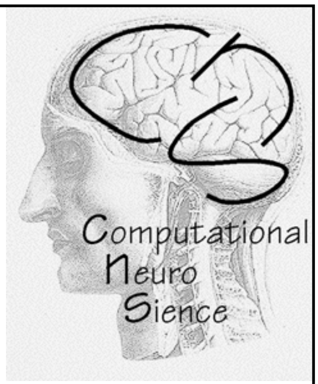
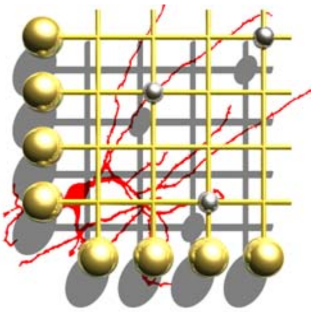
Introduction to Computational Modelling of Brain Functions: Cells, Synapses, Networks and Beyond





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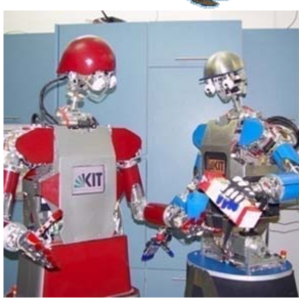
Computational Neuroscience

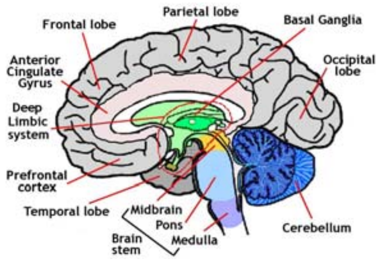


(KIT Armar-1 Robot)

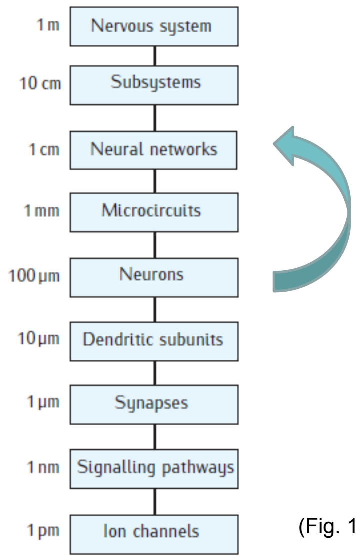
- Discover how the brain works
  - Models that can reproduce and explain experimental results
- Emulate the brain in computational devices
  - Models that retain only the important computational details

Levels of Detail

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



(confrontaal.org)



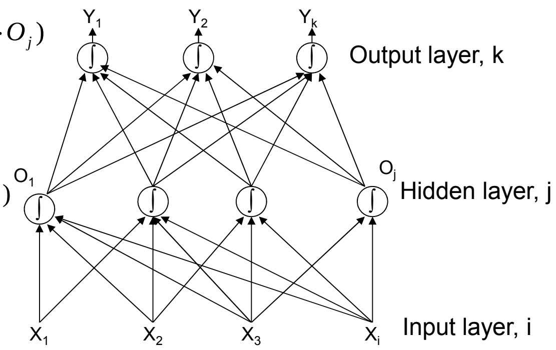
(Fig. 1.3 pg 7)

Artificial Neural Networks

- Networks of simple computing units (“*neurons*”)
- Binary or analog signals and connection weights

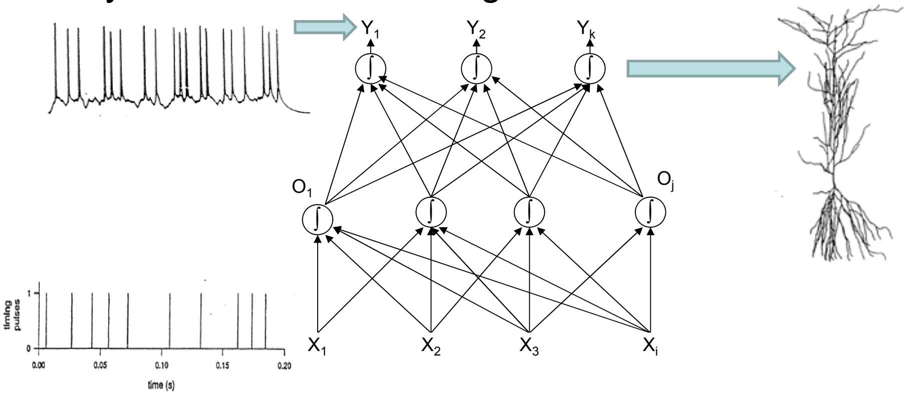
$$Y_k = f(\sum_j w_{kj} \cdot O_j)$$

$$O_j = f(\sum_i w_{ji} \cdot X_i)$$



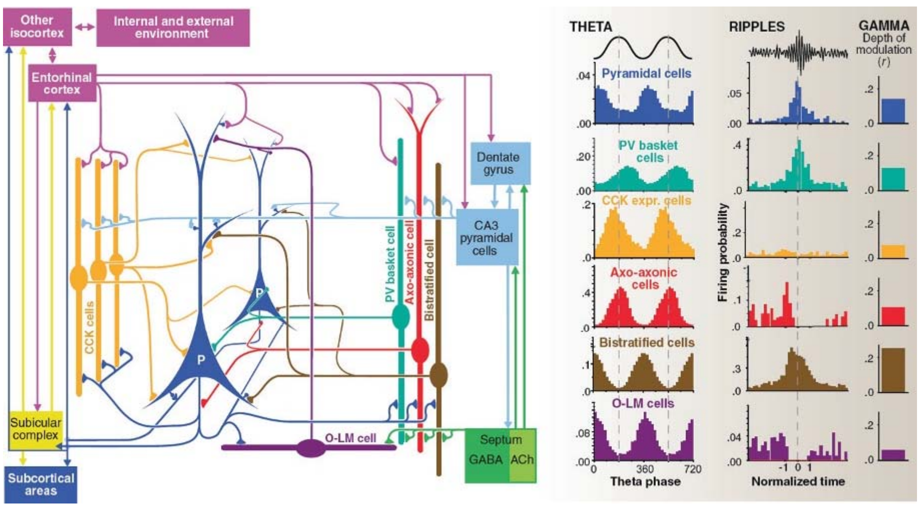
Real Neural Networks

- Networks of complex neurons
- Pulse train signals (*action potentials* or *spikes*)
- Dynamic connection weights



Complicated Neural Circuits

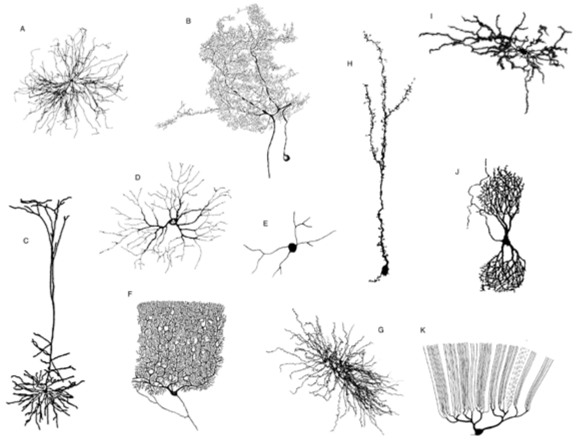
- CA1 region of hippocampus



(Fig. 2, Cobb & Vida in CU)

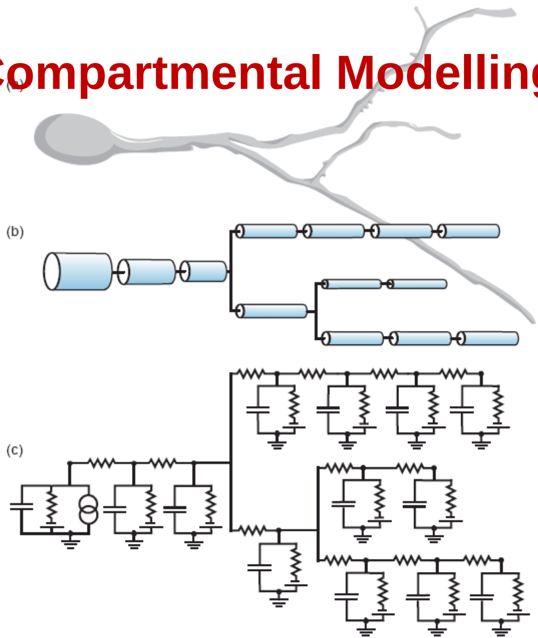
Neurons

- Neurons come in many shapes and sizes



(Dendrites, Hausser et al (eds))

Compartmental Modelling

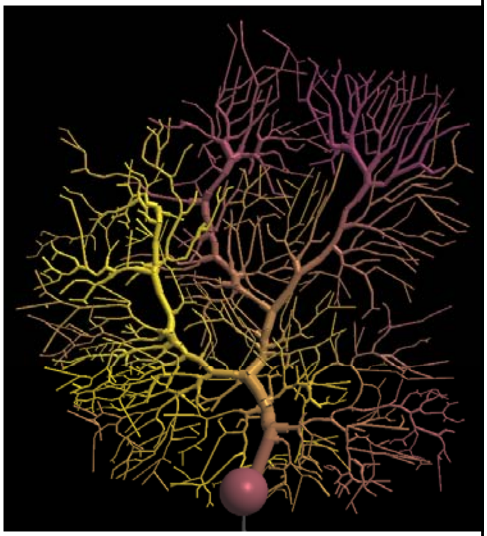


(Fig. 4.1 pg 73)

Large Scale Model

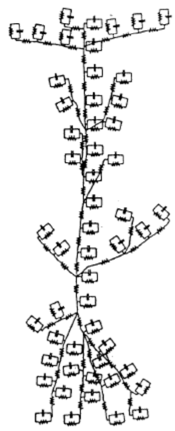
- Cerebellar Purkinje cell
  - De Schutter & Bower, 1994
- 4550 compartments
- 8021 ion channels
- 3500 synapses

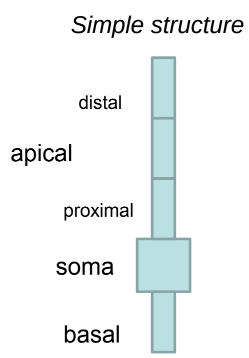
(www.neuroconstruct.org)



Varying Levels of Detail

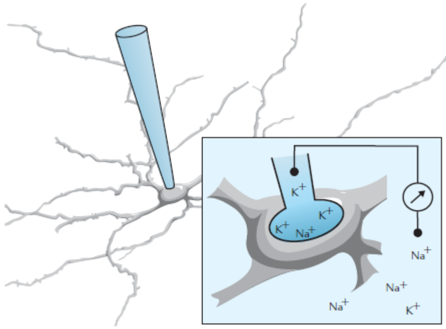
- Capture essential features of morphology



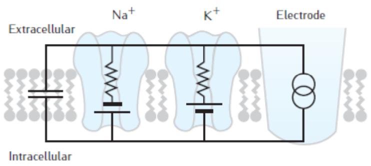


Electrical Potential of a Neuron

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



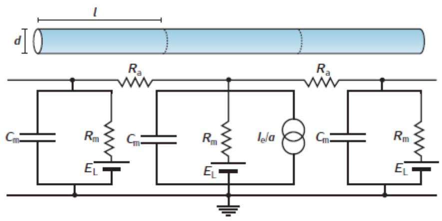
(Fig. 2.1 pg 14)



(Fig. 2.13 pg 31)

A Length of Membrane

- Membrane *compartments* connected by intracellular resistance



(Fig. 2.15 pg 36)

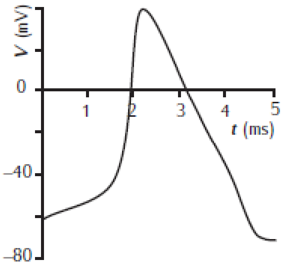
- Compartmental modelling equation

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

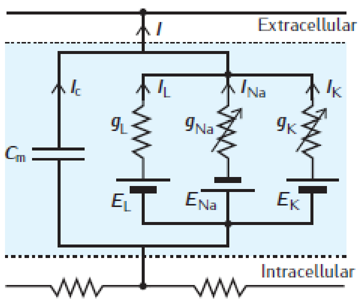
Action Potential Model

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

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



(Fig. 3.1 pg 47)



(Fig. 3.2 pg 50)

Complete Action Potential Model

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

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):

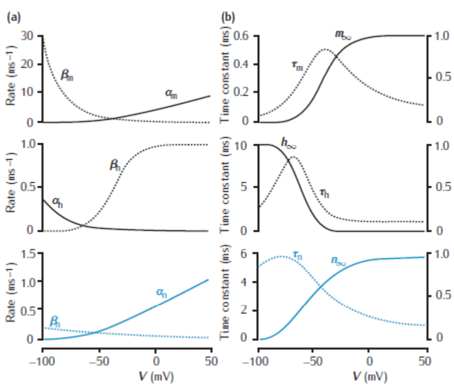
$C_m = 1.0\ \mu F\ cm^{-2}$

$E_{Na} = 50$ mV $\qquad \bar{g}_{Na} = 120\ mS\ cm^{-2}$

$E_K = -77$ mV $\qquad \bar{g}_K = 36\ mS\ cm^{-2}$

$E_L = -54.4$ mV $\qquad \bar{g}_L = 0.3\ mS\ cm^{-2}$

Box 3.5 pg 61



(Fig. 3.10 pg 60)

Many, Many Ion Channels…

Table 5.2 Summary of important currents, their corresponding channel types and sample parameters.

Current	Channel proteins	Other names	Activation $V_{1/2}$ (mV)	Activation σ (mV)	Activation τ (ms)	Inactivation $V_{1/2}$ (mV)	Inactivation σ (mV)	Inactivation τ (ms)	Note
I_{Na}	$Na_v1.1$–1.3,1.6		−30	6	0.2	−67	−7	5	a
I_{NaP}	$Na_v1.1$–1.3,1.6		−52	5	0.2	−49	−10	1500	b
I_{CaL}	$Ca_v1.1$–1.4	HVA_l	9	6	0.5	4	2	400	c
I_{CaN}	$Ca_v2.2$	HVA_m	−15	9	0.5	−13	−19	100	d
I_{CaR}	$Ca_v2.3$	HVA_m	3	8	0.5	−39	−9	20	e
I_{CaT}	$Ca_v3.1$–3.3	LVA	−32	7	0.5	−70	−7	10	f
I_{PO}	$K_v3.1$	Fast rectifier	−5	9	10	—	—	—	g
I_{DR}	$K_v2.2$, $K_v3.2$…	Delayed rectifier	−5	14	2	−68	−27	90	h
I_A	$K_v1.4$,3.4,4.1,4.2…		−1	15	0.2	−56	−8	5	i
I_M	$K_v7.1$–7.5	Muscarinic	−45	4	8	—	—	—	j
I_D	$K_v1.1$–1.2		−63	9	1	−87	−8	500	k
I_h	HCN1–4	Hyperpolarisation-activated	−75	−6	1000	—	—	—	l
I_C	$K_{Ca}1.1$	BK, maxi-K(Ca), fAHP	V & Ca^{2+}-dep			—	—	—	m
I_{AHP}	$K_{Ca}2.1$–2.3	SK1–3, mAHP	0.7 μM		40	—	—	—	n
I_{sAHP}	K_{Ca}?	Slow AHP	0.08 μM		200	—	—	—	o

(Table 5.2 pg 102)

Potassium A-current: K_A

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

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

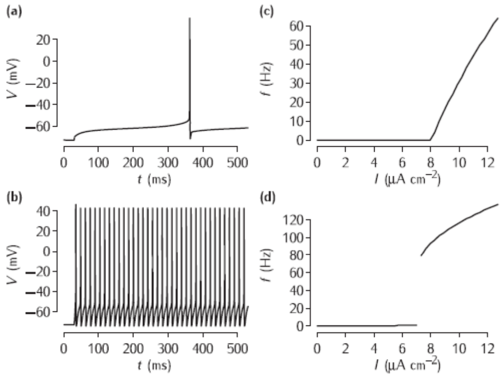
$$I_A = g_A(V - E_A), \qquad g_A = \overline{g}_A a^3 b,$$

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

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

One Effect of A-current

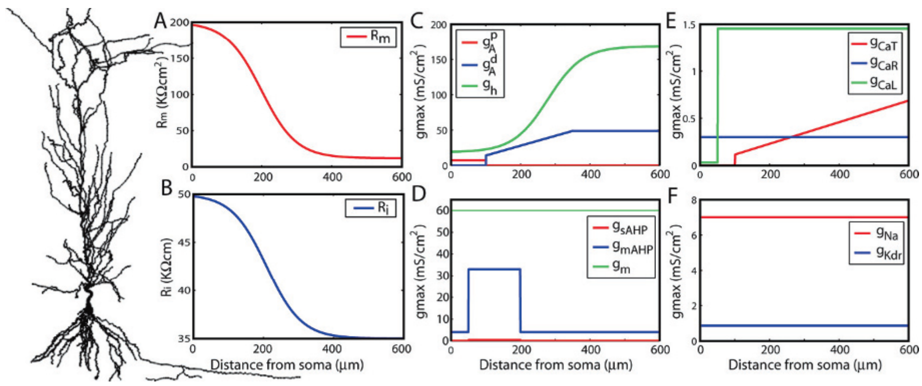
- Low frequency (Type I) firing
- Type I: with KA
  - Steady increase in firing frequency with driving current
- Type II: without KA
  - Suddent jump to non-zero firing rate



(Table 5.9 pg 106)

A Detailed Pyramidal Cell Model

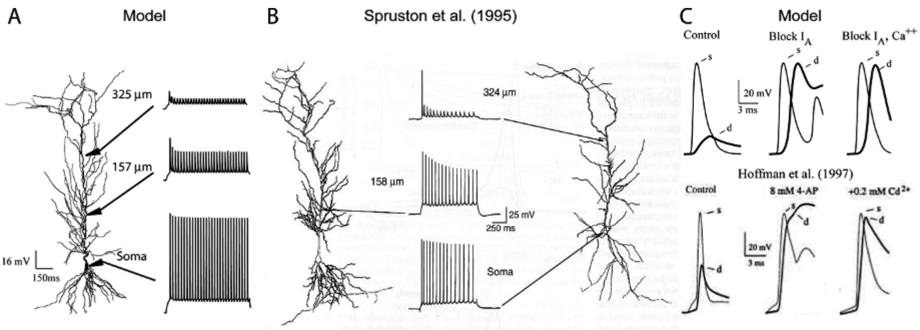
- 183 electrical compartments
- Heterogeneous ion channel population



(Poirazzi & Pissadaki, in CU)

Pyramidal Cell Model Responses

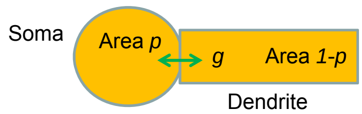
- Reproduces somatic and dendritic current injection experimental results
  - Sodium spiking with distance

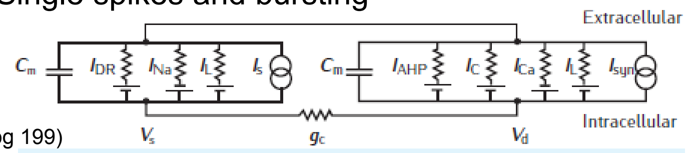


(Poirazzi & Pissadaki, in CU)

Reduced Pyramidal Cell Model

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





(Fig. 8.1 pg 199)

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

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

(Box 8.1 pg 200)

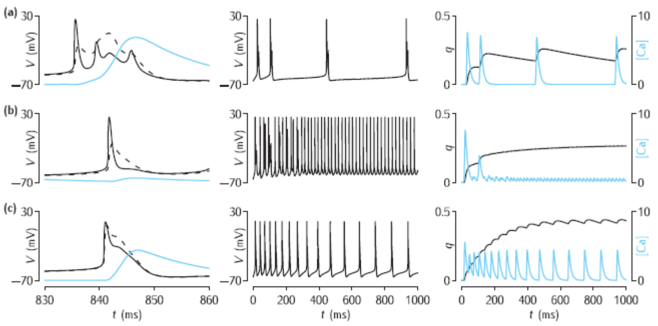
Pinsky-Rinzel Model in Action

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

Low I, low g

High I, low g

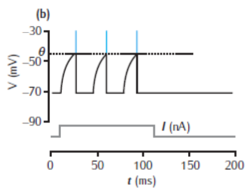
High I, high g



(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



Morris-Lecar Model

- 2-variable model of Ca-mediated Aps
- Instantaneous activation kinetics

$$C_{\mathrm{m}} \frac{\mathrm{d}V}{\mathrm{d}t} = -I_{\mathrm{i}}(V, w) + I_{\mathrm{e}}$$

$$\frac{\mathrm{d}w}{\mathrm{d}t} = \frac{w_\infty(V) - w}{\tau_w(V)}$$

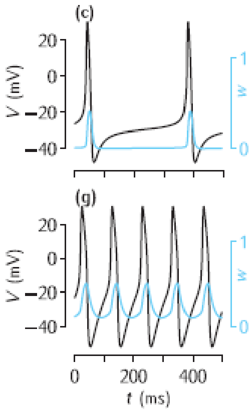
$$I_{\mathrm{i}}(V, w) = \overline{g}_{\mathrm{Ca}} m_\infty(V)(V - E_{\mathrm{Ca}}) + \overline{g}_{\mathrm{K}} w(V - E_{\mathrm{K}}) + g_{\mathrm{L}}(V - E_{\mathrm{L}})$$

$$m_\infty(V) = 0.5(1 + \tanh((V - V_1)/V_2))$$

$$w_\infty(V) = 0.5(1 + \tanh((V - V_3)/V_4))$$

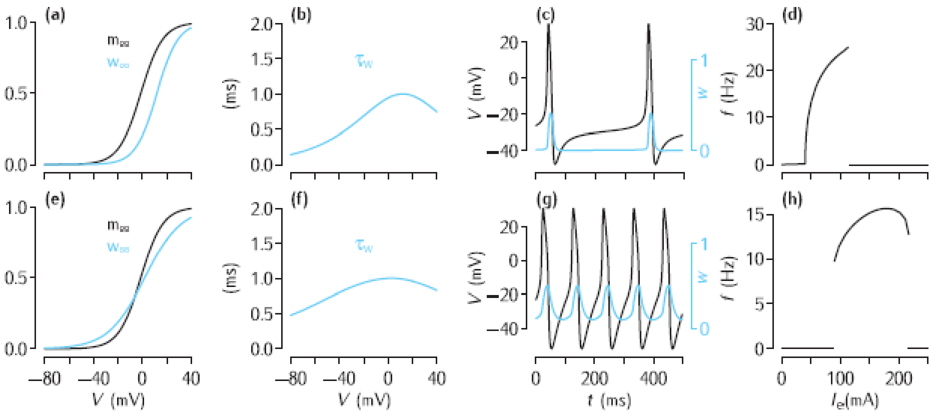
$$\tau_w(V) = \phi / \cosh((V - V_3)/(2V_4)).$$

(Box 8.1 pg 200)



Morris-Lecar Model (2)

- Type I firing: continuous increase in firing rate
- Type II firing: discontinuous jump to nonzero rate

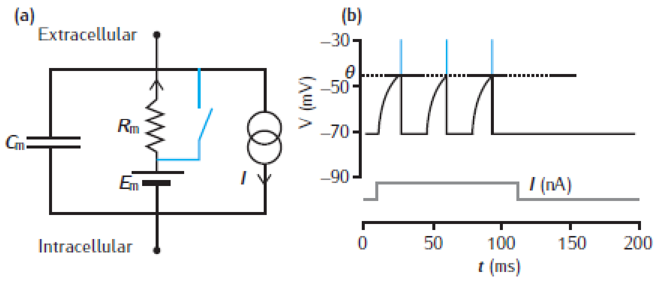


(Fig. 8.3 pg 202)

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

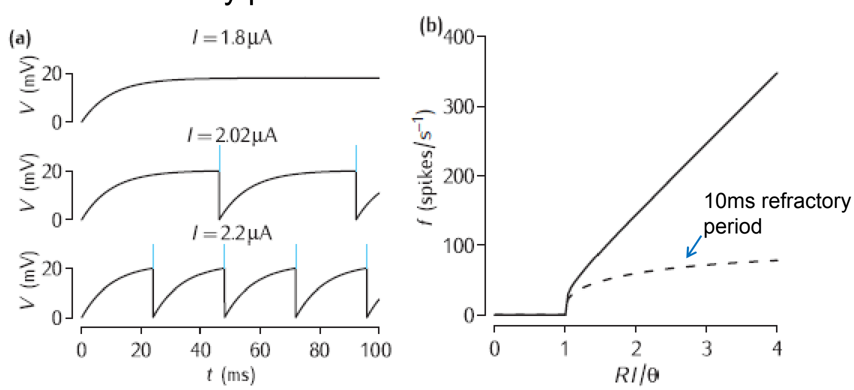
$$C_m \frac{dV}{dt} = -\frac{V - E_m}{R_m} + I$$



(Fig. 8.4 pg 204)

I&F Model Response

- Response to constant current injection
  - No refractory period



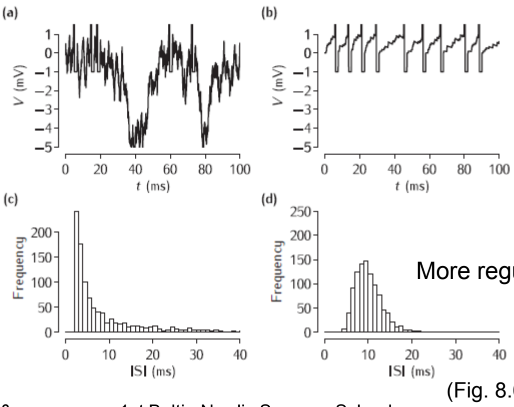
(Fig. 8.5 pg 205)

Application of I&F Neurons

- Variability of neuronal firing
  – Balance of excitation and inhibition
  – I&F neuron driven by 100Hz Poisson spike trains

Excitation + inhibition

Excitation only



Irregular firing

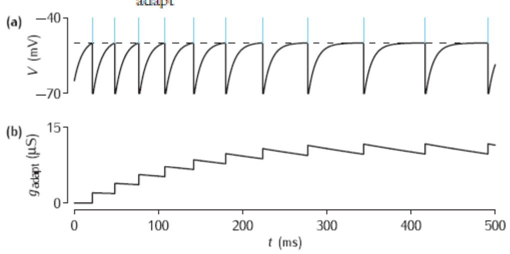
More regular

(Fig. 8.6 pg 209)

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

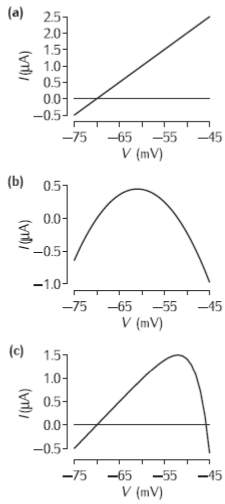
Modelling AP Initiation

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

$$C_m \frac{dV}{dt} = -\frac{(V - E_m)(V_{thresh} - V)}{R_m(V_{thresh} - E_m)} + I.$$

- Exponential I&F

$$C_m \frac{dV}{dt} = -\left(\frac{V - E_m}{R_m} - \frac{\Delta_T}{R_m} \exp\left(\frac{V - V_T}{\Delta_T}\right)\right) + I,$$



(Fig. 8.9 pg 214)

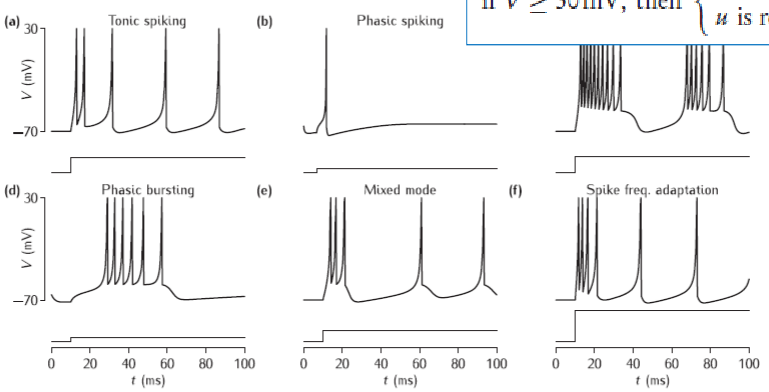
The Izhikevich Model

- Quadratic I&F plus dynamic recovery variable

$$\frac{dV}{dt} = k(V - E_m)(V - V_{thresh}) - u + I$$

$$\frac{du}{dt} = a(b(V - E_m) - u)$$

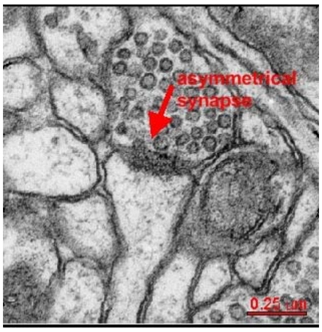
$$\text{if } V \geq 30\,\text{mV, then } \begin{cases} V \text{ is reset to } c \\ u \text{ is reset to } u + d, \end{cases}$$



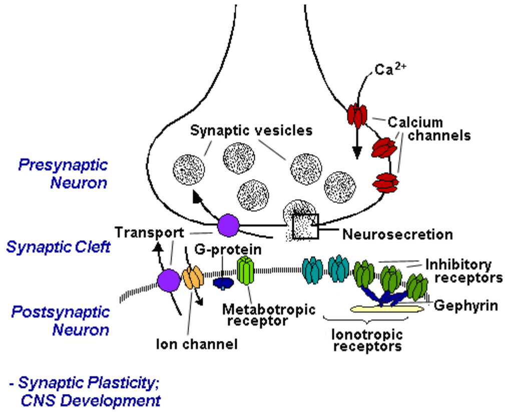
(Fig. 8.10 pg 215)

The Chemical Synapse

- A temporal signal filter
- Complex biochemical signalling pathways



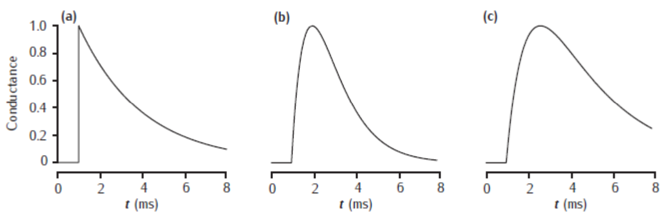
(The Synapse Web)



(biochem.uni-erlangen.de)

Synaptic Conductance

- 3 commonly used simple waveforms
  a) Single exponential $g_{syn}(t) = \bar{g}_{syn} \exp\left(-\frac{t-t_s}{\tau}\right)$
  b) Alpha function $g_{syn}(t) = \bar{g}_{syn} \frac{t-t_s}{\tau} \exp\left(-\frac{t-t_s}{\tau}\right)$
  c) Dual exponential $g_{syn}(t) = \bar{g}_{syn} \frac{\tau_1 \tau_2}{\tau_1 - \tau_2} \left(\exp\left(-\frac{t-t_s}{\tau_1}\right) - \exp\left(-\frac{t-t_s}{\tau_2}\right)\right)$



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

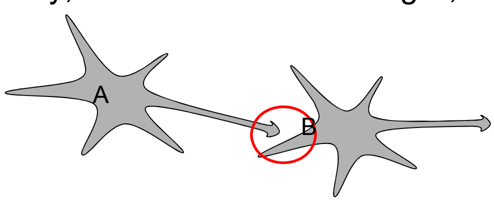
(Fig. 7.2 pg 174)

Learning in the Nervous System

- ANNs "learn" by adapting the connection weights
  - Different learning rules
- Real chemical synapses do change their strength in response to neural activity
  - Short-term changes
    - Milliseconds to seconds
    - Not classified as "learning"
  - Long term potentiation (LTP) and depression (LTD)
    - Changes that last for hours and possibly lifetime
- Evidence that LTP/LTD corresponds to "learning"

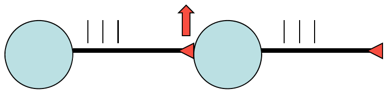
Hebbian Learning

- Hypothesis by Donald Hebb, "The Organization of Behaviour", 1949
  - "When an axon of cell A excites cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells so that A's efficiency, as one of the cells firing B, is increased."

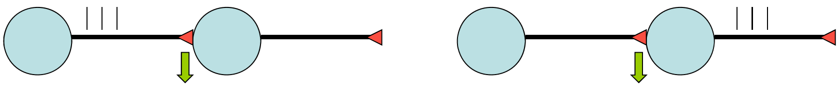


Associative Learning

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

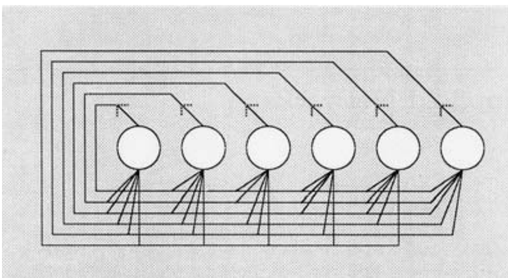


- Decrease synaptic strength when the pre- or postsynaptic neuron is active alone: LTD



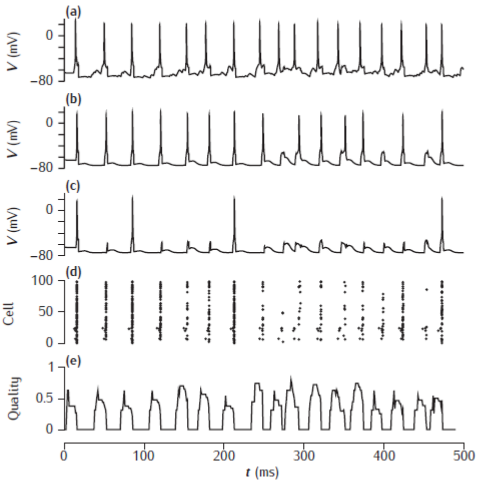
Spiking Associative Network

- Sommers and Wennekers (2000, 2001)
- Pinsky-Rinzel 2-compartment PC model
- 100 PC recurrent network
  - E connections determined by predefined binary Hebbian weight matrix that sets AMPA conductance
  - All-to-all fixed weight inhibitory connections



Cued Recall in Spiking Network

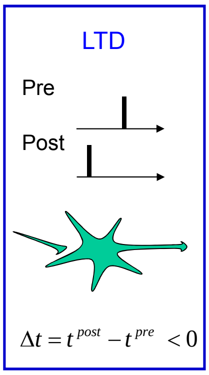
- Cue: 4 of 10 PCs in a stored pattern receive constant excitation
- Network fires with gamma frequency
- Pattern is active cells on each gamma cycle
- Timing and strength of inhibition

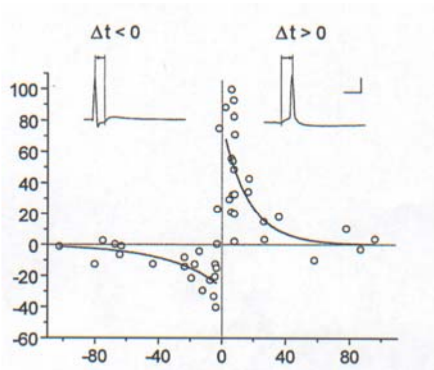


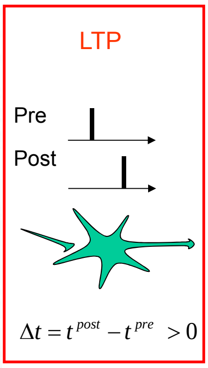
(Fig. 9.10 pg 253)

Spike Time Dependent Plasticity

- STDP depends on relative timing of pre- and postsynaptic spiking activity
  - Single spikes or short bursts



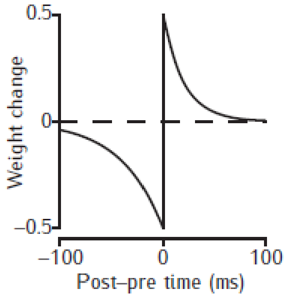




(Bi & Poo, 1998, 2001)

STDP Learning Rule

- Synaptic weight change as a function of pre- and postsynaptic spike times for a single spike pair



(Fig. 7.13 pg 190)

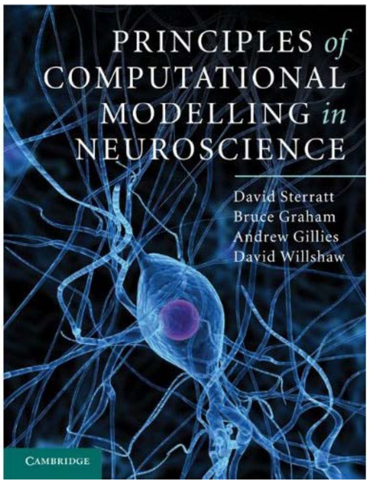
$$\Delta w_{ij} = A^{\mathrm{LTP}} \exp(-\Delta t / \tau^{\mathrm{LTP}}) \quad \text{if } \Delta t \geq 0$$
$$\Delta w_{ij} = -A^{\mathrm{LTD}} \exp(\Delta t / \tau^{\mathrm{LTD}}) \quad \text{if } \Delta t < 0.$$

(Song et al 2000; van Rossum et al 2000)

Typical parameter values:

$A^{LTP} > A^{LTD}$
τ^{LTP} = 20 msecs
τ^{LTD} = 40 msecs

Text Book



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