Over the HH-model

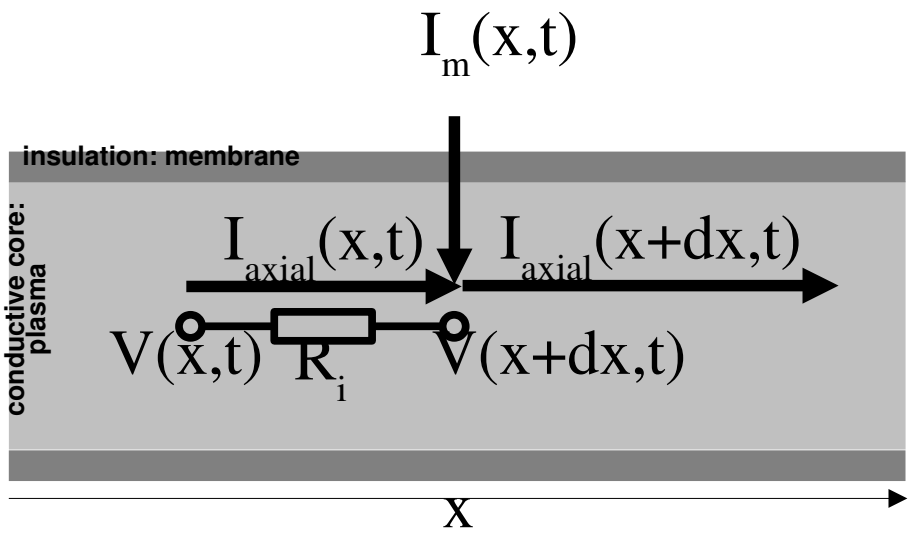
Different currents	**Function**
slow K^+	firing frequency adaptation
perzistent (non-inactivating)	Na^+ burst
Ca^{2+}	burst
Ca^{2+}-(and V-) dependent K^+	burst, adaptation
H hyperpolarization activated	pacemaker

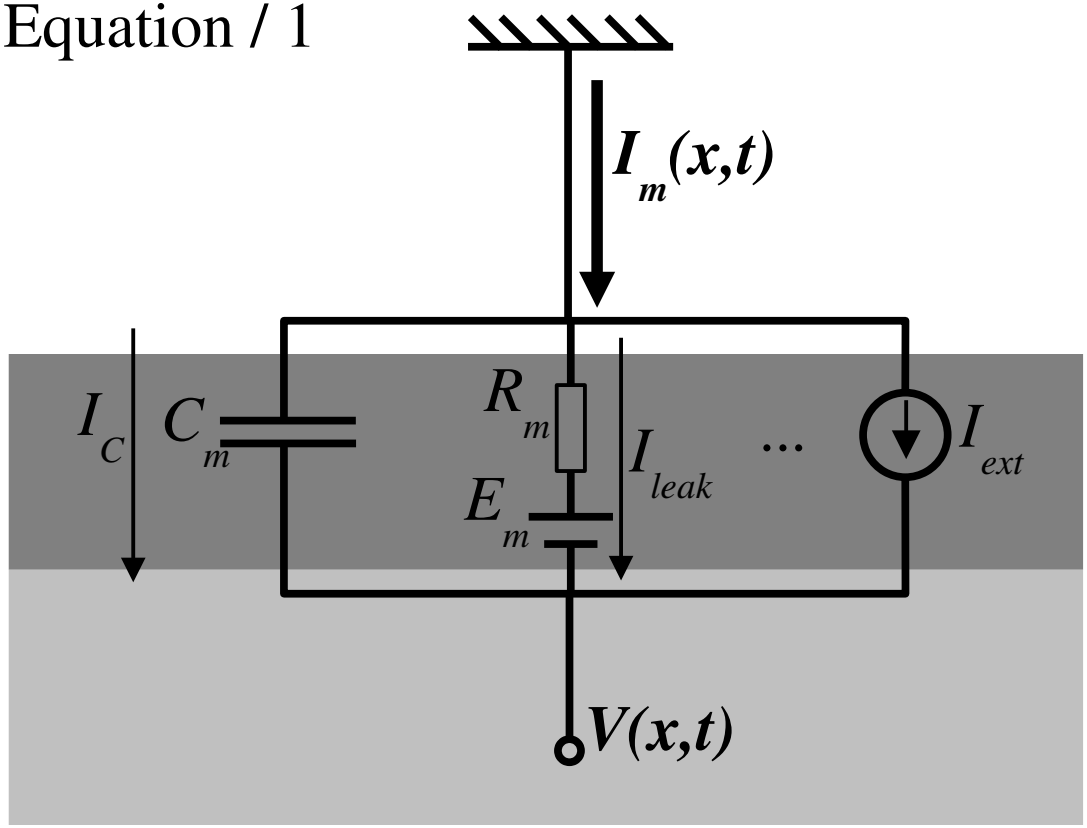
Voltage dependent currents $$I_X = g_X(t)(E_X - V(t)),\ \ g_X(t) = \bar{g}_X \prod_i p_X^{(i)}(t),\ \ \frac{dp_X^{(i)}}{dt} = \frac{p_{X\infty}^{(i)}(V(t)) - p(t)}{\tau_{p_X^{(i)}}(V(t))}$$

Ca^{2+} concentration $$\frac{d[Ca]_i}{dt} = \beta\ I_{Ca}(t) - \frac{[Ca]_i(t)}{\tau_{Ca}}$$

Ca^{2+}-dependent gate $$\frac{dp_X^{(i)}}{dt} = \frac{p_{X\infty}^{(i)}([Ca]_i(t)) - p(t)}{\tau_{p_X^{(i)}}([Ca]_i(t))}$$

The Cable Equation / 1





$$I_{axial}(x,t) = -\frac{1}{R_i}\frac{\partial V}{\partial x}$$

$$\frac{\partial I_{axial}}{\partial x} = I_m(x,t)$$

$$I_m(x,t) = I_C(x,t) + I_{leak}(x,t) + \ldots = -C_m\frac{\partial V}{\partial t} - \frac{V(x,t)}{R_m}$$

simplification: no voltage-dependent currents!

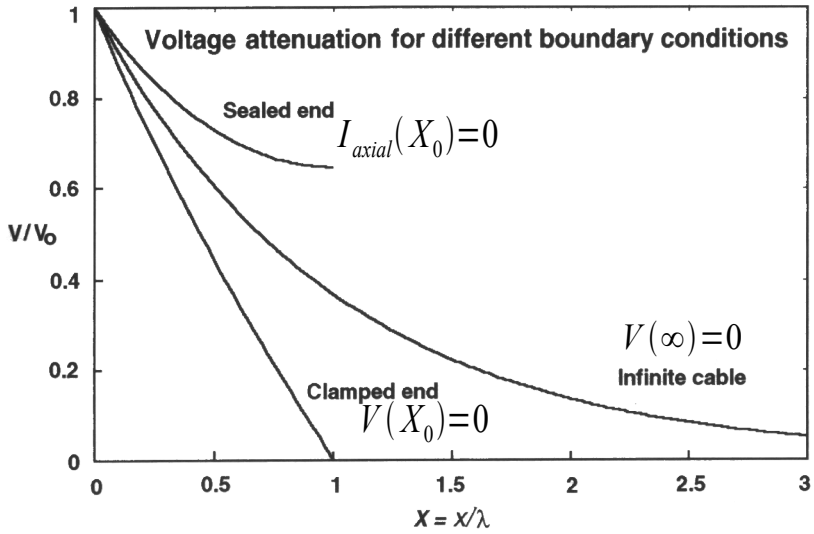
x [cm], t [msec]
V [mV], I_{axial} [μA], I_m [μA/cm]
R_i [kΩ/cm], R_m [kΩcm], C_m [μF/cm]

$$\lambda = \sqrt{R_m / R_i} \quad [cm]$$
$$\tau = R_m C_m \quad [msec]$$

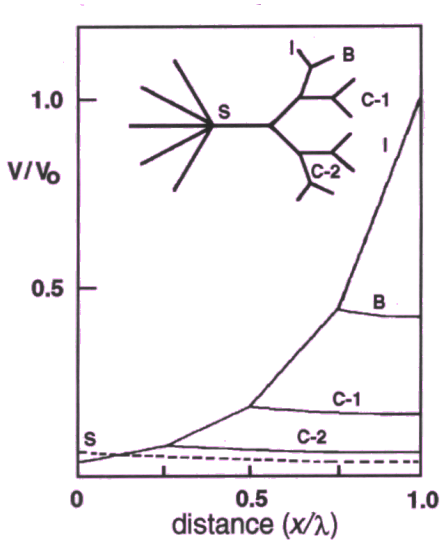
$$\frac{1}{R_i}\frac{\partial^2 V}{\partial x^2} - C_m\frac{\partial V}{\partial t} - \frac{V(x,t)}{R_m} = 0$$

$$\lambda^2\frac{\partial^2 V}{\partial x^2} - \tau\frac{\partial V}{\partial t} - V(x,t) = 0$$

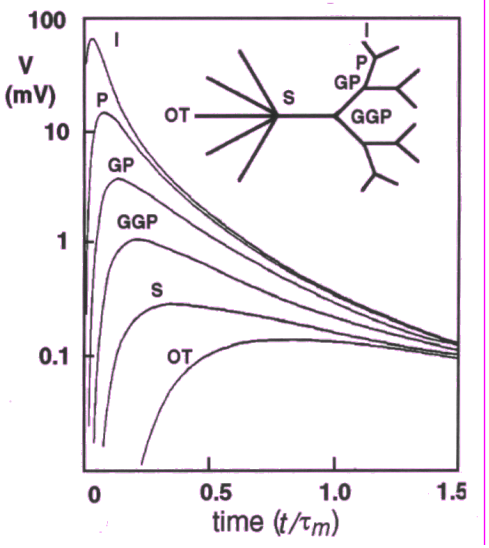
The Cable Equation / 2



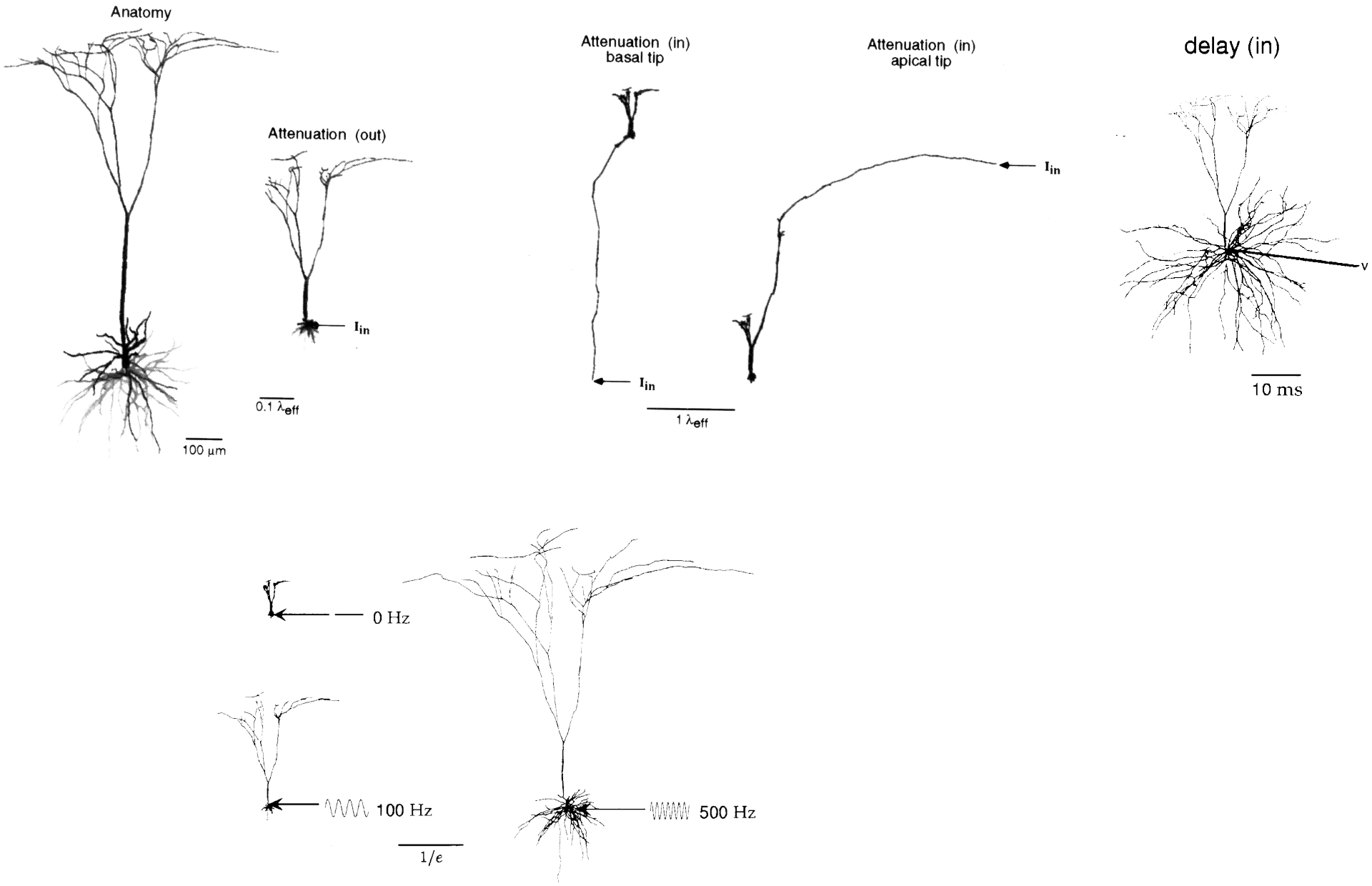
Constant current injection: steady-state **spatial** voltage spread



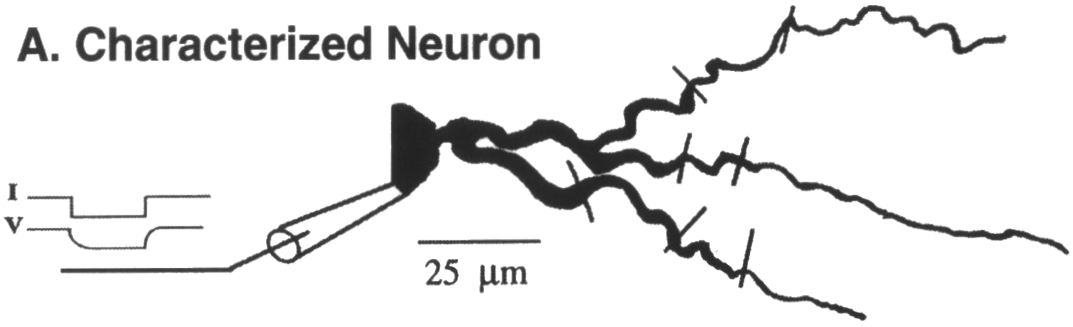
Transient current injection: **temporal** development of voltage spread

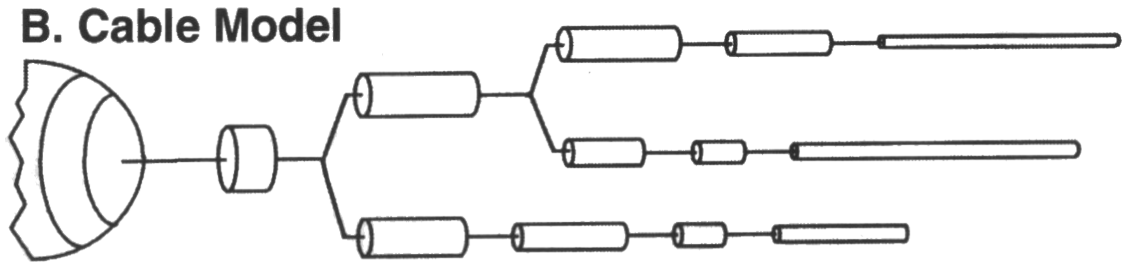


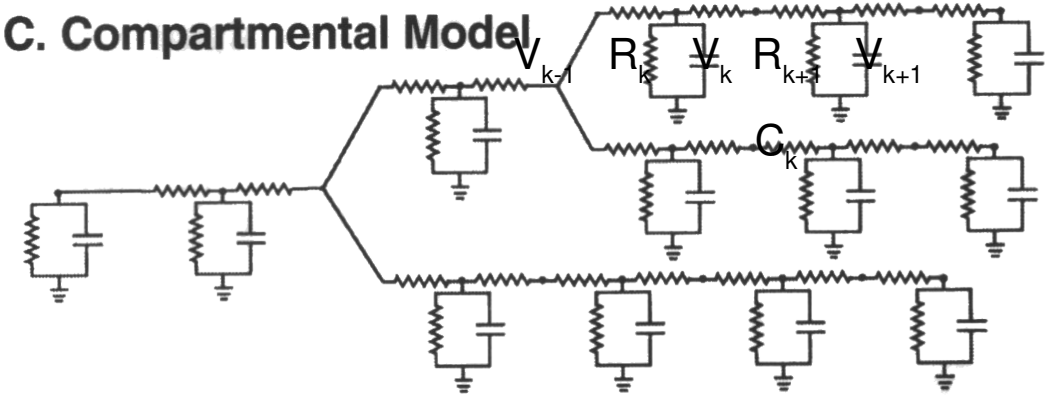
The Cable Equation / 3



Multicompartmental modeling







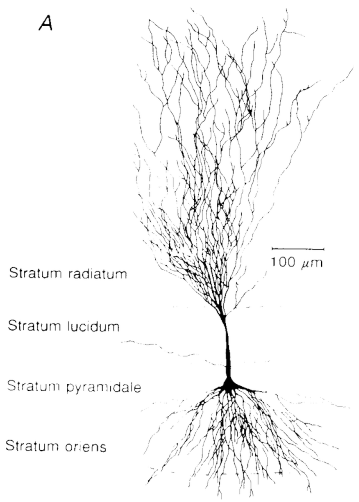
$$\frac{1}{R_i}\frac{\partial^2 V}{\partial x^2} - C_m\frac{\partial V}{\partial t} - \frac{V(x,t)}{R_m} = 0$$

$$C_k\frac{dV_k}{dt} = \underbrace{I_k(t)} + \frac{V_{k-1}(t) - V_k(t)}{R_k} + \frac{V_{k+1}(t) - V_k(t)}{R_{k+1}}$$

all sorts of ionic currents (HH, etc)

Detailed cell models: Why?
I. Reproducing different phenomena (how does it works?)

Traub & Miles (1991, 1994) hippocampal pyramidal cell model



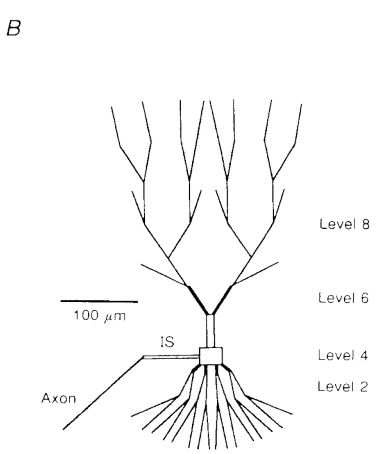
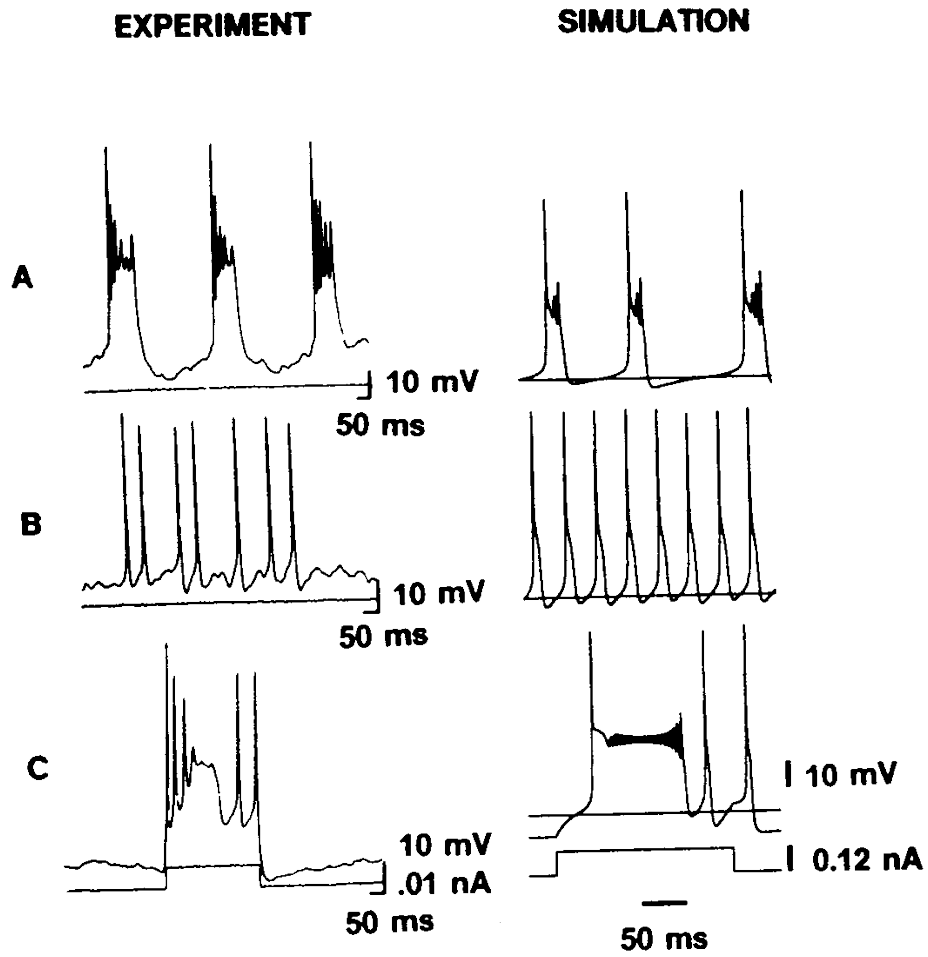


Table 2. Active conductance densities (mS cm^{-2})

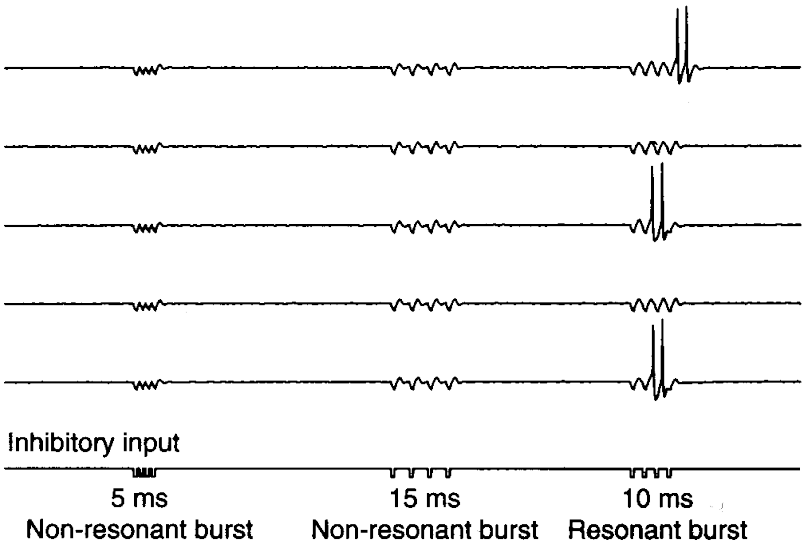
Level	Na^+	Ca^{2+}	K(DR)	K(AHP)	K(C)	K(A)
1	—	1·0	—	0·8	4·0	—
2	—	1·0	—	0·8	4·0	0·5
3	1·0	1·0	15	0·8	8·0	0·5
4	100	1·0	135	0·8	20	0·5
5	3·0	1·0	20	0·8	8·0	0·5
6	3·0	1·0	20	0·8	8·0	0·5
7	—	2·0	—	0·8	4·0	—
8	—	3·0	—	0·8	12	—
9	—	3·0	—	0·8	12	—
10	—	1·0	—	0·8	4·0	—
11	—	1·0	—	0·8	4·0	—
IS	500	—	250	—	—	—
Axon	500	—	250	—	—	—

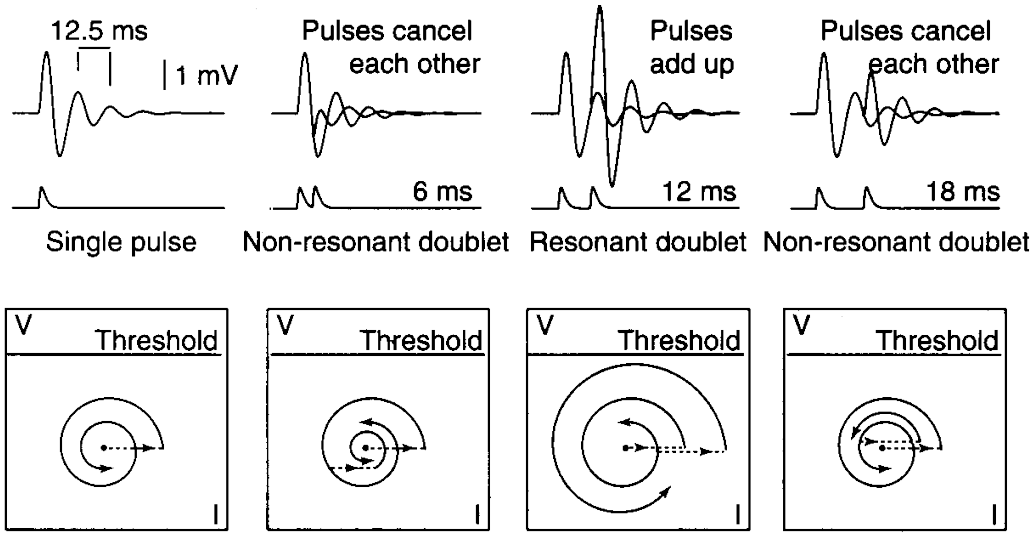


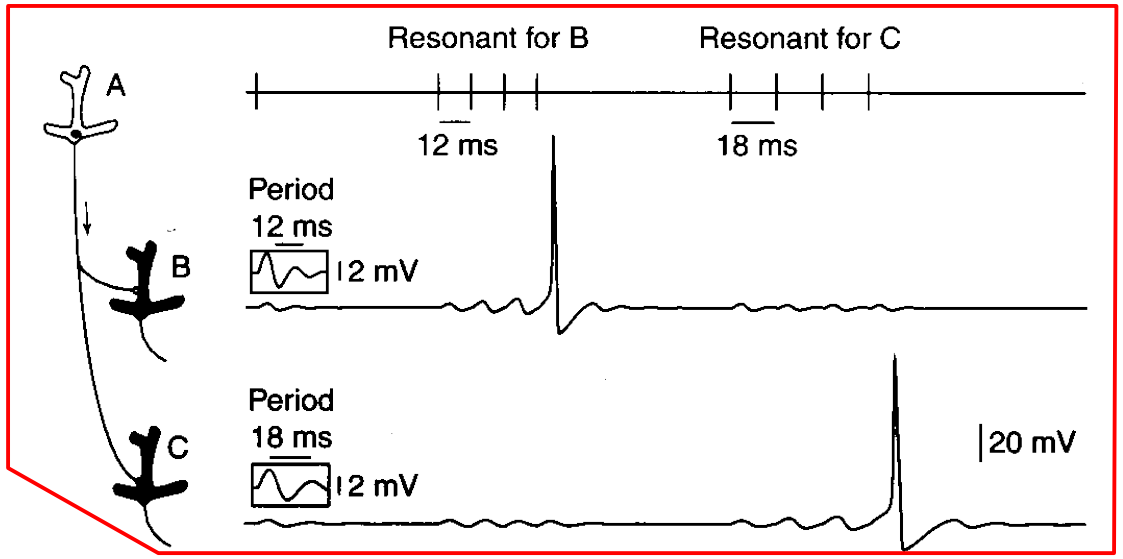
Detailed cell models: Why?
II. Revealing computational functions (What it is good for?) / 1

What is a burst good for?

1. Common sense (Lisman): more robust transmission
2. Izhikevich: selective communication with resonance



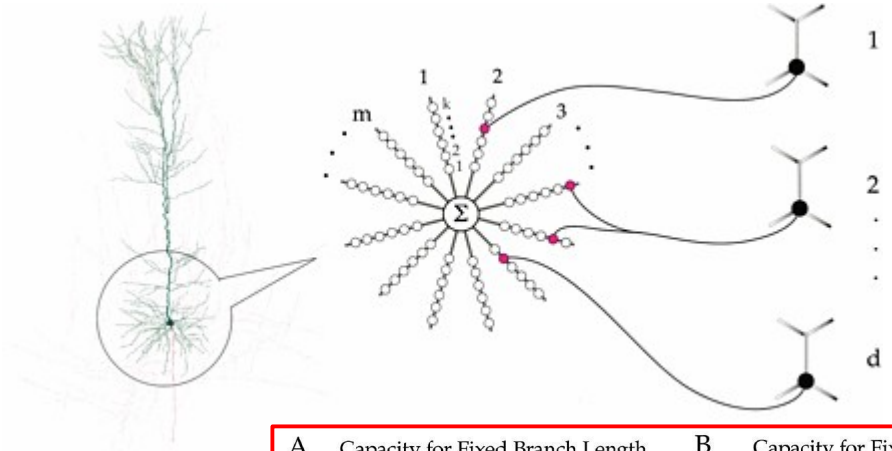




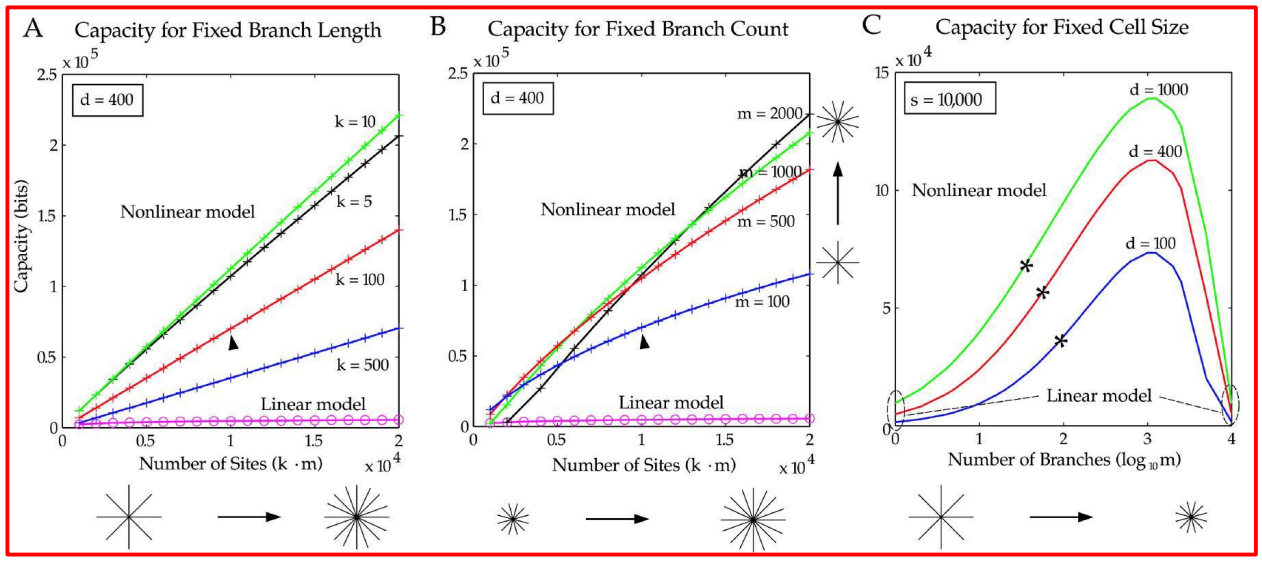
Detailed cell models: why?
II. Revealing computational functions (What it is good for?) / 2

What is the role of the dendrites?

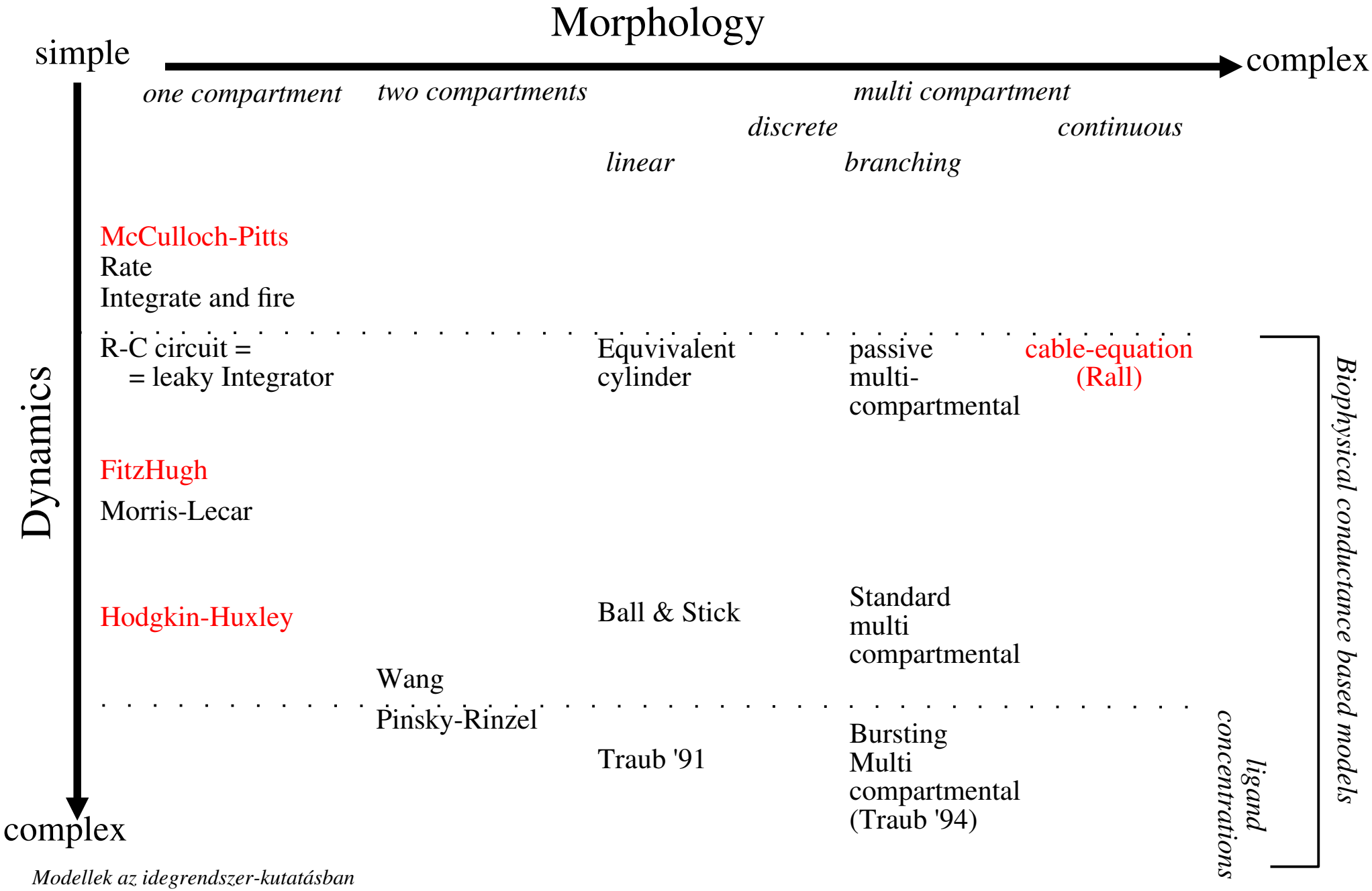
1. Common sense (Cook&Johston): amplification of distal synaptic effects
2. Mel: increasing storage capacity



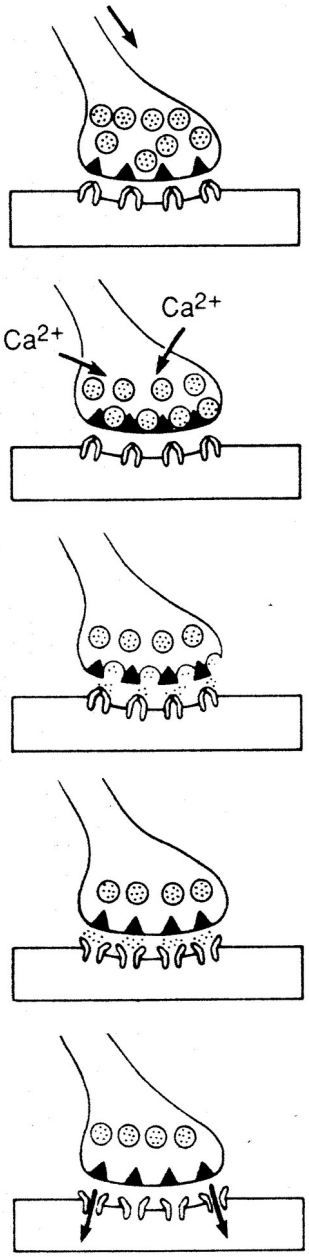
	Linear Cell	Nonlinear Cell
d_1 d_2 d_3 $d,m,k = 3$	$a_L(x)$	$a_N(x)$
Wiring Configurations ①	$4x_1 + 3x_2 + 2x_3$	$b(2x_1 + x_2) + b(2x_1 + x_2) + b(x_2 + 2x_3)$
Wiring Configurations ②	$4x_1 + 3x_2 + 2x_3$	$b(2x_1 + x_3) + b(x_1 + 2x_2) + b(x_1 + x_2 + x_3)$
Total number of distinct i/o functions	110	220



2D taxonomy of single cell modells



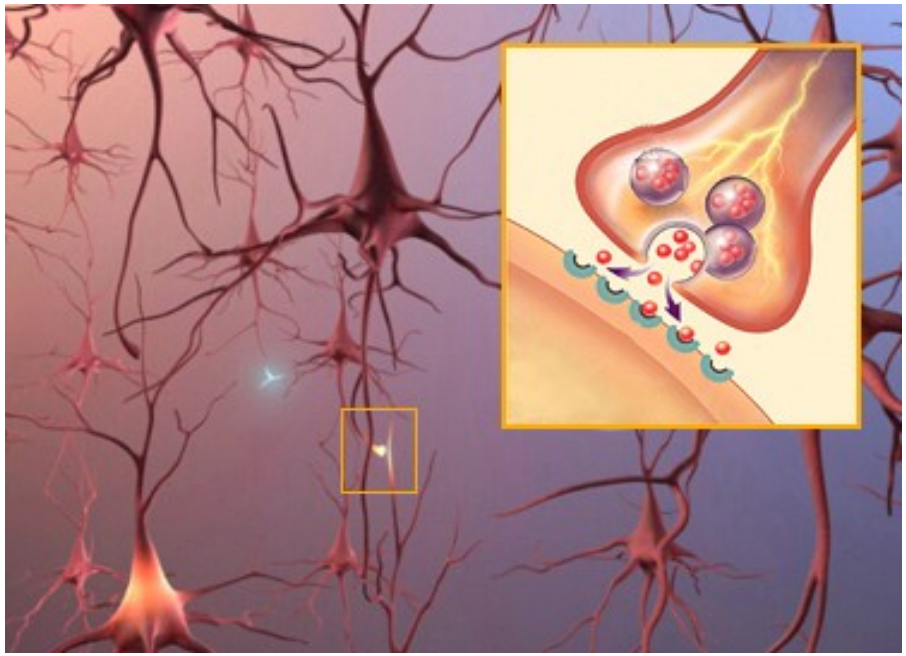
Synaptic models

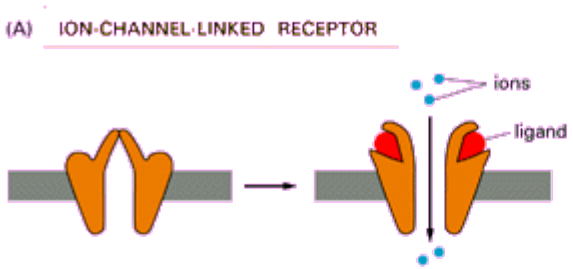


1. presynaptic action potential
2. Ca^{2+} influx
3. transmitter release from the vesicles
4. transmitter-receptor binding
5. postsynaptic conductance ("PSG"), current (PSC) and potential changes (PSP)

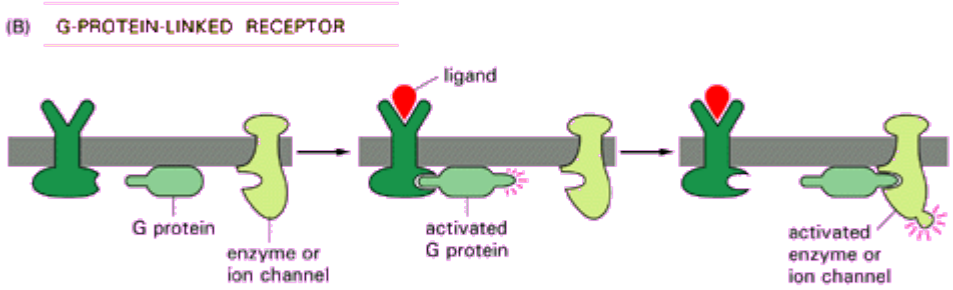
The aim synaptic models:
To calculate the postsynaptic potential changes, based on the presynaptic activity.

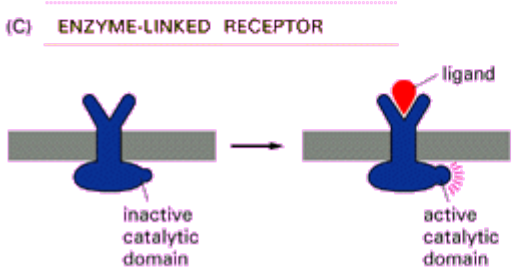
Between two neuron: The synapse

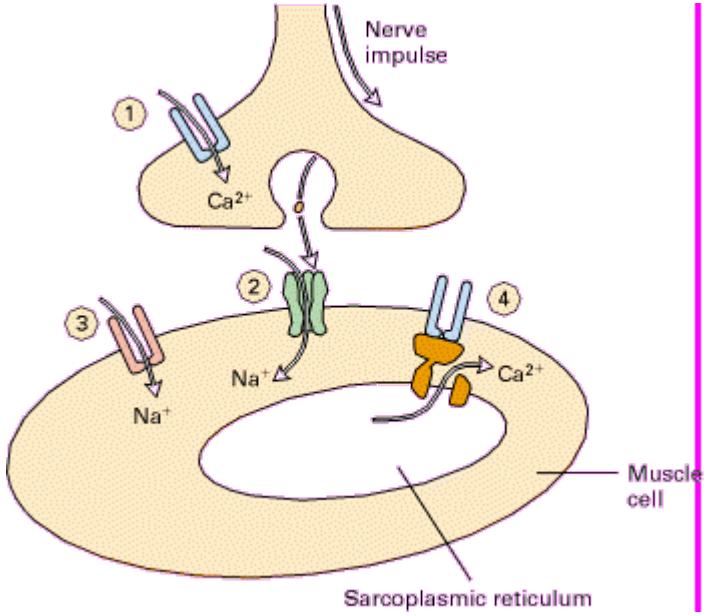




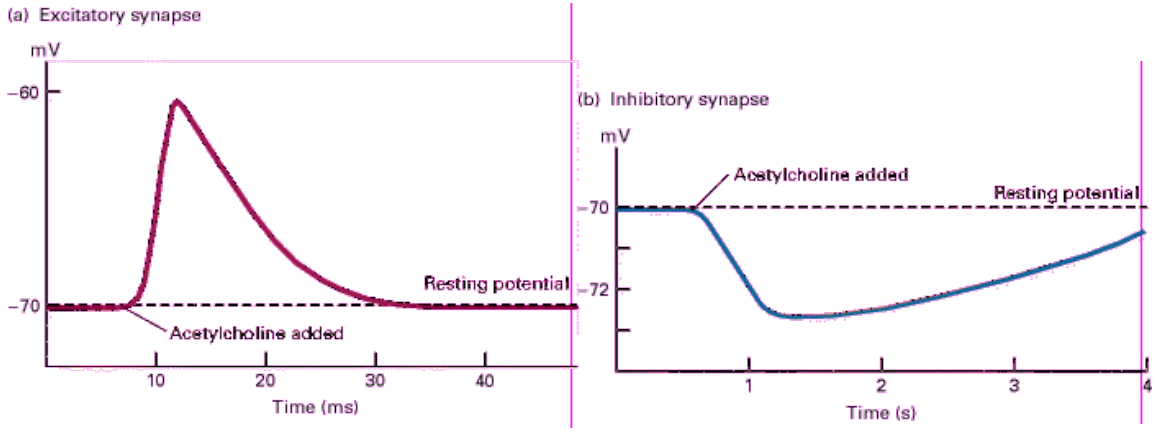
Ionotrophic (A) and metabotrophic (B,C) receptors





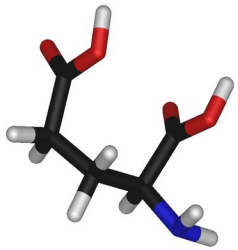


Excitatory and inhibitory postsynaptic potentials

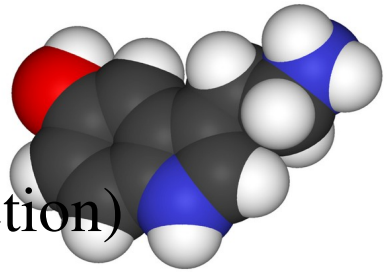


Excitatory and inhibitory neurotransmitters

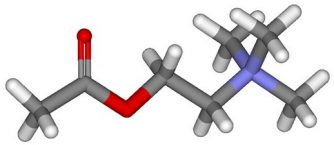
Glutamat
(information transmission)



Serotonin
(mood, wake/sleep)

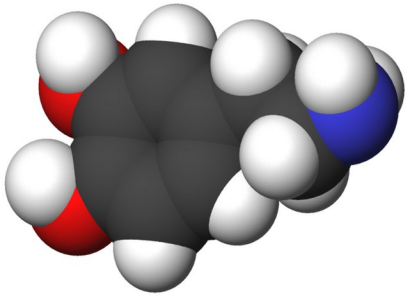


Acetlicholin
(neuromuscular junction)

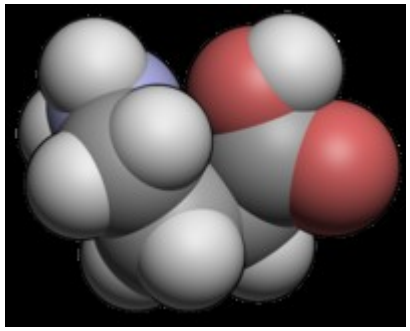


Noradneraline
(arousal)

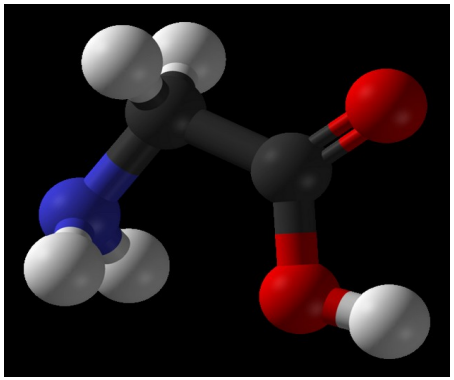
Dopamine
(reward system,
Parkinson disease,
schizophrenia)



GABA-gamma aminobutyric acid
(in the central neural system)

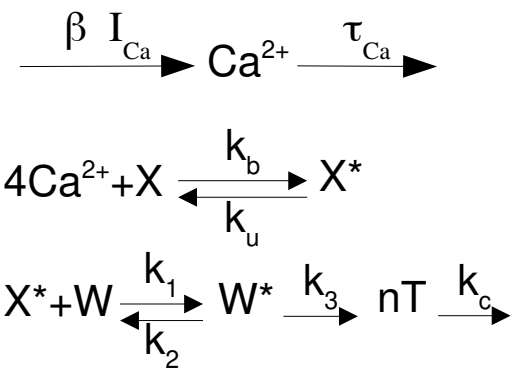


Glycine
(in the periphery)



Detailed kinetic synaptic models: the presynaptic side (1-3.)

kinetic schema (example)



Ca^{2+}	intracellular calcium
X,X*	protein, activated protein
W,W*	vesicle, activated vesicle
T	transmitter

Reminder:

$$I_{Ca}(t) = \bar{g}_{Ca}\, s(t)\left(E_{Ca} - V_{pre}(t)\right)$$

$$\frac{ds}{dt} = \frac{s_\infty\left(V_{pre}(t)\right) - s(t)}{\tau_s\left(V_{pre}(t)\right)}$$

$$\frac{d\left[Ca^{2+}\right]}{dt} = \beta\, I_{Ca}(t) - \frac{\left[Ca^{2+}\right](t)}{\tau_{Ca}} - 4k_b\left[Ca^{2+}\right](t)\,X(t) + 4k_u X^*(t)$$

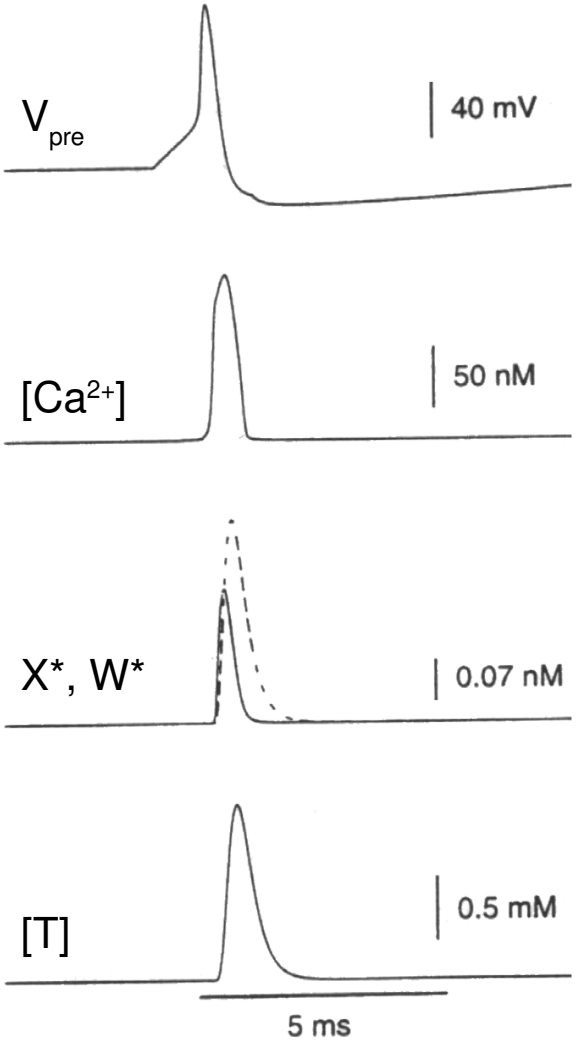
$$\frac{dX}{dt} = -k_b\left[Ca^{2+}\right](t)\,X(t) + k_u X^*(t)$$

$$\frac{dX^*}{dt} = k_b\left[Ca^{2+}\right](t)\,X(t) - k_u X^*(t) - k_1 X^*(t)\,W(t) + k_2 W^*(t)$$

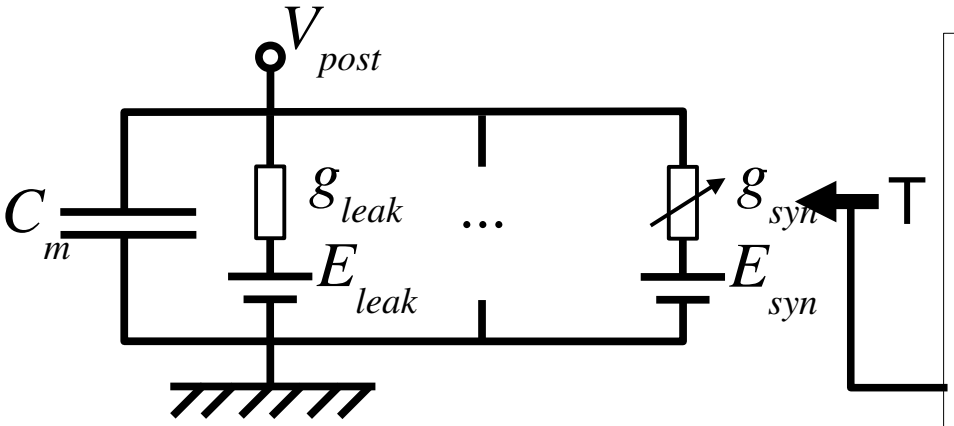
$$\frac{dW}{dt} = -k_1 X^*(t)\,W(t) + k_2 W^*(t)$$

$$\frac{dW^*}{dt} = k_1 X^*(t)\,W(t) - k_2 W^*(t) - k_3 W^*(t)$$

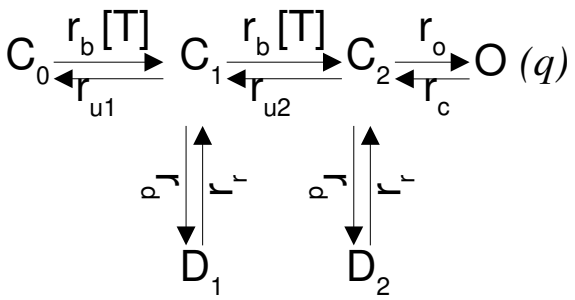
$$\frac{d\left[T\right]}{dt} = k_3 n\, W^*(t) - k_c\left[T\right](t)$$



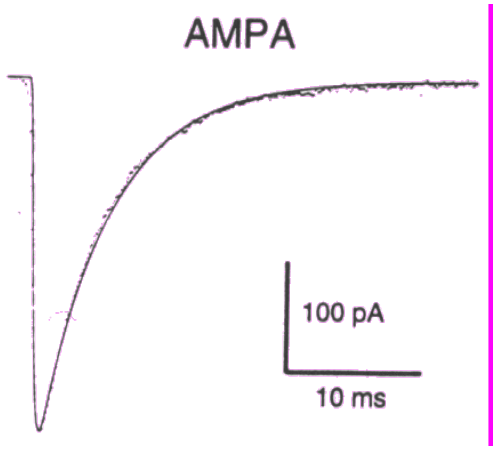
Detailed kinetic synaptic models: the postsynaptic side (4-5.)



kientic schema (example)



T transmitter
C closed receptor
D desensitized receptor
O open receptor



Reminder:

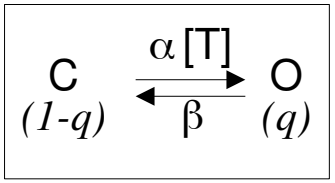
$$I_{syn}(t) = \bar{g}_{syn}\, q(t) \left(E_{syn} - V_{post}(t) \right)$$

Simplified kinetic synaptic models

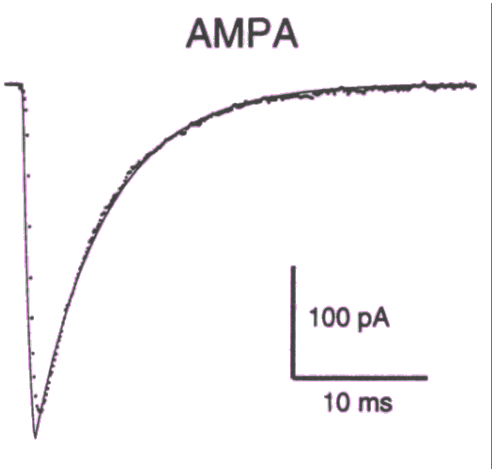
presynaptic side

$$[T]\left(V_{pre}(t)\right) = \frac{T_{max}}{1 + e^{-\frac{V_{pre}(t) - V_{\Theta}}{K_{\Theta}}}}$$

postsynaptic side



$$\frac{dq}{dt} = \alpha [T](t) \left(1 - q(t)\right) - \beta\, q(t)$$

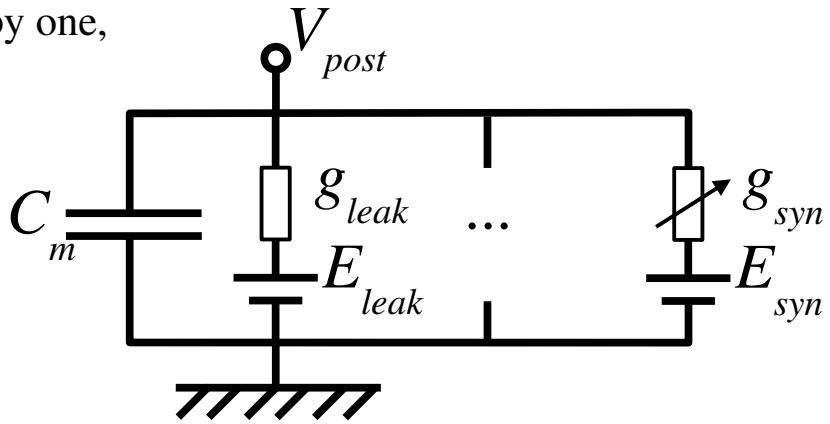


Phemomeological synaptic models

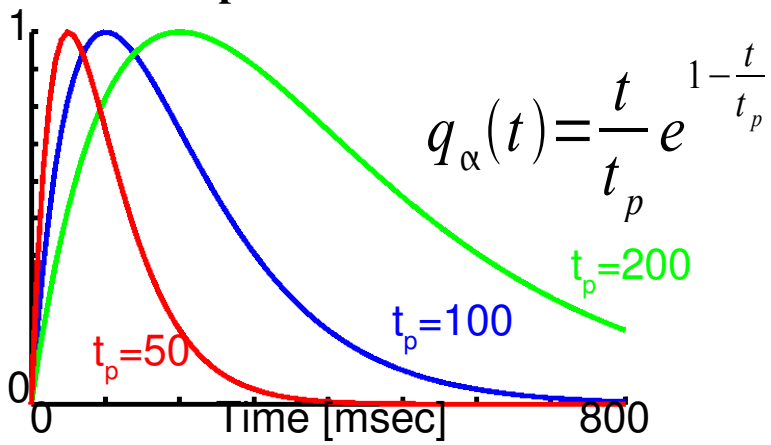
The postsynaptic conductance change, caused by one, single presynaptic action potential

$$I_{syn}(t) = \bar{g}_{syn}\left(E_{syn} - V_{post}(t)\right)\int_0^t \Delta\left(V_{pre}(t_0) - V_\Theta\right)\cdot q(t-t_0)\,dt_0$$

Linear summation of the individual conductance changes
(convolution by Dirac-delta function)

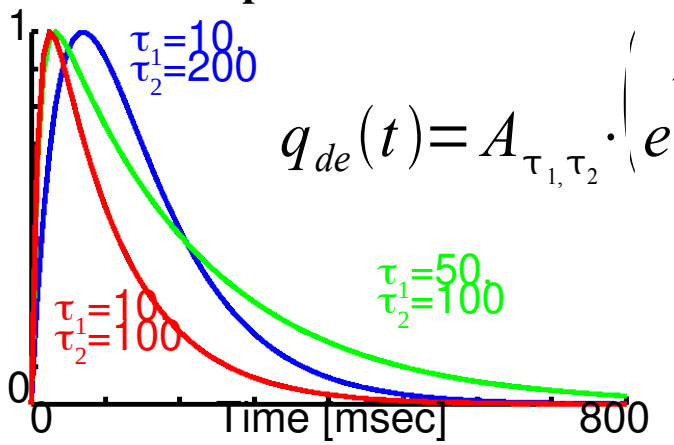


alpha-function



$$q_\alpha(t) = \frac{t}{t_p}e^{1-\frac{t}{t_p}}$$

double exponential function



$$q_{de}(t) = A_{\tau_1,\tau_2}\cdot\left(e^{-\frac{t}{\tau_2}} - e^{-\frac{t}{\tau_1}}\right)$$

Synaptic models: summary

		detailed	simplified	phenomenological
Number of variables	presynaptic	**>=5**	**0**	**0**
	postsynaptic	**~5**	**1**	
reproduced phenomena	senzitisation	**yes**	**no**	**no**
	desenzitisation	**yes**	**no**	**no**
	saturation (PSG, PSC)	**yes**	**no**	**no**
	saturation (PSP)	**yes**	**yes**	**no**