Od neuronu do sieci: modelowanie układu nerwowego

Ośrodkowe generatory wzorców (CPG) jako przykłady małych sieci neuronalnych

dr Daniel Wójcik

na podstawie „The Book of GENESIS”

- Wzorce aktywności mięśniowej: chodzenie, pływanie, latanie, oddychanie, żucie, drapanie
- Przykłady:
  - pływanie uciekającego mięczaka *Tritonia diomedea*
  - rytmy trawienne homara *Panulirus interruptus* i kraba *Cancer borealis*
  - faliste ruchy pływne ryby i minoga
  - kroki karalucha
  - szybki ruch skrzydeł szarańczy w locie
  - skomplikowana lokomocja czworonoga

Tritonia Diomedea

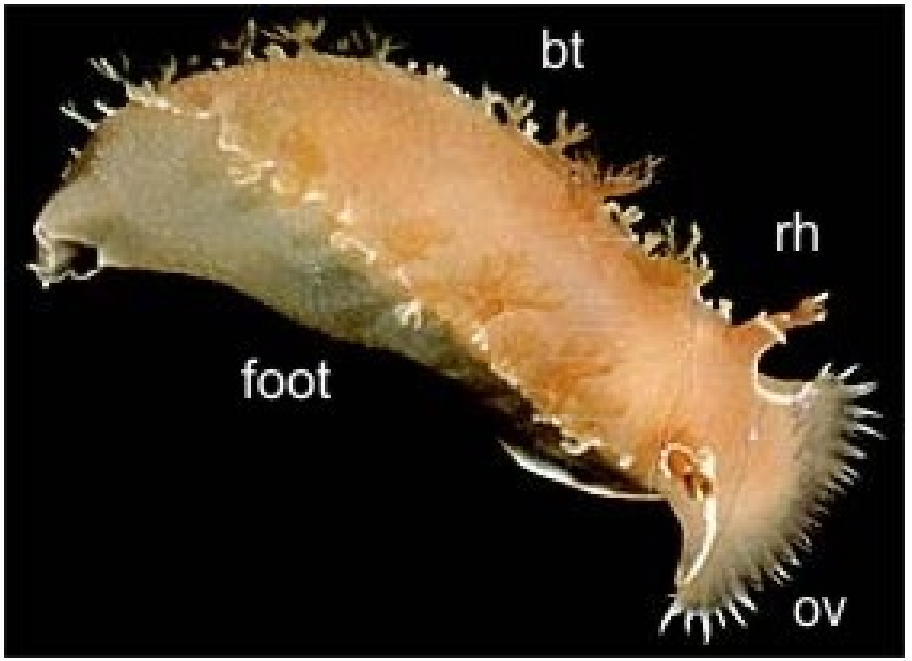
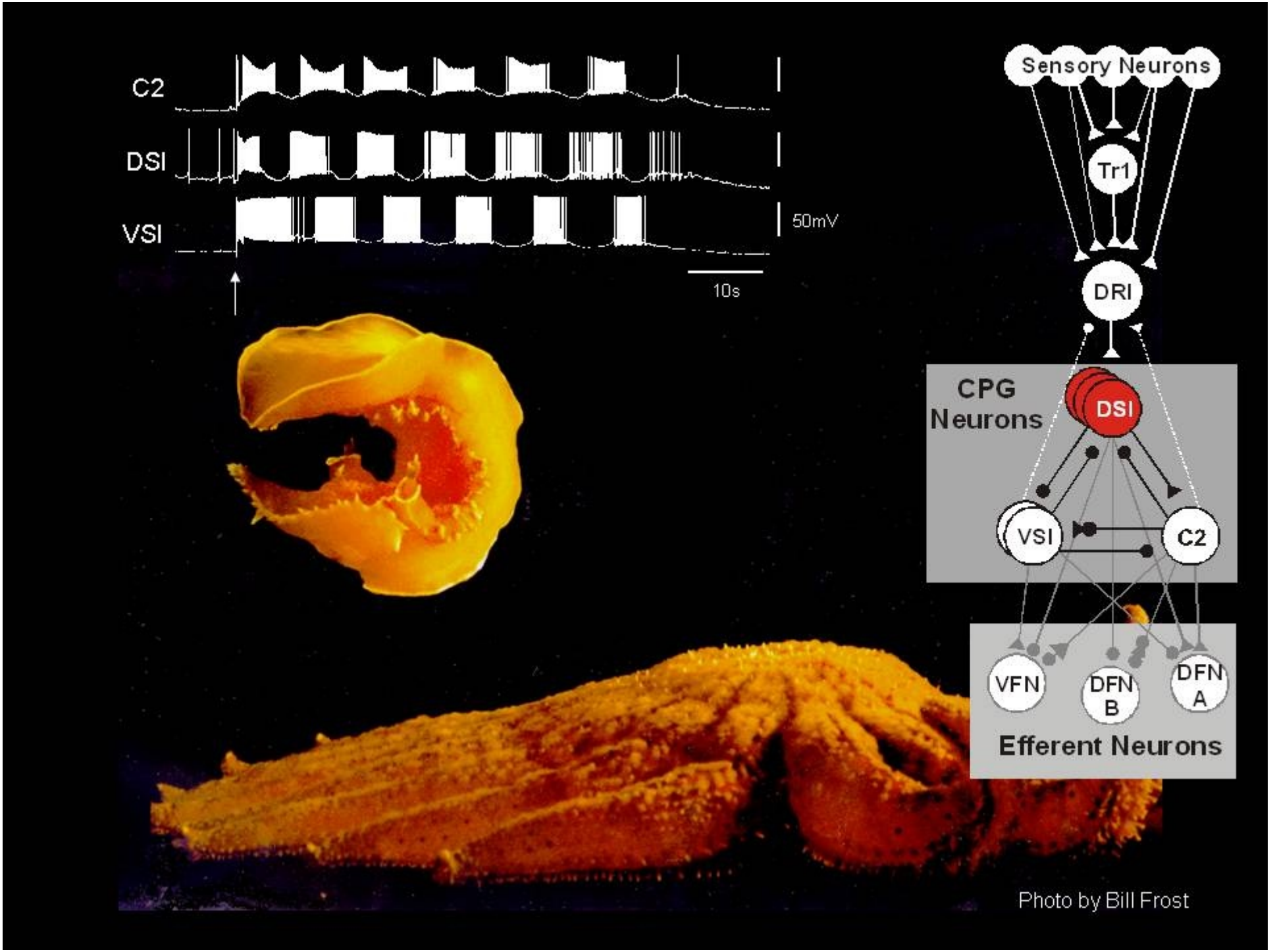


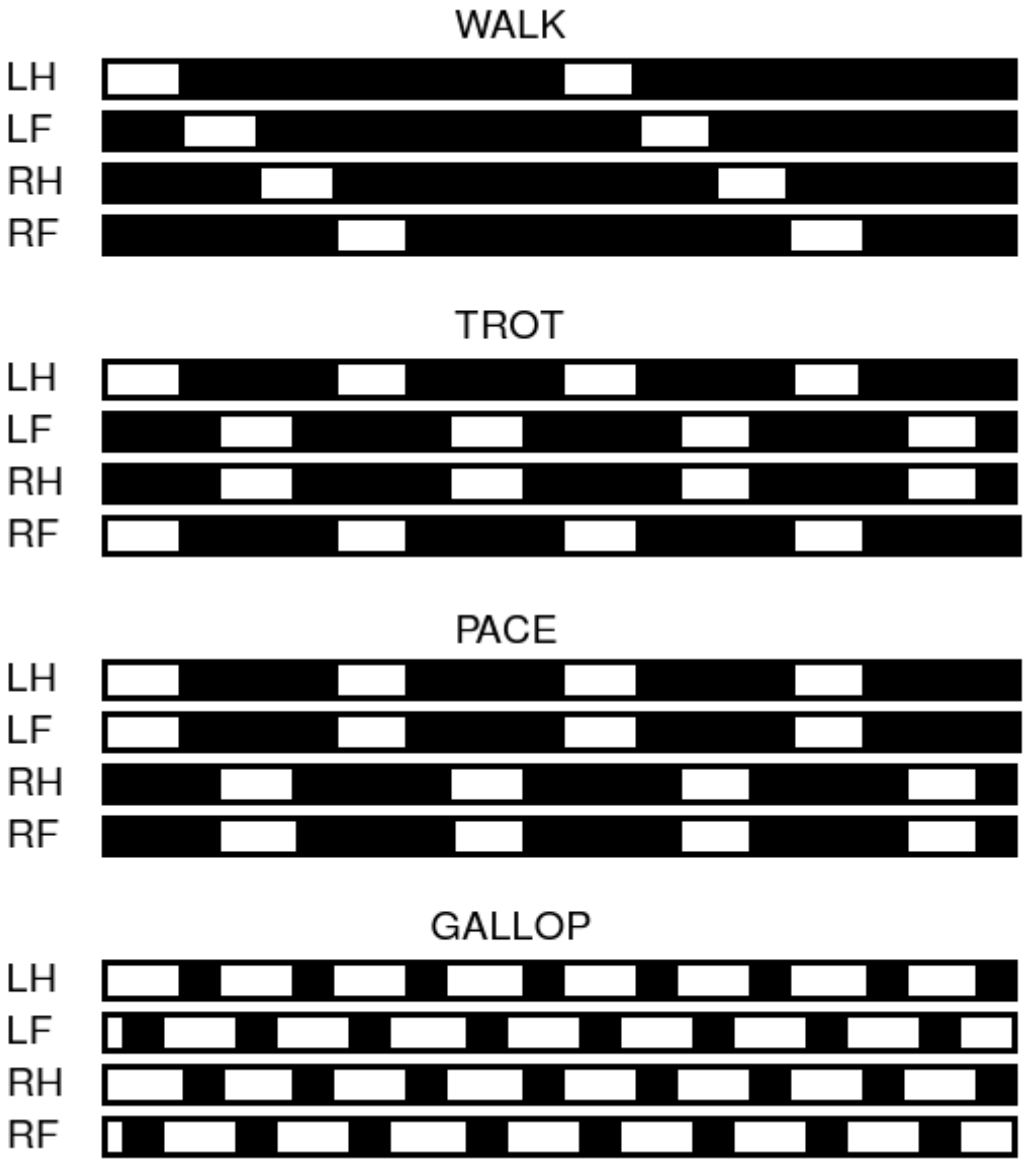
Photo of Tritonia diomedea.
Anterior is to the right.
bt = Branchial Tufts,
rh = Rhinophore,
ov = Oral Veil.

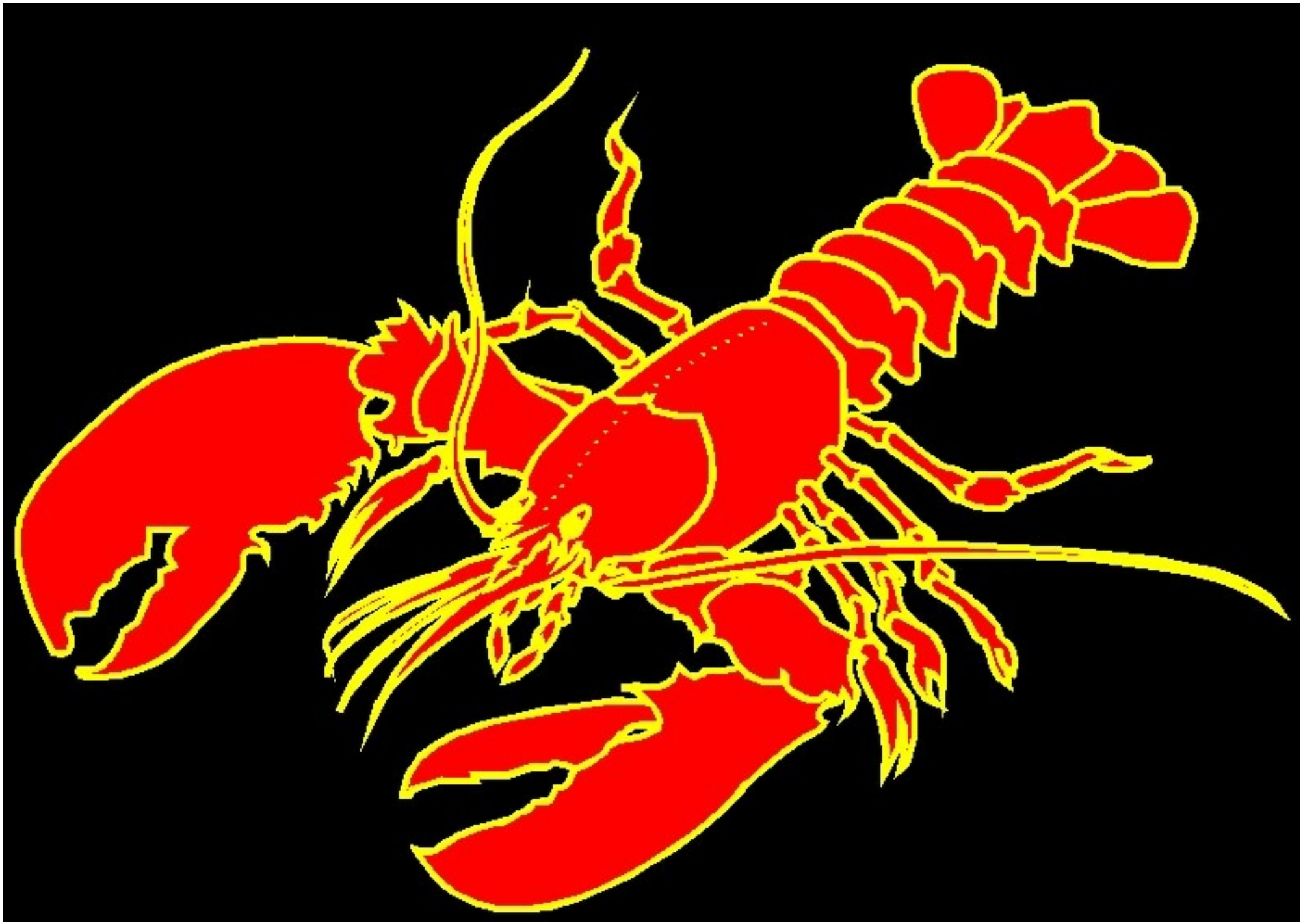
Następna strona: Tritonia escape swimming. The picture shows a Tritonia escaping from a sea star, Pycnopodia. At the top are simultaneous intracellular electrophysiological recordings from the 3 CPG neurons: C2, DSI, and VSI taken from an isolated brain. At the arrow, a body wall nerve was stimulated, producing a pattern of discharges that lasts about a minute. DSI bursts alternate with VSI bursts producing dorsal and ventral body flexions. To the right is the neural circuit from sensory neurons to efferent output.


C2
DSI
VSI
50mV
10s
Sensory Neurons
Tr1
DRI
CPG Neurons
DSI
VSI
C2
VFN
DFN B
DFN A
Efferent Neurons
Photo by Bill Frost

- Ośrodkowe generatory wzorców – obwody nerwowe odpowiedzialne za generację rytmicznych ruchów mięśni
- Generują oscylacje nawet przy braku wejścia
- Łatwa adaptacja ruchów oscylacyjnych do zmiennych warunków wykazuje, że wejście sensoryczne moduluje aktywność CPG
- CPG mogą się przełączać między różnymi wzorcami aktywności pod wpływem bodźców zewnętrznych i kontroli z wyższych centrów UN, dlatego możemy je traktować jako jedną część rozproszonego układu sterowania

- Wiele CPG potrafi generować rytmy o różnym charakterze, np. spacer, trucht, jednochód, galop





Przykład: stomatogastric ganglion

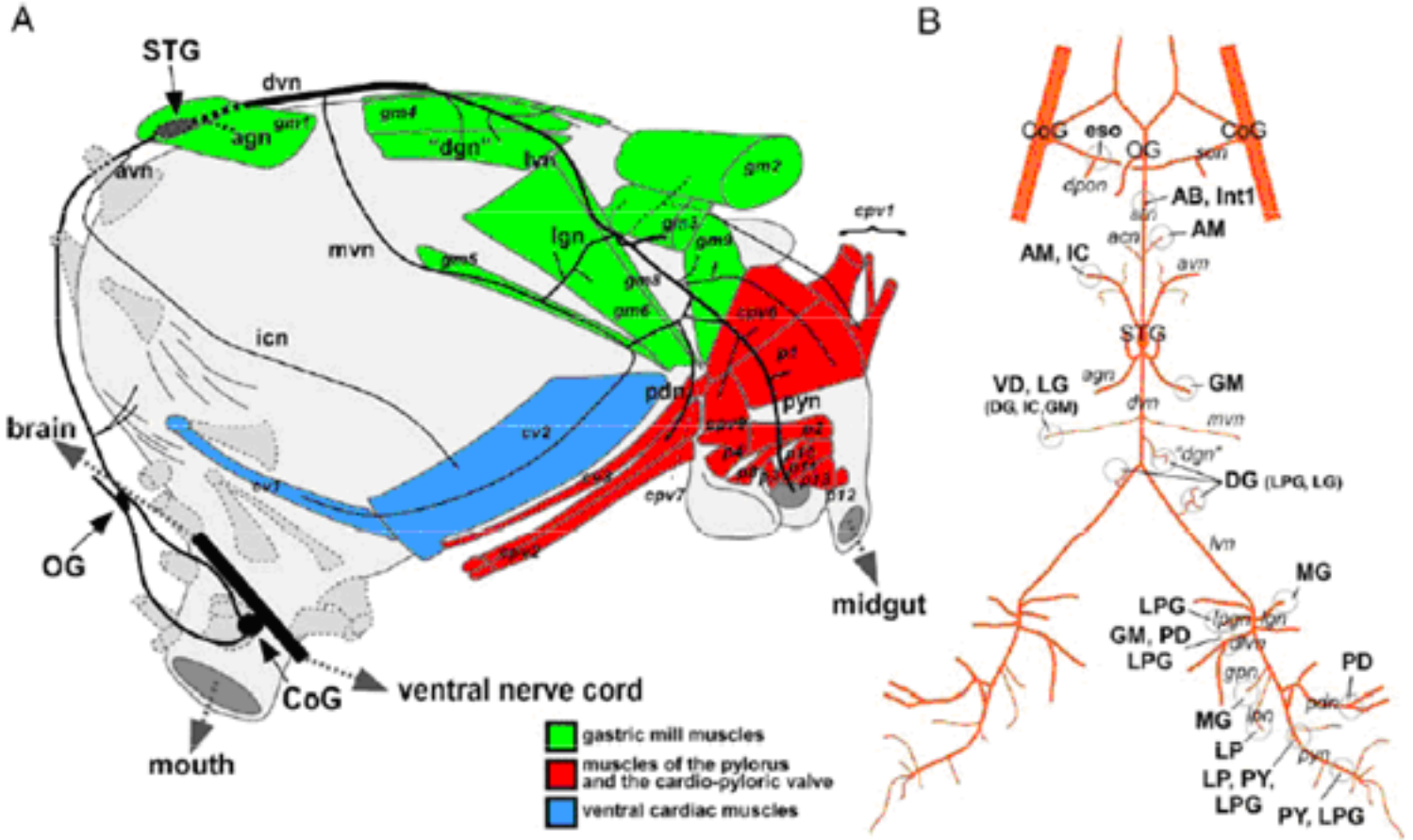
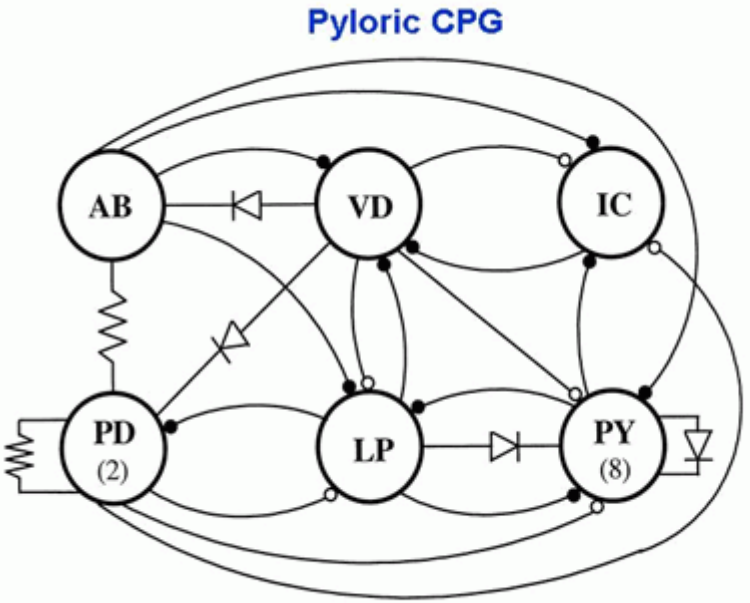


Figure 1: The muscles and nerves of the stomatogastric system. A. Muscles shown in green control the "teeth" of the gastric mill, those in red the pyloric region and blue, part of the cardiac sac. B. Nerves containing the axons of the neurons within the stomatogastric ganglion. Adapted from Heinzel and Boehm (unpublished).



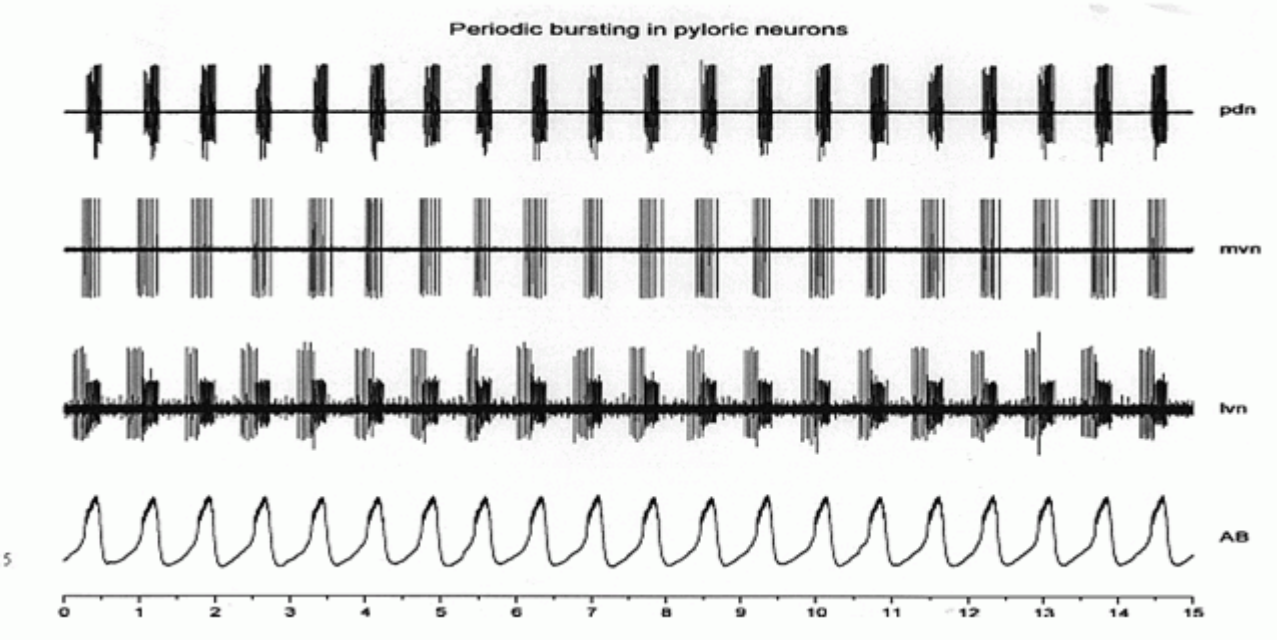


Figure 5: Simplified version of the pyloric circuit and extracellular recordings of the in vitro motor pattern. Black dots represent glutamatergic inhibitory synapses and open circles cholinergic inhibitory synapses. Resistors indicate electrical connections and diodes are rectifying connections. The motor pattern at right shows the two PD axons in the pdn, VD in the mvn, LP (large spike), PD and some PY units in the lvn. The intracellular recording is from the AB interneuron.

Pyloric Neurons

# of copies	Name	Abbr.	Muscle	Transmitter
1	anterior burster	(AB)	interneuron	glu
2	pyloric dilator	(PD)	cpv 1&2	ach
1	lateral pyloric	(LP)	p1	glu
1	ventricular dilator	(VD)	cv 2	ach
1	inferior cardiac	(IC)	cv 3	glu
8	pyloric	(PY)	p 2-4, 7-8, 10-11	glu

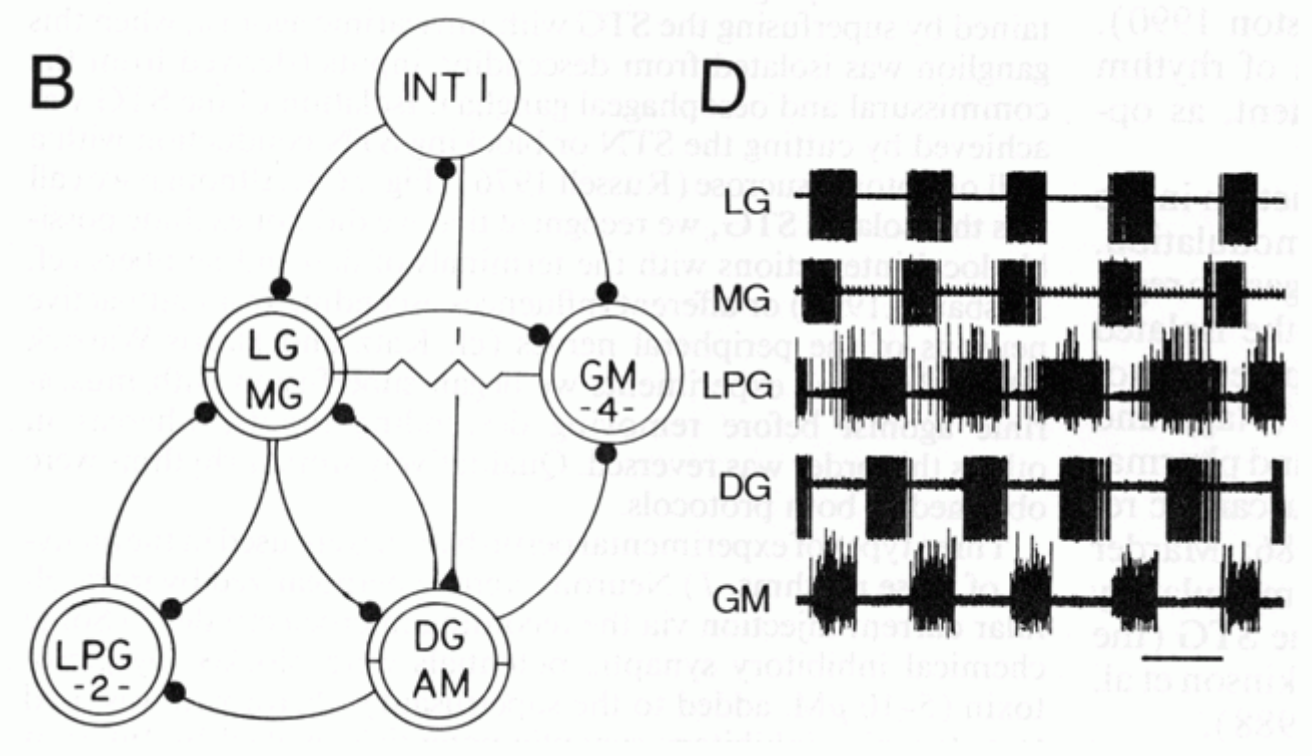
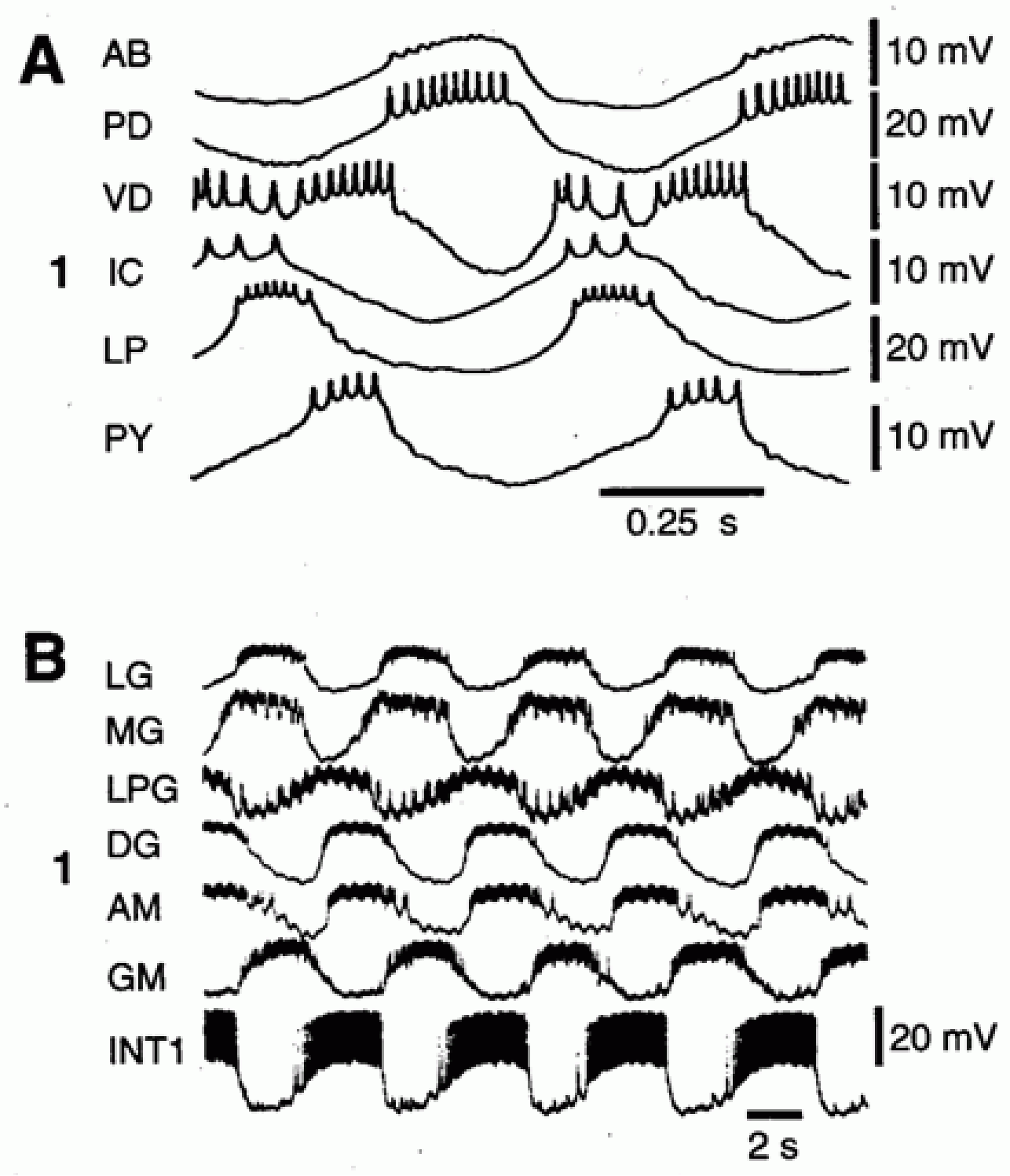


Figure 6: B. Simplified gastric mill circuit and in vitro motor pattern. The symbols are as in Fig.5 except the transmitters are not coded and the triangle from Int 1 is excitatory. D. The motor pattern shown here has five phases. Time bar ca 3 sec. The AM neuron is not shown.

Gastric Mill Neurons

# of copies	Name	Abbr.	Muscle	Transmitter
1	Interneuron 1	(Int 1)	interneuron	glu
4	Gastric Mill	(GM)	gm 1b,2a,b	ach
1	Dorsal Gastric	(DG)	gm 4a,b,c	ach
1	Anterior Median	(AM)	c 6, c7	glu
1	Lateral Gastric	(LG)	gm 5b, 6a	glu
1	Medial Gastric	(MG)	gm 9a, 9c	glu
2	Lateral Posterior Gastric	(LPG)	gm 3	ach

Figure 7: A. Simultaneous intracellular recordings from all neuron types in the pyloric CPG. B. Simultaneous intracellular recordings from gastric mill neurons. Recordings in A made by J.P. Miller and in B by H.G. Heinzel.



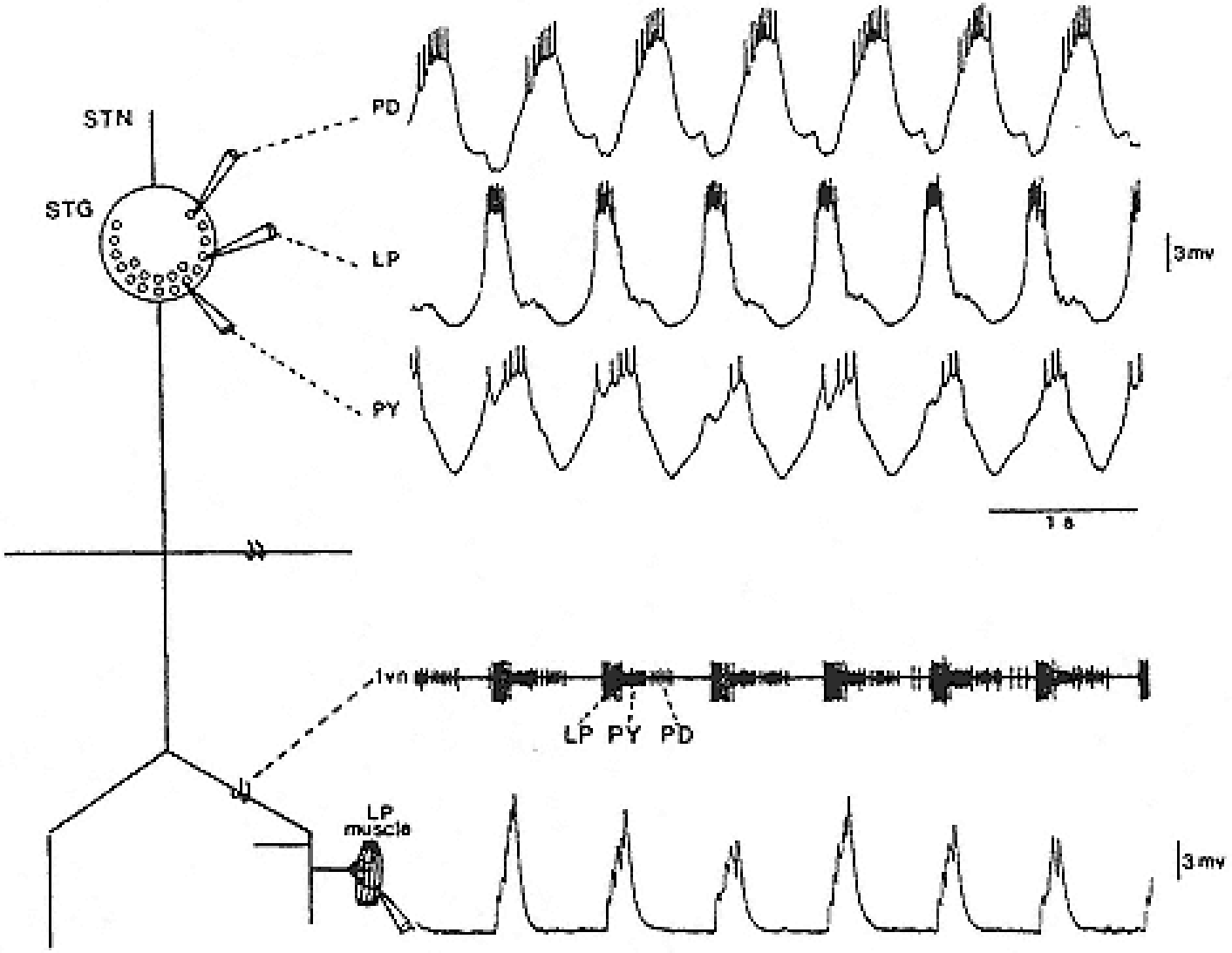


Figure 1: The pyloric rhythm. The stick figure shows the positions of the recordings shown on the right. All recordings were simultaneous. The top three traces are intracellular recordings from the somata of the PD, LP and PY neurons, the next trace is an extracellular recording from the *lvn* and the bottom trace is an intracellular recording from one of the muscles innervated by the LP neuron. Modified from Marder et al. (1987).

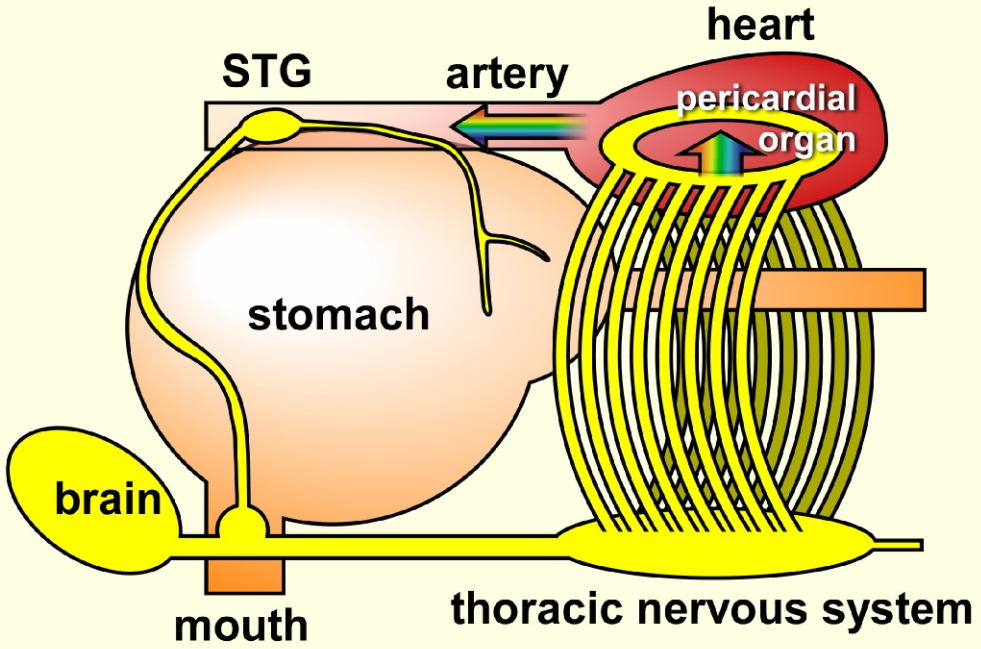
circulating neurohormones

DA
5-HT
AST
ATR
Buc
CabTRP

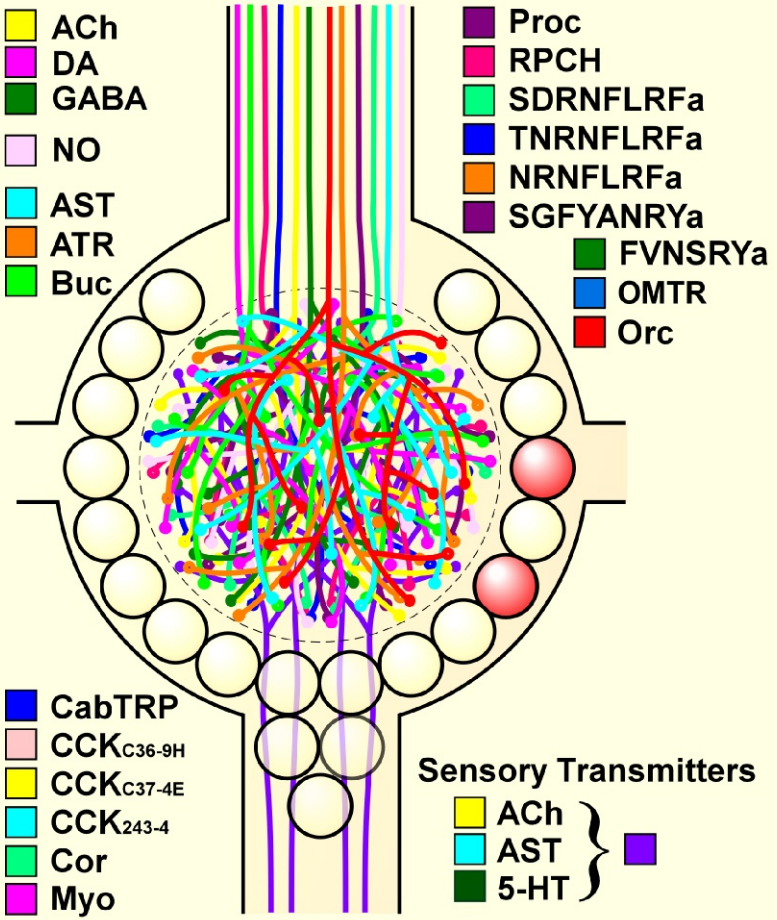
CCAP
RPCH
Cor
Proc
Myo
Orc

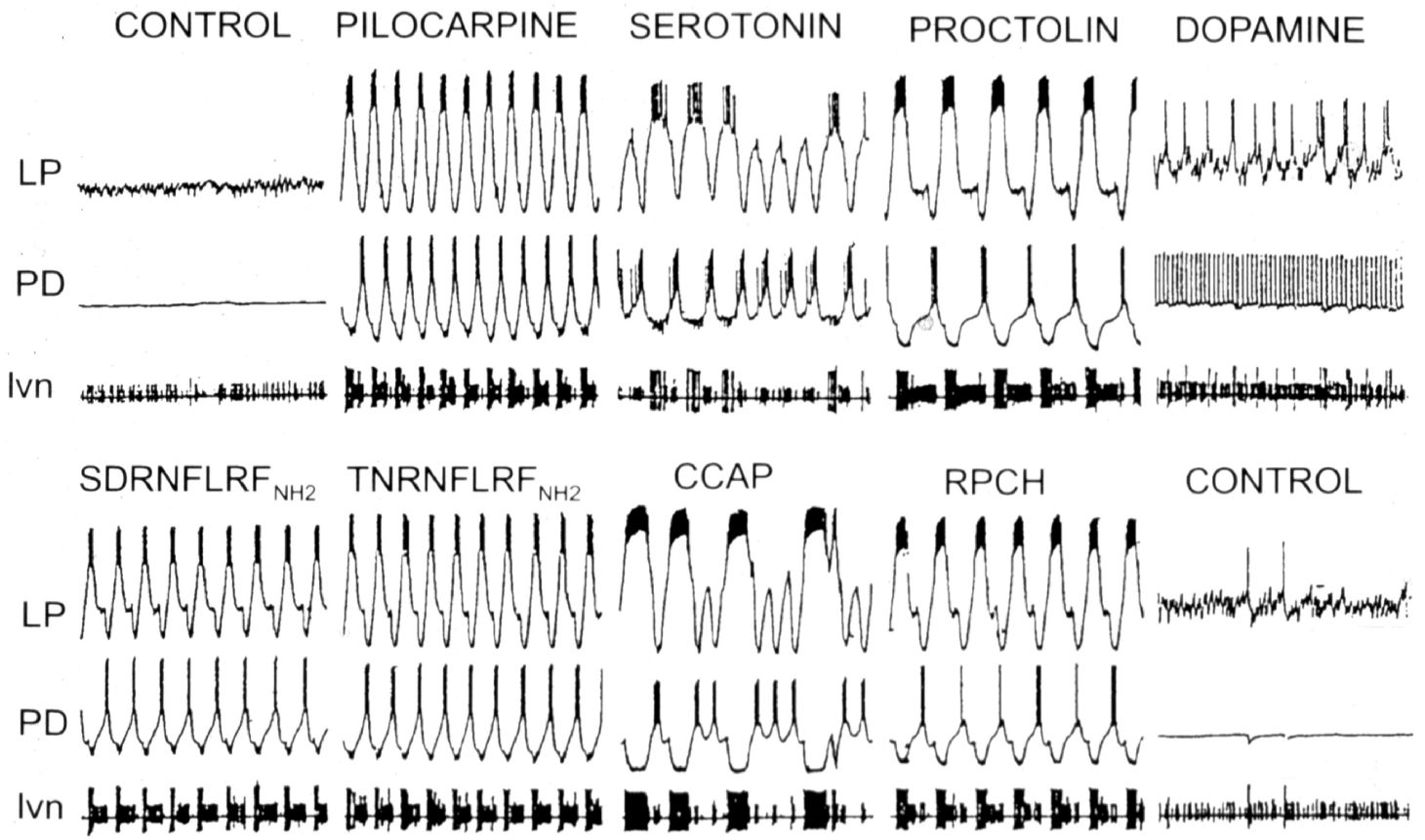
β-PDH
CCK_{C36-9H}
CCK_{243-4}
SDRNFLRFa
TNRNFLRFa
NRNFLRFa

SGFYANRYa
FVNSRYa
PAFYSQRYa
Cor2
Pevkinin
OMTR



locally-delivered neuromodulators




CONTROL
PILOCARPINE
SEROTONIN
PROCTOLIN
DOPAMINE
LP
PD
lvn
SDRNFLRF$_{NH2}$
TNRNFLRF$_{NH2}$
CCAP
RPCH
CONTROL
LP
PD
lvn

$$\dot{\theta}_i(t) = \omega_i$$

$$\dot{\theta}_1(t) = \omega_1 + h_{12}(\theta_1, \theta_2)$$
$$\dot{\theta}_2(t) = \omega_2 + h_{21}(\theta_2, \theta_1),$$

$$\phi(t) = \theta_1(t) - \theta_2(t)$$

$$\begin{aligned} \dot{\phi}(t) &= \dot{\theta}_1(t) - \dot{\theta}_2(t) \\ &= (\omega_1 - \omega_2) + (h_{12}(\theta_1, \theta_2) - h_{21}(\theta_2, \theta_1)) \end{aligned}$$

$$\dot{\phi}(t) = (\omega_1 - \omega_2) - (a_{12} + a_{21}) \sin(\phi(t))$$

$$\dot{\phi}(t) = (\omega_1 - \omega_2) - (a_{12} + a_{21}) \sin(\phi(t))$$

$$\phi = \arcsin\left(\frac{\omega_1 - \omega_2}{a_{12} + a_{21}}\right)$$

$$
\begin{aligned}
\dot{\theta}_1(t) &= \omega_1 + h_{12}(\theta_1, \theta_2) \\
\dot{\theta}_2(t) &= \omega_2 + h_{21}(\theta_2, \theta_1) + h_{23}(\theta_2, \theta_3) \\
\dot{\theta}_3(t) &= \omega_3 + h_{32}(\theta_3, \theta_2) + h_{34}(\theta_3, \theta_4) \\
\dot{\theta}_4(t) &= \omega_4 + h_{43}(\theta_4, \theta_3).
\end{aligned}
$$

$$\phi_i(t) = \theta_i(t) - \theta_{i+1}(t)$$

$$\dot{\phi}(t) = \Omega + AS(t)$$

$$\phi(t) = \begin{bmatrix} \phi_1(t) \\ \phi_2(t) \\ \phi_3(t) \end{bmatrix} \qquad A = a \begin{bmatrix} -2 & 1 & 0 \\ 1 & -2 & 1 \\ 0 & 1 & -2 \end{bmatrix}$$

$$\Omega = \begin{bmatrix} \omega_1 - \omega_2 \\ \omega_2 - \omega_3 \\ \omega_3 - \omega_4 \end{bmatrix} \qquad S = \begin{bmatrix} \sin(\phi_1(t)) \\ \sin(\phi_2(t)) \\ \sin(\phi_3(t)) \end{bmatrix}$$

$\dot{\phi} = 0$ when $S = -A^{-1}\Omega$, and we know that

$$A^{-1} = \frac{-1}{4a}\begin{bmatrix} 3 & 2 & 1 \\ 2 & 4 & 2 \\ 1 & 2 & 3 \end{bmatrix}$$

If we assume that there is a smooth gradient in the intrinsic frequency of oscillation along the cord, then the frequency difference along the chain is constant, and $\omega_1 - \omega_2 = \omega_2 - \omega_3 = \omega_3 - \omega_4 = c$. In this case,

$$\Omega = c\begin{bmatrix} 1 \\ 1 \\ 1 \end{bmatrix} \qquad S = \frac{c}{2a}\begin{bmatrix} 3 \\ 4 \\ 3 \end{bmatrix} \qquad \left|\frac{c}{a}\right| \leq \frac{1}{2}$$