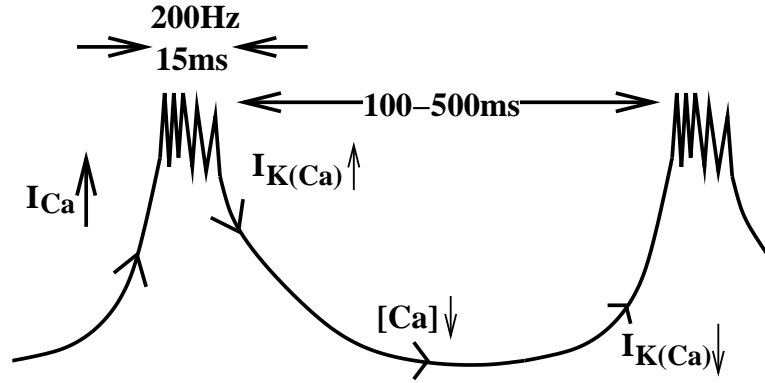


# Bursting, Pacemaking Neurons and Central Pattern Generators

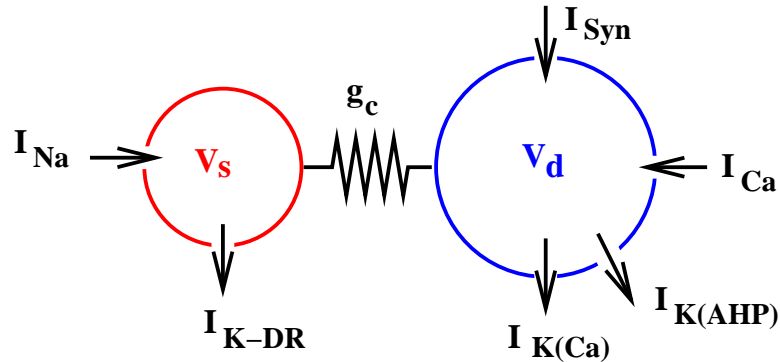
## (1) Pinsky-Rinzel rhythmic burster via calcium influx

See Pinsky and Rinzel J. Comput. Neurosci. 1, 39-60 (1994).

Model of hippocampal, CA3, pyramidal cell see Matlab code PR.m and alternative with persistent sodium and slow potassium currents, PR\_alt.m.



Two-compartment model (soma and dendrite) with *ping-pong* of currents between soma and dendrites during burst.



**Area:  $A_s = pA_{tot}$**

**Area:  $A_d = (1-p)A_{tot}$**

$g_c$  is strength of coupling between soma and dendrites.

$g_c = 0$  no coupling. Soma fires regularly. Dendrites produce regular Ca-spikes (like Na-spikes but slower).

$g_c \mapsto \infty$  isopotential neuron ( $V_s = V_d$ ). No bursting.

$$A_s c_m \frac{dV_s}{dt} = -A_s (i_{L,s} + i_{Na} + i_{K-DR}) - (V_s - V_d) g_c A_{tot} \quad (1)$$

$$A_d c_m \frac{dV_d}{dt} = -A_d (i_{L,d} + i_{K(AHP)} + i_{K(Ca)} + i_{Ca}) - (V_d - V_s) g_c A_{tot} \quad (2)$$

(3)

leads to

$$c_m \frac{dV_s}{dt} = - (i_{L,s} + i_{Na} + i_{K-DR}) - (V_s - V_d) \frac{g_c}{p} \quad (4)$$

$$c_m \frac{dV_d}{dt} = - (i_{L,d} + i_{K(AHP)} + i_{K(Ca)} + i_{Ca}) - (V_d - V_s) \frac{g_c}{1-p} \quad (5)$$

The currents follow

$$i_{L,s} = g_L (V_s - V_L) \quad (6)$$

$$i_{L,d} = g_L (V_d - V_L) \quad (7)$$

$$i_{Na} = g_{Na} m_{\infty}^2 h (V_s - V_{Na}) \quad (8)$$

$$i_{K-DR} = g_{K-DR} n (V_s - V_K) \quad (9)$$

$$i_{Ca} = g_{Ca} s^2 (V_d - V_{Ca}) \quad (10)$$

$$i_{K(Ca)} = g_{K(Ca)} c \chi (V_d - V_K) \quad (11)$$

$$i_{K(AHP)} = g_{K(AHP)} q (V_d - V_K) \quad (12)$$

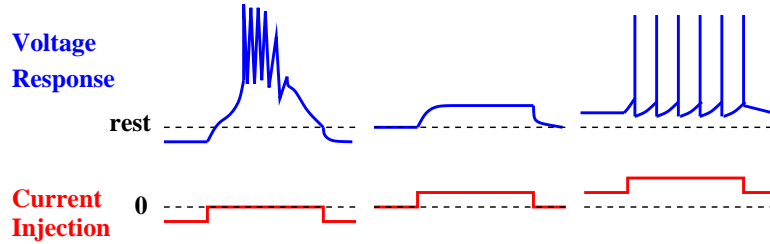
where  $h, n, s, c,$  and  $q$  are gating variables which follow the usual form:

$$\frac{dy}{dt} = [y_{\infty} - y] / \tau_y \quad (13)$$

with  $y_{\infty}$  and  $\tau_y$  functions of  $V_s$  for  $y = h, n,$  functions of  $V_d$  for  $y = s, c$  and functions of  $[Ca]$  for  $y = q.$

## (2) Post-inhibitory rebound and thalamic relay neuron

Arises from a transient (T-type) Ca-current that is deinactivated by hyperpolarization. See Matlab file PIR.m.



Add to a (modified) Hodgkin-Huxley model:

$$i_{Ca,T} = g_{Ca,T} m^2 h (V - V_{Ca}) \quad (14)$$

where  $V_{Ca} = 120\text{mV}, g_{Ca,T} = 0 - 2\text{mS/cm}^2$  and

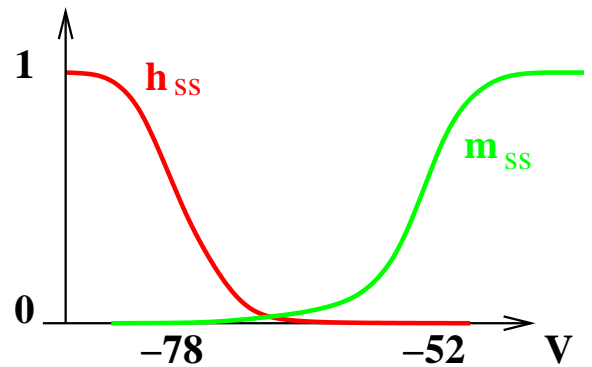
$$m = m_{\infty} = \frac{1}{1 + \exp[-(V + 52)/7.4]} \quad (15)$$

$$\frac{dh}{dt} = \frac{h_{\infty} - h}{\tau_h} \quad (16)$$

where

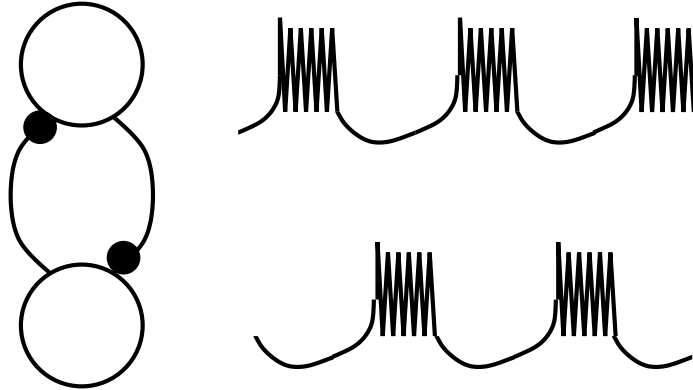
$$h_{\infty} = \frac{1}{1 + \exp[(V + 78)/5]} \quad (17)$$

$$\tau_h = 24 + \frac{119}{1 + \exp[(V + 70)/3]} \quad (18)$$



### (3) Half-center oscillator

Two cells with  $I_{Ca,T}$  coupled by inhibition (Wang and Rinzel, Neural Comput. 4:84, 1992).



If  $g_{Ca,T}$  is low relative to inhibitory coupling, then rebound arises by **release**. Time to switch is determined by decay time of the burst.

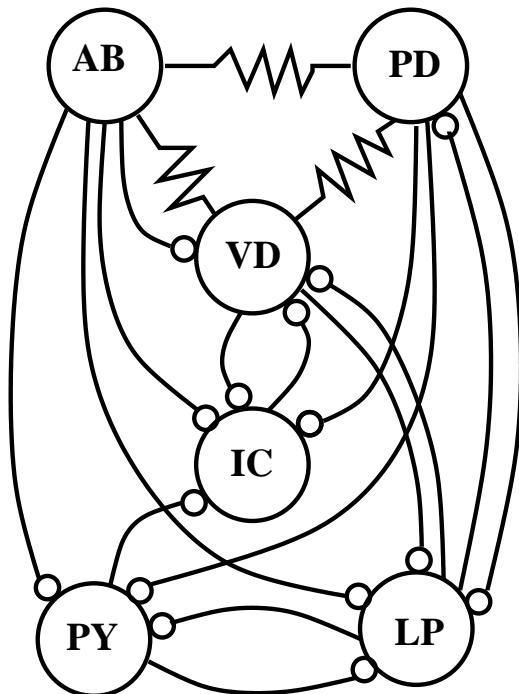
If  $g_{Ca,T}$  is high relative to inhibitory coupling, then rebound arises by **escape**. The hyperpolarized neuron recovers and has enough excitatory current  $i_{Ca,T}$  to escape inhibition and start firing. Time to switch is determined by recovery time of  $i_{Ca,T}$  when cell is hyperpolarized.

Equivalent system is leech heartbeat, see Sorensen et al. J. Neurosci. 24:5427 (2004). Responsible current called  $i_h$  for hyperpolarization-activated inward current. Note the use of **dynamic clamp** and a “silicon cell” to mimic half of the system.

### (4) Central pattern generators: Pyloric rhythm of stomatogastric ganglion (STG) in lobster

Eve Marder’s group has been at the forefront of research in this system for many years.

Well-characterized neuronal circuitry: Marder and Calabrese, Physiol. Rev. 76:687 (1996).



3-phase rhythm, with one pacemaker neuron (the anterior burster, AB).

Electrically coupled cells tend to be in phase (pyloric dilator PD though not quite ventricular dilator, VD).

Lateral pyloric (LP) then pyloric neurons (PY) fire subsequently.

Subtle changes in connection strengths and excitabilities of cells via modulators change rhythm significantly.

## (5) Central pattern generators: Lamprey swimming as a chain of coupled oscillators

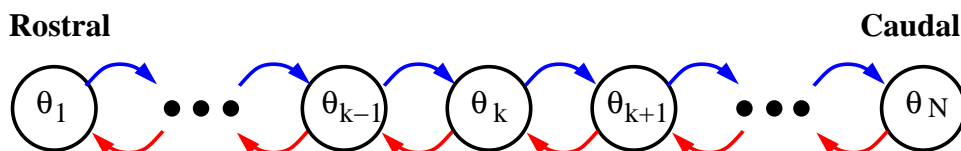
Problem: muscles should contract at a constant relative phase with each other to maintain correct body form while swimming, even though the rate of rhythmic motion can vary ten-fold.

So how are individual neuronal oscillators (which control muscle contraction) maintained at a fixed phase relative to each other?

Answer: via phase response curve. Interactions between oscillators gives a constant phase shift rather than a constant time shift.

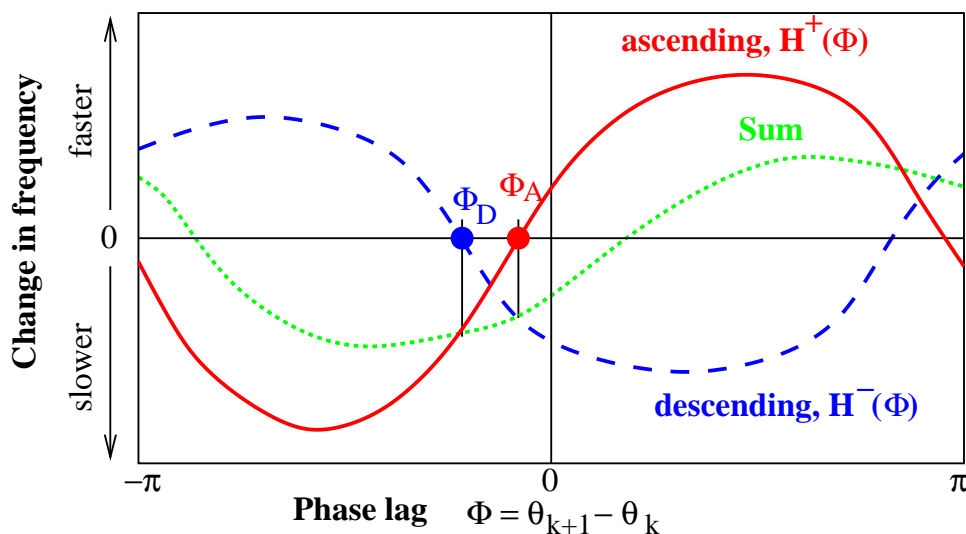
Intuition: constant voltage-kick from one neuron to the other corresponds to a constant change in phase of the voltage-time curve, **not** a constant shift in time.

Model via phases, see eg Cohen et al. Trends Neurosci. 15:434 (1992) and Kopell, Ermentrout and Williams SIAM J. Appl. Math. 51:1397 (1991):



$$\frac{d\theta_k}{dt} = \omega_k + H^+(\theta_{k+1} - \theta_k) + H^-(\theta_{k-1} - \theta_k) \quad (19)$$

Phase-response curves integrated over a cycle become phase-coupling curves:



Two curves, one for ascending coupling (caudal to rostral = high to low  $k$ ) the other for descending coupling (rostral to caudal = low to high  $k$ ).

Stable solution given by the zero-crossing,  $\Phi_A$  of the dominant coupling (ascending in this case).

In reality, each oscillator labeled with phase  $\theta_k$  corresponds to one segment, with two reciprocally inhibiting sets (one set for each side of the body) of at least 5 types of cells.