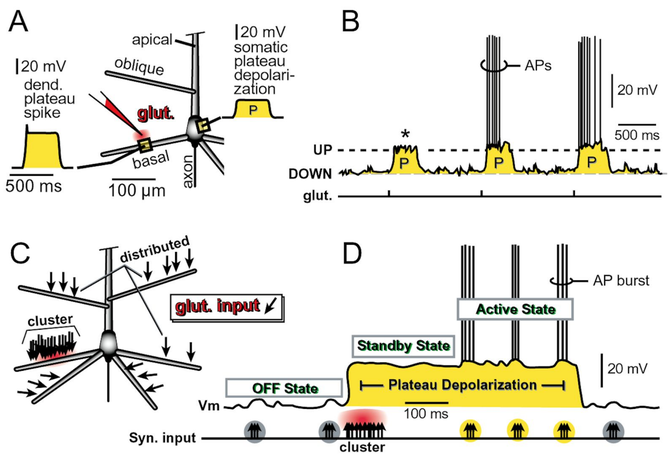
- Strong and clustered excitatory synaptic inputs
- Experimentally applied glutamate (iontophoresis)

These plateau potentials:

- Activate at a threshold
- Are NMDAr dependent
- Last 200 to 500 ms
- Depolarize soma ~20 mV
- Can trigger bAPs

With increase in stim amp:

- Saturate in amplitude
- Increase in duration



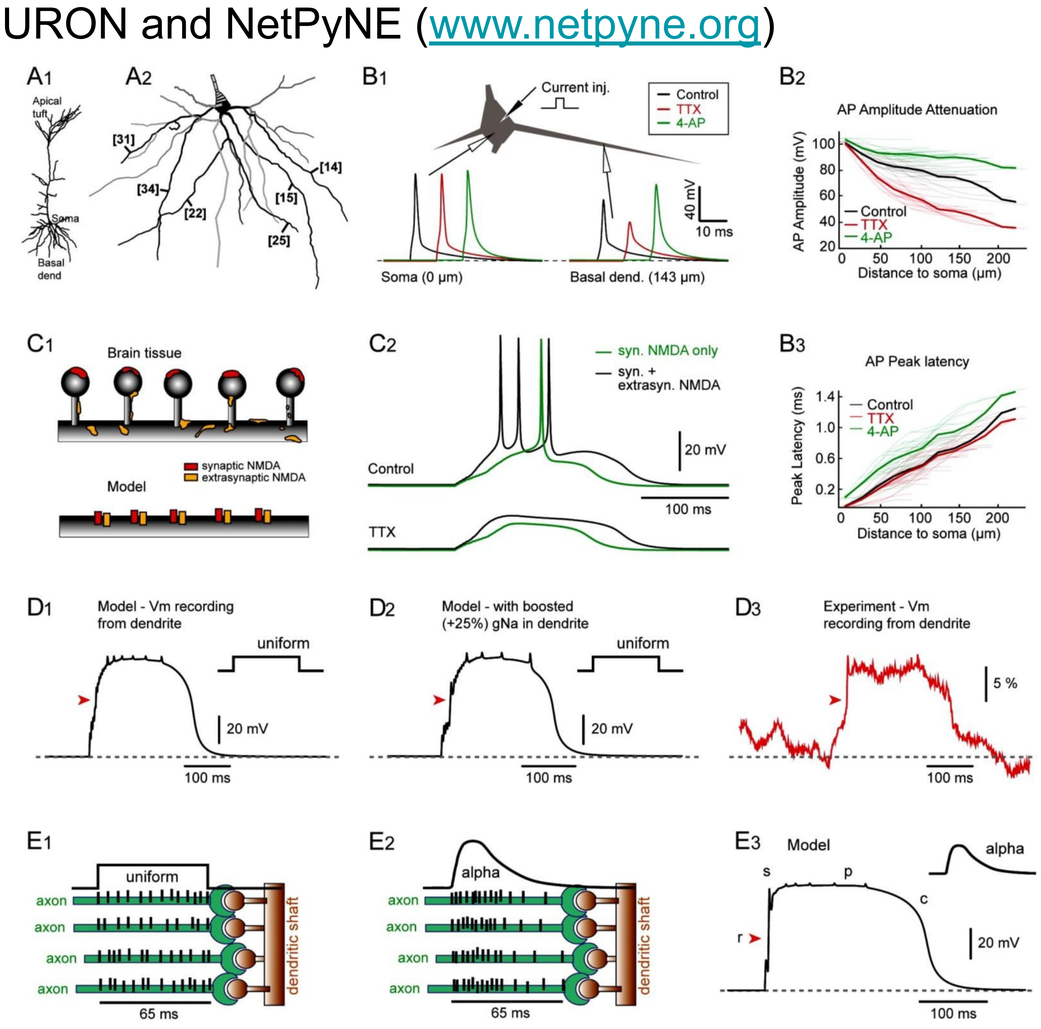
We developed a computer model of cortical pyramidal cells that replicates experimental behavior, and predicts:

- Plateaus last longer when triggered more distal from soma
- Membrane time constant (tau) is reduced during plateau
- Post-synaptic responses are quicker and of larger amplitude during plateaus

Methods

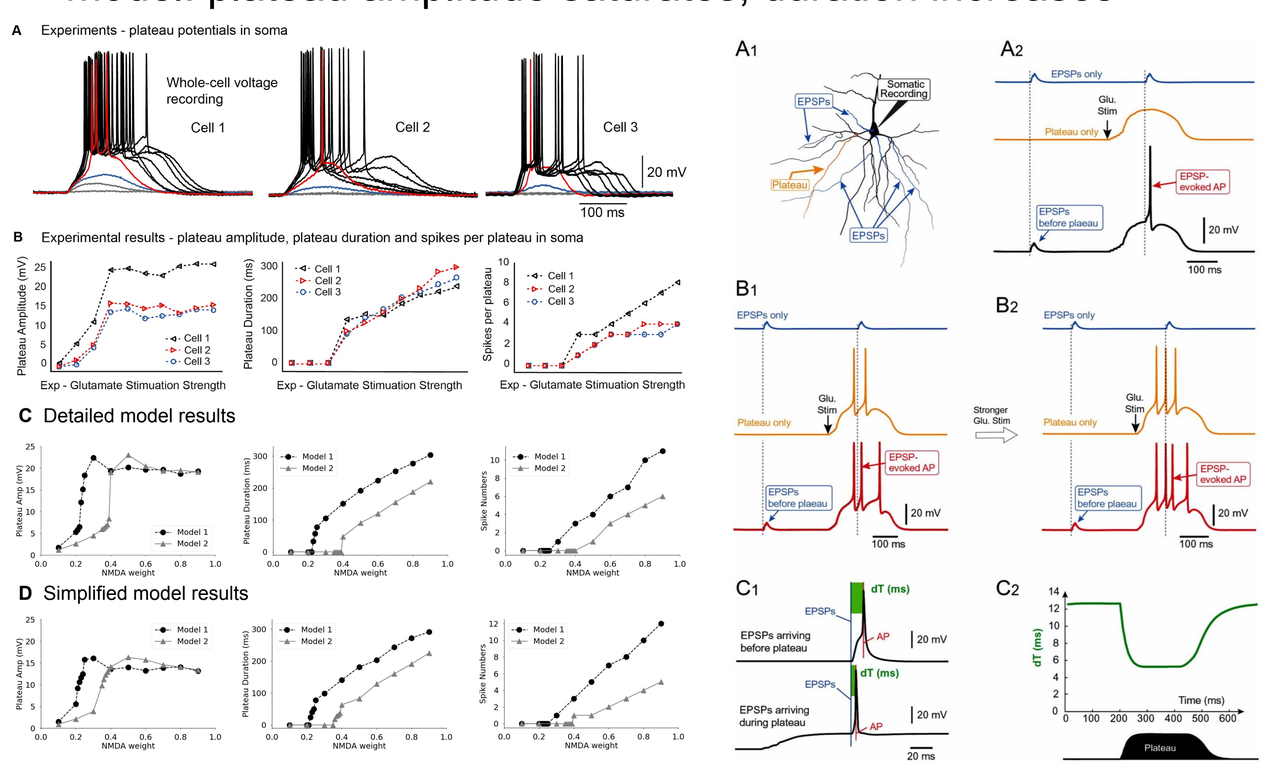
Experimental: in rat prefrontal cortex slices, glutamate microiontophoresis and dendritic voltage-sensitive dye imaging were combined to simultaneously characterize plateau potentials at their site of origin in the basal and oblique dendrites of cortical pyramidal neurons and somatic whole-cell recording was used to record membrane potential.

Modeling: morphologically-detailed, conductance-based L5 pyramidal neuron with channel densities and conductances optimized to match recorded plateaus and back-propagating APs was developed using NEURON/Python, glutamate stimulus modeled with synaptic NMDAr and AMPAr along with extrasynaptic NMDAr. Cell model was simplified using equivalent cylinders for use in network simulations (800 pyramidals/200 interneurons), built and simulated with NEURON and NetPyNE (www.netpyne.org)



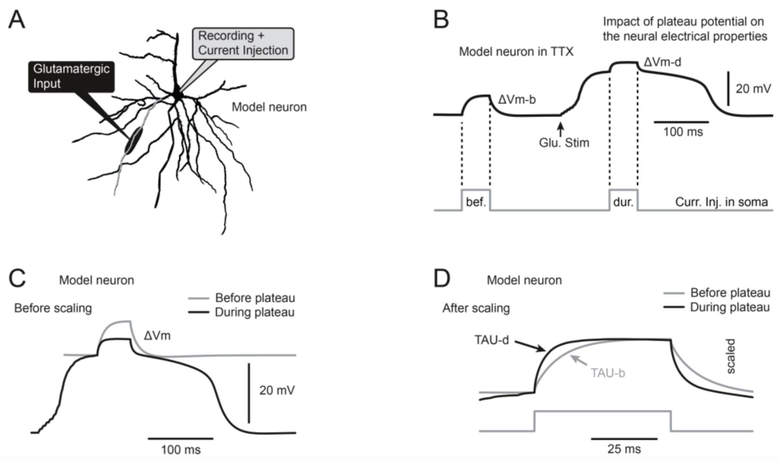
Results

- Simplified model maintains plateau behavior of detailed model: plateau amplitude saturates, duration increases



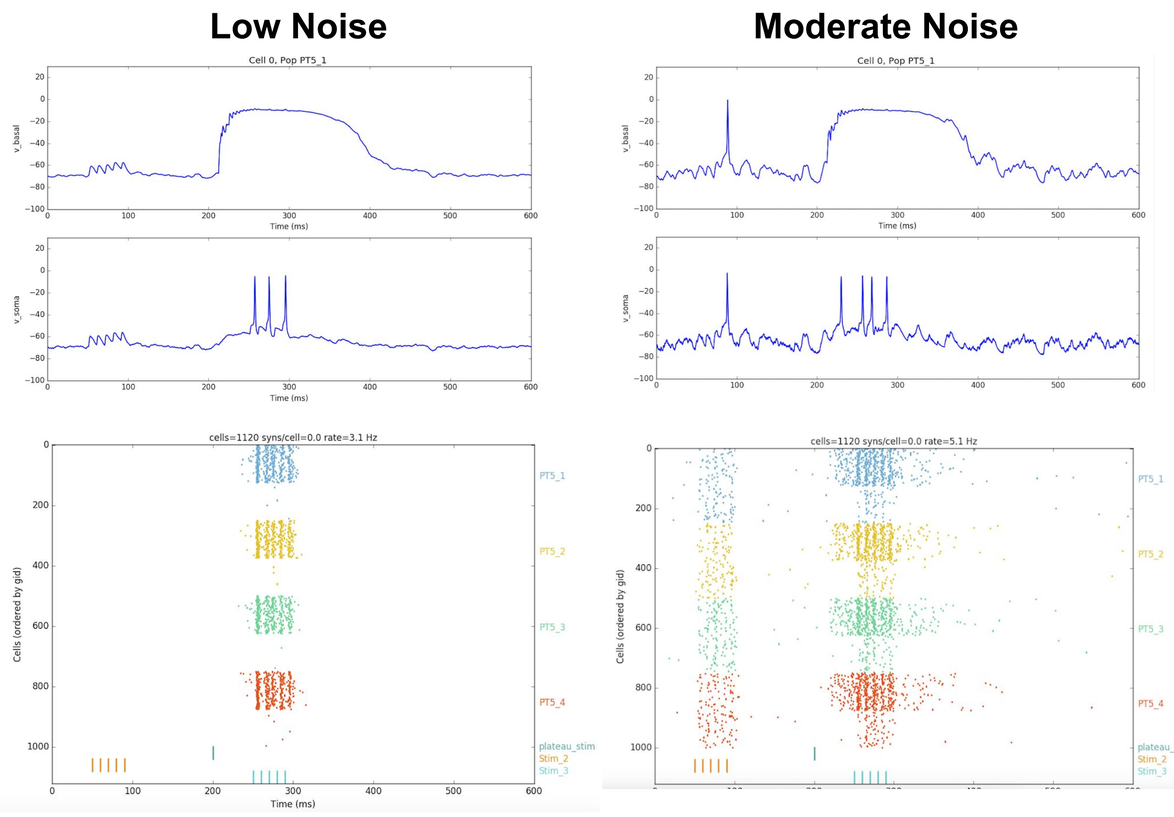
During plateau:

- Membrane time constant becomes faster
- Membrane potential is depolarized
- Post-synaptic responses are faster and larger



Dendritic plateaus increase network synchrony

- Simulated glutamate input at 200 ms
- Five excitatory synaptic inputs at 100 Hz into apical dendrite before and during plateau
- Inputs during plateau result in more network synchrony



Discussion

At the network level, this predicts that sets of cells with simultaneous plateaus would provide an activated ensemble of responsive cells with increased firing. Synchronously spiking subsets of these cells would then create an embedded ensemble. This embedded ensemble would demonstrate a temporal code, at the same time as the activated (embedding) ensemble showed rate coding.

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