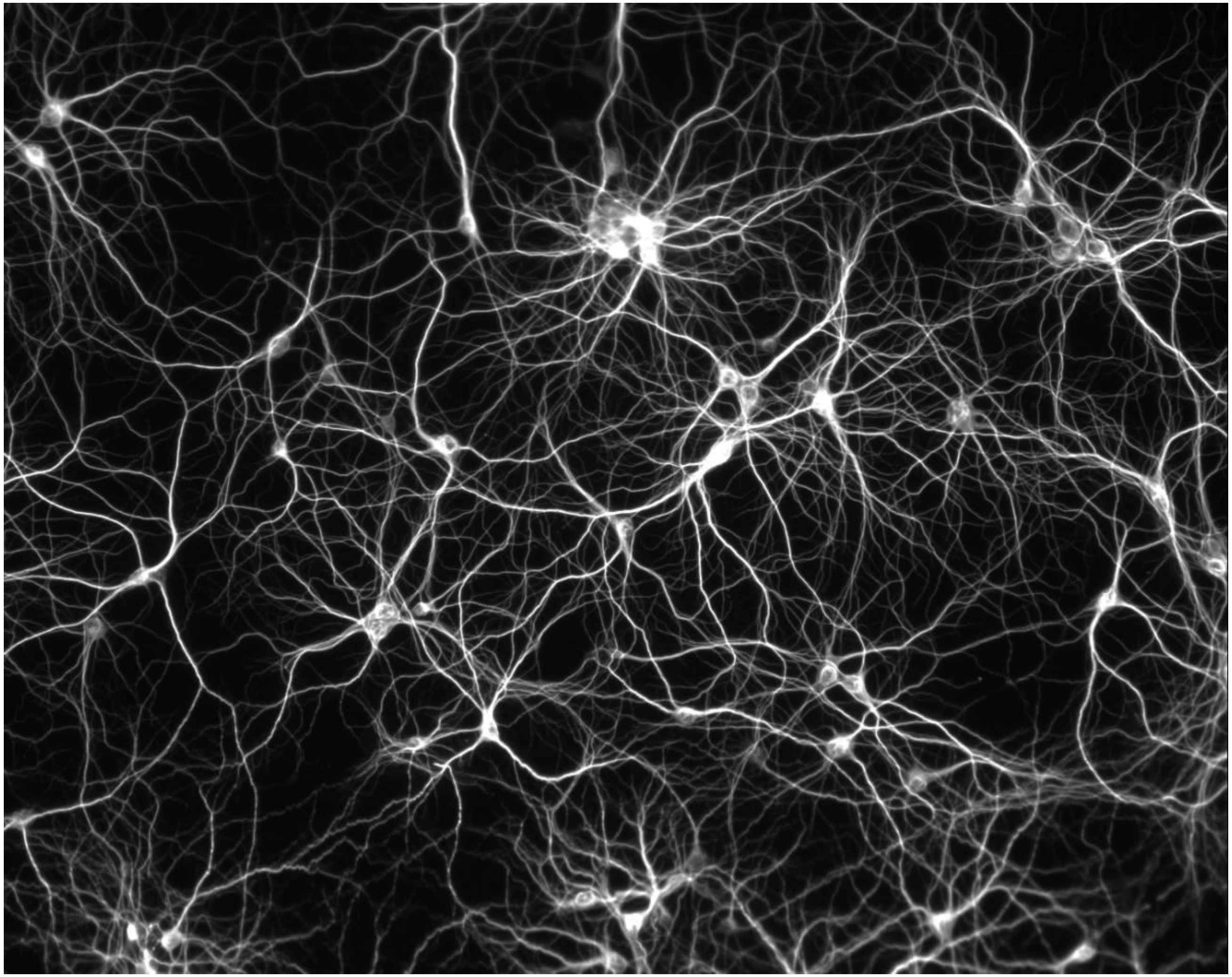
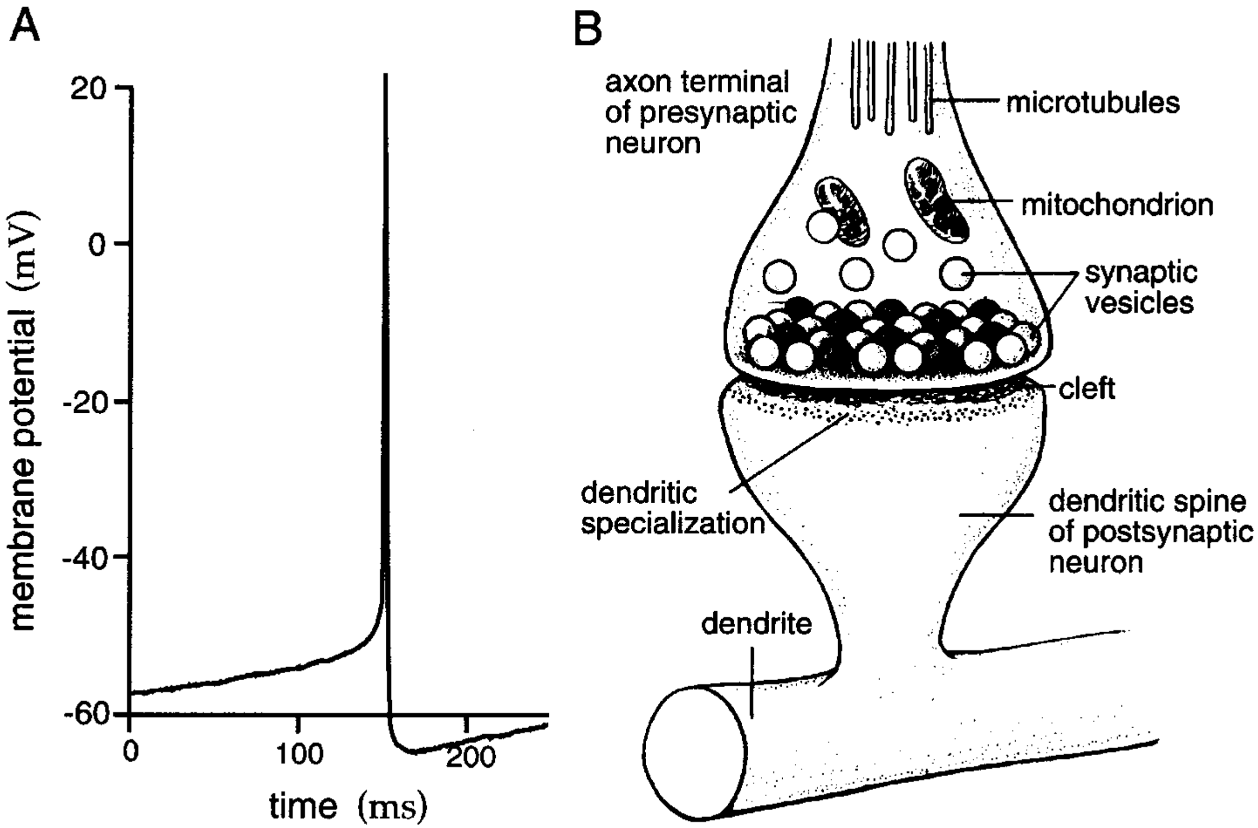
Recalling: neurons create circuits

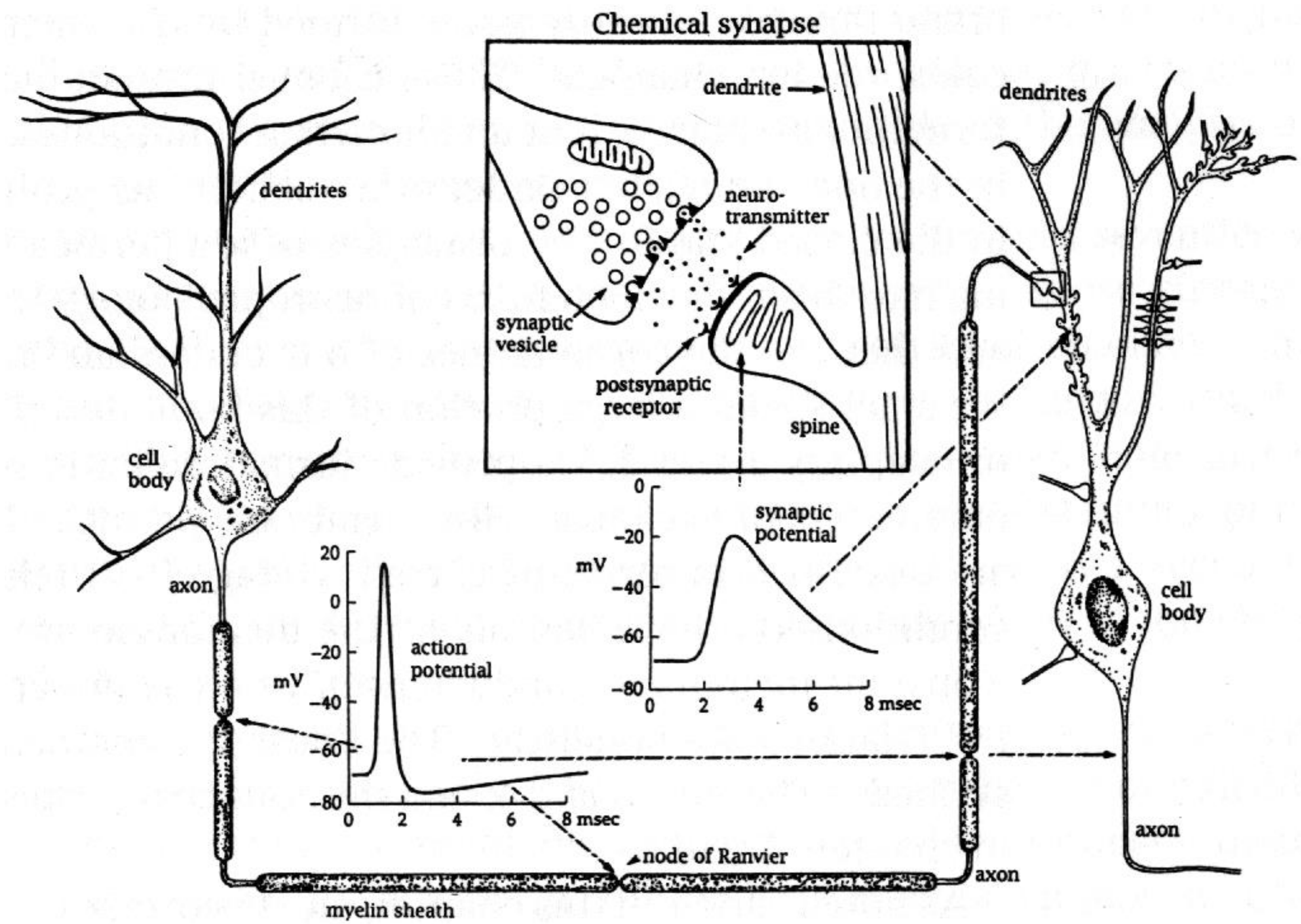


Synapses



Each action potential evokes neurotransmitter release at the axon

The effect of postsynaptic receptors at the arrival of neurotransmitters is the generation of a postsynaptic potential.



Synapse models:

General form for the synaptic current: $I_{syn}(t) = g_{syn}(t) \cdot (V(t) - E_{syn})$

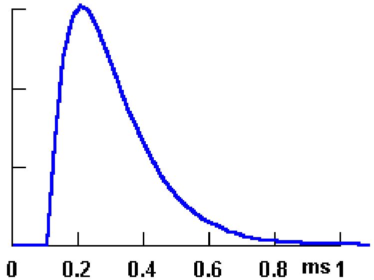
Models for the description of $g_{syn}(t)$:

- $g_{syn}(t) = g_{max} \cdot t \cdot e^{(1 - t/\tau)} / \tau$ (alpha function)

- $g_{syn}(t) = A \cdot g_{max} \cdot (e^{-t/\tau_1} - e^{-t/\tau_2}) / (\tau_1 - \tau_2)$, with $\tau_1 > \tau_2$

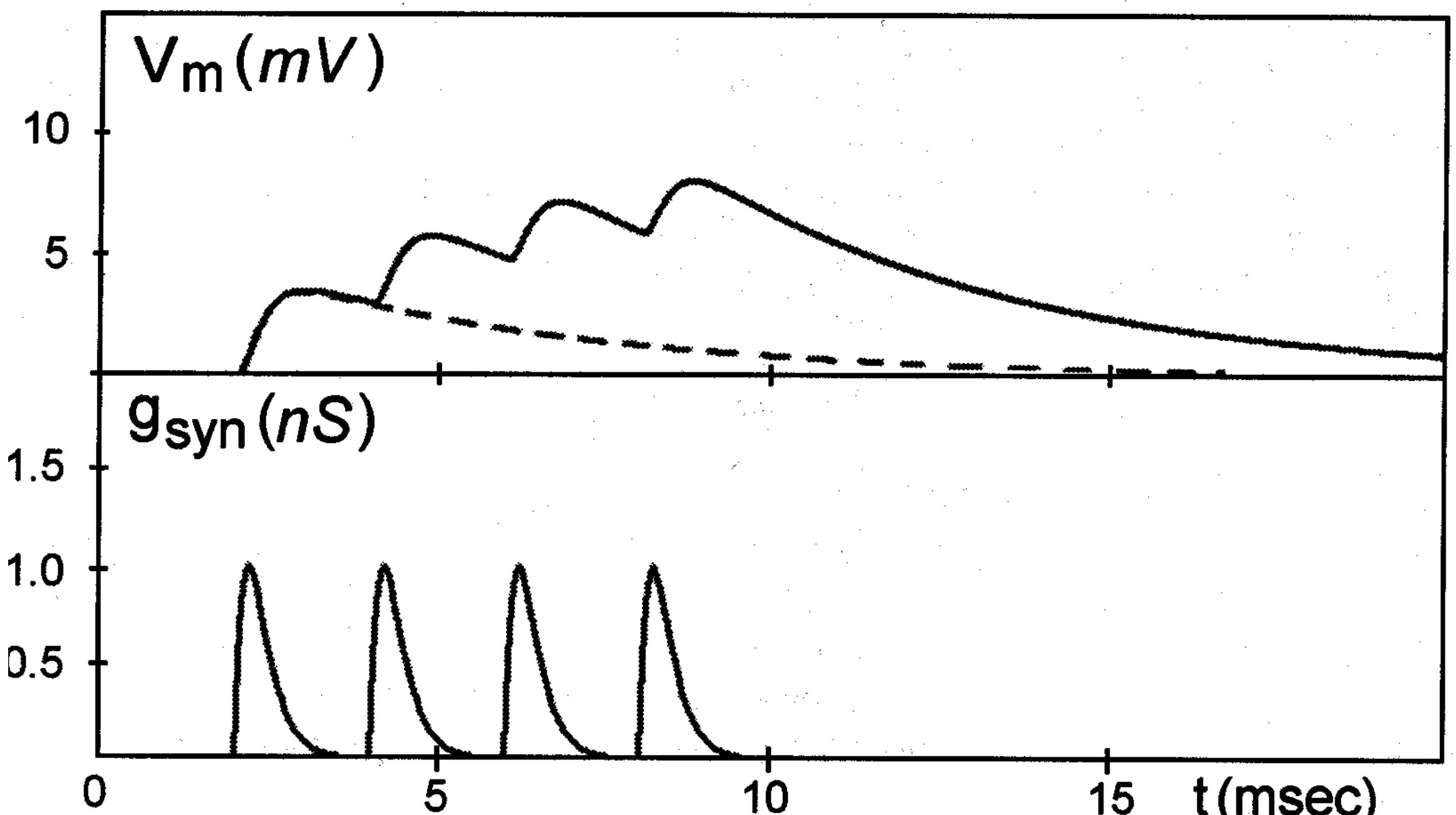
When $\tau_1 = \tau_2 \equiv \tau$ we recover the alpha function

A is a normalization constant so that $\max(g_{syn}(t)) = g_{max}$



A neuron can receive several synapses in a short period of time

$$C_m dV/dt + I_{ion} + g^{(1)}_{syn}(t)\cdot(V-E^{(1)}_{syn}) + g^{(2)}_{syn}(t)\cdot(V-E^{(2)}_{syn}) + \ldots = 0$$



Synapse models II:

The binding of neurotrasnsmitter moleculets T to the postsynaptic receptors can be described as:

$$R + T \underset{\beta}{\overset{\alpha}{\rightleftarrows}} TR^*$$

R represents the unbound postsynaptic receptor

TR* is the bound form of the postsynaptic receptor

α and β are the rate constants for the forward and backward transmitter binding.

If r represents the fraction of bound receptors and [T] the transmitter concentration, the kinetics can be described with the following ODE:

$$dr/dt = \alpha\,[T] \cdot (1-r) \; - \; \beta \cdot r$$

Destexhe et al. 1994

Modelos de sinapsis II:

$$dr/dt = \alpha\,[T] \cdot (1-r) \; - \; \beta \cdot r$$

If the transmitter concentration in the cleft rises and falls very rapidly, we can assume that [T] occurs as a pulse:

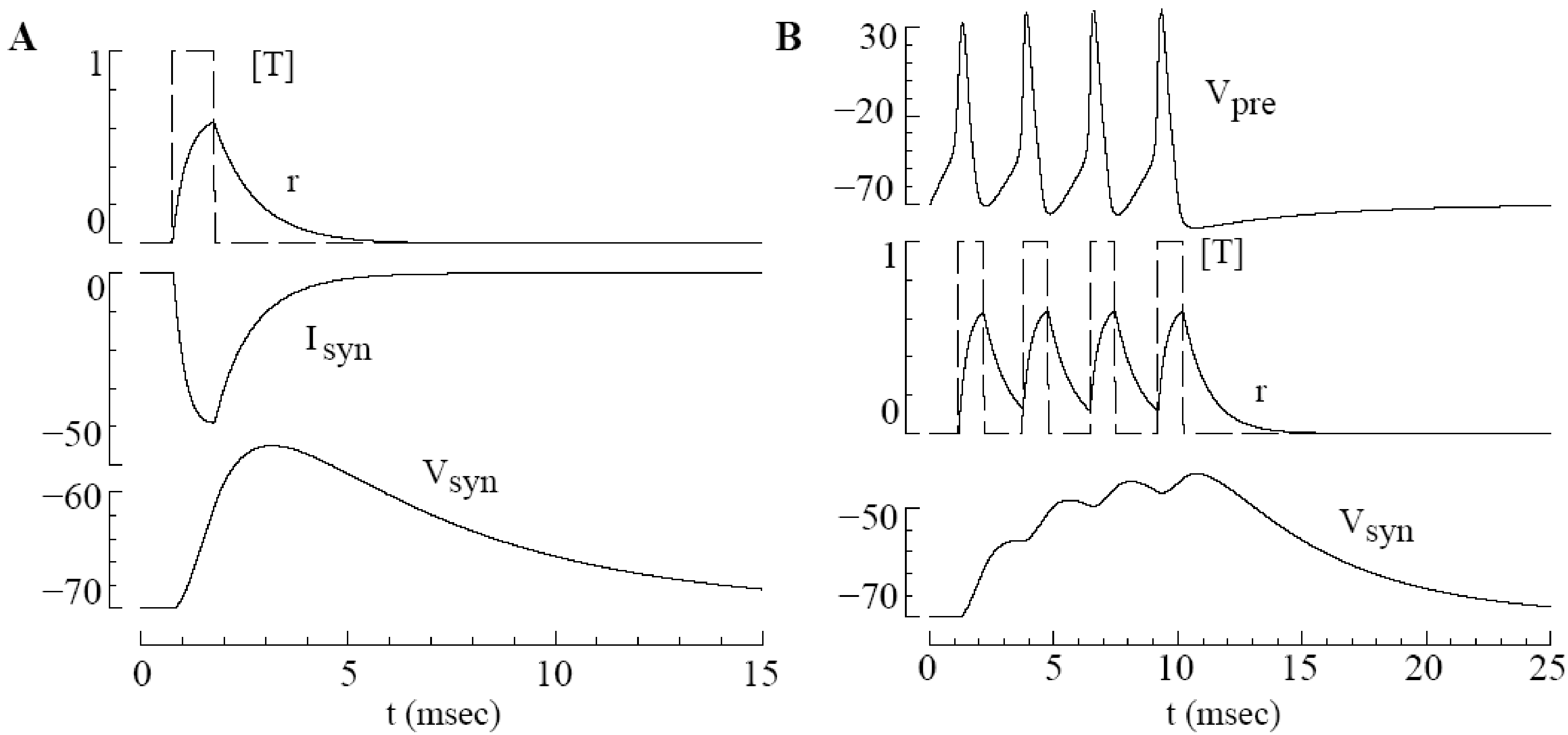
1- During the pulse ($t_0 < t < t_1$), $[T]=T_{max}$ and $r(t-t_0) = r_\infty + (r(t_0)-r_\infty)\cdot exp[-(t-t_0)/\tau_r]$

where $r_\infty = \alpha T_{max} / (\alpha T_{max} + \beta)$ and $\tau_r = 1 / (\alpha T_{max} + \beta)$

2- After the pulse ($t>t_1$), $[T]=0$ and $r(t-t_1) = r(t_1)\cdot exp[-\beta(t-t_1)]$

and the synaptic current can be written as: $I_{syn}(t) = g_{syn}\, r(t)\, [V_{syn}(t)-E_{syn}]$

Excitatory synapses:

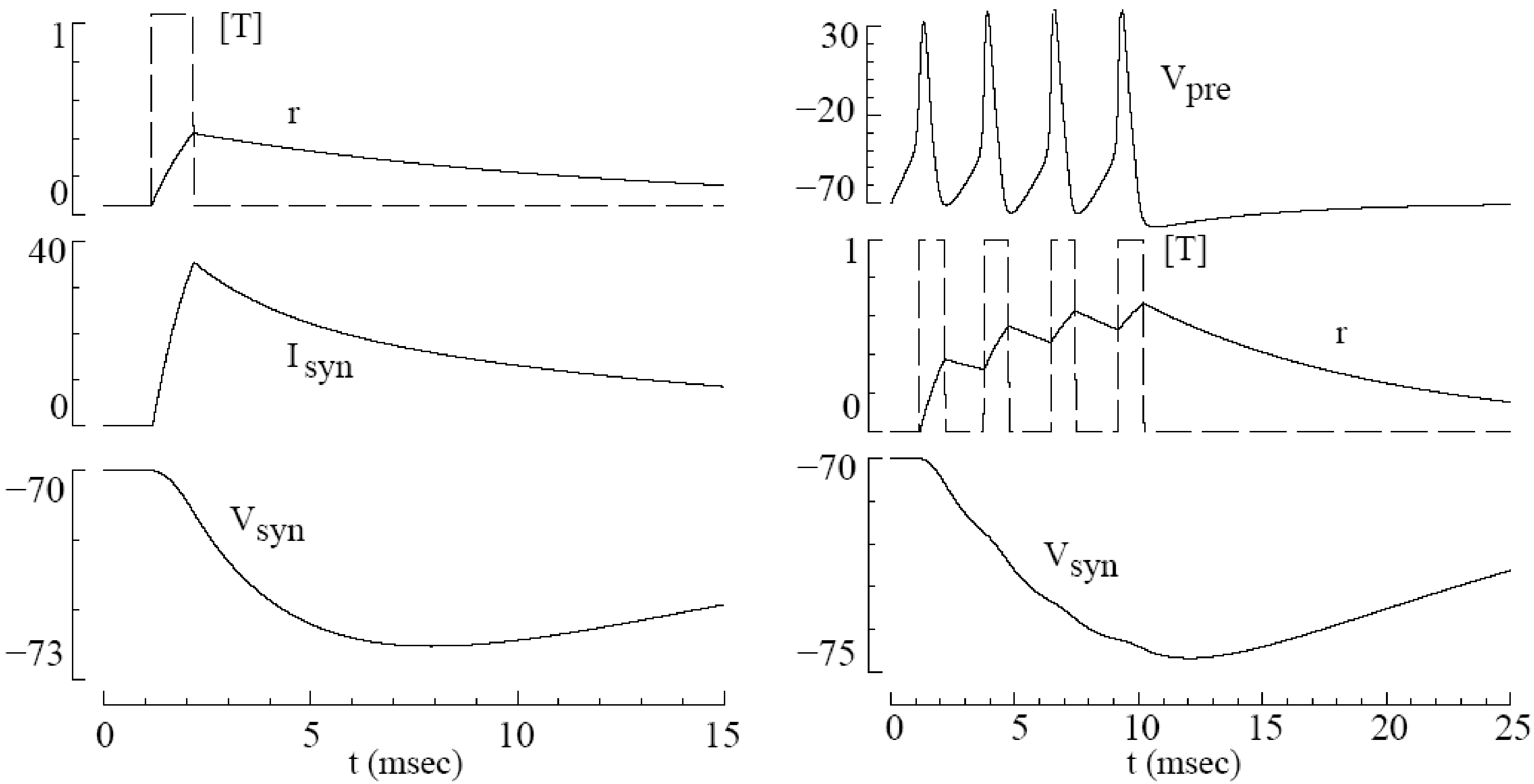


$\alpha = 2\ ms^{-1} mM^{-1}$ $\quad \bar{g}_{syn} = 1\ nS,\ T_{max} = 1\ mM$

$\beta = 1\ ms^{-1},\ E_{syn} = 0\ mV$ $\quad (t_1 - t_0) = 1\ msec$

Destexhe et al. 1994

Inhibitory synapses:



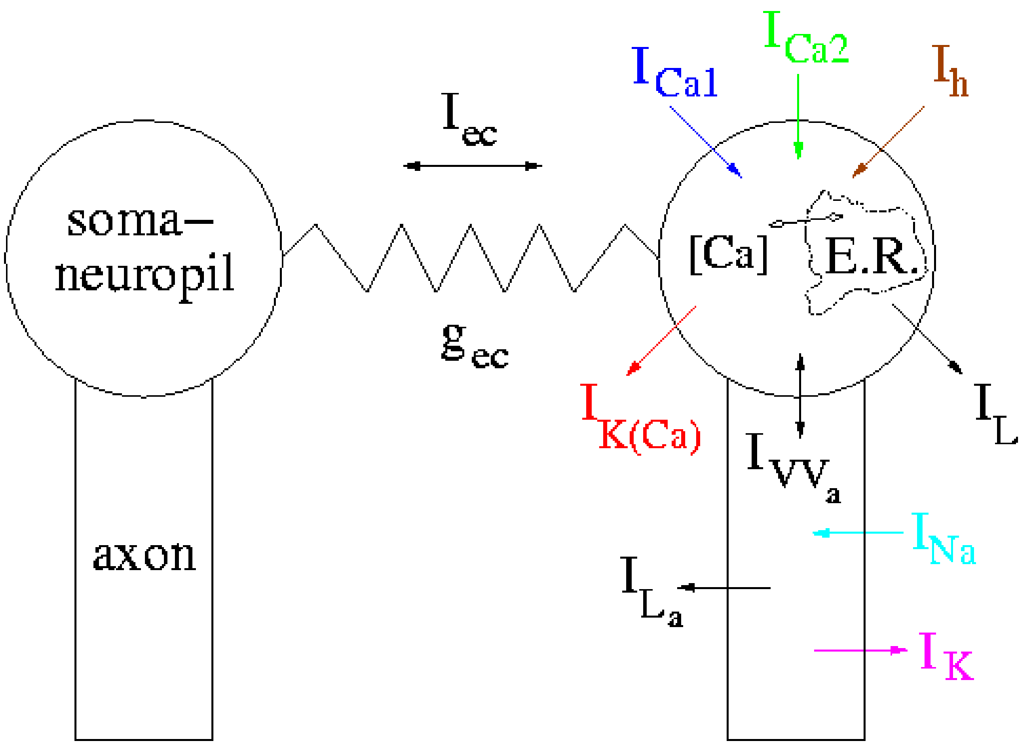
$\alpha = 0.5\ ms^{-1} mM^{-1}$, $\beta = 0.1\ ms^{-1}$, $E_{syn} =$ -80 mV

Destexhe et al. 1994 $\quad \bar{g}_{syn} = 1\ nS$, $T_{max} = 1\ mM \qquad (t_1 - t_0) = 1\ msec$

Electrical synapses or *gap junctions*

- They can be rectifying or symmetric:

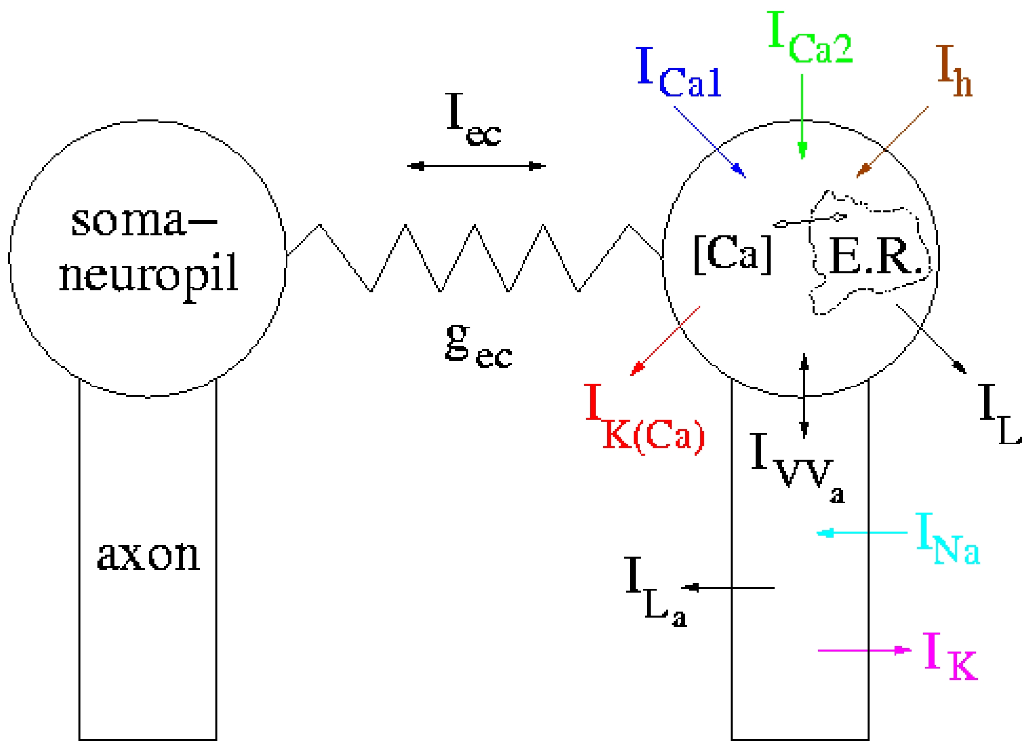
$$\mathbf{I_{ec} = g_{ec}\,(V_1\text{-}V_2)}$$



Electrical synapses or *gap junctions*

- In some synapses the coupling conductance depends on the voltage:

$$g_{ec} = g\ f(V)$$



Graded synapses

These synapses release neurotransmitters even before the action potential:

$$I_{syn}(t) = g_{syn} S(t)(V_{rev} - x_{post}(t))$$

$$\tau \frac{dS(t)}{dt} = \frac{S_\infty(x(t)) - S(t)}{S_0 - S_\infty(x(t))}$$

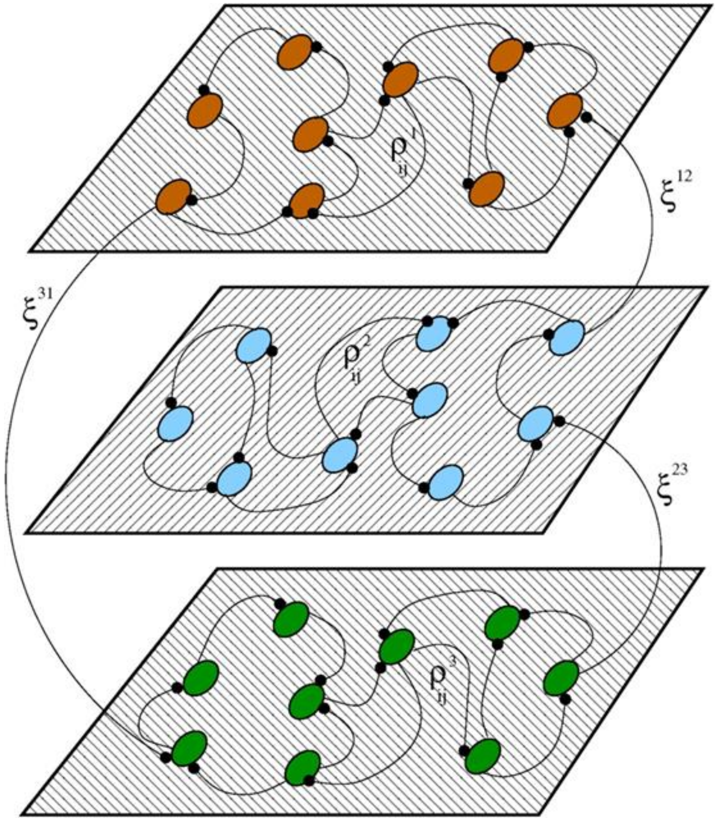
$$S_\infty(x) = \begin{cases} \tanh[(x - V_{th})/V_{slope}] & \text{if } V_{pre} > V_{th} \\ 0 & \text{if } V_{pre} \leq V_{th} \end{cases}$$

where x (V_{pre}) is the postsynaptic potential

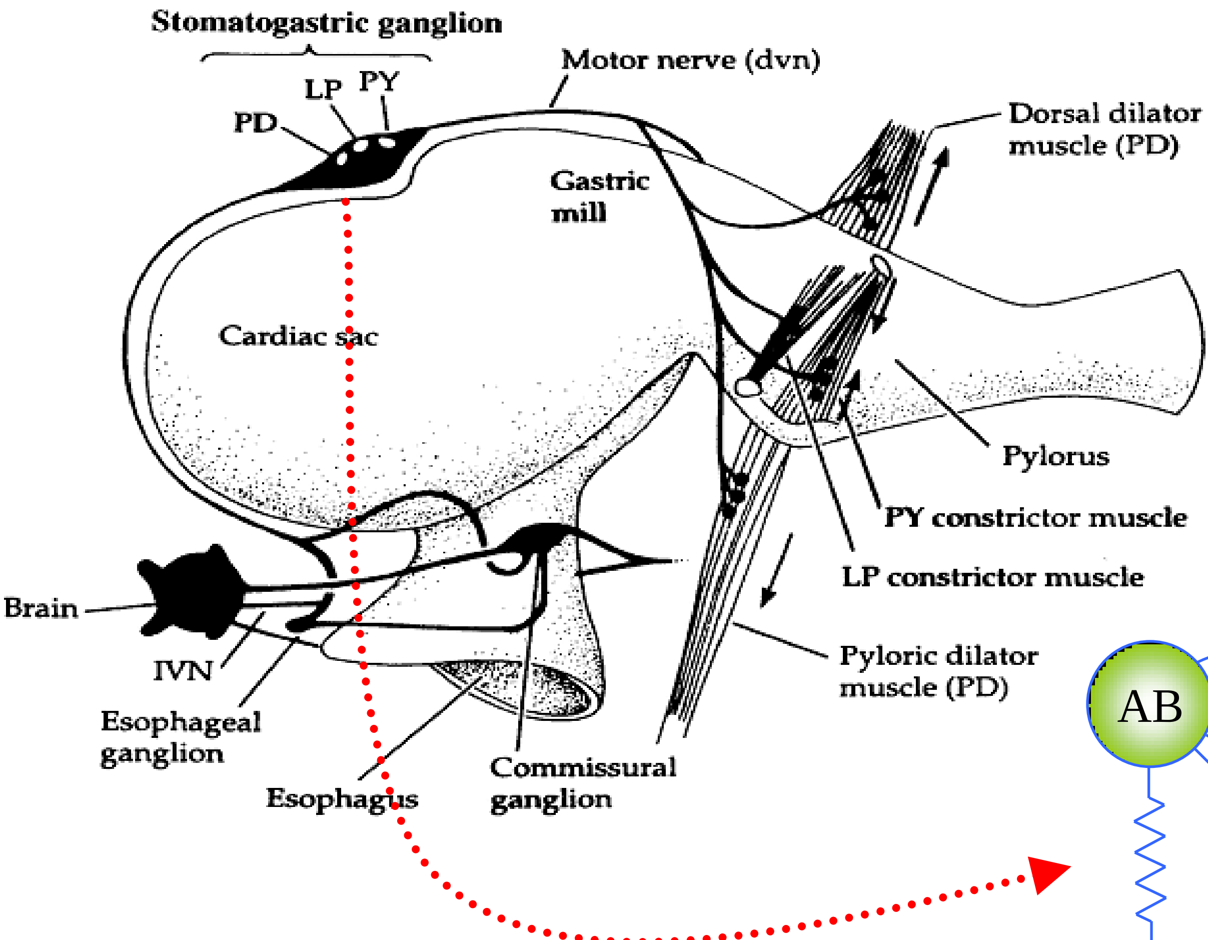
Synapses in simplified models

$$\dot{a}_i \quad = \quad a_i(\sigma(\boldsymbol{H}, \boldsymbol{S}) - \sum_{j=1}^{N} \rho_{ij} a_j + H_i(t)) + S_i(t)$$

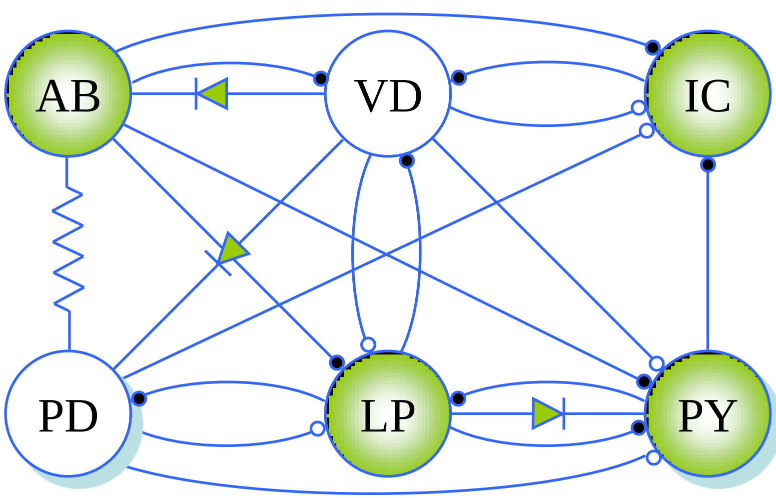
$$\tau_i \frac{dx_i^m}{dt} = x_i^m \left(\sigma_i^m - \sum_{j=1}^{N} \rho_{ij}^m x_j^m - \sum_{k=1}^{M} \sum_{j=1}^{N} \xi_{ij}^{mk} x_j^k \right), \quad i, j = 1, \ldots, N; \; m, k = 1, \ldots, M$$



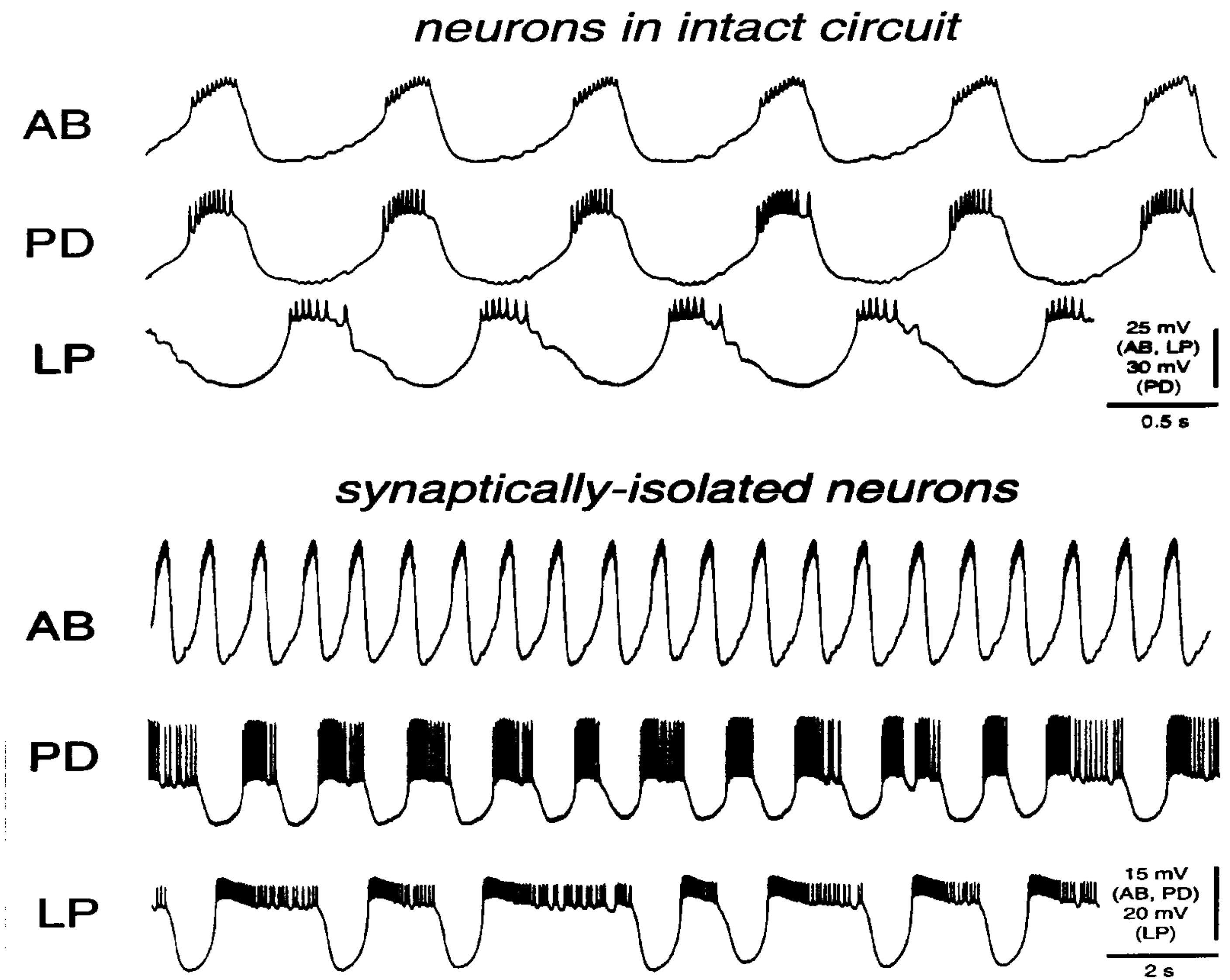
Example: model of a central pattern generator (CPG)



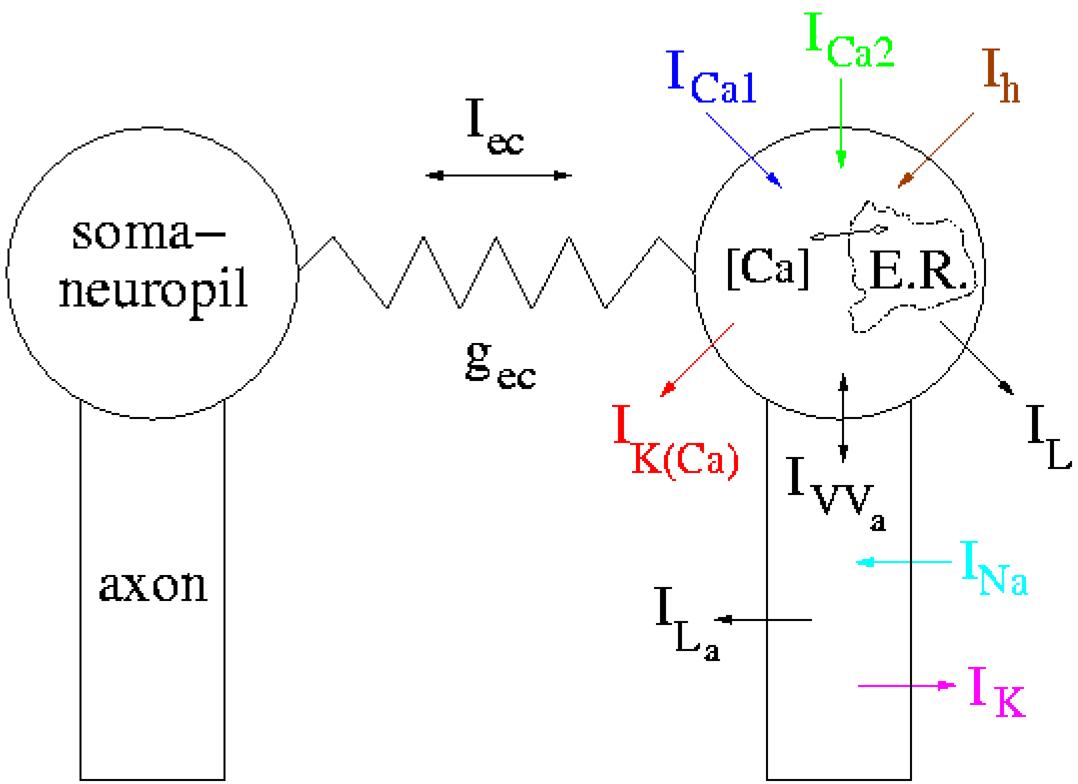
Pyloric CPG



El CPG produces periodic and precise rhythms in spite that the isolated neurons are highly irregular

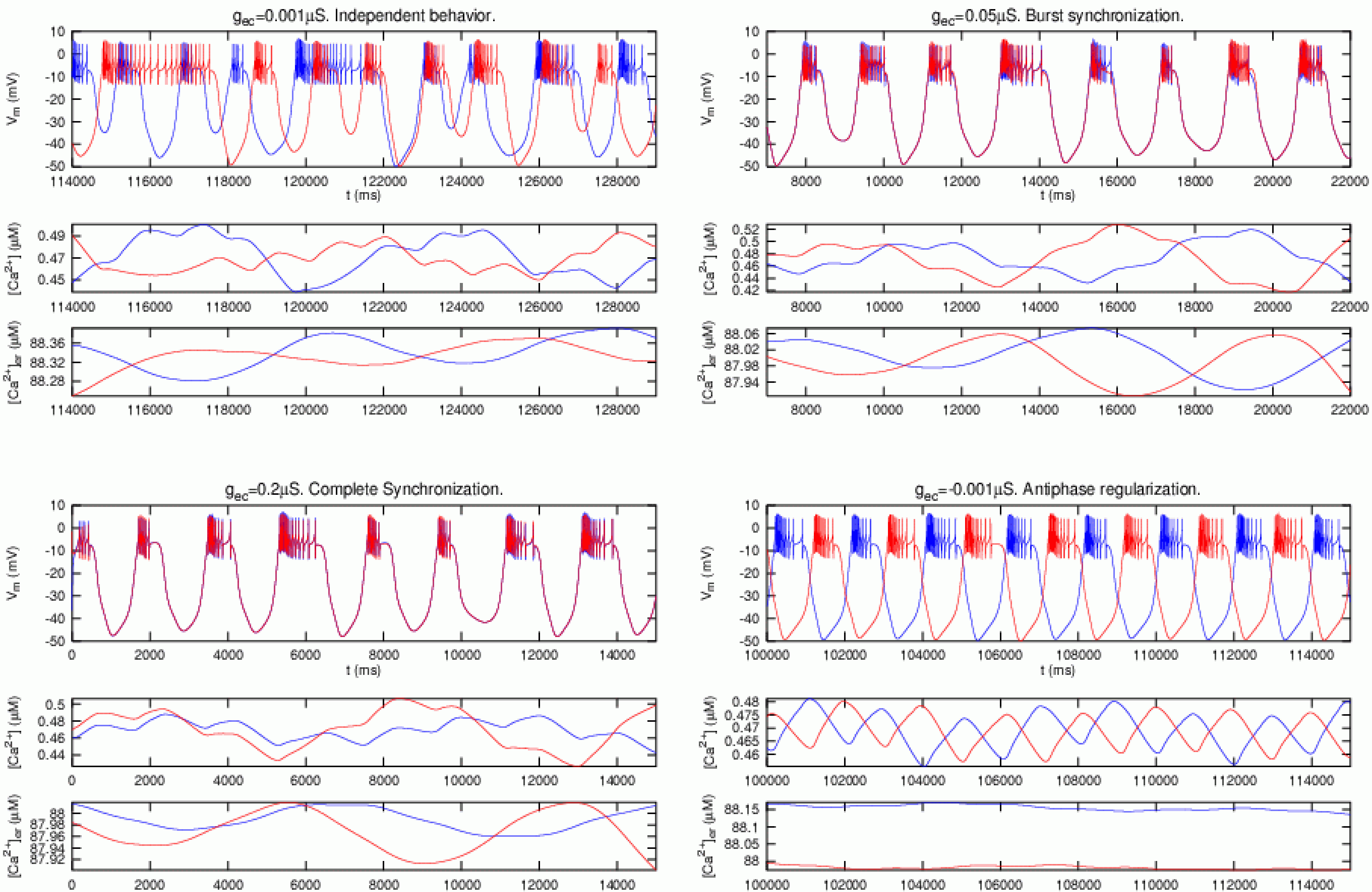


H-H model of pyloric neurons

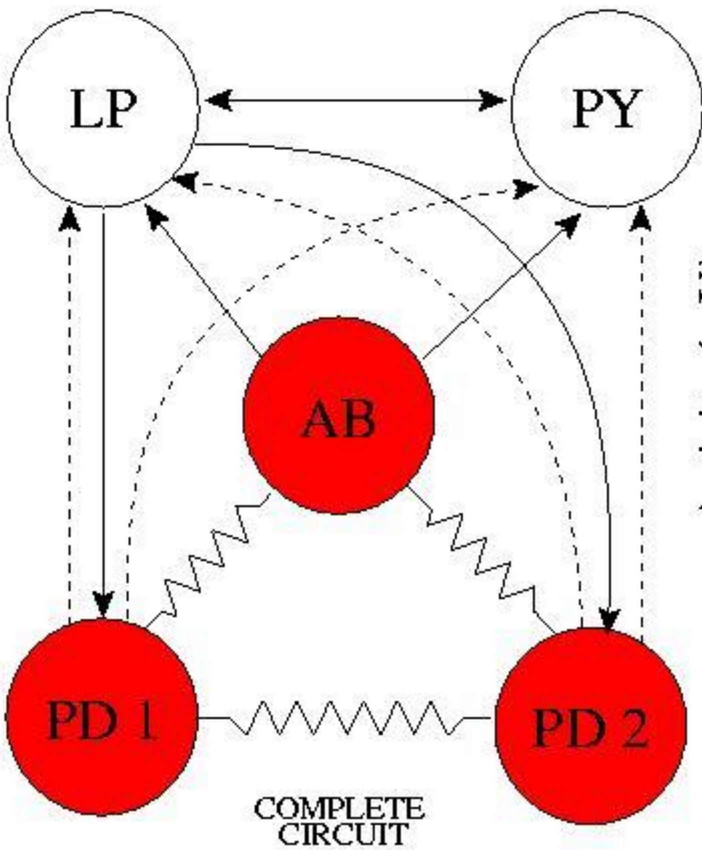


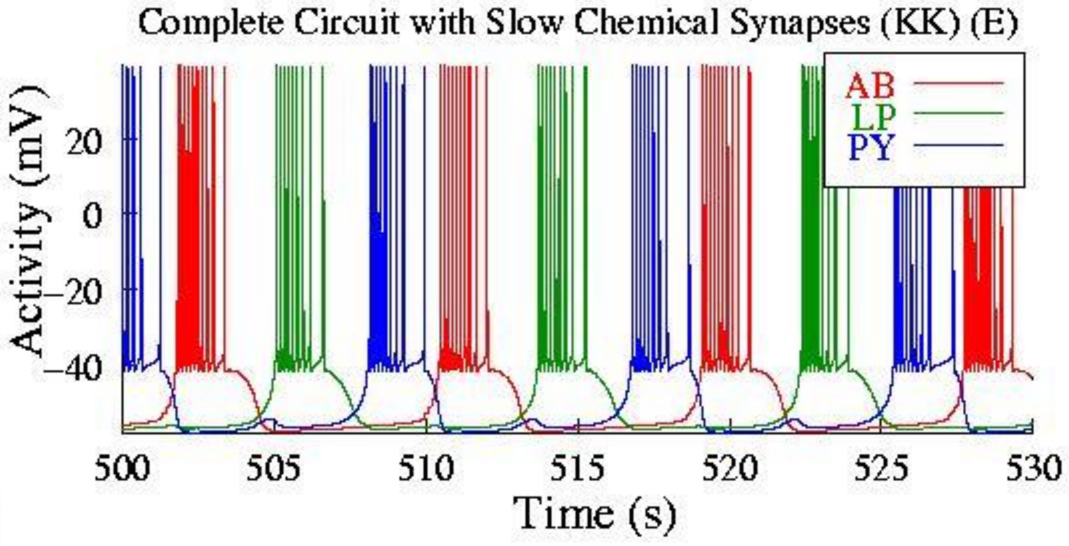
P. Varona, J.J. Torres, R. Huerta, H.D.I. Abarbanel, M.I. Rabinovich. 2001. Regularization mechanisms of spiking-bursting neurons. *Neural Networks*, 14: 865-875.

Two STG model neurons coupled ellectrically



Modelo de CPG

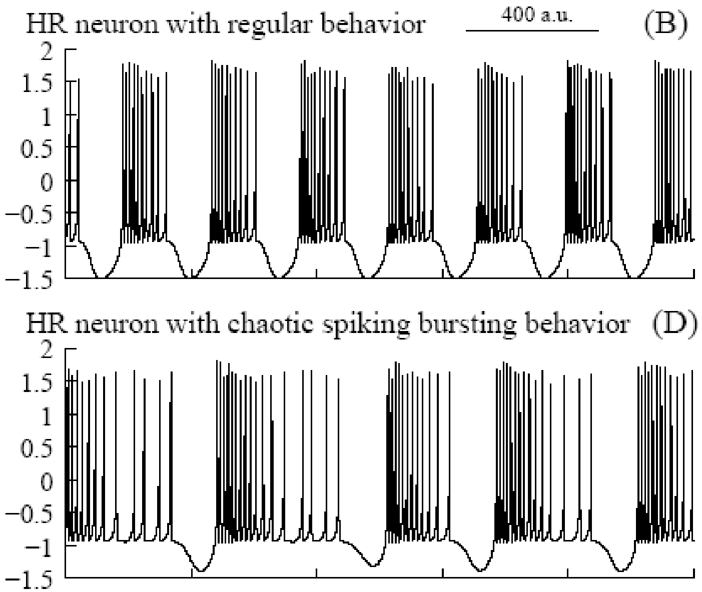




Hindmarsh-Rose model

$$\frac{dx_i(t)}{dt} = y_i(t) + 3x_i^2(t) - x_i^3(t) - z_i(t) + e_i$$

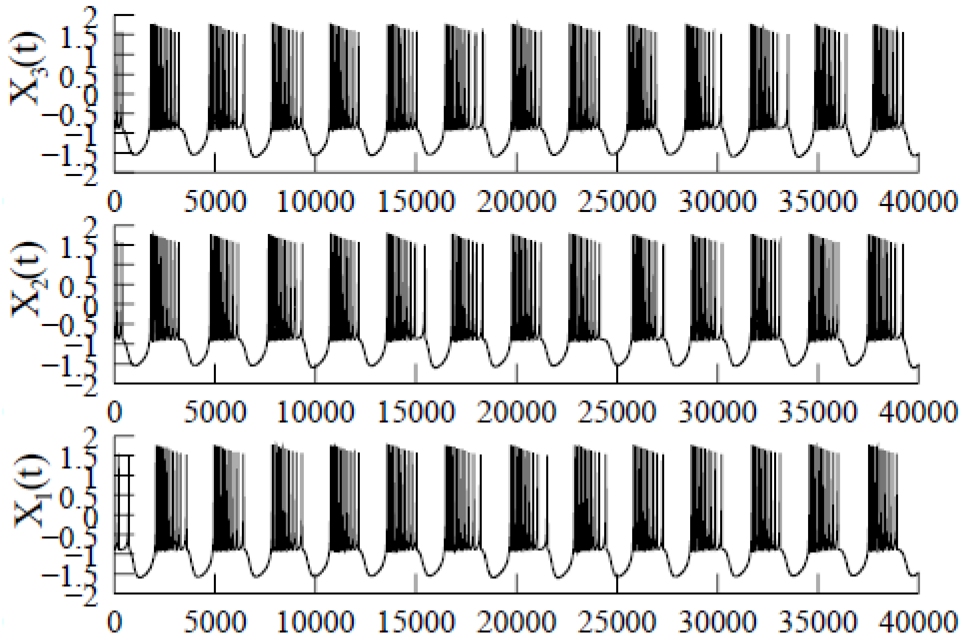
$$\frac{dy_i(t)}{dt} = 1 - 5x_i^2(t) - y_i(t), \qquad \frac{1}{\mu}\frac{dz_i(t)}{dt} = -z_i(t) + S\left[x_i(t) + 1.6\right],$$



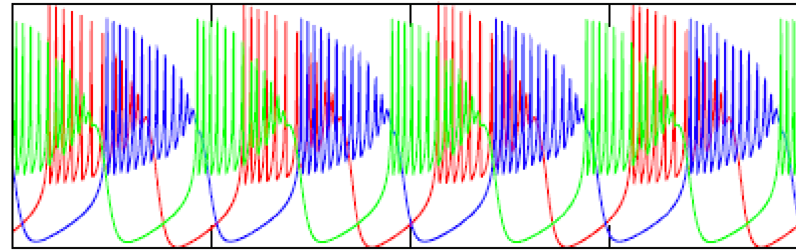
Electrically coupled Hindmarsh-Rose neurons

$$\frac{dx_i(t)}{dt} = y_i(t) + 3x_i^2(t) - x_i^3(t) - z_i(t) + e_i - \sum_{j \neq i} g_{ij}(x_i(t) - x_j(t))$$

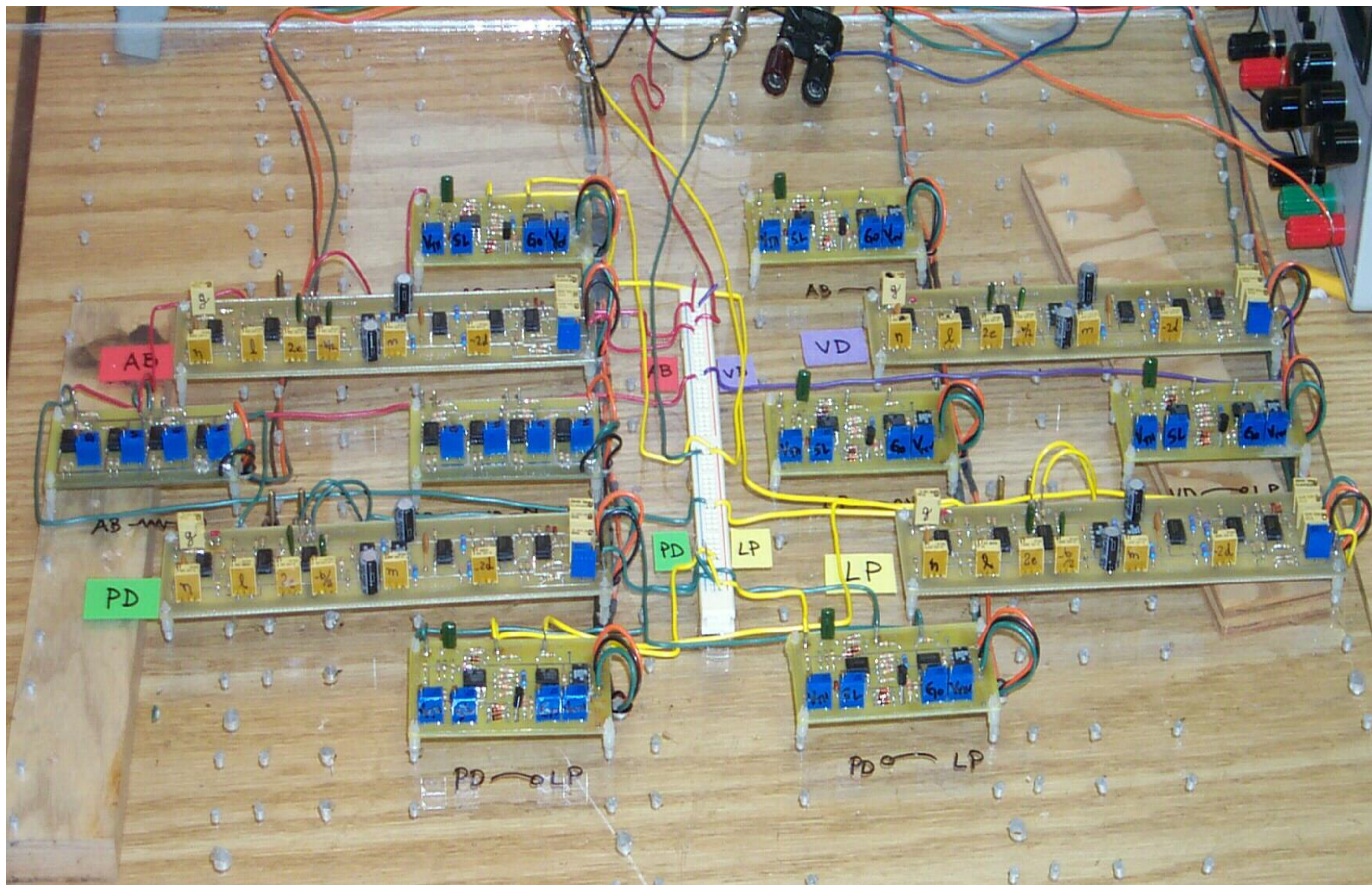
$$\frac{dy_i(t)}{dt} = 1 - 5x_i^2(t) - y_i(t), \qquad \frac{1}{\mu}\frac{dz_i(t)}{dt} = -z_i(t) + S\left[x_i(t) + 1.6\right]$$



F.B. Rodríguez, P. Varona, R. Huerta, M.I. Rabinovich, H.D.I. Abarbanel. 2001. Richer network dynamics of intrinsically non-regular neurons measured through mutual information. *Lect. Notes Comput. Sc.*, 2084: 490-497.



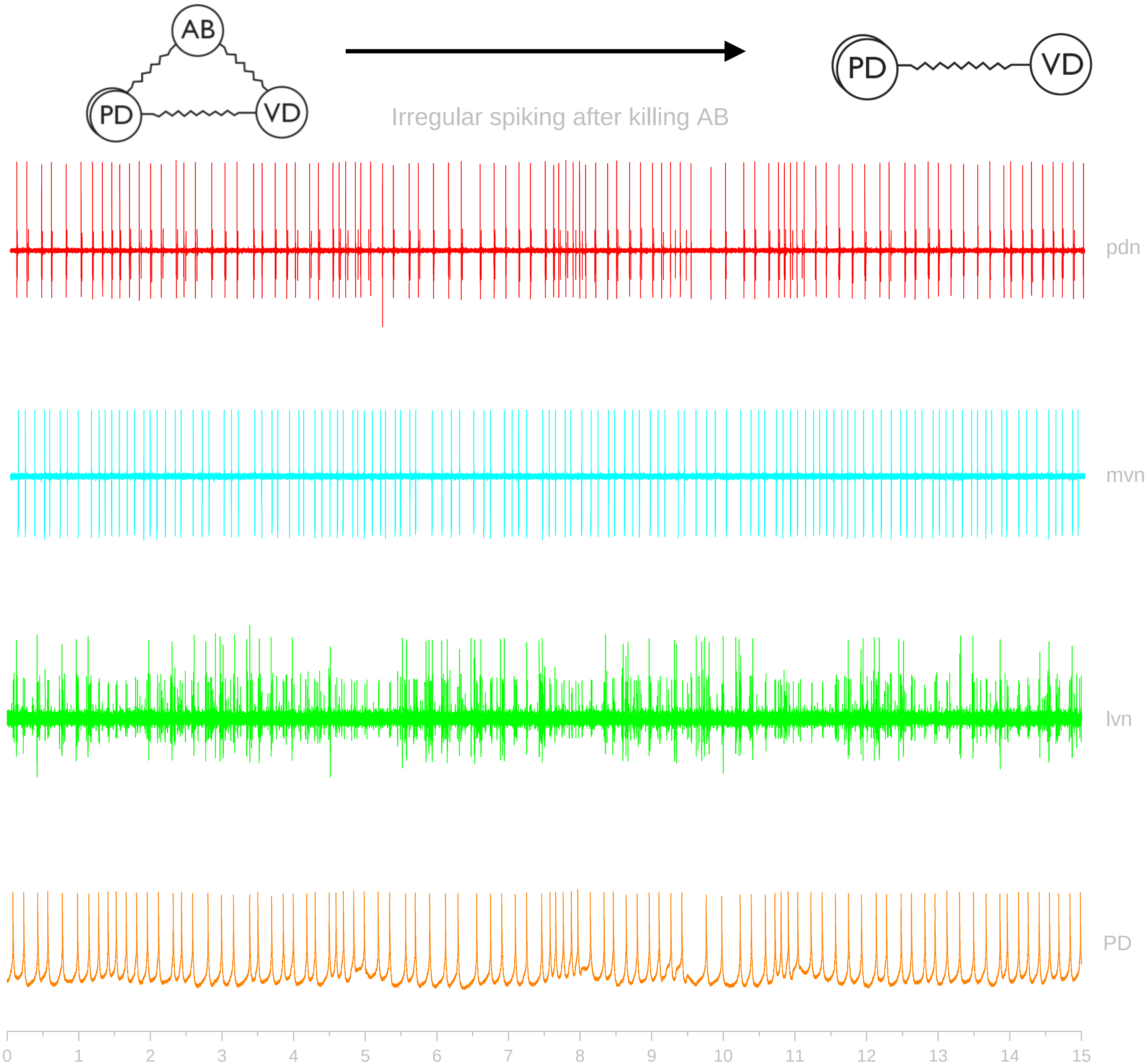
Artificial Syapses

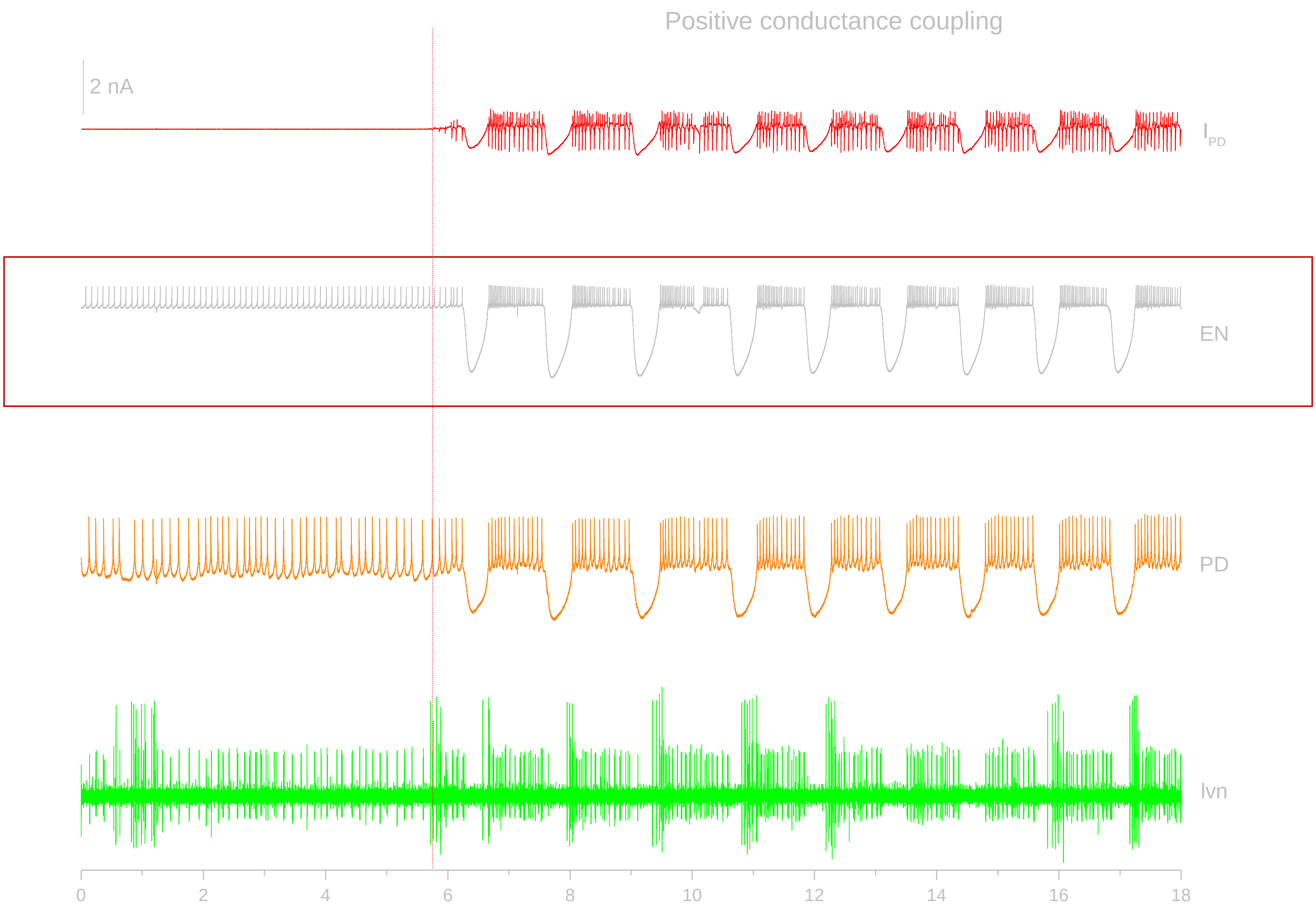


Pyloric CPG implemented with electronic neurons

(H-R model)

Damaged biological circuit: one neuron was killed

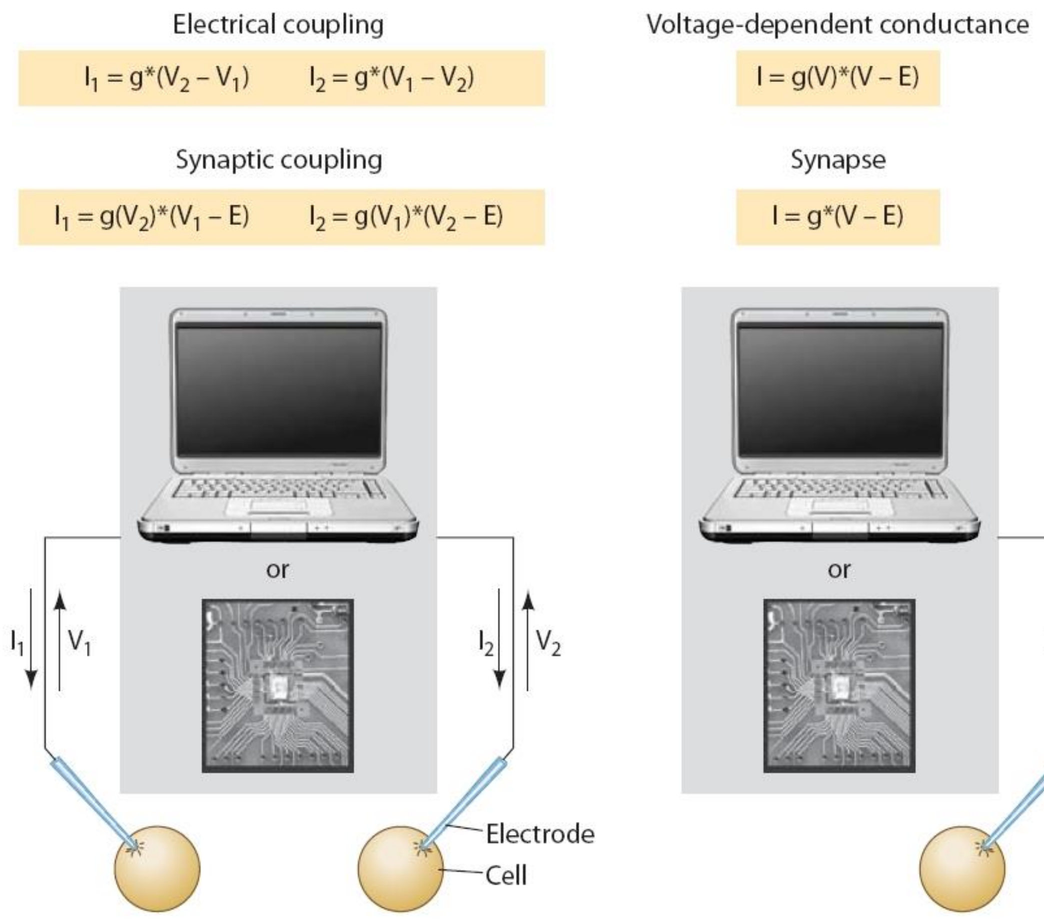




Hybrid circuit where an artificial neuron recovers the rhythm

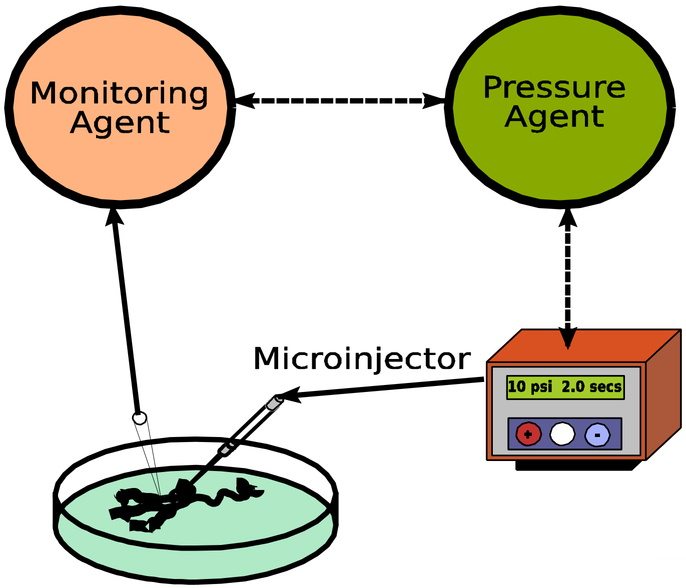
Dynamic Clamp
(Robinson ’91, Sharp et al. ’93)

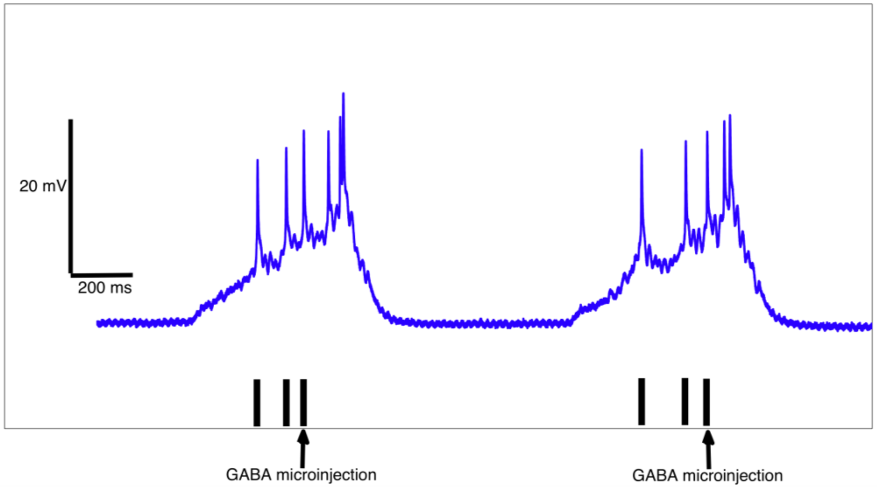
Activity-dependent stimulation has been previously exploited to build dynamic clamp protocols in electrophysiological preparations



From Goaillard, Marder (2006)

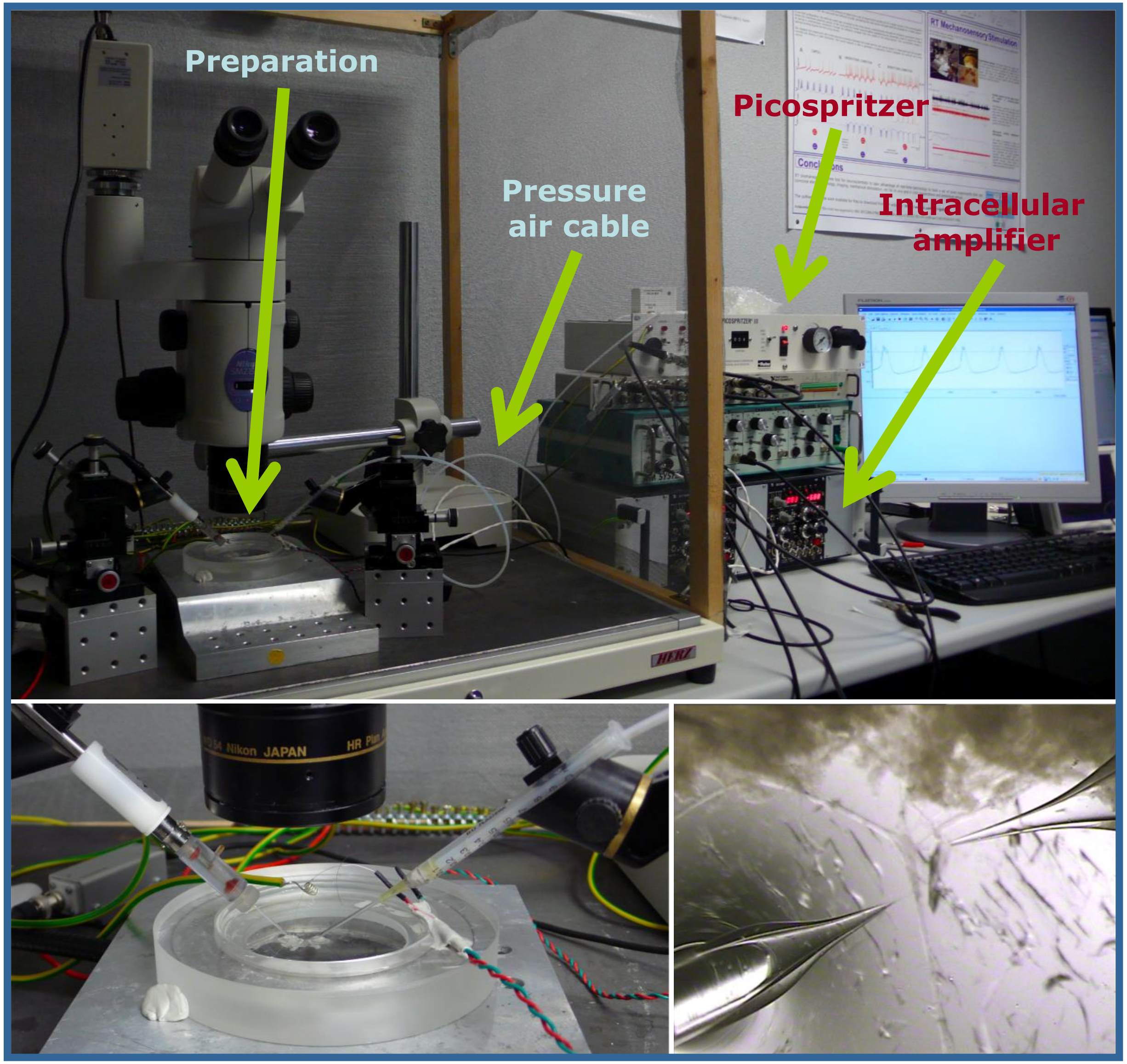
Activity-dependent drug microinjection



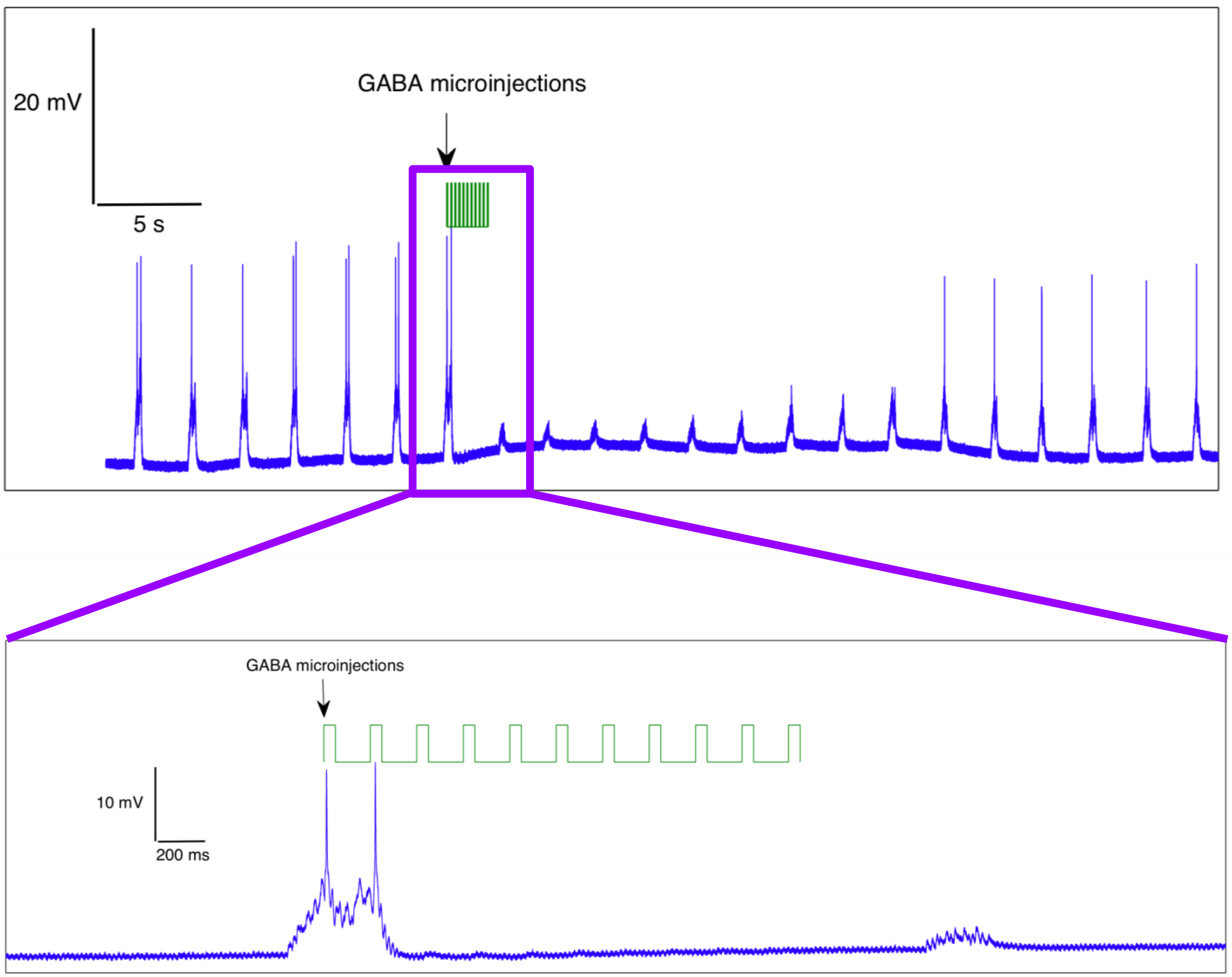


The membrane potential of a neuron is measured and an activity-dependent stimulation protocol of GABA microinjection is implemented with RT software technology. The duration of the micro-injections and the stimulation precise instant are controlled through the activity-dependent protocol.

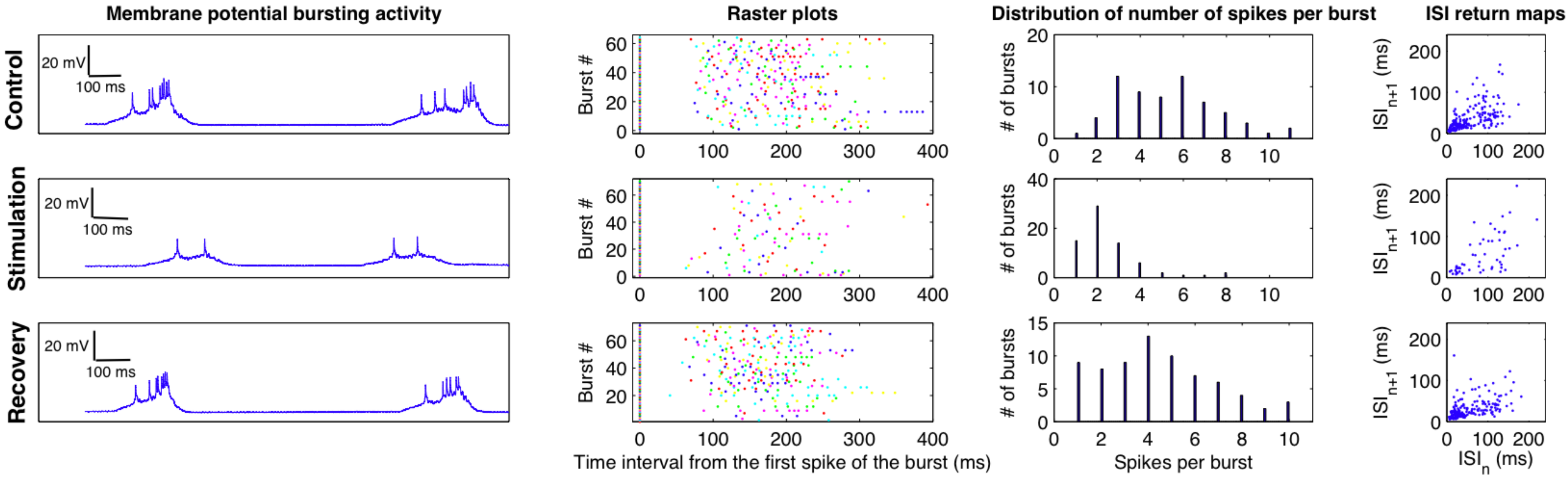
Experimental setup

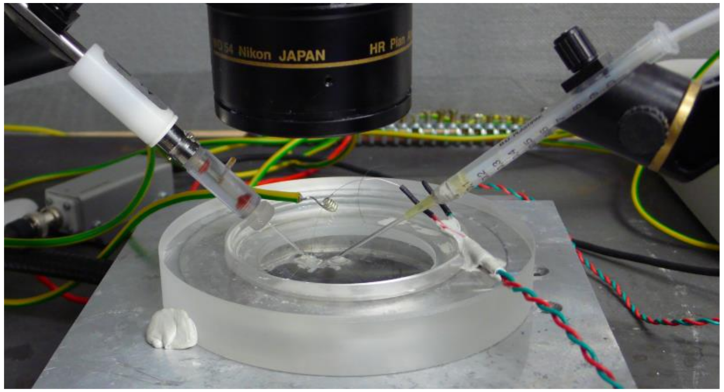


Effect of GABA on the heart CPG neurons of Carcinus maenas



Example of the effect of the activity-dependent GABA microinjection





Chamorro et al. *BMC Neuroscience* 10: P296 (2009)