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)

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

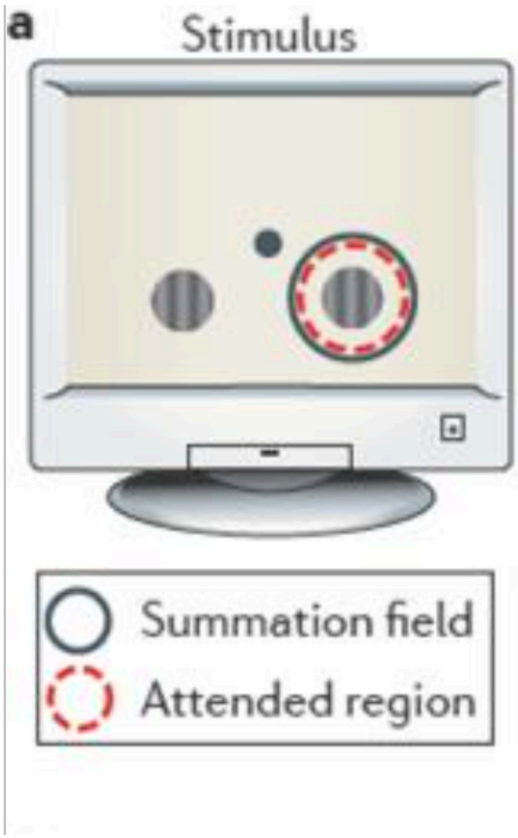
How can a neuron change its gain?

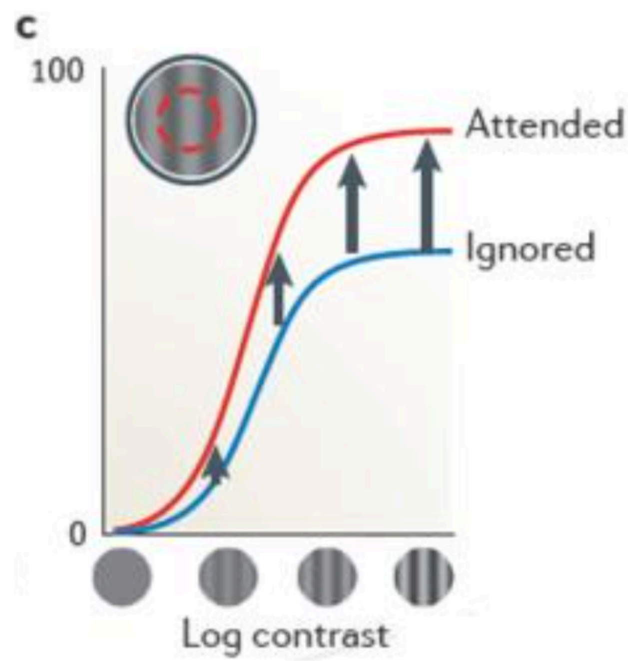
- Integrate and fire model
- Hodgkin-Huxley model
- Dynamic Clamp

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

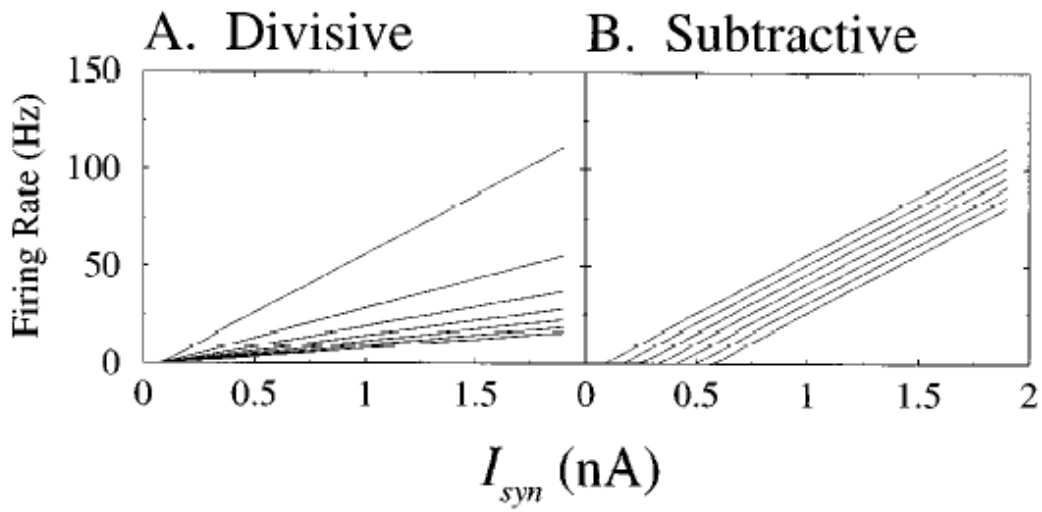


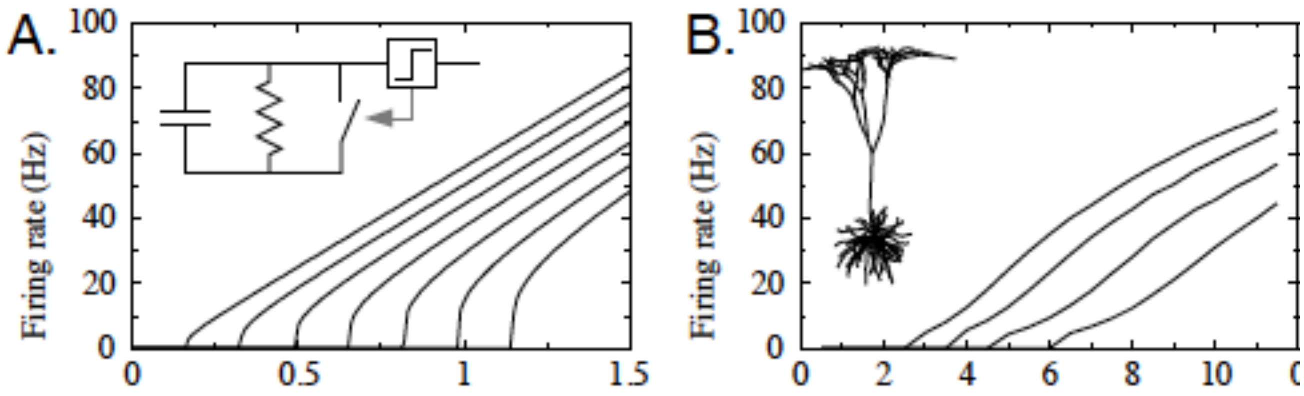


Reynolds & Heeger, 2009

Integrate and fire neuron

- Derivation
- Effect of changing conductance



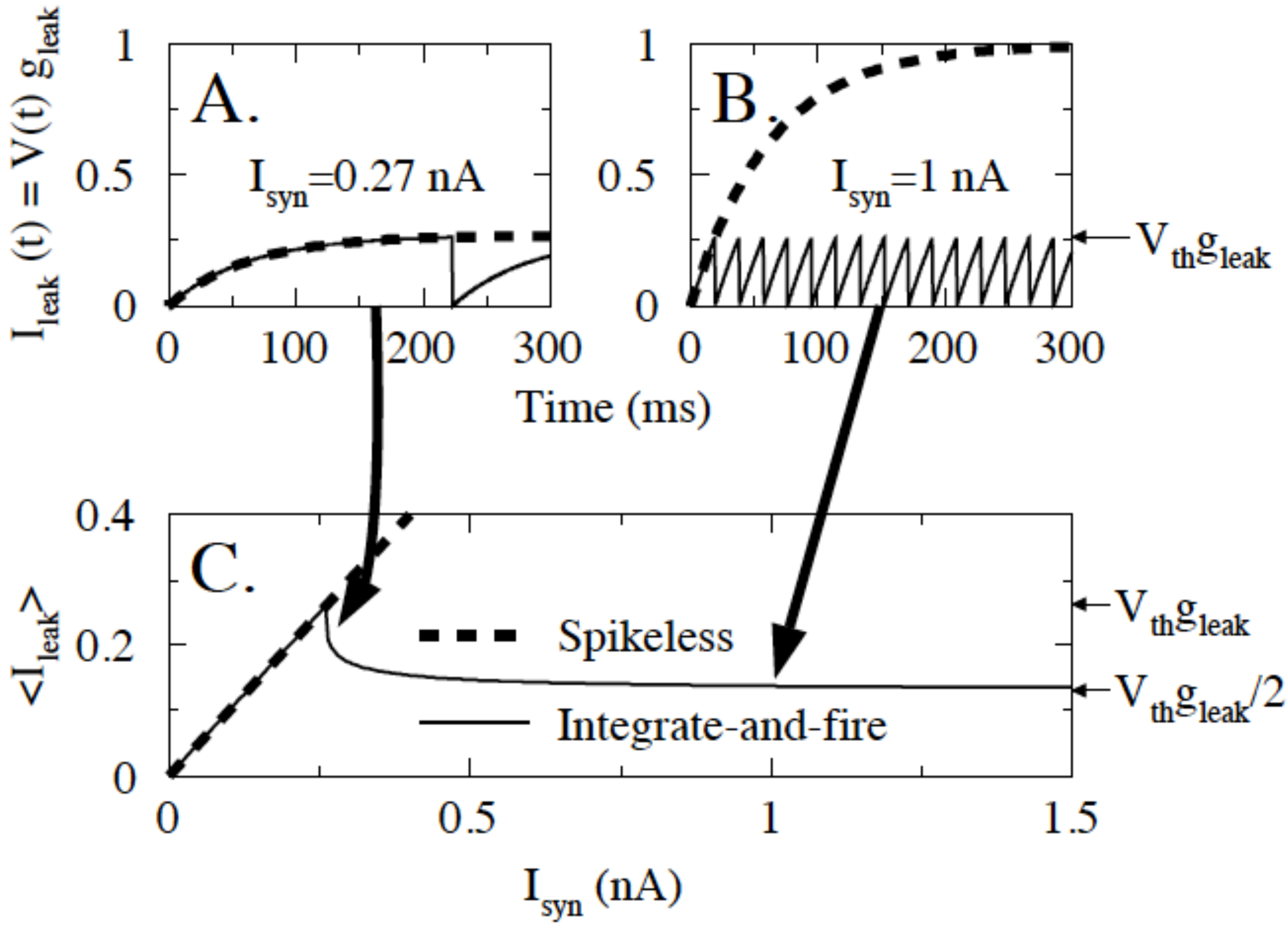


Current (nA)

Excitatory synaptic input rate (Hz)

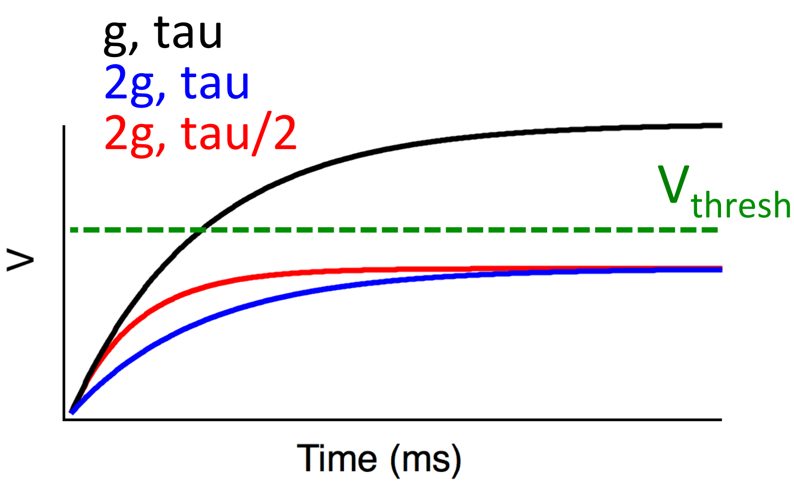
Holt & Koch, 1997. Shunting inhibition does not have a divisive effect on firing rates

Rapid spiking "clamps" the voltage making it independent of injected current

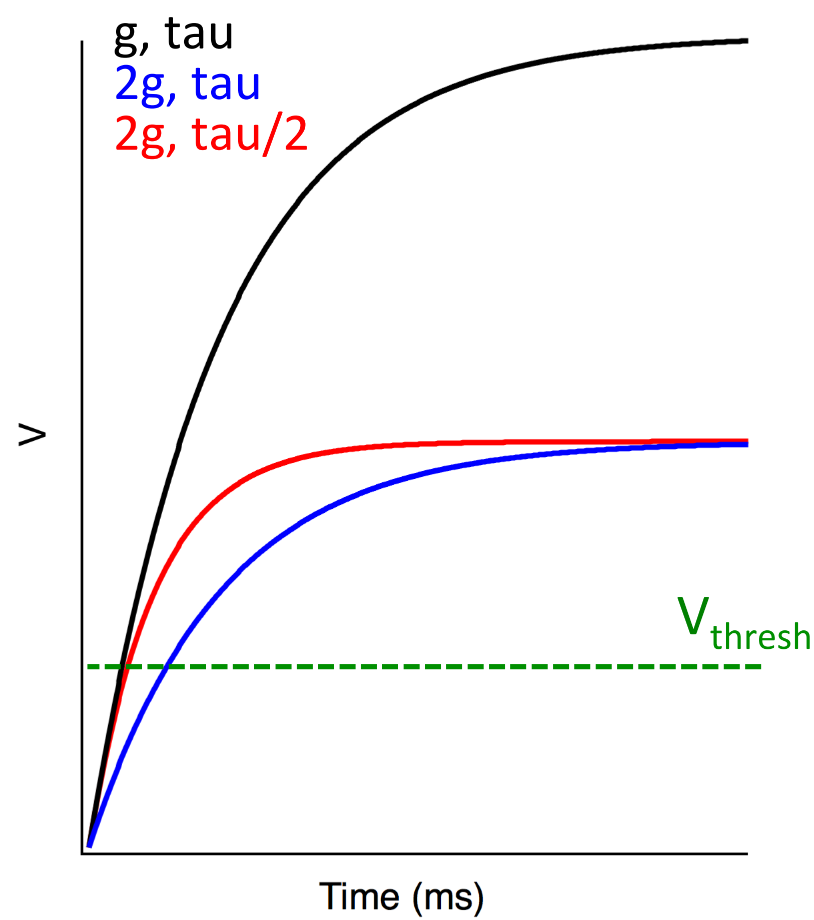


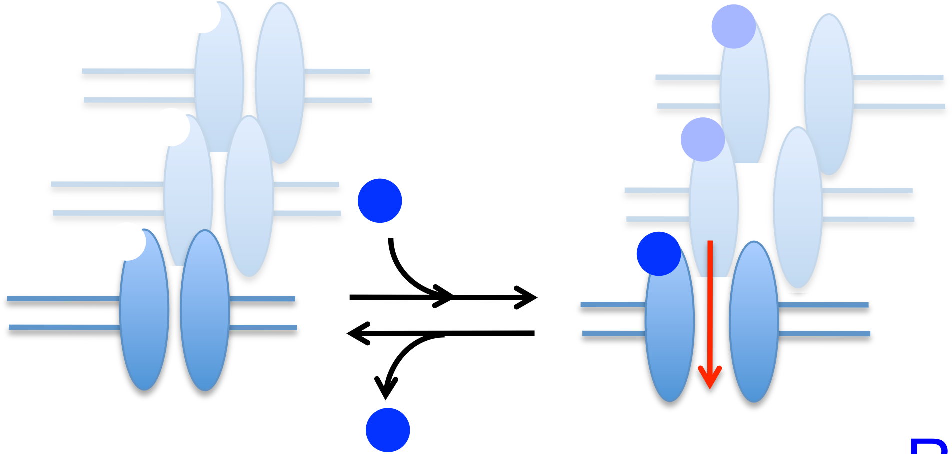
Shunting changes conductance, but also tau with different effects for small and large currents

Small currents



Large currents





Rate constants

Closed | Open

$$R \underset{k_{\text{off}}}{\overset{[L]k_{\text{on}}}{\rightleftharpoons}} A$$

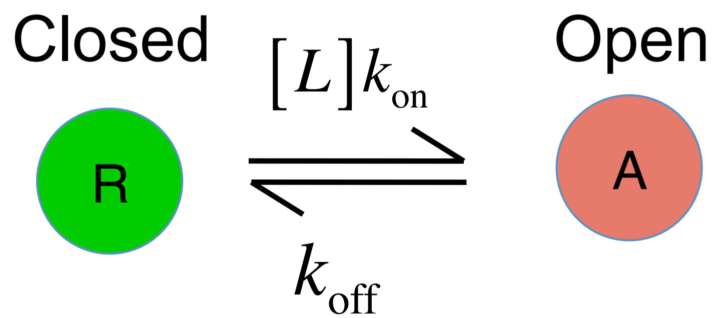
State Occupancies (sum to 1)

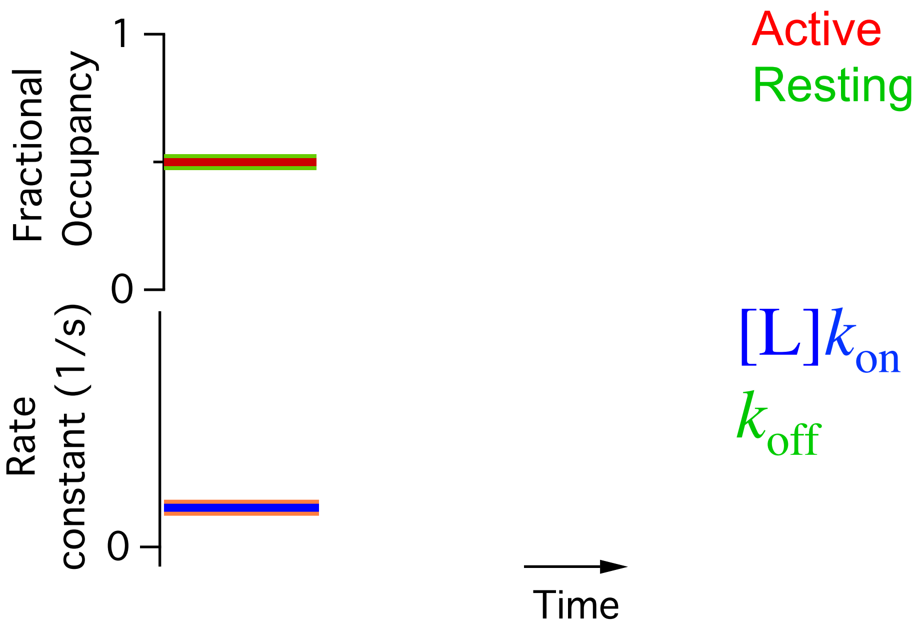
Change in activity = Inflow – Outflow

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

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:

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

Rate "constants":

$$\begin{aligned} \alpha_n(V) &= \frac{10-V}{100\left(\exp\left((10-V)/10\right)-1\right)} \\ \alpha_m(V) &= \frac{25-V}{10\left(\exp\left((25-V)/10\right)-1\right)} \\ \alpha_h(V) &= 0.07\exp(-V/20) \end{aligned}$$

$$\begin{aligned} \beta_n(V) &= 0.125\exp(-V/80) \\ \beta_m(V) &= 4\exp(-V/18) \\ \beta_h(V) &= \frac{1}{\exp\left((30-V)/10\right)+1} \end{aligned}$$

Constants:

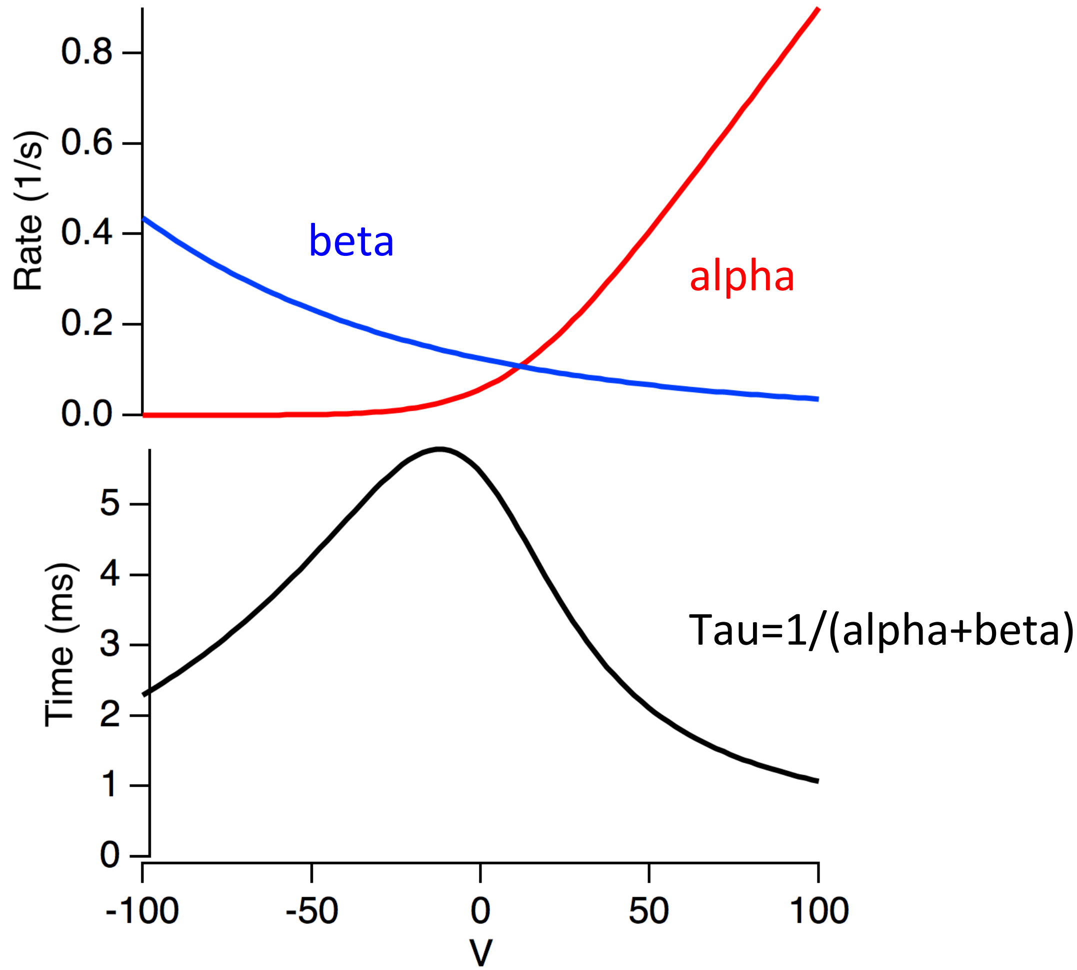
$$C = 1\,\mu\mathrm{F/cm}^2$$

$$\begin{aligned} \bar{g}_{\mathrm{K}} &= 36\,\mathrm{mS/cm}^2 \\ \bar{g}_{\mathrm{Na}} &= 120\,\mathrm{mS/cm}^2 \\ \bar{g}_l &= 0.3\,\mathrm{mS/cm}^2 \end{aligned}$$

$$\begin{aligned} E_K &= -12\,\mathrm{mV} \\ E_{Na} &= +115\,\mathrm{mV} \\ E_l &= +10.613\,\mathrm{mV} \end{aligned}$$

Note: these are given in the original form, relative to V_{rest} =~ -66 mV

Tau is slow when both rate constants are slow



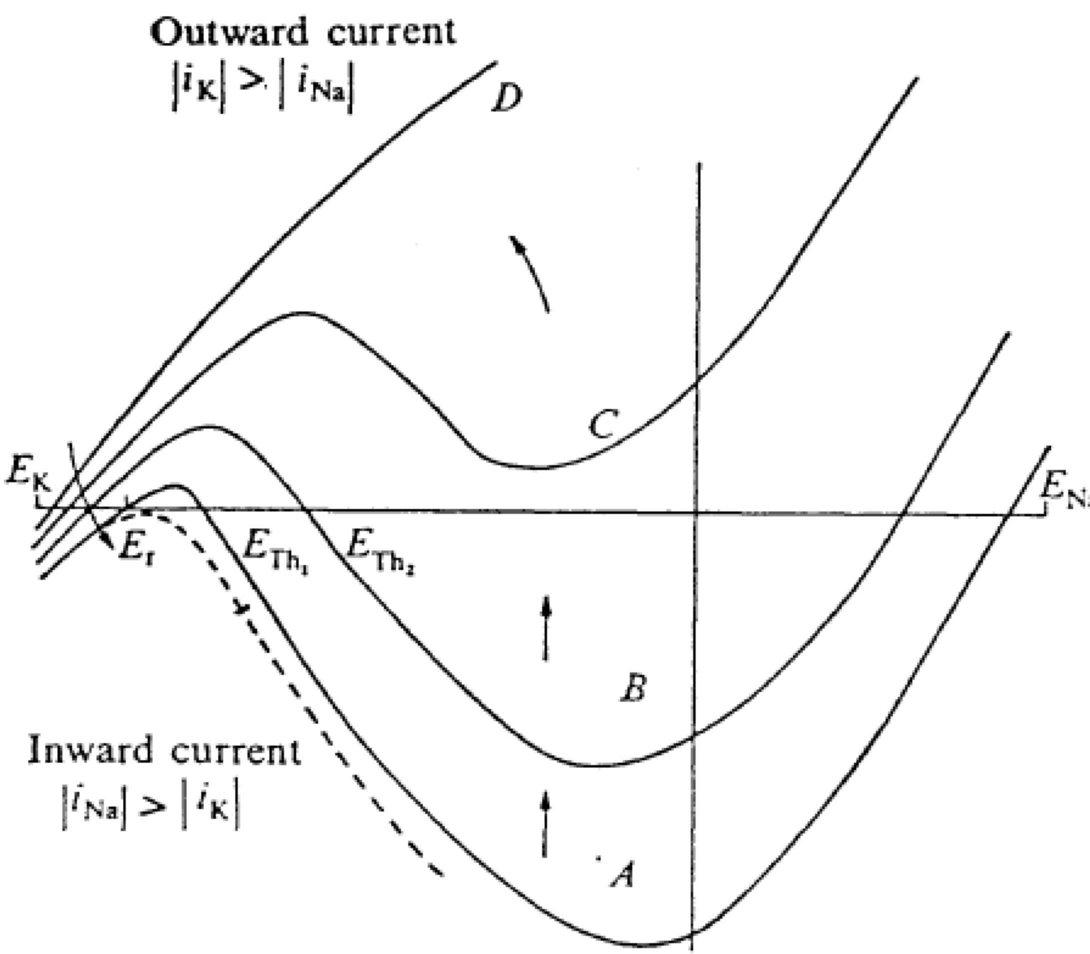
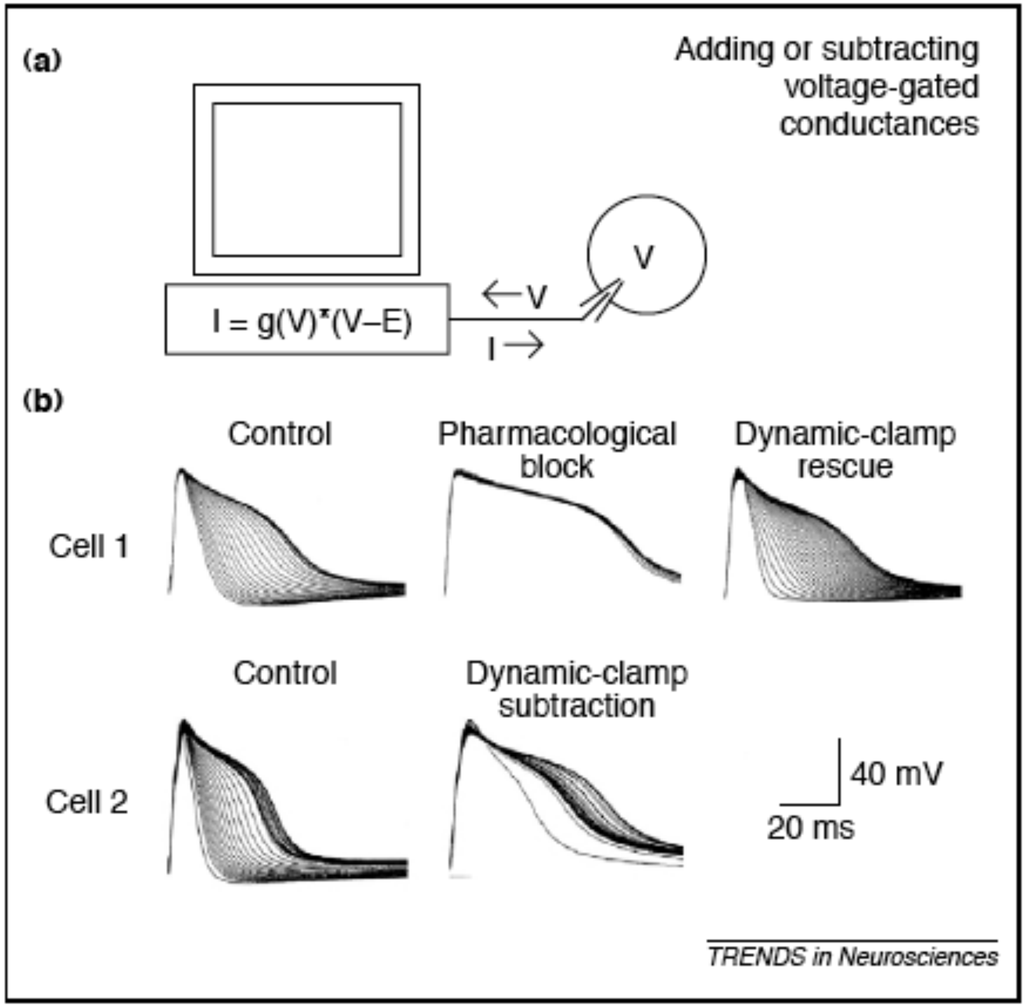


FIG. 8.12. Diagram illustrating change in momentary current–voltage relations with time on depolarization.

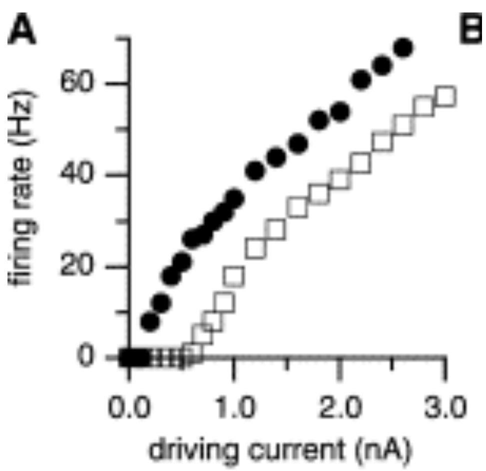
The dynamic clamp
Artificially adding or subtracting membrane mechanisms



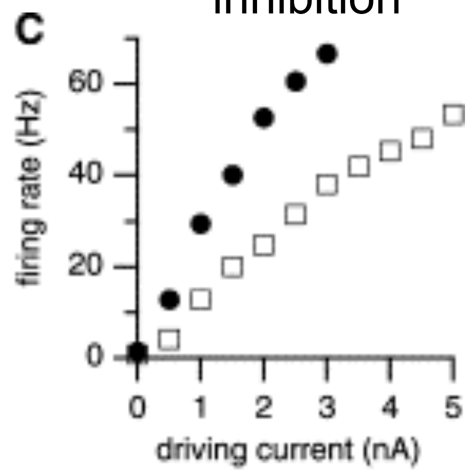
Balanced excitation and inhibition can change gain

Rat somatosensory cortex slice

Shunting inhibition alone



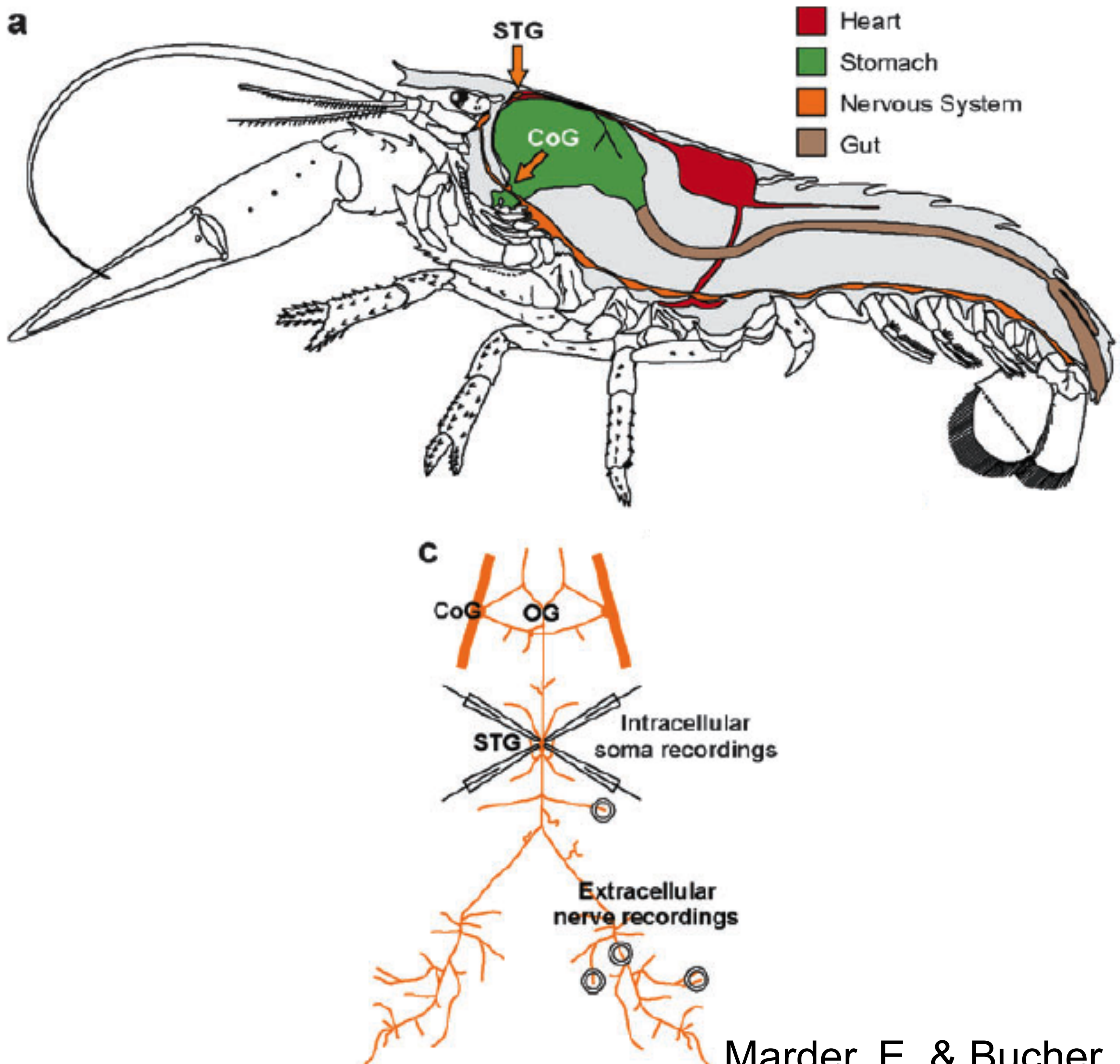
Balanced excitation and inhibition



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

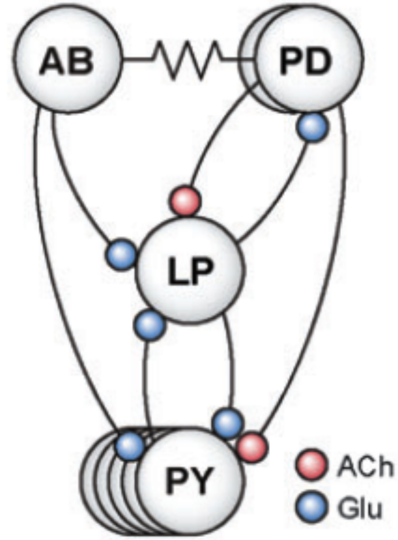
How can a neuron maintain a stable firing pattern?

Crustacean stomatogastric ganglion



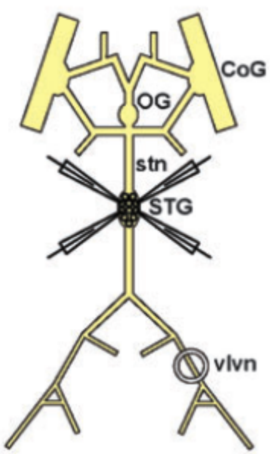
Marder, E. & Bucher, D., 2006

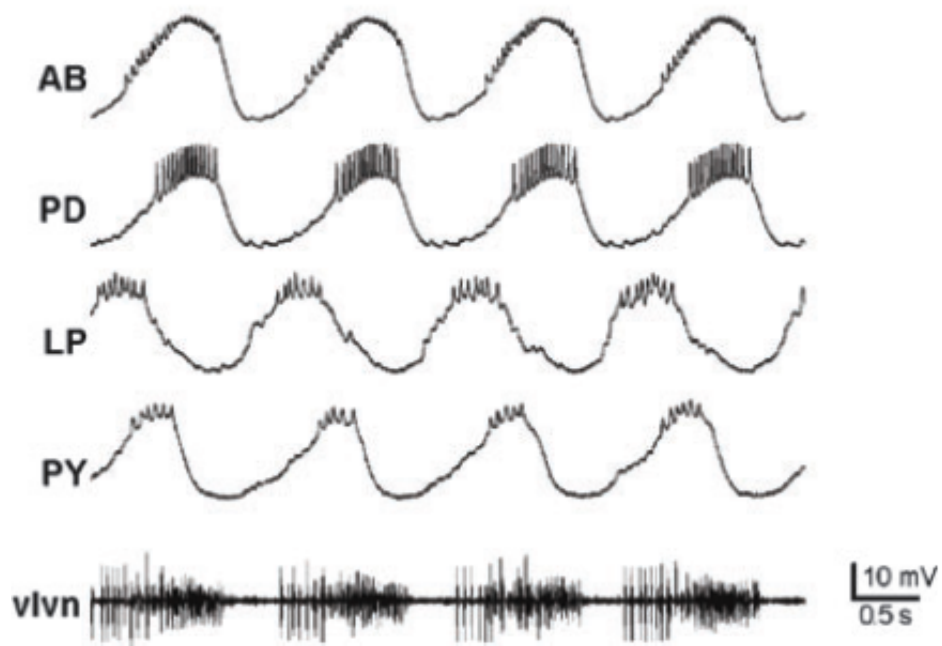
Pyloric oscillator of the stomatogastric ganglion



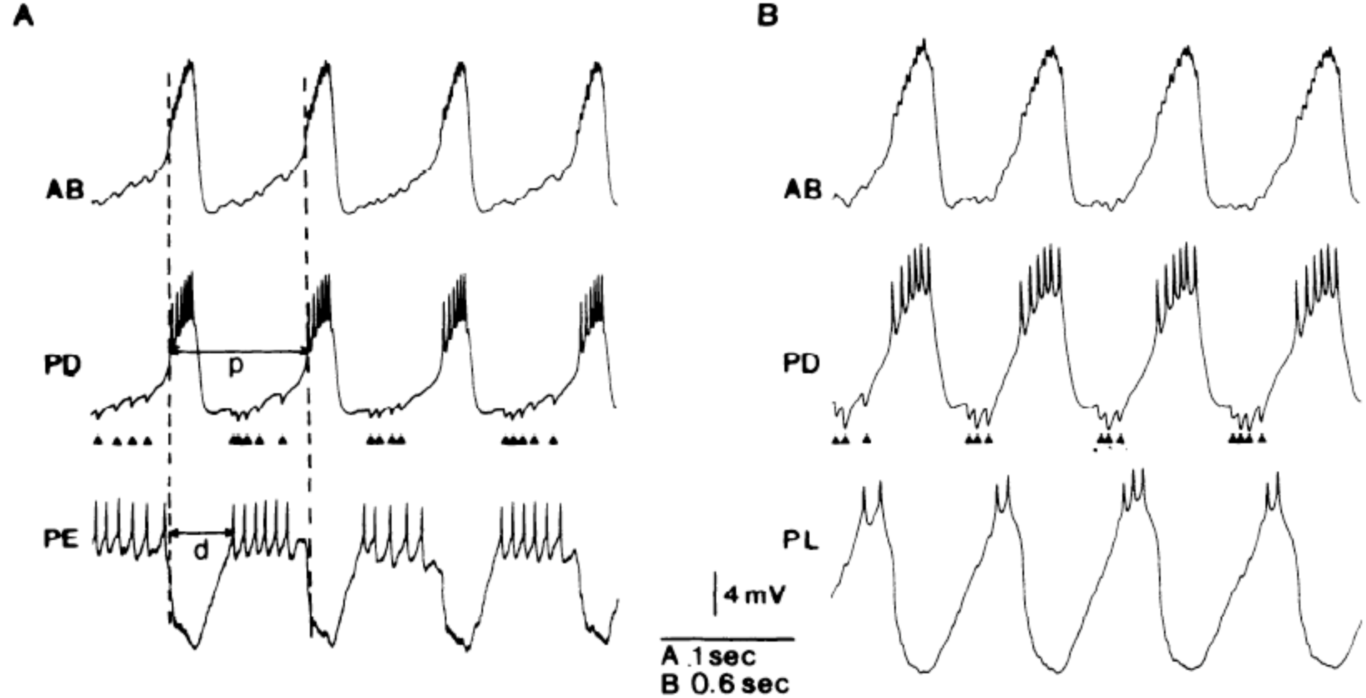
AB: Anterior burster
PD: Pyloric dilator
LP: Lateral Pyloric
PY: Pyloric

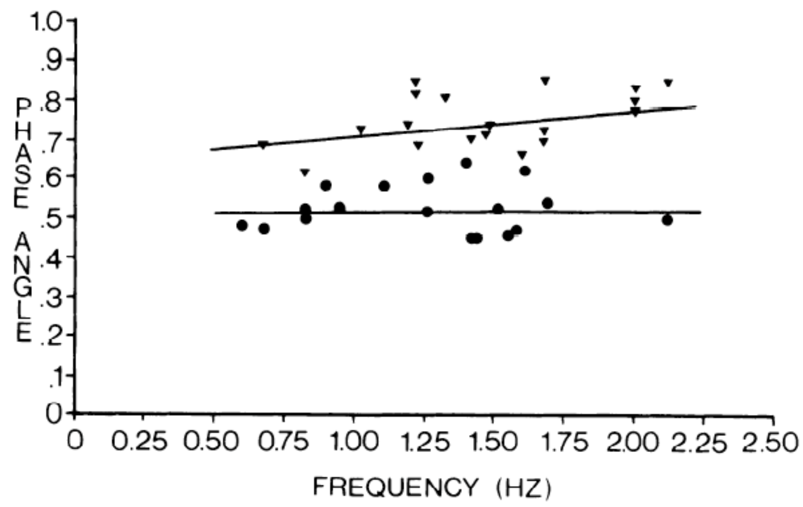
Note: these are *inhibitory*





Phase constancy across oscillation frequency

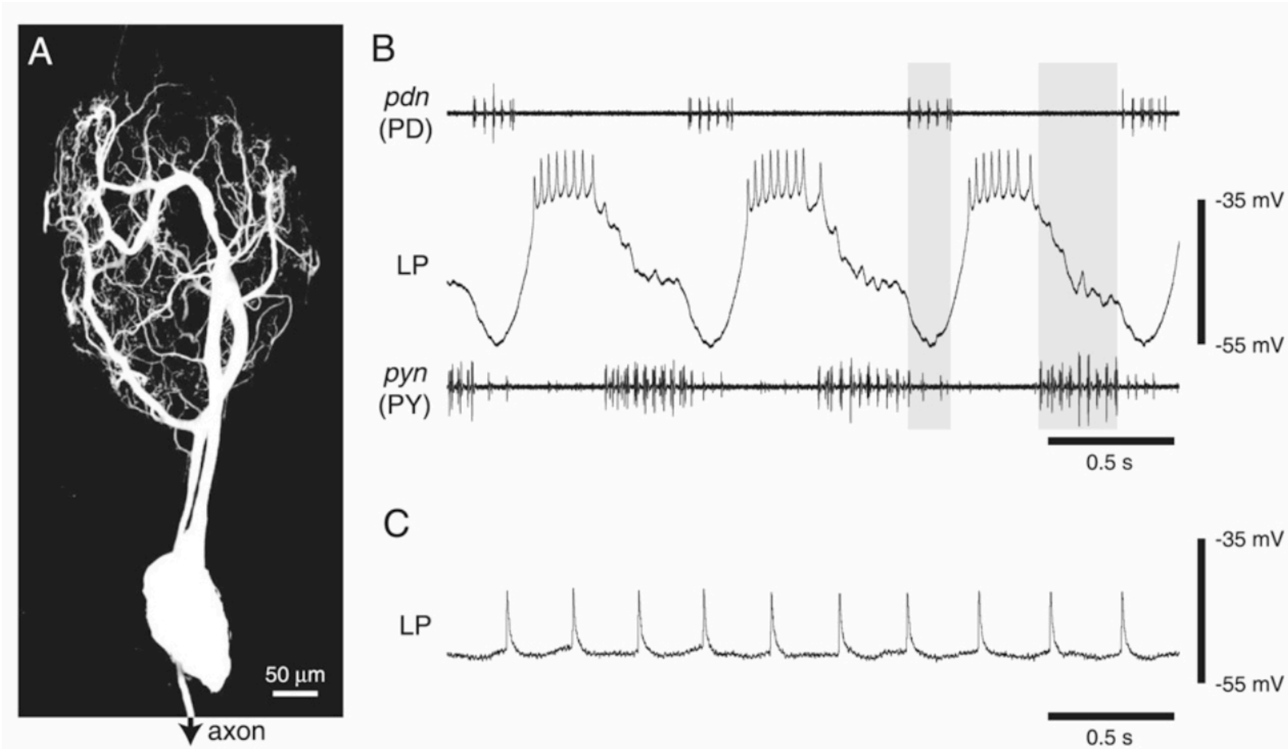




Many conductances, how are they regulated?

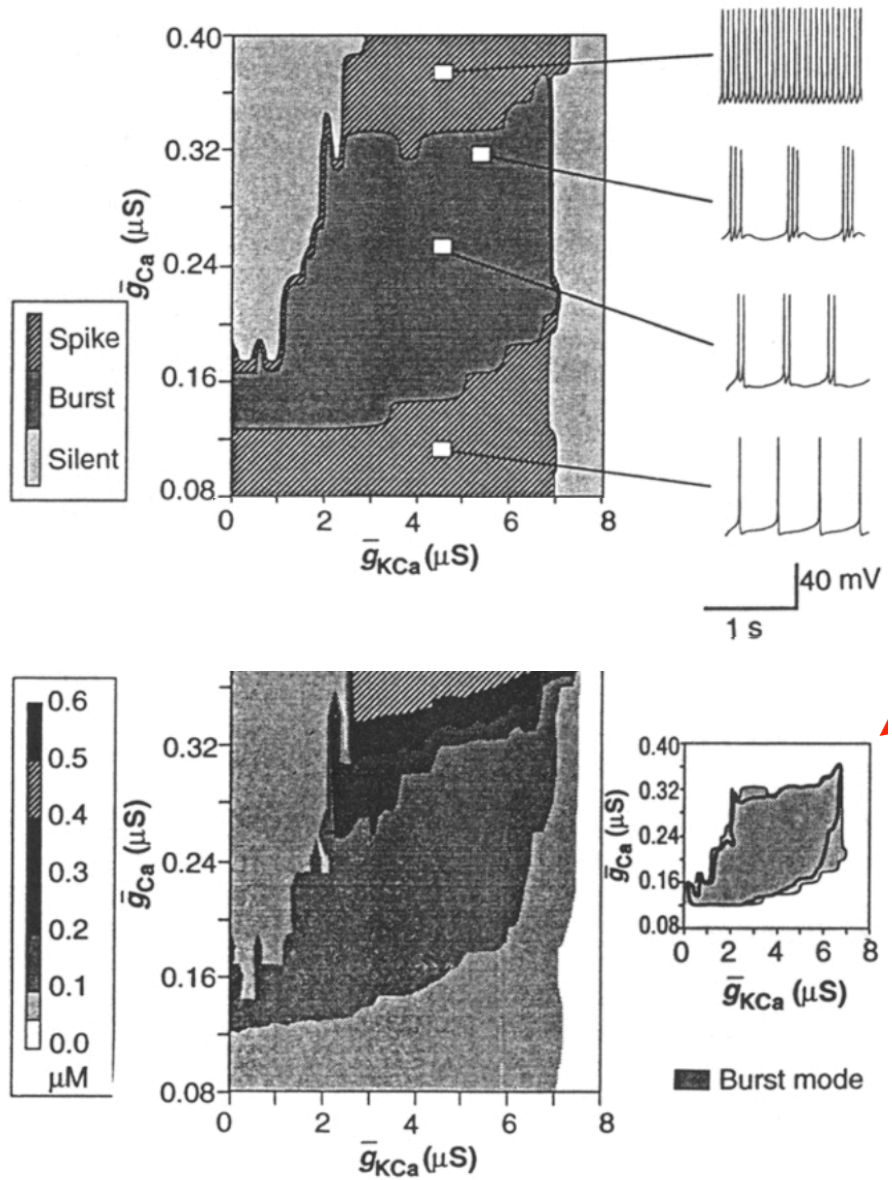
Table 1. Equations describing the activation and inactivation properties of the ionic currents of the model STG neuron

Current	p	m_∞	h_∞	τ_m	τ_h
I_{Na}	3	$\frac{1}{1+\exp\left[\frac{-V-25.5}{5.29}\right]}$	$\frac{1}{1+\exp\left[\frac{V+48.9}{5.18}\right]}$	$1.32-\frac{1.26}{1+\exp\left[\frac{-120-V}{25}\right]}$	$0.67\cdot\left[\frac{1}{1+\exp\left[\frac{-62.9-V}{10}\right]}\right]\cdot\left[1.5+\frac{1}{1+\exp\left[\frac{V+34.9}{3.6}\right]}\right]$
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	$\frac{1}{1+\exp\left[\frac{V+78.3}{6.5}\right]}$		$272-\frac{-1499}{1+\exp\left[\frac{-V-42.2}{8.73}\right]}$	



A
50 µm
axon
B
pdn
(PD)
LP
pyn
(PY)
-35 mV
-55 mV
0.5 s
C
LP
-35 mV
-55 mV
0.5 s

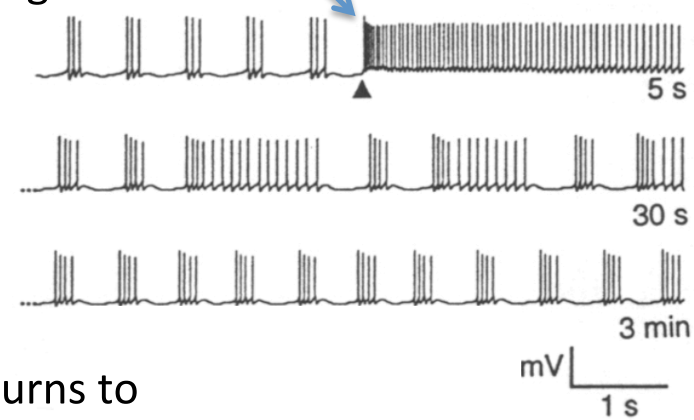
Different dynamic behavior in different regions of parameter space



LeMasson, Abbott and Marder, 1993

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

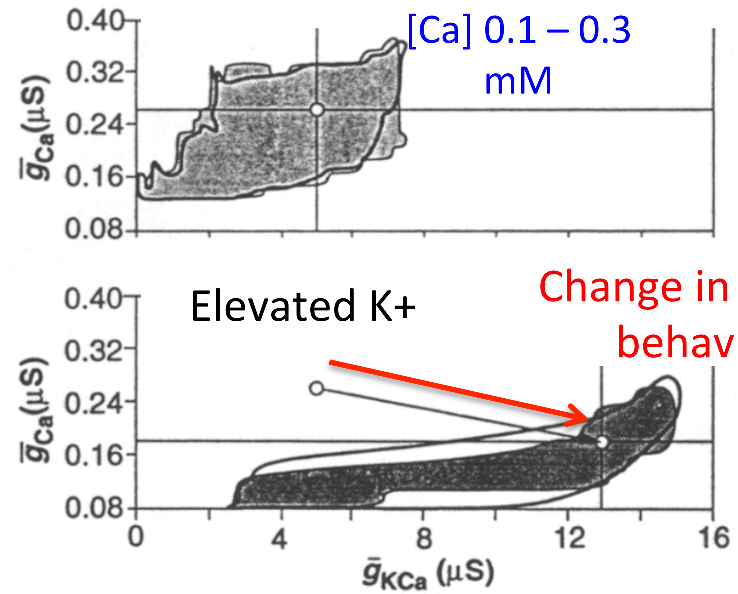
Bursting



Returns to bursting

Normal K+

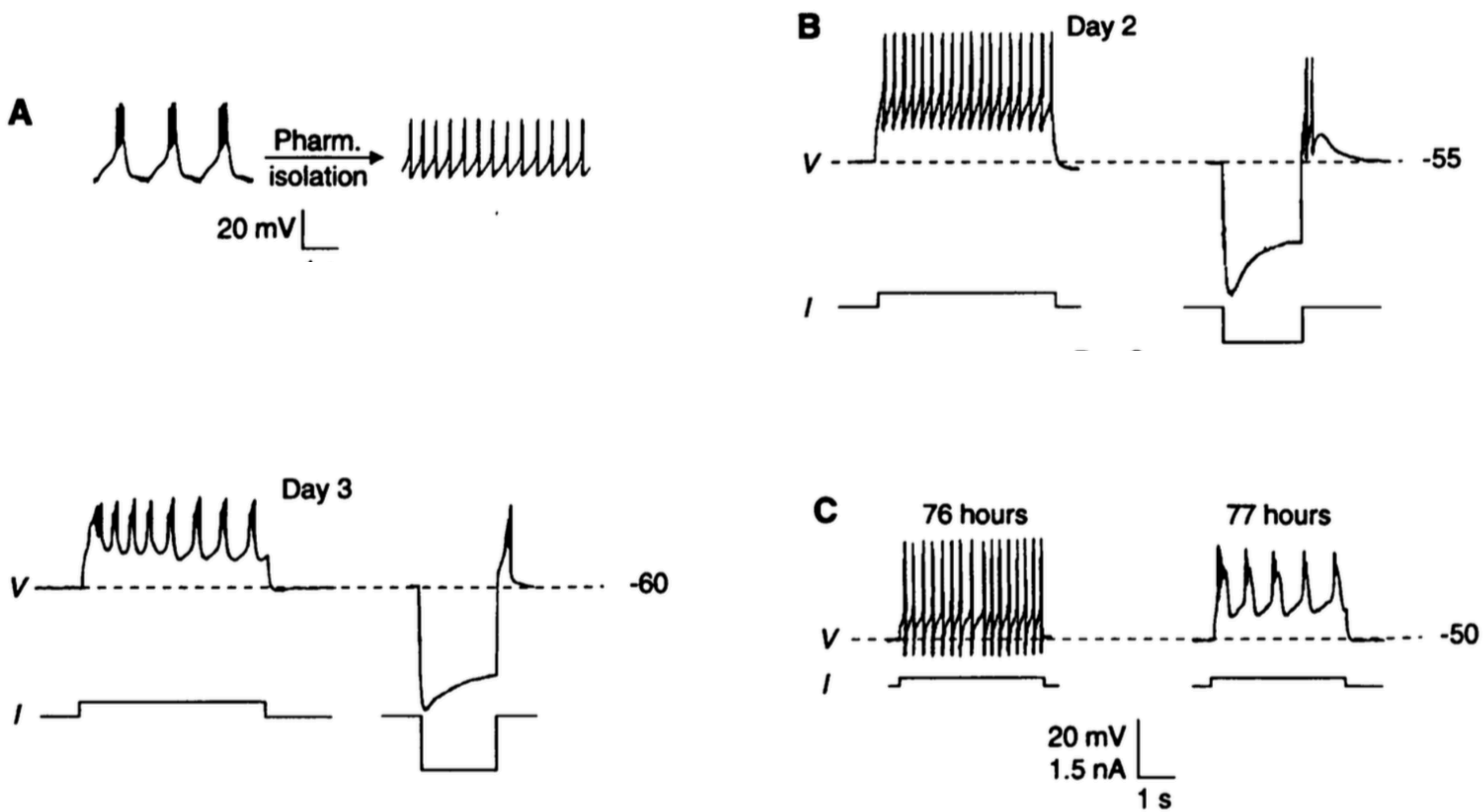
[Ca] 0.1 – 0.3 mM



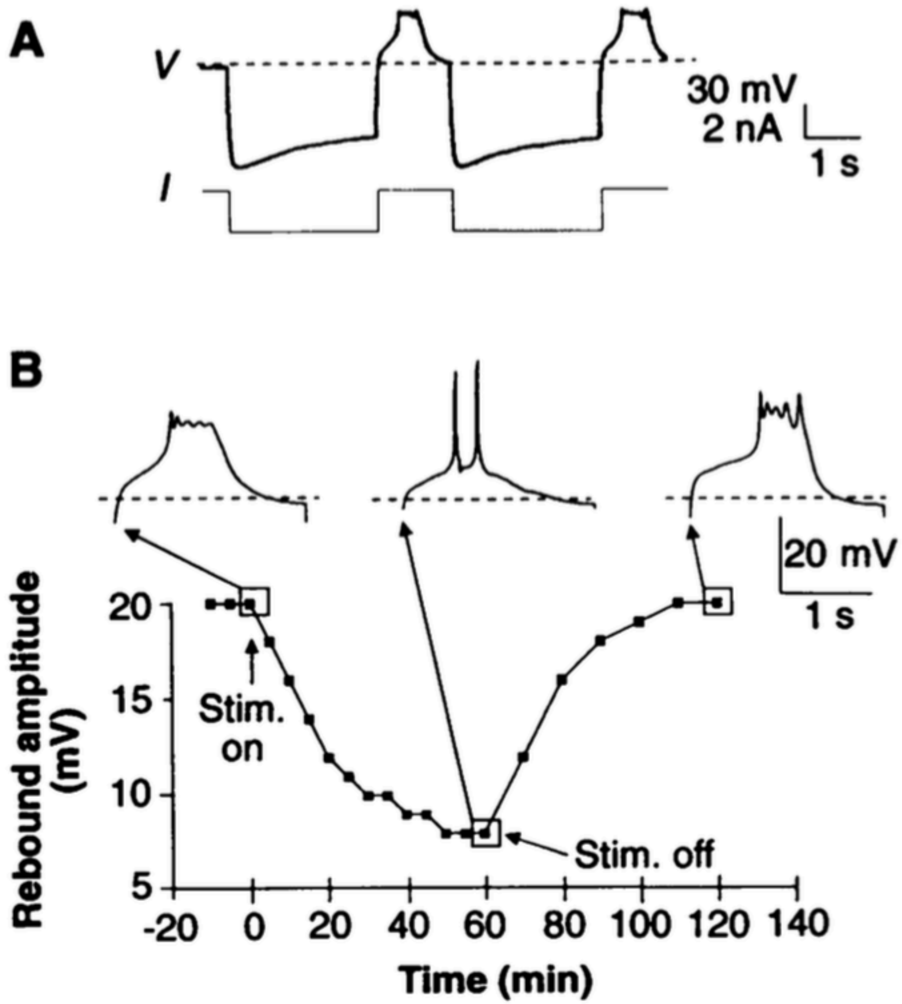
Elevated K+

Change in model behavior

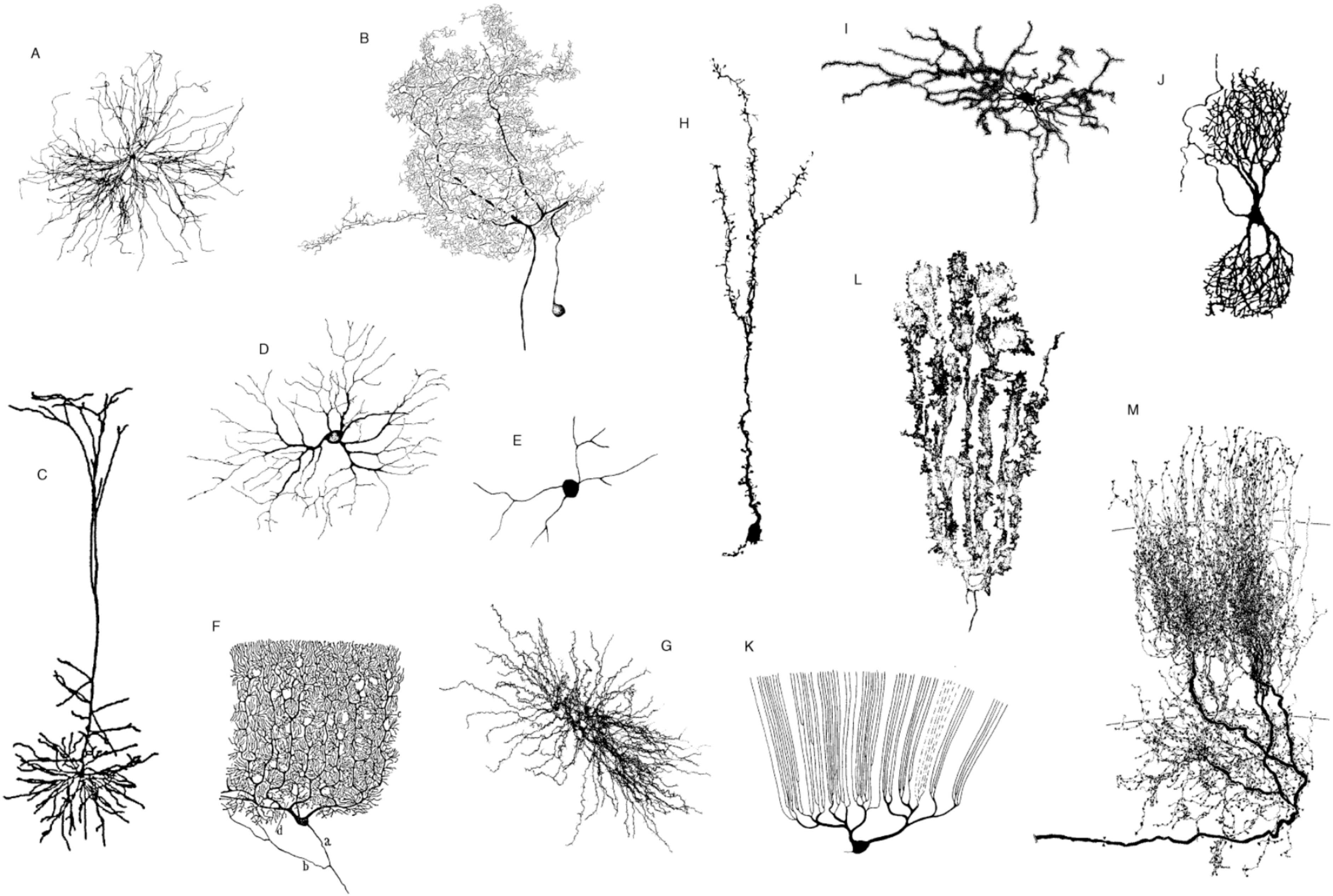
Cells change their physiological properties to burst



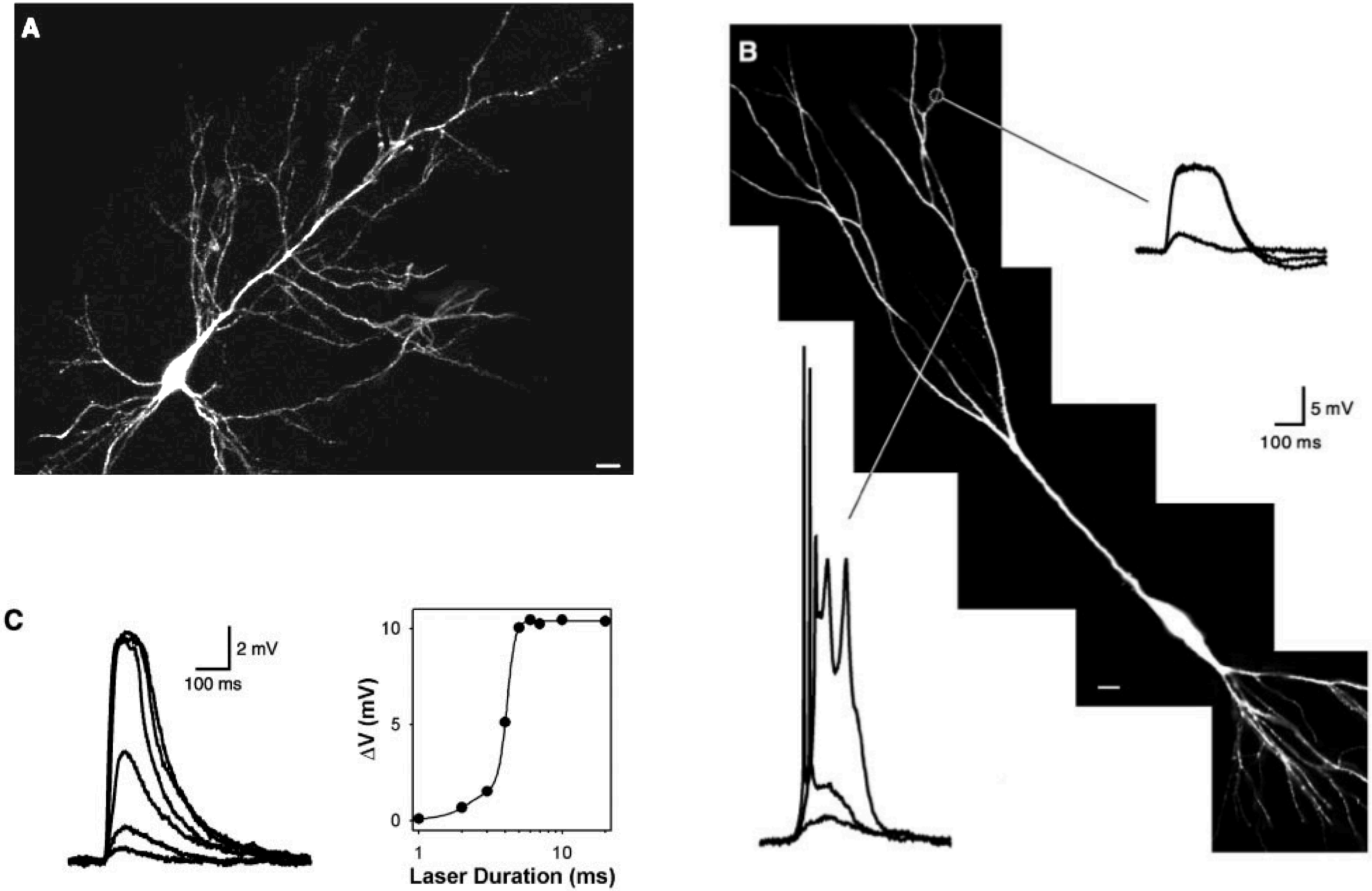
Turrigiano et al., 1994


A
V
30 mV
2 nA
1 s
I
B
20 mV
1 s
Rebound amplitude (mV)
20
15
10
5
Stim. on
Stim. off
-20
0
20
40
60
80
100
120
140
Time (min)

What influence do dendrites have on computation?

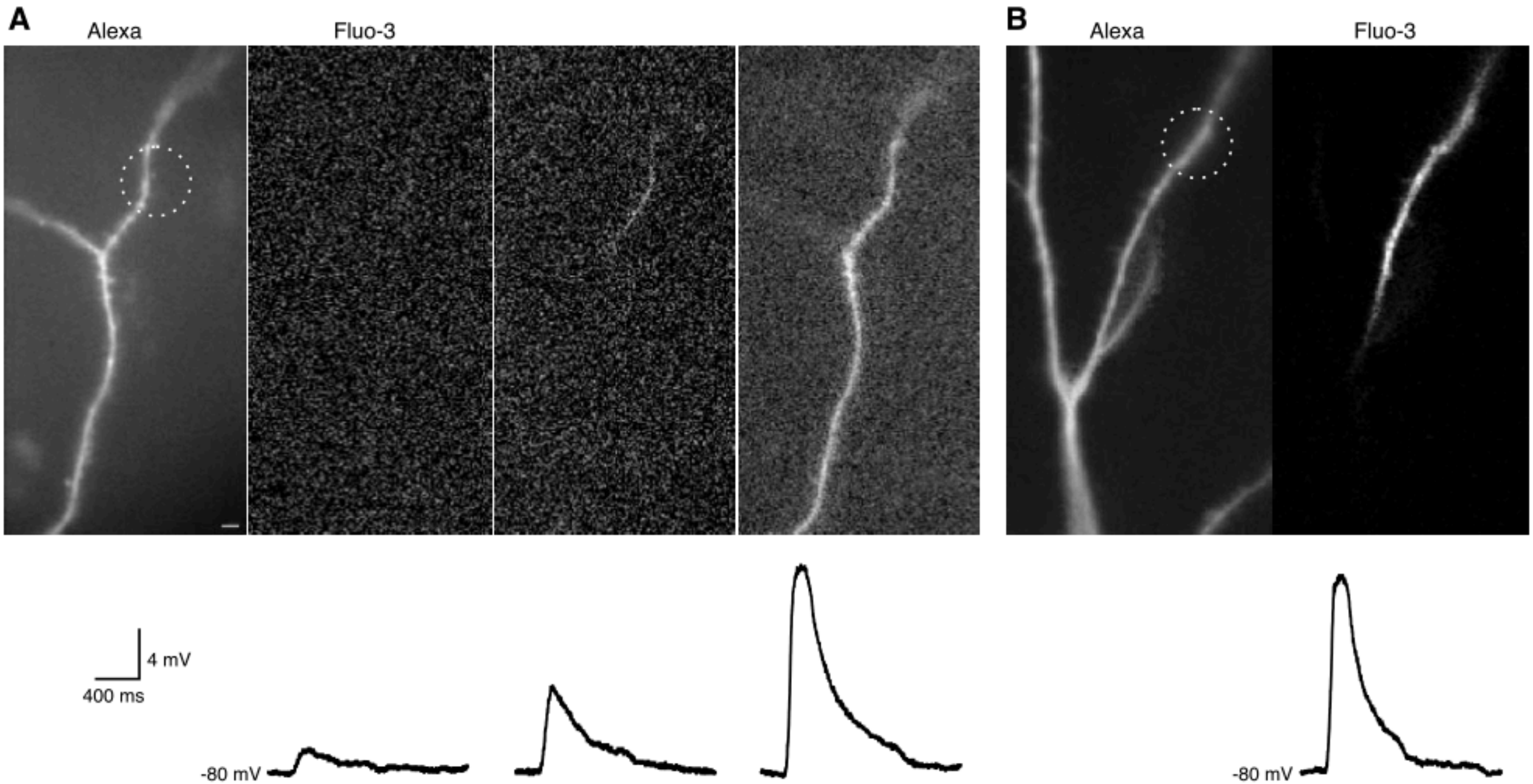

A
B
C
D
E
F
G
H
I
J
K
L
M
d
a
b

All or none calcium action potentials in pyramidal cell dendrites



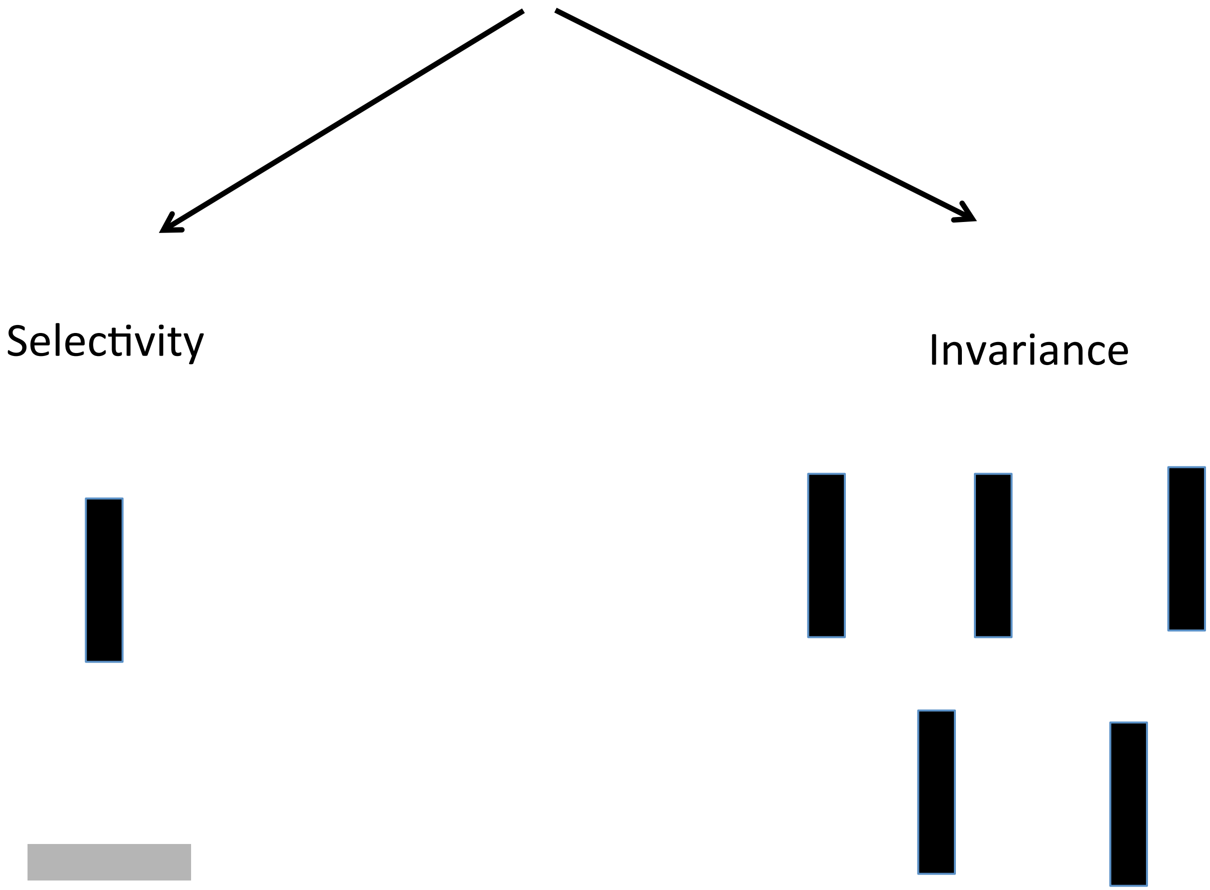
Wei et al., 2001. Compartmentalized and Binary Behavior of Terminal Dendrites in Hippocampal Pyramidal Neurons

Action potential failure at a dendritic branch point

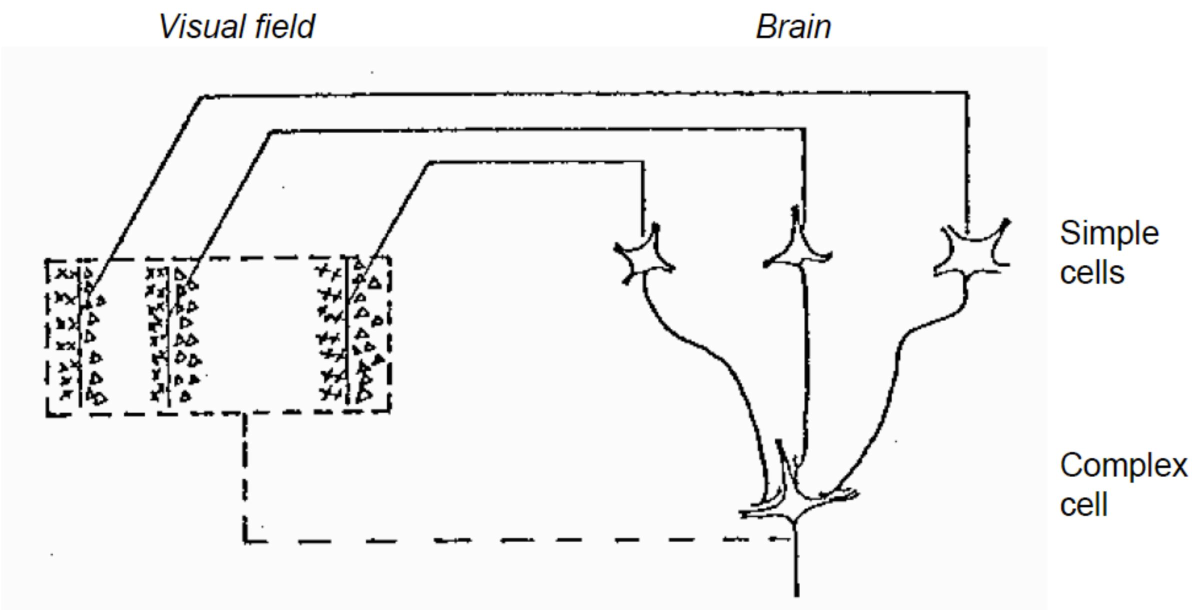


Wei et al., 2001. Compartmentalized and Binary Behavior of Terminal Dendrites in Hippocampal Pyramidal Neurons

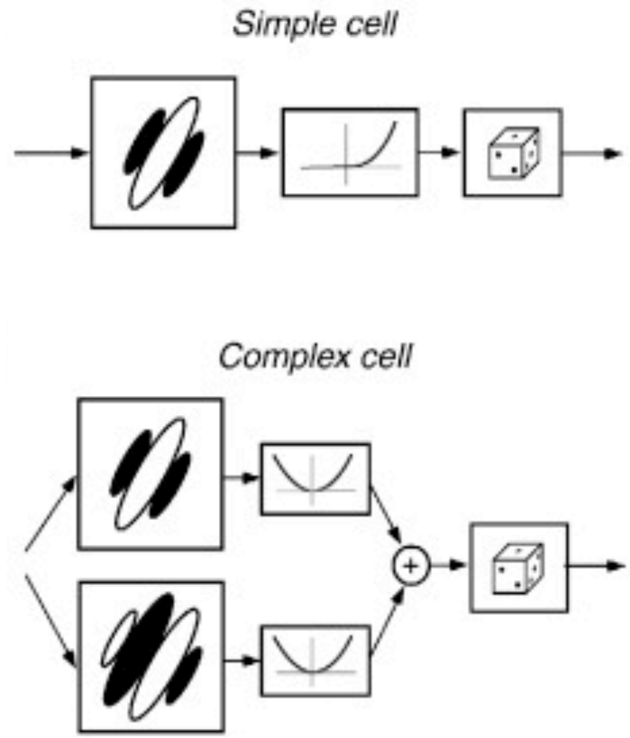
Properties of feature detection



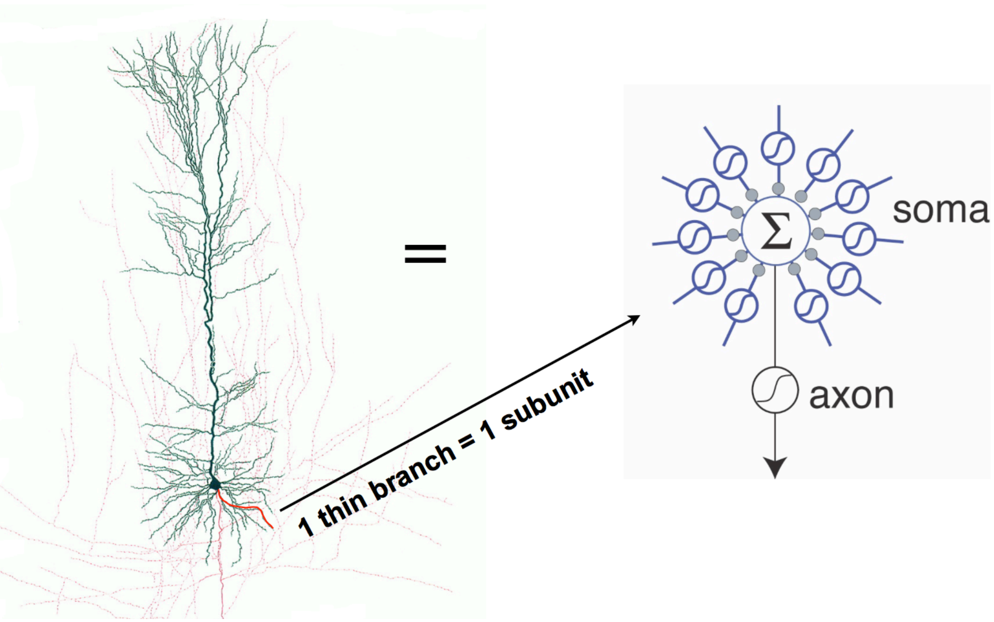
Models of selectivity and invariance in primary visual cortex

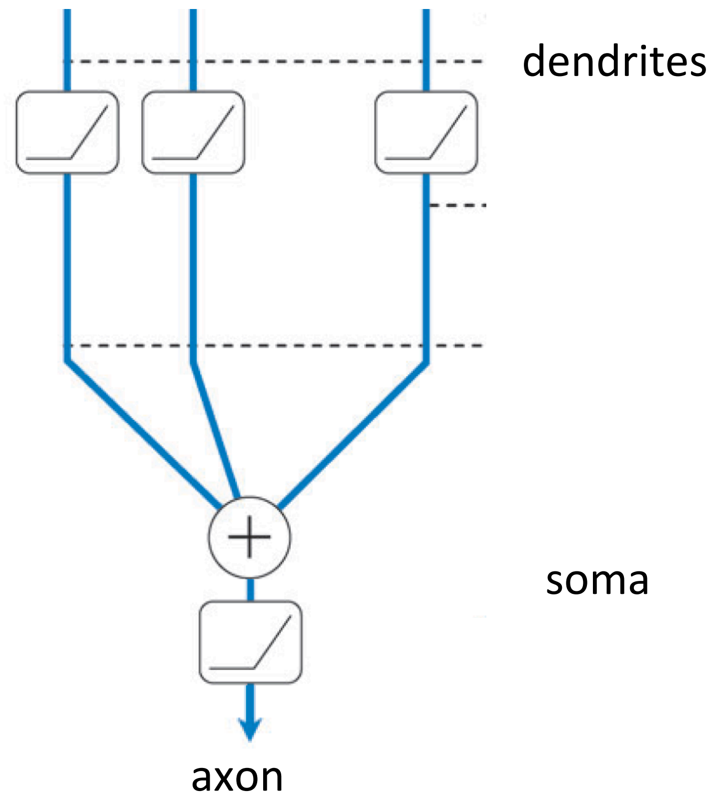


Hubel & Wiesel, 1963



Rust et al., 2005

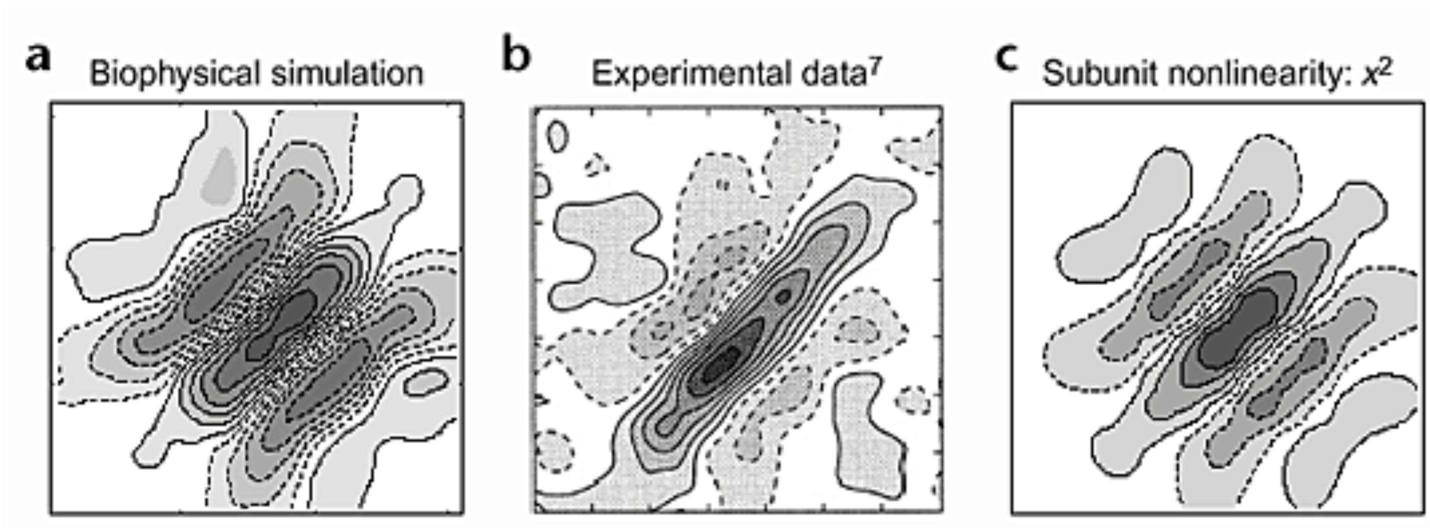

=
1 thin branch = 1 subunit
soma
Σ
axon


dendrites
+
soma
axon

Model of Binocular Disparity Representation

Bar presented to left & right eyes

Right eye pos. (deg)



Left eye pos. (deg)

Archie & Mel (2000)