Introduction to Computational Neuroscience
NEPR208

Theory

Biological Function ⟷ Computation ⟷ Mechanism

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Spring 2017

Why Model?

Joshua Epstein

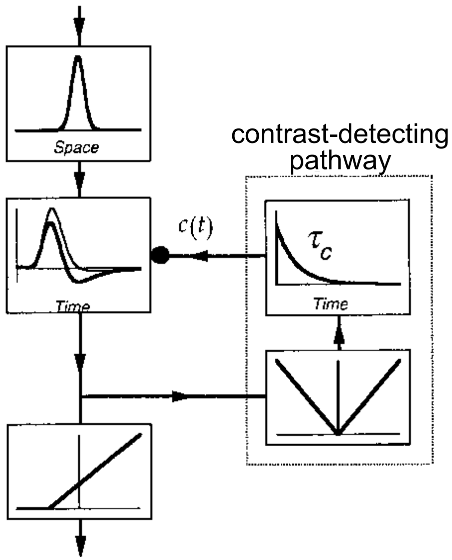
Sixteen Reasons Other Than Prediction to Build Models

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)

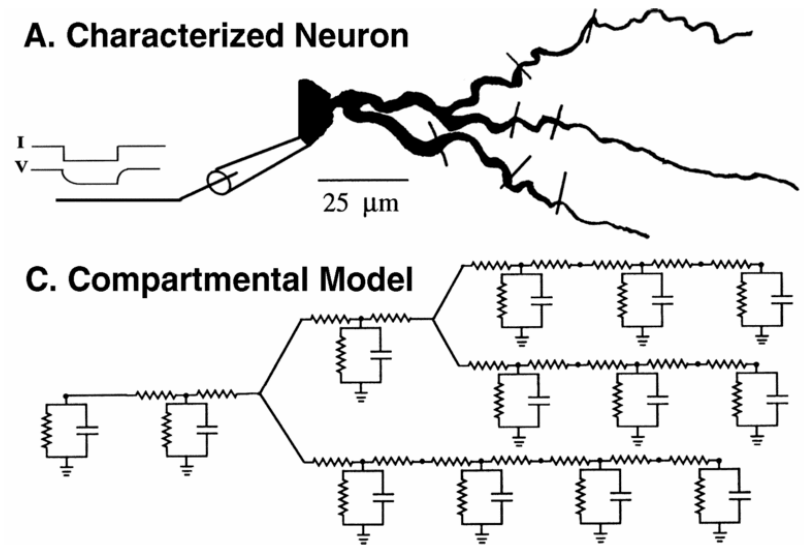
http://jasss.soc.surrey.ac.uk/11/4/12.html

Many types of models for different purposes

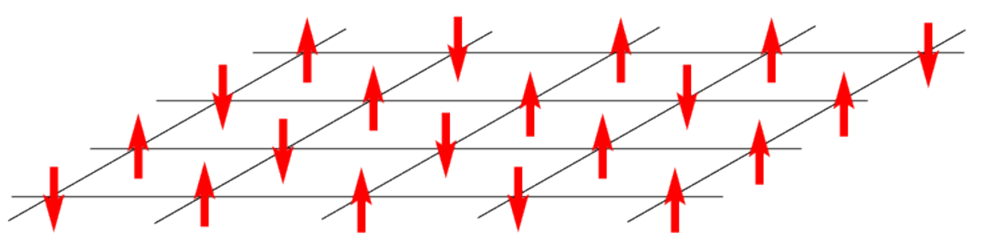
Abstract



Biophysical



Statistical

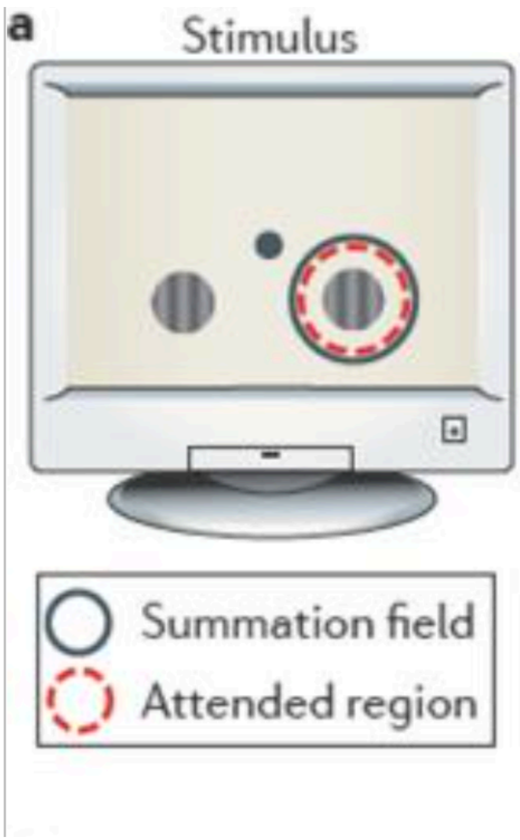


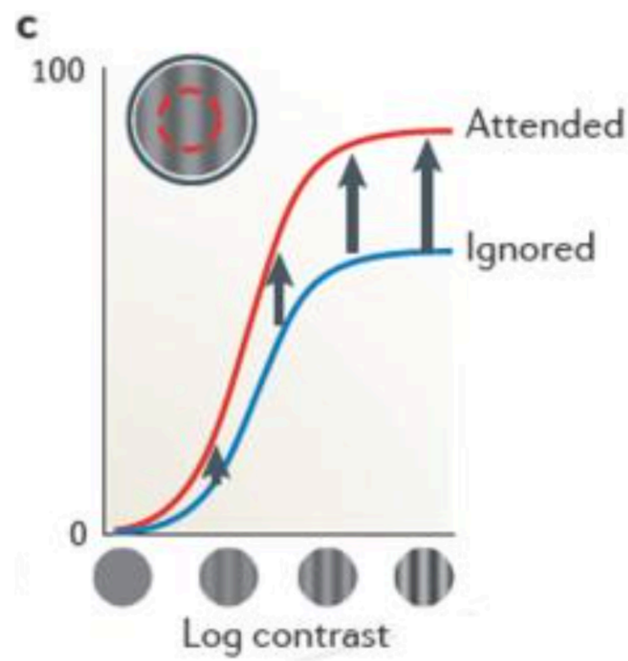
2–D Ising Model

How can a neuron change its gain?

How can a neuron maintain a stable firing pattern?

Changing gain in the nervous system



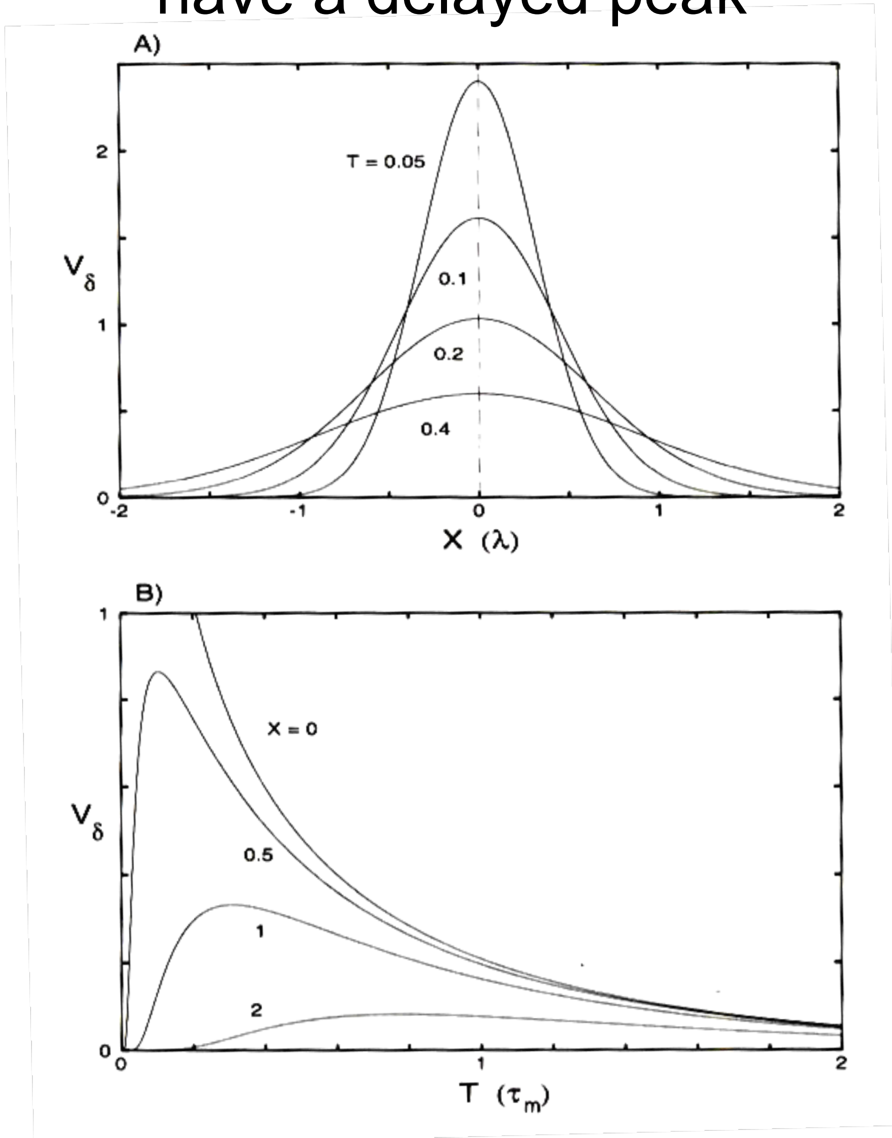


Reynolds & Heeger, 2009

How can a neuron control its gain?

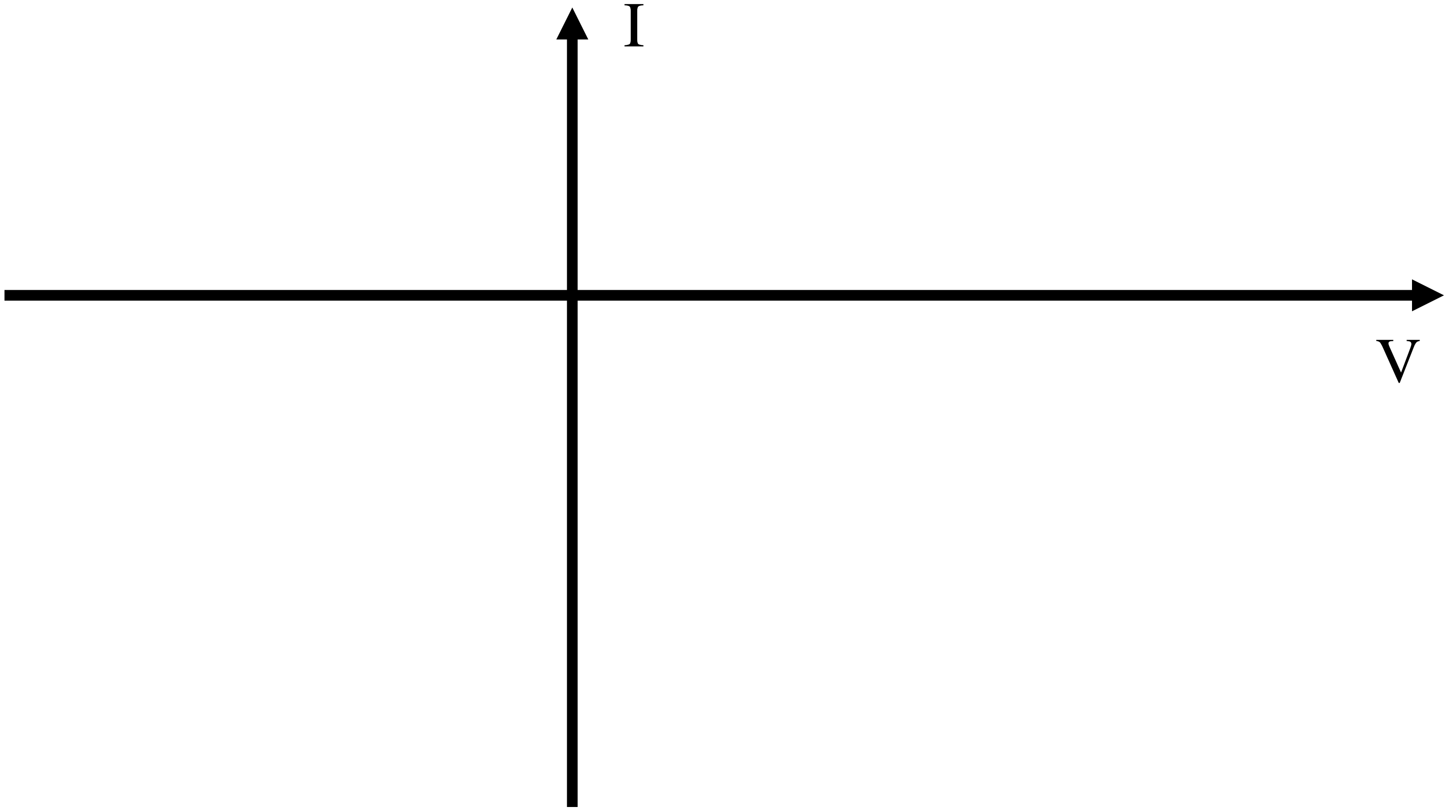
- Integrate and fire neuron
  - Sum of currents
  - Tau
- Conductance models

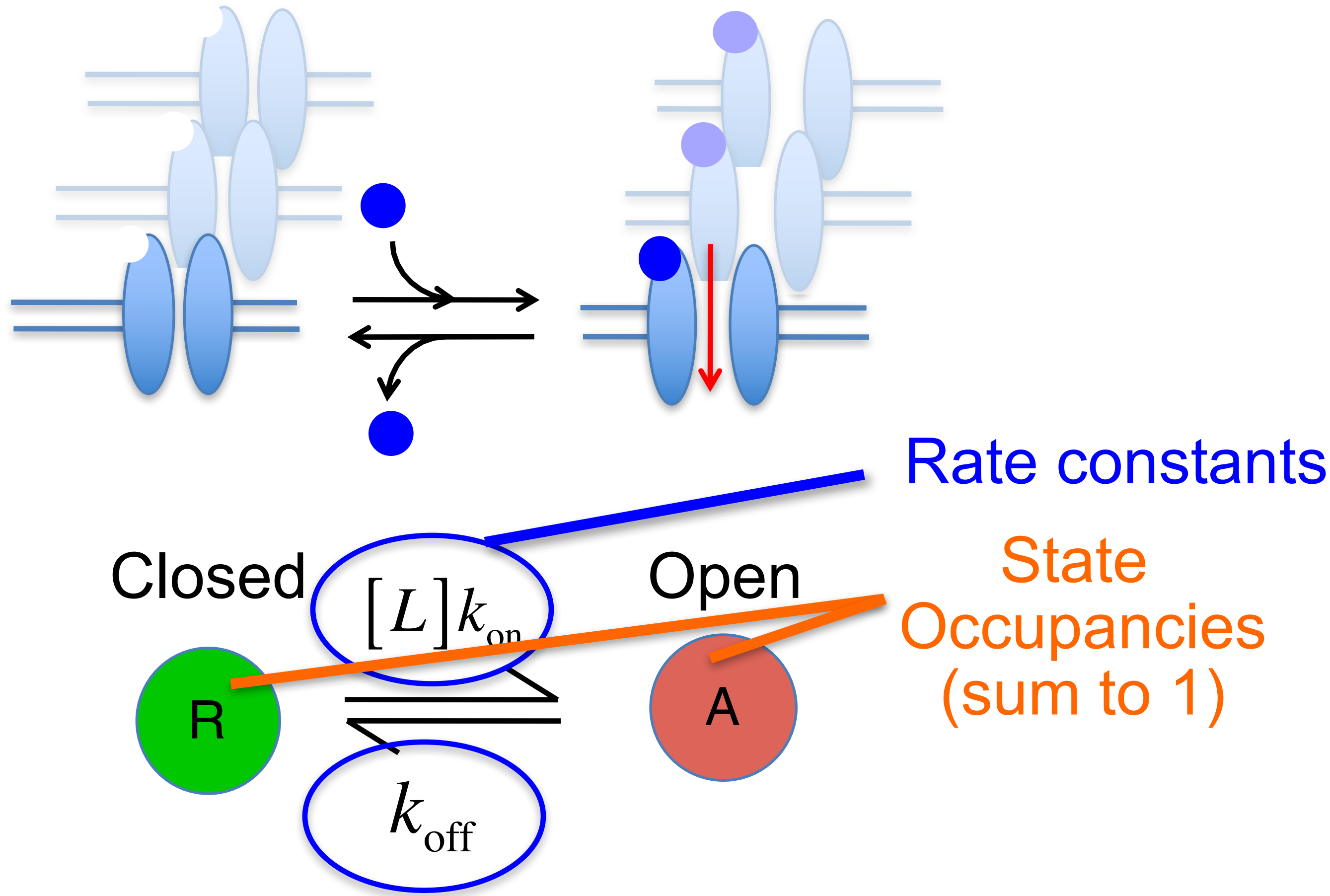
Due to filtering along a cable, distant locations have a delayed peak



From Koch, Biophysics of Computation, Oxford Press, 1999

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



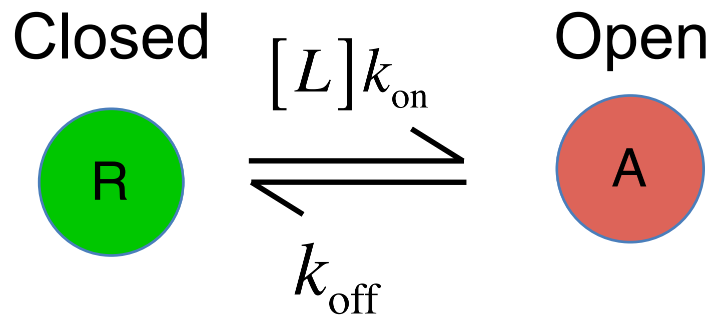


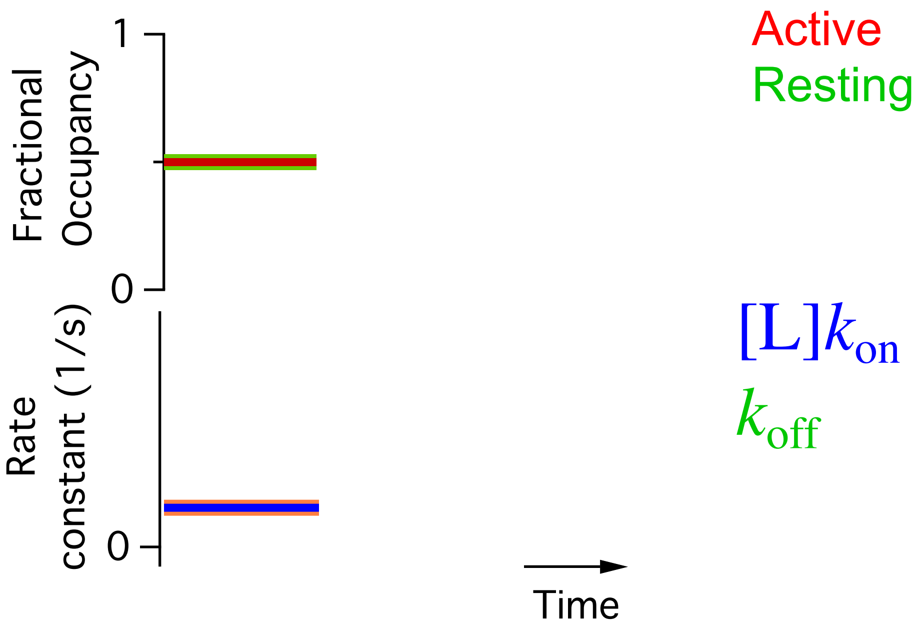
Change in activity = Inflow − Outflow

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

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:

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

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:

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

$$\begin{aligned} \bar{g}_{\mathrm{K}} &= 36\,\mathrm{mS/cm^2} & E_K &= -12\,\mathrm{mV} \\ \bar{g}_{\mathrm{Na}} &= 120\,\mathrm{mS/cm^2} & E_{Na} &= +115\,\mathrm{mV} \\ \bar{g}_l &= 0.3\,\mathrm{mS/cm^2} & E_l &= +10.613\,\mathrm{mV} \end{aligned}$$

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

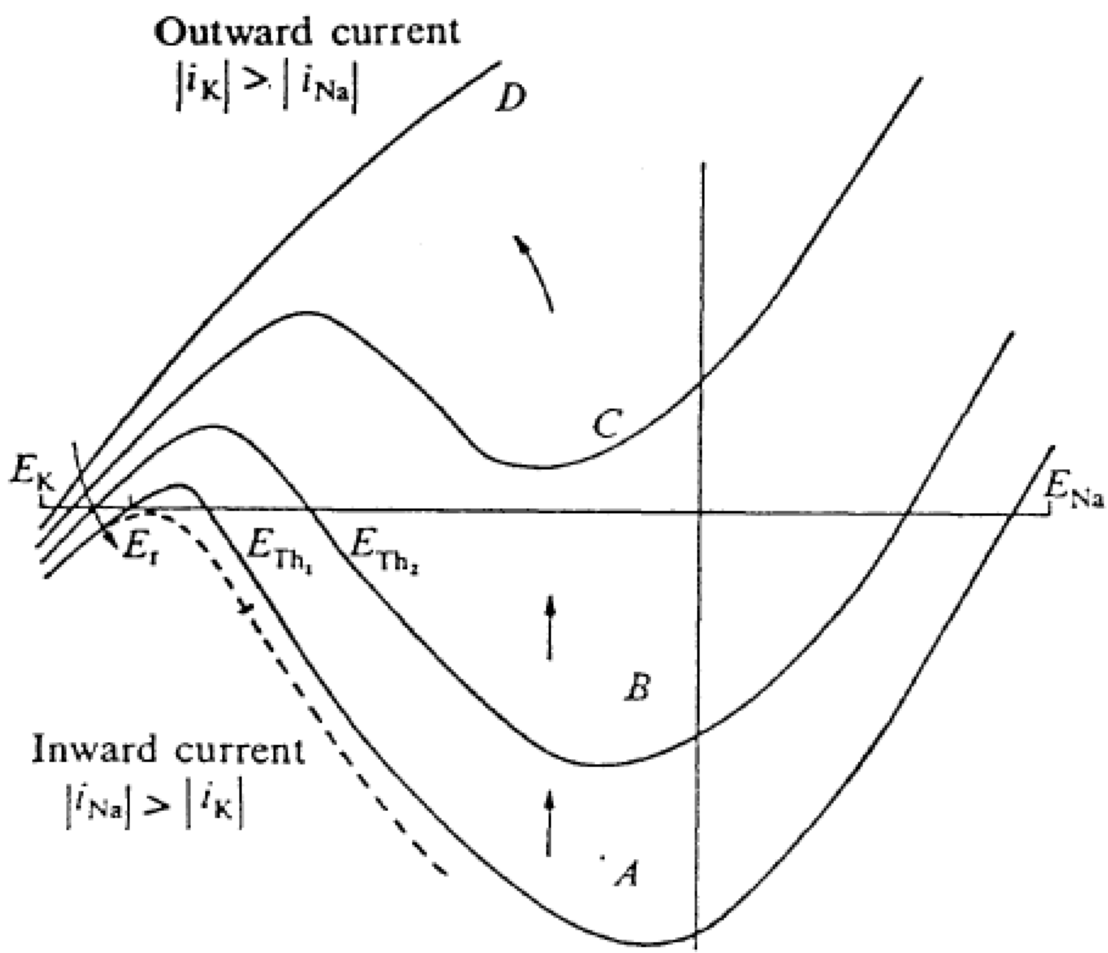
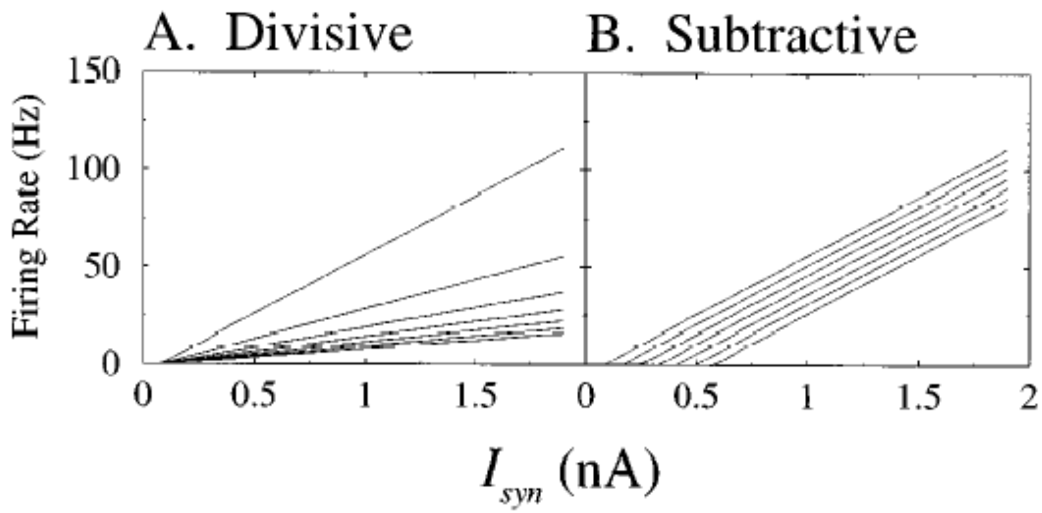
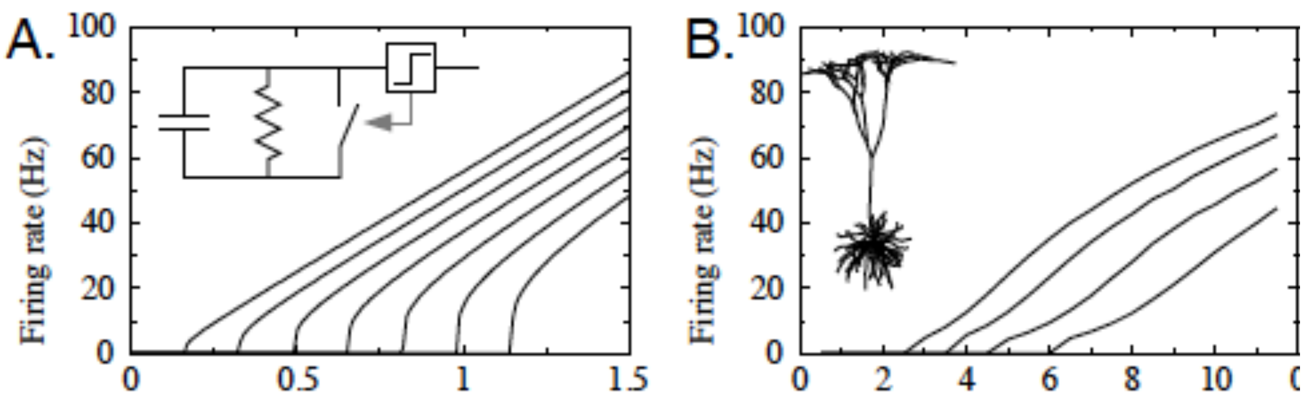


FIG. 8.12. Diagram illustrating change in momentary current–voltage relations with time on depolarization.



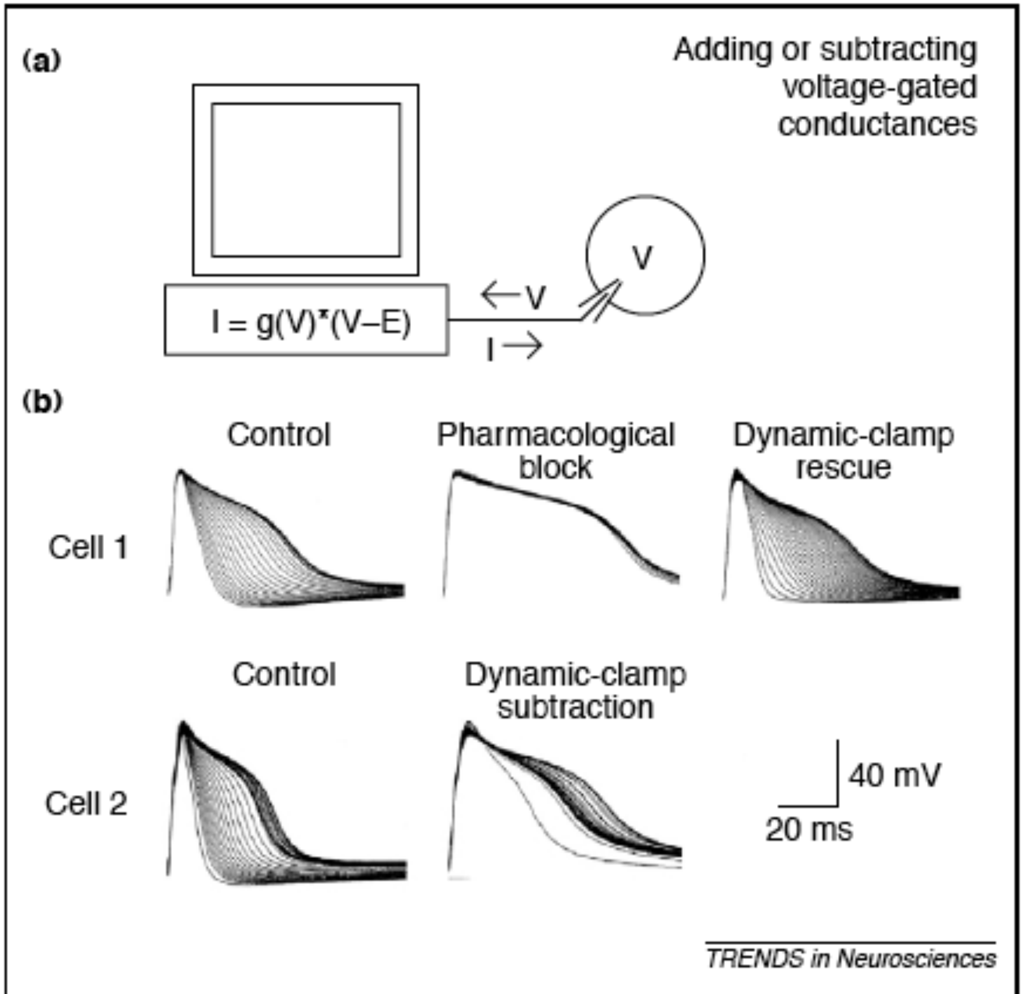


Current (nA) Excitatory synaptic input rate (Hz)

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

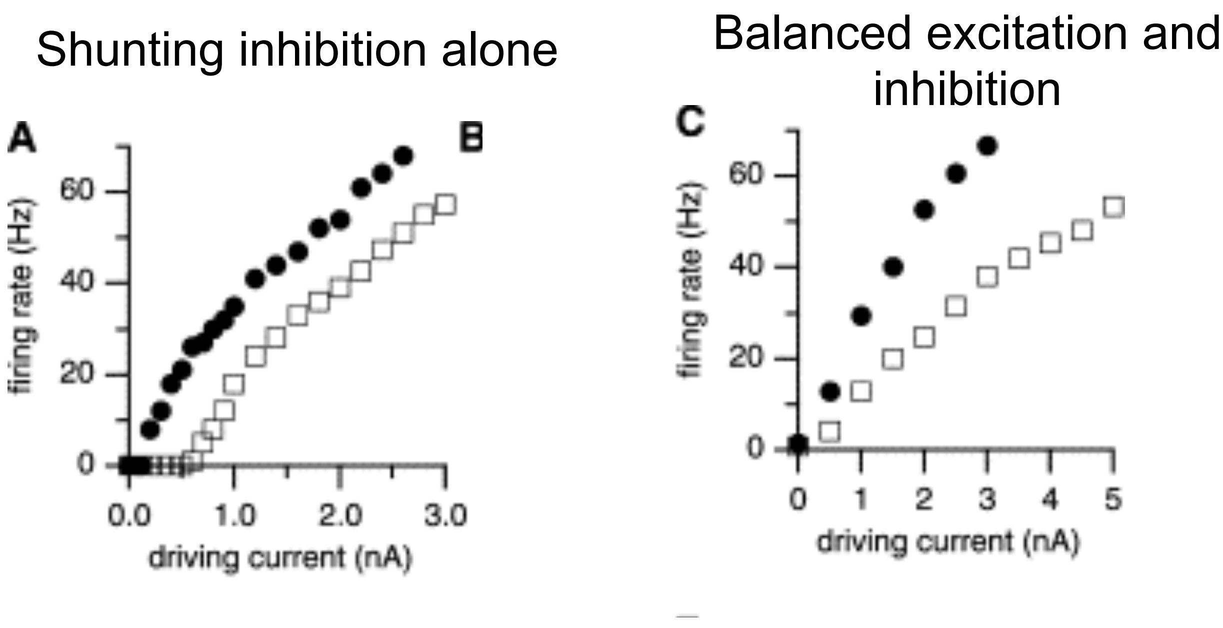
The dynamic clamp

Artificially adding or subtracting membrane mechanisms



Balanced excitation and inhibition can change gain

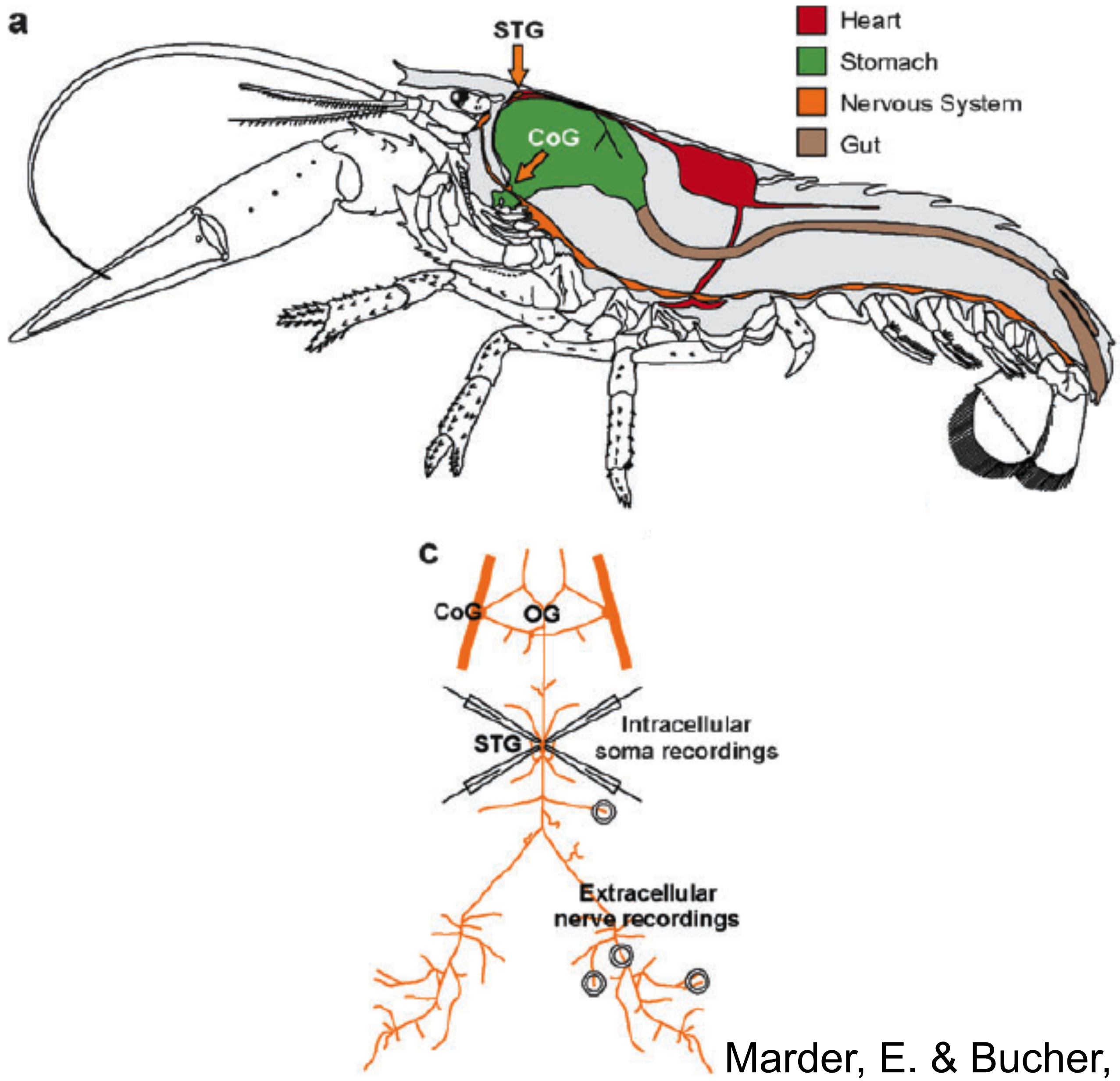
Rat somatosensory cortex slice



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

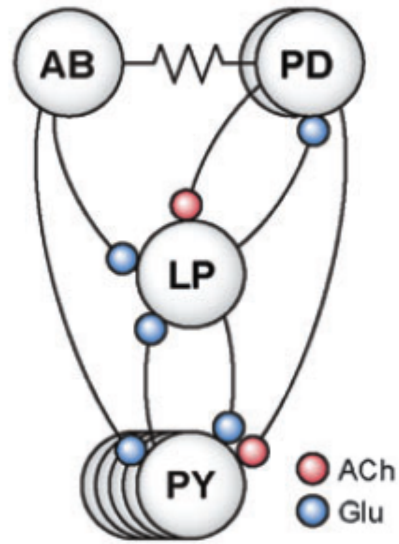
How can a neuron maintain a stable firing pattern?

Crustacean stomatogastric ganglion



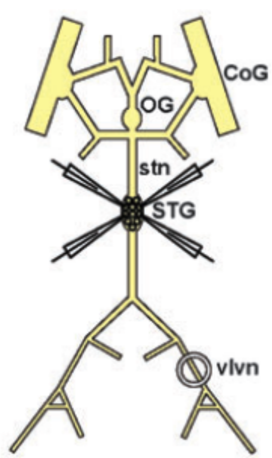
Marder, E. & Bucher, D., 2006

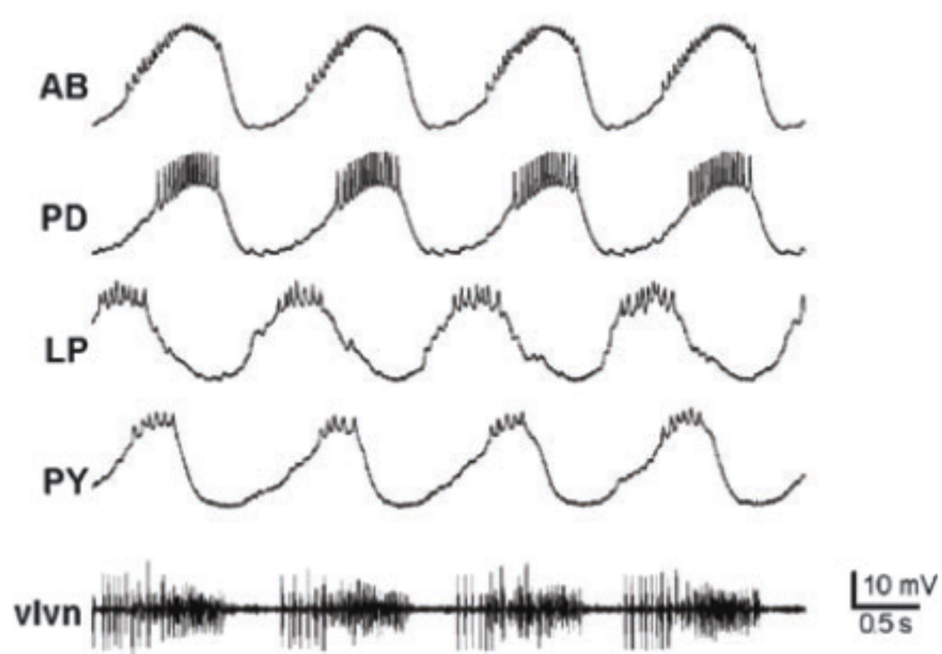
Pyloric oscillator of the stomatogastric ganglion



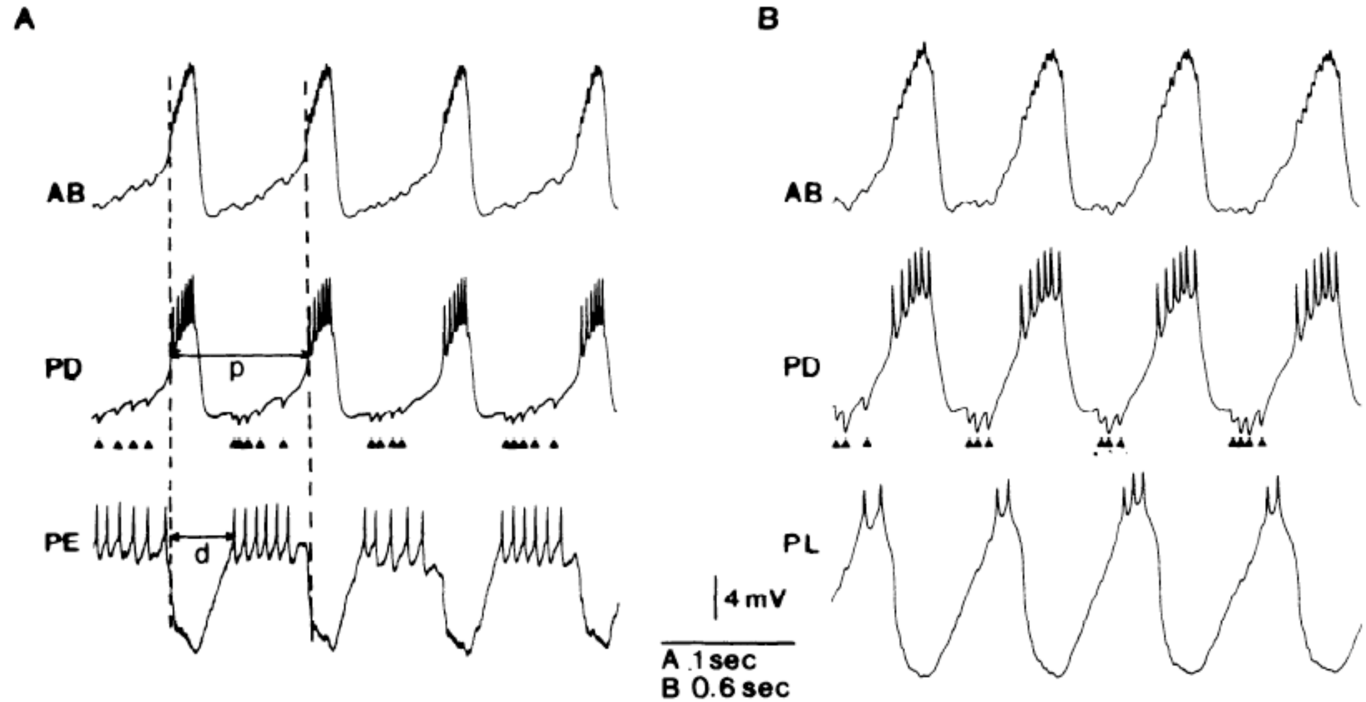
AB: Anterior burster
PD: Pyloric dilator
LP: Lateral Pyloric
PY: Pyloric

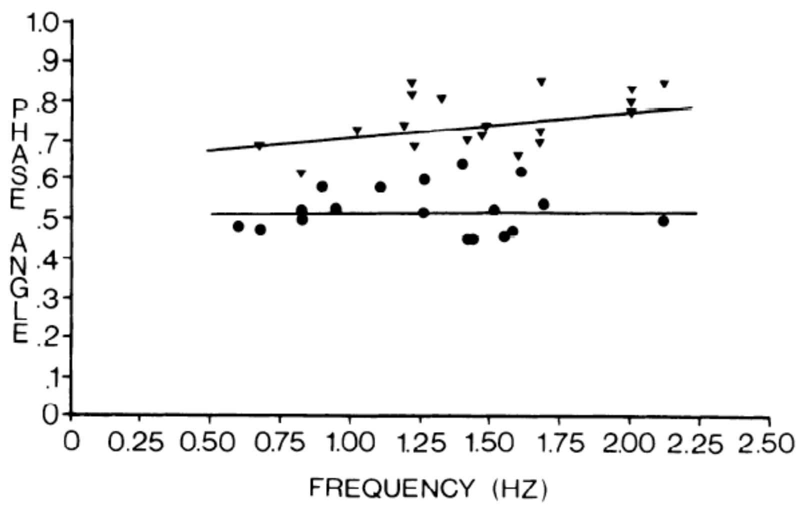
Note: these are *inhibitory*





Phase constancy across oscillation frequency

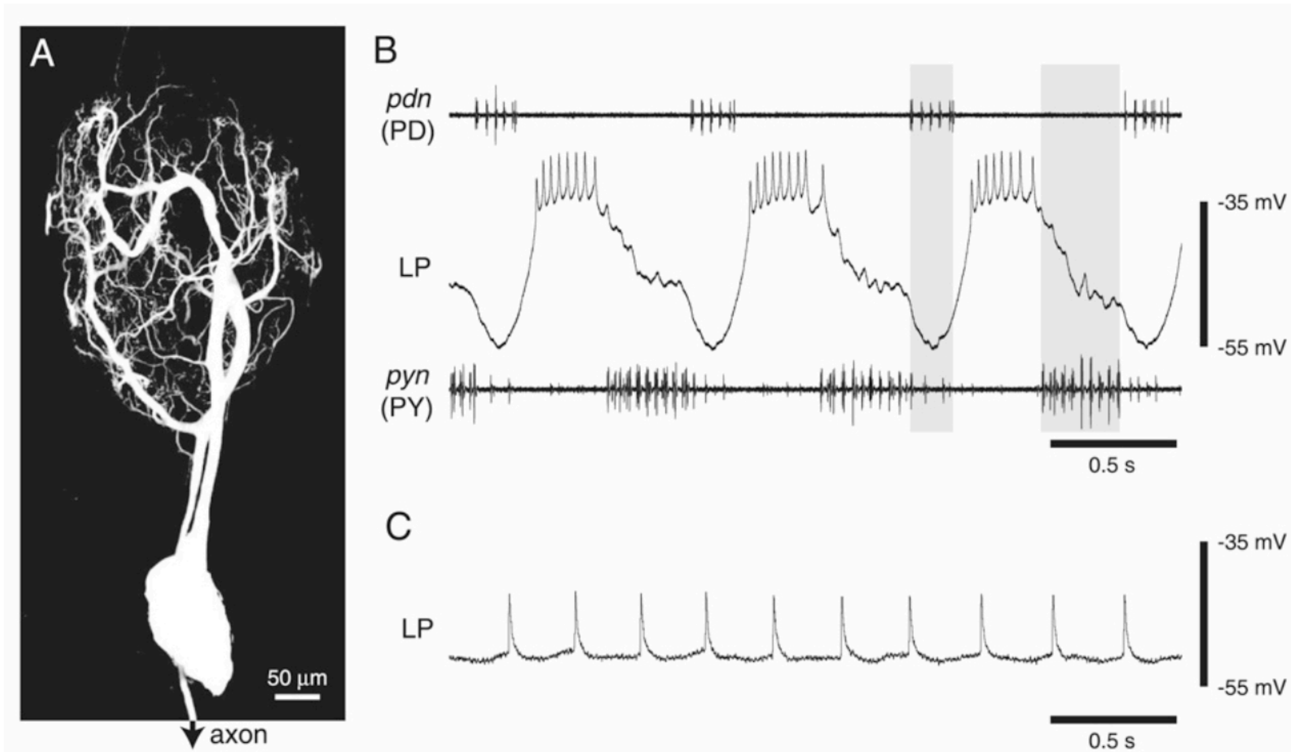




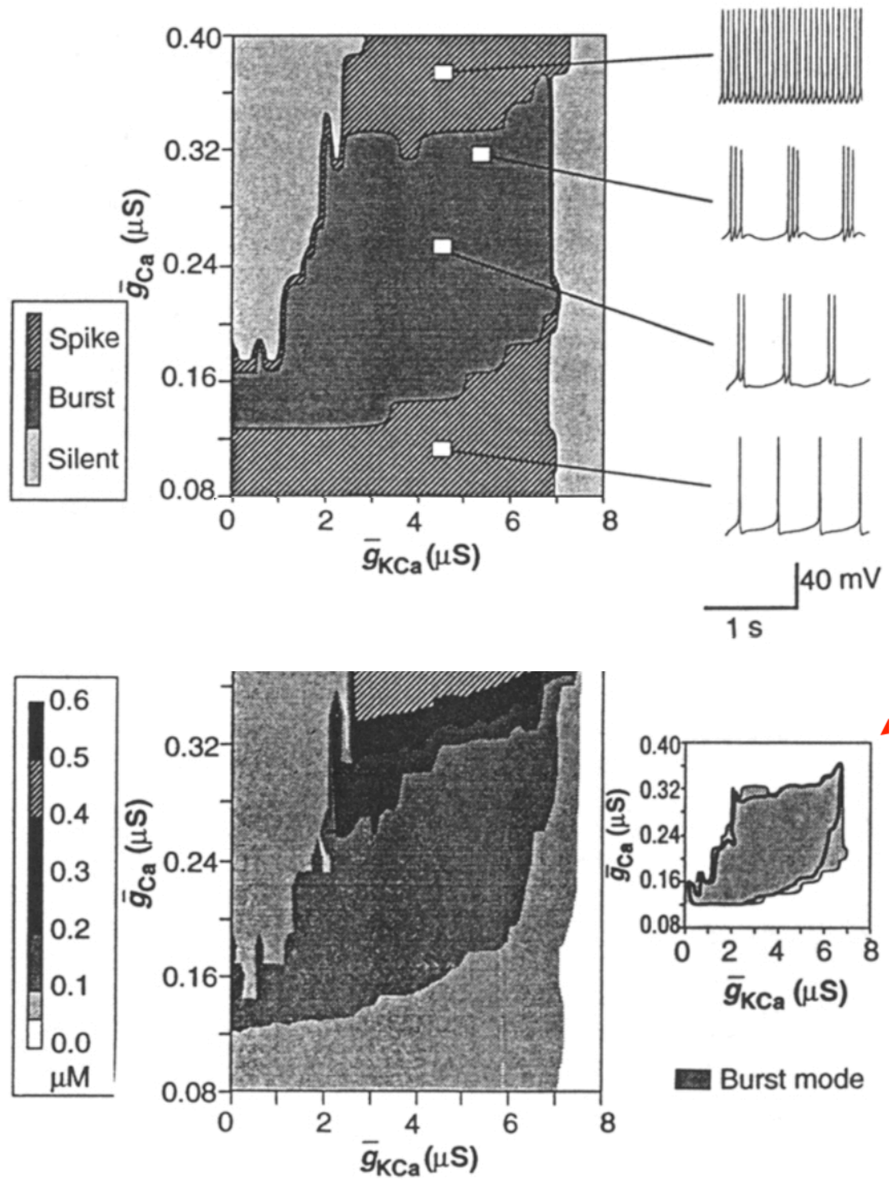
Many conductances, how are they regulated?

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

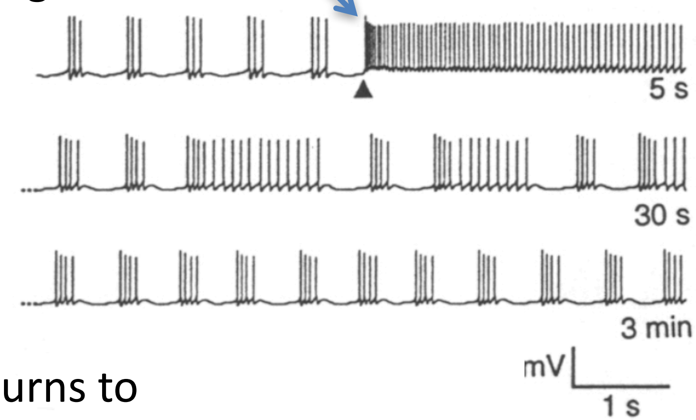
Different dynamic behavior in different regions of parameter space



LeMasson, Abbott and Marder, 1993

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

Bursting



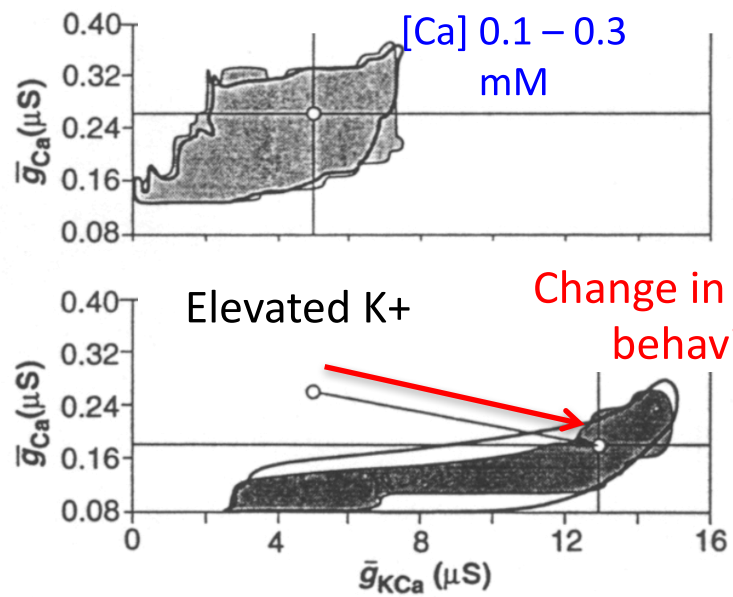
Returns to bursting

Normal K+

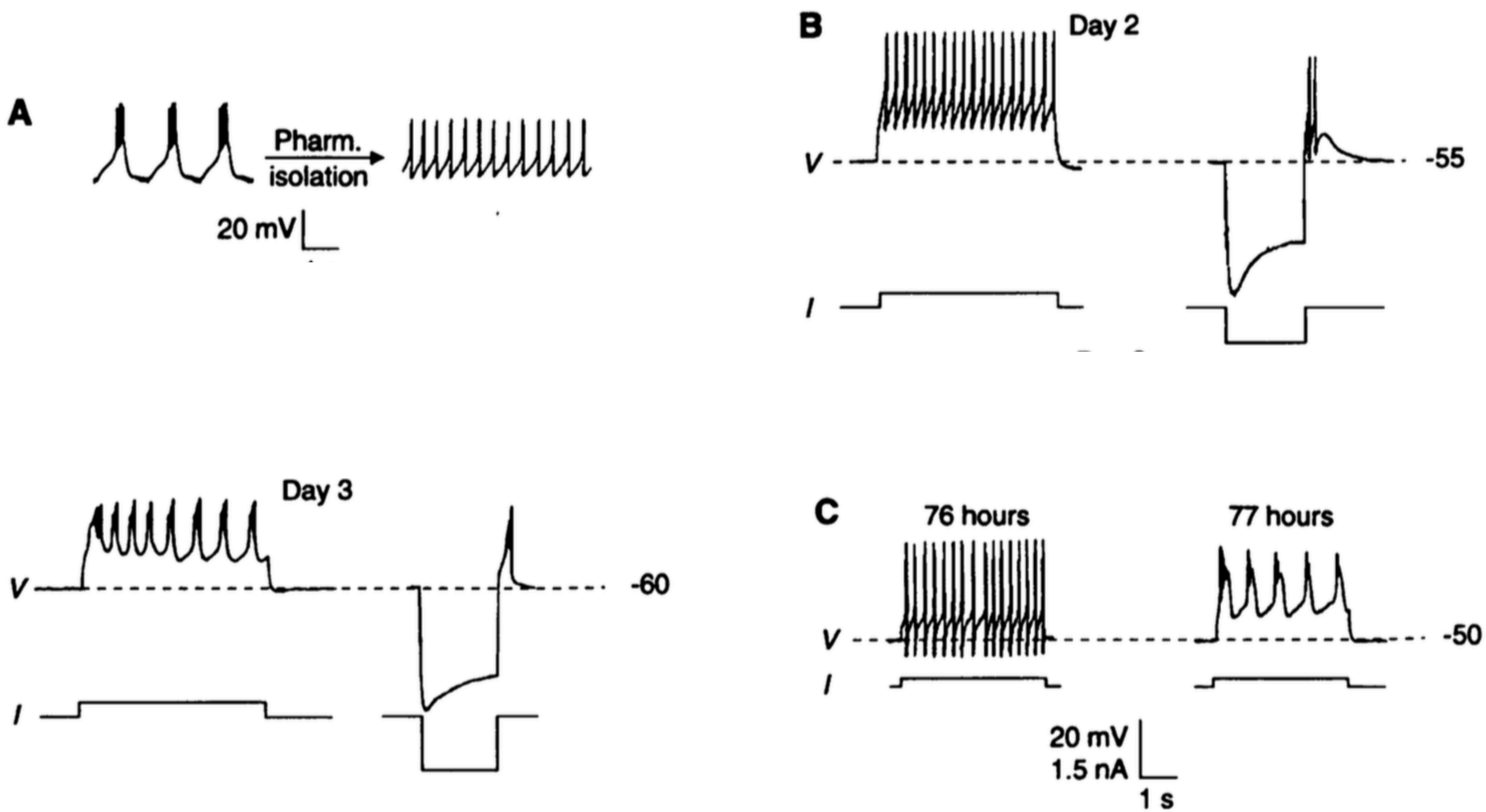
[Ca] 0.1 – 0.3 mM

Elevated K+

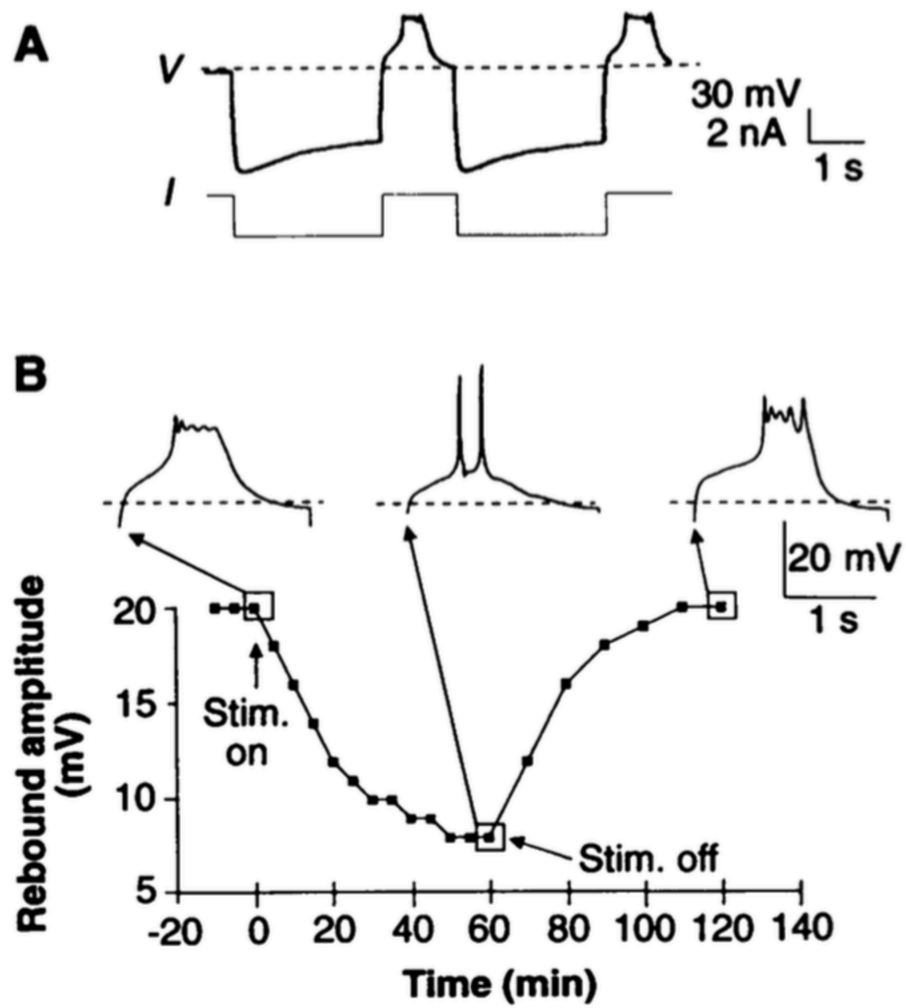
Change in model behavior



Cells change their physiological properties to burst

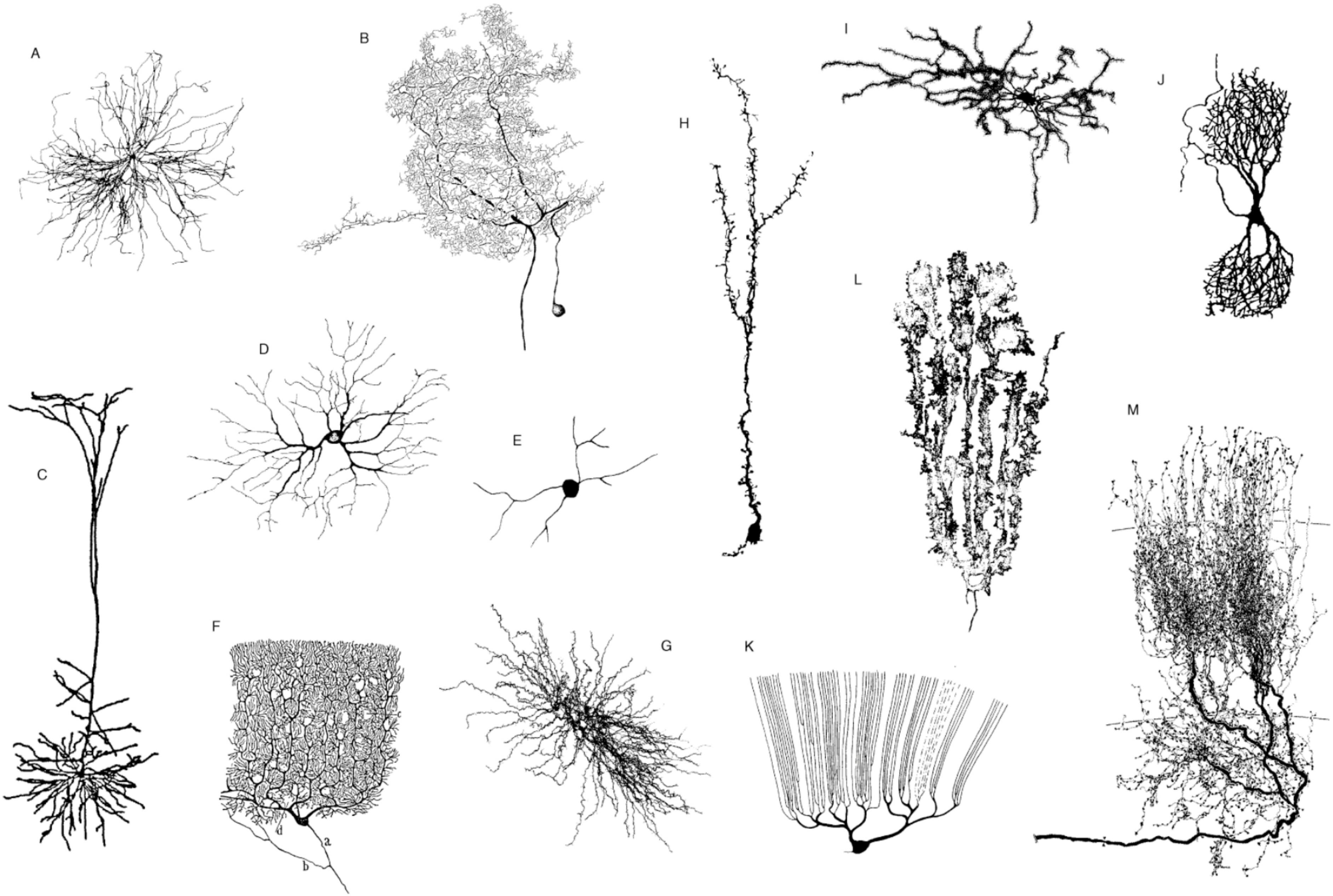


Turrigiano et al., 1994



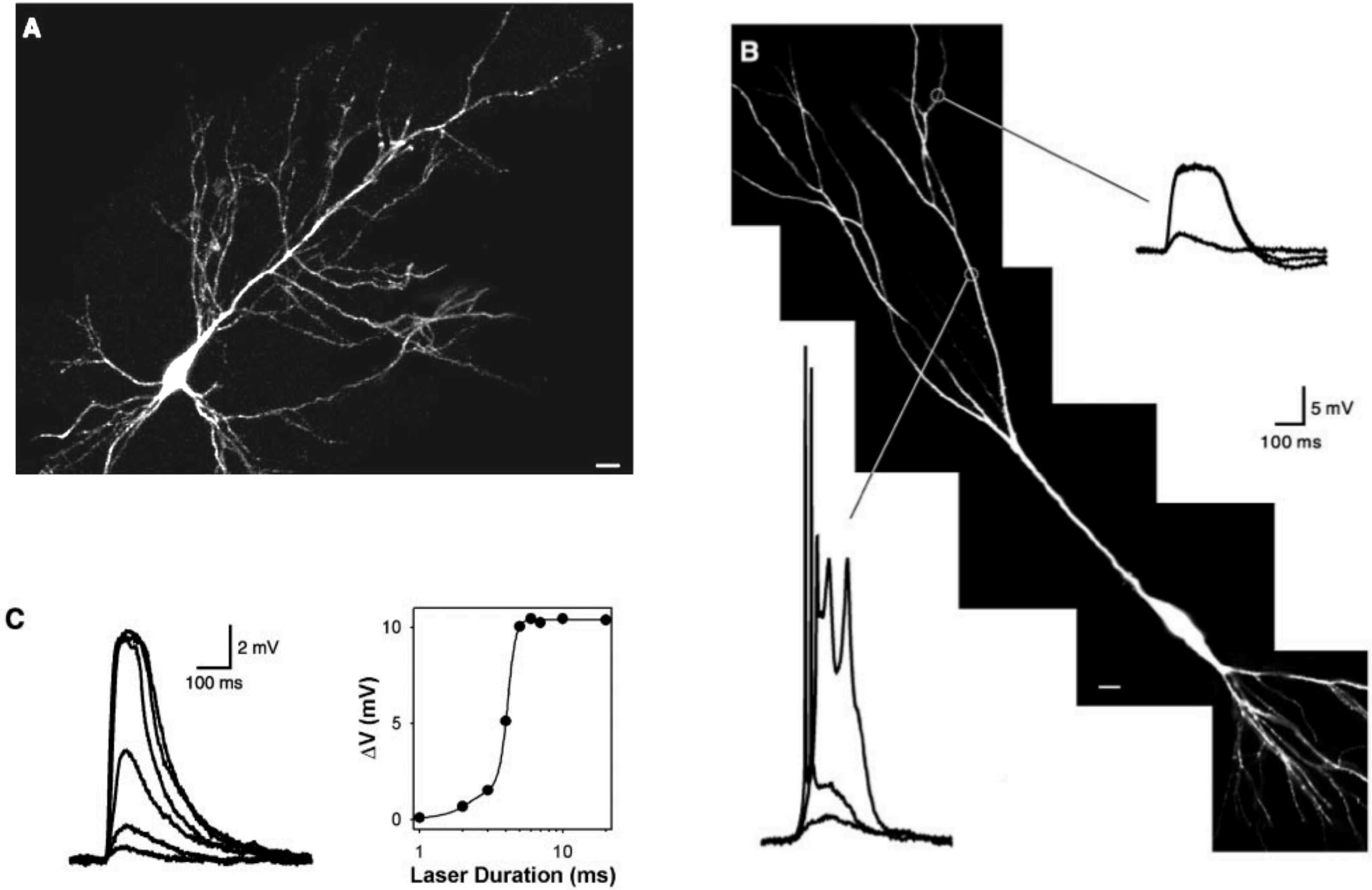
A
V
I
30 mV
2 nA
1 s
B
20 mV
1 s
Rebound amplitude (mV)
Stim. on
Stim. off
20
15
10
5
-20
0
20
40
60
80
100
120
140
Time (min)

What influence do dendrites have on computation?



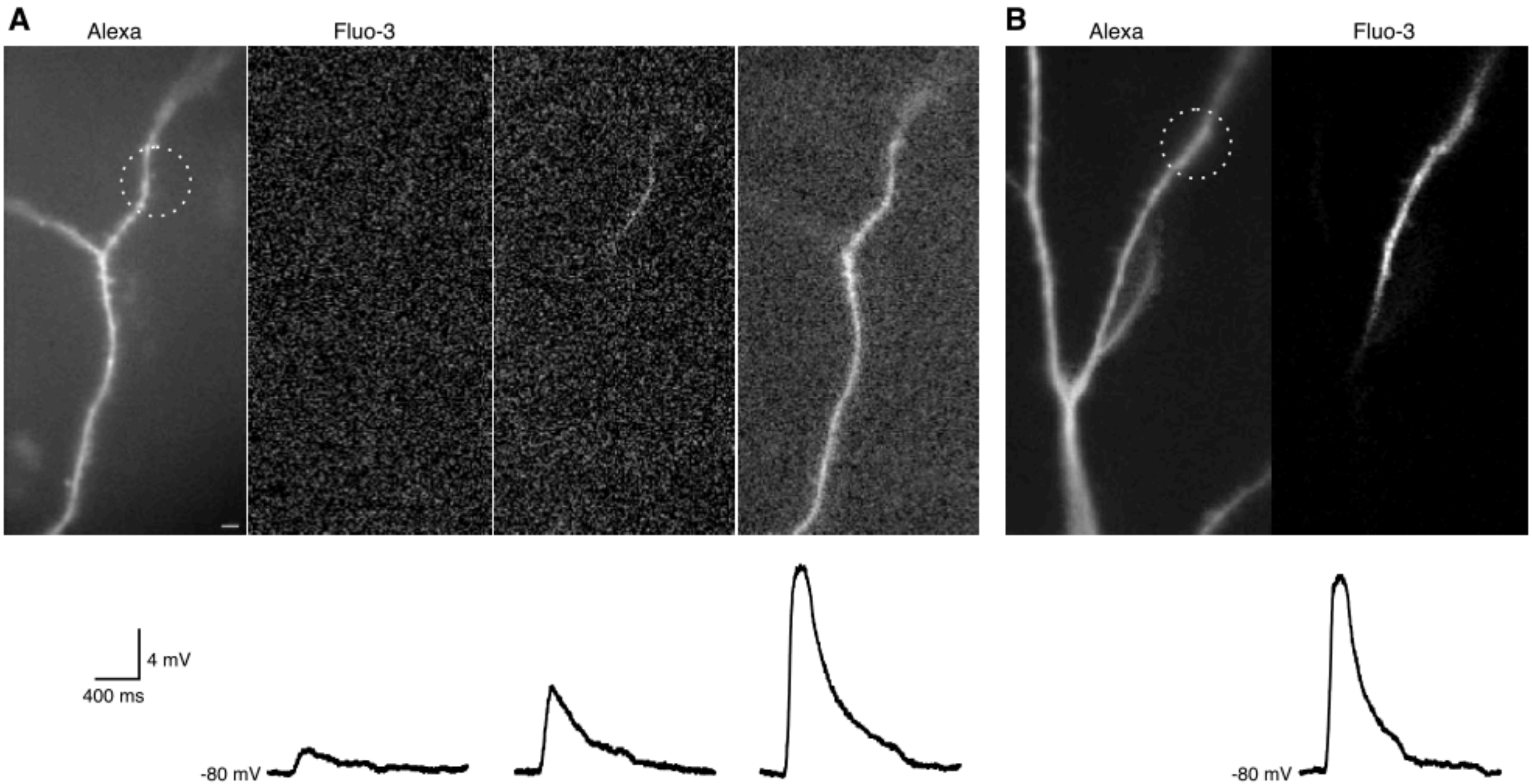
A
B
H
I
J
L
D
C
E
M
F
G
K
d
a
b

All or none calcium action potentials in pyramidal cell dendrites



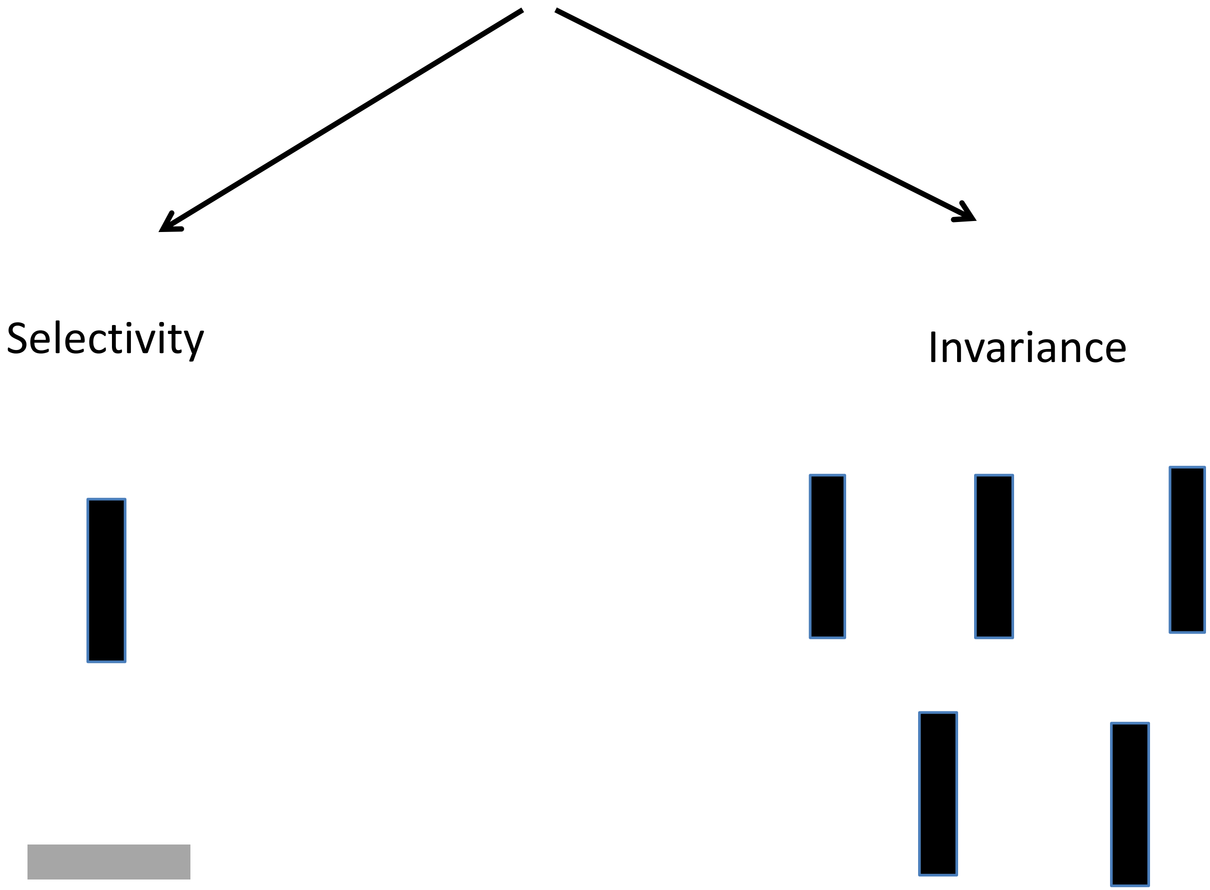
Wei et al., 2001. Compartmentalized and Binary Behavior of Terminal Dendrites in Hippocampal Pyramidal Neurons

Action potential failure at a dendritic branch point

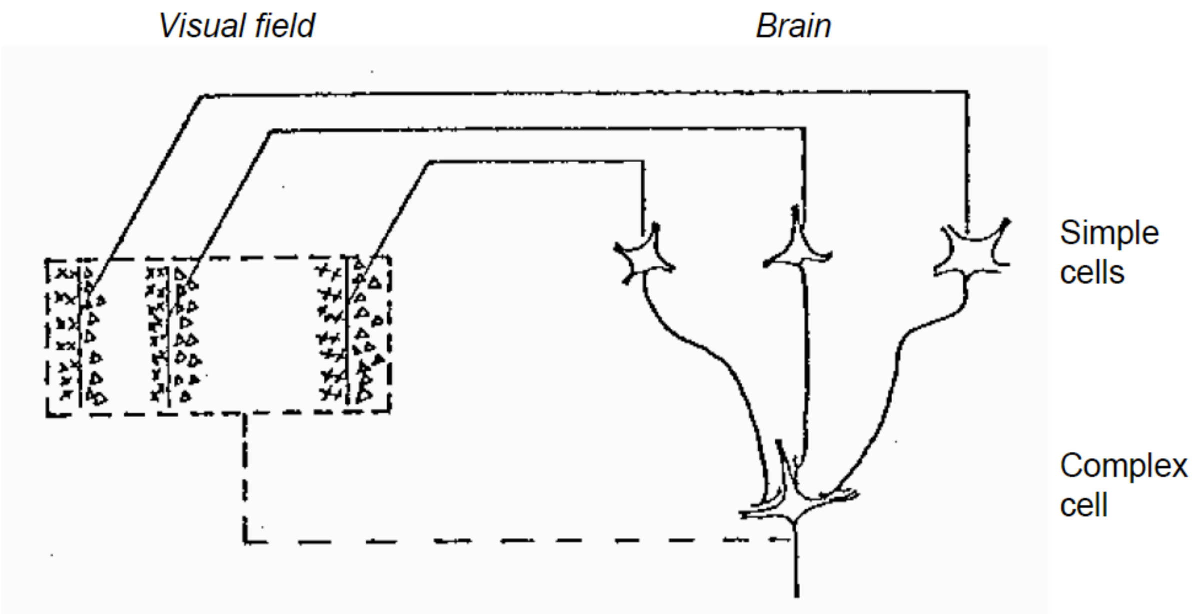


Wei et al., 2001. Compartmentalized and Binary Behavior of Terminal Dendrites in Hippocampal Pyramidal Neurons

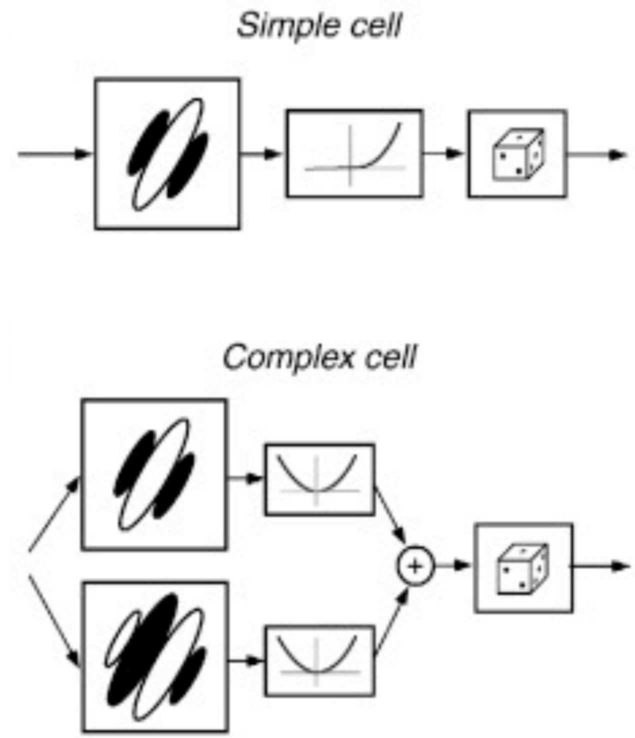
Properties of feature detection



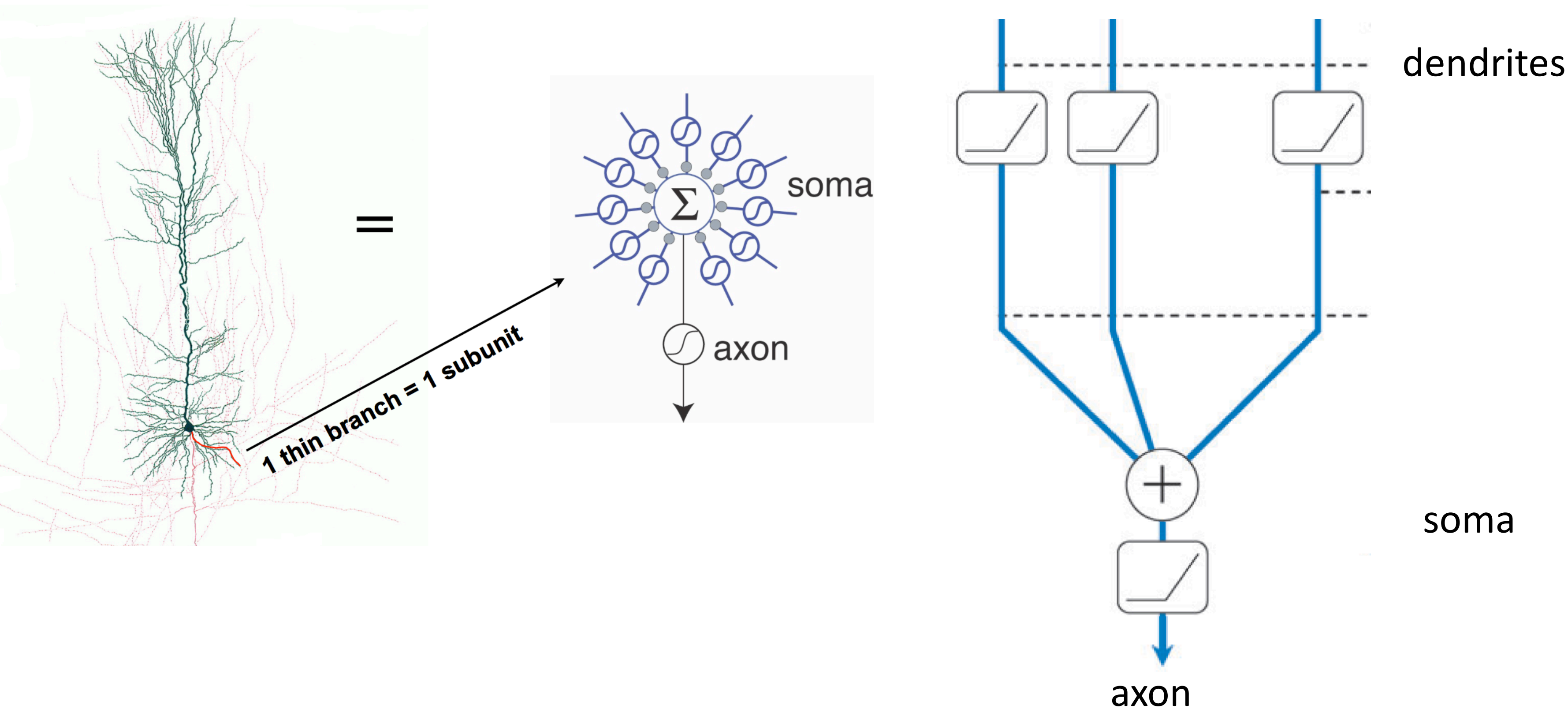
Models of selectivity and invariance in primary visual cortex



Hubel & Wiesel, 1963



Rust et al., 2005

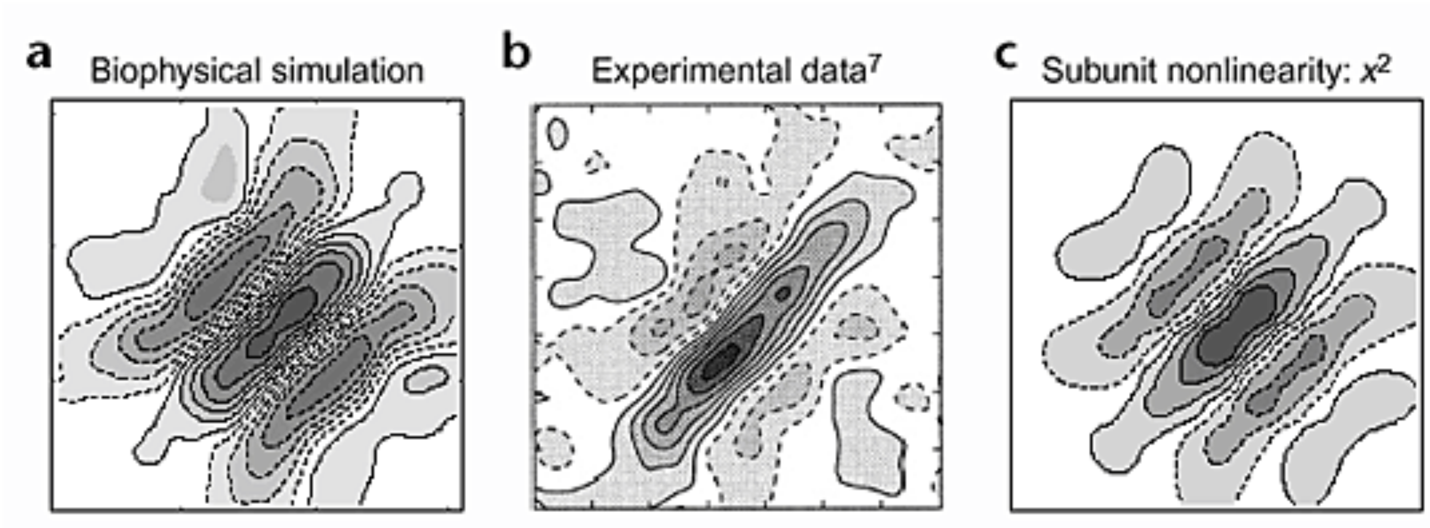


=
1 thin branch = 1 subunit
soma
axon
dendrites
soma
axon

Model of Binocular Disparity Representation

Bar presented to left & right eyes

Right eye pos. (deg)



Left eye pos. (deg)

Archie & Mel (2000)