# Intrinsic neuron firing properties, rhythms and intrinsic plasticity

8 September, 2016

# Outline

- Cortical neuron firing patterns
- Computational implications
- Diverse ion currents
- Thalamic neurons and rhythms
- Intrinsic plasticity

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# Recording cortical neurons *in vitro*

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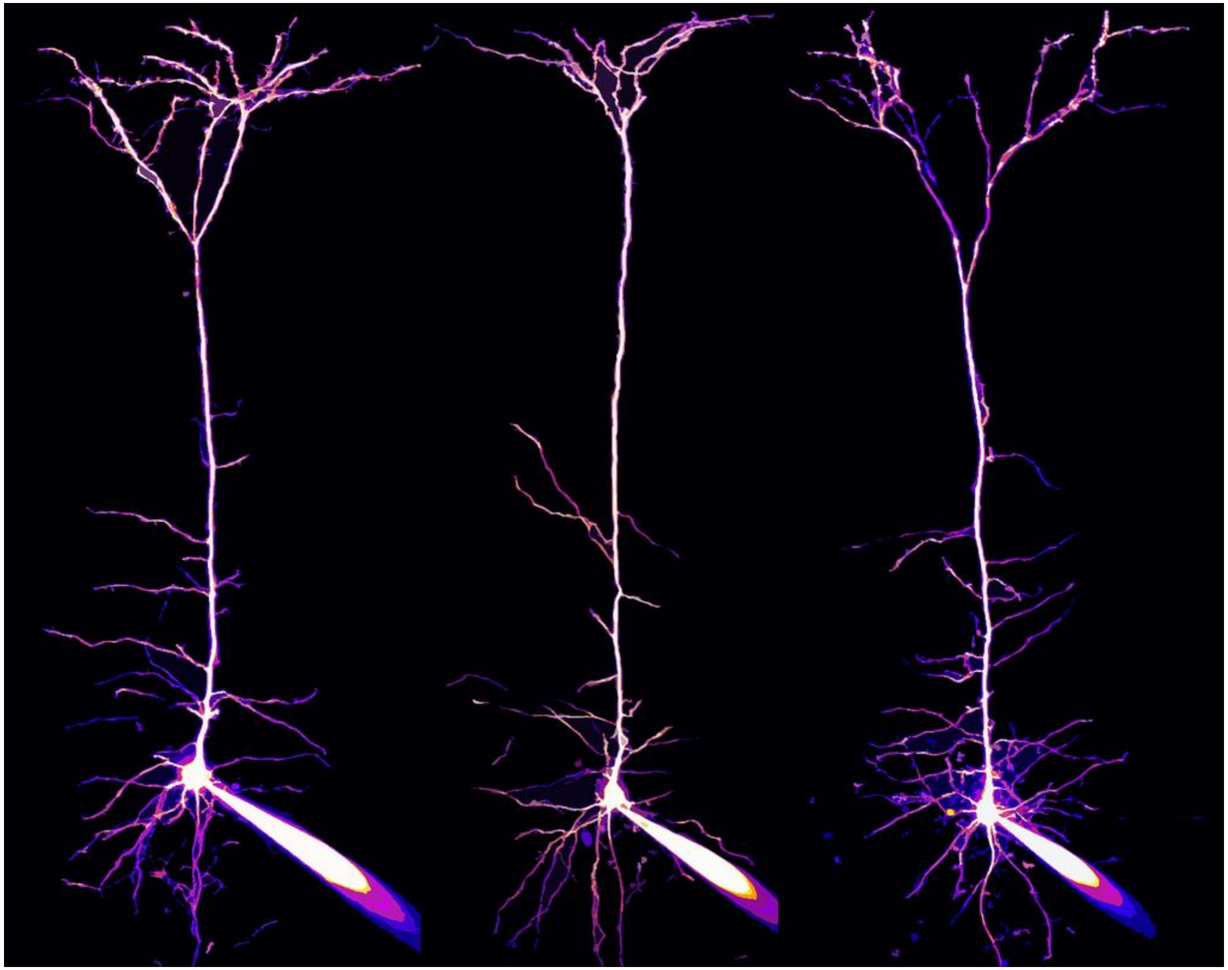
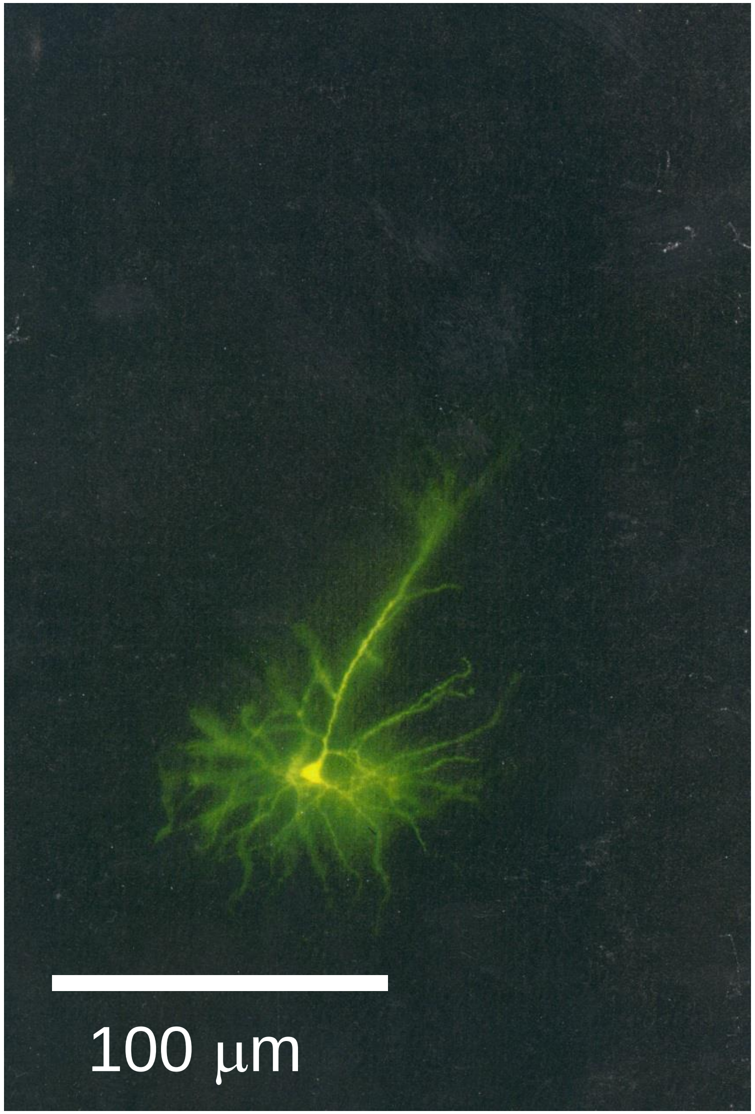
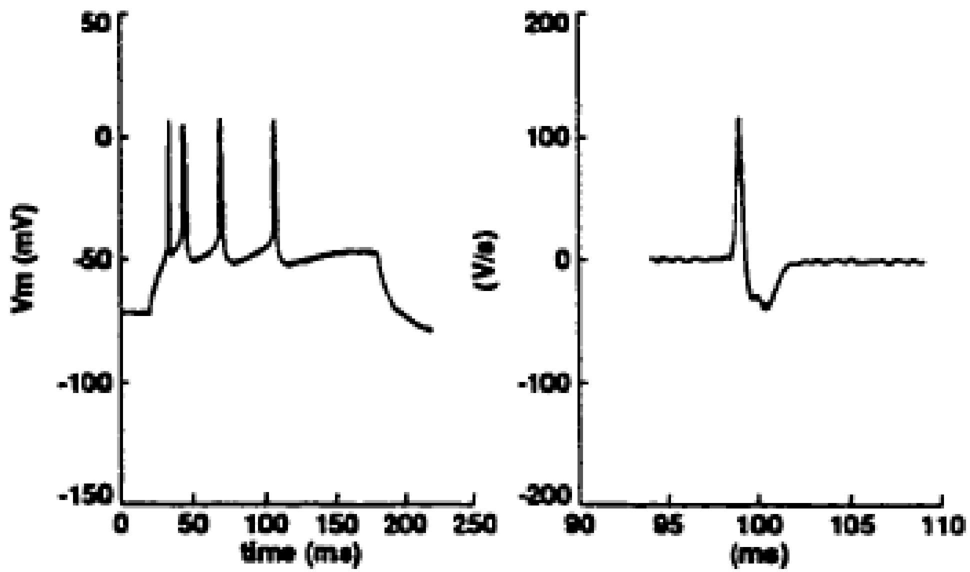
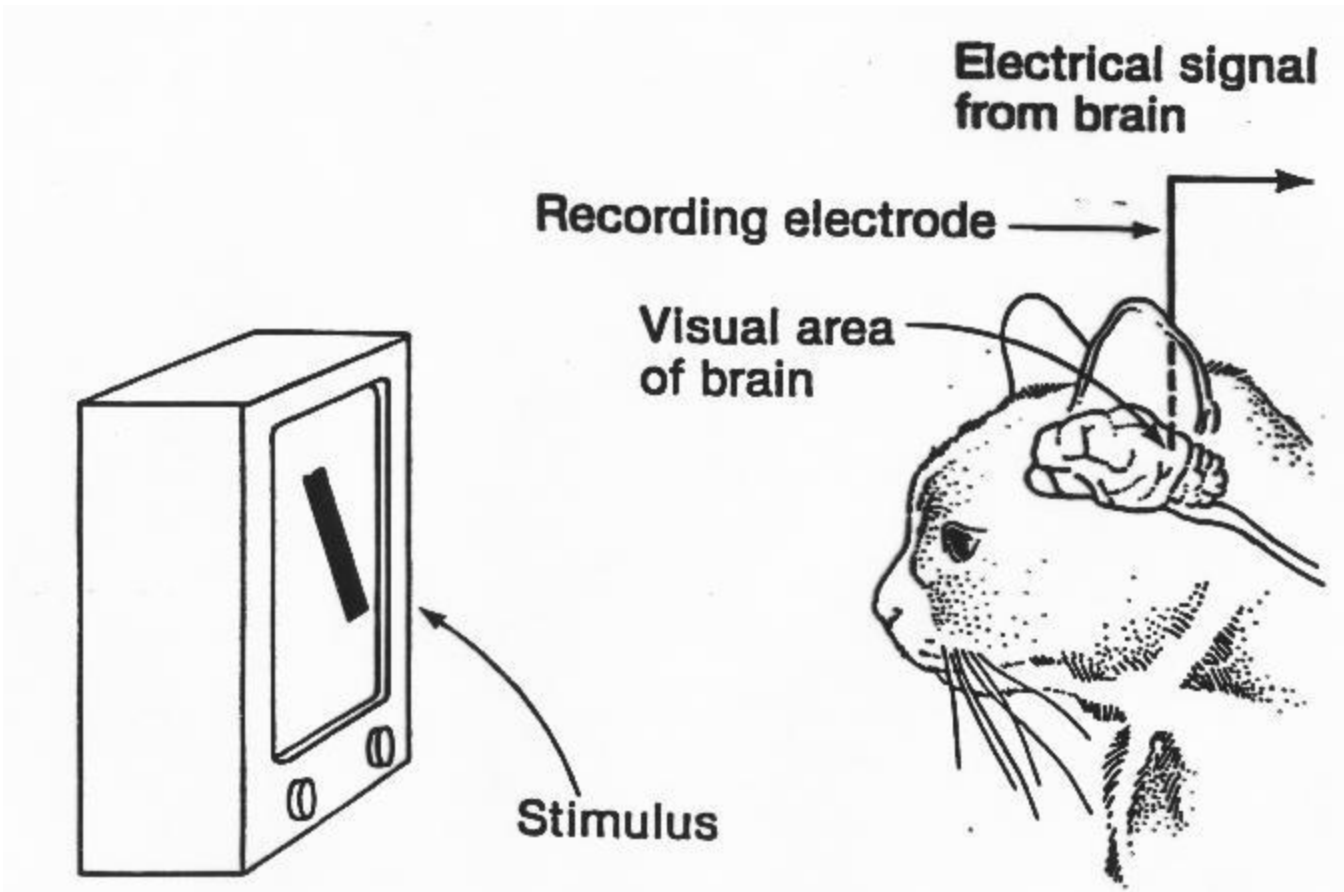


# Regular spiking cell (RS)



# Recording cortical neurons *in vivo*



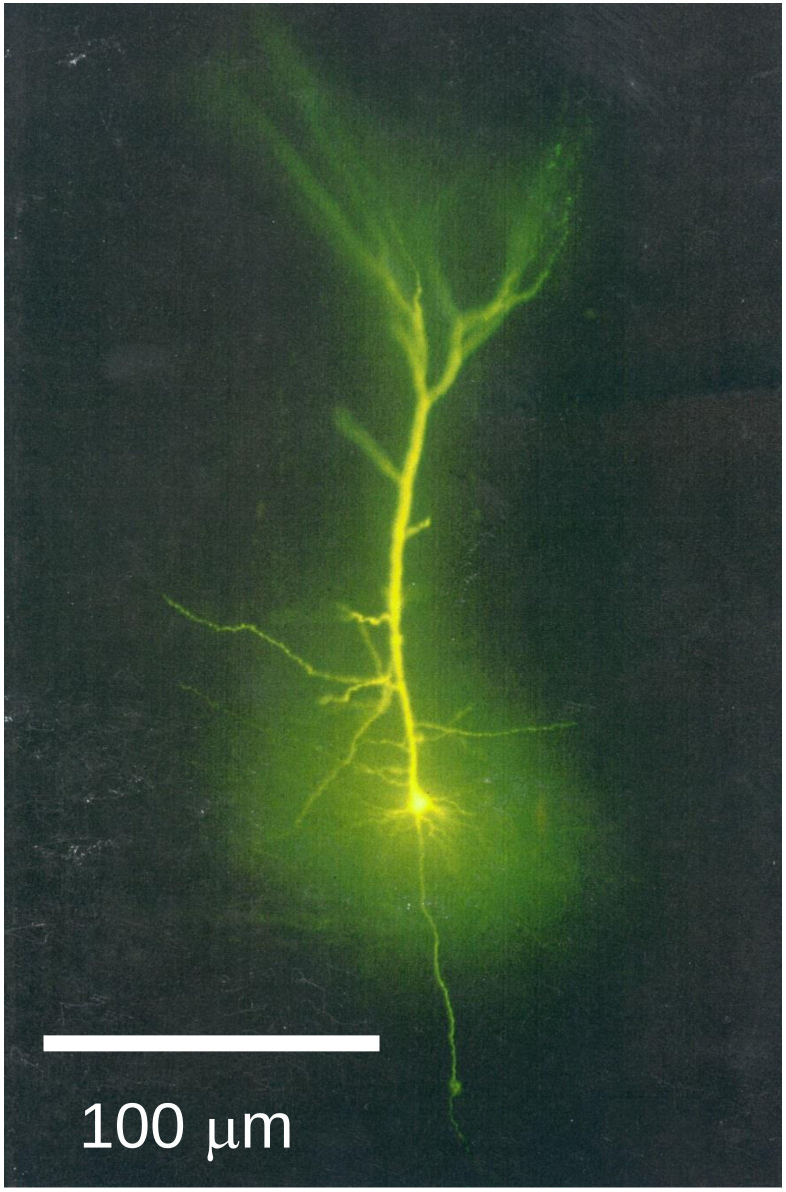
# Movies of RS cell

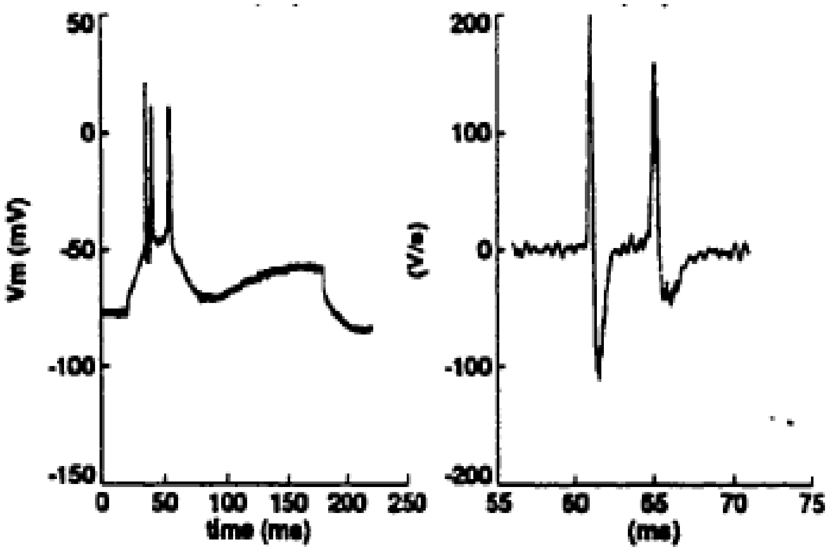
- To current pulses:

- To visual stimulation:

- http://medicine.yale.edu/lab/mccormick/movies/corticalneurons.aspx

# Intrinsically bursting cell (IB)



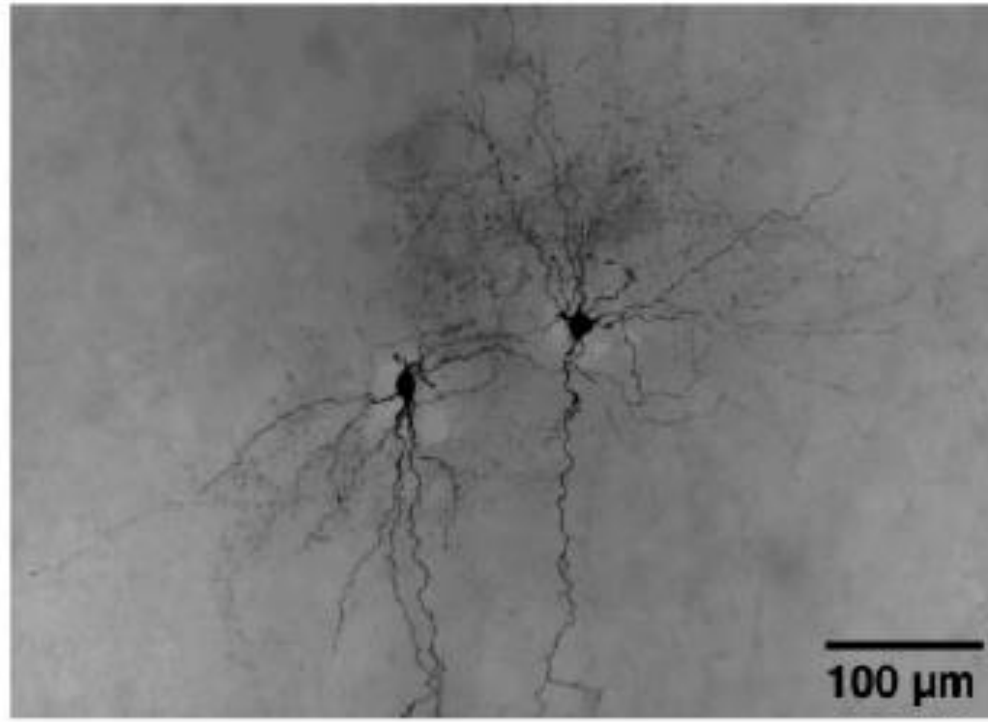
# Movies of IB cell

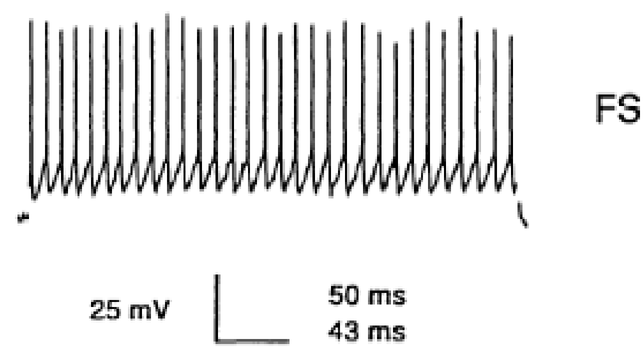
- To current pulse:

- To visual stimulation:

- http://medicine.yale.edu/lab/mccormick/movies/corticalneurons.aspx

# Fast spiking cell (FS)



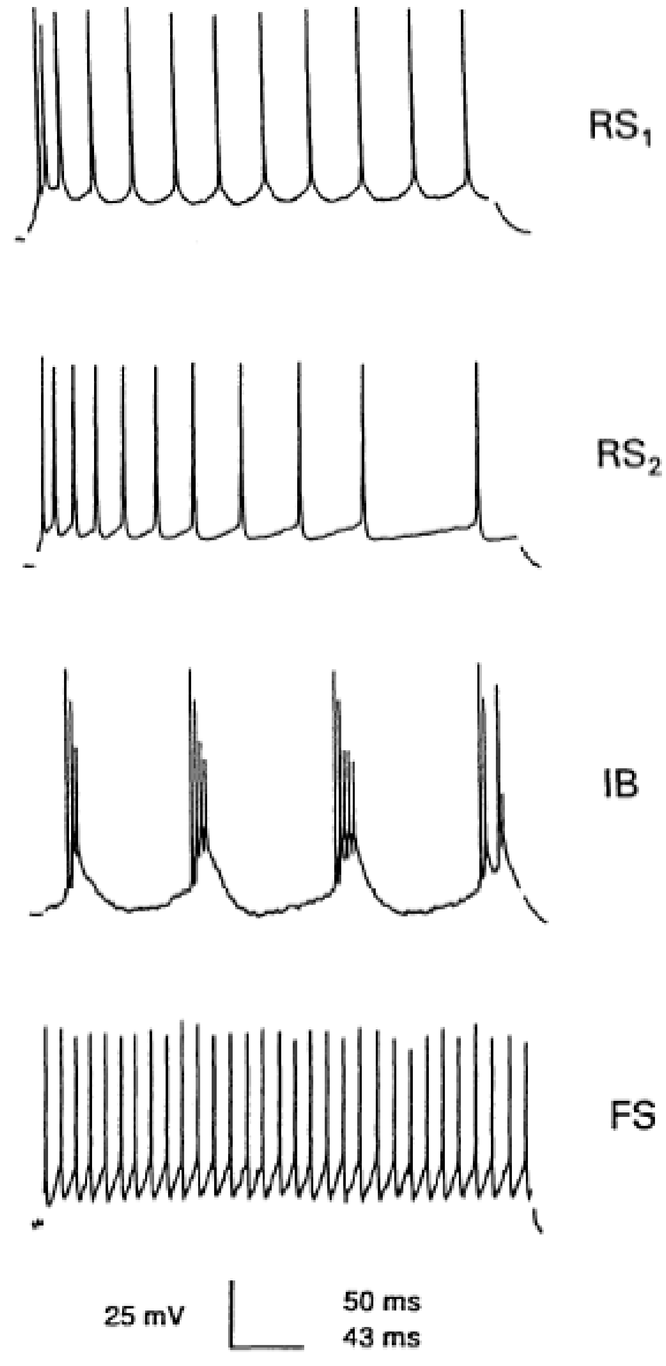
# Movies of FS cell

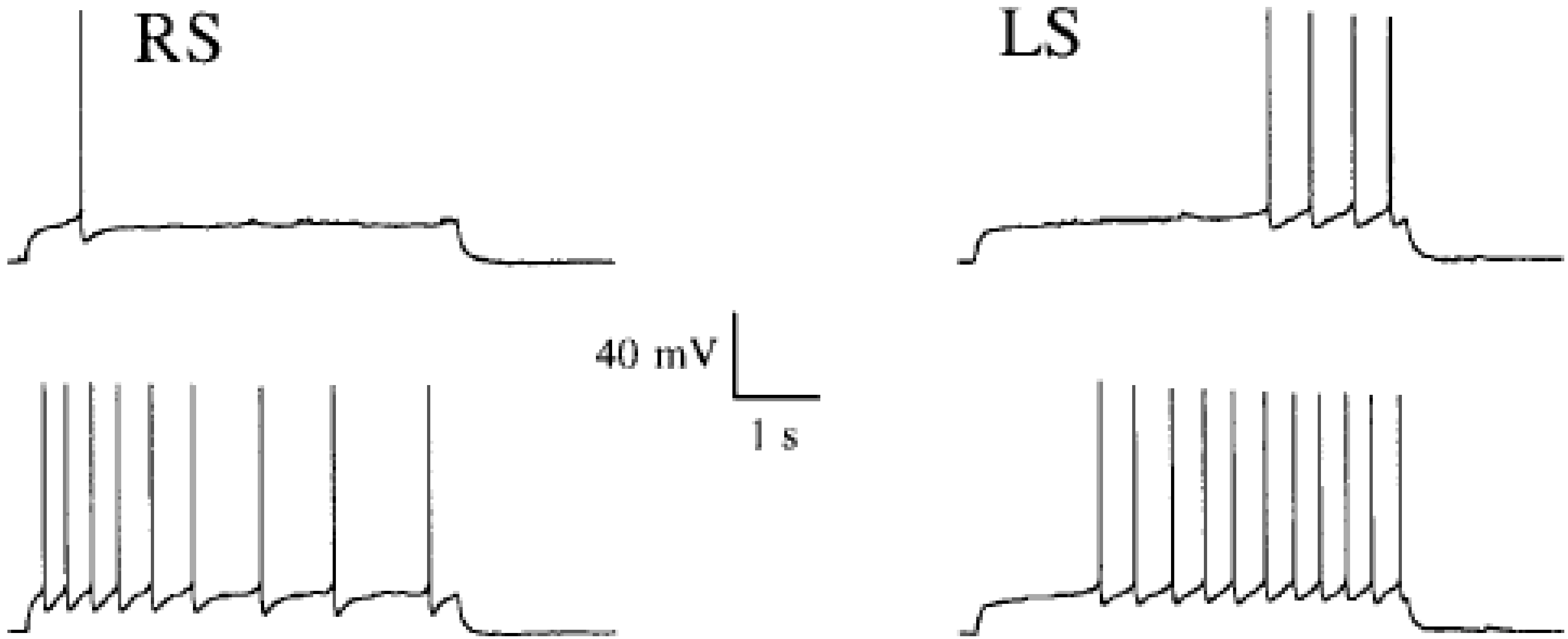
- To current pulse:

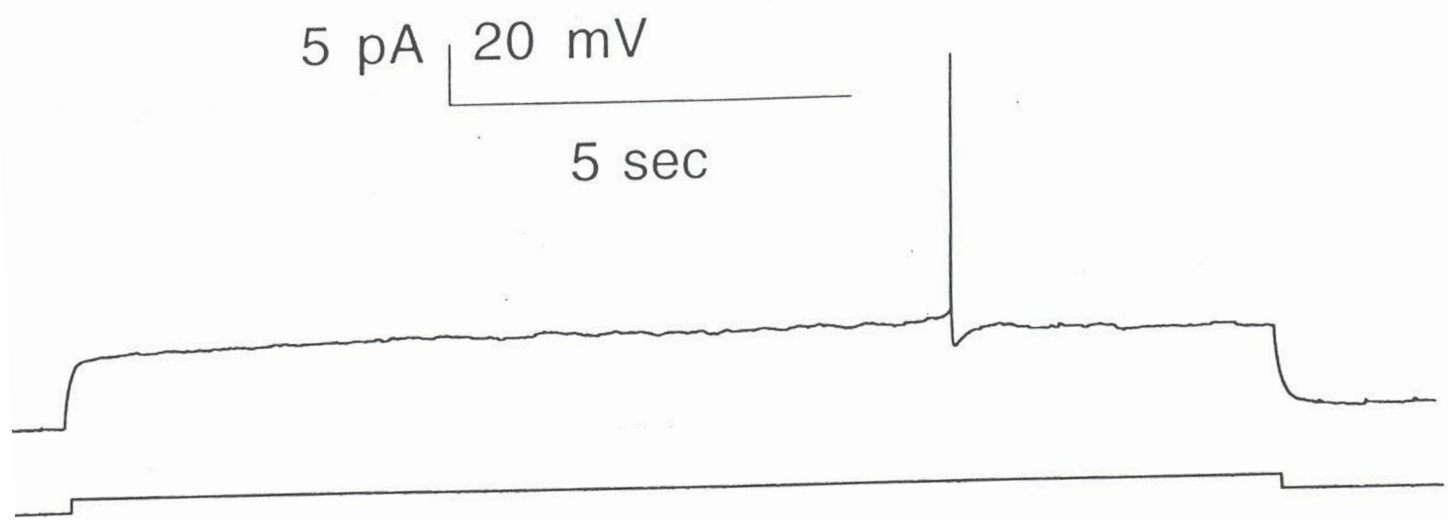
- To visual stimuli:

- http://medicine.yale.edu/lab/mccormick/movies/corticalneurons.aspx

# Cortical neuron firing patterns




RS
LS
40 mV
1 s


5 pA
20 mV
5 sec

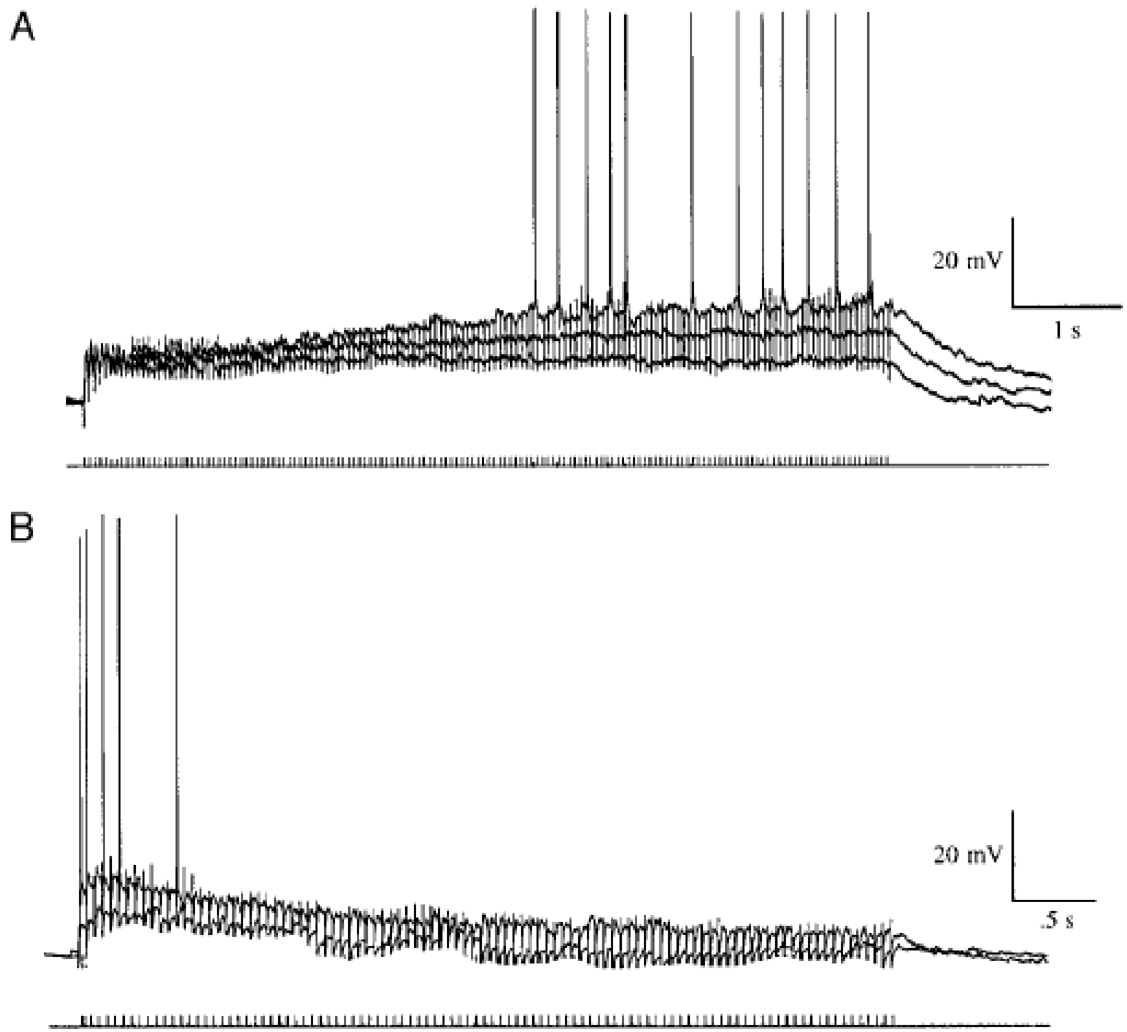



FIG. 2. Responses of LS and RS neurons to synaptic trains produced by electrical stimulation of layer I afferents. *A*: delayed response of an LS neuron to synaptic stimulation. Three different strengths of repetitive synaptic stimulation (150 pulses at 20 Hz; 7.5 s) are shown, one of which was just above spike threshold. Notice the long delay (>4 s) before the cell fired its first action potential and that once it began the cell continued firing for the duration of the synaptic train. *B*: typical RS neuron that quickly reached threshold and rapidly accommodated during the synaptic stimulation (100 pulses at 20 Hz; 5 s).

# Chattering cells?

**Chattering Cells: Superficial Pyramidal Neurons Contributing to the Generation of Synchronous Oscillations in the Visual Cortex**

Charles M. Gray and David A. McCormick

SCIENCE • VOL. 274 • 4 OCTOBER 1996

http://medicine.yale.edu/lab/mccormick/movies/corticalneurons.aspx

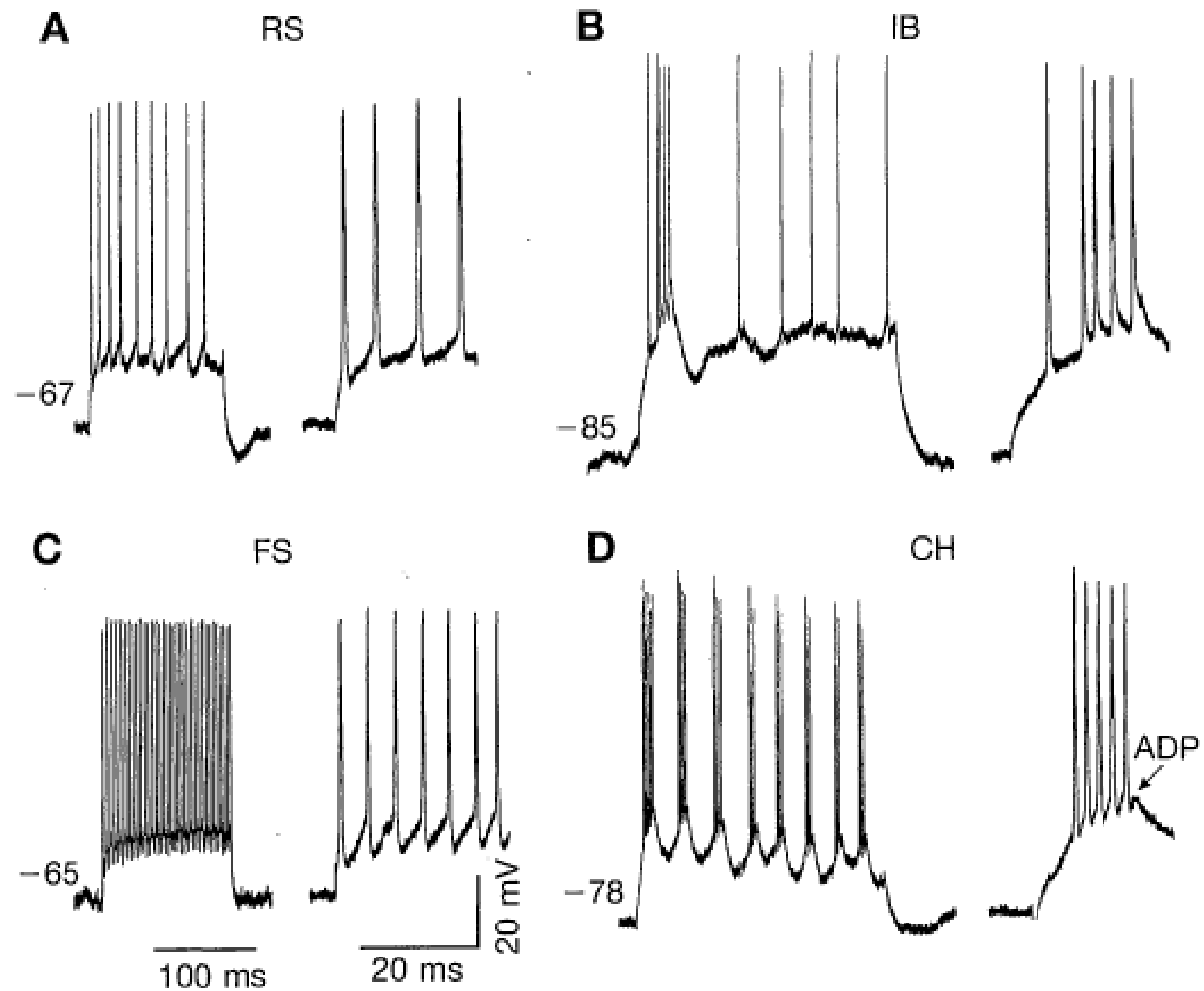



**Fig. 1.** Responses of the four cell classes to intracellular depolarizing current injection. The initial phase of the response is displayed on a faster time scale to the right. (**A**) RS pyramidal cell in layer VI. (**B**) IB pyramidal cell in layer V. (**C**) FS cell. (**D**) CH cell in layer III. Note the switch from burst to tonic firing with depolarization in the IB neuron (B), the high-frequency train of action potentials in the FS neuron (C), and the repetitive burst discharges in the CH neuron (D). Action potentials in the CH neuron are associated with the generation of an ADP. The current intensities were 0.6 nA for the RS and FS cells and 0.9 nA for the IB and CH cells. The RS, IB, and CH neurons were all recorded and labeled in the same animal. The data presented in Figs. 2 through 5 are from different cells recorded in six different animals. The data for this and additional figures are available at http://info.med.yale.edu/neurobio/mccormick/mccormick.

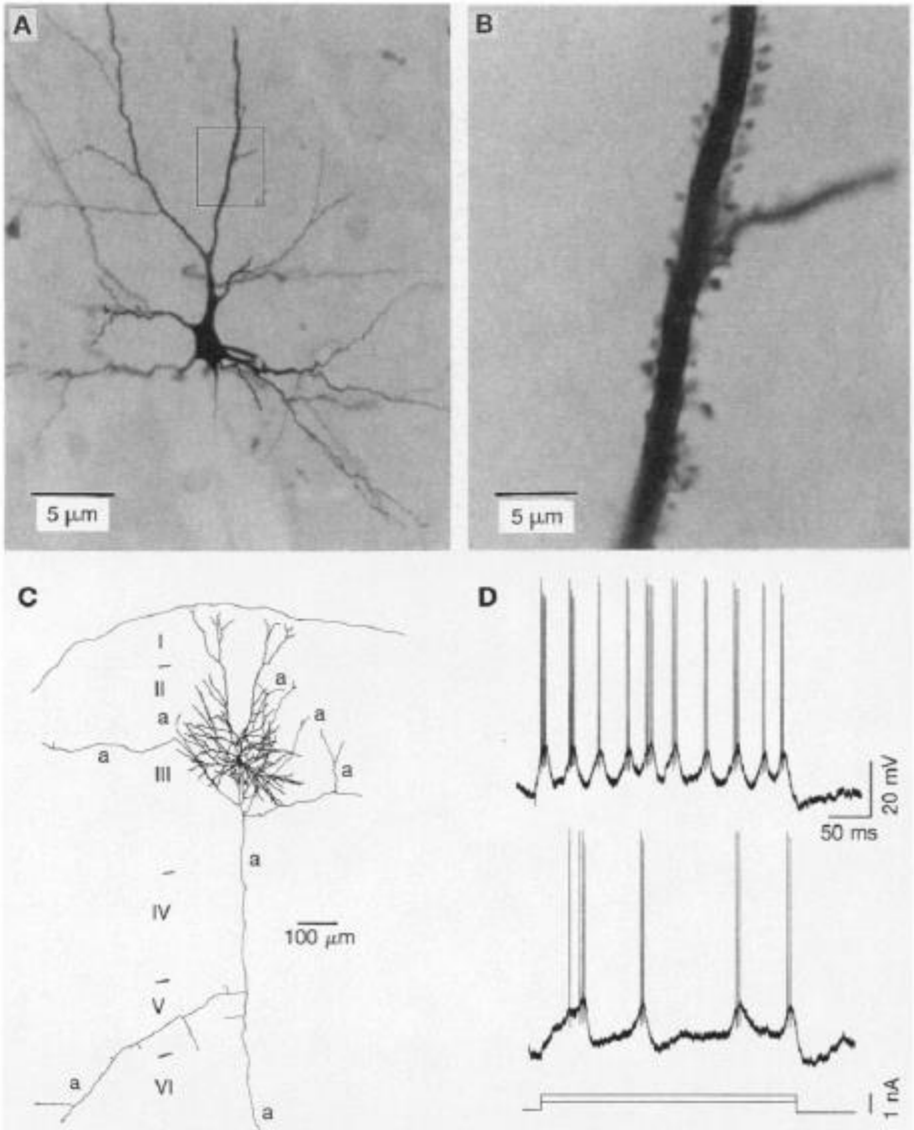



**Fig. 5.** Example of a labeled CH cell having spiny pyramidal morphology, with its soma located in layer III. (**A**) Low-power light field micrograph showing that the filled cell has morphological features that are characteristic of superficial pyramidal neurons. (**B**) High-power micrograph of apical dendritic region outlined by the rectangle in (A). There is a high density of dendritic spines. (**C**) Camera lucida reconstruction of the cell. The dendrites and axon are indicated by the thick and thin lines, respectively. The cortical layers are indicated by the roman numerals I through VI. The axon branches and sends out collaterals in layers II, III, and V. Local axon collaterals are indicated by the letter a. The axon also projects into the white matter (not shown). (**D**) Responses of the cell to two different levels of intracellular depolarizing current pulses. In both traces, the cell exhibits high-frequency bursts of action potentials that are characteristic of CH cells. The pattern of burst firing is rhythmic when the cell is depolarized strongly. At lower levels of depolarization, the cell continues to burst, but in a temporally disorganized manner. There is no apparent evidence of an underlying subthreshold membrane potential oscillation in the lower trace.

# Outline

- Cortical neuron firing patterns
- **Computational implications**
- Diverse ion currents
- Thalamic neurons and rhythms
- Intrinsic plasticity

# Puzzle

- A spiking neuron receiving auditory input drives two cell types: RS and LS
- Which cell type will tell you when an auditory tone begins?
- Can you use RS and LS cells to measure how long the tone lasts?
- Can you build a circuit that will identify a particular frequency of input spikes, say 50  Hz?

What causes such different firing patterns?

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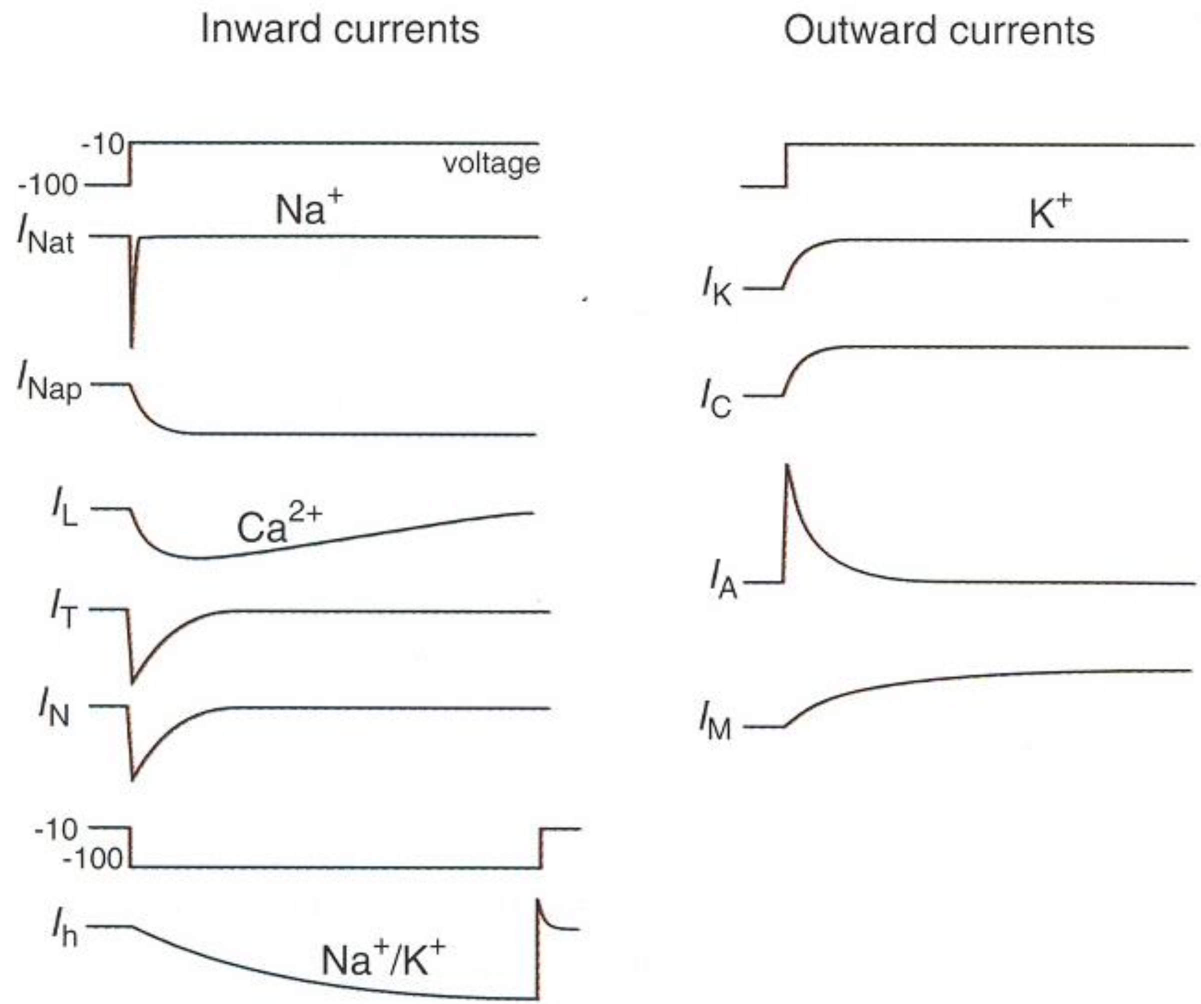
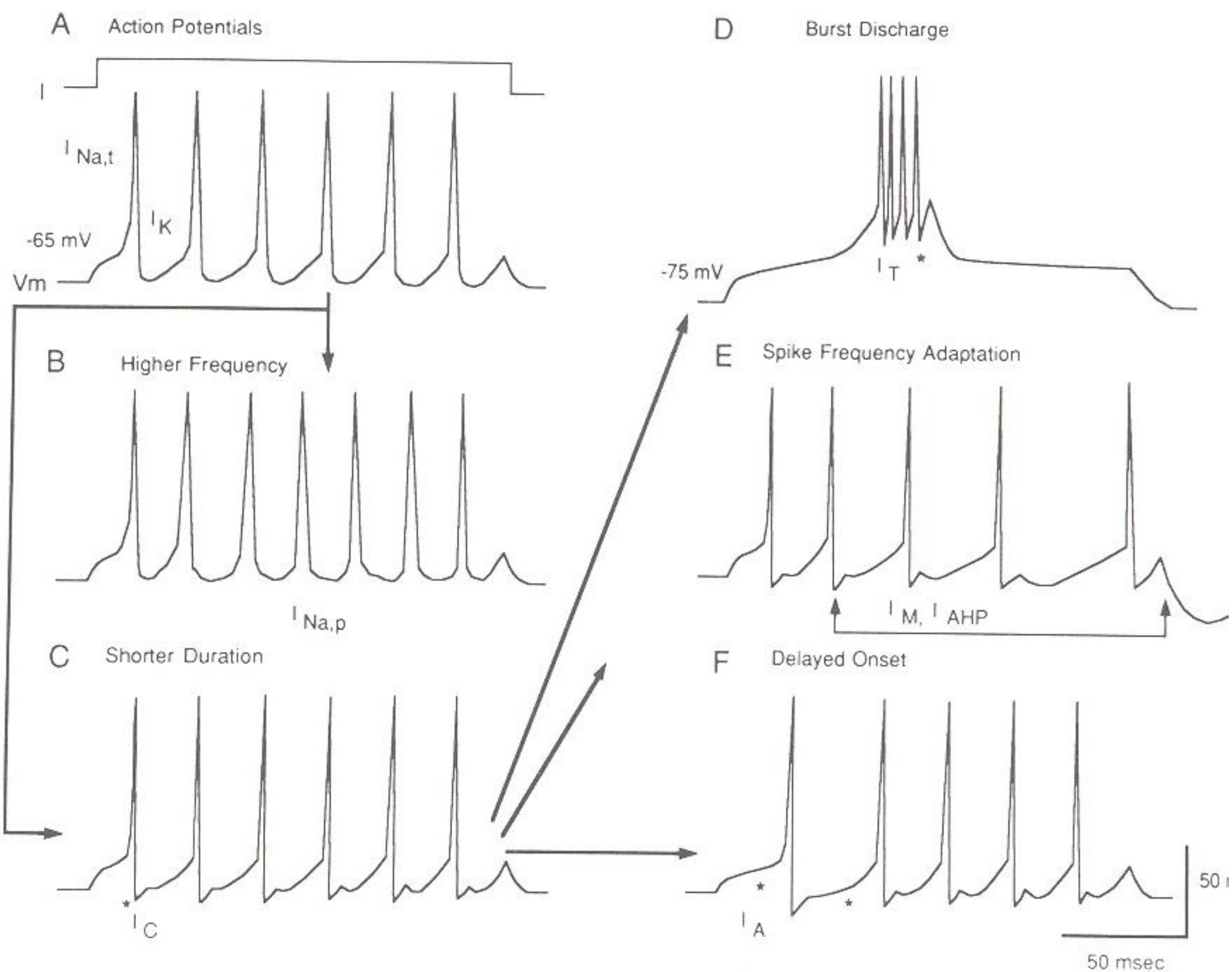


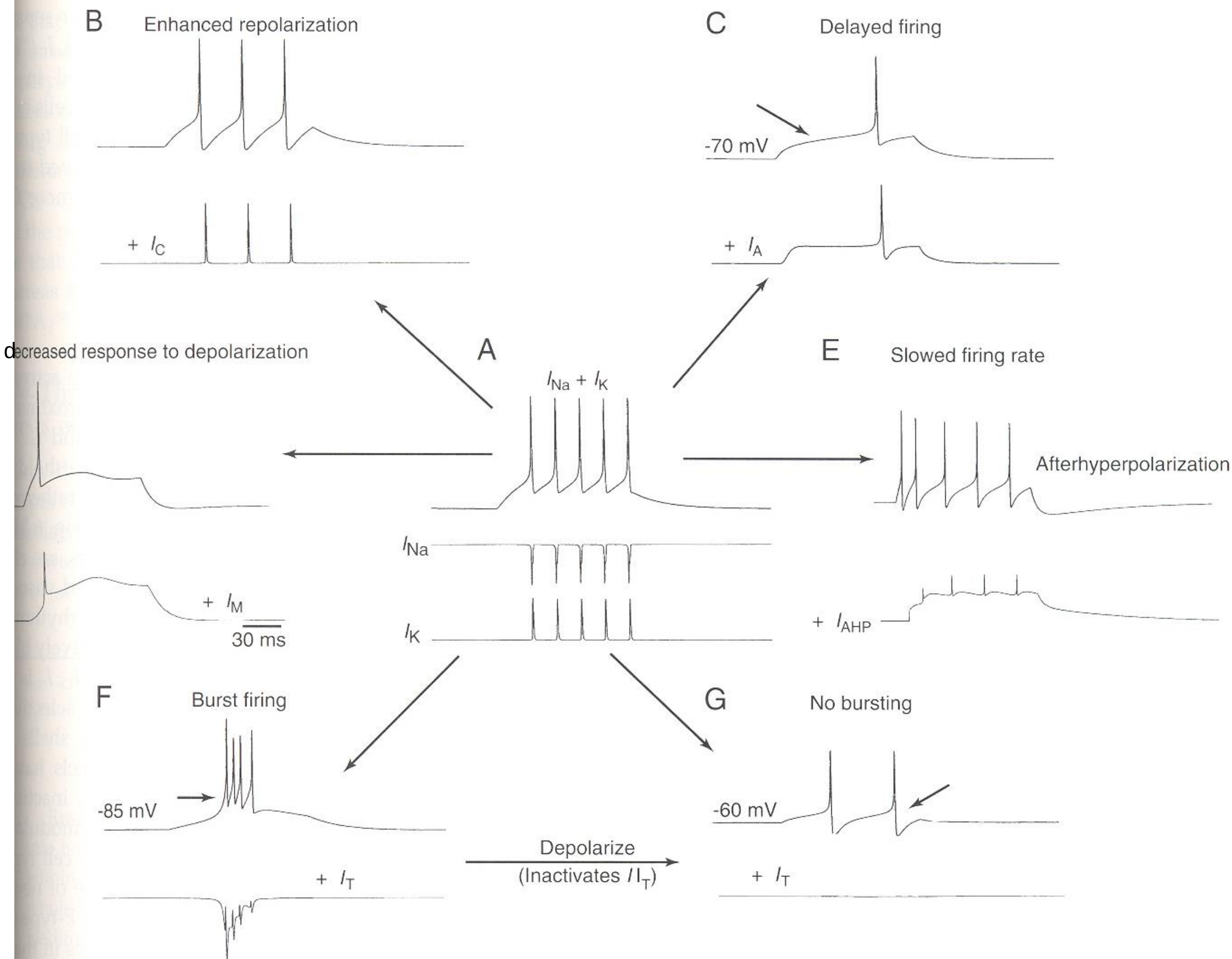

**FIGURE 6.11** Voltage dependence and kinetics of different ionic currents in the mammalian brain. Depolarization of the membrane potential from −100 to −10 mV results in the activation of currents entering or leaving neurons.

TABLE 6.2 Neuronal Ionic Currents

| Current | Description | Function |
|---|---|---|
| $Na^+$ currents | | |
| $I_{Na,t}$ | Transient; rapidly activating and inactivating | Action potentials |
| $I_{Na,p}$ | Persistent; noninactivating | Enhances depolarization; contributes to steady-state firing |
| $Ca^{2+}$ currents | | |
| $I_T$, low threshold | Transient; rapidly inactivating; threshold negative to −65 mV | Underlies rhythmic burst firing |
| $I_L$, high threshold | Long-lasting; slowly inactivating; threshold around −20 mV | Underlies $Ca^{2+}$ spikes that are prominent in dendrites; invol synaptic transmission |
| $I_N$ | Neither; rapidly inactivating; threshold around −20 mV | Underlies $Ca^{2+}$ spikes that are prominent in dendrites; invol synaptic transmission |
| $I_P$ | Purkinje; threshold around −50 mV | |
| $K^+$ currents | | |
| $I_K$ | Activated by strong depolarization | Repolarization of action potential |
| $I_C$ | Activated by increases in $[Ca^{2+}]_i$ | Action potential repolarization and interspike interval |
| $I_{AHP}$ | Slow afterhyperpolarization; sensitive to increases in $[Ca^{2+}]_i$ | Slow adaptation of action potential discharge; the block of t rent by neuromodulators enhances neuronal excitability |
| $I_A$ | Transient; inactivating | Delayed onset of firing; lengthens interspike interval; action tial repolarization |
| $I_M$ | Muscarine sensitive; activated by depolarization; noninactivating | Contributes to spike frequency adaptation; the block of this by neuromodulators enhances neuronal excitability |
| $I_h$ | Depolarizing (mixed cation) current that is activated by hyperpolarization | Contributes to rhythmic burst firing and other rhythmic acti |
| $I_{K,leak}$ | Contributes to neuronal resting membrane potential | Block of this current by neuromodulators can result in a sus change in membrane potential |



A Action Potentials
I
I Na,t
I K
-65 mV
Vm
B Higher Frequency
I Na,p
C Shorter Duration
I C
D Burst Discharge
-75 mV
I T
E Spike Frequency Adaptation
I M, I AHP
F Delayed Onset
I A
50 msec



B
Enhanced repolarization
+ $I_C$
C
Delayed firing
-70 mV
+ $I_A$
decreased response to depolarization
+ $I_M$
30 ms
A
$I_{Na} + I_K$
$I_{Na}$
$I_K$
E
Slowed firing rate
Afterhyperpolarization
+ $I_{AHP}$
F
Burst firing
-85 mV
+ $I_T$
Depolarize
(Inactivates $I$ I$_T$)
G
No bursting
-60 mV
+ $I_T$

What causes such different firing patterns?

…an alternative view

# Influence of dendritic structure on firing pattern in model neocortical neurons

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Howard Hughes Medical Institute, Computational Neurobiology Laboratory, Salk Institute for Biological Studies, La Jolla, California 92037, and Department of Biology, University of California, San Diego, La Jolla, California 92093, USA

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**NEOCORTICAL neurons display a wide range of dendritic morphologies, ranging from compact arborizations to highly elaborate branching patterns[1]. *In vitro* electrical recordings from these neurons have revealed a correspondingly diverse range of intrinsic firing patterns, including non-adapting, adapting and bursting types[2,3]. This heterogeneity of electrical responsivity has generally been attributed to variability in the types and densities of ionic channels. We show here, using compartmental models of reconstructed cortical neurons, that an entire spectrum of firing patterns can be reproduced in a set of neurons that share a common distribution of ion channels and differ only in their dendritic geometry. The essential behaviour of the model depends on partial electrical coupling of fast active conductances localized to the soma and axon and slow active currents located throughout the dendrites, and can be reproduced in a two-compartment model. The results suggest a causal relationship for the observed correlations between dendritic structure and firing properties[3–7] and emphasize the importance of active dendritic conductances in neuronal function[8–10].**

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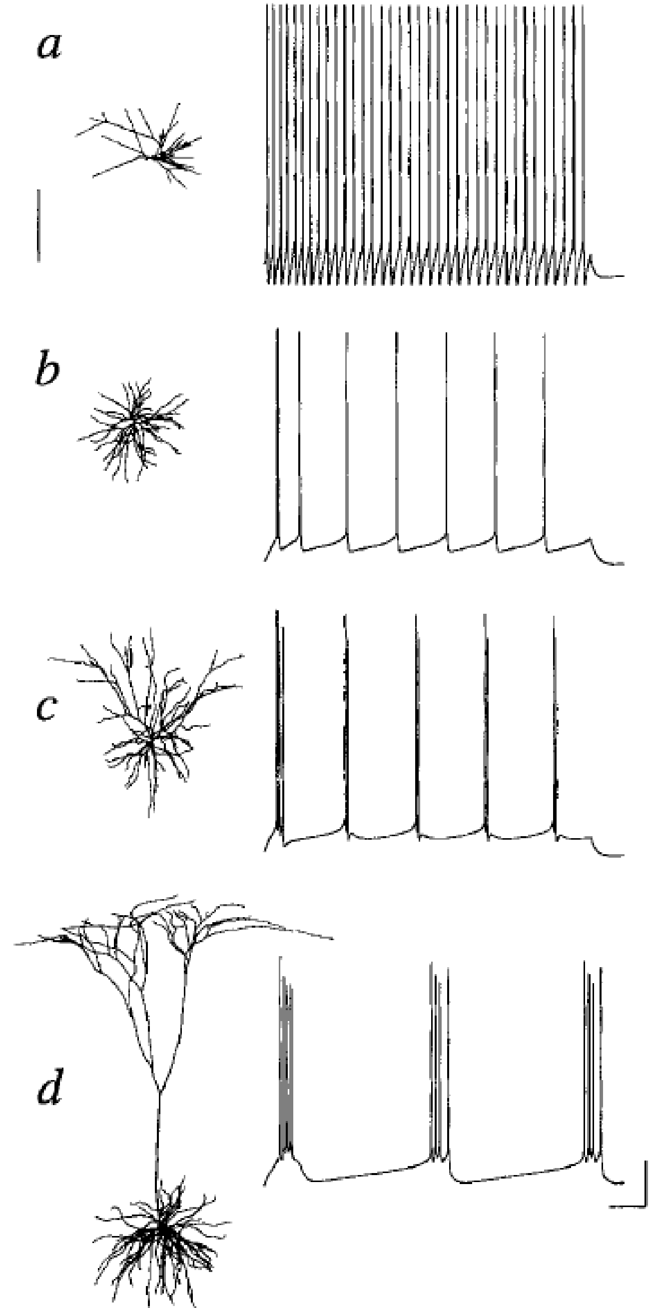
FIG. 1 Distinct firing patterns in model neurons with identical channel distributions but different dendritic morphology. Digital reconstructions of dendritic arborizations of neurons from rat somatosensory cortex (*a*) and cat visual cortex (*b*–*d*). *a*, Layer 3 aspiny stellate. *b*, Layer 4 spiny stellate. *c*, Layer 3 pyramid. *d*, Layer 5 pyramid. Somatic current injection (50, 70, 100, 200 pA for *a*–*d*, respectively) evoked characteristic firing patterns. *a* shows only the branch lengths and connectivity whereas *b*–*d* show a two-dimensional projection of the three-dimensional reconstruction. Scale bars: 250 μm (anatomy), 100 ms, 25 mV.



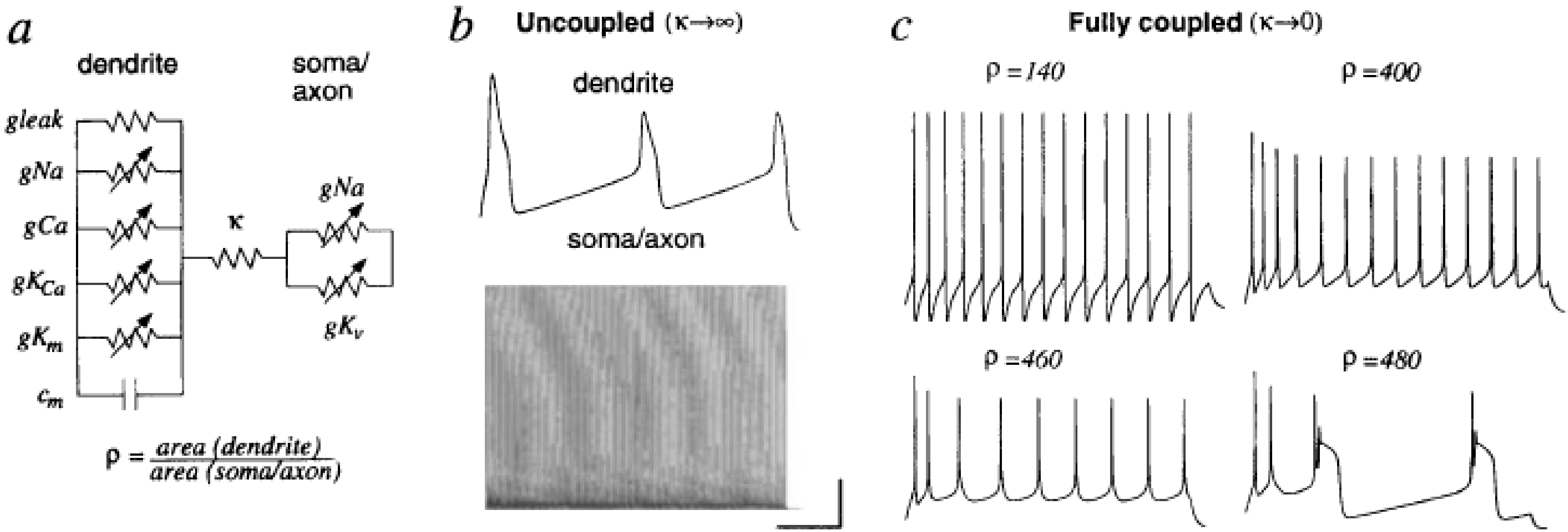



FIG. 2 Effects of electrical structure on firing pattern in a reduced model. *a*, A two-compartment model incorporating the same channels modelled in Fig. 1. The two compartments correspond to the dendritic tree ('dendrite') and the soma and axon initial segment ('axon–soma'). The parameter $\kappa$ specifies the electrical resistance (coupling) between the two compartments. The parameter $\rho$ specifies the ratio of dendritic to axo–somatic area and thereby sets the strength of dendritic currents relative to axo–somatic currents. The channels and membrane properties of each compartment are depicted. *b*, Uncoupled dendritic (top) and axo-somatic (bottom) compartments ($\kappa \to \infty$) are each capable of discharging repetitively when current is injected (top, 400 pA; bottom, 10 pA). Note that the firing frequency of the axo-somatic compartment, which is driven by the fast $I_{Na}$ and $I_{Kv}$ is much higher than for the dendritic compartment, which is driven by $I_{Ca}$, $I_{KCa}$ and $I_{Km}$. *c*, When fully coupled ($\kappa \to 0$), eliminating electrotonic effects, the amount of spike-frequency adaptation varies with the size of the dendritic compartment, but the model does not display bursting or spike ADPs. *d*, *e*, Partial coupling produces voltage gradients between axo-somatic (left) and dendritic (right) compartments and supports bursting and ADPs. When partially coupled,

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Two modes of thalamic neurons:

http://medicine.yale.edu/lab/mccormick/movies/index.aspx#3-165535

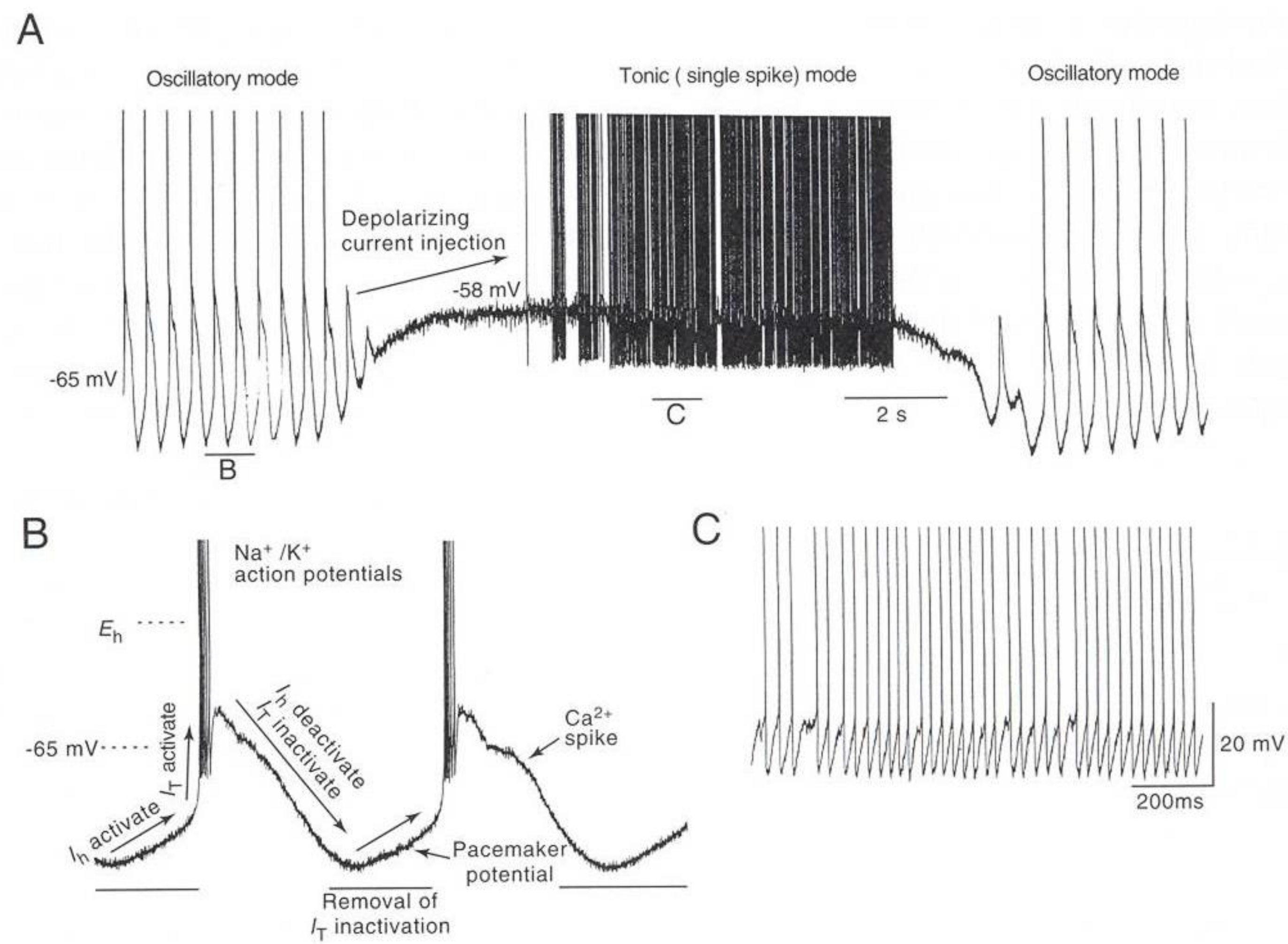


**FIGURE 6.13** Two different patterns of activity generated in the same neuron, depending on membrane potential. (A) The thalamic neuron spontaneously generates rhythmic bursts of action potentials owing to the interaction of the $Ca^{2+}$ current $I_T$ and the inward "pacemaker" current $I_h$. Depolarization of the neuron changes the firing mode from rhythmic burst firing to tonic action potential generation in which spikes are generated one at a time. Removal of this depolarization reinstates the rhythmic burst firing. This transition from rhythmic burst firing to tonic activity is similar to that which occurs in the transition from sleep to waking. (B) Expansion of detail of rhythmic burst firing. (C) Expansion of detail of tonic firing. From McCormick and Pape.[110]

# Thalamic bursting

- When the cell is hyperpolarized, $I_h$ is activated, and this slowly depolarizes the cell
- Hyperpolarization also removes inactivation from $I_t$ , allowing it to contribute later to a burst
- After the burst, $I_t$ is inactivated, so bursting stops. Also $I_h$ is no longer on, and the cell hyperpolarizes
- The cell is not sensitive to weak sensory input, and only sends rhythmic bursts to the cortex (sleep)

# Thalamic transfer mode

- When you open your eyes, the thalamic cell is depolarized by strong sensory input and $I_t$ is inactivated.
- Now, when synaptic input comes into the cell, it leads to individual action potentials, not bursts.
- Patterned sensory input to the thalamus is therefore transferred to the cortex (awake)

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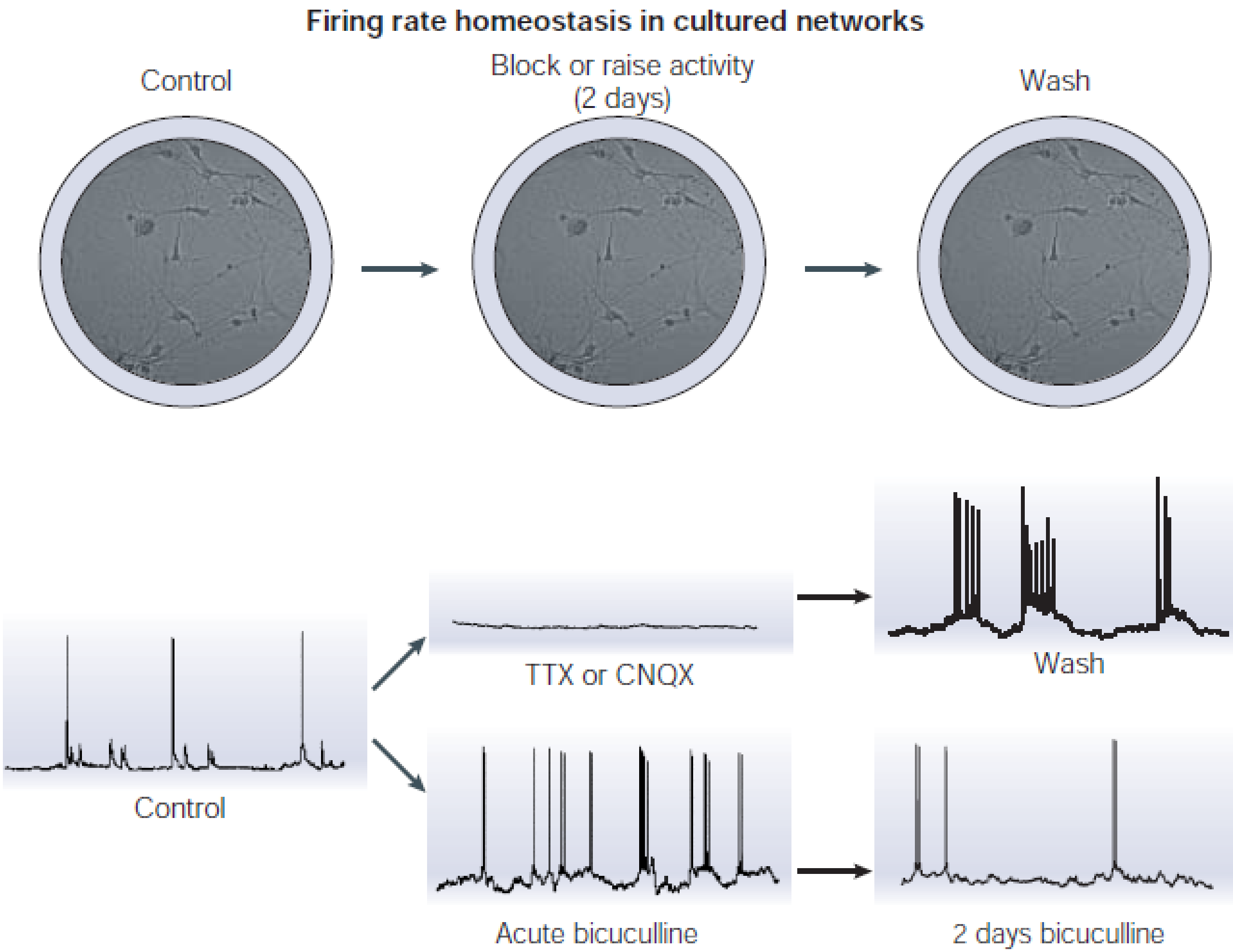
# HOMEOSTATIC PLASTICITY IN THE DEVELOPING NERVOUS SYSTEM

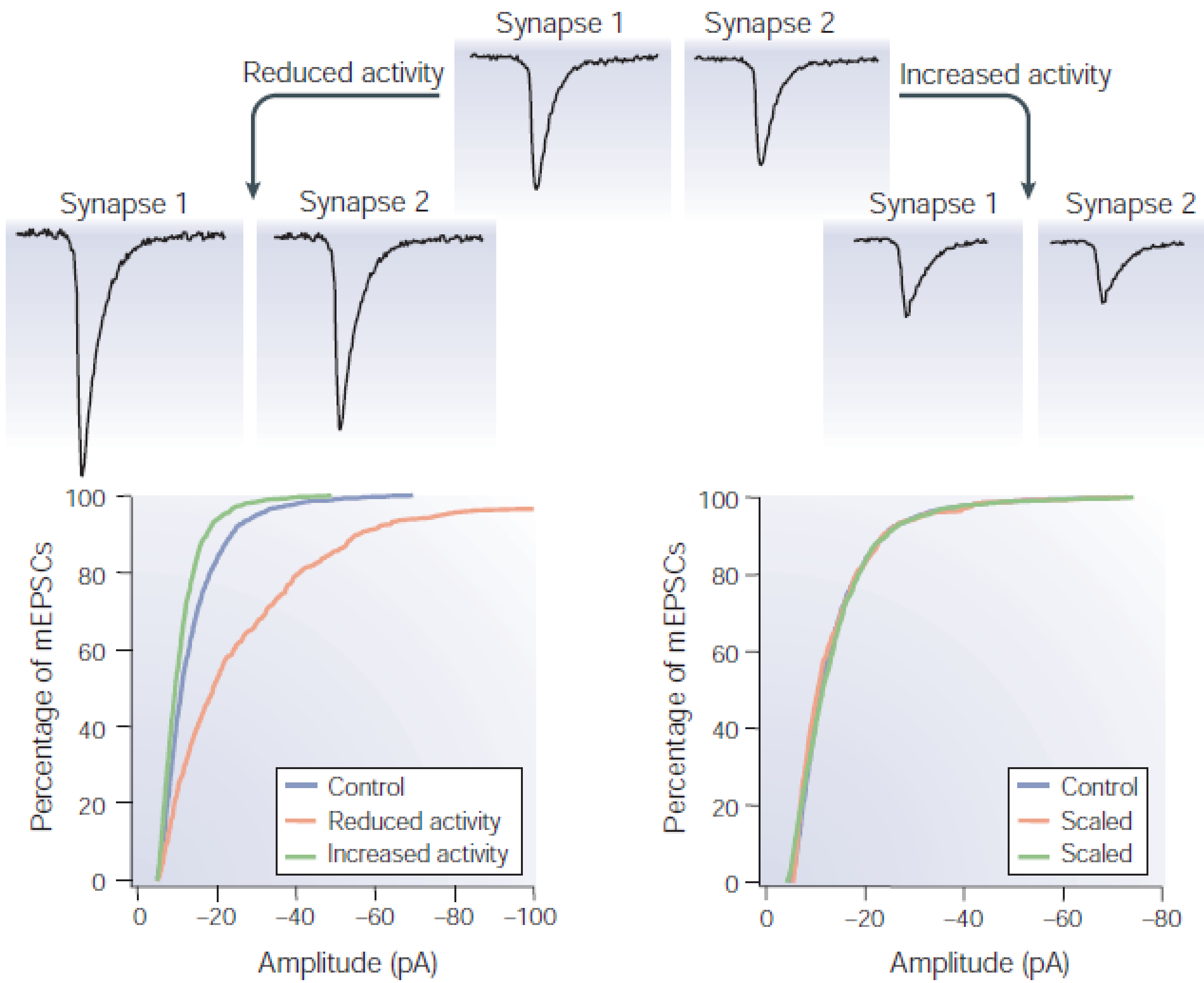
*Gina G. Turrigiano and Sacha B. Nelson*

Activity has an important role in refining synaptic connectivity during development, in part through 'Hebbian' mechanisms such as long-term potentiation and long-term depression. However, Hebbian plasticity is probably insufficient to explain activity-dependent development because it tends to destabilize the activity of neural circuits. How can complex circuits maintain stable activity states in the face of such destabilizing forces? An idea that is emerging from recent work is that average neuronal activity levels are maintained by a set of homeostatic plasticity mechanisms that dynamically adjust synaptic strengths in the correct direction to promote stability. Here we discuss evidence from a number of systems that homeostatic synaptic plasticity is crucial for processes ranging from memory storage to activity-dependent development.

# Firing rate homeostasis



# Synaptic scaling



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