McCormick Lab













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The Holistic (Integrated) Neuron and Network



Rapid Dynamic States of the Cortex:

Attention and Working Memory

Cortical UP and DOWN States during SWS



Selective Attention



Cortical Persistent Activity









Slow Wave Sleep is Associated with a Slow Oscillation in Cortical Networks





Steriade et al., 2001 . J. Neurophysiol. 85, 1969-1985

Slow Oscillation in vivo - Prefrontal Cortex



UP state reversal potential is steady throughout

Average currents during the UP states

Reversal potential during the UP state





Conclusions II: The Cortex Operates Through a Balance of Excitatory and Inhibitory Conductances

Balance of Gi and Ge over time

Balance of Gi and Ge (group data)



High frequency fluctuations permit precise, repeatable spike timing





Inhibition carries high-frequency fluctuations during recurrent network activity





Synchronous barrages of inhibition in nearby pyramidal neurons *in vivo*



Synchrony between gamma-band network oscillations and spiking



Conclusions I: Activated States of the Cortex are Associated with Generation of Higher Frequencies by Inhibitory Networks, Which Give Rise To Precise Spike Timing





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





Somatic and Dendritic Recording



Apical dendrite



UP States Result in Barrages of PSPs in the Apical Dendrite and Soma



The General Pattern of Synaptic Activity is Broadly Distributed in the Dendrites

Overlay of UP states



Ratio of UP state area (d/s)



Distance from soma (µm)

Ratio =

Dendritic UP State Somatic UP State

X 100

Subthreshold synaptic potential travels on axon



The Axon Exhibits a Long Length Constant During Synaptic Activity



Cortical Pyramidal Cells Typically Exhibit a High Density of Local Synaptic Connections



Binzegger T, Douglas RJ, Martin KA. Axons in cat visual cortex are topologically self-similar. Cereb Cortex. 2005 15(2):152-65. 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



A significant number of boutons are located near the soma





Recording Connected Pairs of Pyramidal Cells



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!





The Modulation of EPSP Amplitude by Presynaptic Somatic Vm Requires > 1 Second to Develop and Dissipate



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



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



First Demonstration of Membrane Potential Effects on Evoked Release













What are the Cellular Mechanisms of the Facilitatory Effect?

Is there a role for axonal conduction failures?



Huguenard, John R. (2000) Proc. Natl. Acad. Sci. USA 97, 9349-9350

Imaging Experiments Typically Reveal that Axonal Propagation in Cortical Networks is Highly Reliable

Koester and Sakmann J. Physiol. 529: 625



Calyx of Held Preparation for Presynaptic Recording



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)

Calcium Levels and Facilitation Rise and Fall Slowly in the Calyx of Held Presynaptic Terminal



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

(room temperature)

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)



Action Potential Duration in the Axon is Slowly Affected by Membrane Potential in the Soma



a effect of Vm on somatic and axonal action potential







В

4-AP 40 μM

have a second and

E α -dendrotoxin 100 nM







Conclusion: Although the Cell (and Network) has Distinct Parts, These Often Work Together, not Apart. The neuron and network operate in a more "Holistic" manner than is often emphasized. Also: Information transmission in the brain is a mix of "analog" and "digital"!



Computing with Axons?

Cortical Axons contain High Densities of Na+ and K+ currents (Transient Na+ Low threshold K+ A-current D-current Ca2+ - activated K+ Na+ activated K+ H-current M-current)



Inda et al., PNAS 103: 2920 (2006)

KCNQ2 in Rat Cortex



Devauex et al., J. Neurosci. 24: 1236 (2004).

The Holistic Neuron and Network

