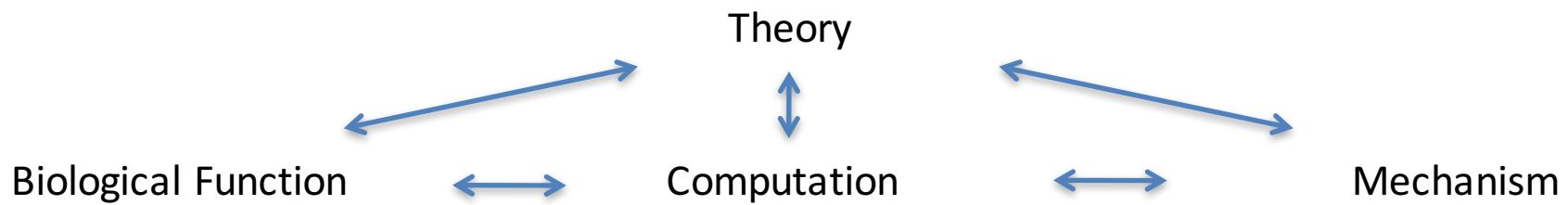


Introduction to {computation | theory | data analysis} in neuroscience



Stephen Baccus
John Huguenard
Surya Ganguli

Niru Maheswaranathan

Why Model?

Joshua Epstein

Sixteen Reasons Other Than Prediction to Build Models

Explain (very distinct from predict)

Illuminate core dynamics

Suggest dynamical analogies

Discover new questions

Bound (bracket) outcomes to plausible ranges

Illuminate core uncertainties

Demonstrate tradeoffs / suggest efficiencies

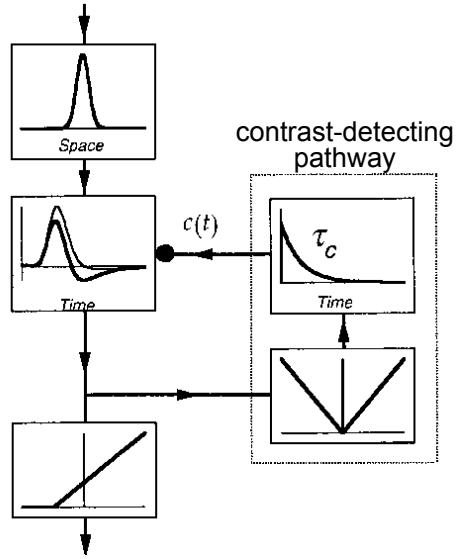
Challenge the robustness of prevailing theory through perturbations

Expose prevailing wisdom as incompatible with available data

Reveal the apparently simple (complex) to be complex (simple)

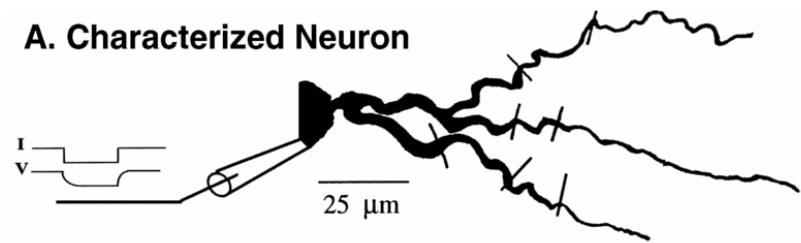
Many types of models for different purposes

Abstract

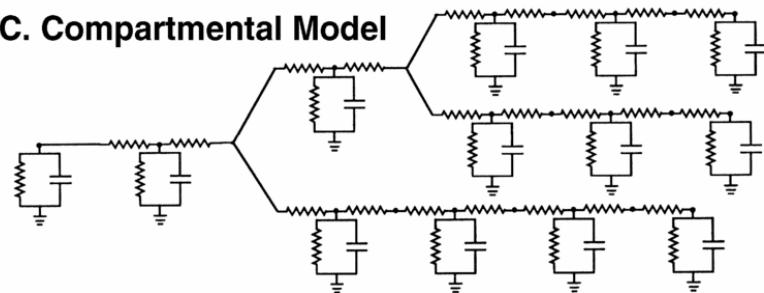


Biophysical

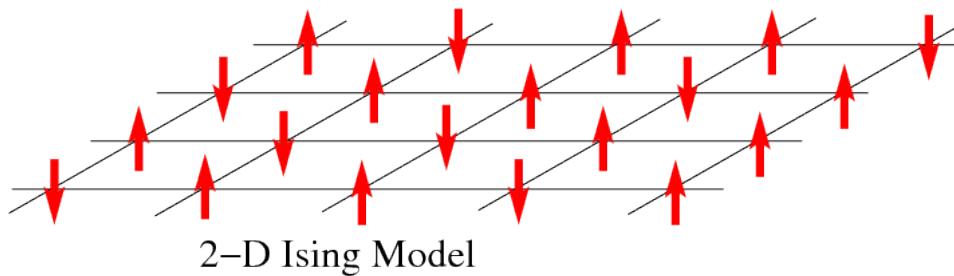
A. Characterized Neuron



C. Compartmental Model



Statistical

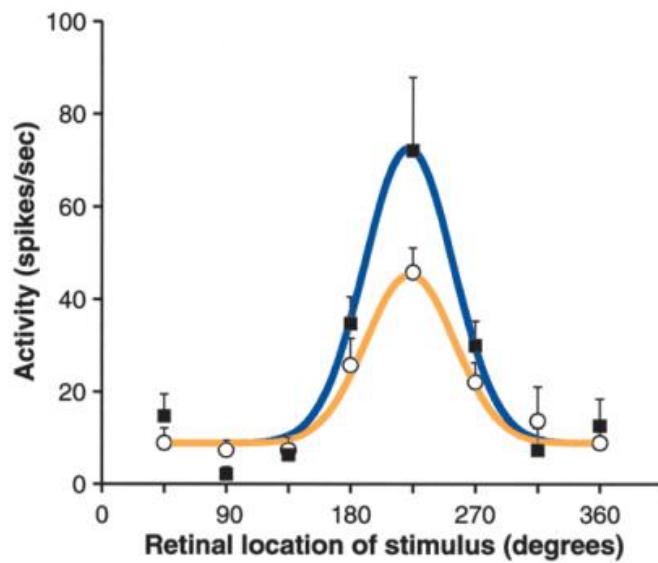
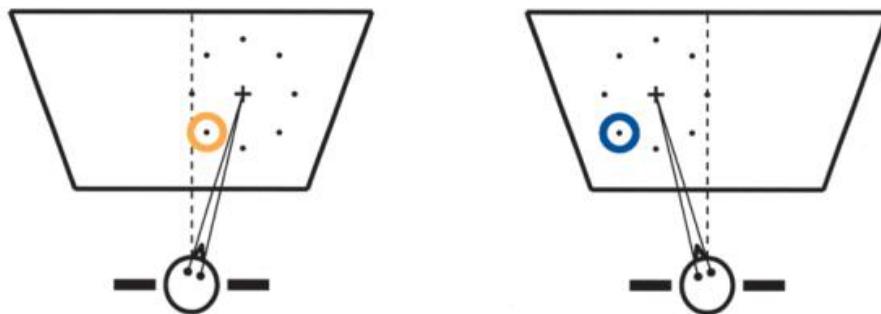


How can a neuron change its gain?

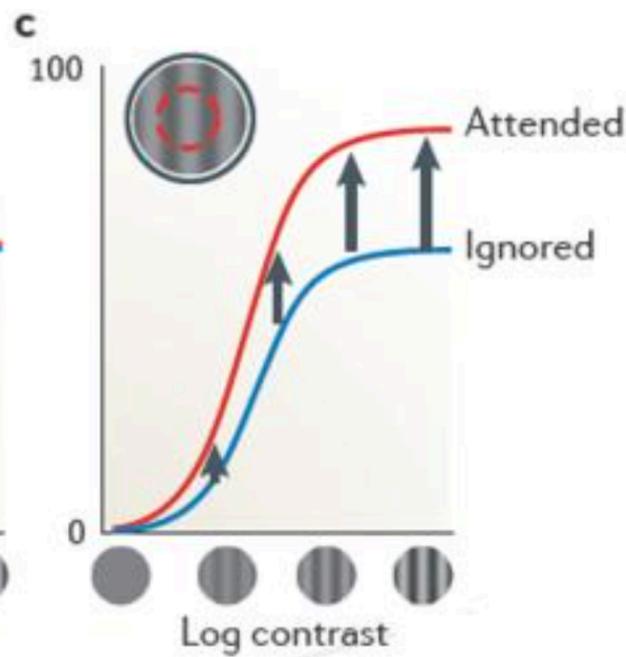
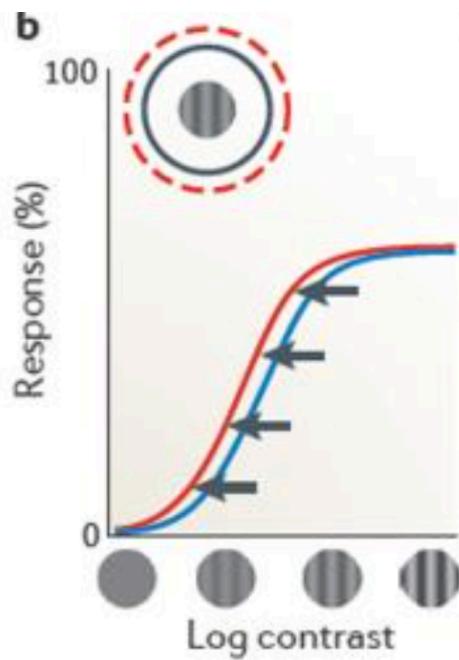
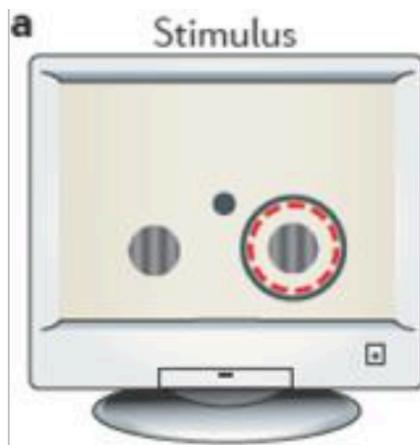
How can a neuron maintain a stable firing pattern?

What influence do dendrites have on computation?

Gain modulation



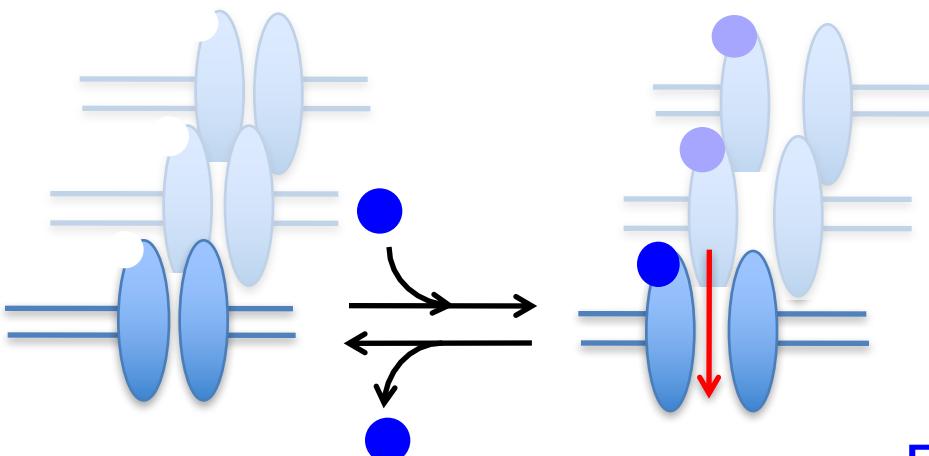
Salinas & Sejnowski, 2001



Reynolds & Heeger, 2009

How can a neuron control its gain?

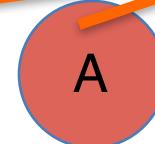
- Integrate and fire neuron
 - Sum of currents
 - Tau
- Conductance models



Closed



Open



$$[L]k_{on}$$

$$k_{off}$$

Rate constants

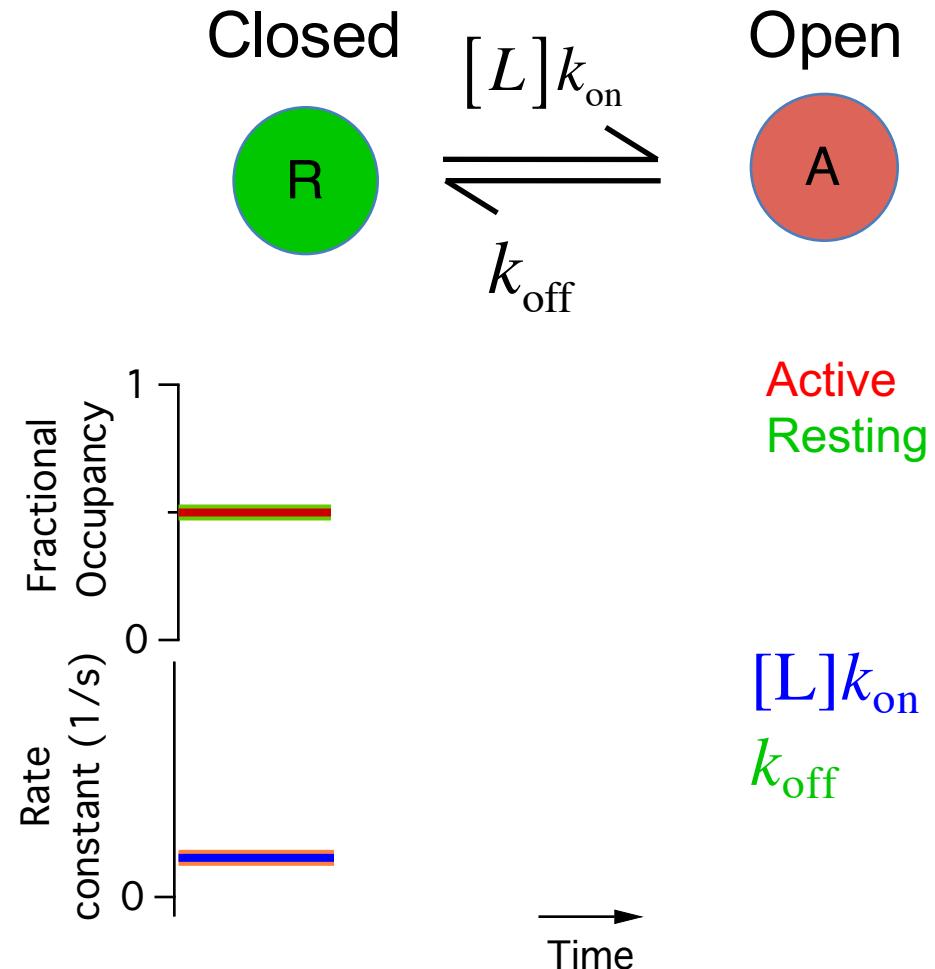
State
Occupancies
(sum to 1)

$$\text{Change in activity} = \text{Inflow} - \text{Outflow}$$

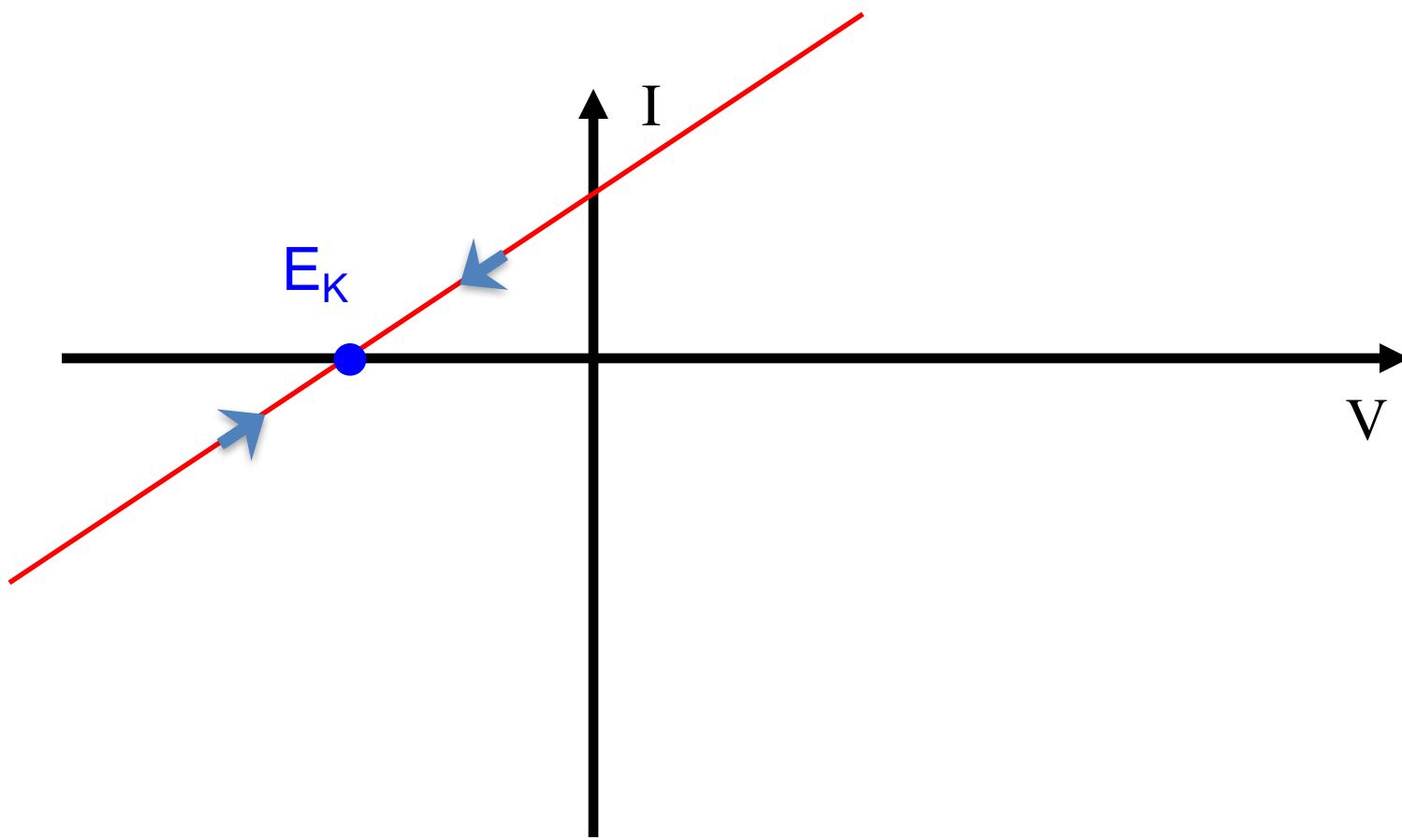
$$\frac{dA}{dt} = R[L]k_{on} - Ak_{off}$$

Kinetic model

Input and output in a kinetic model



Idea of Driving Force
linear (ohmic) input output relationship for individual
channel type



Hodgkin Huxley Model

Voltage state variable (membrane equation):

$$C \frac{dV}{dt} = I(t) - \bar{g}_K n^4 (V - E_K) - \bar{g}_{Na} m^3 h (V - E_{Na}) - \bar{g}_l (V - E_l)$$

Conductance state variables:

$$\begin{aligned} dn/dt &= \alpha_n(V)(1-n) - \beta_n(V)n \\ dm/dt &= \alpha_m(V)(1-m) - \beta_m(V)m \\ dh/dt &= \alpha_h(V)(1-h) - \beta_h(V)h \end{aligned}$$

Rate “constants”:

$$\begin{aligned} \alpha_n(V) &= \frac{10 - V}{100 (\exp((10 - V)/10) - 1)} & \beta_n(V) &= 0.125 \exp(-V/80) \\ \alpha_m(V) &= \frac{25 - V}{10 (\exp((25 - V)/10) - 1)} & \beta_m(V) &= 4 \exp(-V/18) \\ \alpha_h(V) &= 0.07 \exp(-V/20) & \beta_h(V) &= \frac{1}{\exp((30 - V)/10) + 1} \end{aligned}$$

Constants:

| | | | |
|---------------------------------|---|----------------------------|---|
| $C = 1 \mu\text{F}/\text{cm}^2$ | $\bar{g}_K = 36 \text{ mS}/\text{cm}^2$ | $E_K = -12 \text{ mV}$ | Note: these are given in the original form, relative to $V_{\text{rest}} = \sim -66 \text{ mV}$ |
| | $\bar{g}_{Na} = 120 \text{ mS}/\text{cm}^2$ | $E_{Na} = +115 \text{ mV}$ | |
| | $\bar{g}_l = 0.3 \text{ mS}/\text{cm}^2$ | $E_l = +10.613 \text{ mV}$ | |

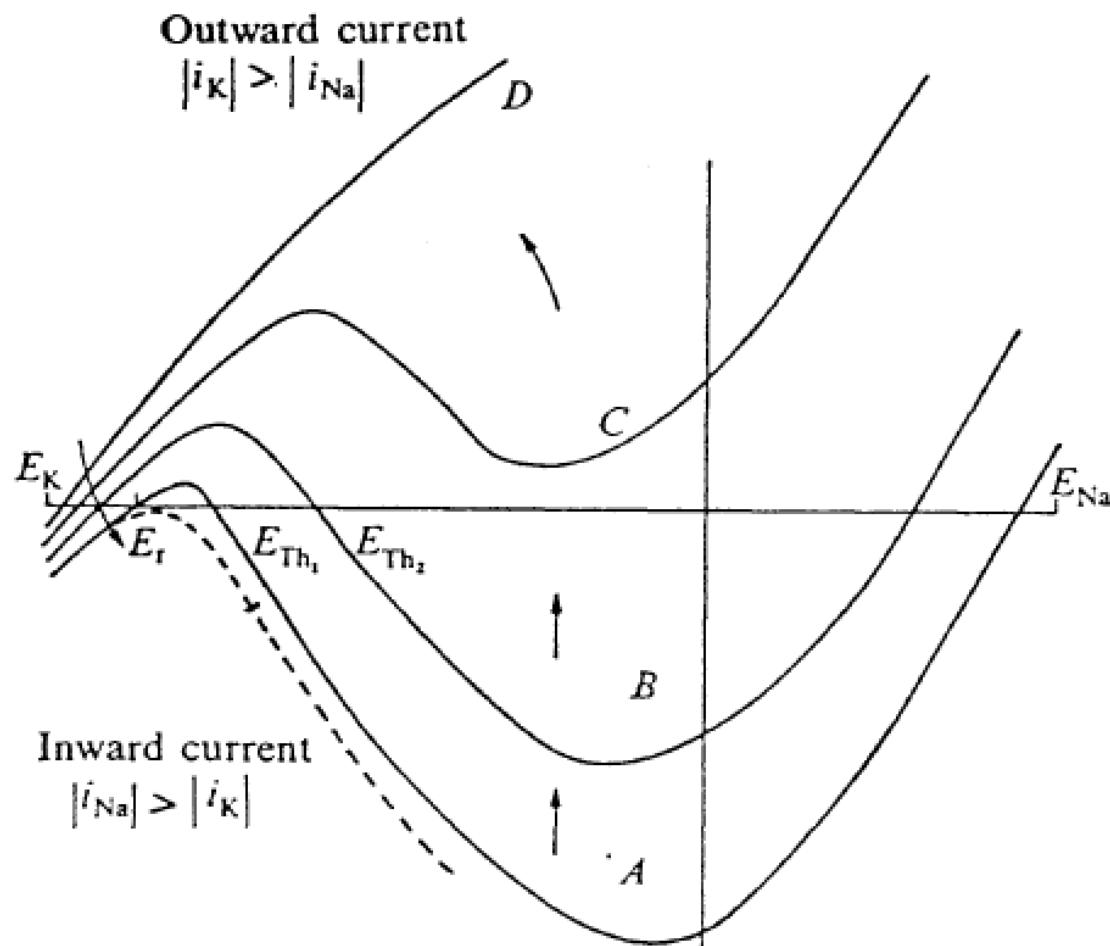
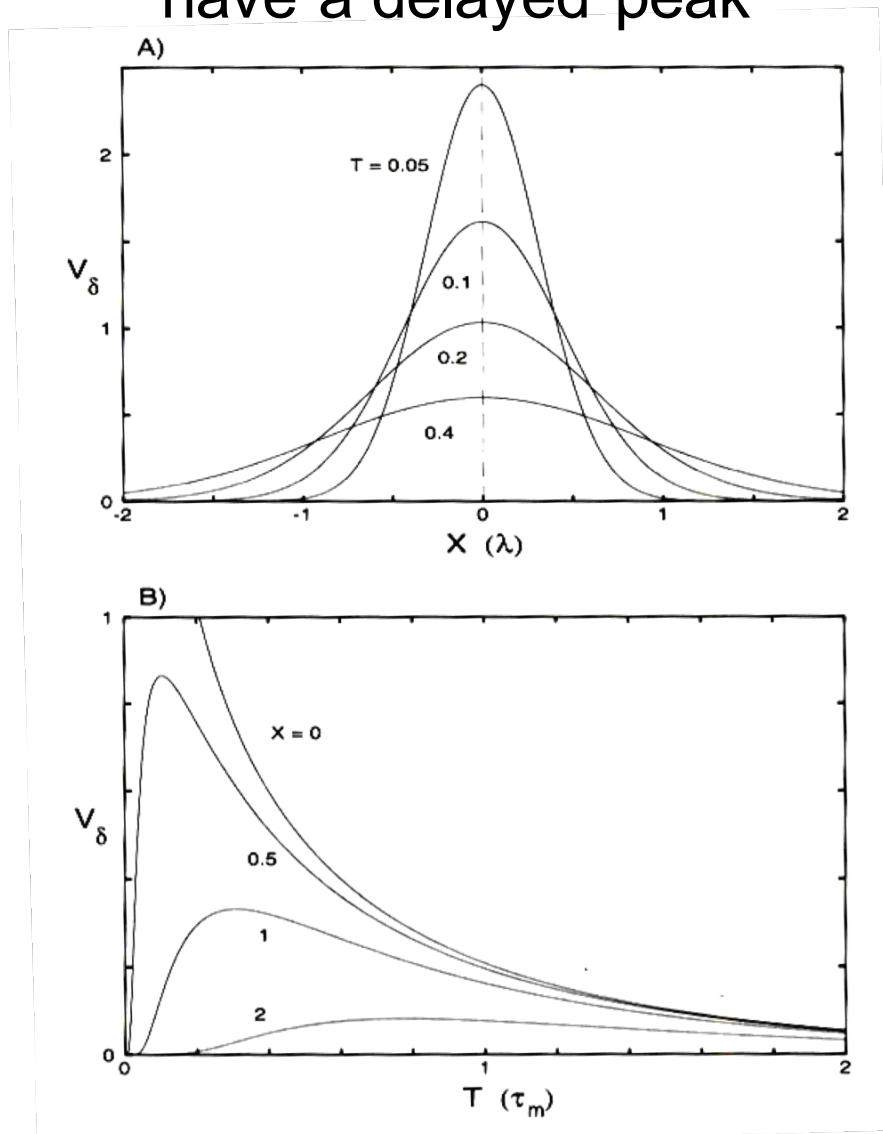
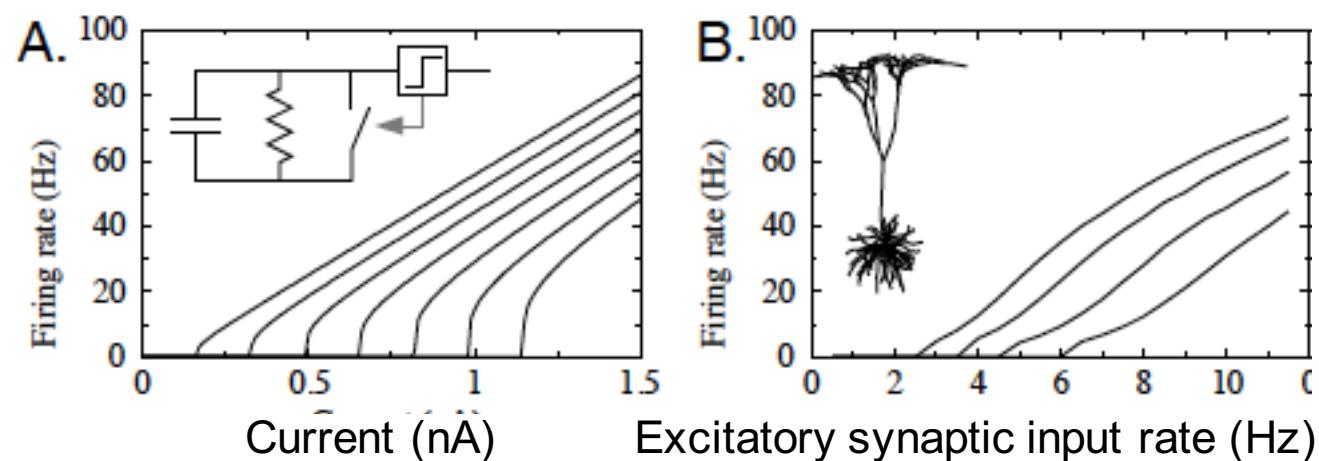
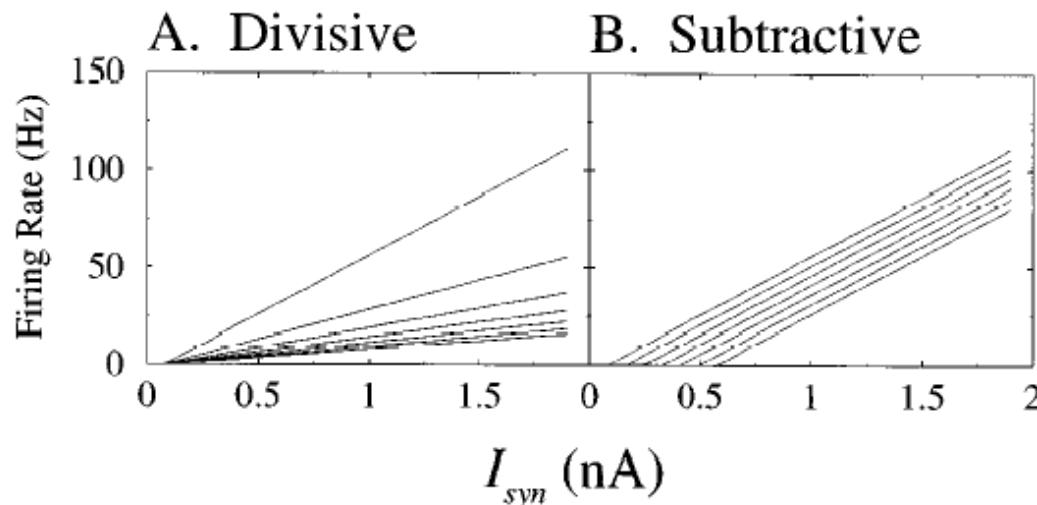


FIG. 8.12. Diagram illustrating change in momentary current-voltage relations with time on depolarization.

Due to filtering along a cable, distant locations have a delayed peak

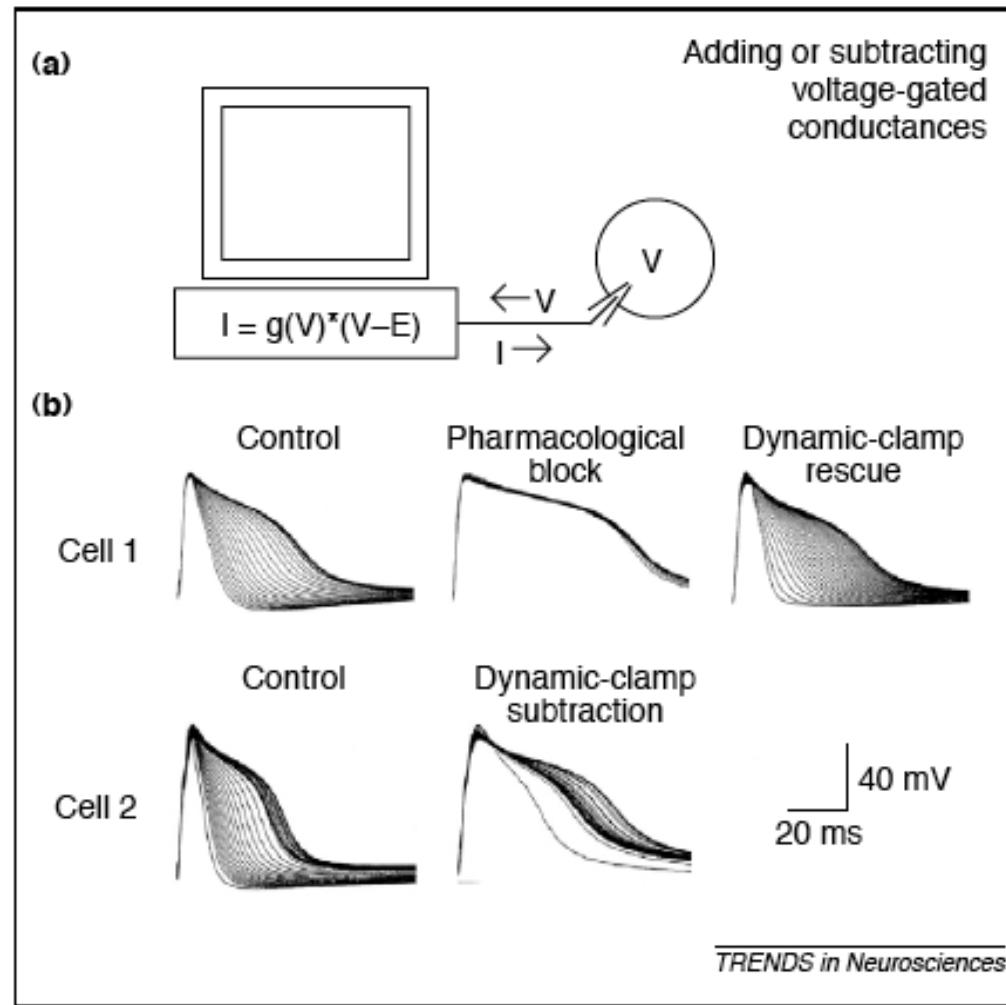




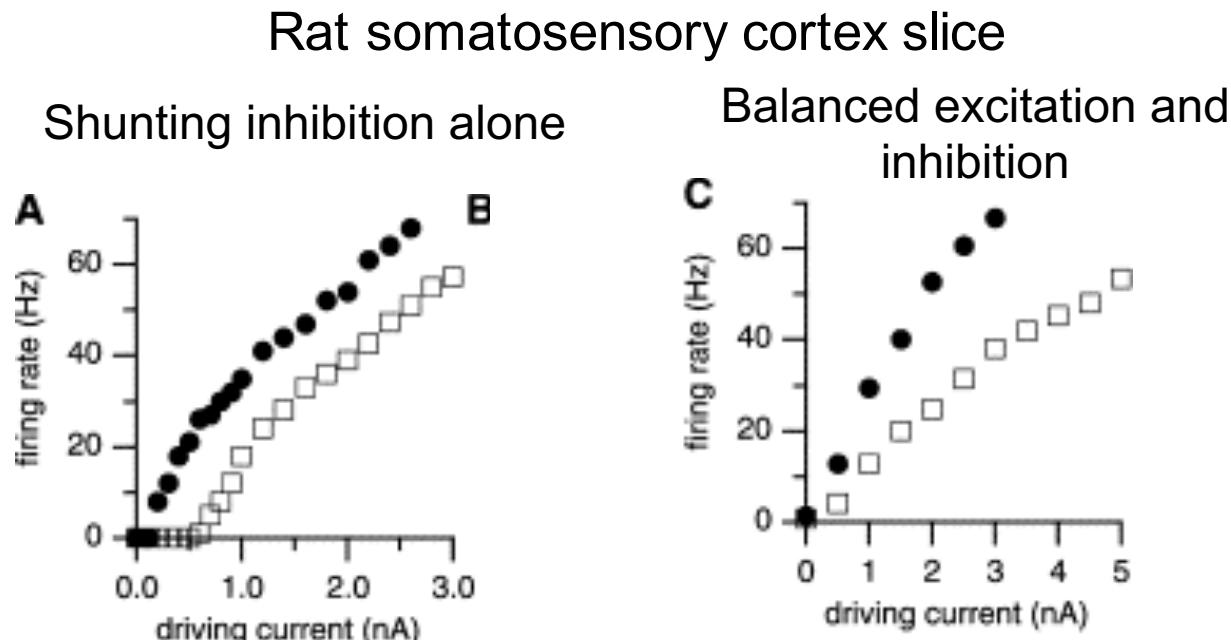
Holt & Koch, 1997. Shunting inhibition does not have a divisive effect on firing rates

The dynamic clamp

Artificially adding or subtracting membrane mechanisms



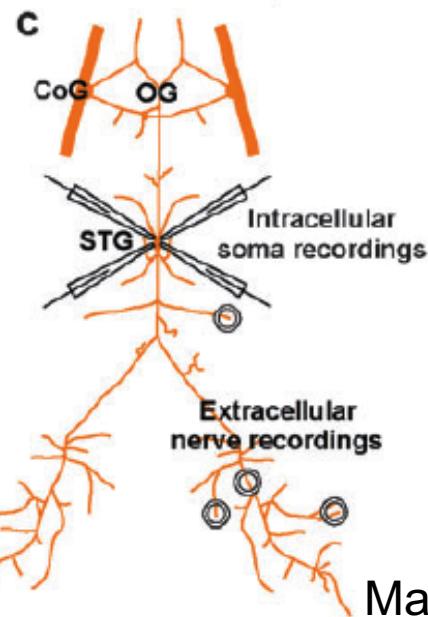
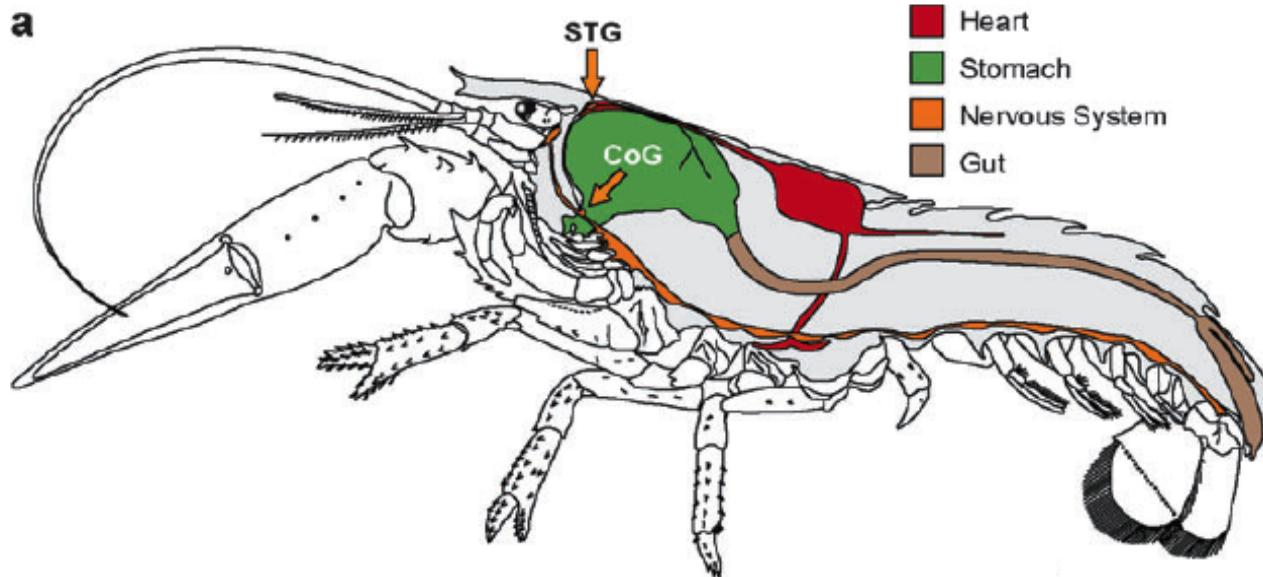
Balanced excitation and inhibition can change gain



Chance, Abbott & Reyes. (2002) Gain modulation from background synaptic input.

How can a neuron maintain a stable firing pattern?

Crustacean stomatogastric ganglion

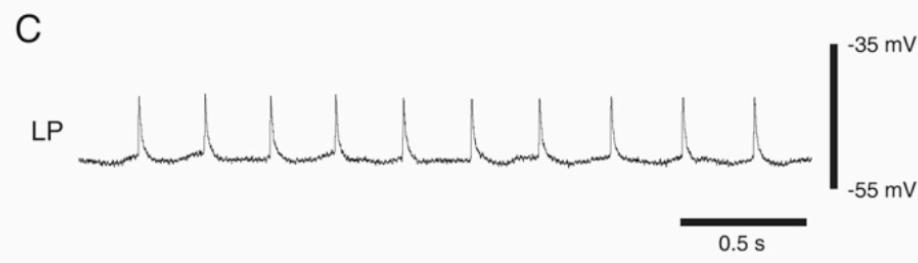
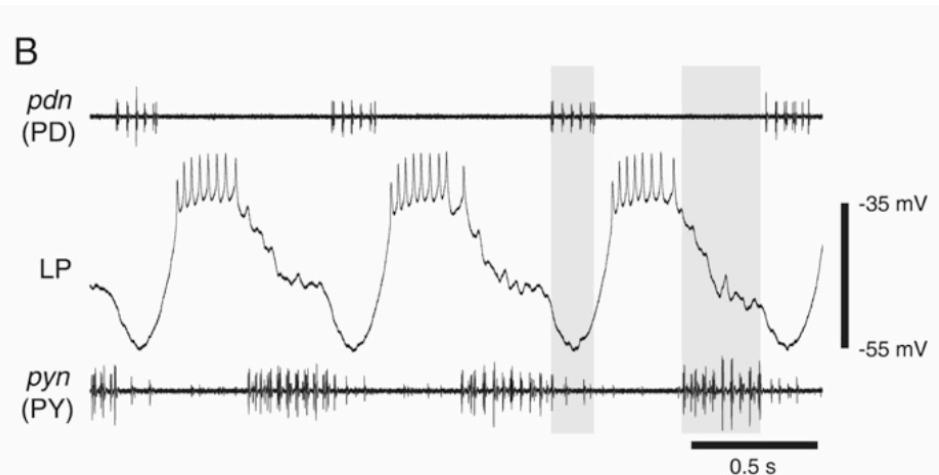


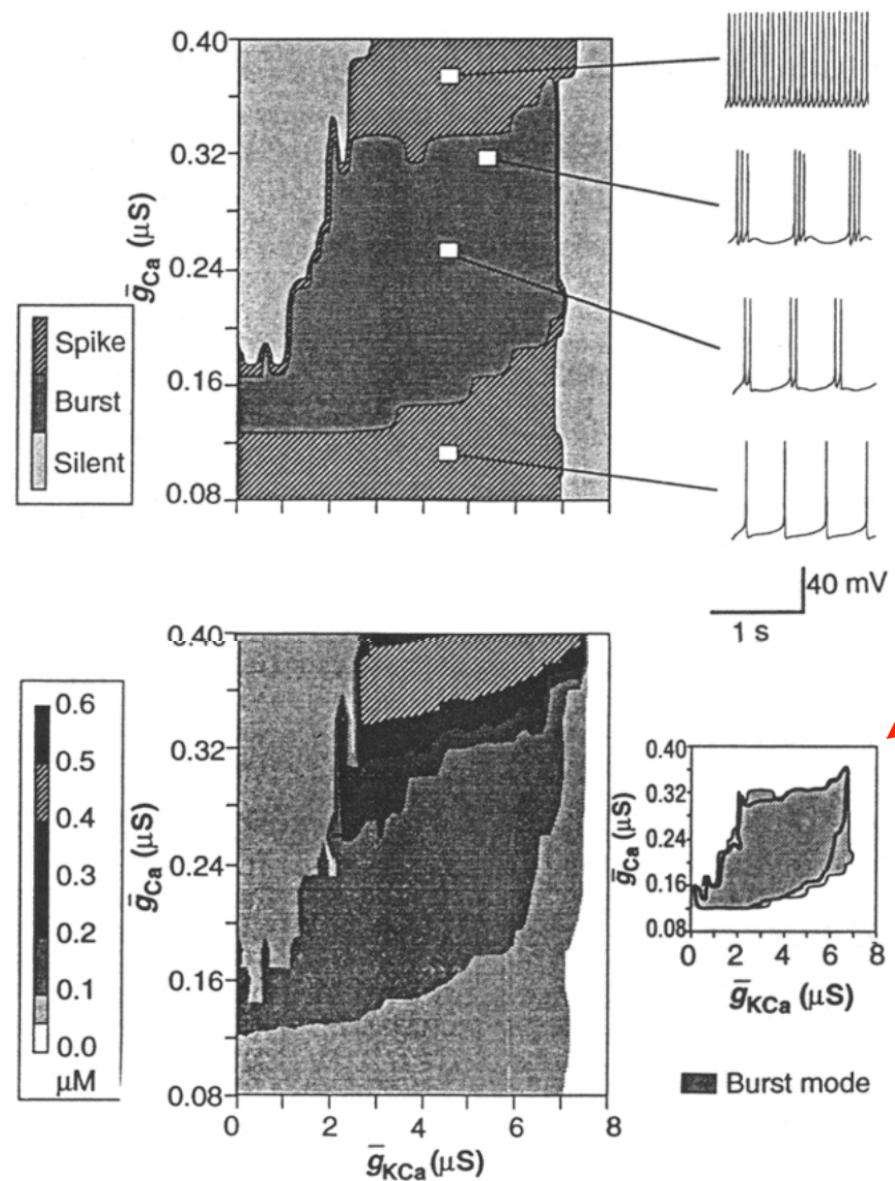
Marder, E. & Bucher, D., 2006

Many conductances, how are they regulated?

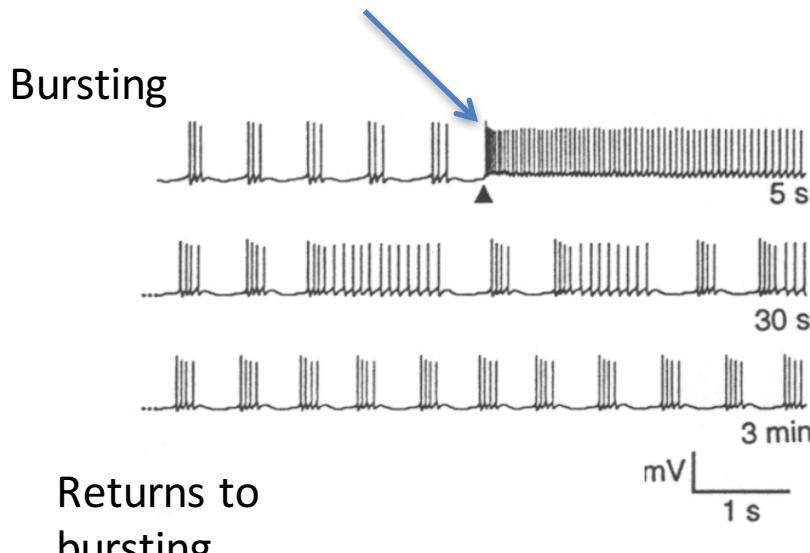
Table 1. Equations describing the activation and inactivation properties of the ionic currents of the model STG neuron

| Current | P | m_∞ | h_∞ | τ_m | τ_h |
|-------------|-----|--|---|--|--|
| I_{Na} | 3 | $\frac{1}{1 + \exp \left[\frac{-V - 25.5}{5.29} \right]}$ | $\frac{1}{1 + \exp \left[\frac{V + 48.9}{5.18} \right]}$ | $1.32 - \frac{1.26}{1 + \exp \left[\frac{-120 - V}{25} \right]}$ | $0.67 - \frac{1}{1 + \exp \left[\frac{-62.9 - V}{10} \right]} \parallel 1.5 + \frac{1}{1 + \exp \left[\frac{V + 34.9}{3.6} \right]}$ |
| I_{Nap} | 3 | $\frac{1}{1 + \exp \left[\frac{-V - 26.8}{8.2} \right]}$ | $\frac{1}{1 + \exp \left[\frac{V + 48.5}{4.8} \right]}$ | $19.8 - \frac{10.7}{1 + \exp \left[\frac{-26.5 - V}{8.6} \right]}$ | $666 - \frac{379}{1 + \exp \left[\frac{-33.6 - V}{11.7} \right]}$ |
| I_{Ca1} | 3 | $\frac{1}{1 + \exp \left[\frac{-V - 27.1}{7.18} \right]}$ | $\frac{1}{1 + \exp \left[\frac{V + 30.1}{5.5} \right]}$ | $21.7 - \frac{21.3}{1 + \exp \left[\frac{-68.1 - V}{20.5} \right]}$ | $105 - \frac{89.8}{1 + \exp \left[\frac{-V - 55.0}{16.9} \right]}$ |
| I_{Ca2} | 3 | $\frac{1}{1 + \exp \left[\frac{-V - 21.6}{8.5} \right]}$ | | $16 - \frac{13.1}{1 + \exp \left[\frac{-V - 25.1}{26.4} \right]}$ | |
| I_{KCa}^* | 4 | $\frac{[Ca]}{[Ca] + 3} \cdot \frac{1}{1 + \exp \left[\frac{-V - 28.3}{12.6} \right]}$ | | $90.3 - \frac{75.1}{1 + \exp \left[\frac{-V - 46}{22.7} \right]}$ | |
| I_{Kd} | 4 | $\frac{1}{1 + \exp \left[\frac{-V - 12.3}{11.8} \right]}$ | | $7.2 - \frac{6.4}{1 + \exp \left[\frac{-V - 28.3}{19.2} \right]}$ | |
| I_A | 3 | $\frac{1}{1 + \exp \left[\frac{-V - 27.2}{8.7} \right]}$ | $\frac{1}{1 + \exp \left[\frac{V + 56.9}{4.9} \right]}$ | $11.6 - \frac{10.4}{1 + \exp \left[\frac{-V - 32.9}{15.2} \right]}$ | $38.6 - \frac{29.2}{1 + \exp \left[\frac{-V - 38.9}{26.5} \right]}$ |
| I_{As} | 3 | $\frac{1}{1 + \exp \left[\frac{-V - 24.3}{9.4} \right]}$ | $\frac{1}{1 + \exp \left[\frac{V + 61.3}{6.6} \right]}$ | $13.3 - \frac{9.0}{1 + \exp \left[\frac{-V - 50.3}{11.8} \right]}$ | $9821 - \frac{9269}{1 + \exp \left[\frac{-V - 69.9}{4.6} \right]}$ |
| I_h | 1 | $\frac{1}{1 + \exp \left[\frac{V + 78.3}{6.5} \right]}$ | | $272 - \frac{-1499}{1 + \exp \left[\frac{-V - 42.2}{8.73} \right]}$ | |



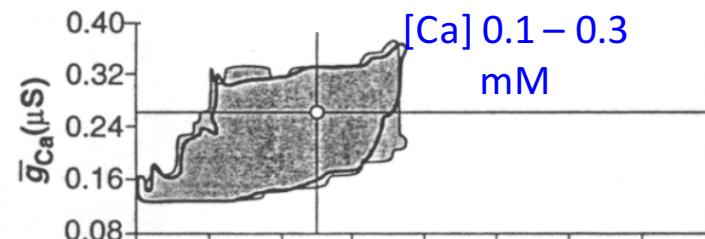


K^+ is increased here, E_K changed from -80 to -60 mV



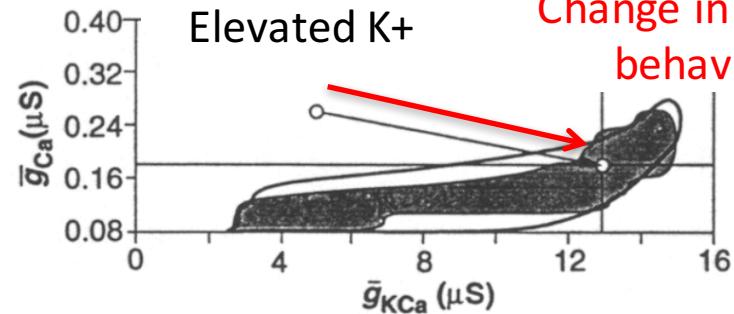
Returns to bursting

Normal K^+

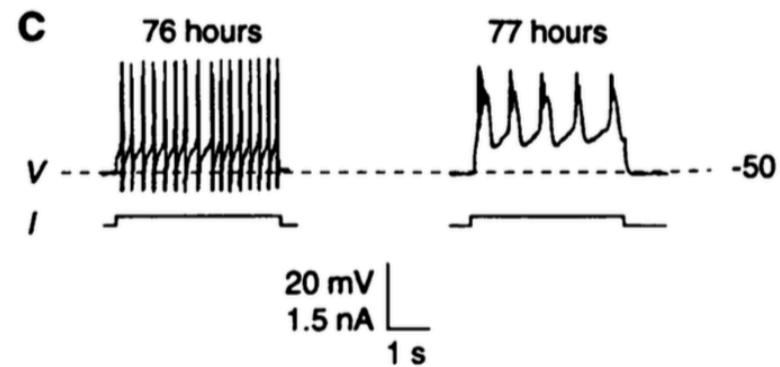
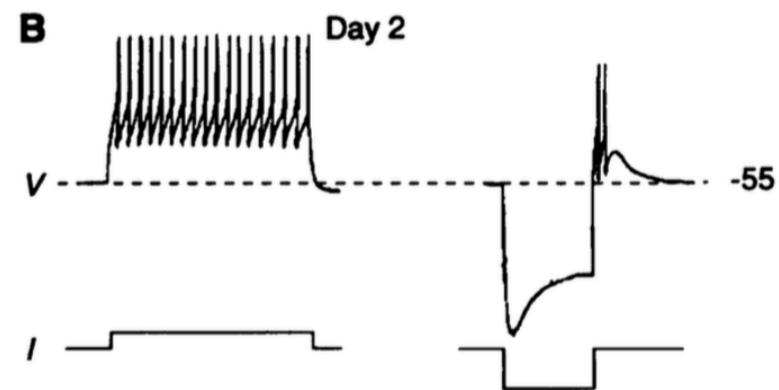
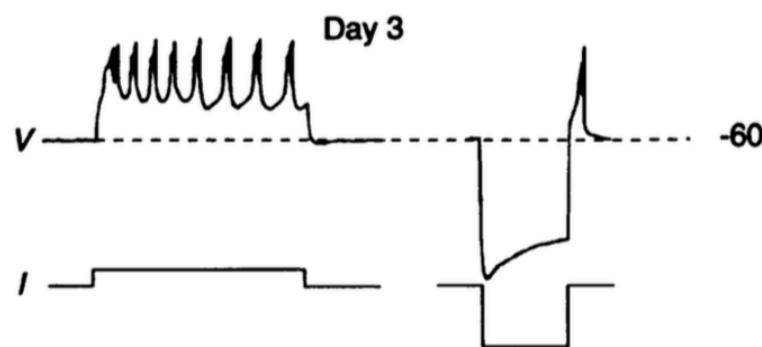
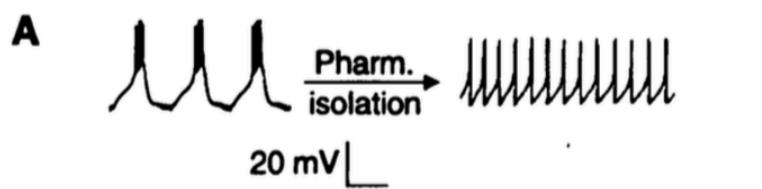


Elevated K^+

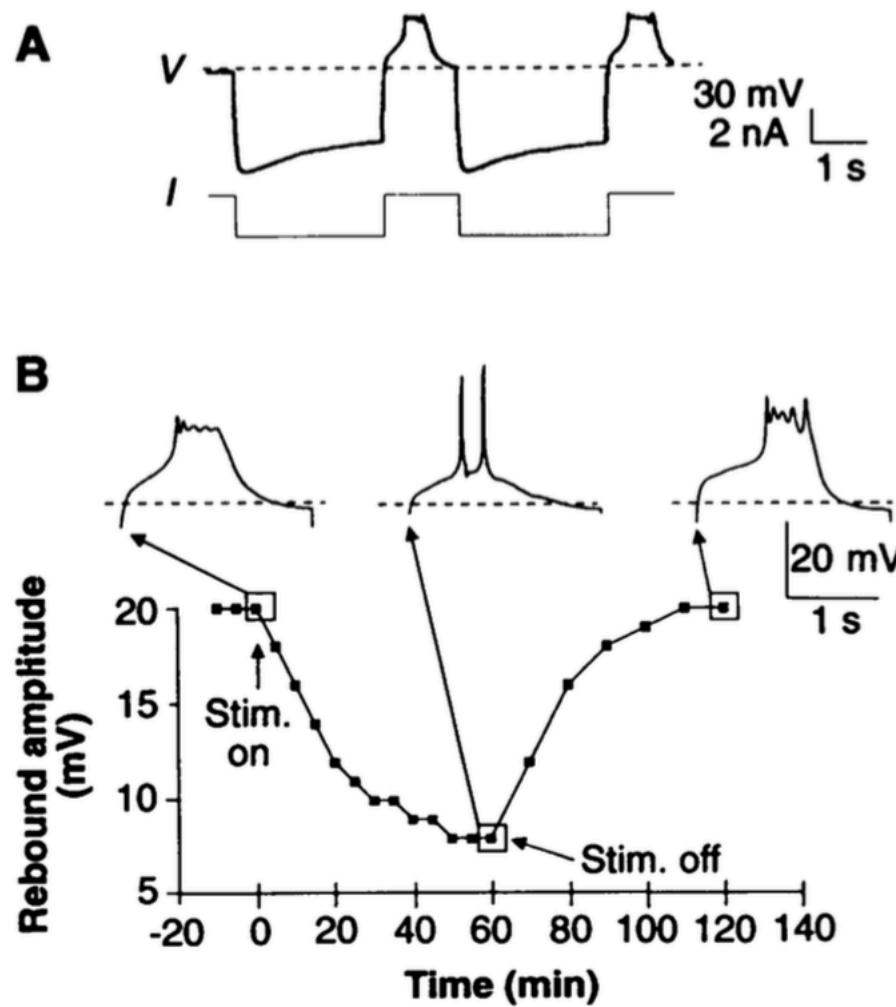
Change in model behavior



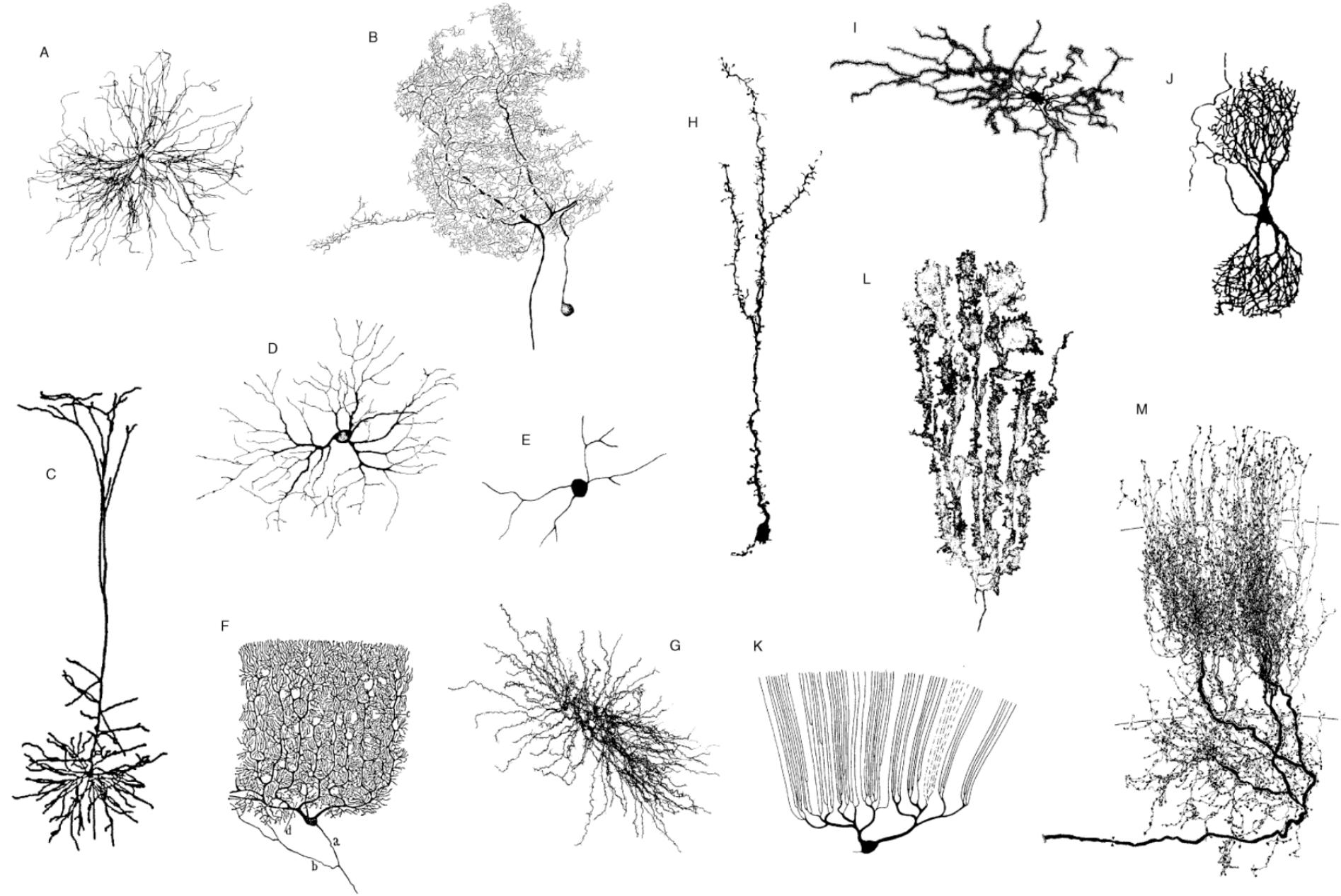
Cells change their physiological properties to burst



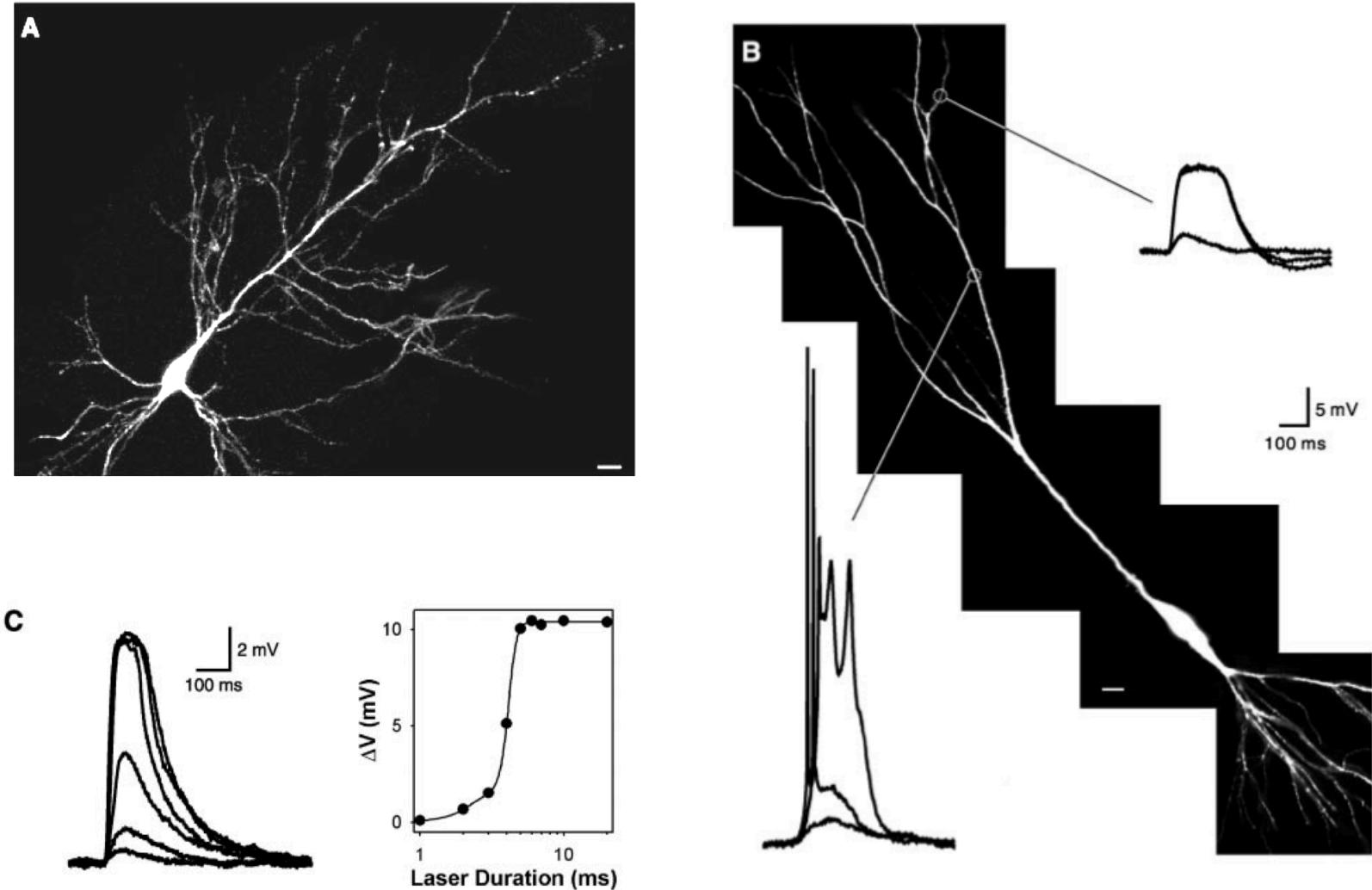
Turrigiano et al., 1994



What influence do dendrites have on computation?

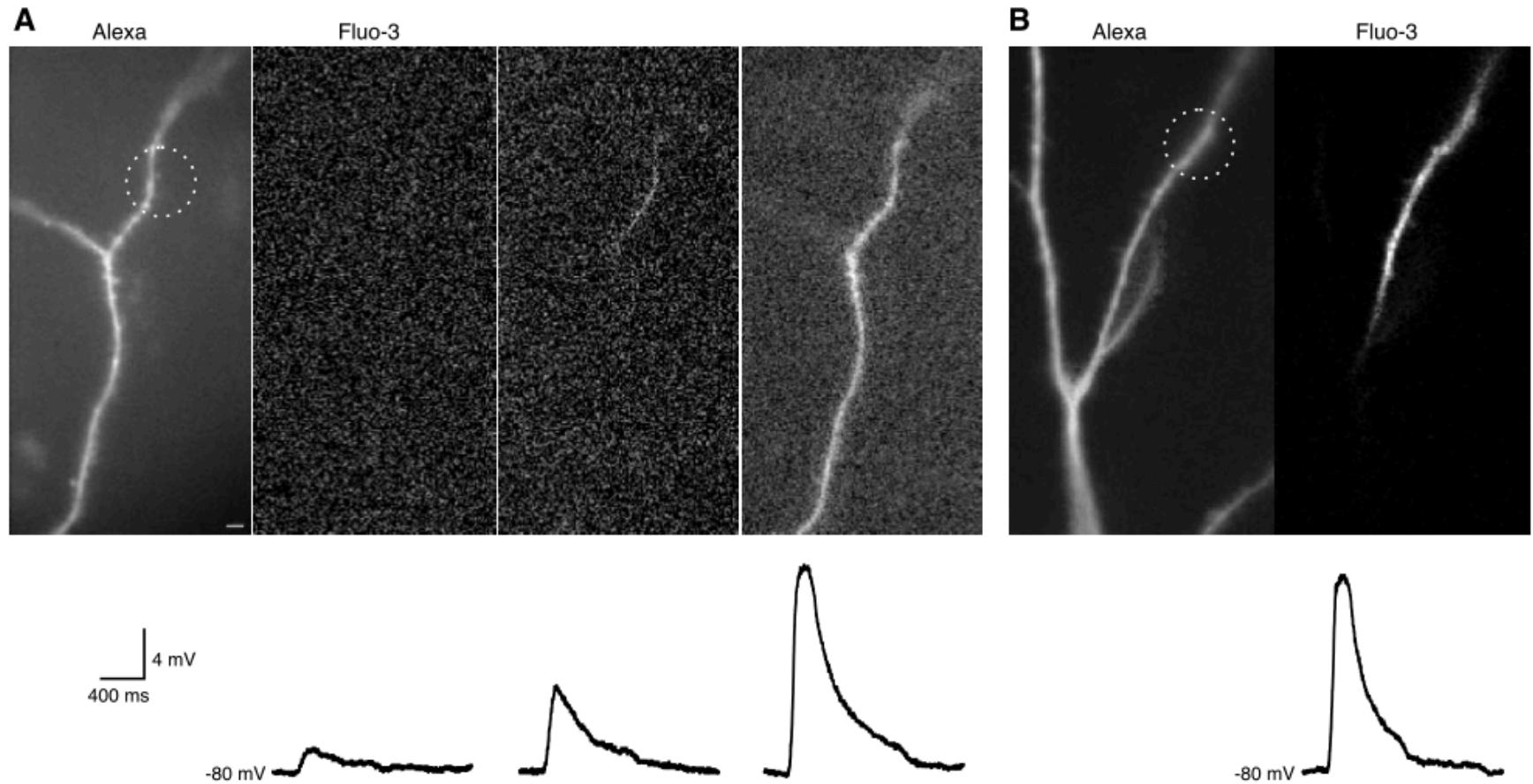


All or none calcium action potentials in pyramidal cell dendrites



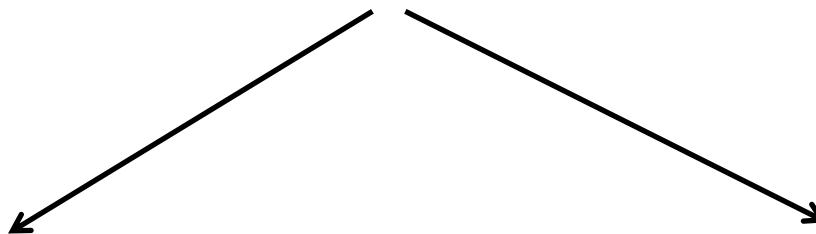
Wei et al., 2001. Compartmentalized and Binary Behavior of Terminal Dendrites in Hippocampal Pyramidal Neurons

Action potential failure at a dendritic branch point



Wei et al., 2001. Compartmentalized and Binary Behavior of Terminal Dendrites in Hippocampal Pyramidal Neurons

Properties of feature detection



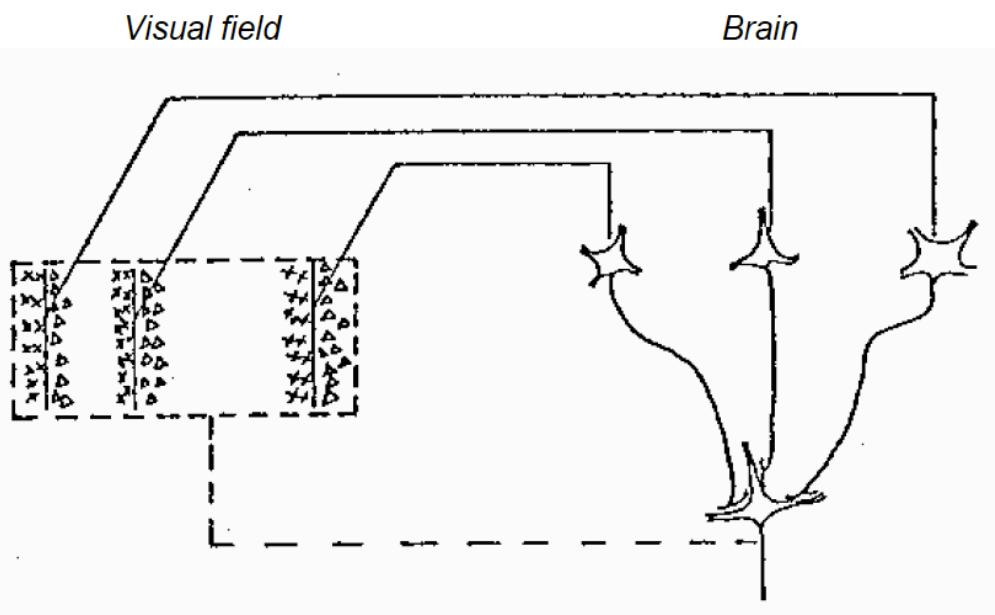
Selectivity



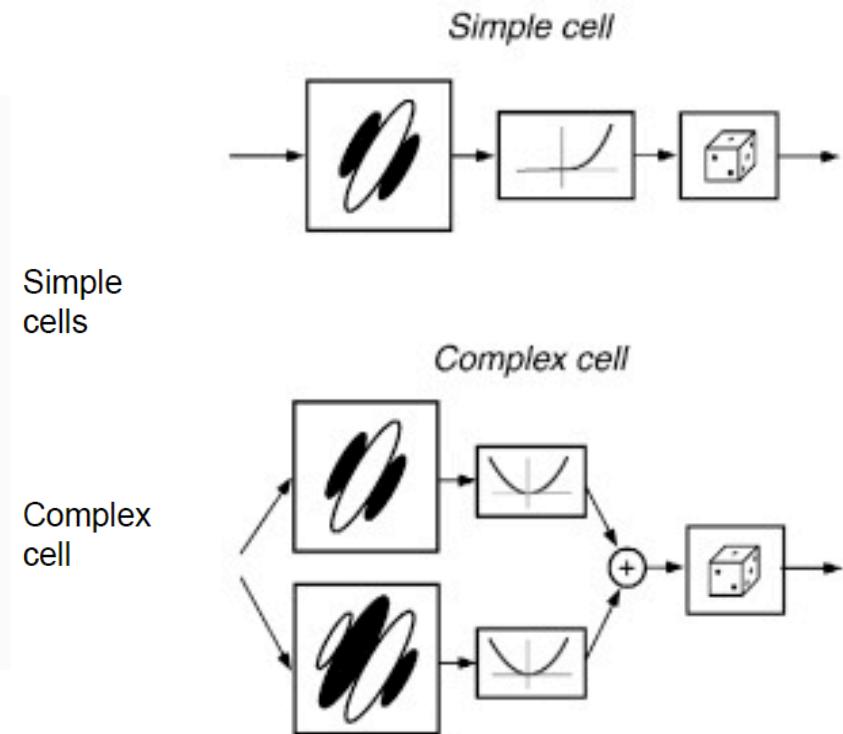
Invariance



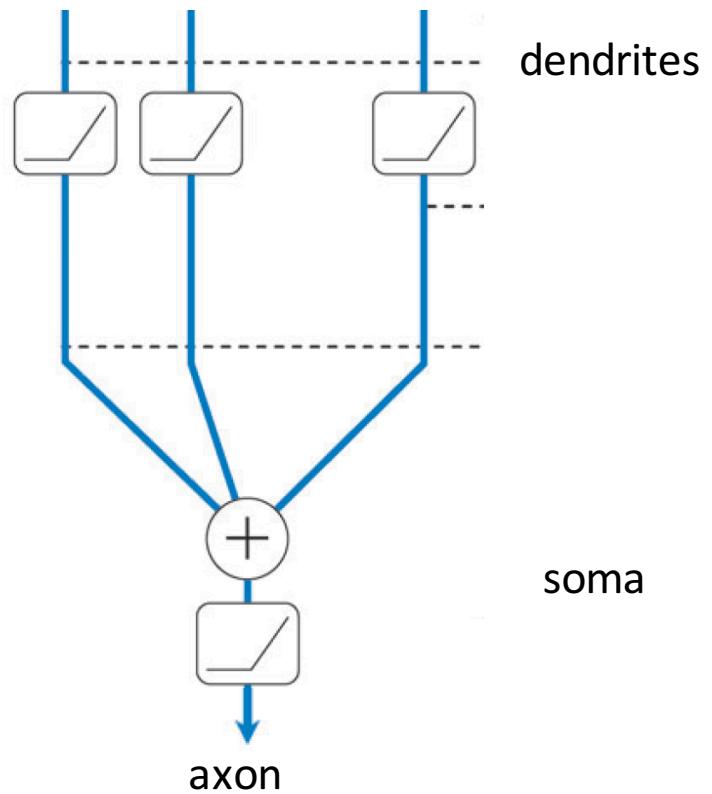
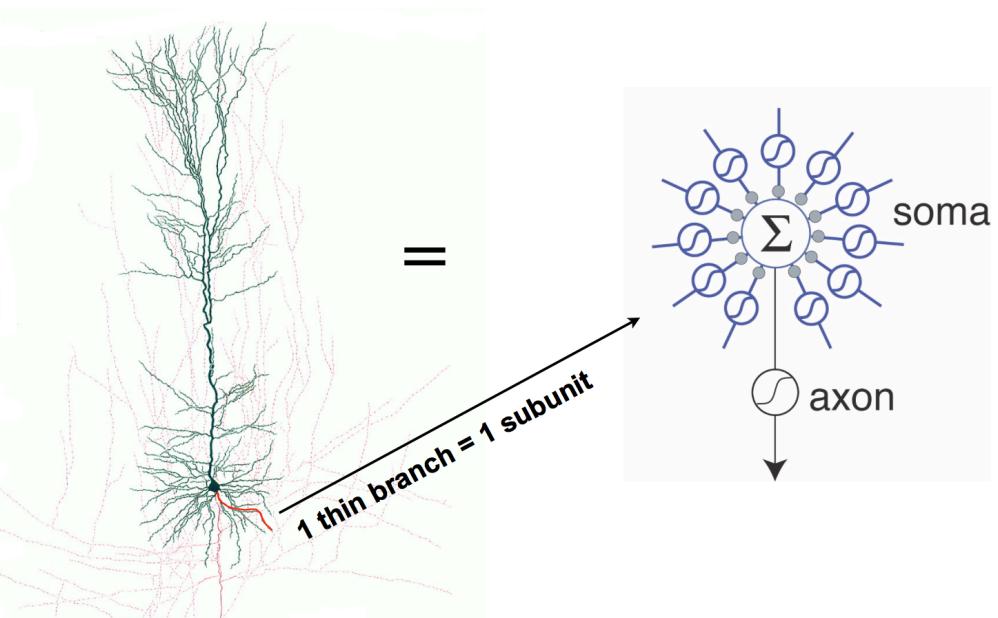
Models of selectivity and invariance in primary visual cortex



Hubel & Wiesel, 1963

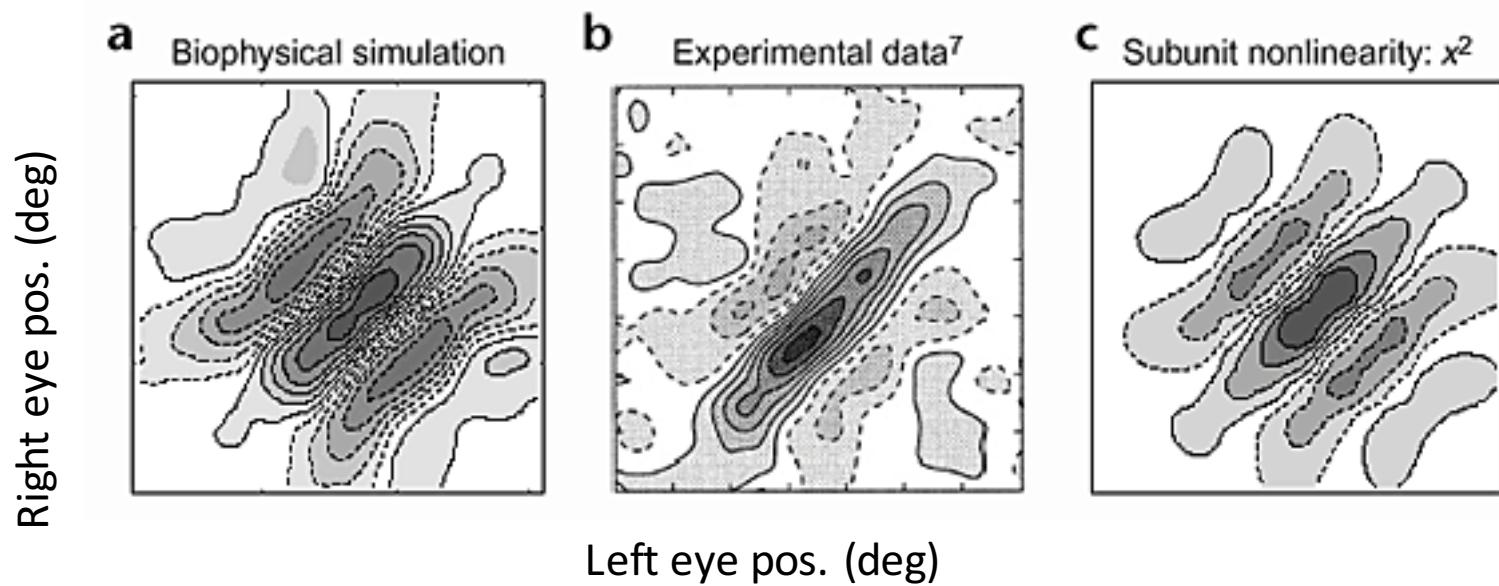


Rust et al., 2005



Model of Binocular Disparity Representation

Bar presented to left & right eyes



Archie & Mel (2000)