

NEPR 208 Introduction to Computational Neuroscience

Instructors:

Stephen Baccus (director)

John Huguenard

Surya Ganguli

Shaul Druckmann

Teaching Assistant: Gabriel Mel

Some questions of computational neuroscience

Neural Dynamics: How do the properties of individual neurons influence dynamics in neural networks?

Neural coding: What is the representation of information used by brains for sensory processing, information transmission, and motor control?

Circuit stability: How are circuits formed by genetics and experience, then maintained over the animal's lifespan despite extensive experience-dependent plasticity?

Actions: How are complex patterns generated? How are they modified by past performance?

Decisions: How do animals choose between different actions? What biophysical and circuit mechanisms underlie the process of accumulating information, and then making distinct motor action.

Memory: How are short-term and long-term memory supported by neuronal circuits? What biochemical, synaptic, and network mechanisms involved?

Cognition: How is perception represented in the human brain, how are motivated decisions executed, and how does this process fail during disease?

Why Model?

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)

Joshua Epstein

<http://jasss.soc.surrey.ac.uk/11/4/12.html>

Outline for today

How can a neuron change its gain?

Integrate and fire model

Hodgkin-Huxley model

Dynamic Clamp

How can a neuron maintain a stable firing pattern?

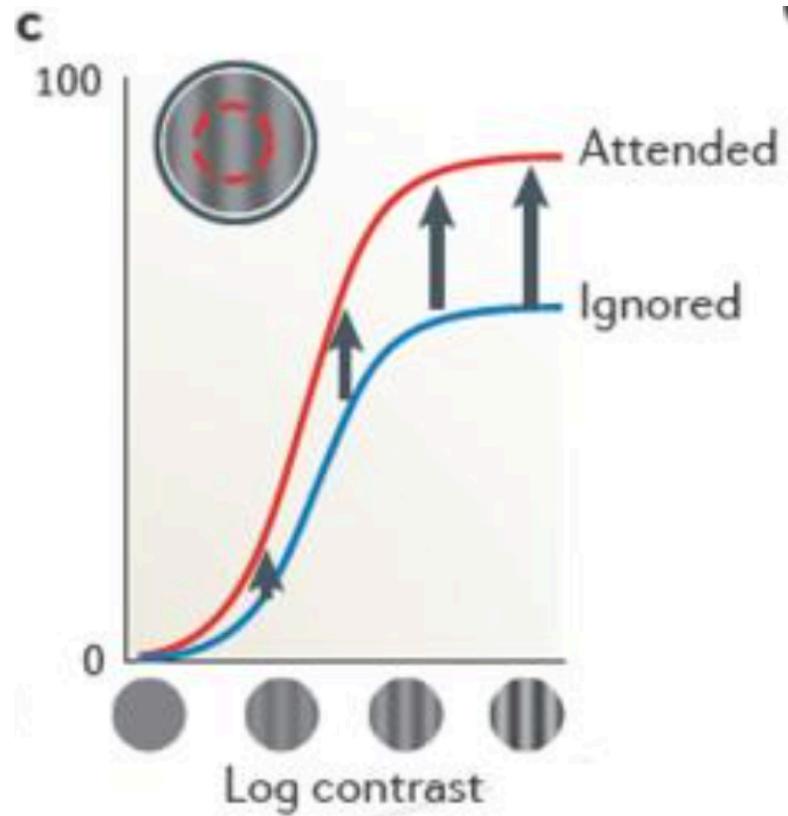
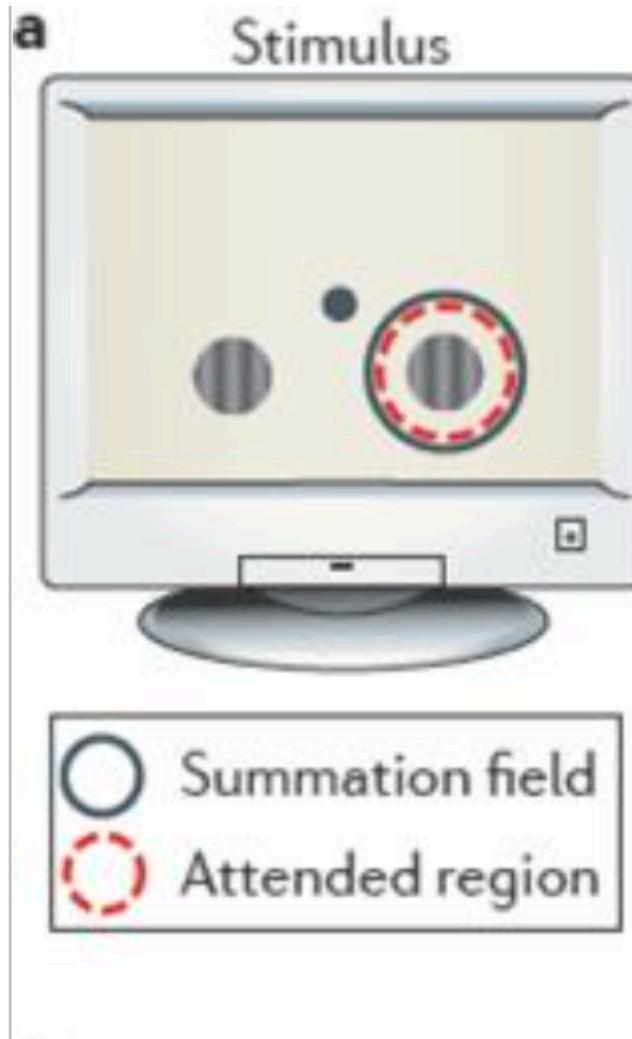
Crustacean stomatogastric ganglion

Phase constancy

Calcium as a feedback mechanism

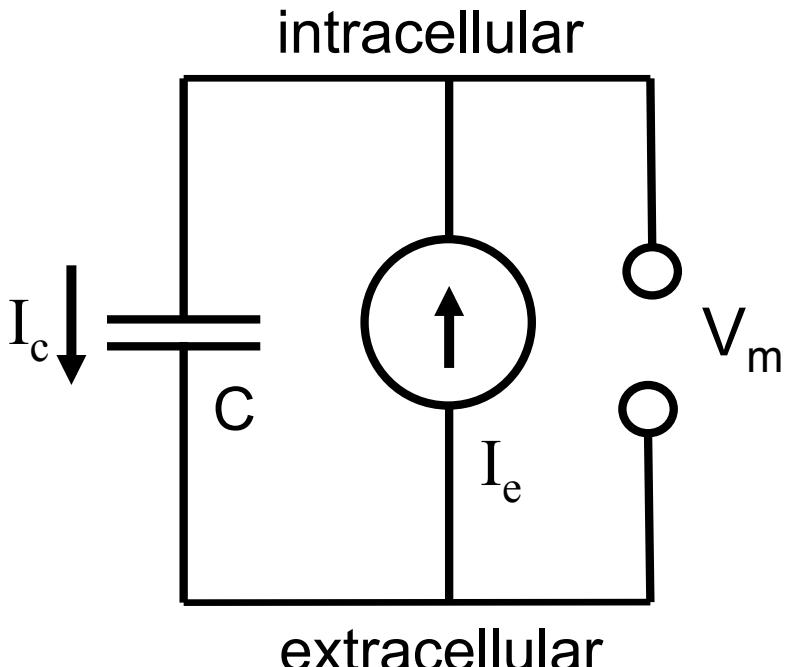
Changing gain in the nervous system

What cellular mechanisms could change the gain of a system?



Reynolds & Heeger, 2009

Membrane capacitance integrates the input



$$\Delta Q = C \cdot \Delta V$$

Definition of capacitive current

$$I_c(t) = \frac{dQ}{dt} = C \frac{dV_m}{dt} + V \cancel{\frac{dC}{dt}}$$

$$I_e(t) = C \frac{dV_m}{dt}$$

I_e has units of Amperes, which is Coulombs per second

$$V_m(t) = V_0 + \frac{1}{C} \int_0^t I_e(\tau) d\tau$$

Membranes have resistance and capacitance

Kirchhoff's Current Law

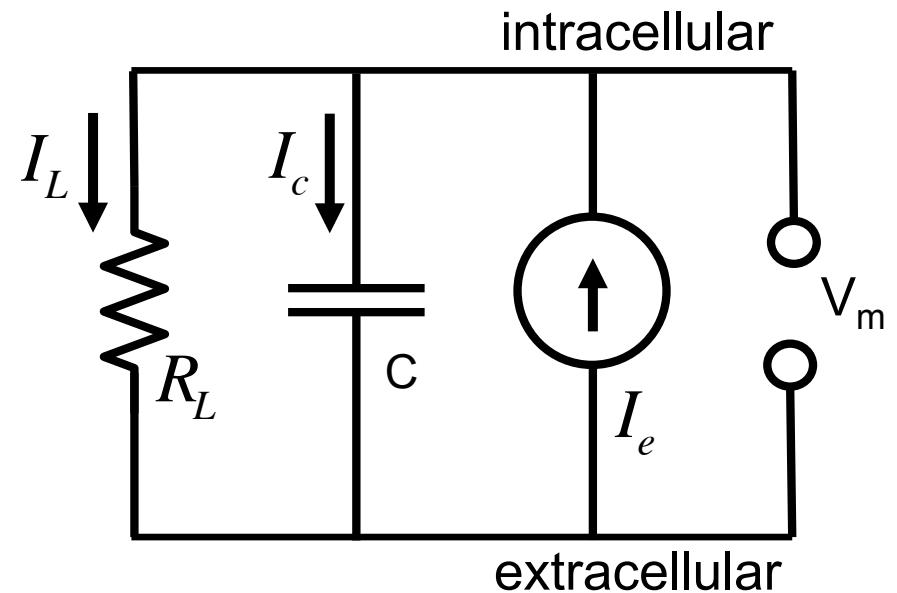
$$I_L + I_c - I_e = 0$$

$$I_L + C \frac{dV_m}{dt} = I_e$$

membrane capacitive current
membrane ionic current

$$\frac{V_m}{R_L} + C \frac{dV_m}{dt} = I_e$$

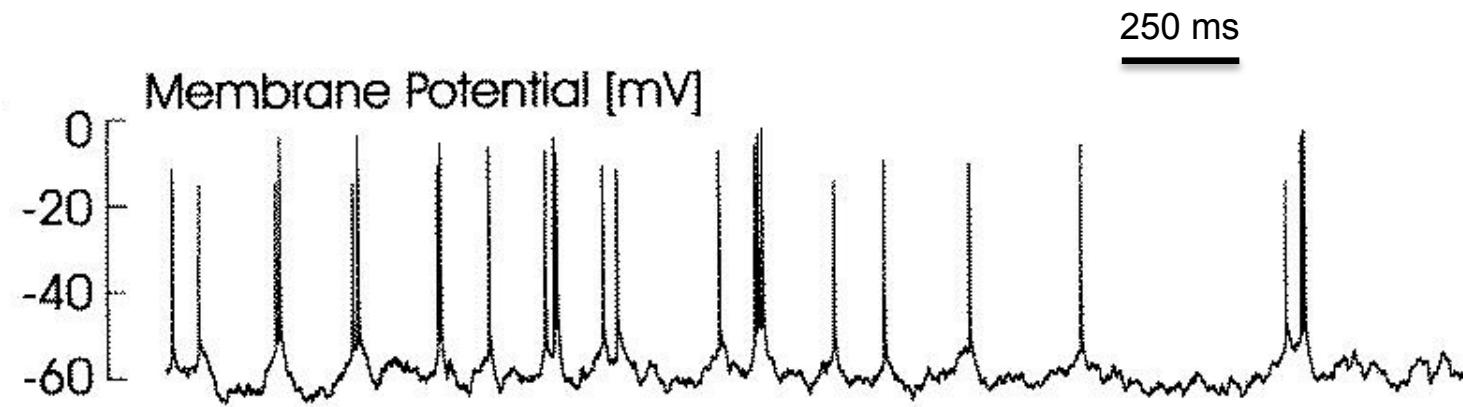
outward current
'leaving the cell' \Rightarrow positive

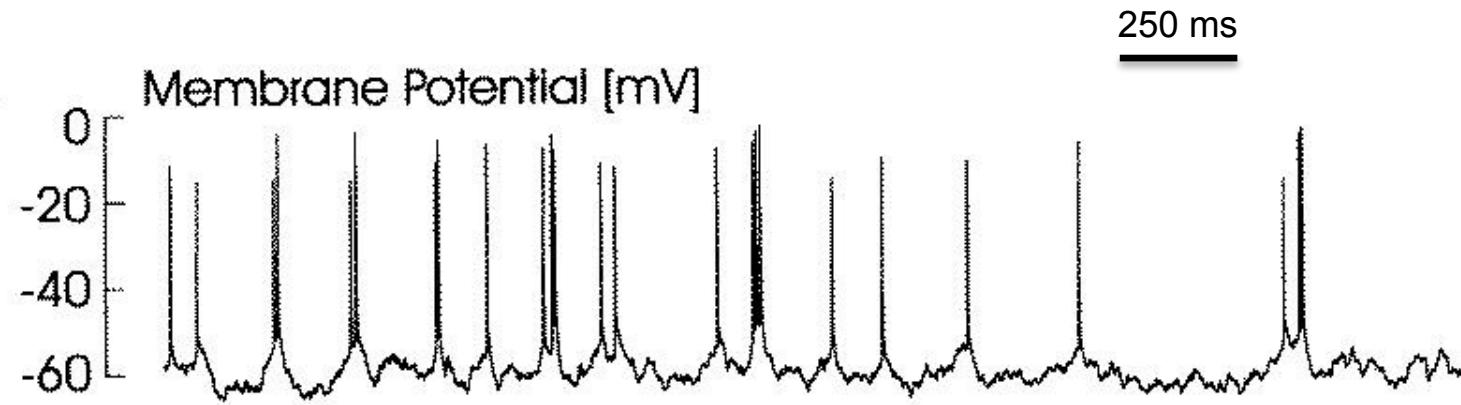


electrode current

inward current
'+' entering the cell \Rightarrow negative

Neurons spike, how do we model that?





Action potentials are fast (~ 1 ms), and usually occur infrequently.

Most of the time, a neuron is ‘integrating’ its inputs.

All spikes are the same, only occurrence of spikes matter (mostly).

What if we want to represent, roughly, integration of inputs and crossing a threshold?

Multiplying by R_L , we get:

$$V_m + R_L C \frac{dV_m}{dt} = R_L I_e$$

What is the steady state solution?

$$V_m \Rightarrow V_\infty = R_L I_e$$

Thus, we can rewrite our equation as follows

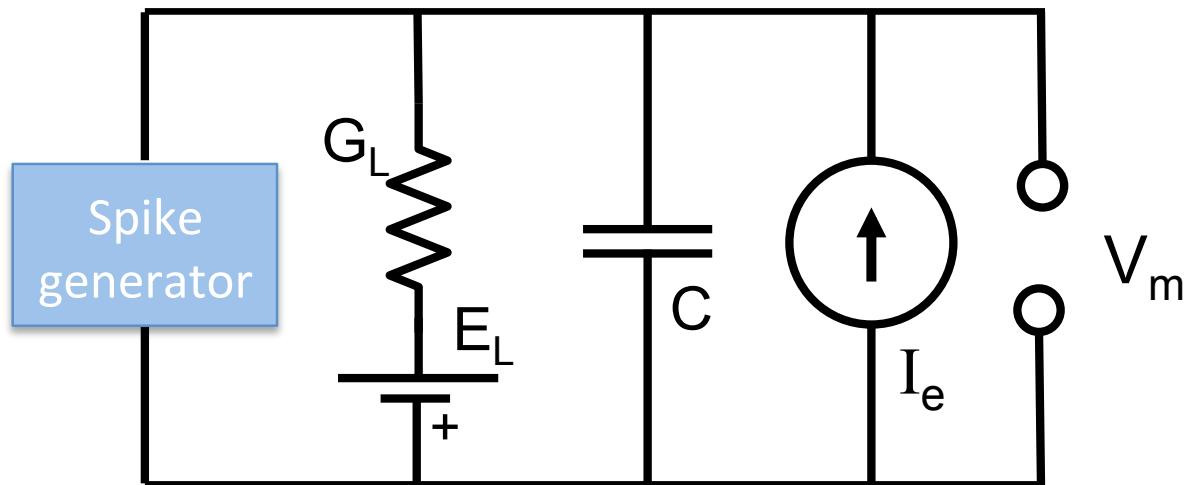
$$V_m + \tau \frac{dV_m}{dt} = V_\infty \quad \text{where } \tau = R_L C$$

When I_e is constant (and thus V_∞ is constant):

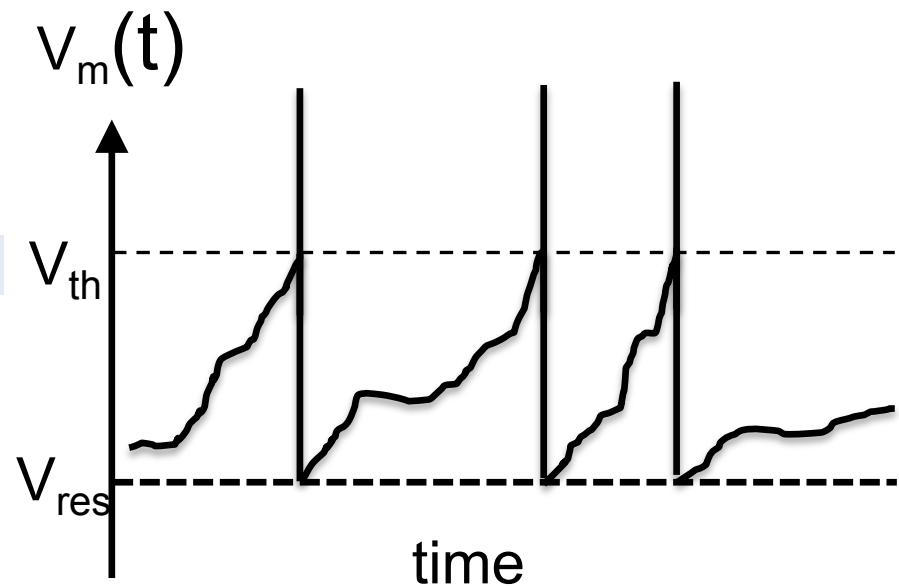
$$V(t) - V_\infty = (V_0 - V_\infty) e^{-t/\tau}$$

Integrate and fire model of a neuron

spikes as ‘events’. When the voltage reaches the threshold V_{th} , it resets the neuron to a hyper-polarized voltage V_{res} .



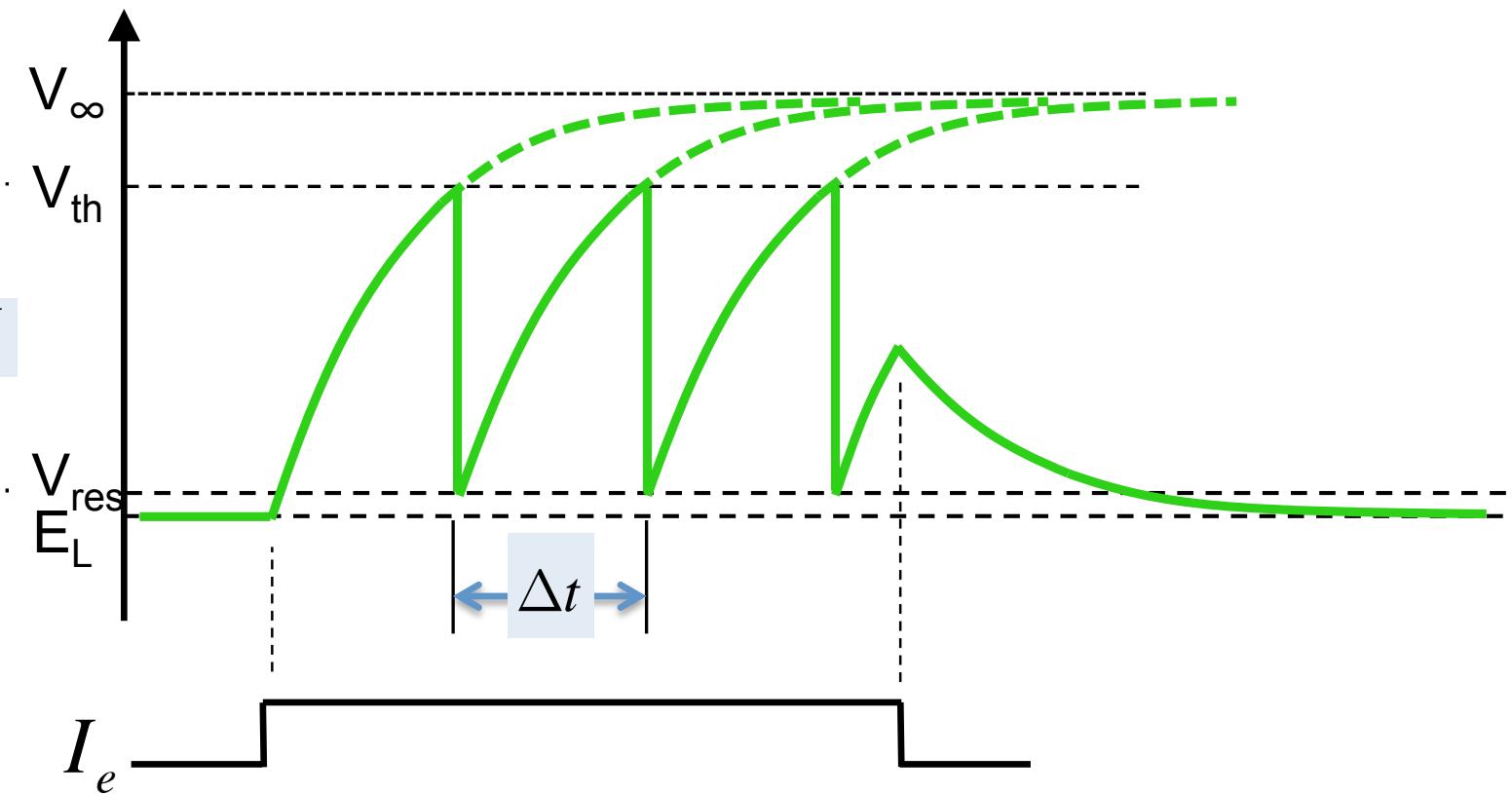
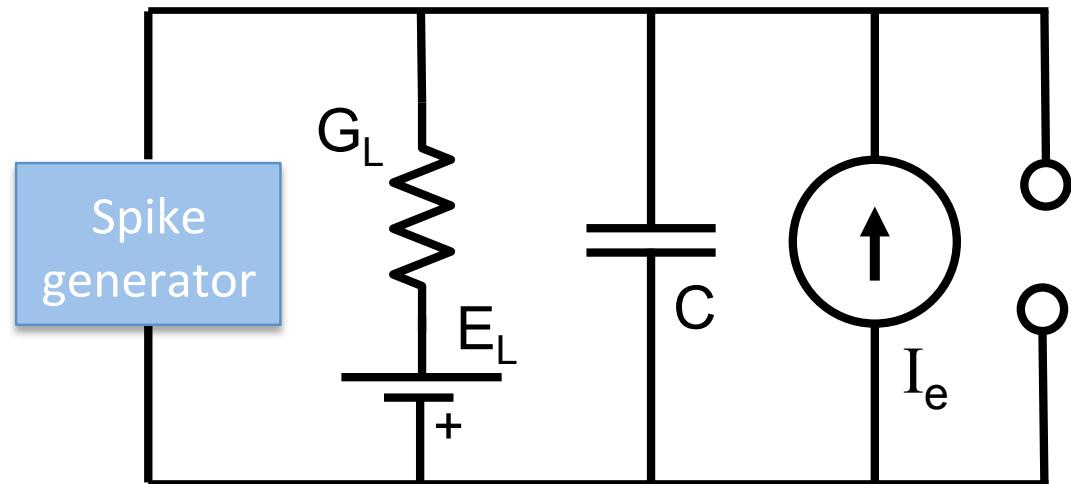
Louis Lapique, 1907



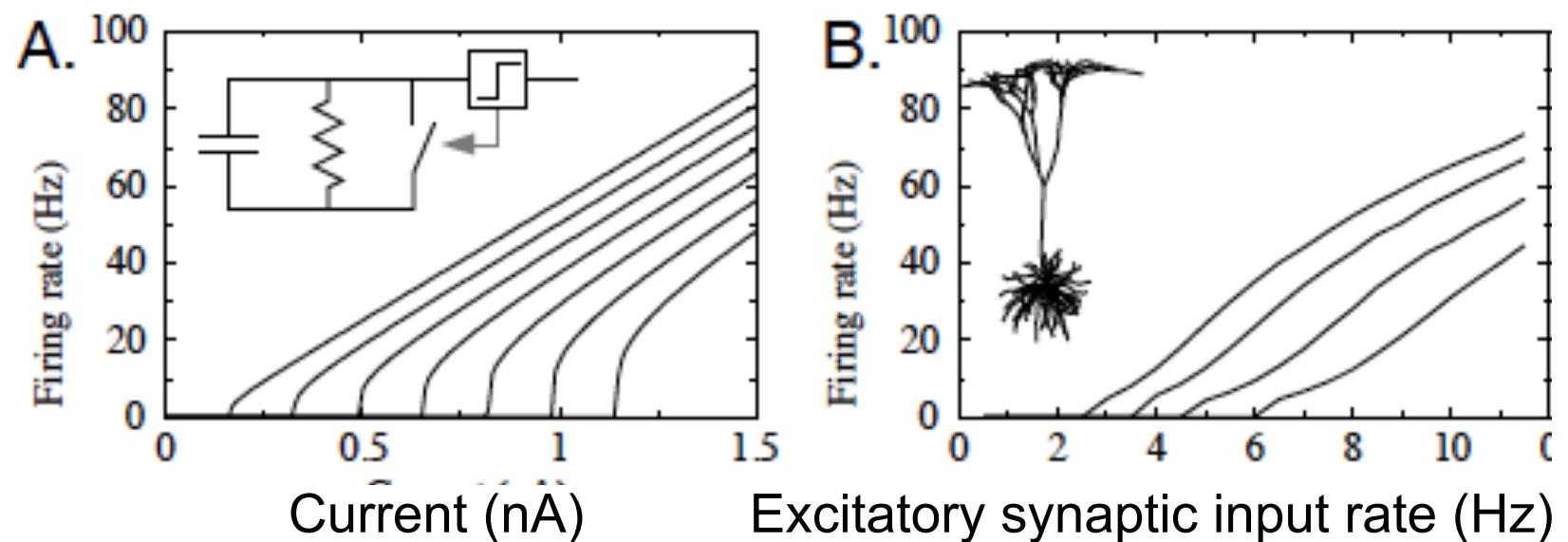
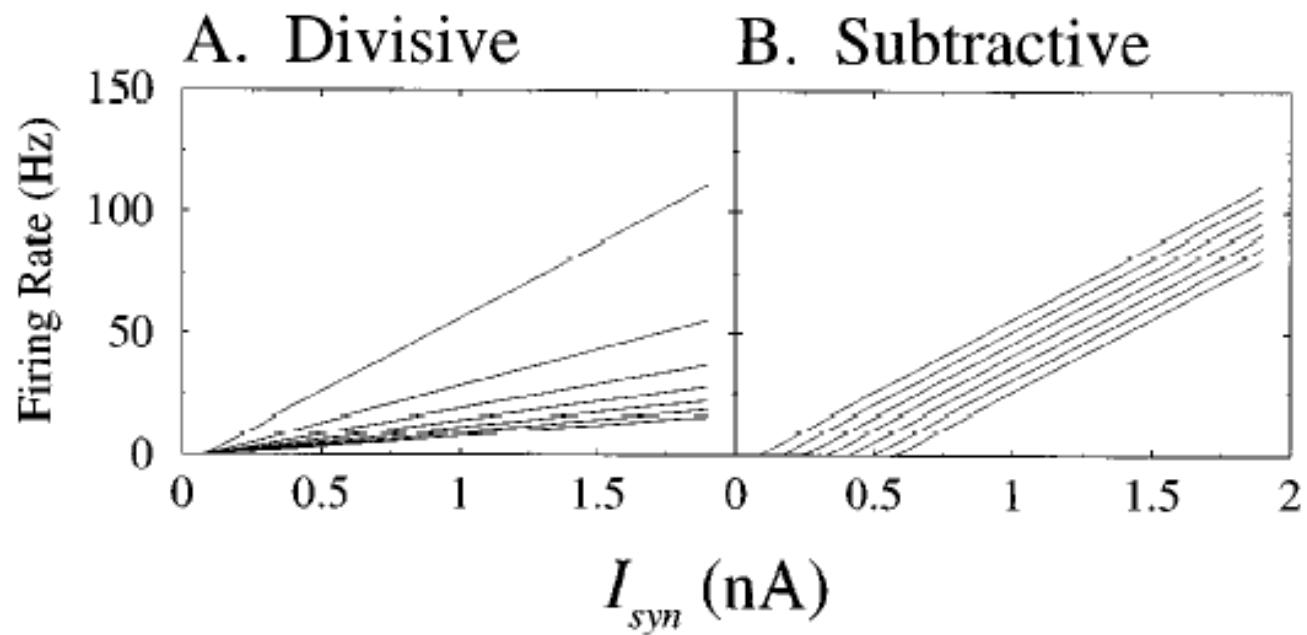
Integrate and fire model of a neuron

Conductance called 'leak'

$$+ \tau \frac{dV}{dt} = V_\infty, \quad V_\infty = E_L + R_L I_e$$

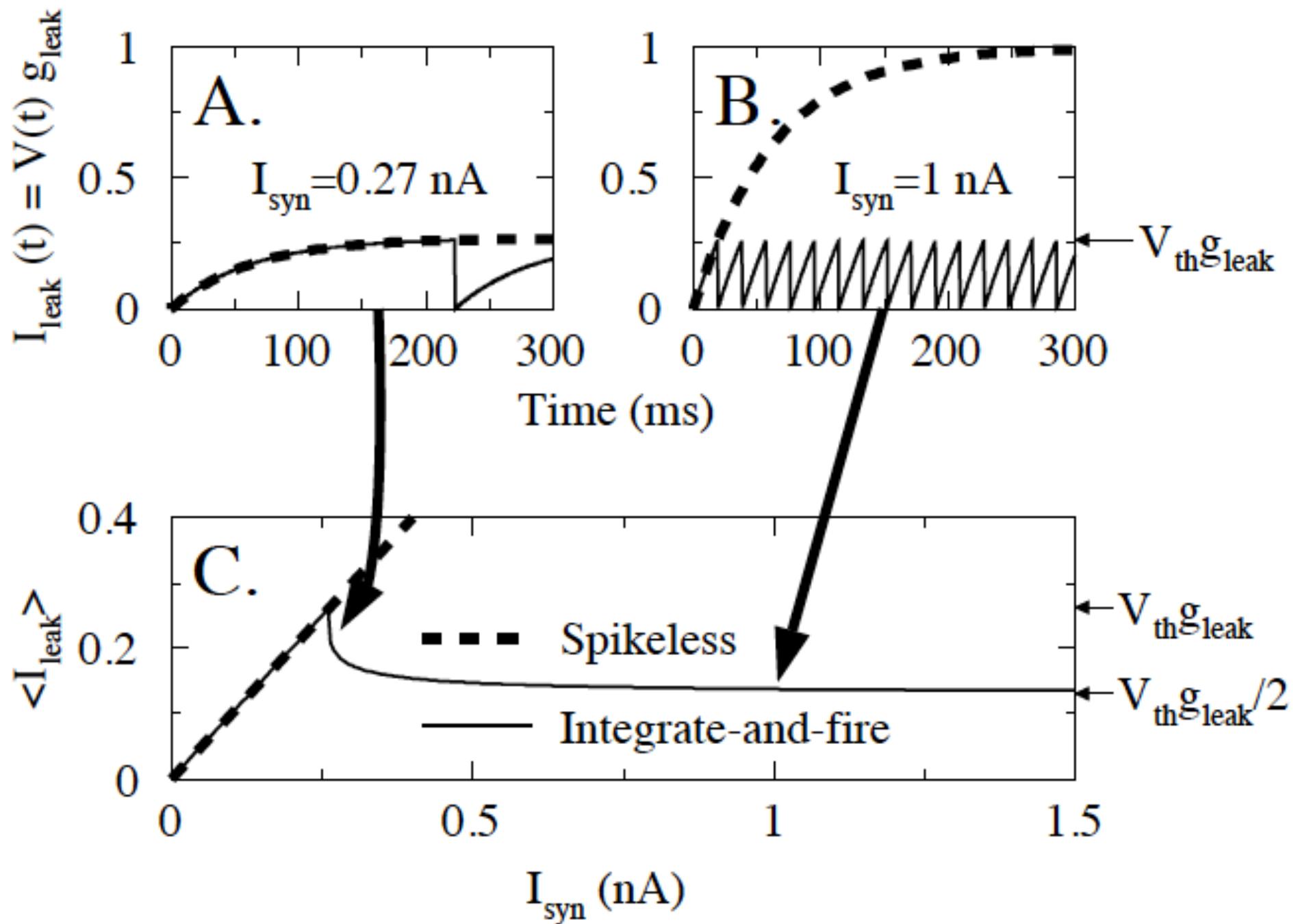


$$f.r. = \frac{1}{\Delta t}$$



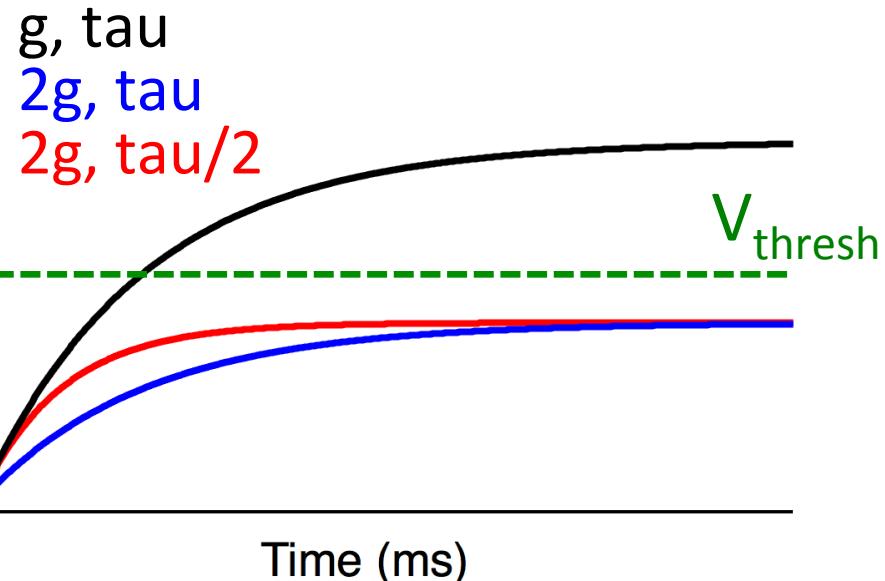
Holt & Koch, 1997. Shunting inhibition does not have a

Rapid spiking “clamps” the voltage making it independent of injected current

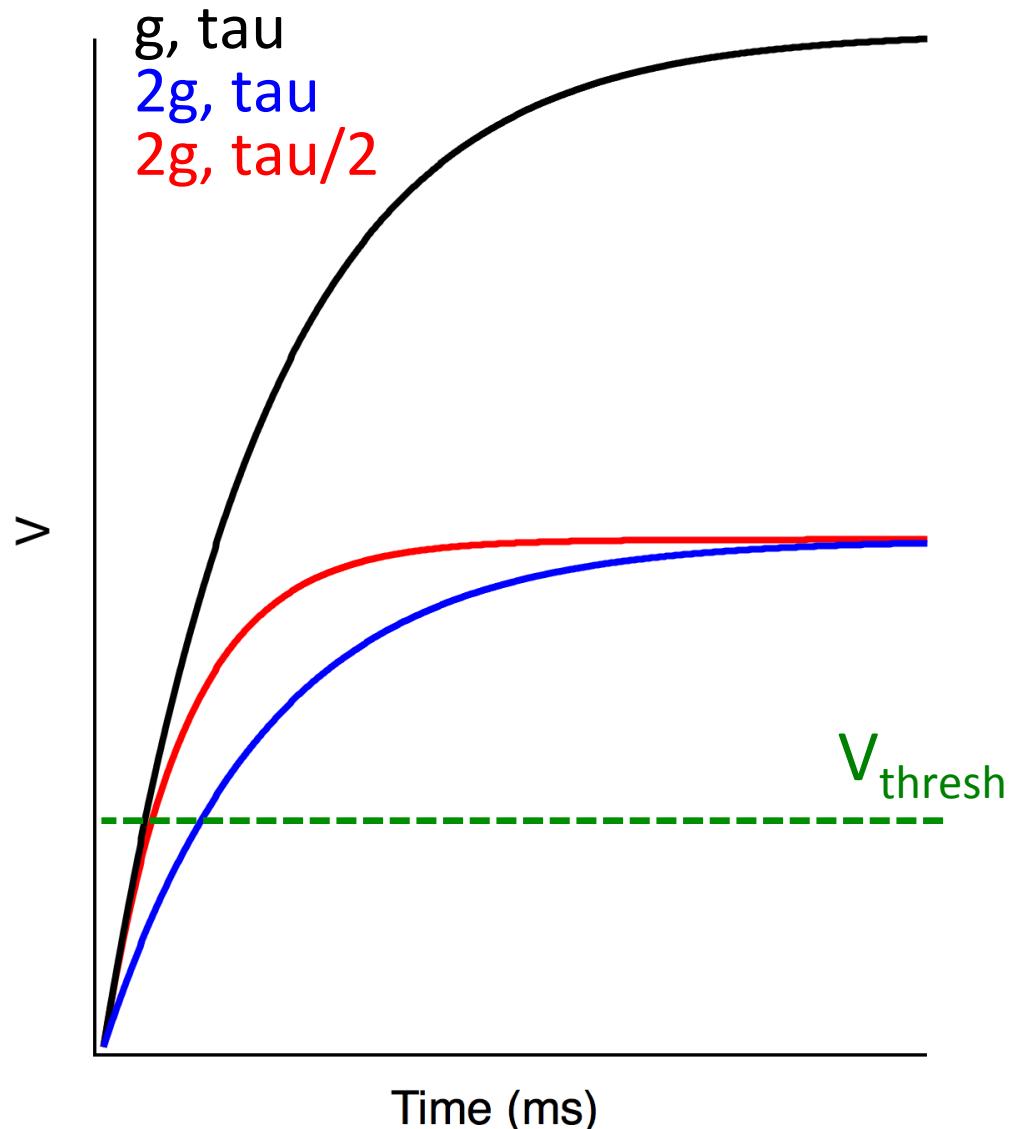


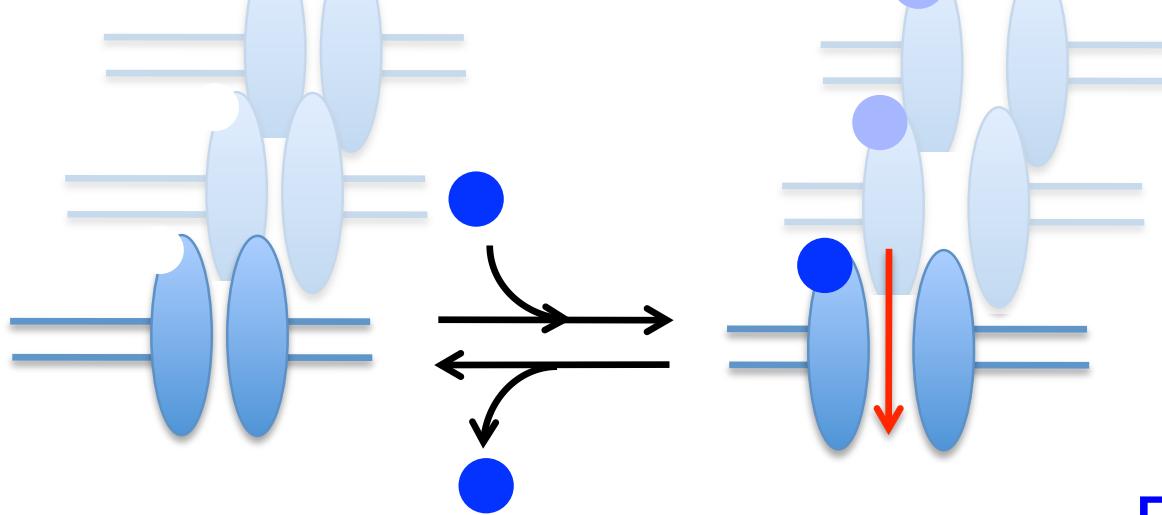
Shunting changes conductance, but also tau
with different effects for small and large currents

Small currents

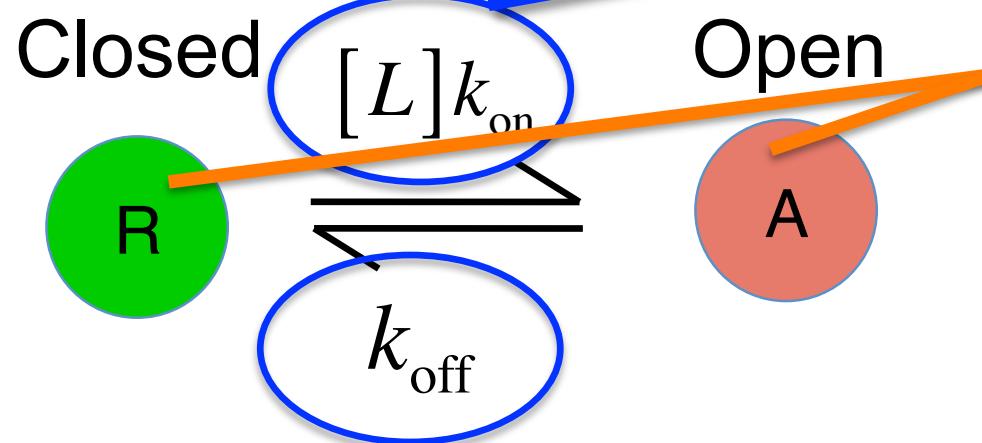


Large currents





Rate constants



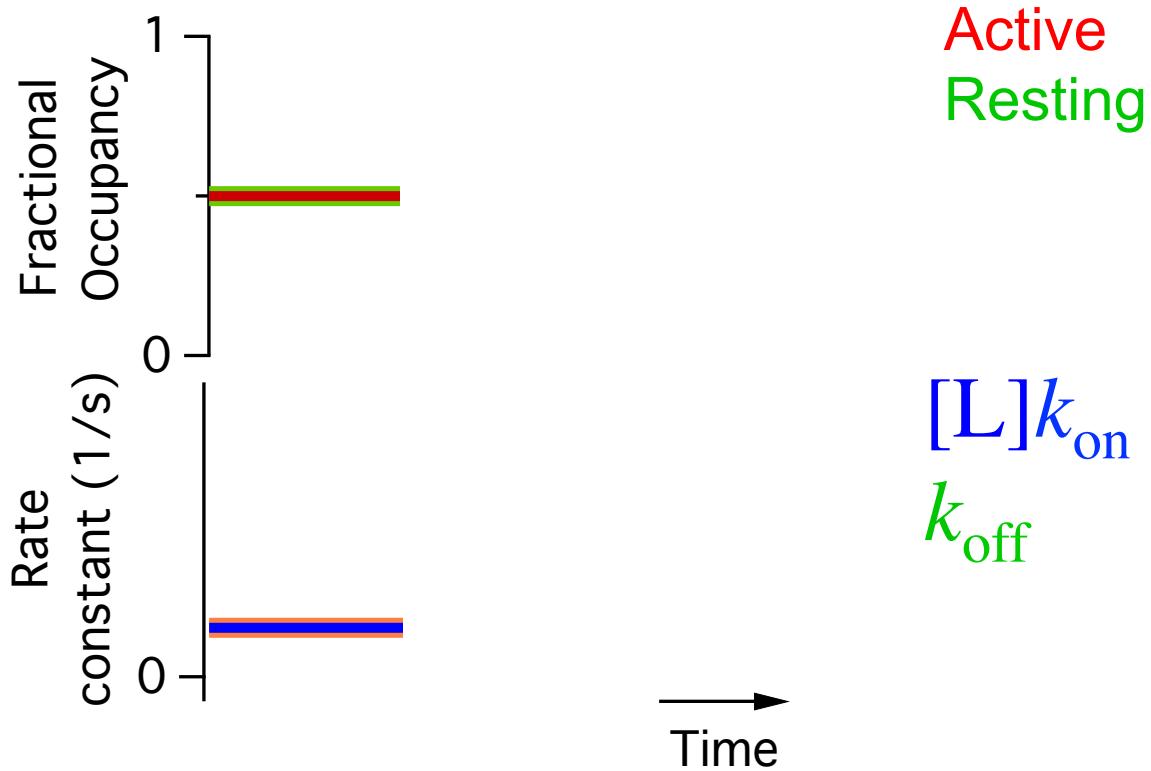
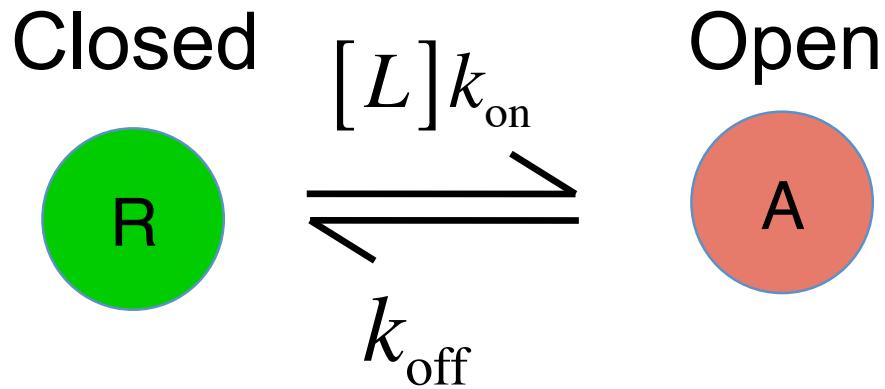
State
Occupancies
(sum to 1)

Change in activity = Inflow - Outflow

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

Kinetic model

Input and output in a kinetic model



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:

$$dn/dt = \alpha_n(V)(1 - n) - \beta_n(V)n$$

$$dm/dt = \alpha_m(V)(1 - m) - \beta_m(V)m$$

$$dh/dt = \alpha_h(V)(1 - h) - \beta_h(V)h$$

Rate “constants”:

$$\alpha_n(V) = \frac{10 - V}{100 (\exp((10 - V)/10) - 1)}$$

$$\alpha_m(V) = \frac{25 - V}{10 (\exp((25 - V)/10) - 1)}$$

$$\alpha_h(V) = 0.07 \exp(-V/20)$$

$$\beta_n(V) = 0.125 \exp(-V/80)$$

$$\beta_m(V) = 4 \exp(-V/18)$$

$$\beta_h(V) = \frac{1}{\exp((30 - V)/10) + 1}$$

Constants:

$$C = 1 \mu\text{F}/\text{cm}^2$$

$$\bar{g}_K = 36 \text{ mS}/\text{cm}^2$$

$$\bar{g}_{Na} = 120 \text{ mS}/\text{cm}^2$$

$$\bar{g}_l = 0.3 \text{ mS}/\text{cm}^2$$

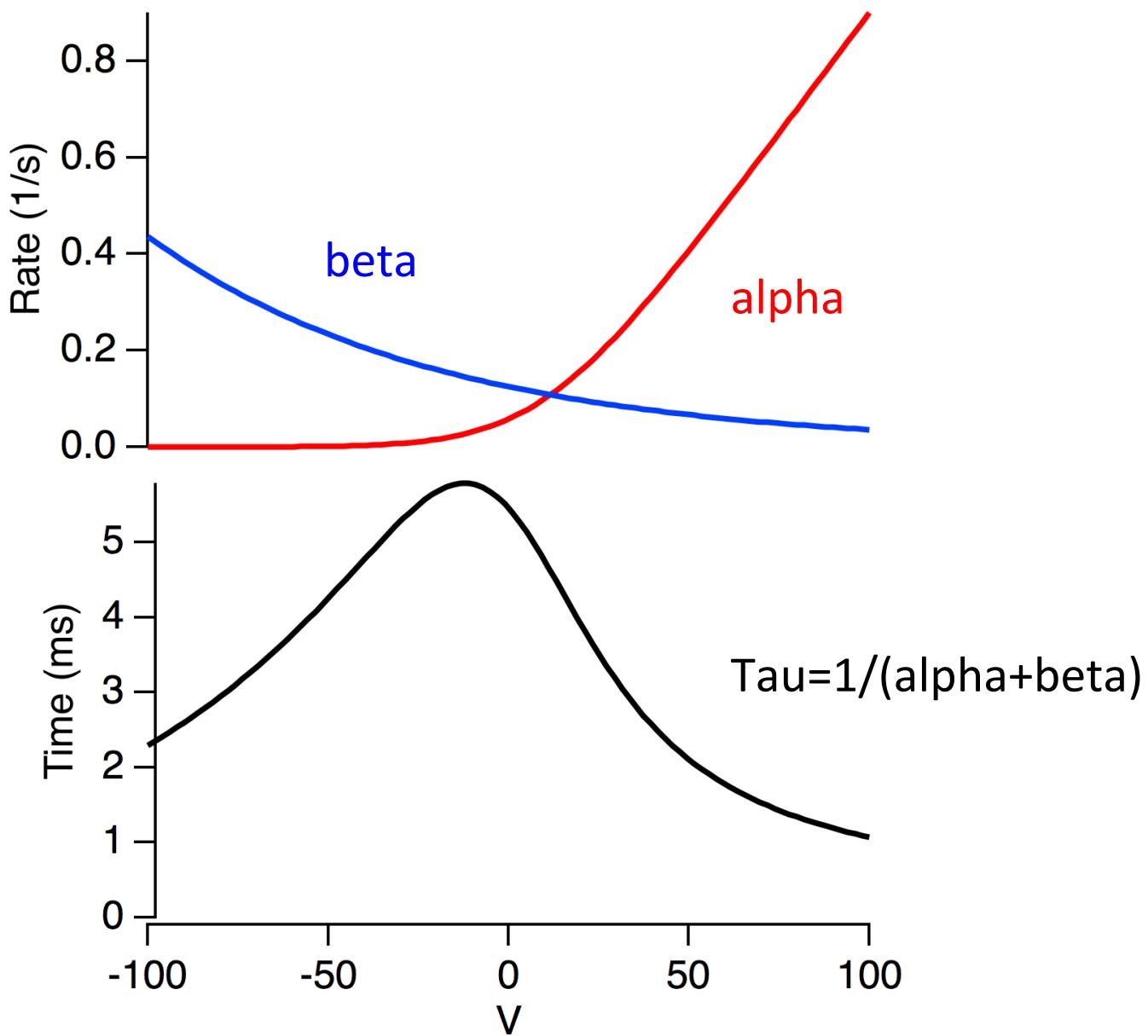
$$E_K = -12 \text{ mV}$$

$$E_{Na} = +115 \text{ mV}$$

$$E_l = +10.613 \text{ mV}$$

Note: these are given in the original form, relative to $V_{\text{rest}} \approx -66 \text{ mV}$

Tau is slow when both rate constants are slow



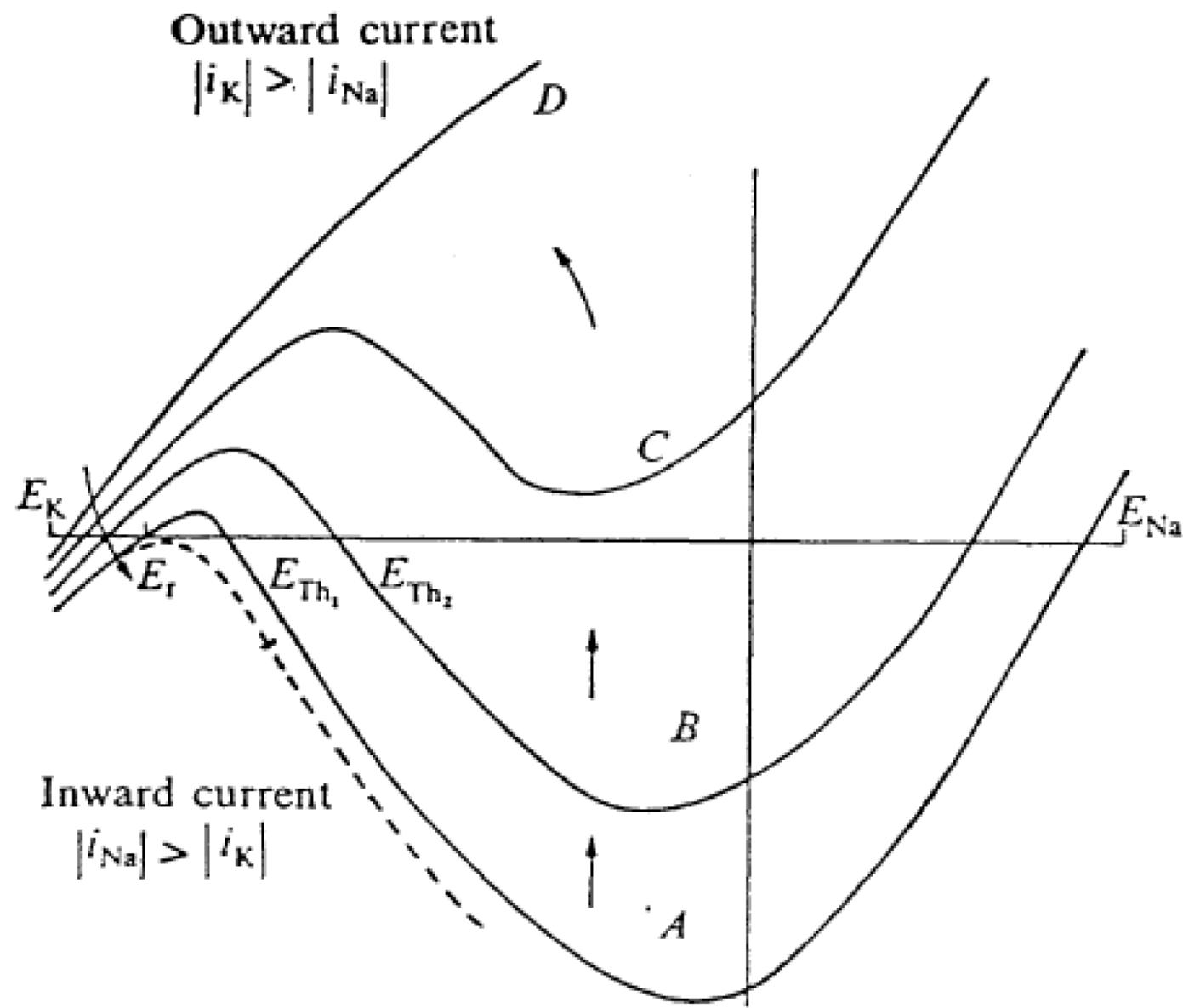
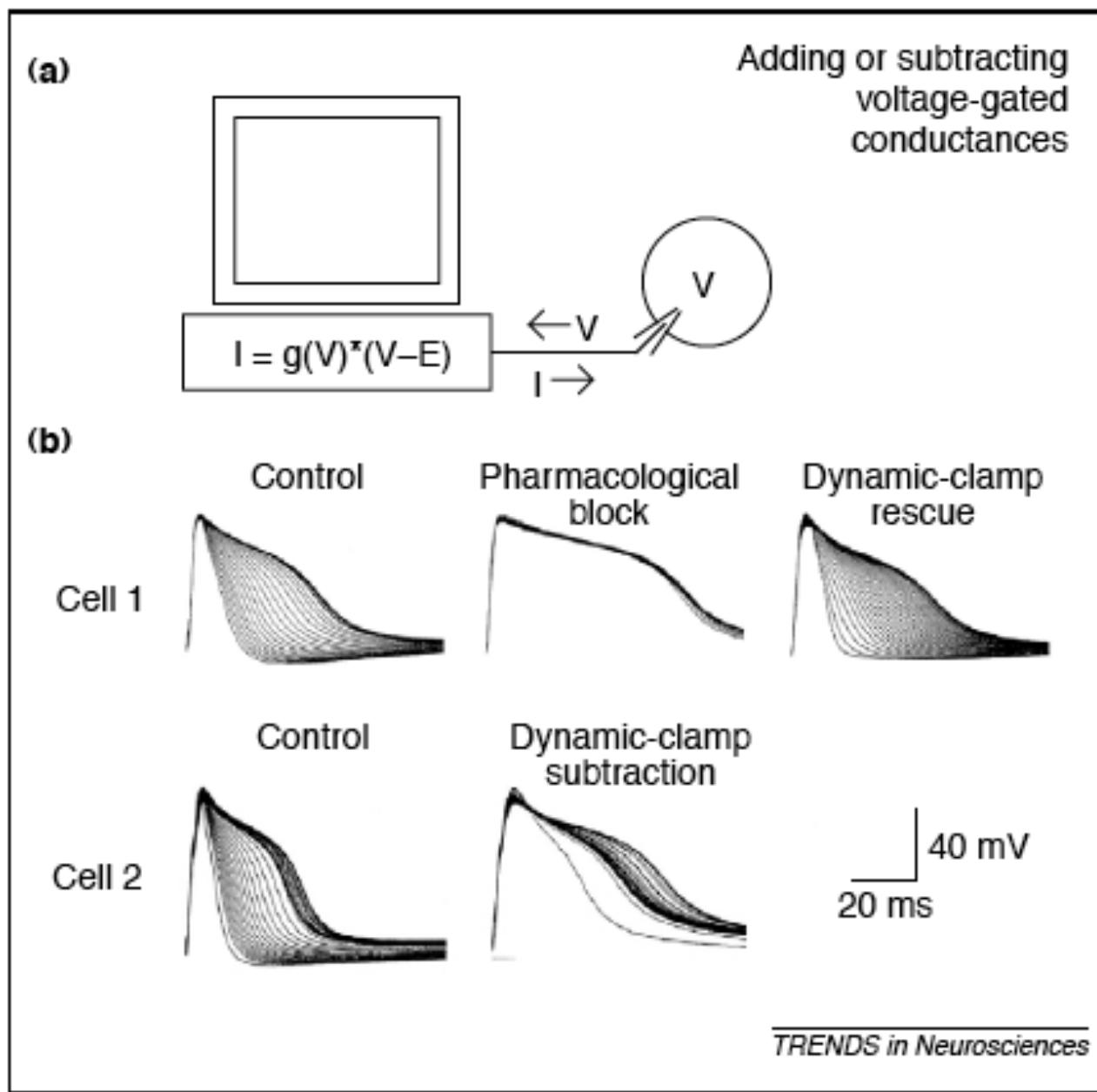


FIG. 8.12. Diagram illustrating change in momentary current-voltage relations with time on depolarization.

The dynamic clamp

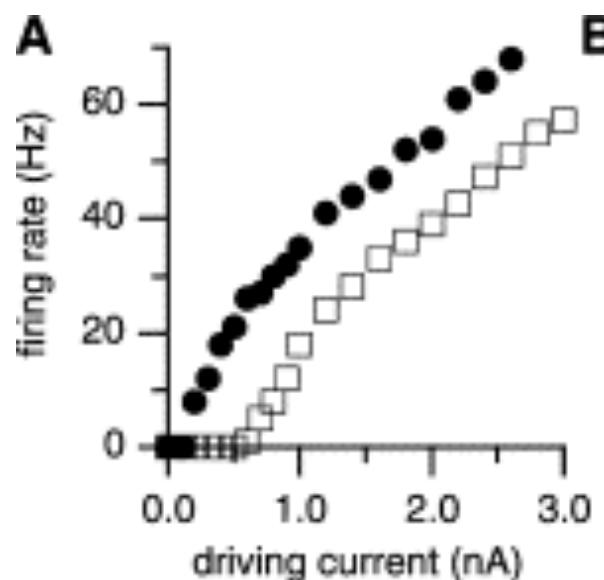
Artificially adding or subtracting membrane mechanisms



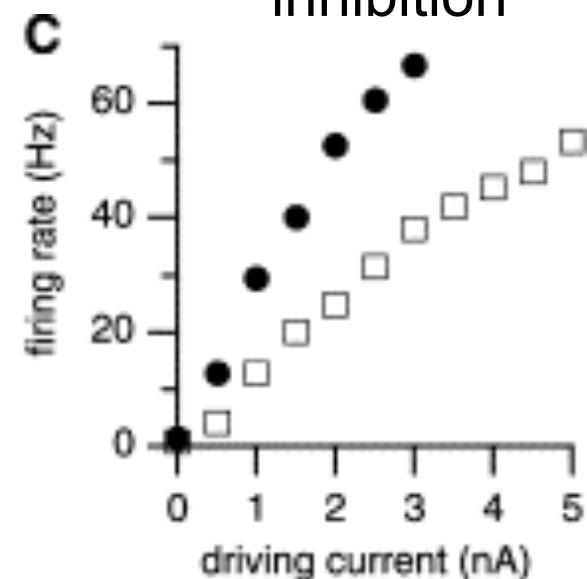
Balanced excitation and inhibition can change gain

Rat somatosensory cortex slice

Shunting inhibition alone



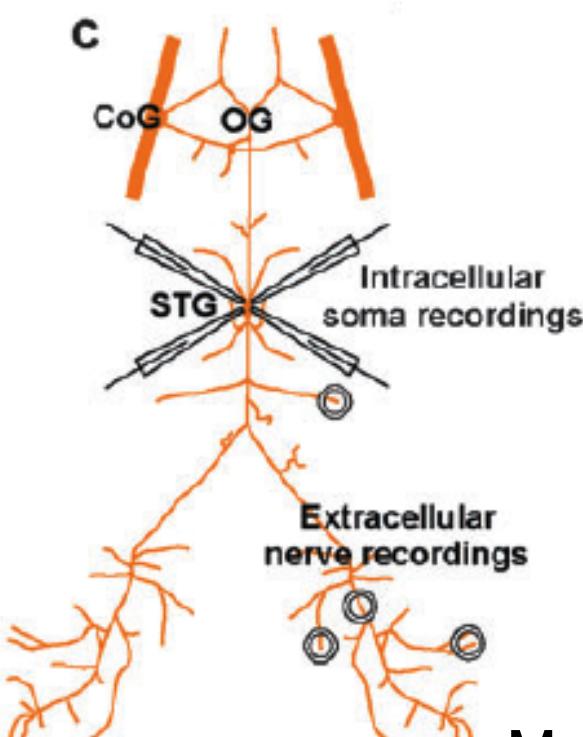
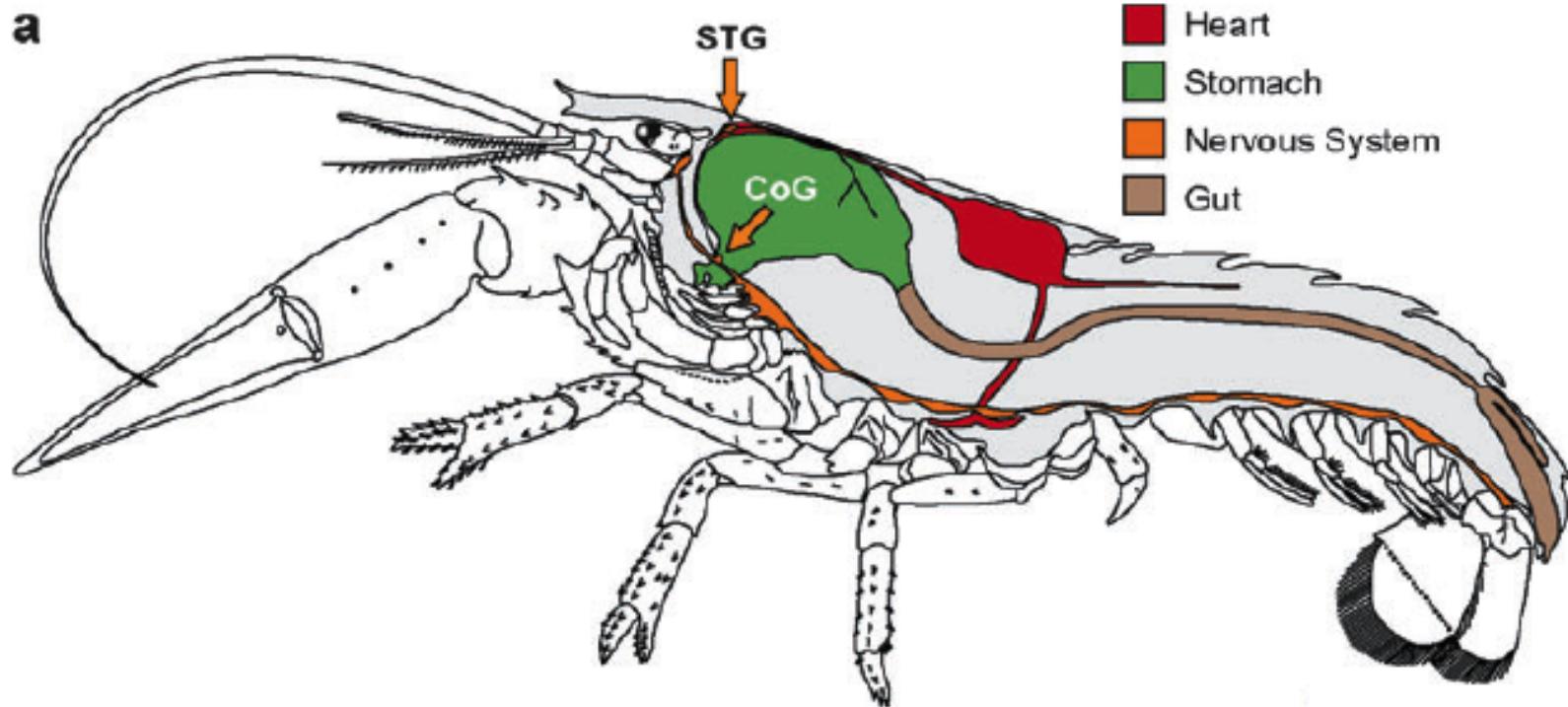
Balanced excitation and inhibition



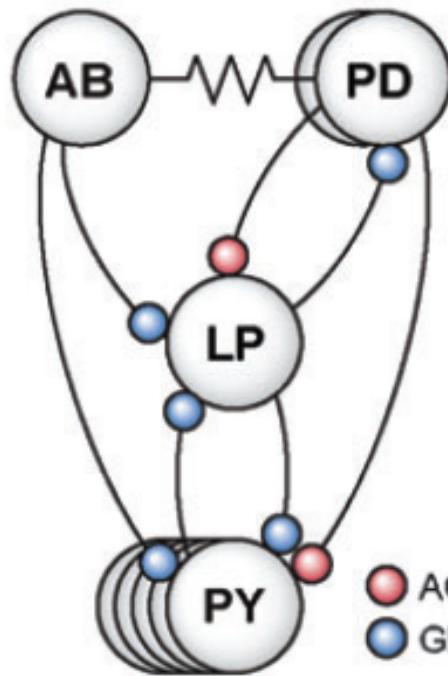
Chance, Abbott & Reyes. (2002) Gain modulation from background synaptic input.

How can a neuron maintain a stable firing pattern?

Crustacean stomatogastric ganglion

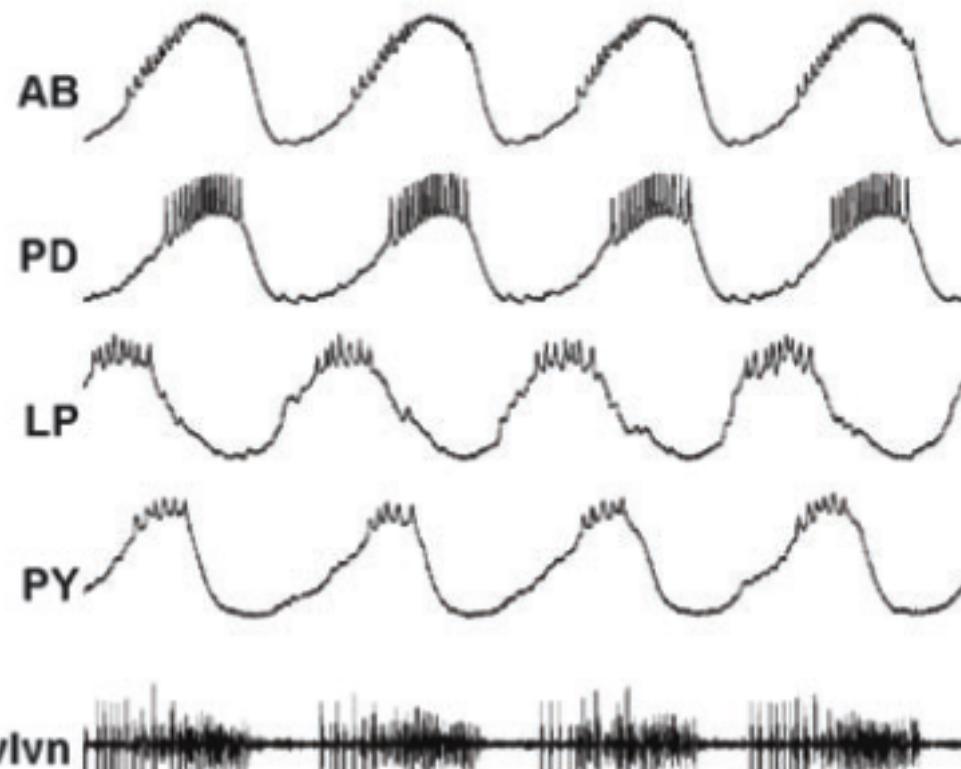
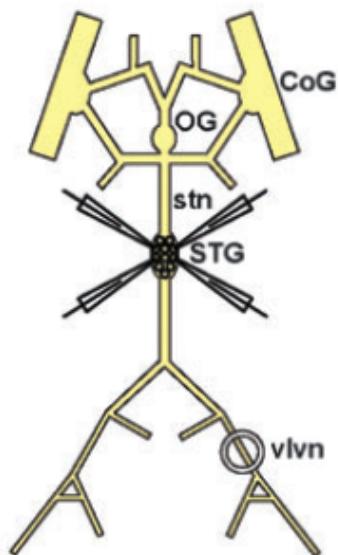


Pyloric oscillator of the stomatogastric ganglion

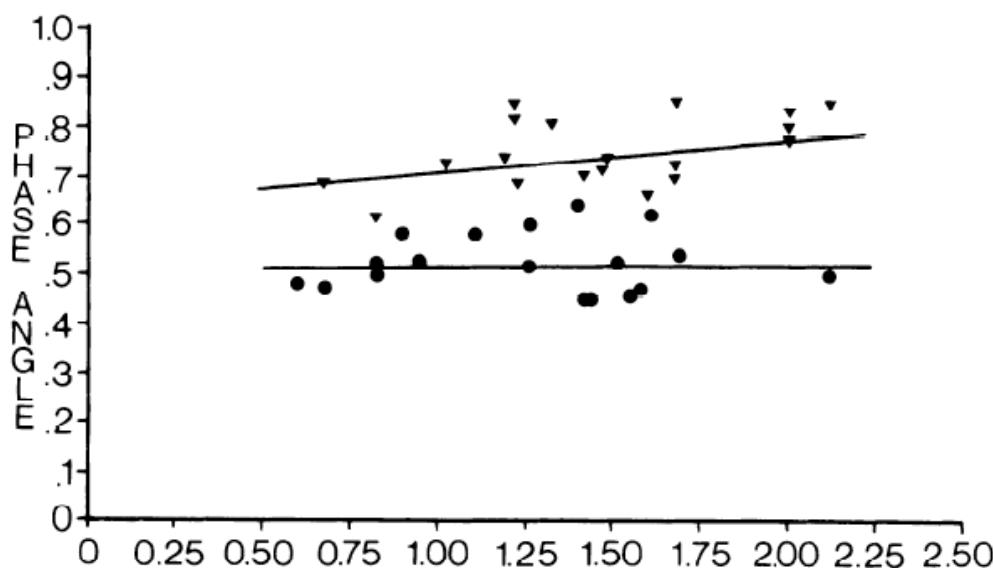
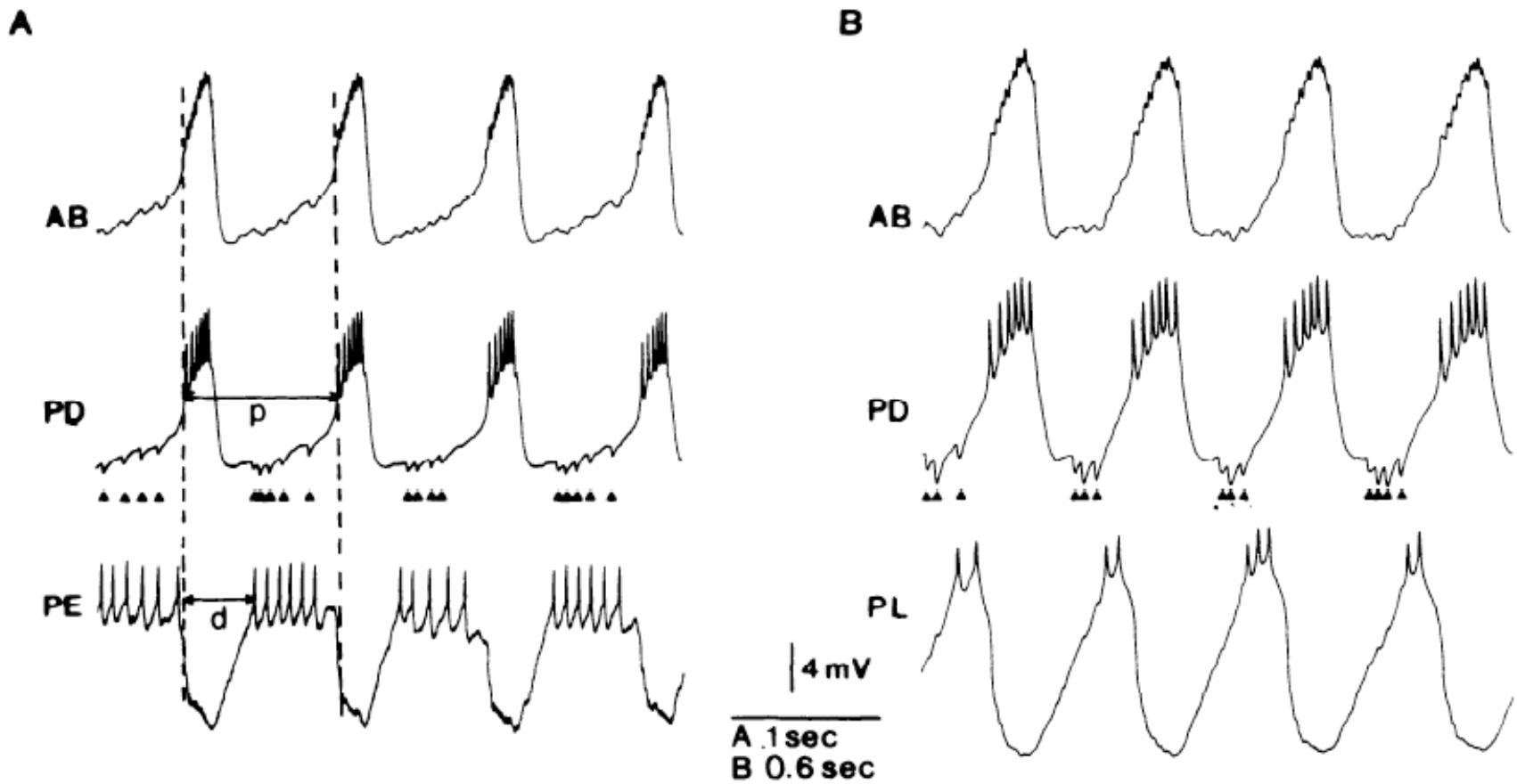


AB: Anterior burster
PD: Pyloric dilator
LP: Lateral Pyloric
PY: Pyloric

Note: these are *inhibitory*



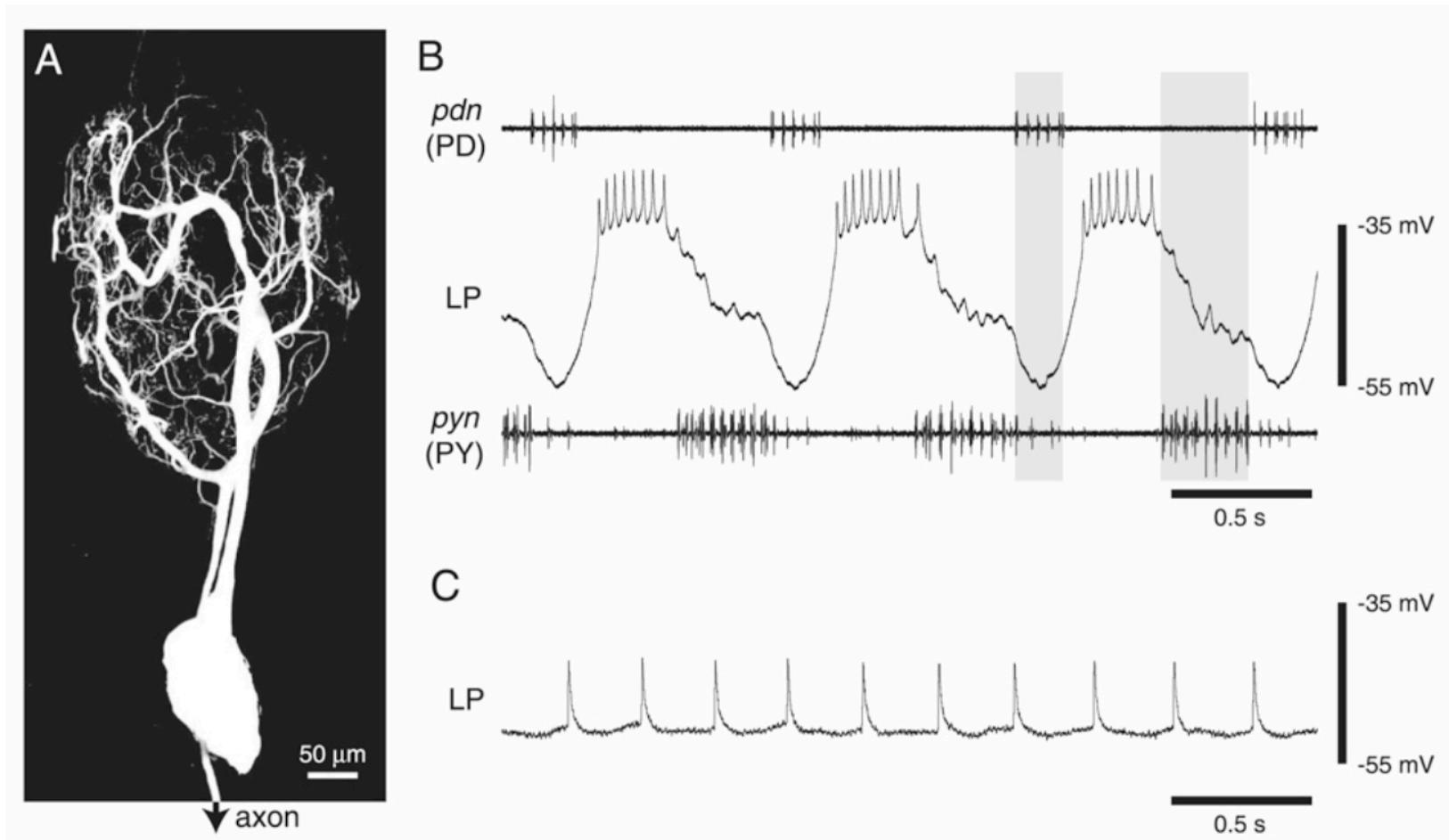
Phase constancy across oscillation frequency



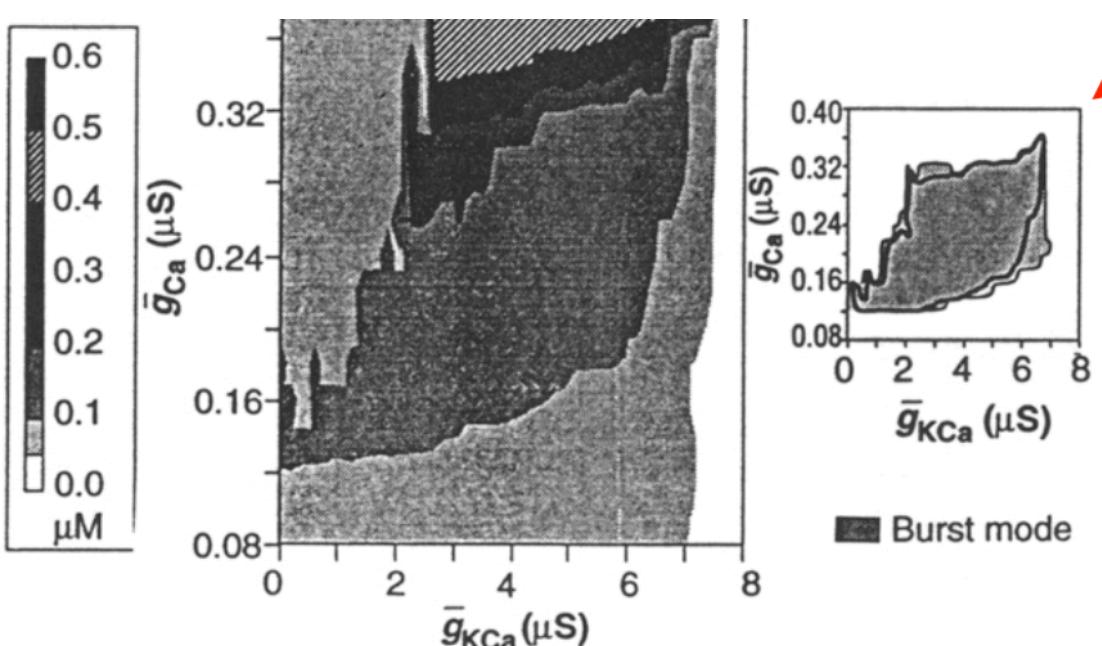
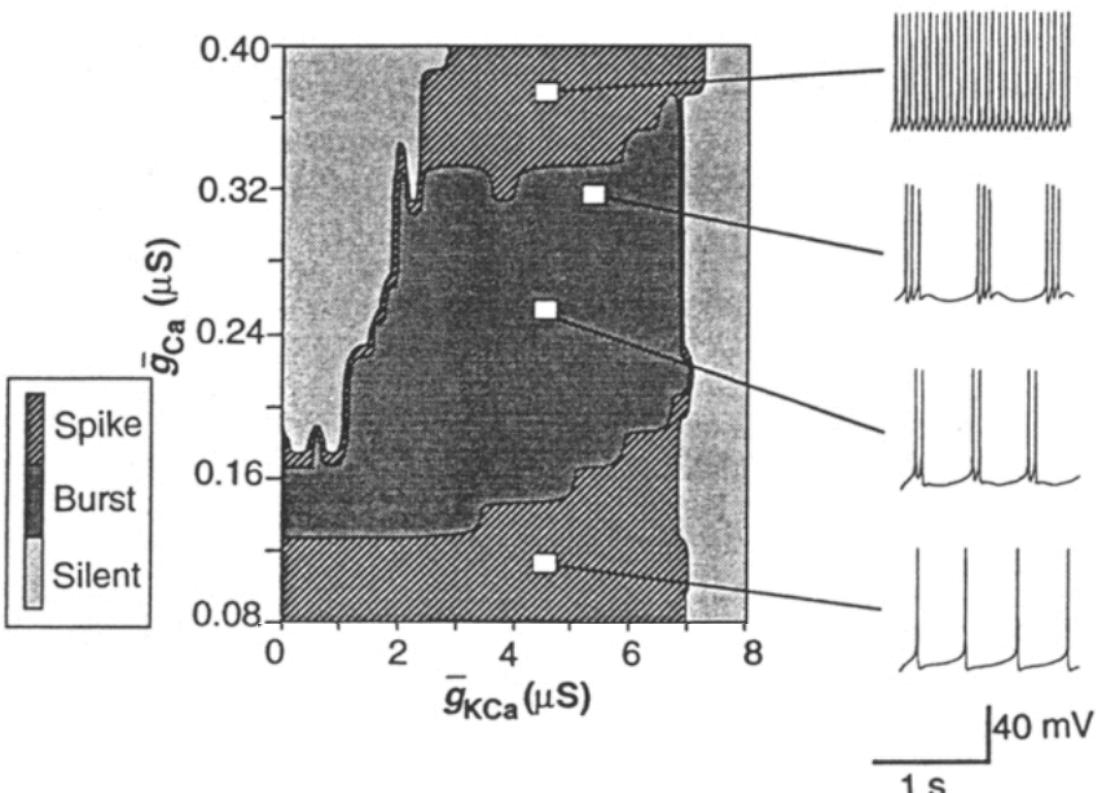
Many conductances, how are they regulated?

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

Current	<i>p</i>	m_∞	h_∞	τ_m	τ_h
I_{Na}	3	$\frac{1}{1 + \exp \left[\frac{-V - 25.5}{5.29} \right]}$	$\frac{1}{1 + \exp \left[\frac{V + 48.9}{5.18} \right]}$	$1.32 - \frac{1.26}{1 + \exp \left[\frac{-120 - V}{25} \right]}$	$0.67 * \frac{1}{1 + \exp \left[\frac{-62.9 - V}{10} \right]} * \frac{1}{1 + \exp \left[\frac{V + 34.9}{3.6} \right]}$
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	$\frac{[Ca]}{[Ca] + 3} * \frac{1}{1 + \exp \left[\frac{-V - 28.3}{12.6} \right]}$		$90.3 - \frac{75.1}{1 + \exp \left[\frac{-V - 46}{22.7} \right]}$	
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	$\frac{1}{1 + \exp \left[\frac{V + 78.3}{6.5} \right]}$		$272 - \frac{-1499}{1 + \exp \left[\frac{-V - 42.2}{8.73} \right]}$	

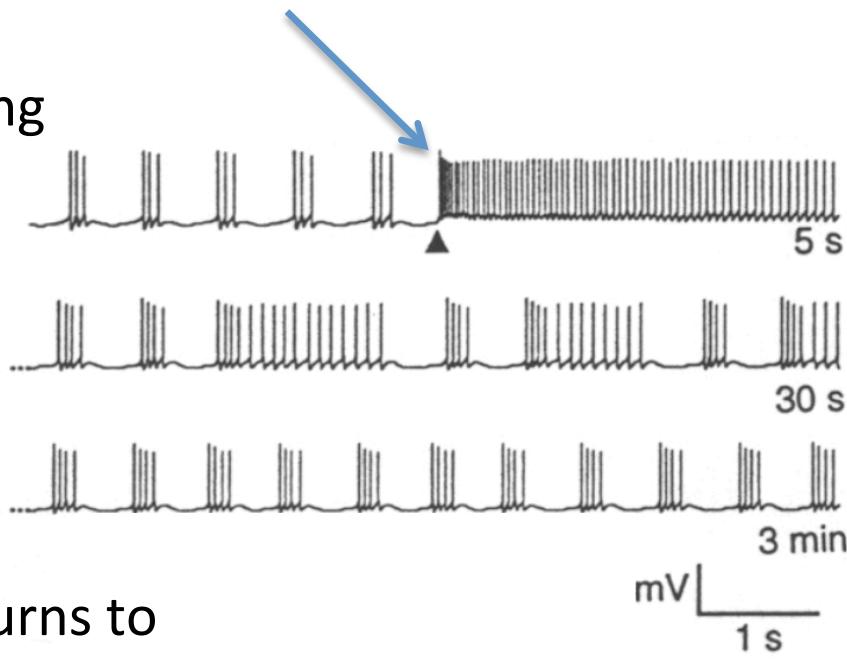


Different dynamic behavior in different regions of parameter space



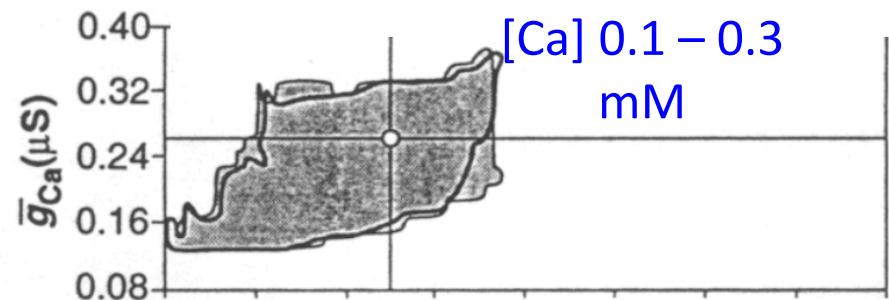
K^+ is increased here, E_K changed from -80 to -60 mV

Bursting



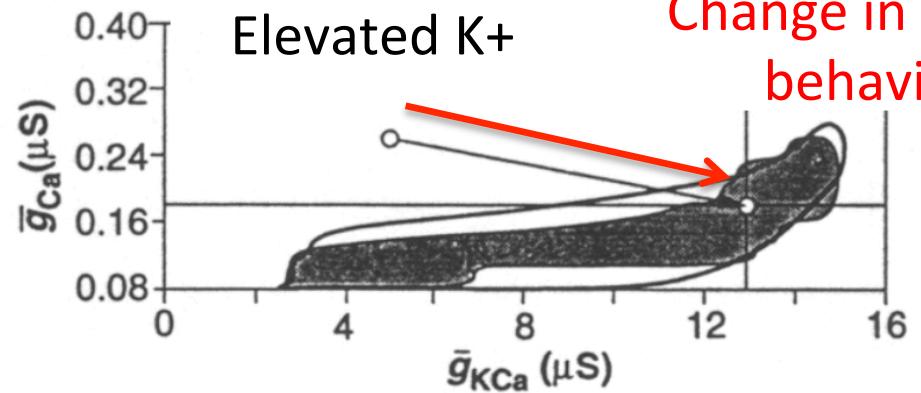
Returns to bursting

Normal K^+

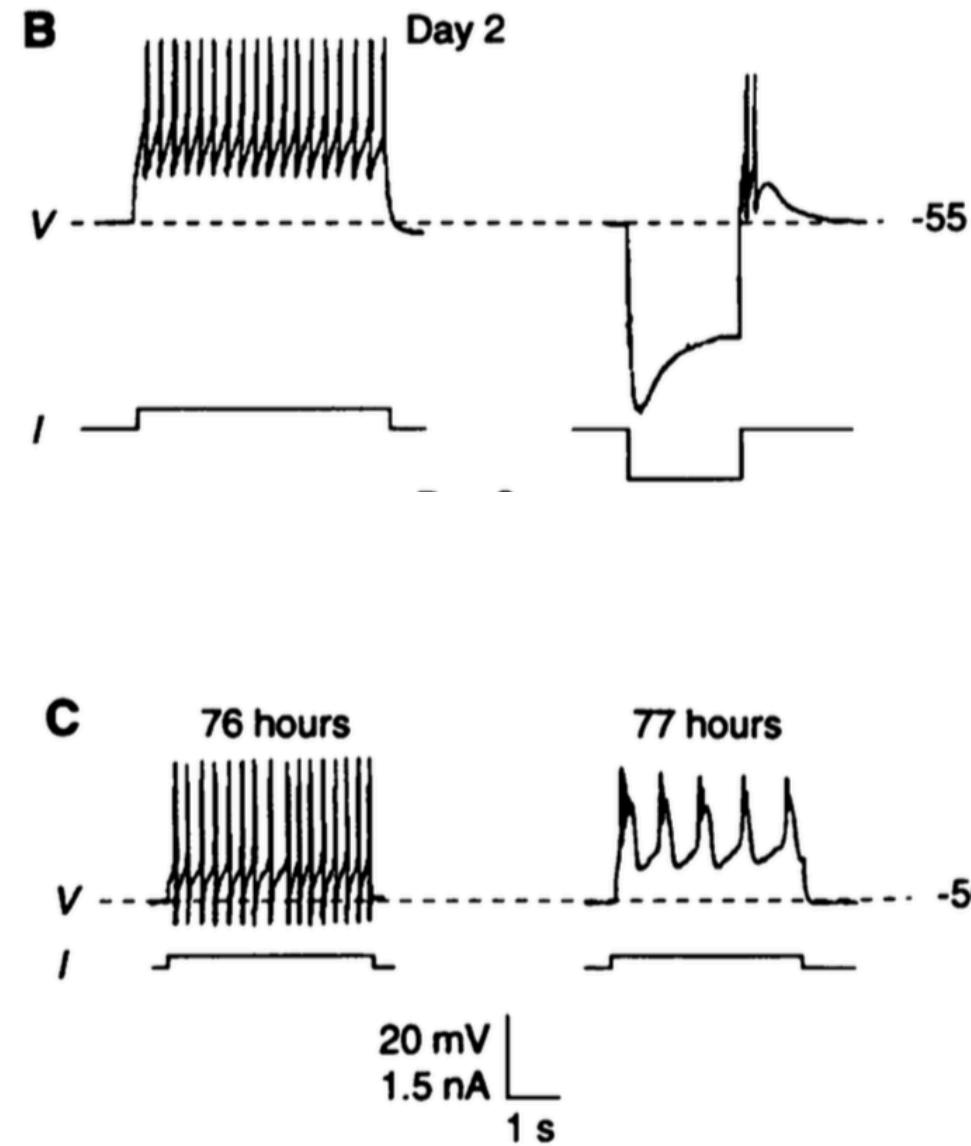
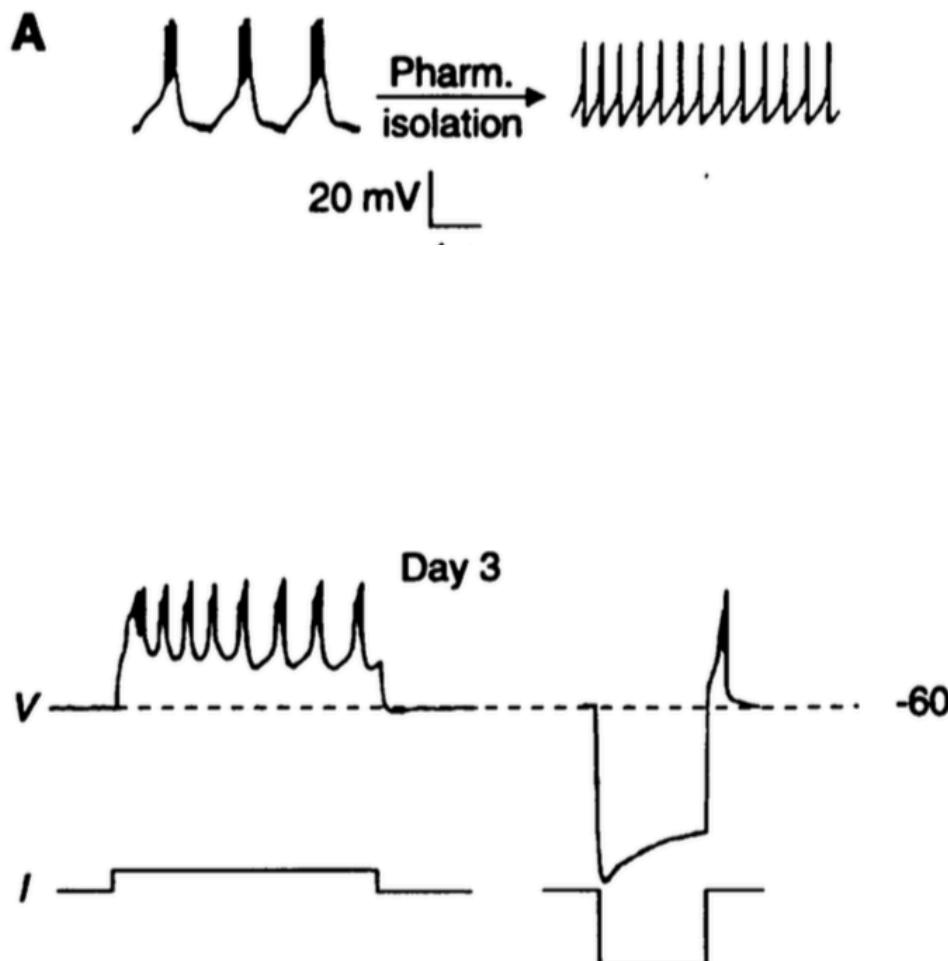


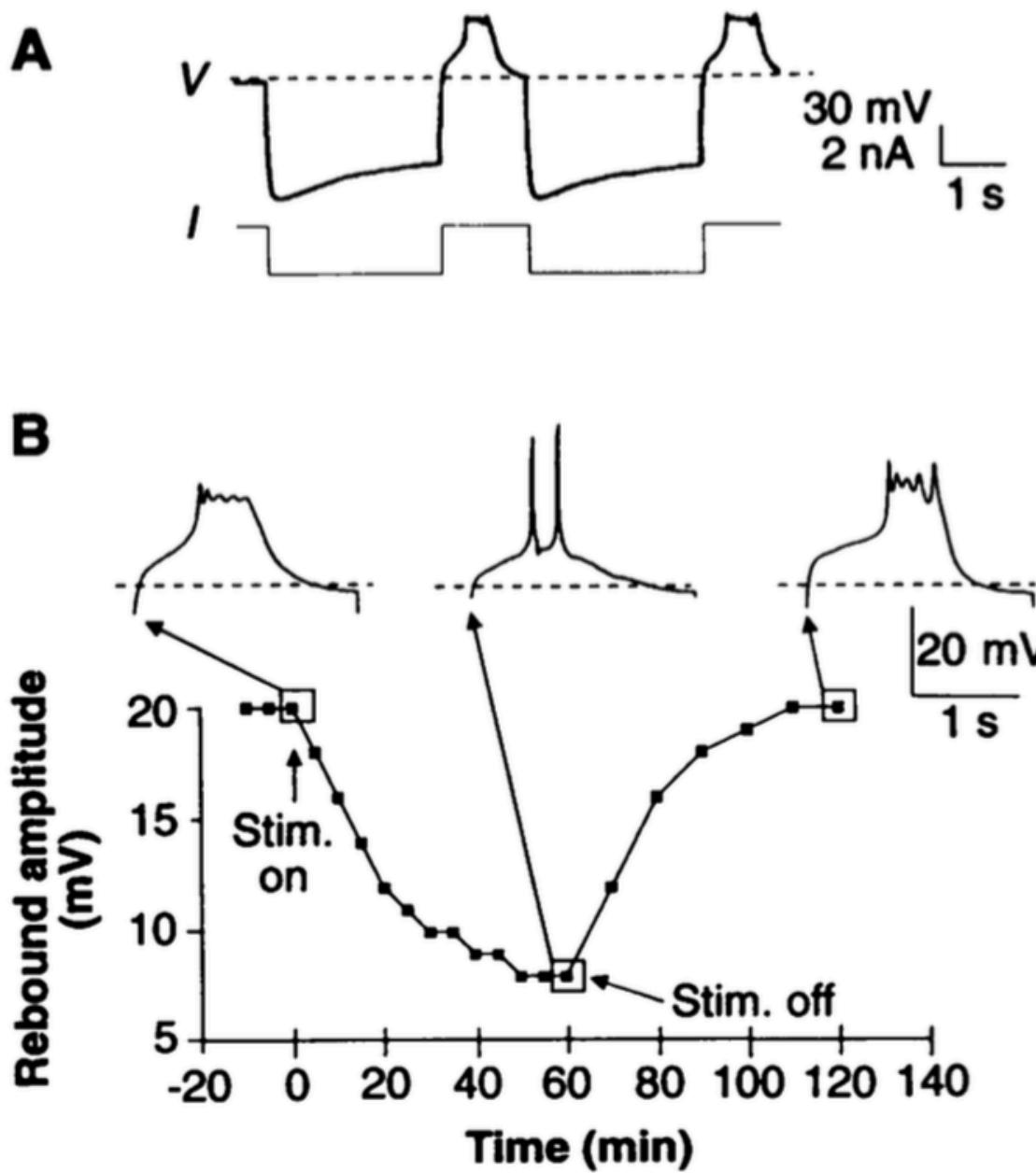
Elevated K^+

Change in mode behavior

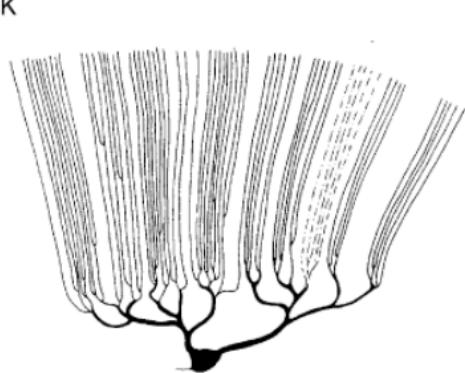
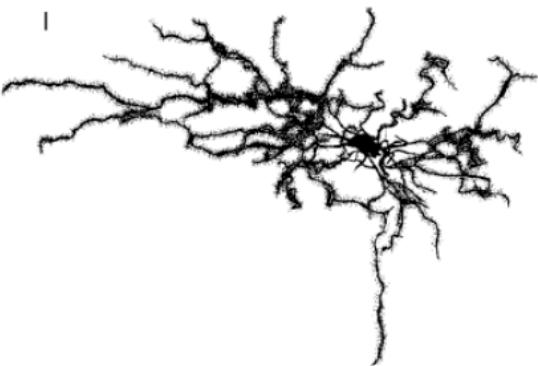
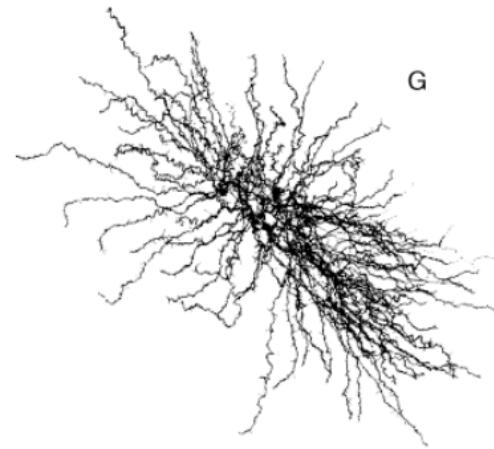
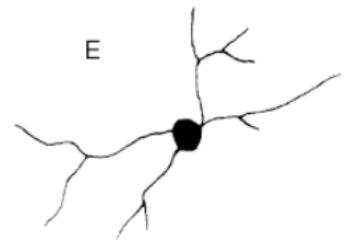
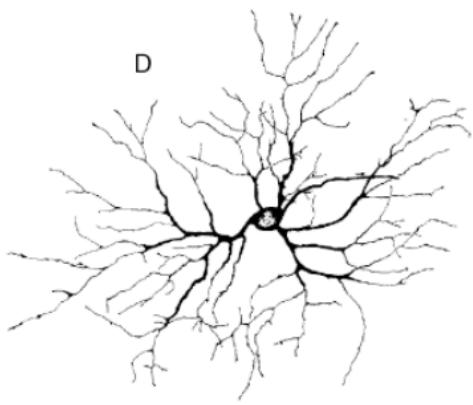
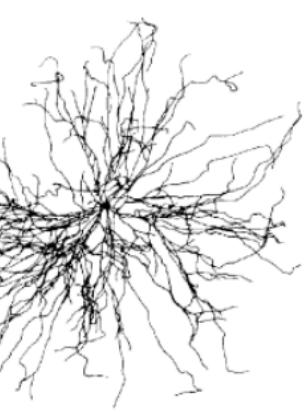


Cells change their physiological properties to burst

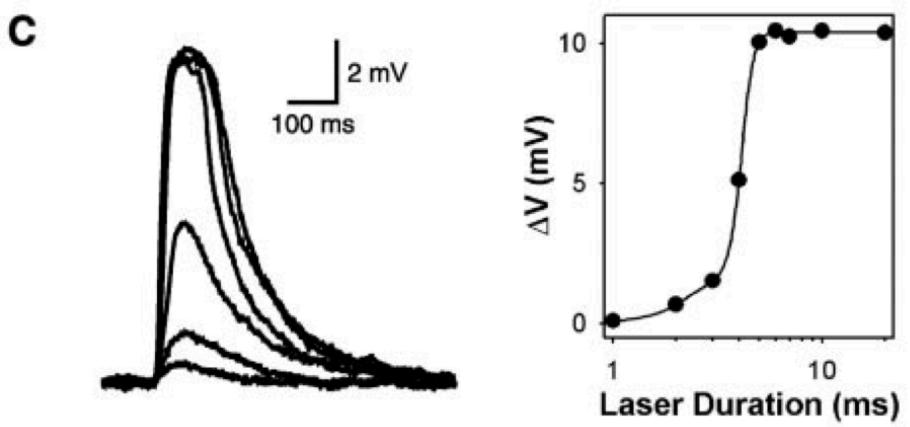
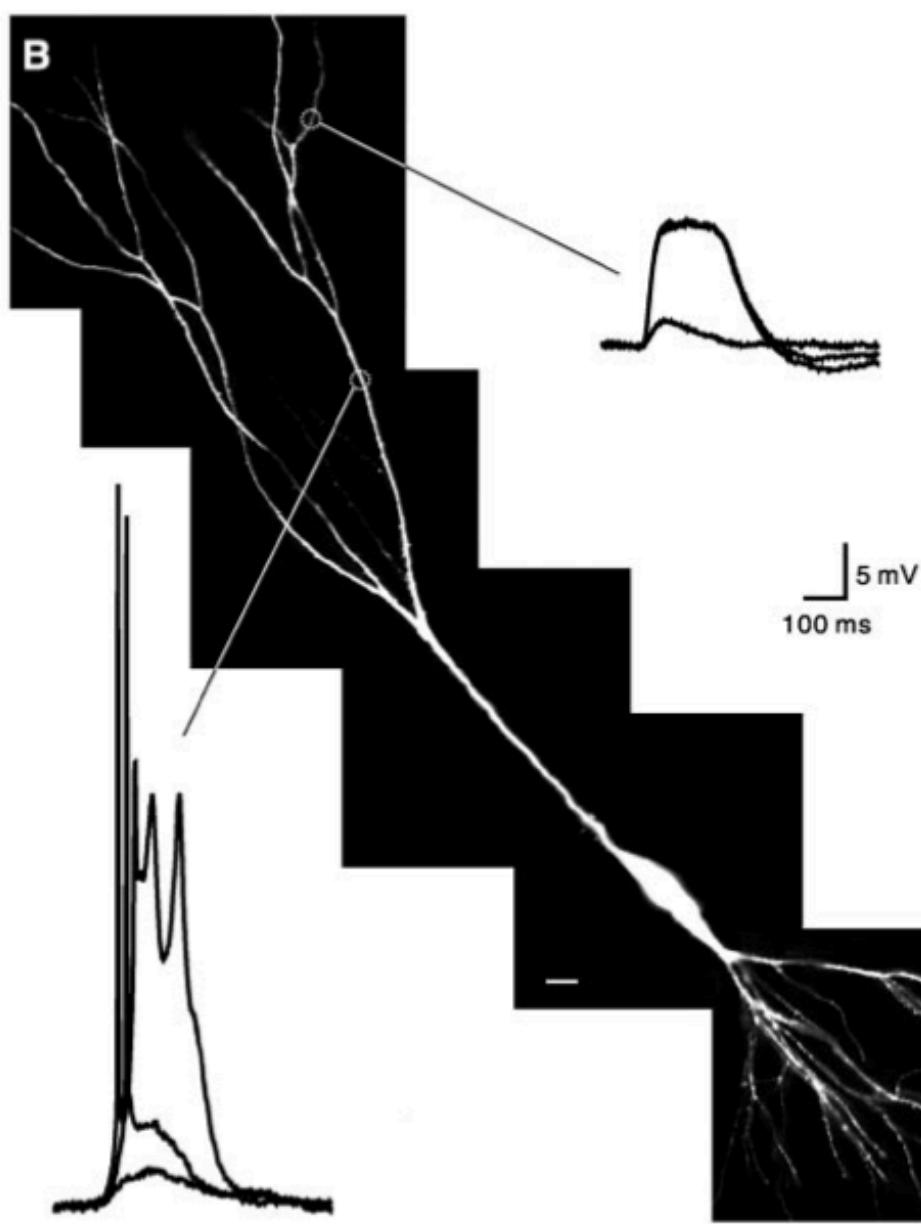
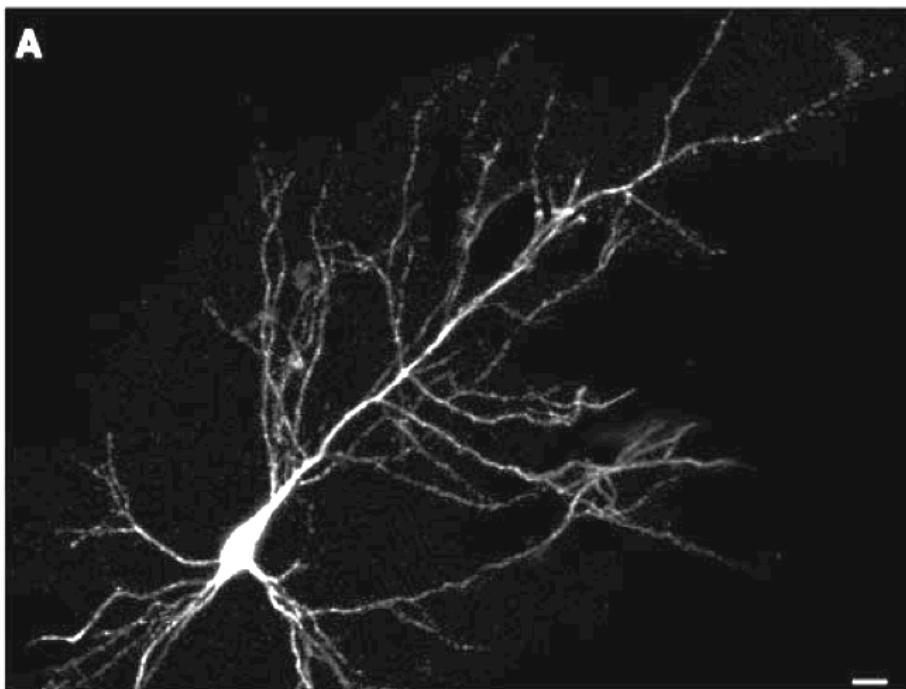




What influence do dendrites have on computation?

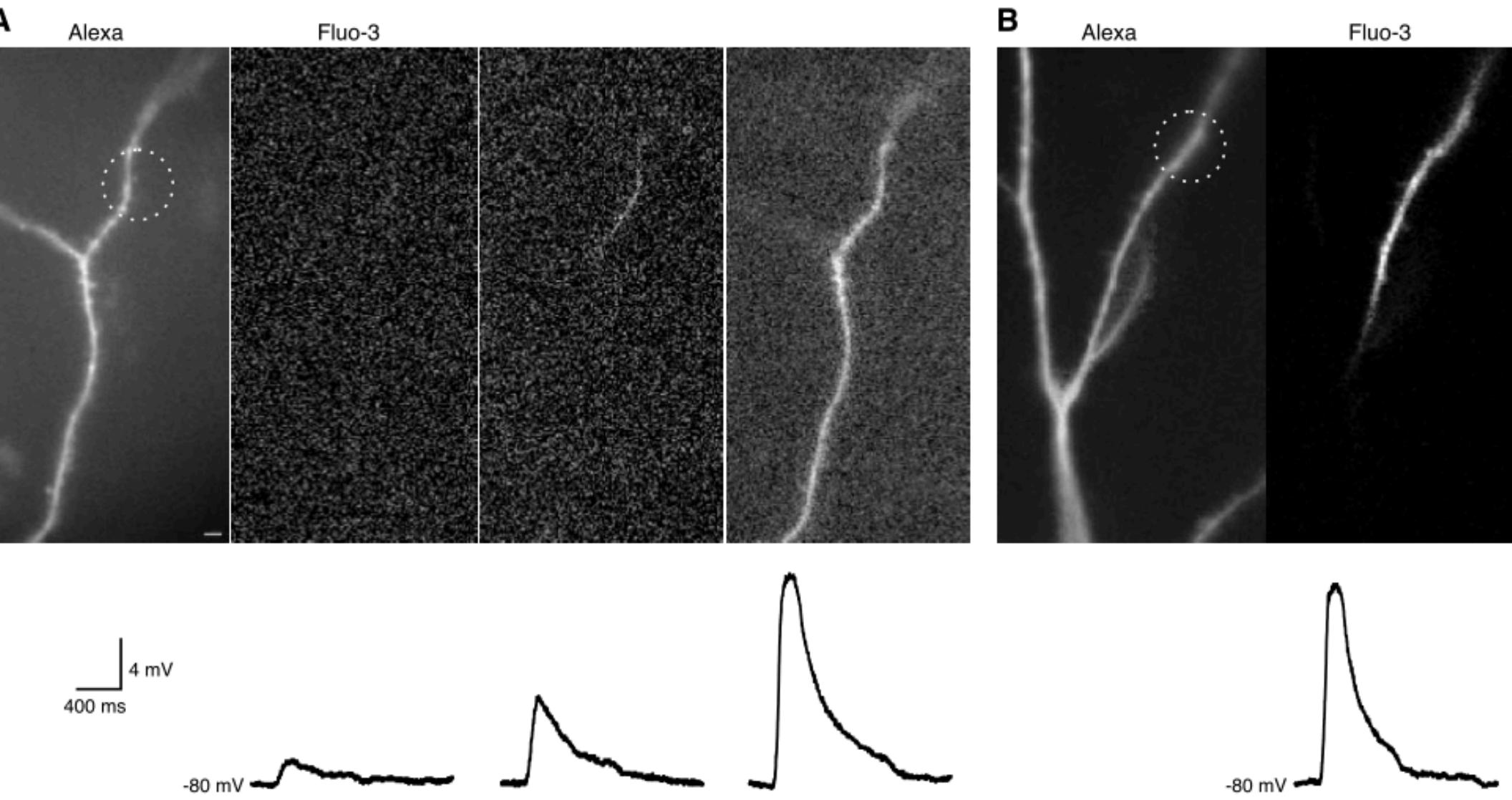


or none calcium action potentials in pyramidal cell dendrites



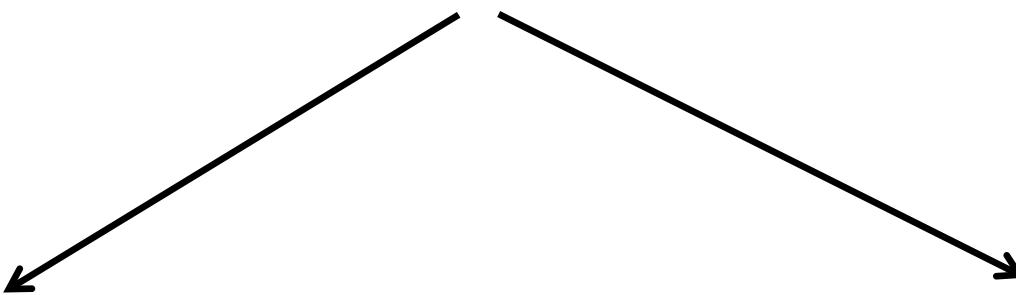
Wei et al., 2001. Compartmentalized and Binary Behavior of Terminal Dendrites in Hippocampal Pyramidal Neurons

Action potential failure at a dendritic branch point

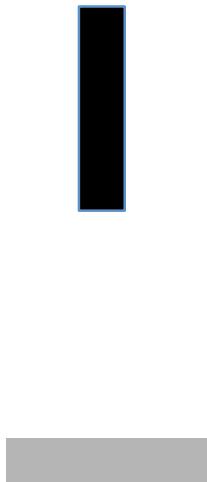


Wei et al., 2001. Compartmentalized and Binary Behavior of Terminal Dendrites in Hippocampal Pyramidal Neurons

Properties of feature detection



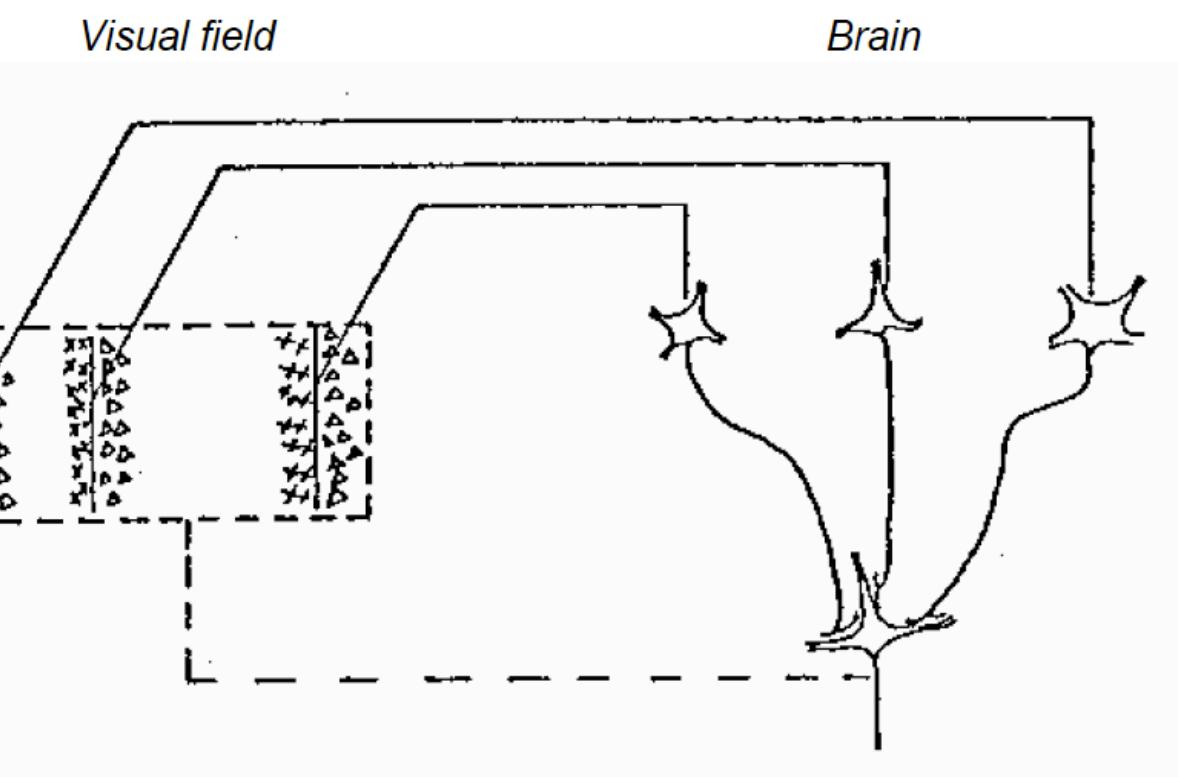
Selectivity



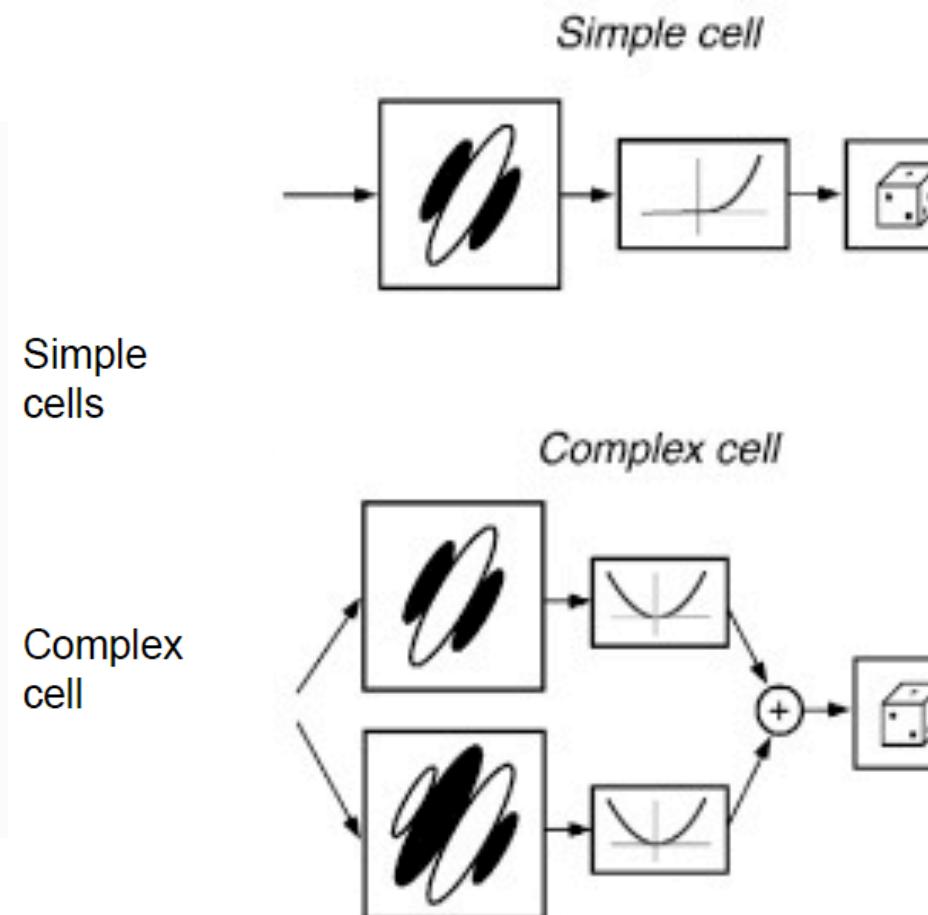
Invariance



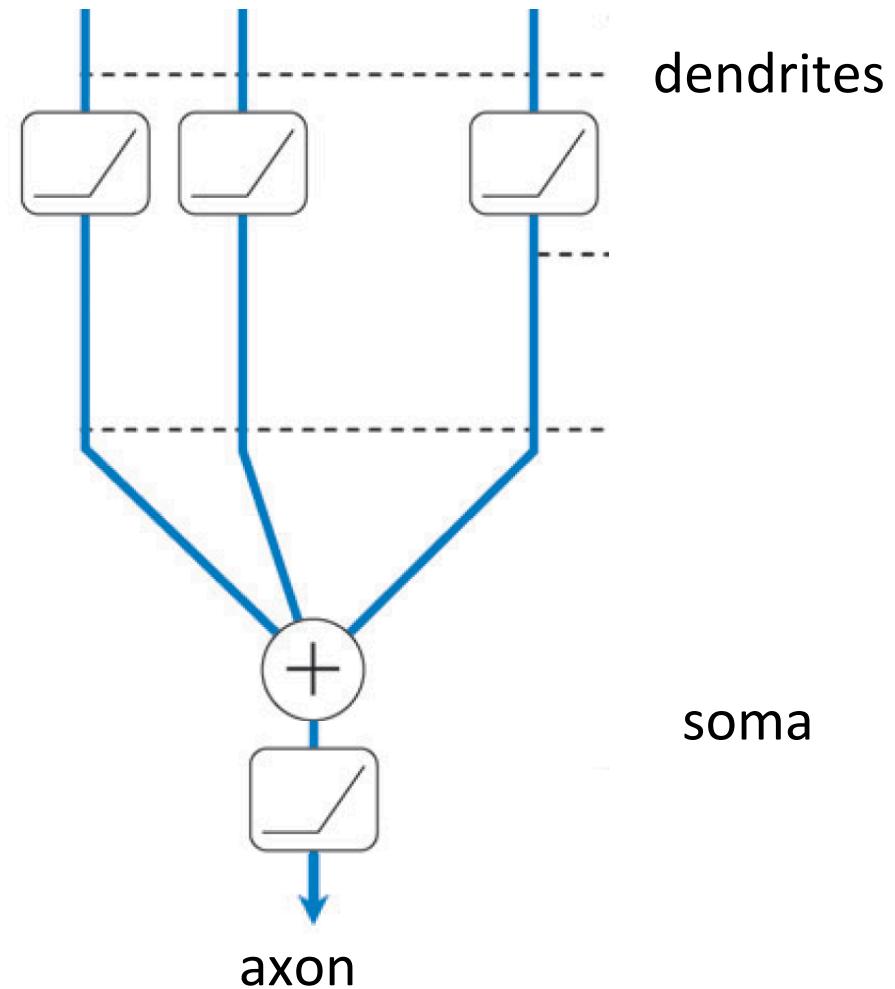
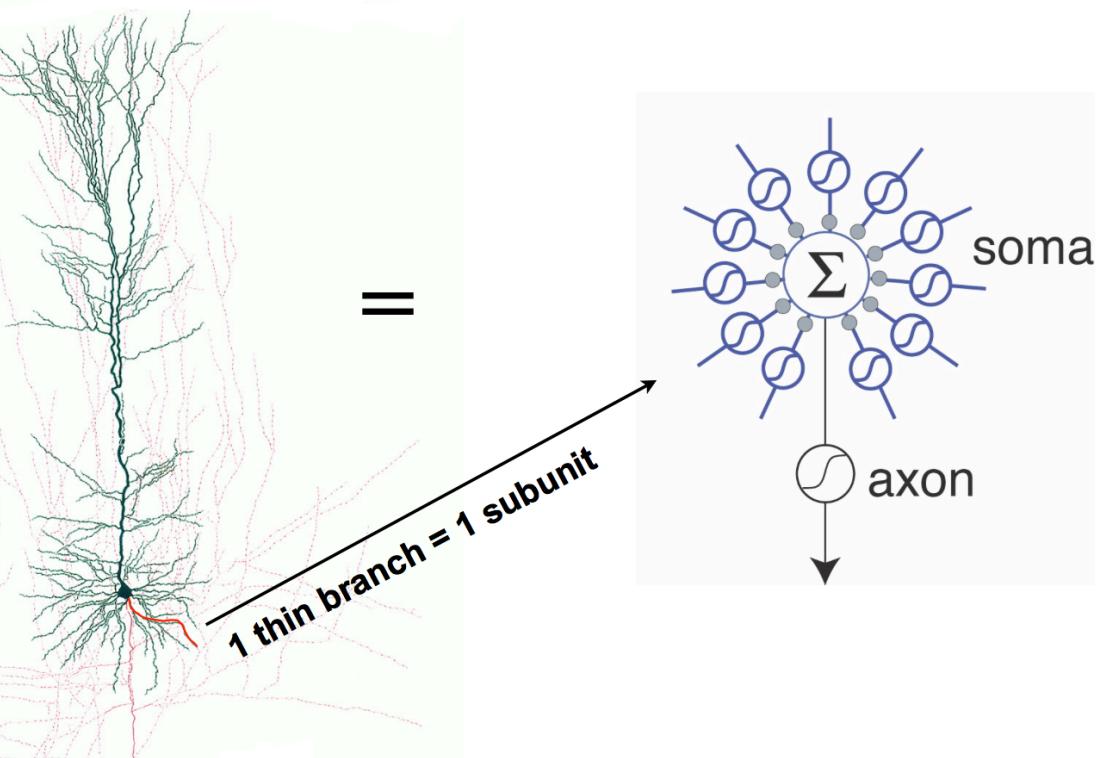
Models of selectivity and invariance in primary visual cortex



Hubel & Wiesel, 1963



Rust et al., 2005



Model of Binocular Disparity Representation

Bar presented to left & right eyes

Right eye pos. (deg)

