Dynamics of storage and recall in associative memories

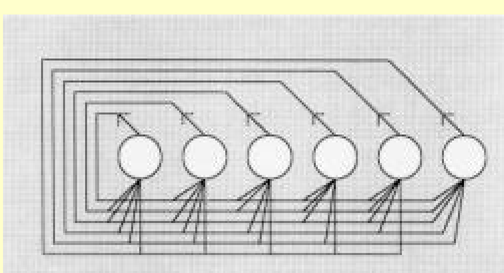
What can we learn from cortical control structures?

1. Single Cell Properties

Bruce Graham
Department of Computing Science & Mathematics
University of Stirling, Scotland, U.K.

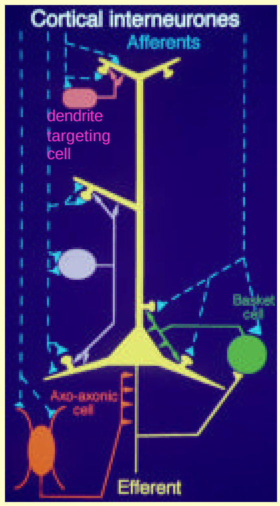
Associative Memory

- Content addressable

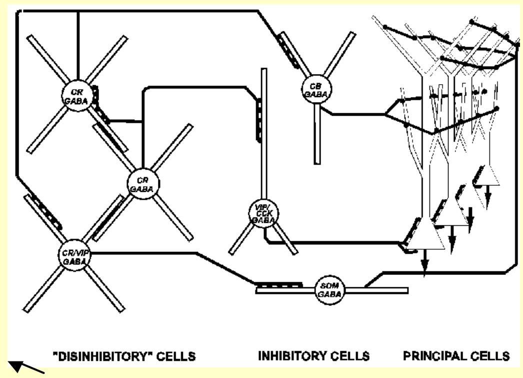


Hippocampal Microcircuit

Control synaptic excitatory input to cell



Control action potential output of cell

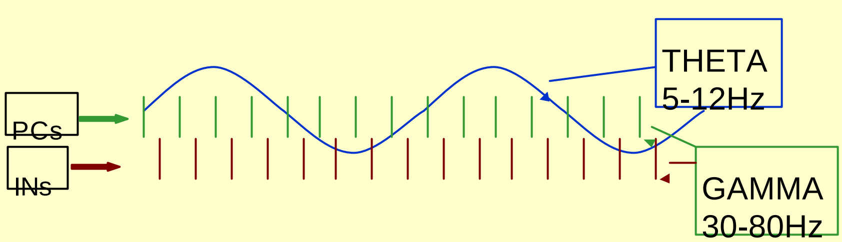


Control integration of synaptic inputs

Freund & Buzsaki , Hippocampus 6:347-470, 1996

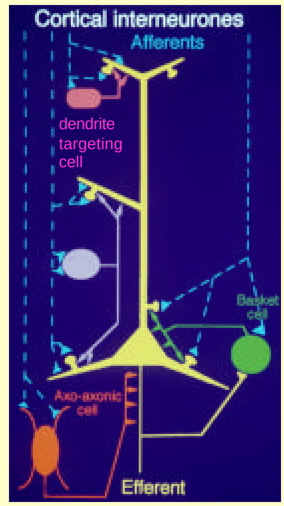
Dynamics of Operation

- Rhythms and animal behaviour
- Rhythms = clock cycles?
- Phasing of storage and recall
  - varying network plasticity over time



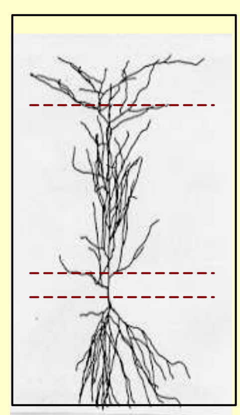
Components of the Microcircuit

- CA3 / CA1
- Pyramidal cells
  - excitatory
- Interneurons
  - inhibitory
  - various



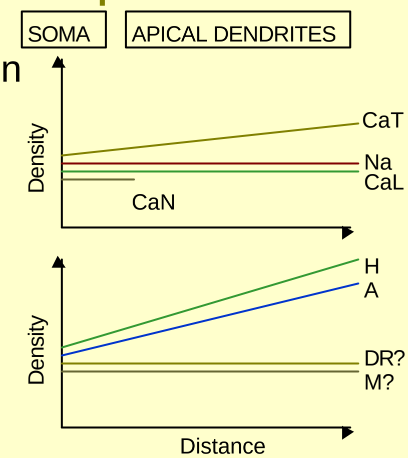
Pyramidal Cells - CA1

- Spatial segregation of inputs
- 2 major excitatory pathways
  - perforant path from EC
  - Schaffer collaterals from CA3
- Multiple sites of inhibition
  - perisomatic
  - proximal & distal dendrites
  - axon initial segment



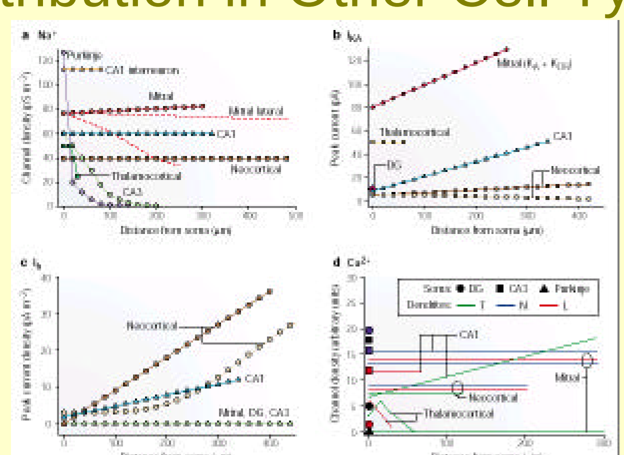
Intrinsic PC Properties

- Spatial distribution of ion channel types
- Na & Ca
  - fast Na, persistent Na
  - T, L & N type Ca
- K & mixed cation
  - DR, A, C, AHP, D
  - M, H



Migliore & Shepherd, Nature Rev. Neurosci 3:362-370, 2002

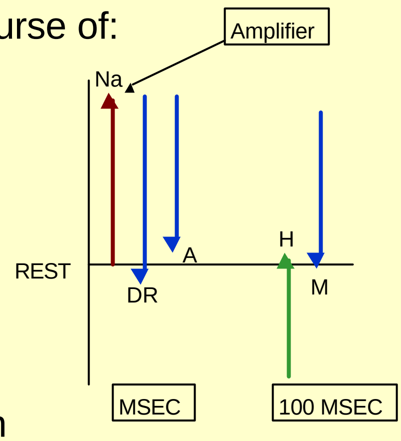
Distribution in Other Cell Types



Migliore & Shepherd, Nature Rev. Neurosci 3:362-370, 2002

Ion Channel Dynamics

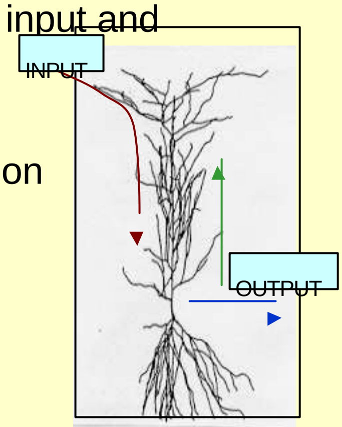
- Voltage range and time course of:
  - activation / deactivation
  - inactivation / reactivation
- Amplifiers
  - Na and Ca currents
- Suppressors
  - K and mixed cation
- EPSP / spike shaping
- Spike frequency adaptation



Borg-Graham, Cerebral Cortex vol 13, 1998

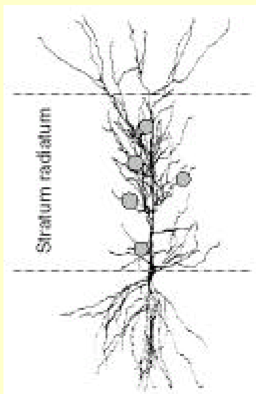
Signal Integration

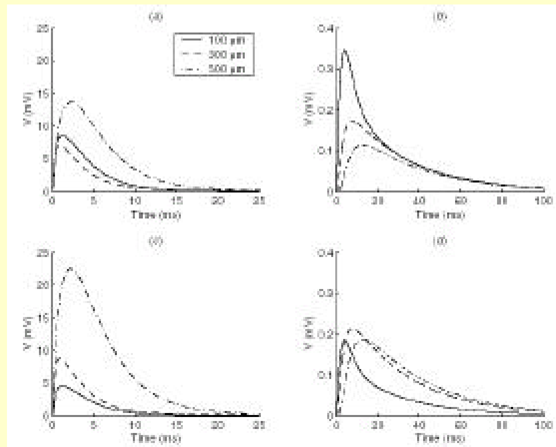
- Interactions between synaptic input and intrinsic cellular properties
- Synaptic scaling with distance
- Time course of signal integration
  - temporal summation
  - roles of A and H currents
- Linearity of summation
  - signal amplification
  - linear versus nonlinear



Synaptic Scaling

- Strength of AMPA synapses may increase with distance from soma



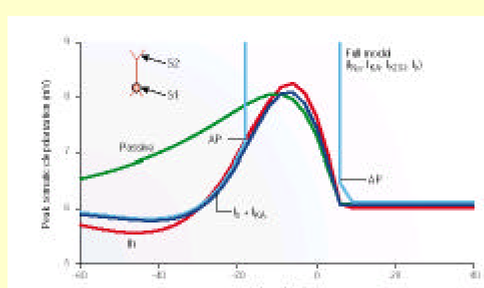


Magee & Cook, Nature Neurosci 3:895-903, 2000

Figures from Graham, 2001

Integration of Two Pathways

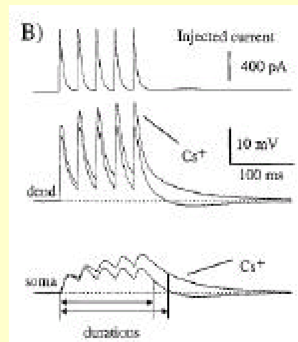
- 20msec integration window
- Roles for A and H currents
  - high densities in distal dendrites
  - rapid activation of A
  - deactivation of H



Migliore, J. Comput Neuro. 14:185-192, 2003

Temporal Summation

- Role for H current
  - high density in distal dendrites
  - deactivation shortens time course of distal EPSPs
- Equal temporal summation of proximal and distal inputs

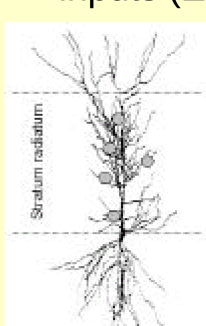


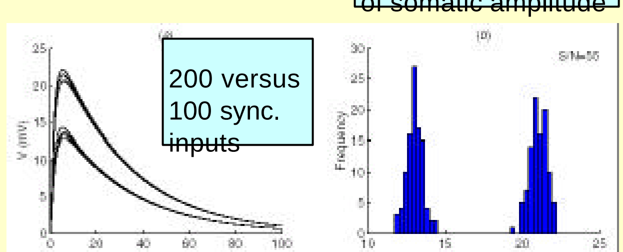
Magee, J. Neurosci 18:7613-7624, 1998 and Nature Neurosci 2:508-514, 1999

Signal Amplification

- Nonlinear summation of inputs
  - roles of NMDA, persistent Na and Ca currents
- Can a neuron *count* the number of active inputs (EPSPs)?

Signal-to-noise ratio of somatic amplitude

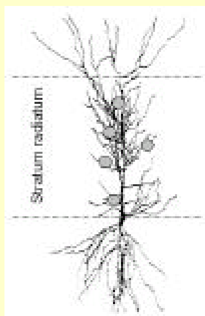




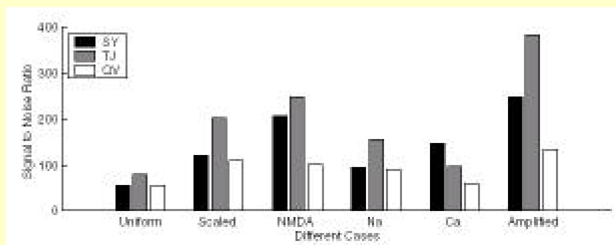
Graham, Network: Comput. Neural Syst. 12:473-492, 2001

Signal Amplification (2)

- Inputs:
  - SY: synchronous
  - TJ: asynchronous over 20msecs
  - QV: quantal variance of 30%



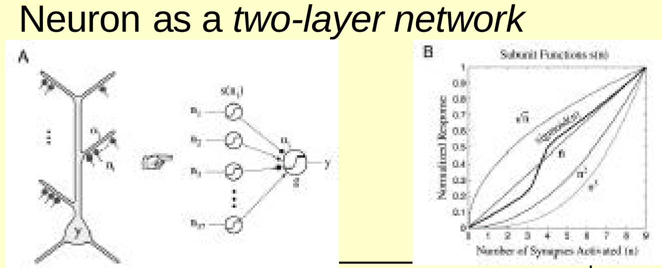
- Amplification:
  - synaptic AMPA scaling
  - AMPA / NMDA synapses
  - uniform persistent NA
  - uniform LVA T-type Ca



Graham, Network: Comput. Neural Syst. 12:473-492, 2001

Spatial Integration

- Spatial interactions of inputs
  - linear summation of spatially separate inputs
    - rectification by A current
  - nonlinear interaction of nearby inputs
    - amplification by NMDA, Na and Ca currents
- Neuron as a *two-layer network*



Poirazi et al, Neuron 37:977-987 & 989-999, 2003

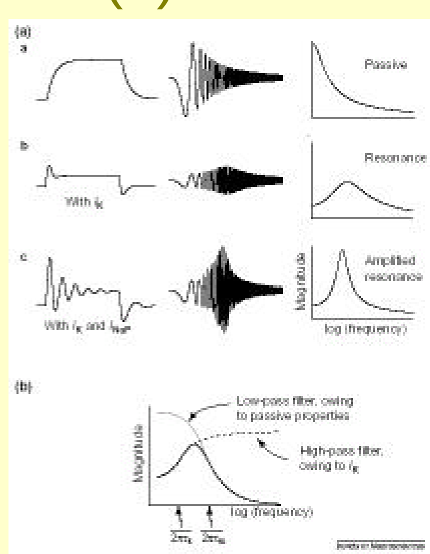
Resonance

- Dynamics of membrane and ion channels causes resonance
  - Membrane leak conductance and capacitance provides low-pass filtering
  - Slowly activating ion channels that oppose membrane potential changes provide high-pass filtering
  - Fast activating channels that boost membrane potential changes act as amplifiers
- Intrinsic subthreshold oscillations
- Band-pass filtering of inputs

Resonance (2)

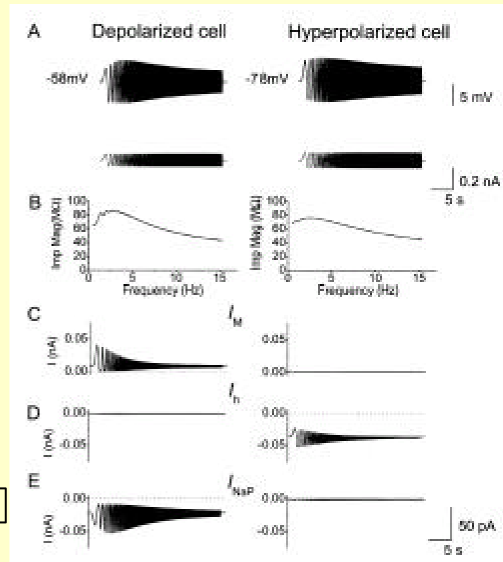
- High pass filters
  - *slow* ion channels that activate when membrane potential moves *away* from their reversal potential
- Amplifiers
  - *fast* ion channels that activate when potential moves *towards* from their reversal potential

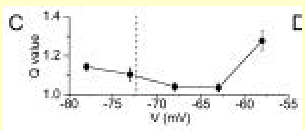
~~*Hutcheon & Yarom, TINS 23:216-222, 2000*~~



Resonance in PCs

- Resonate at theta frequencies (7Hz)
- Roles for H, M and persistent Na

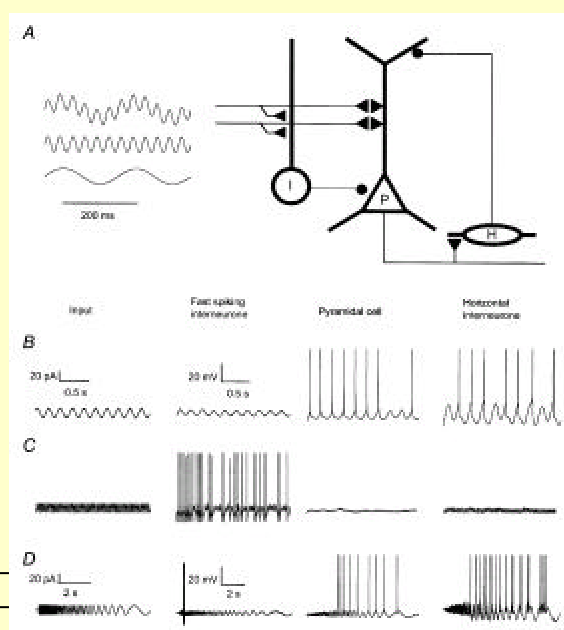




Hu et al, J. Physiol. 545:783-805, 2002

Resonance in INs

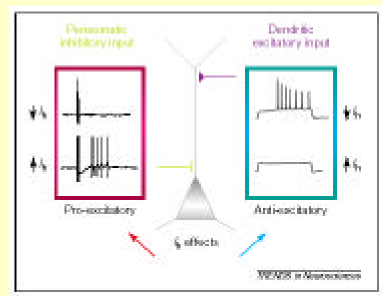
- Different neuronal types resonate at different frequencies
  - PCs and horizontal INs at theta (1-10Hz)
  - fast spiking INs at beta-gamma (10-50Hz)
    - role for fast Na?



Pike et al, J. Physiol. 529:205-213, 2000

Multiple Roles for H current

- Depolarising deactivation shortens time course of distal EPSPs
- Hyperpolarising activation can lead to rebound excitation
  - interaction of inhibition and H current
  - rhythmic inhibition can phase PC firing

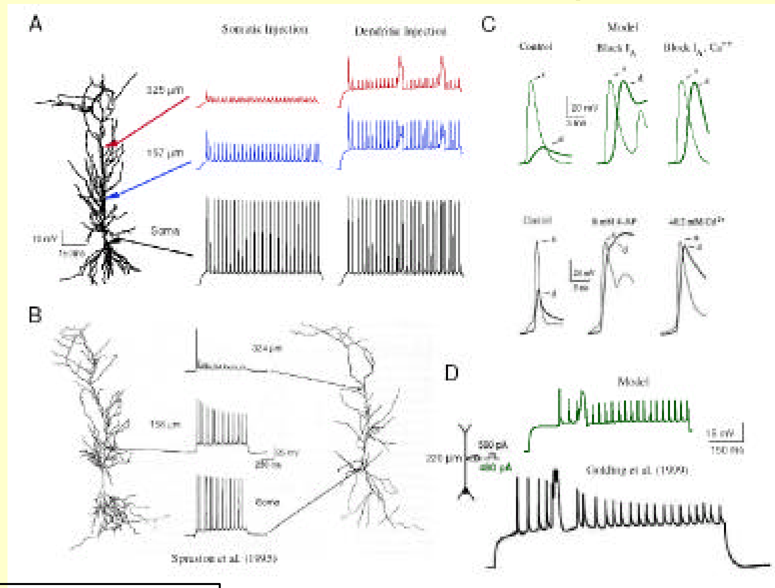


Santoro & Baram, TINS 26:550-554, 2003
Cobb et al, Nature 378:75-78, 1995

Internal Signals

- Synaptic input interacting with intracellular properties determines internal PC signals
  - as well as PC output
- Internal signals within dendritic tree:
  - calcium spikes
  - back-propagating action potentials (BPAPS)
- Roles in synaptic plasticity
  - spike timing dependent plasticity

BPAPs and Calcium Spikes



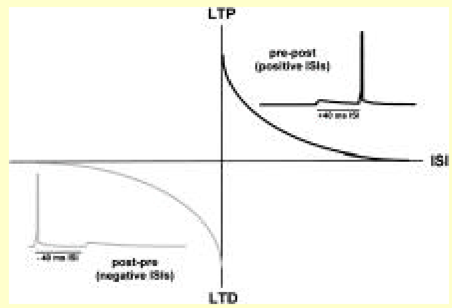
Poirazi et al, Neuron, 2003

Control of BPAPs

- Potassium A current attenuates BPAPs in distal dendrites
  - increasing density of A channels with distance
- BPAP amplitude increased by anything that reduces A current
  - preceding depolarising synaptic activity
  - suppression by neuromodulators e.g. Ach
- Large amplitude BPAPs may lead to slow calcium spikes

Spike Timing Dependent Plasticity

- Relative timing of pre- and postsynaptic activity determines plasticity
  - Post before Pre = LTD
  - Pre before Post = LTP
- Presynaptic spike time
- Postsynaptic signal?
  - Axonal spike / burst
  - BPAP
  - Calcium level



Karmarkar & Buonomano, J. Neurophysiol. 88:507-513, 2002

Postsynaptic Activity and Plasticity

- LTP / LTD determined by level of Ca
- Postsynaptic depolarisation
  - Ca entry through NMDA and voltage-gated channels
- LTP is possible with the following:
  - single somatic/axonal spike leading to BPAP
    - tight timing constraints relative to presynaptic input
  - burst of somatic/axonal spikes
  - dendritic spike only

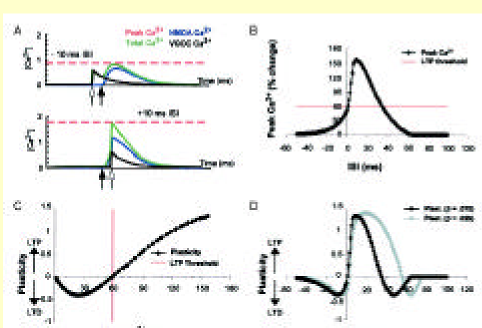
STDP Models 1&2

- Model 1
  - interaction of synaptic input and BPAPS
    - BPAPs with slow ADP
  - calcium entry through NMDA channels and voltage-gated channels
  - plasticity determined by peak combined Ca
- Model 2
  - peak NMDA Ca determines LTP
  - mGluR activity due to voltage-gated Ca determines LTD

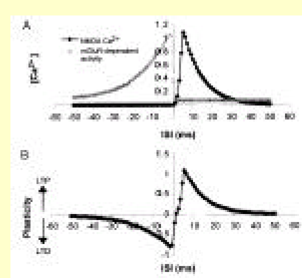
Karmarkar & Buonomano, J. Neurophysiol. 88:507-513, 2002

STDP Models 1&2 - Results

Model 1



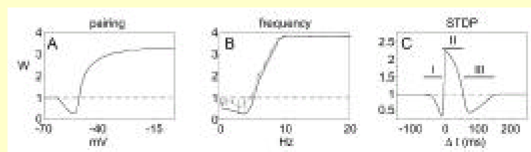
Model 2



Karmarkar & Buonomano, J. Neurophysiol. 88:507-513, 2002

STDP Model 3

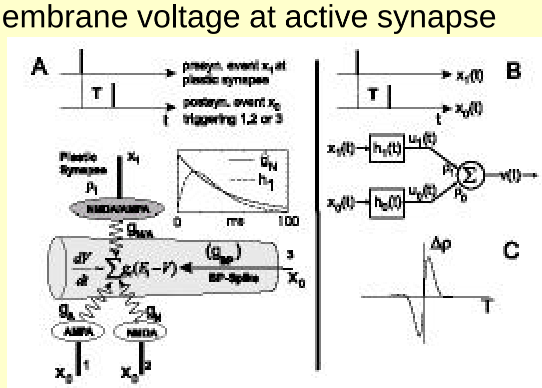
- Model 3
  - interaction of synaptic input and BPAPS
    - BPAPs with slow ADP
  - calcium entry through NMDA channels only
  - plasticity determined by continuous calcium concentration
  - learning rate varies with Ca



Shouval et al, PNAS 99:10831-10836, 2002

STDP Model 4

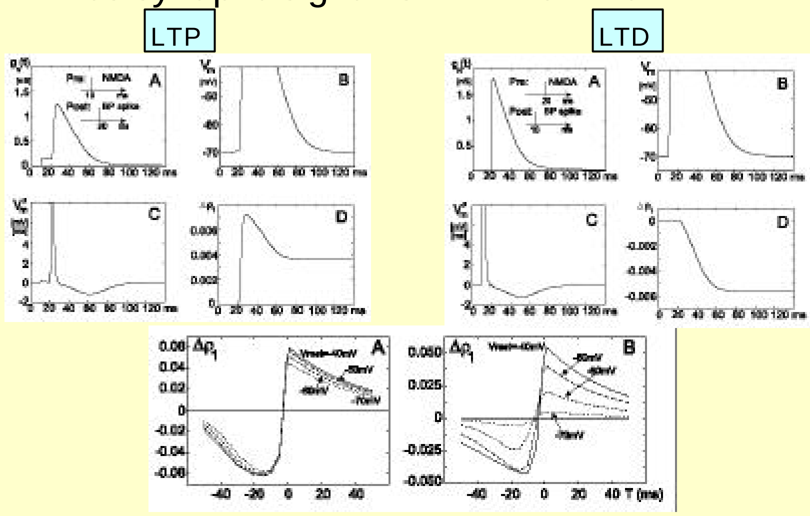
- Model 4
  - plasticity determined by rate of change of membrane voltage at active synapse



Saudargiene et al, Neural Computation, 2003

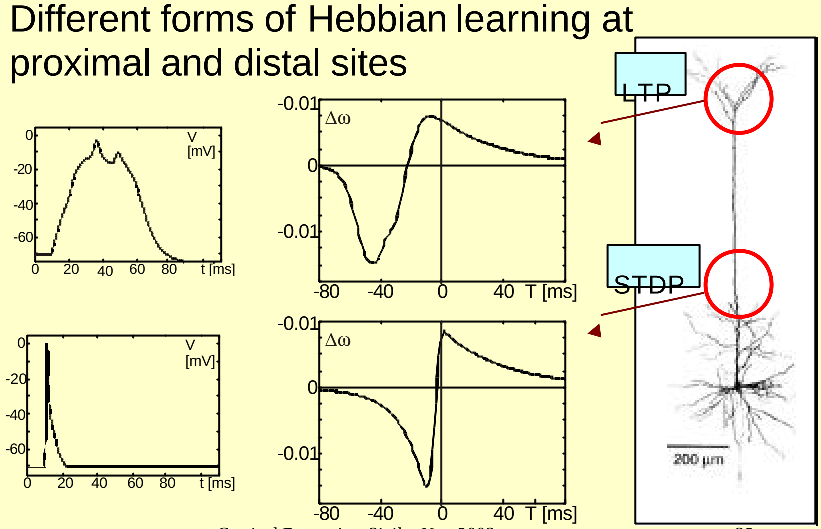
STDP Model 4 - Results

- Postsynaptic signal is BPAP or 2nd NMDA



STDP Model 4 - Results (2)

- Different forms of Hebbian learning at proximal and distal sites



Metaplasticity

- *Plasticity:* relationship between pre- and postsynaptic activity and synaptic LTP/LTD
- *Metaplasticity*: altering this relationship so that same activity levels result in different synaptic weight changes
  - relationship between activity and Ca levels
  - relationship between Ca and LTP / LTD

Abraham et al, PNAS, 98:10924-10929, 2001
Castellani et al, PNAS, 98:12772-12777, 2001

Summary

- Neurons are dynamic devices
- Integration of inputs from multiple synaptic pathways interacting with complex intrinsic cellular dynamics determines
  - PC output
  - synaptic plasticity
- Inhibition is not as simple as it sounds
  - disinhibition
  - rebound excitation