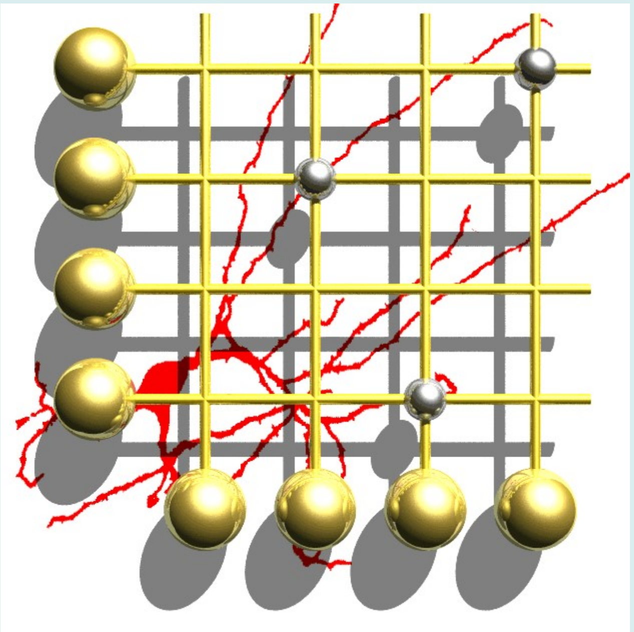
Synapses, Neurons, Circuits Introduction to Computational Neuroscience



Bruce Graham

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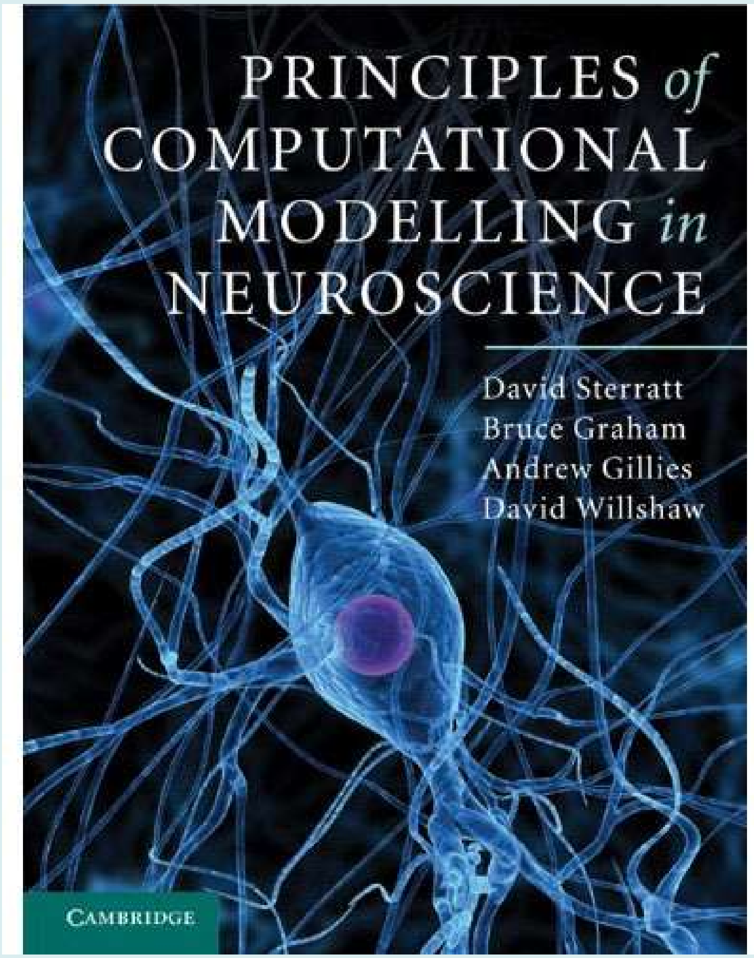
Useful Book



David Sterratt, Bruce Graham, Andrew Gillies, David Willshaw

Cambridge University Press, 2011

compneuroprinciples.org

2nd Edition due 2022 (now with Gaute Einevoll too!)

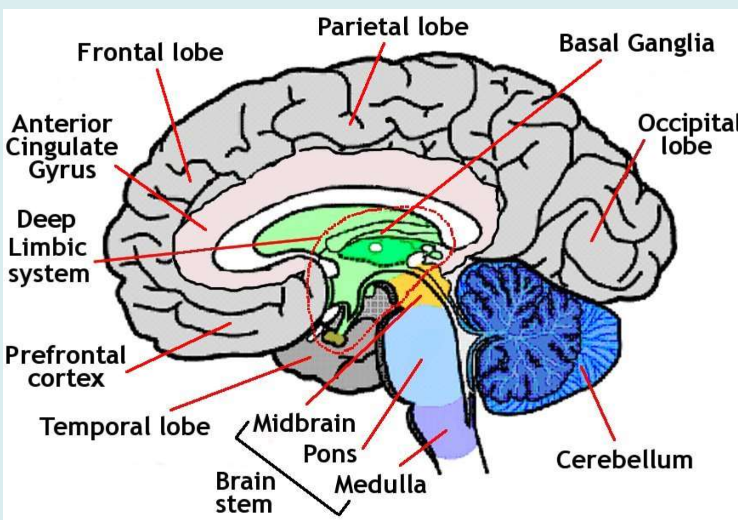
NEURON Exercises

- Simulating neurons and neural networks with the NEURON software:

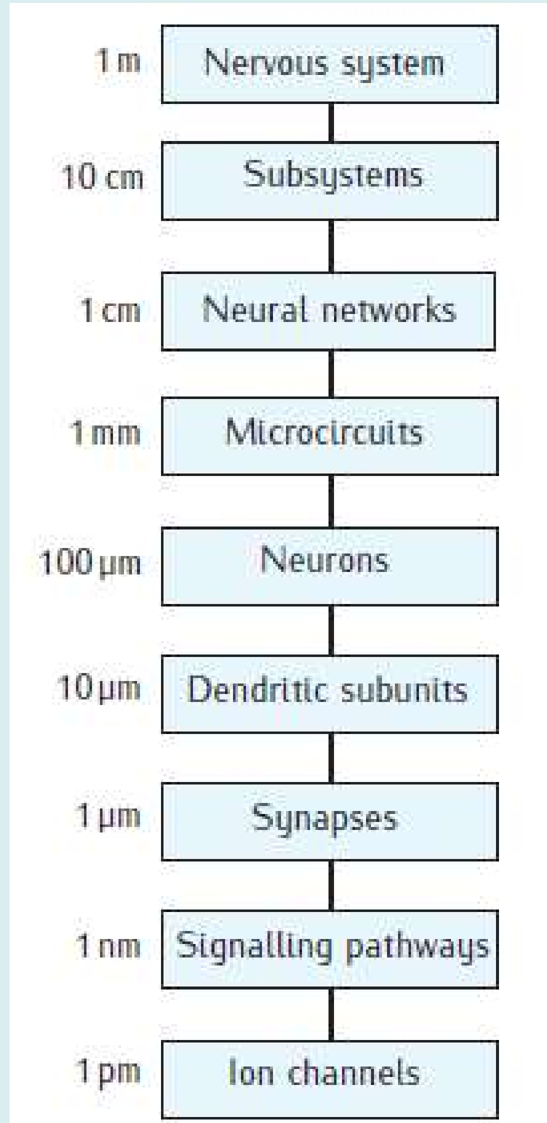
1. Frequency-Input Current (F-I) Firing Curve of a Neuron
    1. F-I curve of a basic neuron
    2. F-I curve types I and II
2. Electrical activity in a CA1 Pyramidal Cell
3. Simple Excitation-Inhibition (E-I) Oscillator
4. Excitation-Inhibition Balance
    1. Single I&F Neuron
    2. Network of I&F Neurons
5. STDP in Action
    1. Phase precession of spike timing
    2. Sequence learning
6. Associative Memory in a Network of Spiking Neurons

Levels of Detail

- Whole brain
- Brain nuclei
    - Lumped models
- Networks of neurons
- Single neurons
- Subcellular



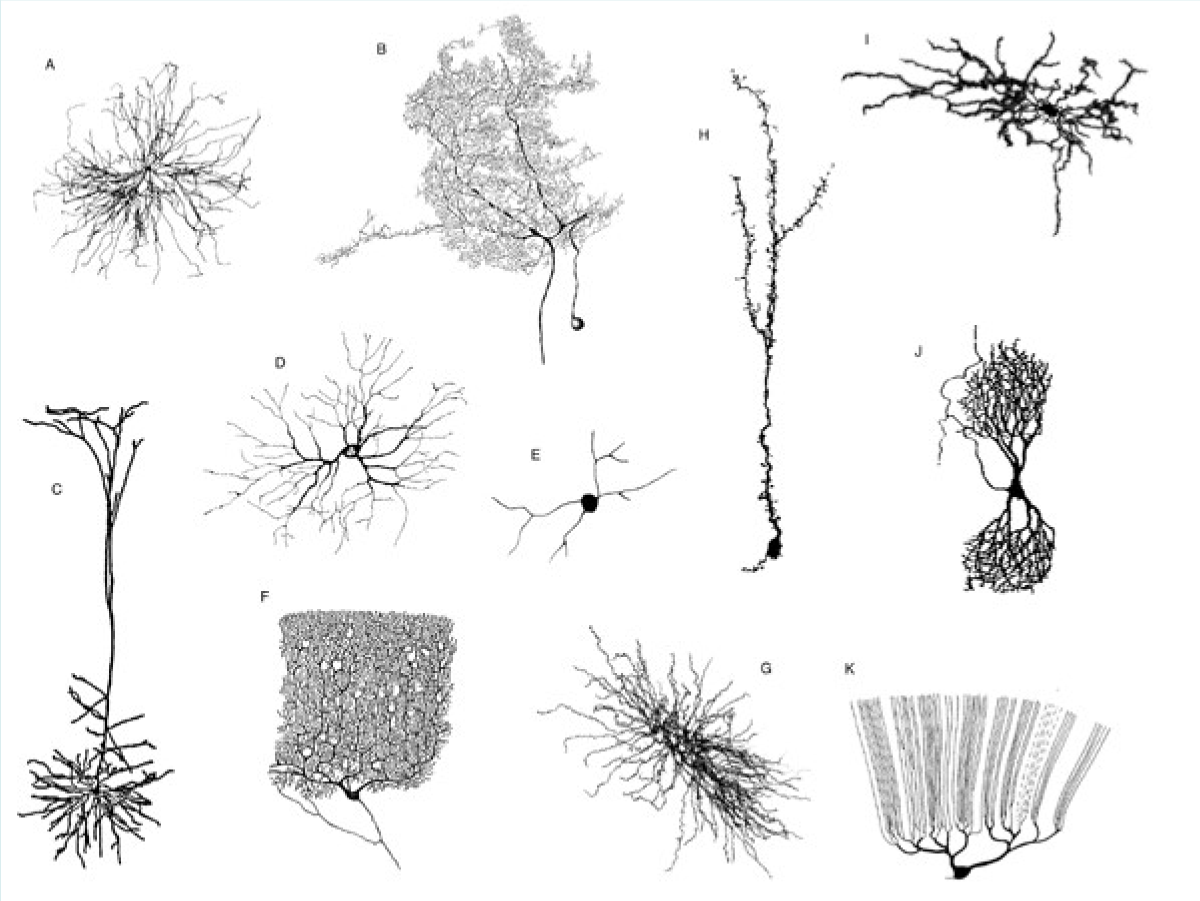
(confrontaal.org)



(PCMN Fig. 1.3 pg 7)

Neurons

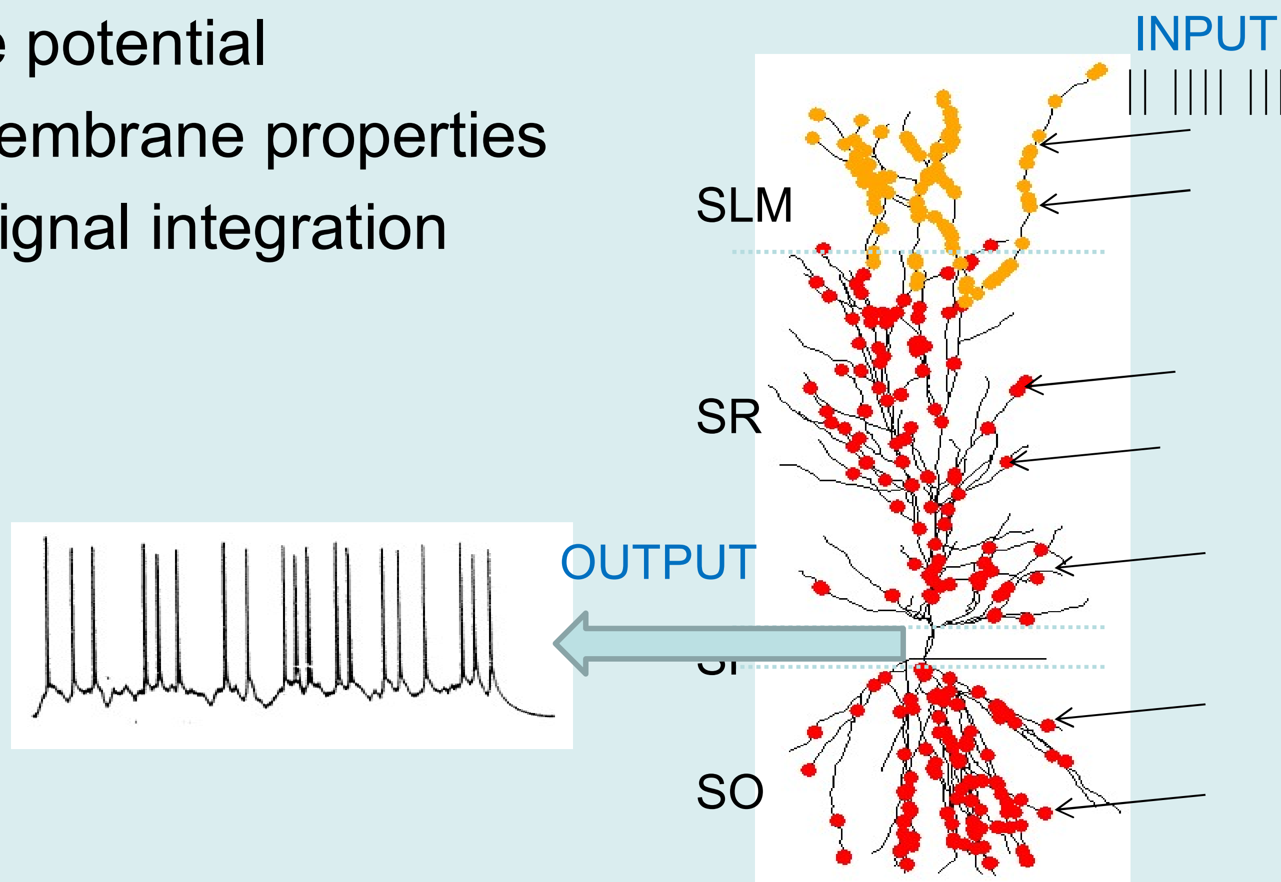
- Neurons come in many shapes and sizes



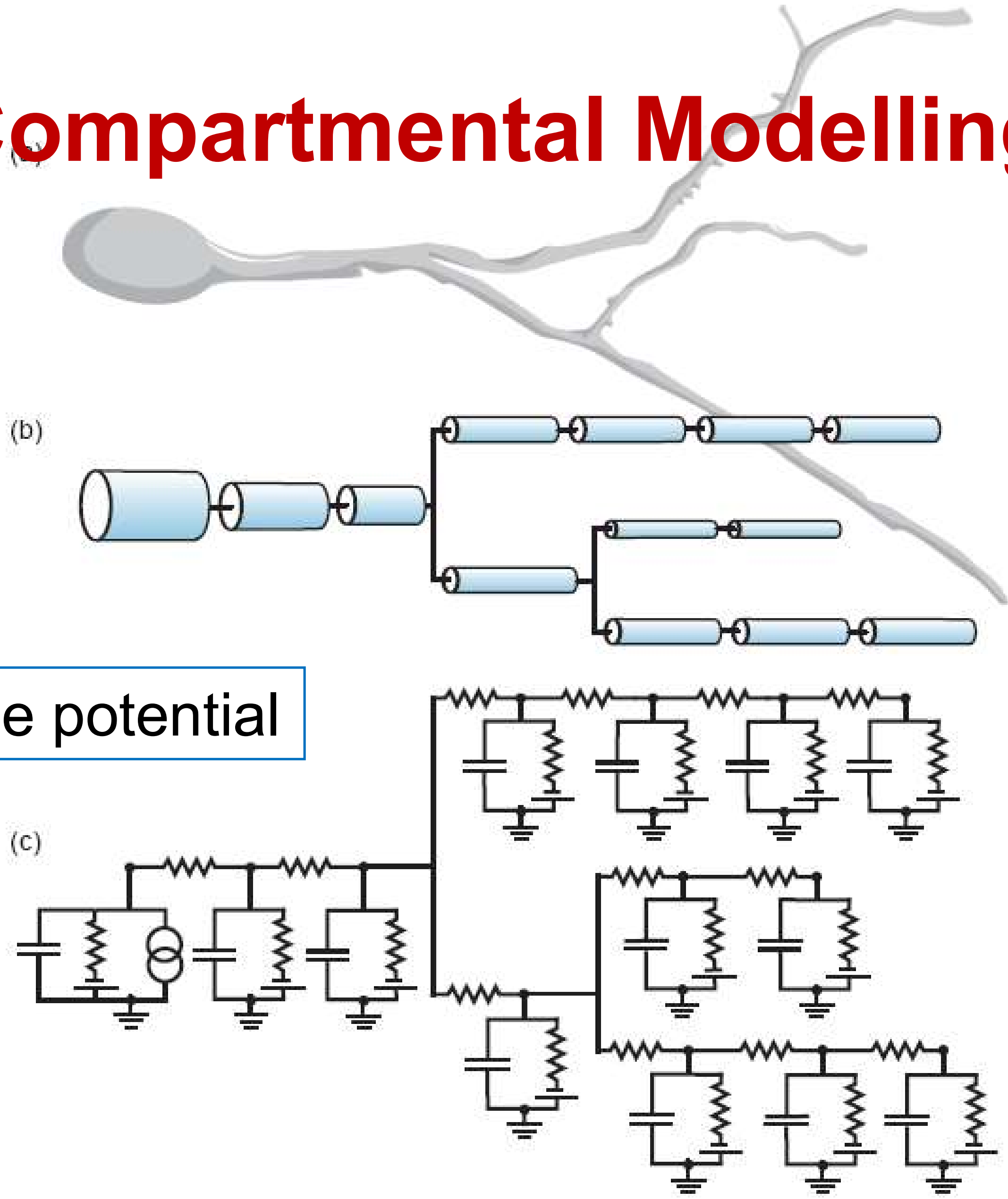
(Dendrites, Hausser et al (eds))

Why Model a Neuron?

- Response to inputs from other neurons?
  - Membrane potential
  - Intrinsic membrane properties
  - Synaptic signal integration



Compartmental Modelling

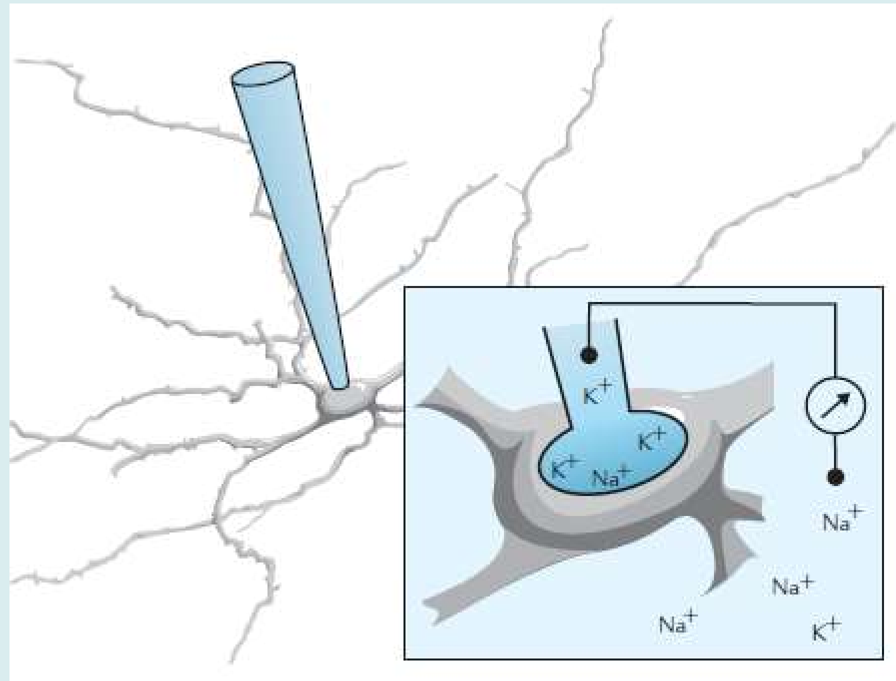


Membrane potential

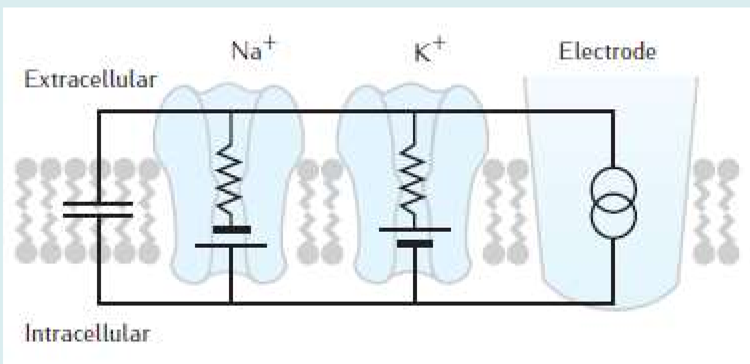
(Fig. 4.1 pg 73)

Electrical Potential of a Neuron

- Differences in ionic concentrations
- Transport of ions
  - Sodium (Na)
  - Potassium (K)



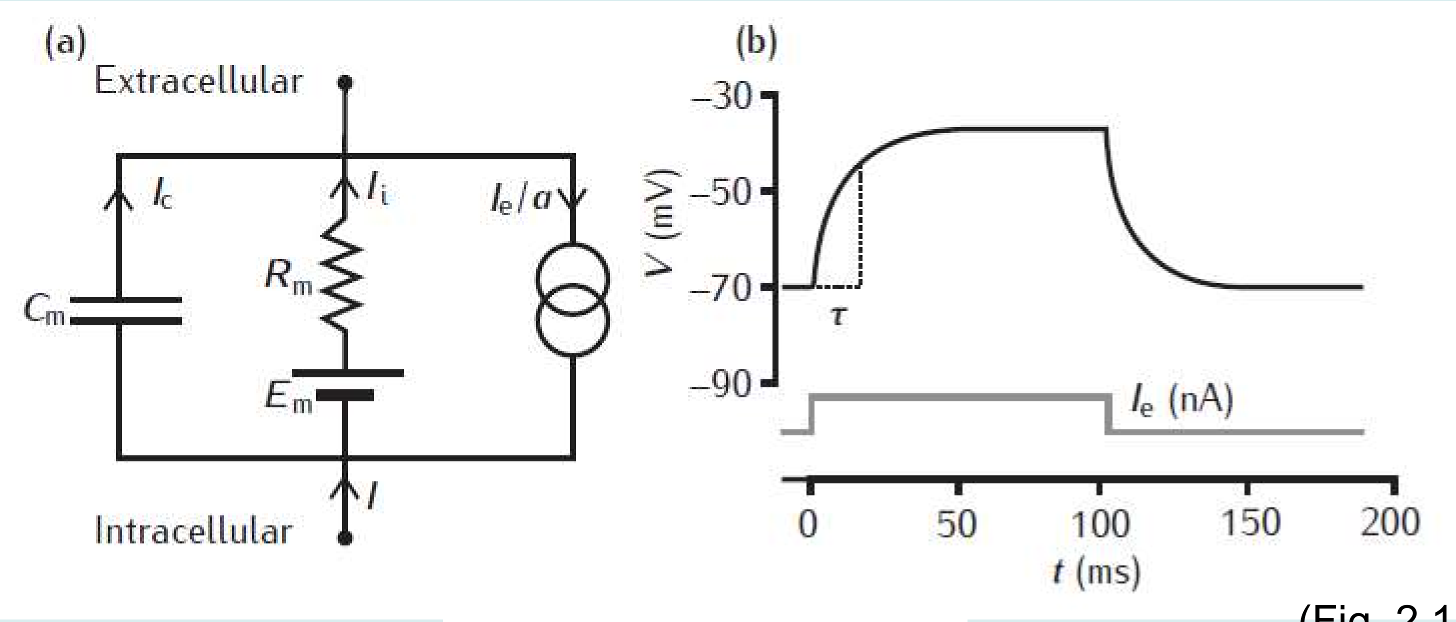
(Fig. 2.1 pg 14)



(Fig. 2.13 pg 31)

A Model of Passive Membrane

- A resistor and a capacitor
- Kirchhoff's current law

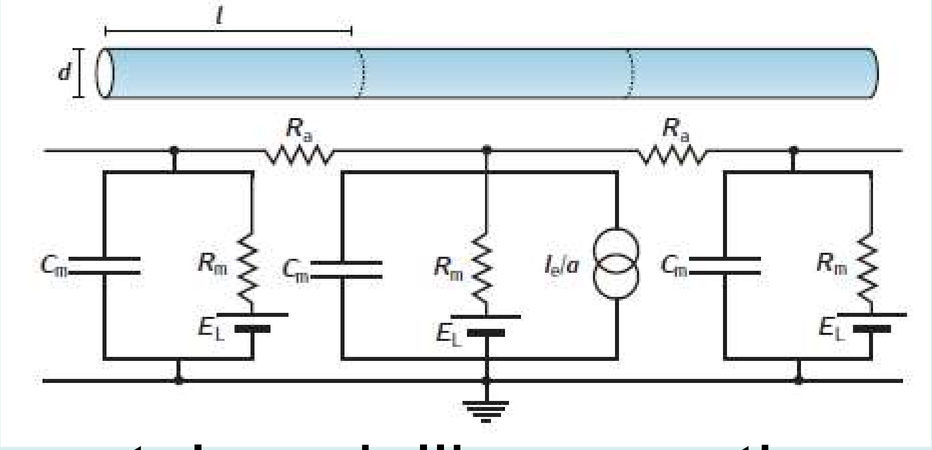


(Fig. 2.14 pg 32)

$$C_m \frac{dV}{dt} = \frac{E_m - V}{R_m} + \frac{I_e}{a}.$$

A Length of Membrane

- Membrane *compartments* connected by intracellular resistance



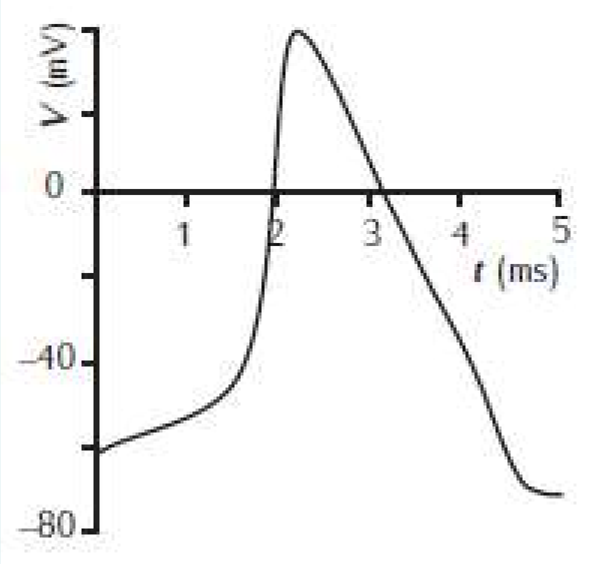
(Fig. 2.15 pg 36)

- Compartmental modelling equation

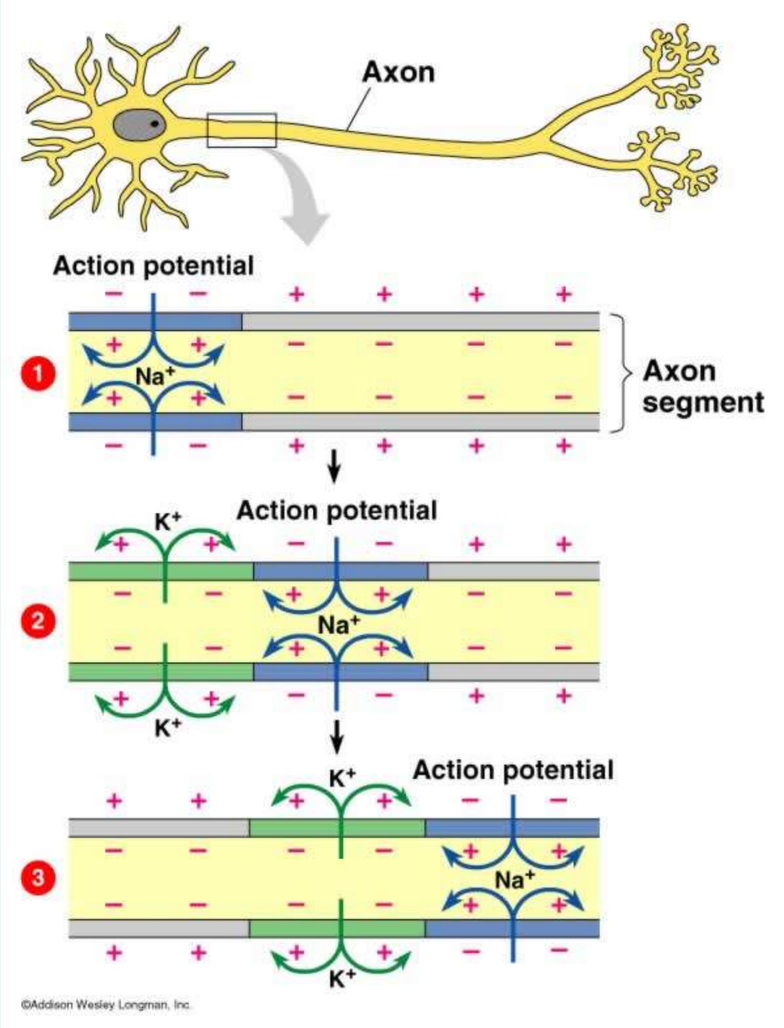
$$C_m \frac{dV_j}{dt} = \frac{E_m - V_j}{R_m} + \frac{d}{4R_a}\left(\frac{V_{j+1} - V_j}{l^2} + \frac{V_{j-1} - V_j}{l^2}\right) + \frac{I_{e,j}}{\pi d l}. \qquad (2.23)$$

The Action Potential

- Output signal of a neuron
  - Rapid change in membrane potential
  - Flow of Na and K ions



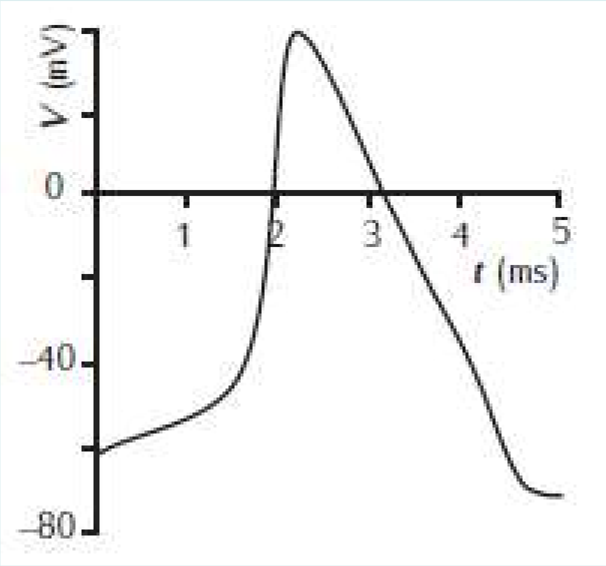
(Fig. 3.1 pg 47)



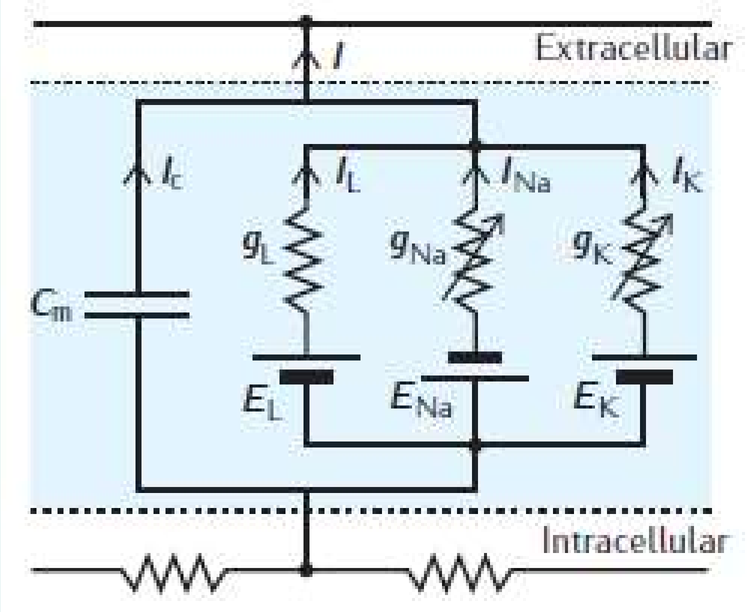
Action Potential Model

- Empirical model by Hodgkin and Huxley, 1952
  - Voltage-dependent Na and K channels

$$C_m \frac{dV}{dt} = -\overline{g}_L(V - E_L) - \overline{g}_{Na} m^3 h(V - E_{Na}) - \overline{g}_K n^4 (V - E_K) + I,$$



(Fig. 3.1 pg 47)



(Fig. 3.2 pg 50)

Time Varying Conductances

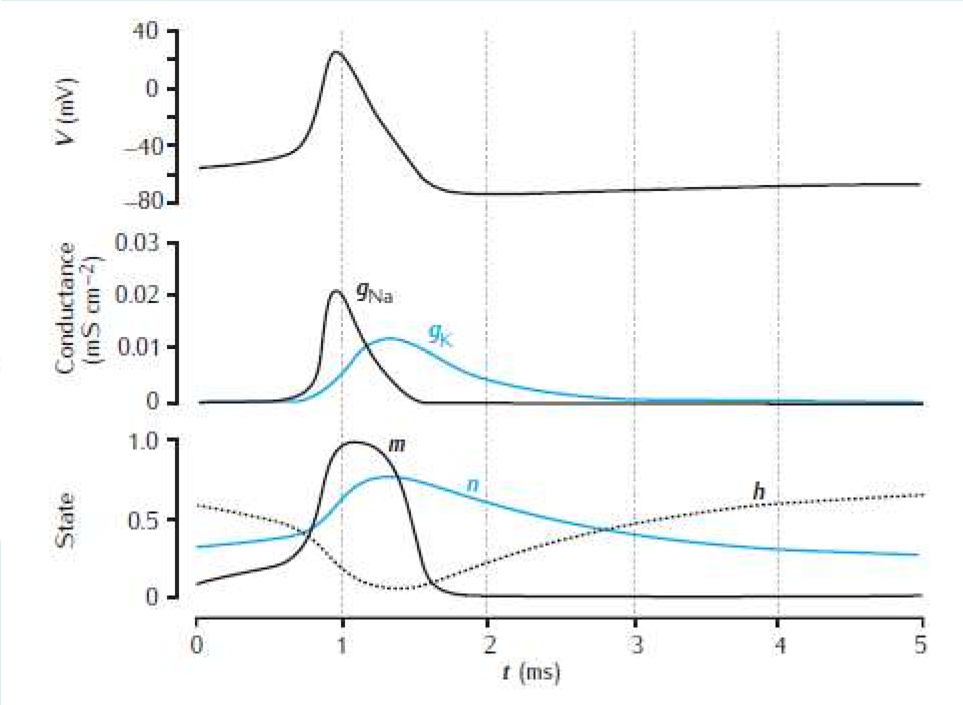
- K conductance: *n* a function of time and voltage

$$I_K = \bar{g}_K n^4 (V - E_K),$$

$$\frac{dn}{dt} = \alpha_n (1-n) - \beta_n n,$$

$$\alpha_n = 0.01 \frac{V+55}{1-\exp(-(V+55)/10)},$$

$$\beta_n = 0.125 \exp(-(V+65)/80).$$



(Fig. 3.12 pg 63)

Complete Action Potential Model

$$C_m \frac{dV}{dt} = -\overline{g}_L(V - E_L) - \overline{g}_{Na} m^3 h (V - E_{Na}) - \overline{g}_K n^4 (V - E_K).$$

Sodium activation and inactivation gating variables:

$$\frac{dm}{dt} = \alpha_m(1-m) - \beta_m m, \qquad \frac{dh}{dt} = \alpha_h(1-h) - \beta_h h,$$

$$\alpha_m = 0.1 \frac{V+40}{1-\exp(-(V+40)/10)}, \qquad \alpha_h = 0.07 \exp(-(V+65)/20),$$

$$\beta_m = 4 \exp(-(V+65)/18), \qquad \beta_h = \frac{1}{\exp(-(V+35)/10)+1}.$$

Potassium activation gating variable:

$$\frac{dn}{dt} = \alpha_n(1-n) - \beta_n n,$$

$$\alpha_n = 0.01 \frac{V+55}{1-\exp(-(V+55)/10)},$$

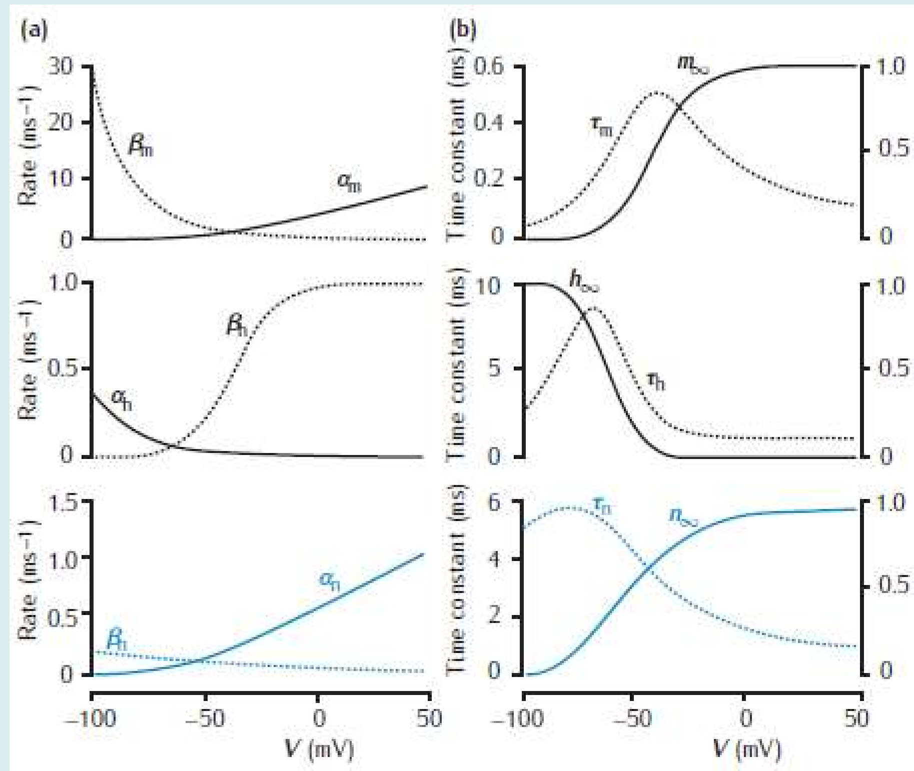
$$\beta_n = 0.125 \exp(-(V+65)/80).$$

Parameter values (from Hodgkin and Huxley, 1952d):

$C_m = 1.0\ \mu\text{F cm}^{-2}$

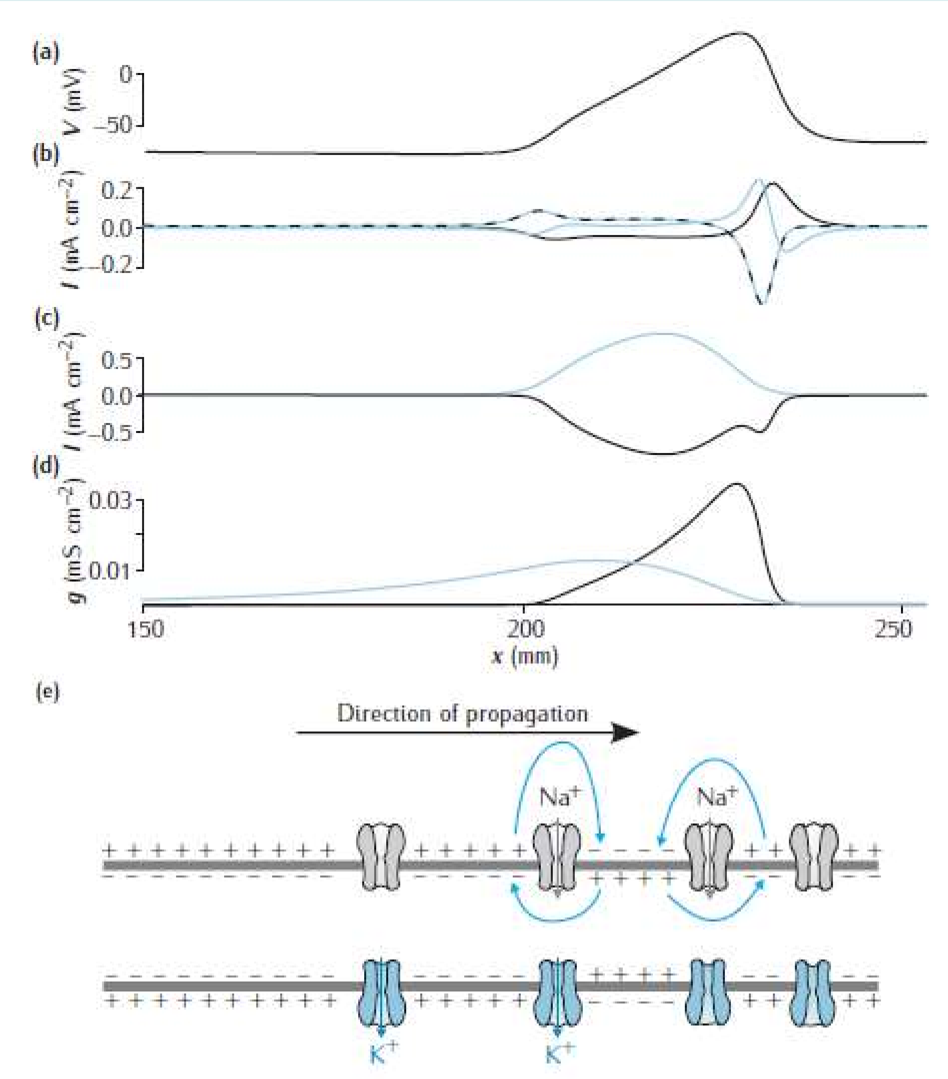
$E_{Na} = 50$ mV	$\overline{g}_{Na} = 120$ mS cm^{-2}
$E_K = -77$ mV	$\overline{g}_K = 36$ mS cm^{-2}
$E_L = -54.4$ mV	$\overline{g}_L = 0.3$ mS cm^{-2}

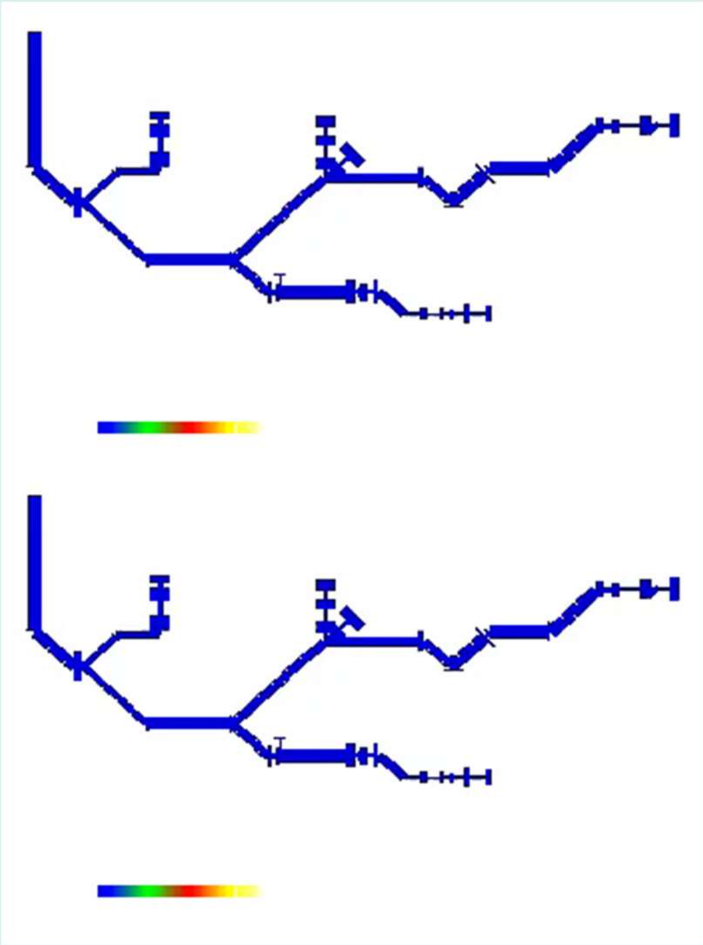
Box 3.5 pg 61



(Fig. 3.10 pg 60)

Propagating Action Potential





(Fig. 3.15 pg 65)

Families of Ion Channels

- Sodium (Na): fast, persistent
- Potassium (K): delayed rectifier, A, M
- Calcium (Ca): low and high voltage activated
  - L, N, R, T
- Calcium-activated potassium: sAHP, mAHP
- Non-specific cation: H

Around 140 different voltage-gated ion channel types.
A neuron may express 10 to 20 types.

Potassium A-current: K_A

- Different characteristics from delayed rectifier: K_{DR}
- Low threshold activating / inactivating current

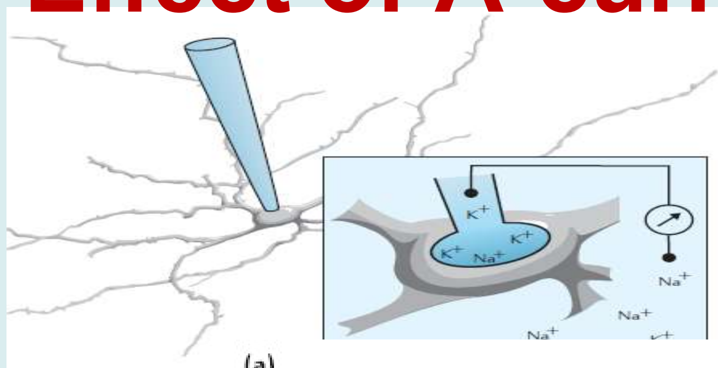
$$C_m \frac{dV}{dt} = -g_{Na}(V - E_{Na}) - g_K(V - E_K) - g_A(V - E_A) - g_L(V - E_L).$$

$$I_A = g_A(V - E_A), \qquad g_A = \bar{g}_A a^3 b,$$

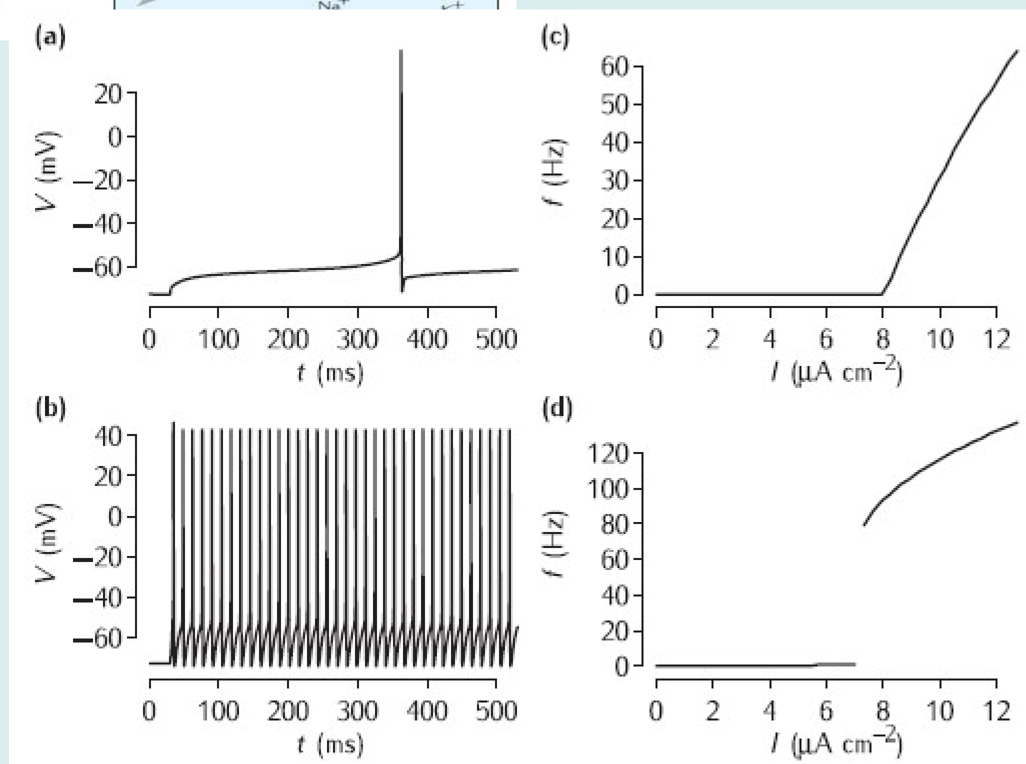
$$a_\infty = \left(\frac{0.0761 \exp\left(\frac{V+99.22}{31.84}\right)}{1 + \exp\left(\frac{V+6.17}{28.93}\right)} \right)^{\frac{1}{3}}, \qquad \tau_a = 0.3632 + \frac{1.158}{1 + \exp\left(\frac{V+60.96}{20.12}\right)},$$

$$b_\infty = \frac{1}{\left(1 + \exp\left(\frac{V+58.3}{14.54}\right)\right)^4}, \qquad \tau_b = 1.24 + \frac{2.678}{1 + \exp\left(\frac{V-55}{16.027}\right)}.$$

One Effect of A-current



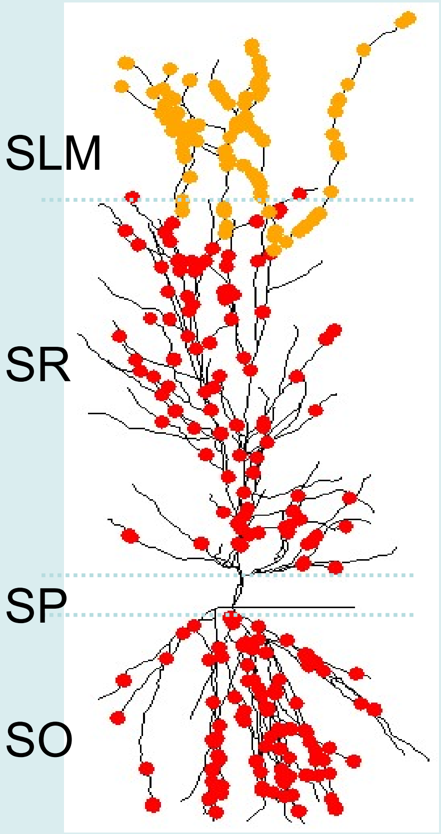
- Type I: with K_A
  - Steady increase in firing frequency with driving current
- Type II: without K_A
  - Suddent jump to non-zero firing rate



(Fig. 5.9 pg 106)

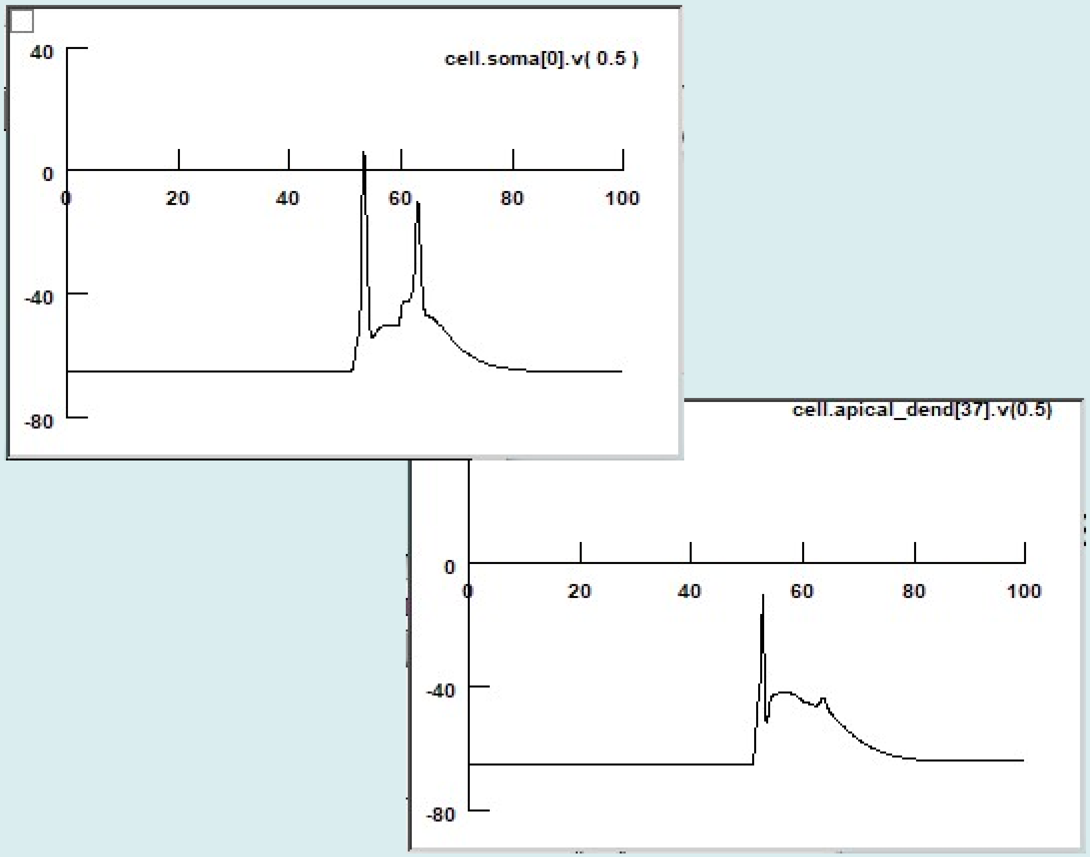
Large Scale Neuron Model

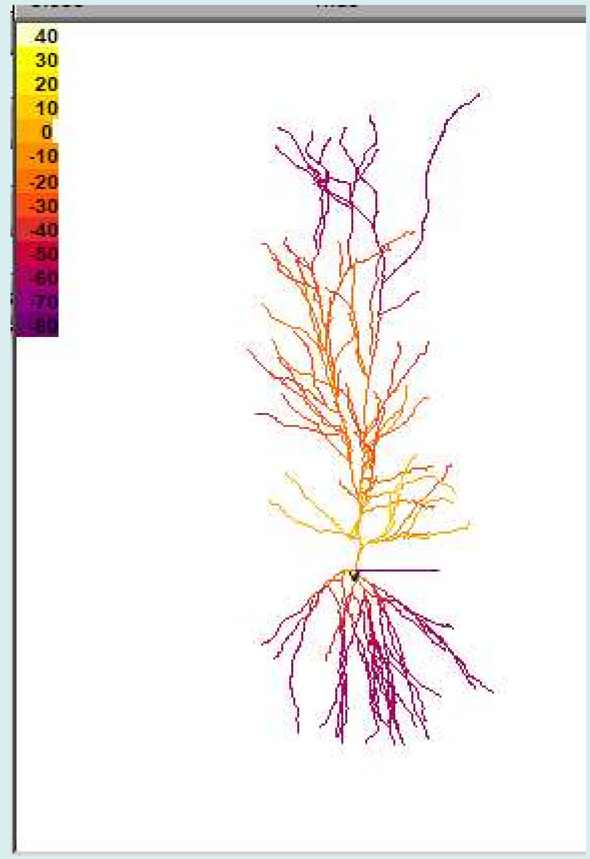
- Hippocampal pyramidal cell (HPC)
- 337 electrical compartments
  - Plus synaptic spines
- 6 ion channel types
  - Heterogeneous distribution
- Current injection and synaptic inputs



HPC Voltage Responses

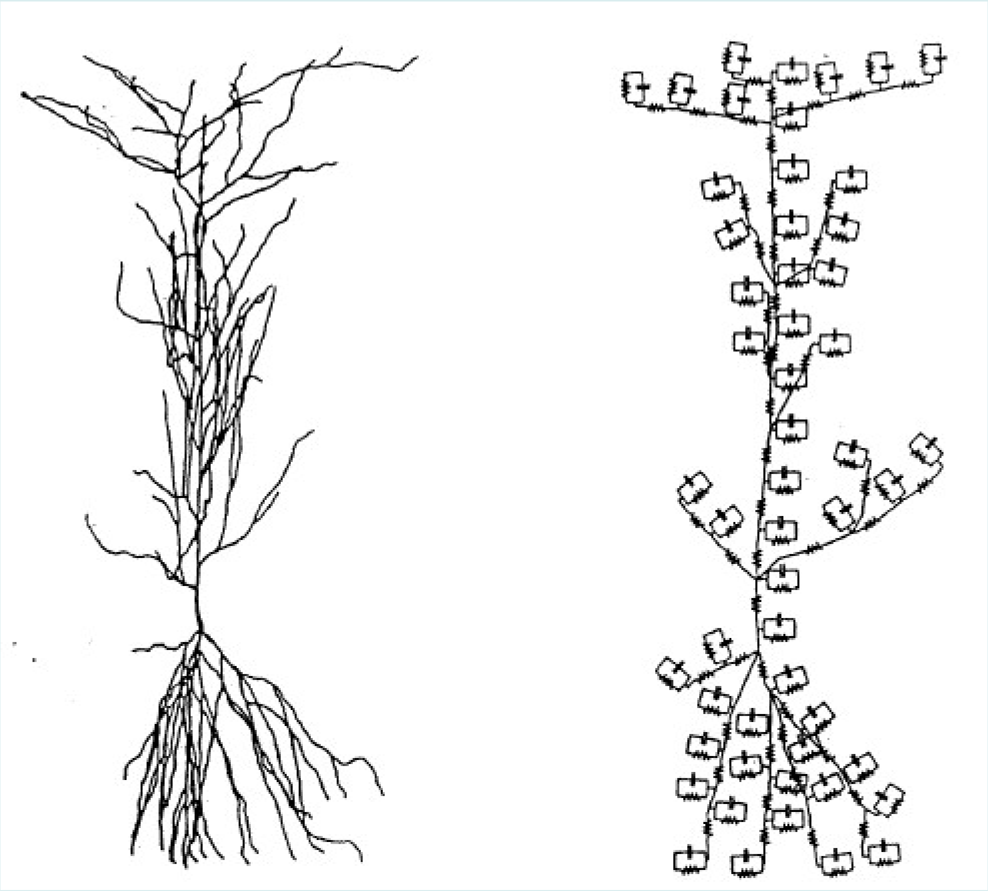
- Sodium and calcium spikes

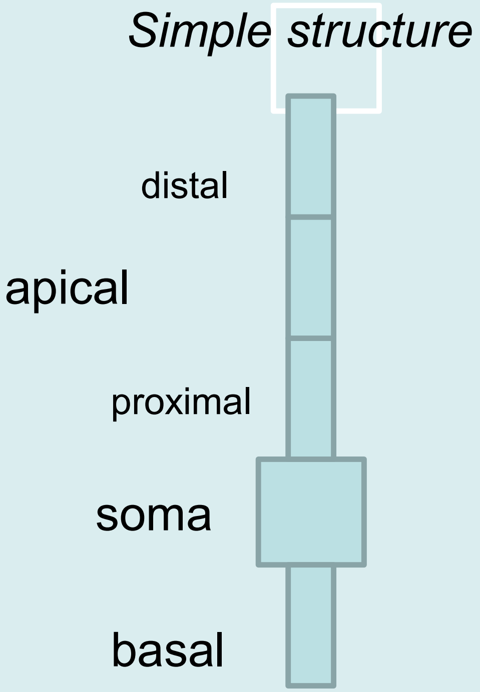




Varying Levels of Detail

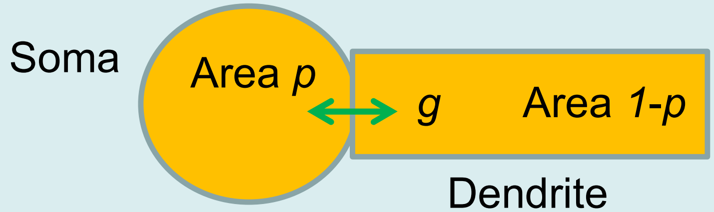
- Capture essential features of morphology

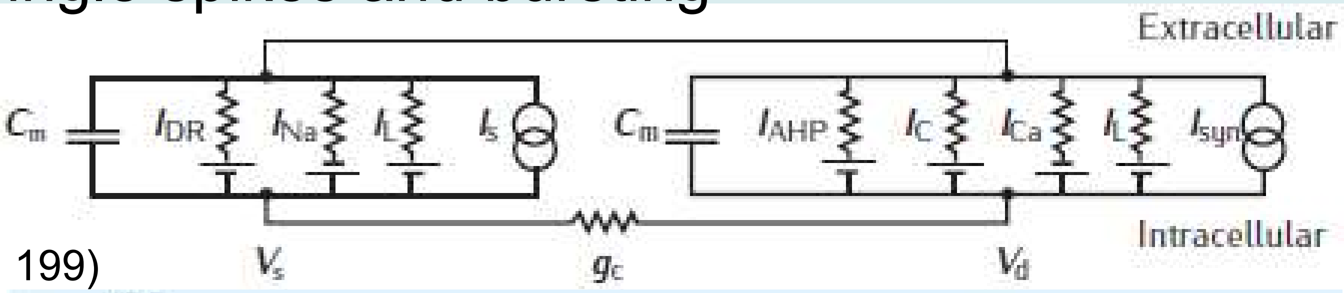




Reduced Pyramidal Cell Model

- 2-compartment model
  - Pinsky & Rinzel (1994)
- Captures essence of PC behaviour
  - Single spikes and bursting





(Fig. 8.1 pg 199)

$$C_m \frac{dV_s}{dt} = -\overline{g}_L(V_s - E_L) - g_{Na}(V_s - E_{Na}) - g_{DR}(V_s - E_K) + \frac{g_c}{p}(V_d - V_s) + \frac{I_s}{p}$$

$$C_m \frac{dV_d}{dt} = -\overline{g}_L(V_d - E_L) - g_{Ca}(V_d - E_{Ca}) - g_{AHP}(V_d - E_K) - g_C(V_d - E_K) + \frac{g_c}{1-p}(V_s - V_d) + \frac{I_{syn}}{1-p}.$$

(Box 8.1 pg 200)

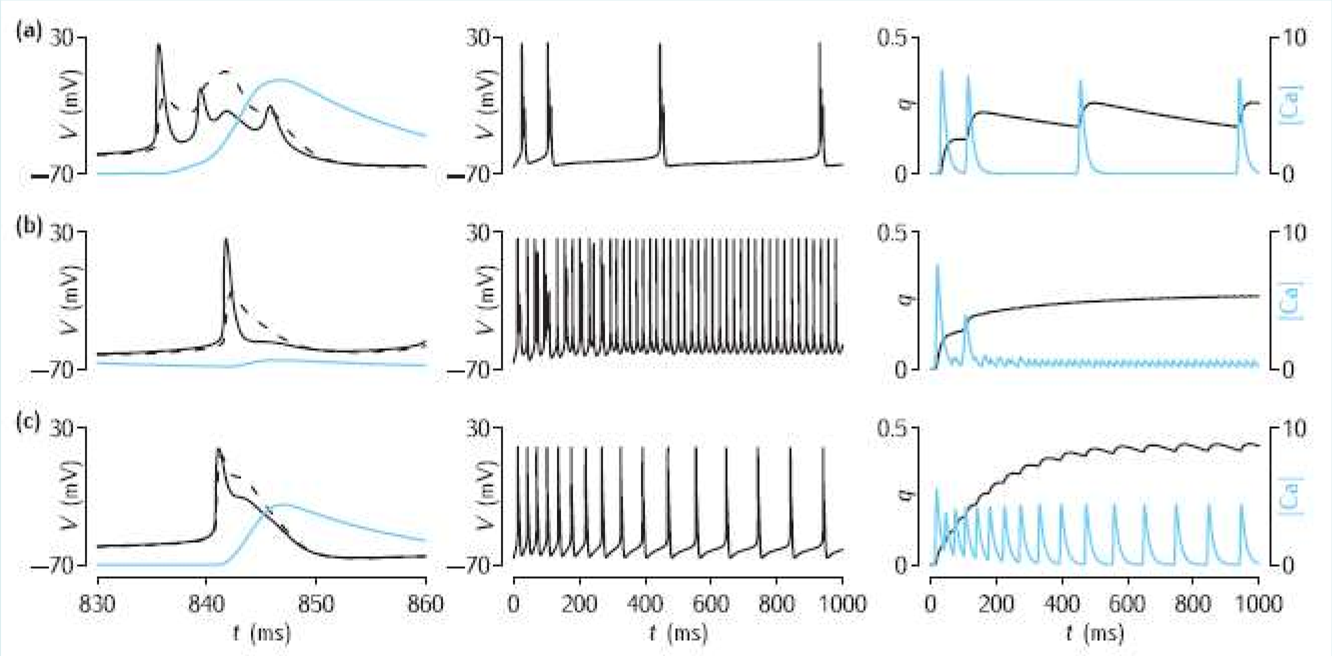
Pinsky-Rinzel Model in Action

- Behaviour depends on
  - Compartment coupling strength (g)
  - Magnitude of driving current (I)

Low I, low g

High I, low g

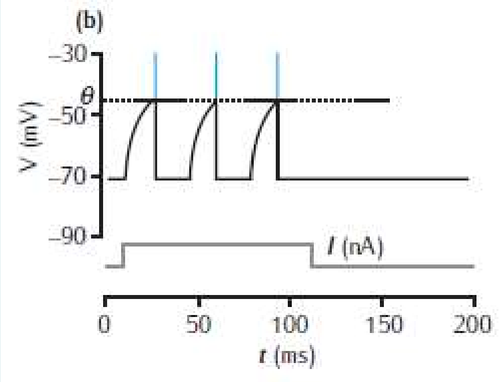
High I, high g



(Fig. 8.2 pg 201)

Simple Spiking Neuron Models

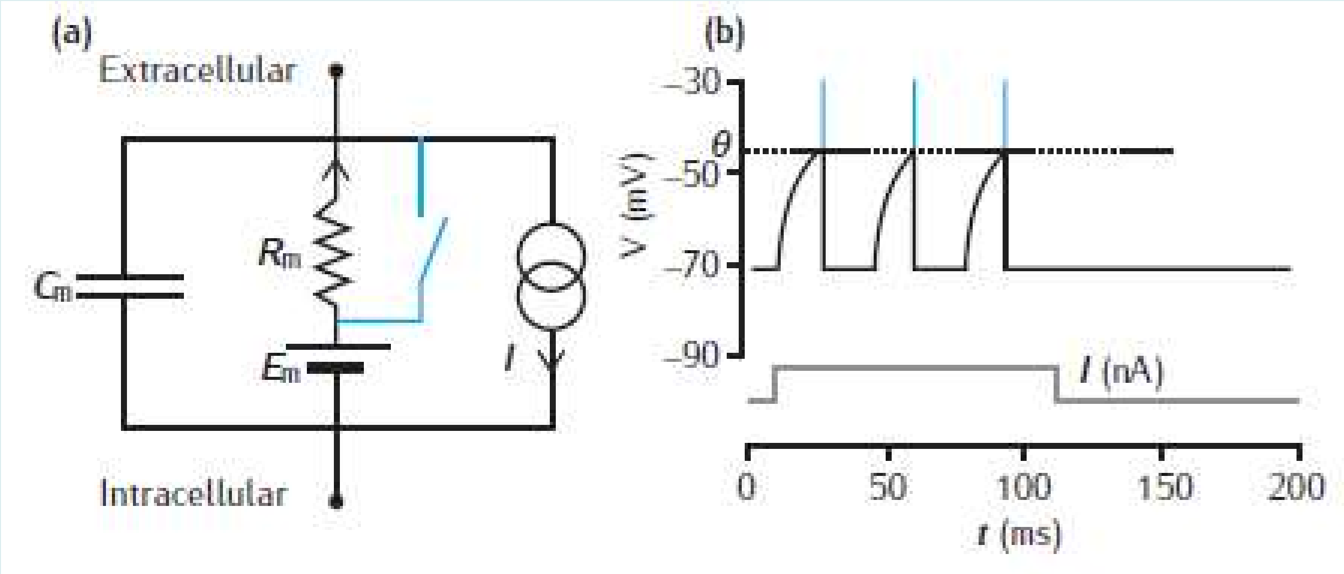
- Simplified equations for generating action potentials (APs)
  - FitzHugh-Nagumo; Kepler; Morris-Lecar
  - 2 state variables: voltage plus one other
    - H-H model contains 4 variables: V, m, h, n
- Simple spiking models that DO NOT model the AP waveform
  - Integrate-and-fire models



Integrate-and-Fire Model

- RC circuit with spiking and reset mechanisms
  - When V reaches a threshold
    - A spike (AP) event is "signalled"
    - Switch closes and V is reset to E_m
    - Switch remains closed for refractory period

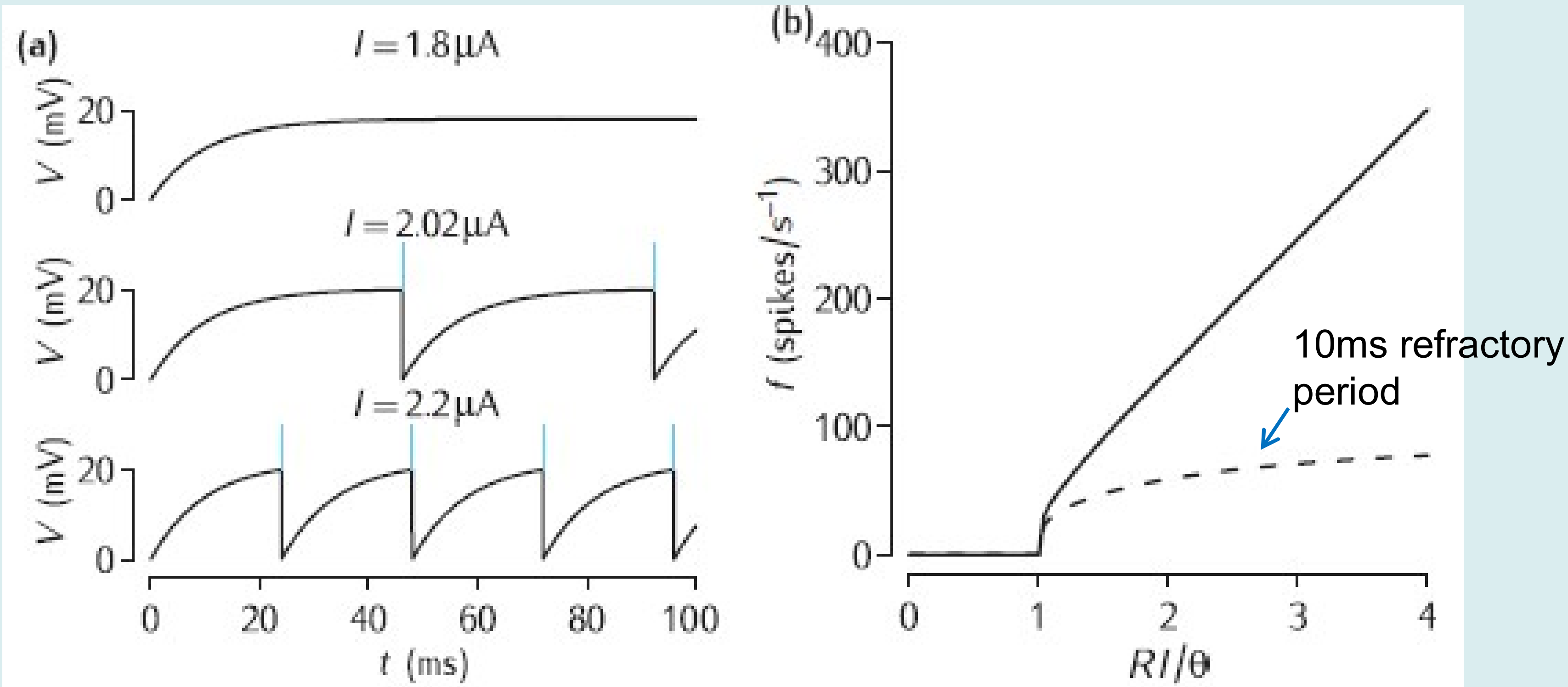
$$C_m \frac{dV}{dt} = -\frac{V - E_m}{R_m} + I$$



(Fig. 8.4 pg 204)

I&F Model Response

- Response to constant current injection
  – No refractory period

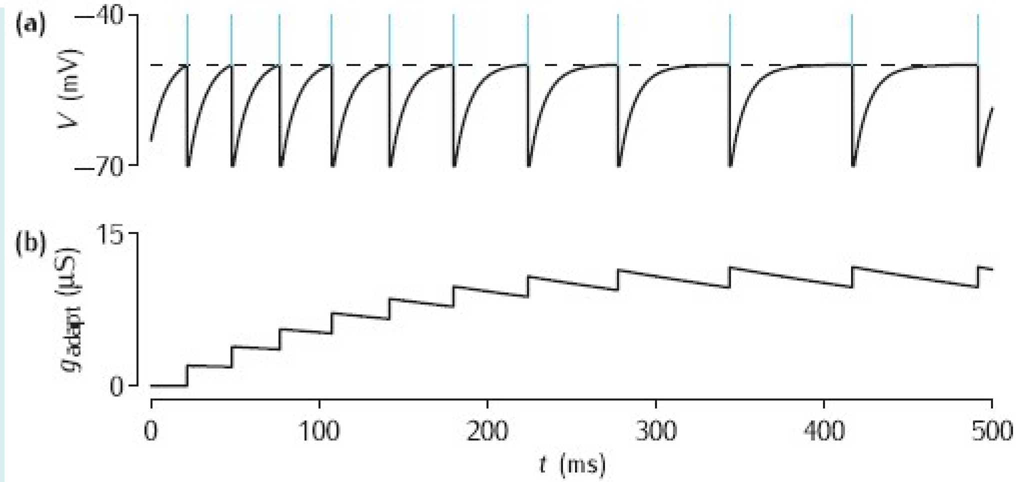


(Fig. 8.5 pg 205)

More Realistic I&F Neurons

- Basic I&F model does not accurately capture the diversity of neuronal firing patterns
  - Adaptation of interspike intervals (ISIs) over time

$$\frac{\mathrm{d}g_{\mathrm{adapt}}}{\mathrm{d}t} = -\frac{g_{\mathrm{adapt}}}{\tau_{\mathrm{adapt}}} \quad \text{and} \quad I_{\mathrm{adapt}} = g_{\mathrm{adapt}}(V - E_{\mathrm{m}}).$$



(Fig. 8.8 pg 213)

  - Precise timing of AP initiation
  - Noise

Modelling AP Initiation

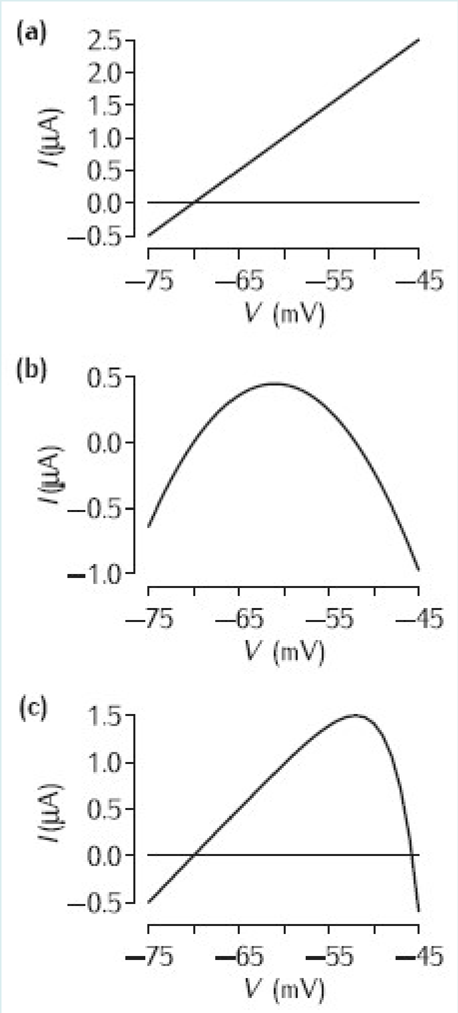
- Basic I&F is a poor model of the ionic currents near AP threshold

- Quadratic I&F

$$C_{\mathrm{m}} \frac{\mathrm{d}V}{\mathrm{d}t} = -\frac{(V - E_{\mathrm{m}})(V_{\mathrm{thresh}} - V)}{R_{\mathrm{m}}(V_{\mathrm{thresh}} - E_{\mathrm{m}})} + I.$$

- Exponential I&F

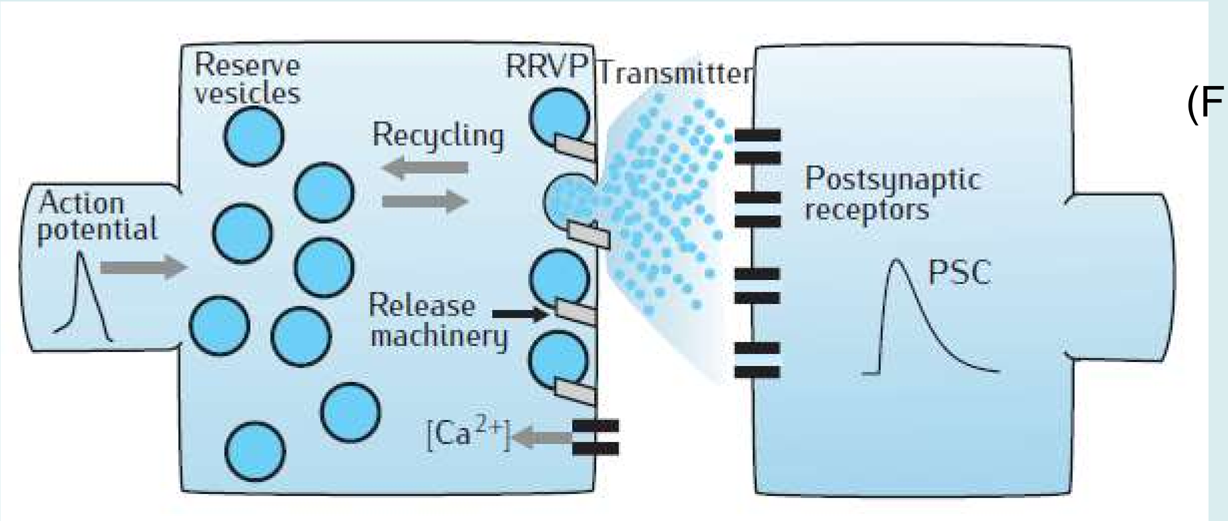
$$C_{\mathrm{m}} \frac{\mathrm{d}V}{\mathrm{d}t} = -\left(\frac{V - E_{\mathrm{m}}}{R_{\mathrm{m}}} - \frac{\Delta_{\mathrm{T}}}{R_{\mathrm{m}}} \exp\left(\frac{V - V_{\mathrm{T}}}{\Delta_{\mathrm{T}}}\right)\right) + I,$$



(Fig. 8.9 pg 214)

Neural Connections: Synapses

- Presynaptic AP causes neurotransmitter release
- Binding to postsynaptic receptors generates a response



(Fig. 7.1 pg 173)

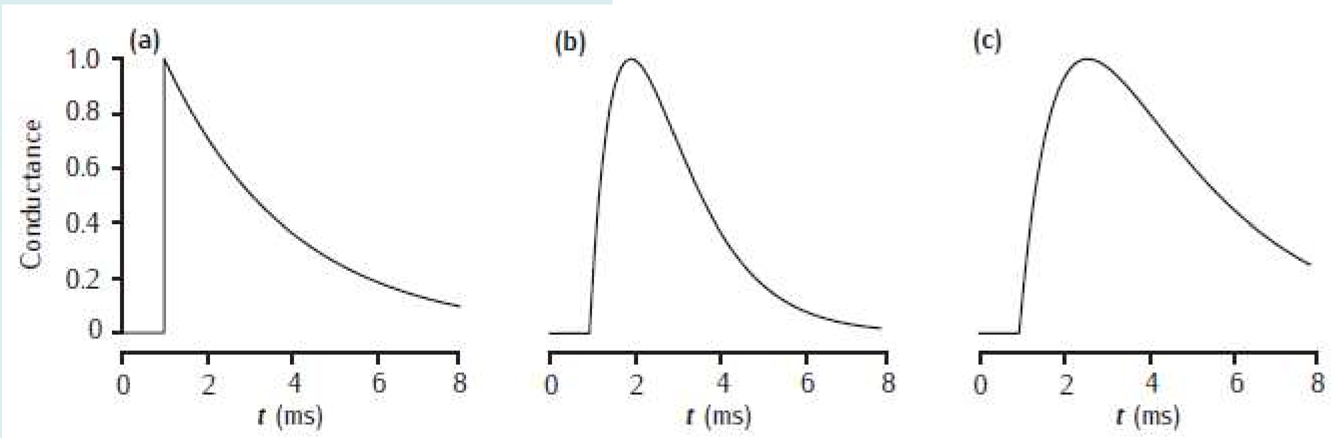
Synaptic Conductance

- 3 commonly used simple waveforms
  a) Single exponential
  b) Alpha function
  c) Dual exponential

$$g_{syn}(t) = \bar{g}_{syn} \exp\left(-\frac{t - t_s}{\tau}\right)$$

$$g_{syn}(t) = \bar{g}_{syn} \frac{t - t_s}{\tau} \exp\left(-\frac{t - t_s}{\tau}\right)$$

$$g_{syn}(t) = \bar{g}_{syn} \frac{\tau_1 \tau_2}{\tau_1 - \tau_2} \left(\exp\left(-\frac{t - t_s}{\tau_1}\right) - \exp\left(-\frac{t - t_s}{\tau_2}\right)\right)$$

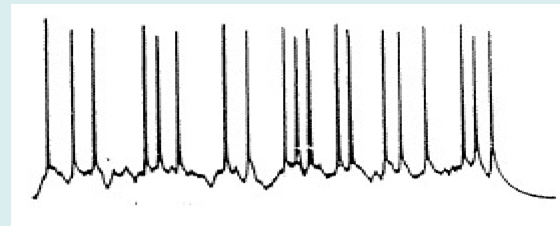


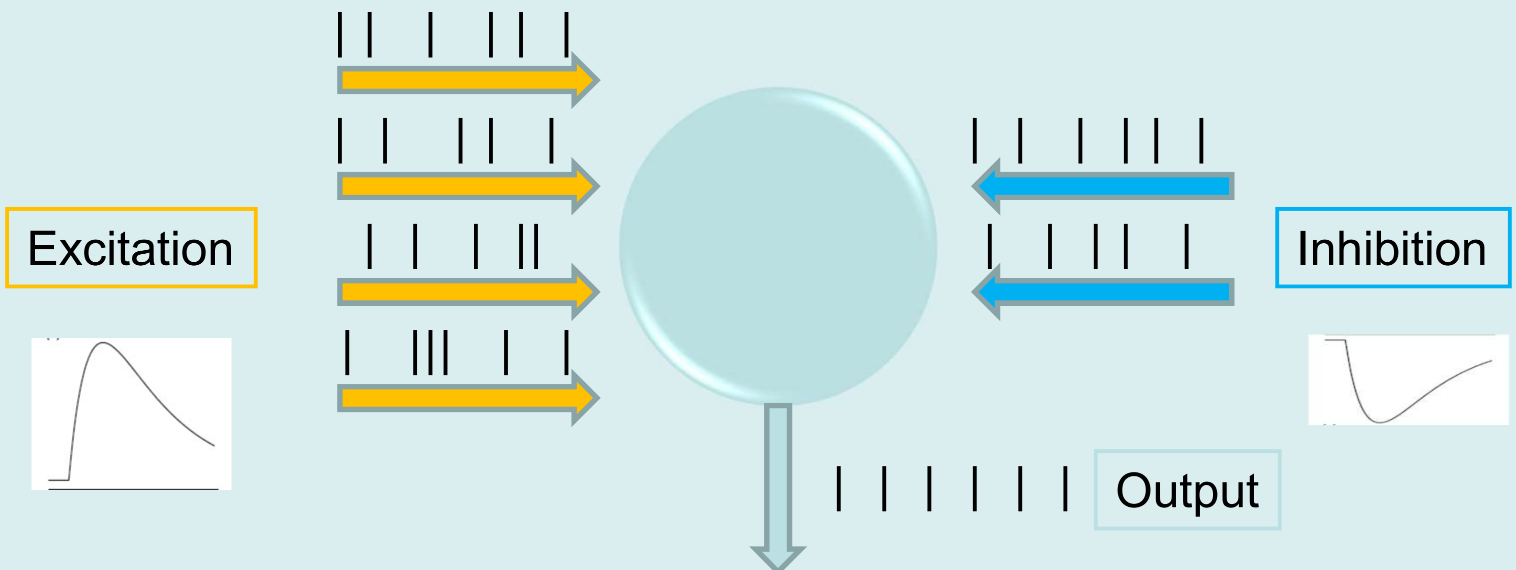
  – Current: $I_{syn}(t) = g_{syn}(t)(V(t)-E_{syn})$

(Fig. 7.2 pg 174)

Neuronal Firing Patterns

- Neuronal firing activity is often irregular
- How does this arise?
  - Intrinsic or network property?
  - Balance of excitation and inhibition





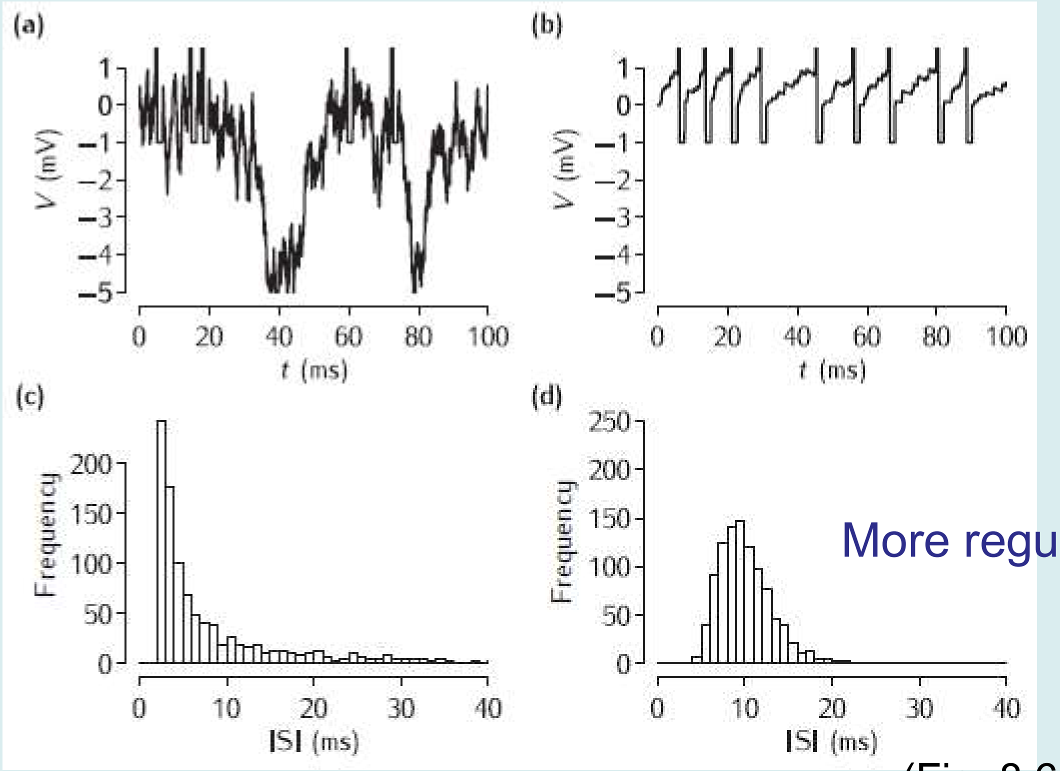
$I_{syn}(t) = g_{syn}(t)(V(t)-E_{syn})$

Model using I&F Neuron

- I&F neuron driven by 100Hz Poisson spike trains
  - Via excitatory and inhibitory synapses
- Alter balance of excitation and inhibition

300 Excitation + 150 inhibition

18 Excitation only



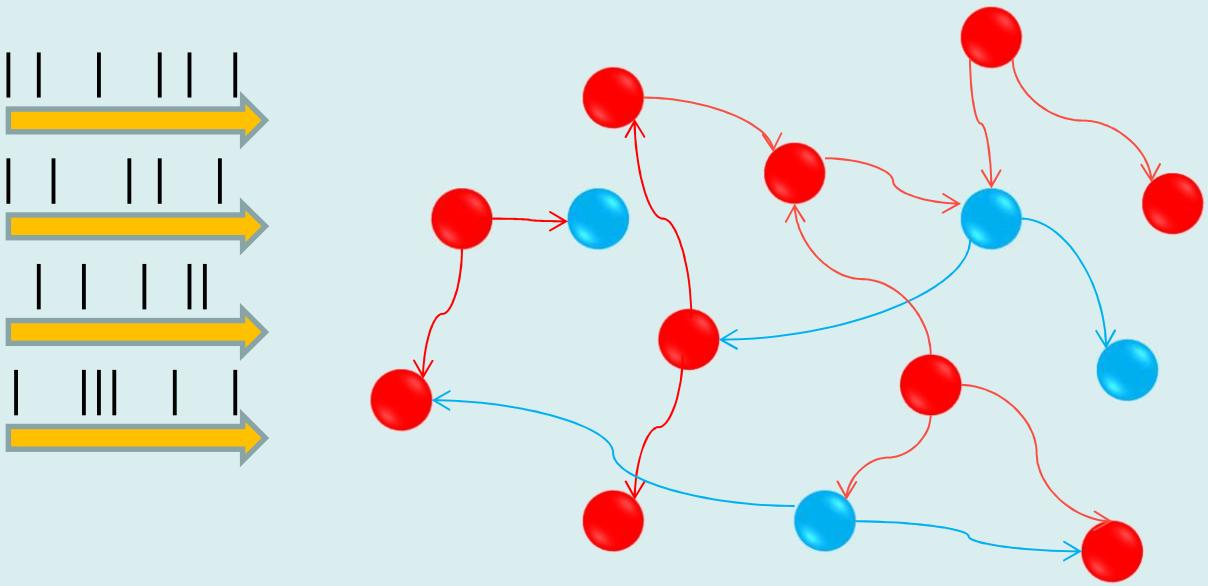
Irregular firing

More regular

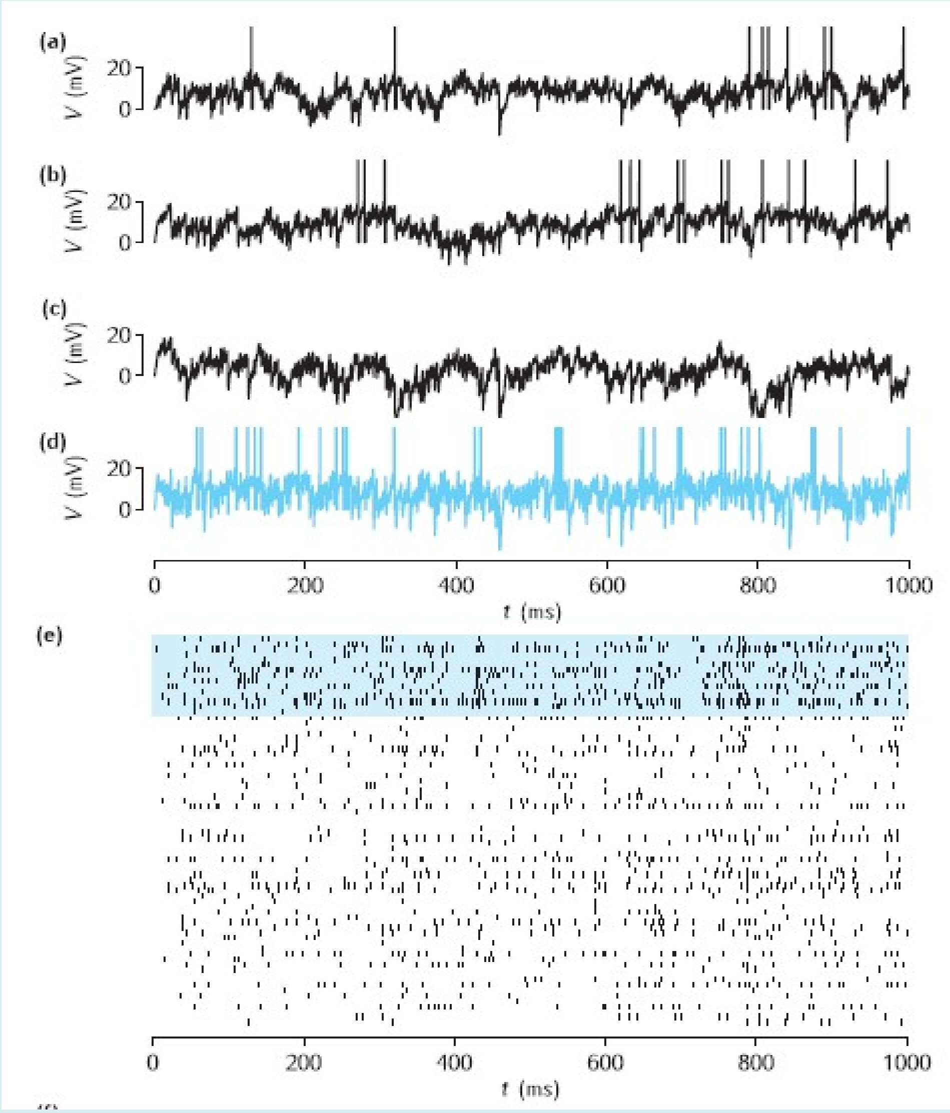
(Fig. 8.6 pg 209)

Network Model with I&F Neurons

- Randomly connected network of 80% excitatory and 20% inhibitory neurons
- External excitatory drive to all neurons
  - Noisy Poisson spike trains

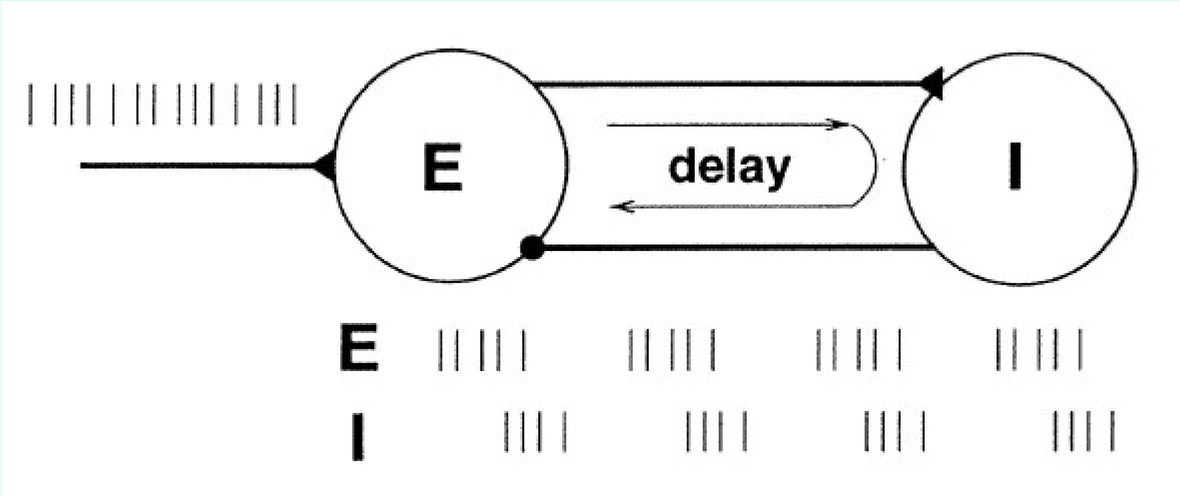


Network Model: Random Firing



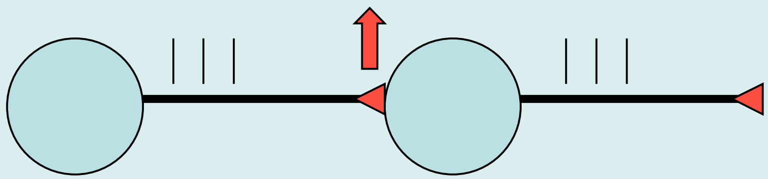
Rhythm Generation

- E-I oscillator
  - Reciprocally coupled *excitatory* and *inhibitory* neurons
  - Constant drive to excitatory neuron
  - Delay around the loop

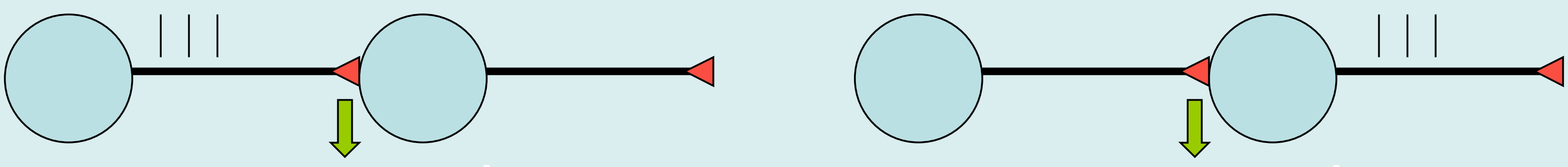


Associative Learning: Hebbian

- Increase synaptic strength if both pre- and postsynaptic neurons are active: LTP

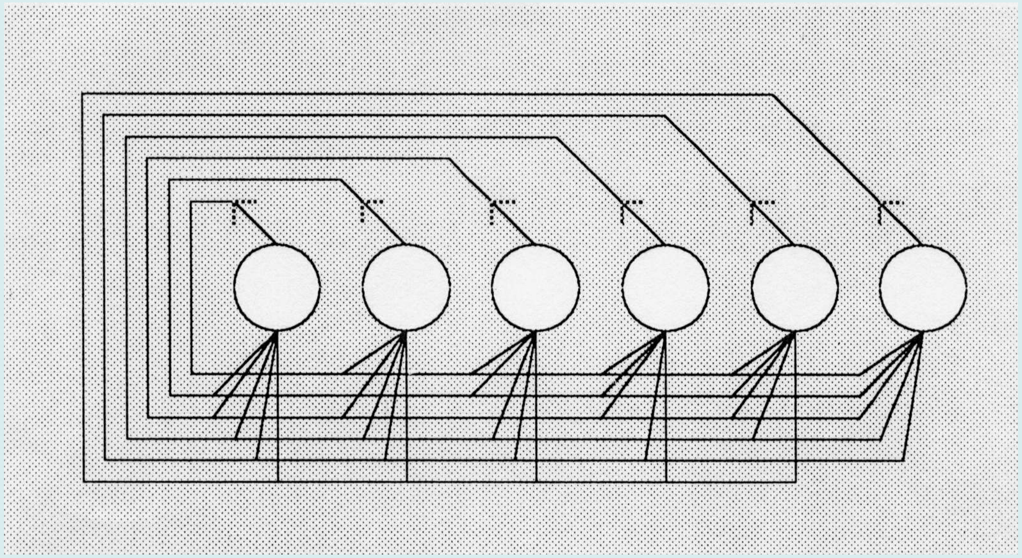


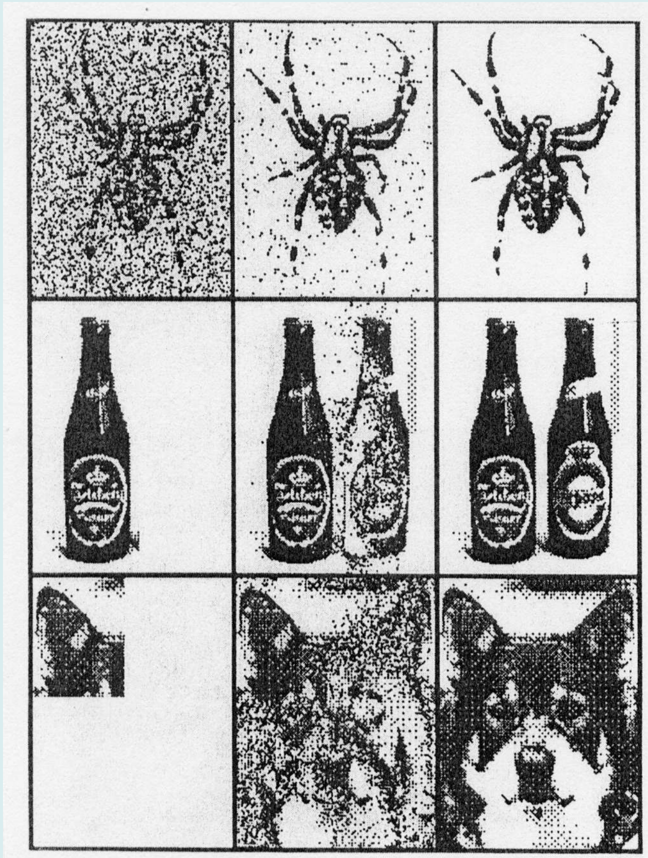
- Decrease synaptic strength when the pre- or postsynaptic neuron is active alone: LTD



Example: Associative Memory

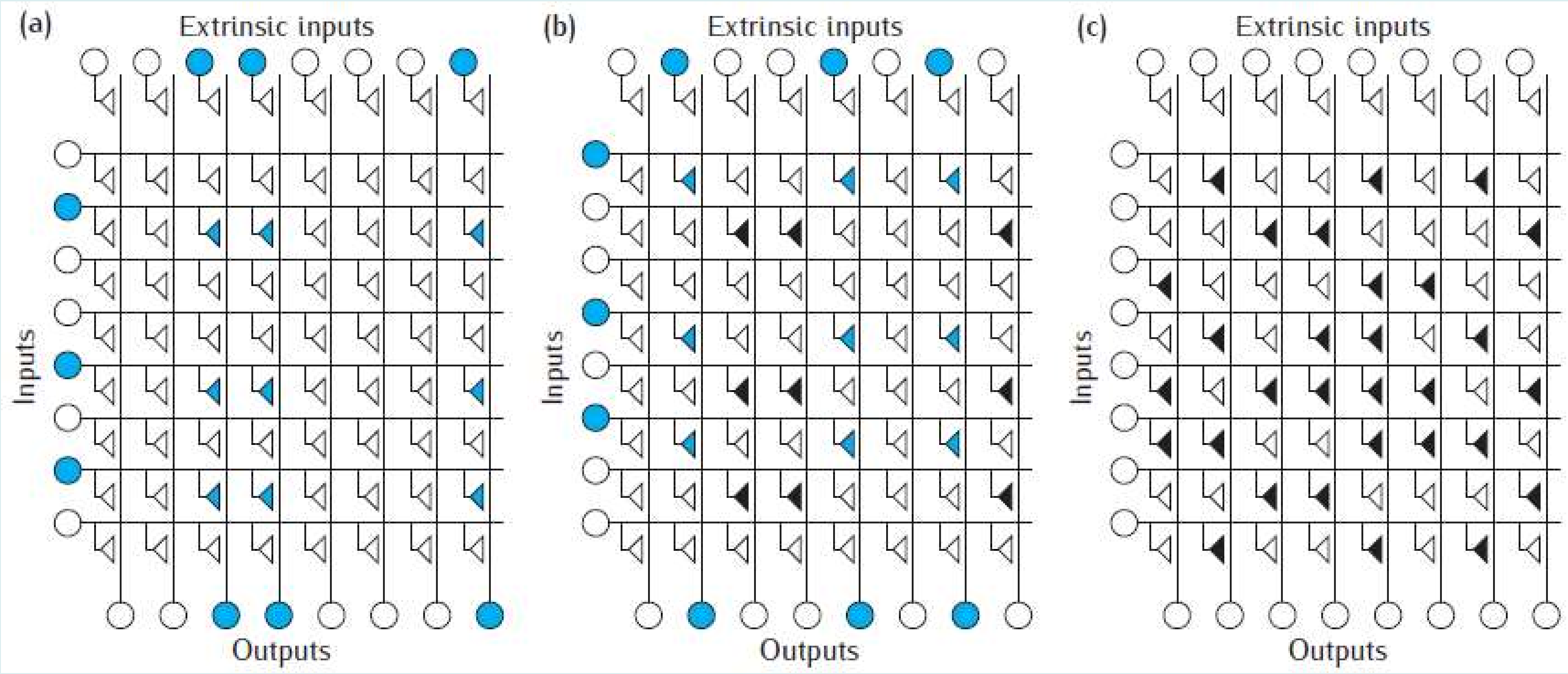
- Autoassociation and heteroassociation
- Hebbian learning of weights
- Content addressable





Heteroassociative Memory

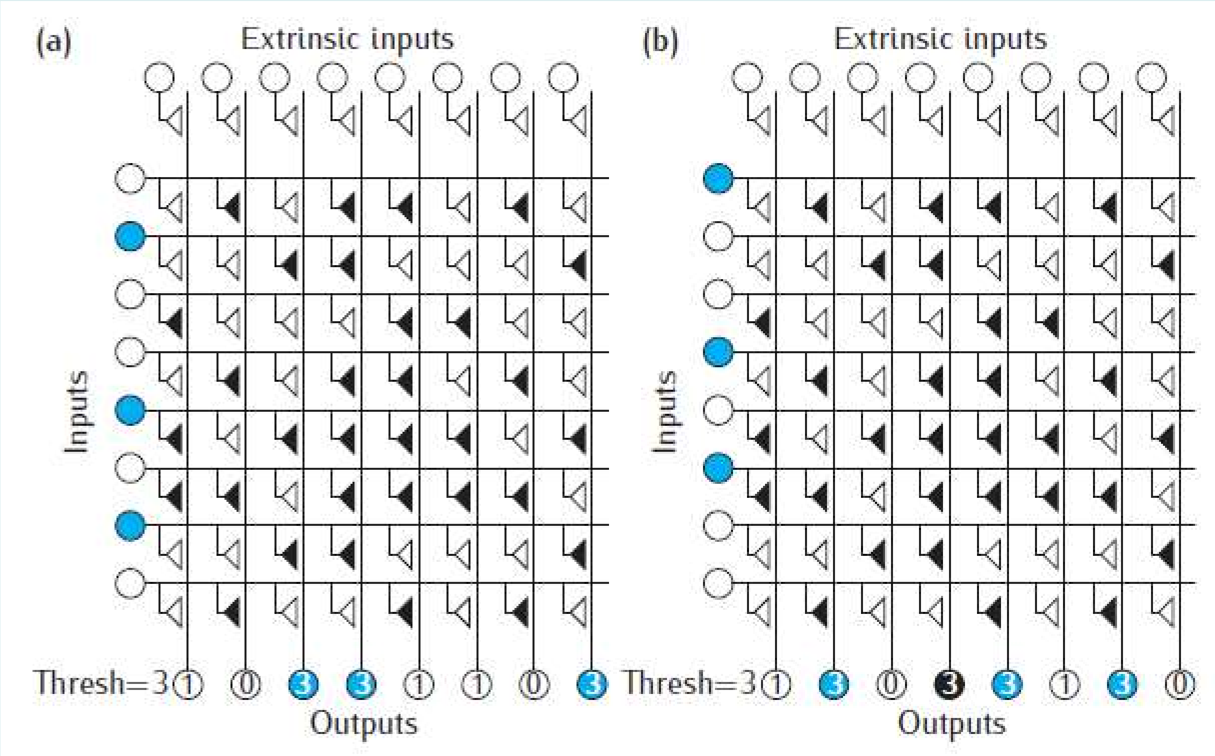
- Associations between binary patterns
- Hebbian learning: $\Delta w_{ij} = p_i . p_j$
- Store multiple patterns



(Fig. 9.4 pg 234)

Memory Recall

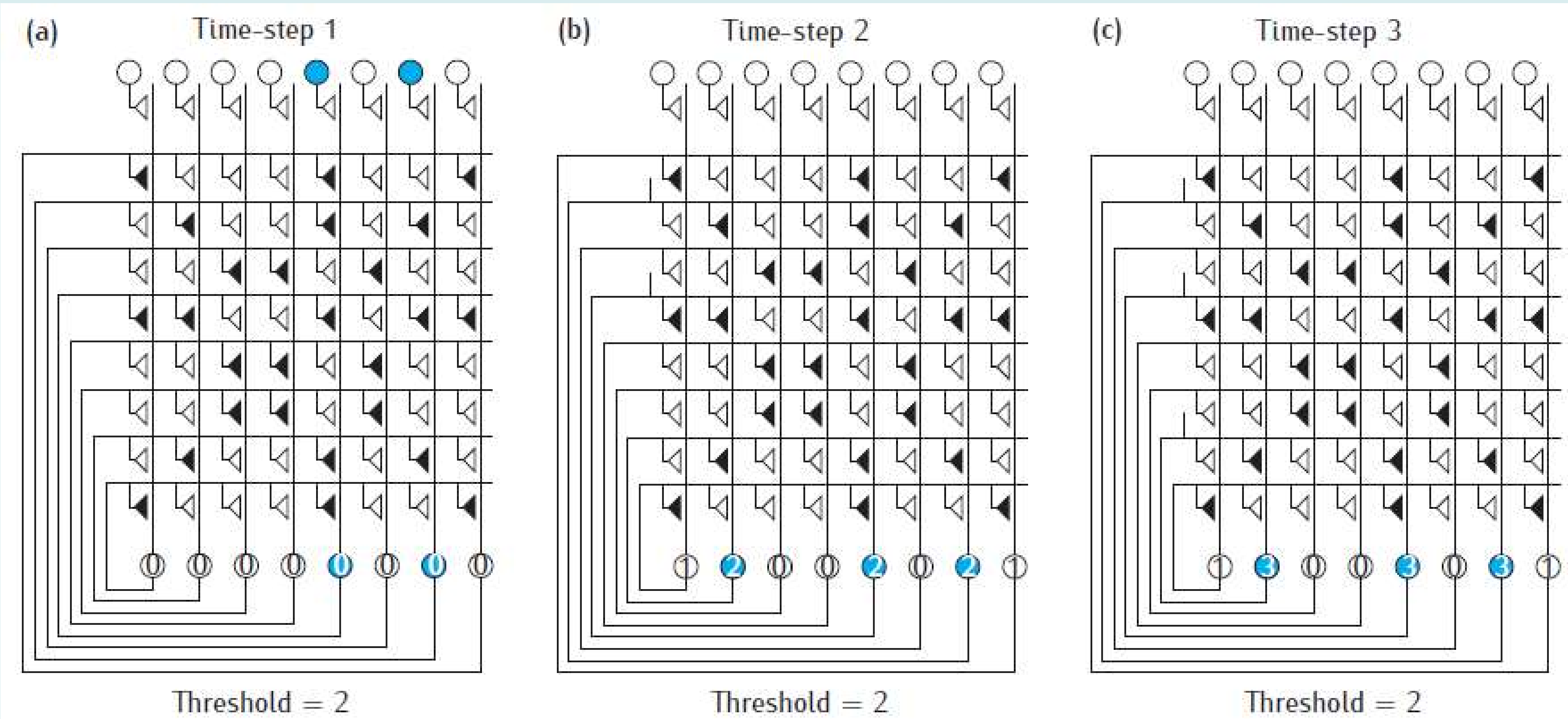
- Weighted synaptic input from memory cue
- Threshold setting on output



(Fig. 9.5 pg 235)

Multistep Memory Recall

- Autoassociative recurrent network



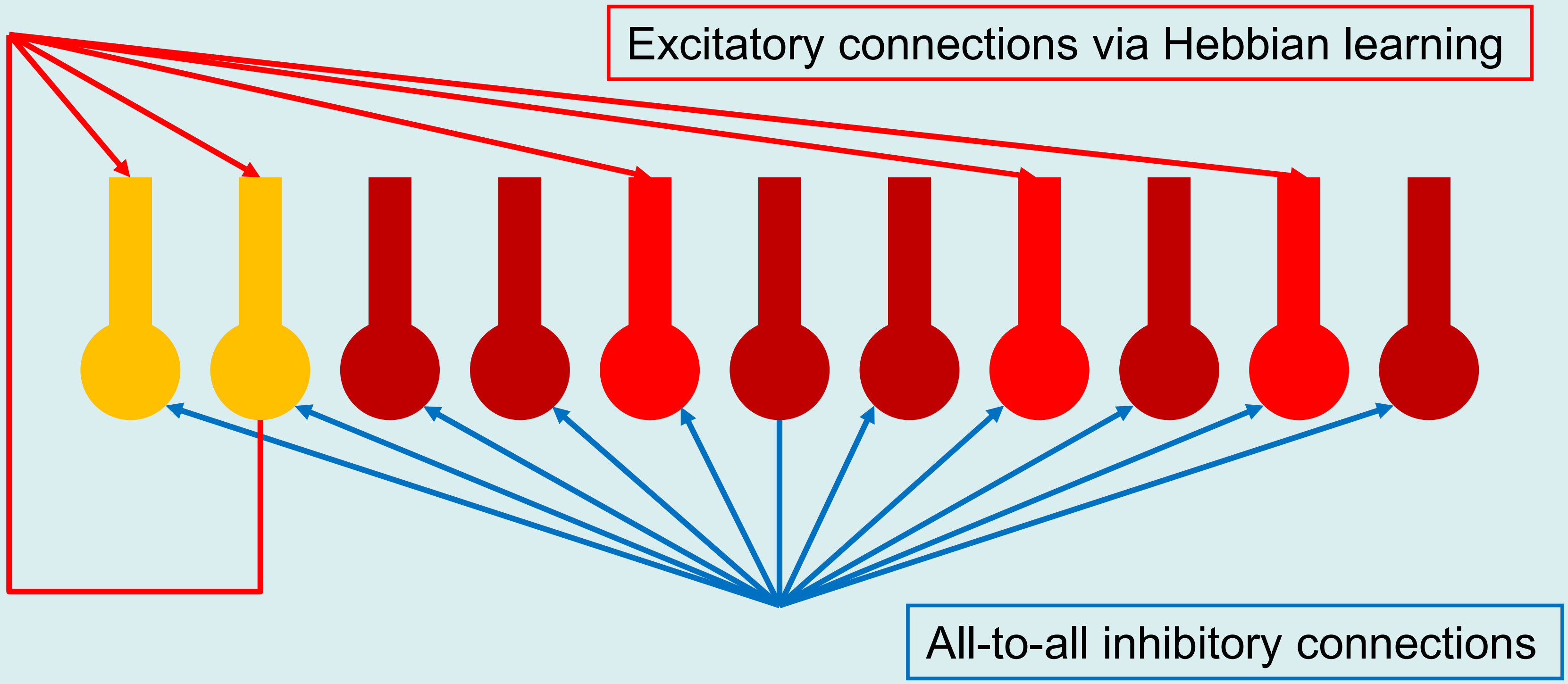
(Fig. 9.6 pg 236)

Spiking Associative Network

- How could this be implemented by spiking neurons?
  - Sommers and Wennekers (2000, 2001)
- 100 Pyramidal cell recurrent network
  - Pinsky-Rinzel 2-compartment PC model
  - E connections determined by predefined binary Hebbian weight matrix that sets AMPA conductance
  - All-to-all fixed weight inhibitory connections
- Tests autoassociative memory recall

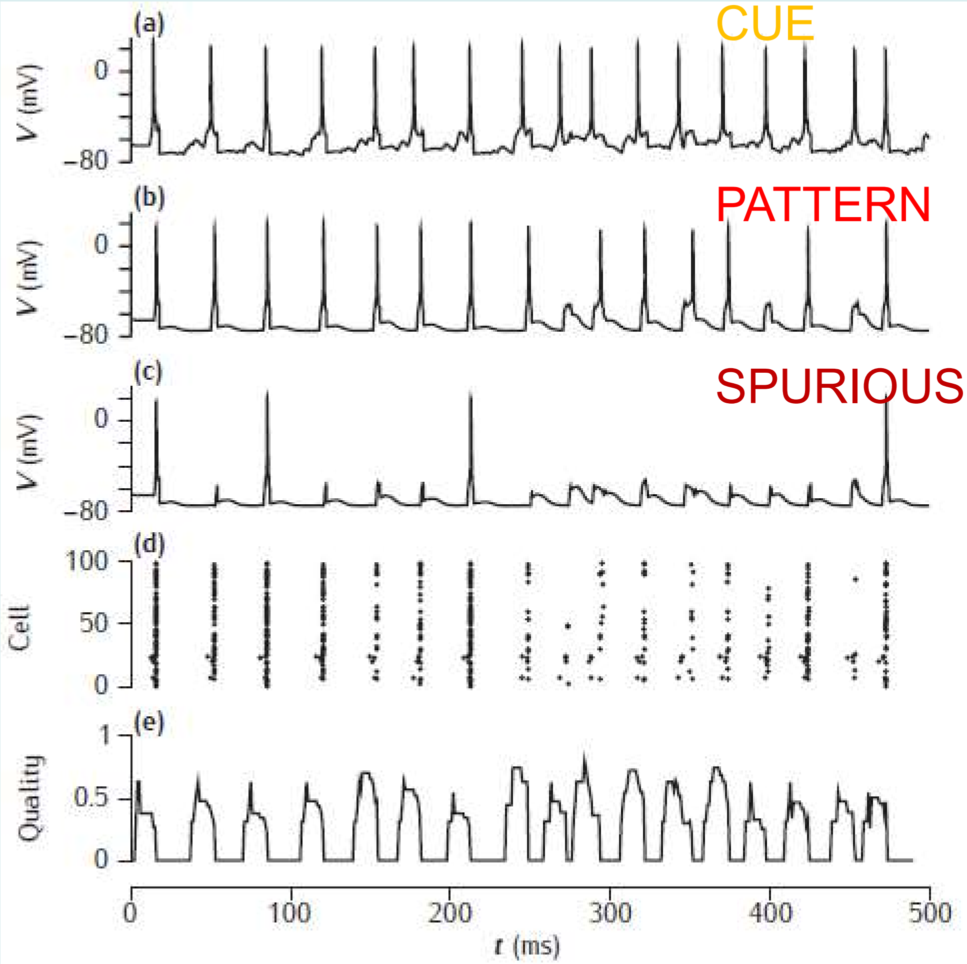
Spiking Associative Network

- Pattern is 10 active neurons out of 100
- 50 random patterns stored
- 4 active neurons as recall cue



Cued Recall in Spiking Network

- Cue: 4 of 10 PCs in a stored pattern receive constant excitation
- Network fires with gamma frequency
- Pattern is active cells on each gamma cycle
- Timing and strength of inhibition



(Fig. 9.10 pg 253)

The End

Any questions?