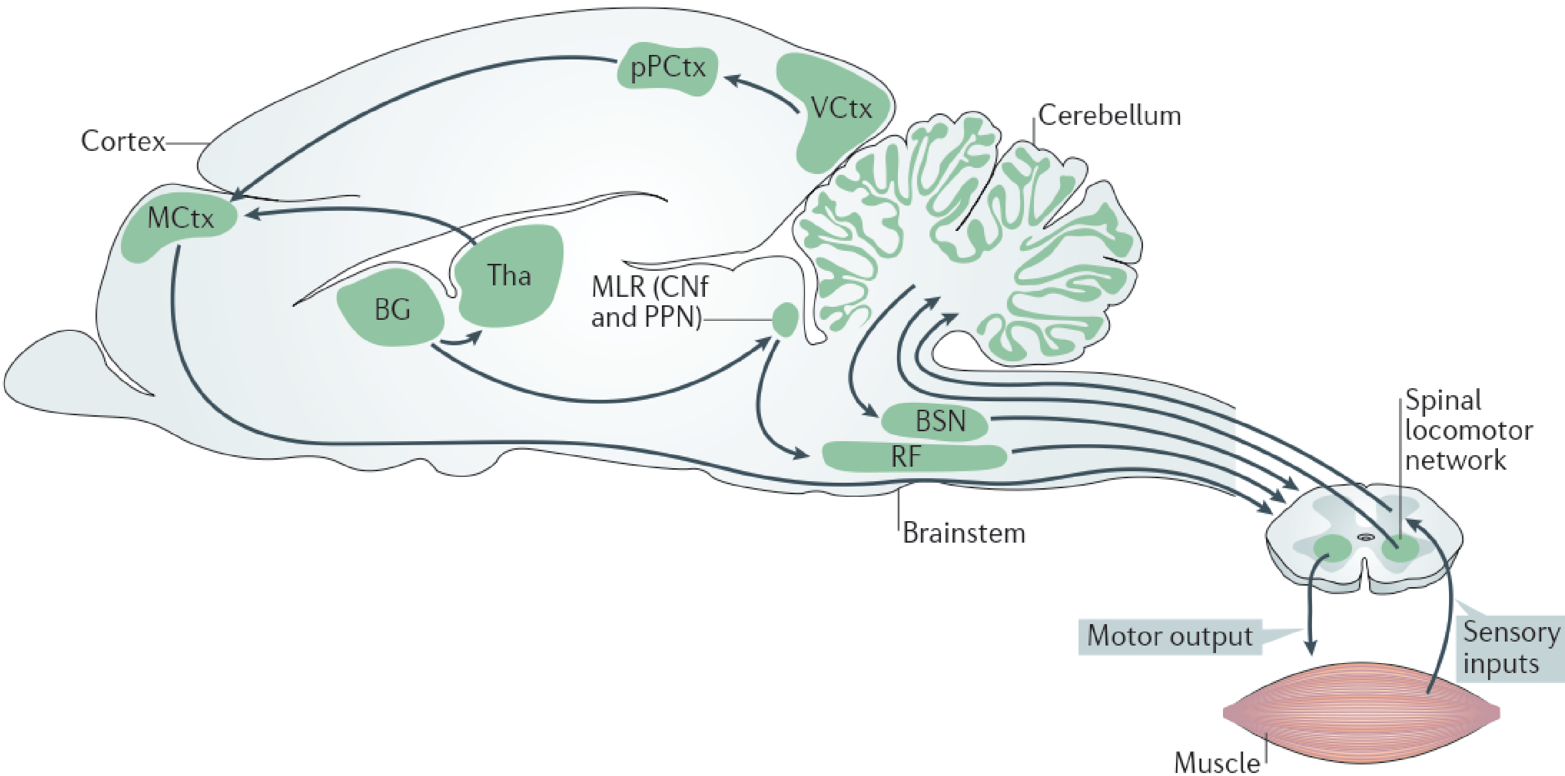
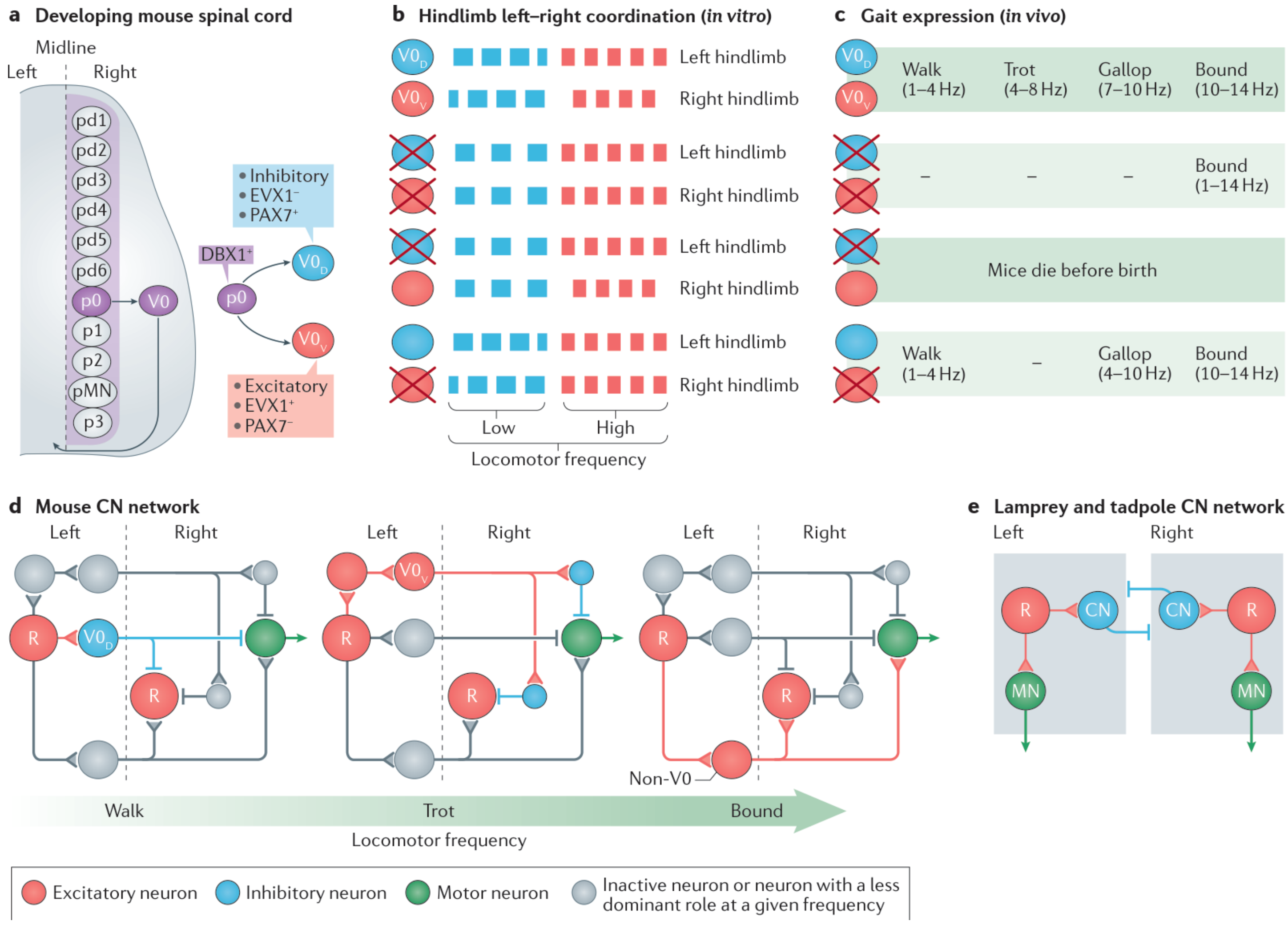
Lecture slides for locomotion, SWC lecture on Nov. 4, 2016, giving by Li Zhaoping


pPCtx
VCtx
Cerebellum
Cortex
MCtx
Tha
BG
MLR (CNf and PPN)
BSN
RF
Brainstem
Spinal locomotor network
Motor output
Sensory inputs
Muscle

Kiehn 2016

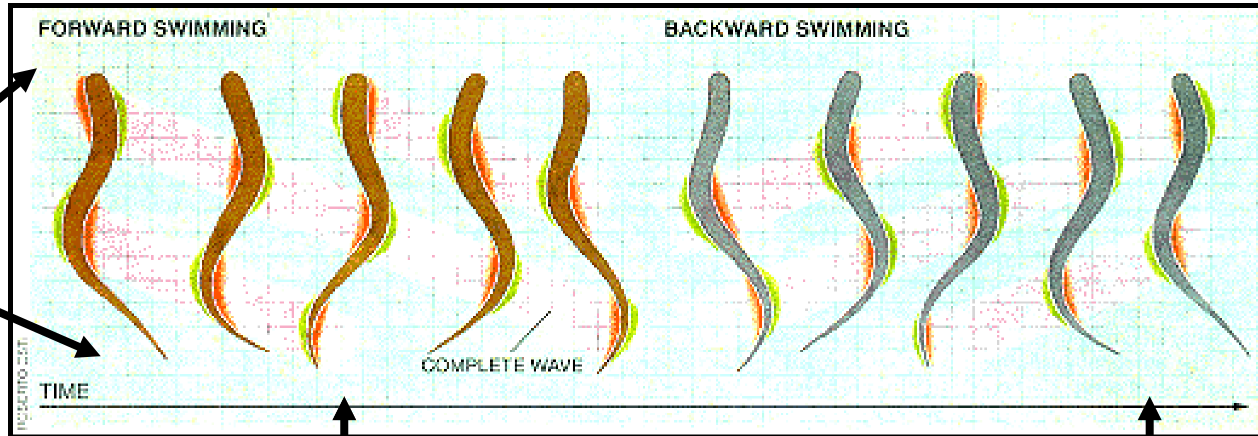


a Developing mouse spinal cord
Midline
Left
Right
pd1
pd2
pd3
pd4
pd5
pd6
p0
p1
p2
pMN
p3
V0
DBX1+
p0
• Inhibitory
• EVX1−
• PAX7+
• Excitatory
• EVX1+
• PAX7−
b Hindlimb left–right coordination (in vitro)
Left hindlimb
Right hindlimb
Low
High
Locomotor frequency
c Gait expression (in vivo)
Walk (1–4 Hz)
Trot (4–8 Hz)
Gallop (7–10 Hz)
Bound (10–14 Hz)
Bound (1–14 Hz)
Mice die before birth
Walk (1–4 Hz)
Gallop (4–10 Hz)
Bound (10–14 Hz)
d Mouse CN network
Left
Right
R
Non-V0
Walk
Trot
Bound
Locomotor frequency
e Lamprey and tadpole CN network
Left
Right
CN
R
MN
Excitatory neuron
Inhibitory neuron
Motor neuron
Inactive neuron or neuron with a less dominant role at a given frequency

Kiehn 2016

Lamprey, locomotion (swimming)

One wave length over about 100 body segments



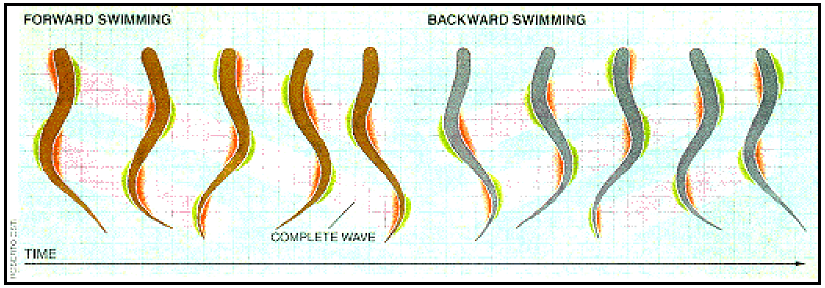
Head oscillation leads tail
forward swimming

Head oscillation lags tail
backward swimming

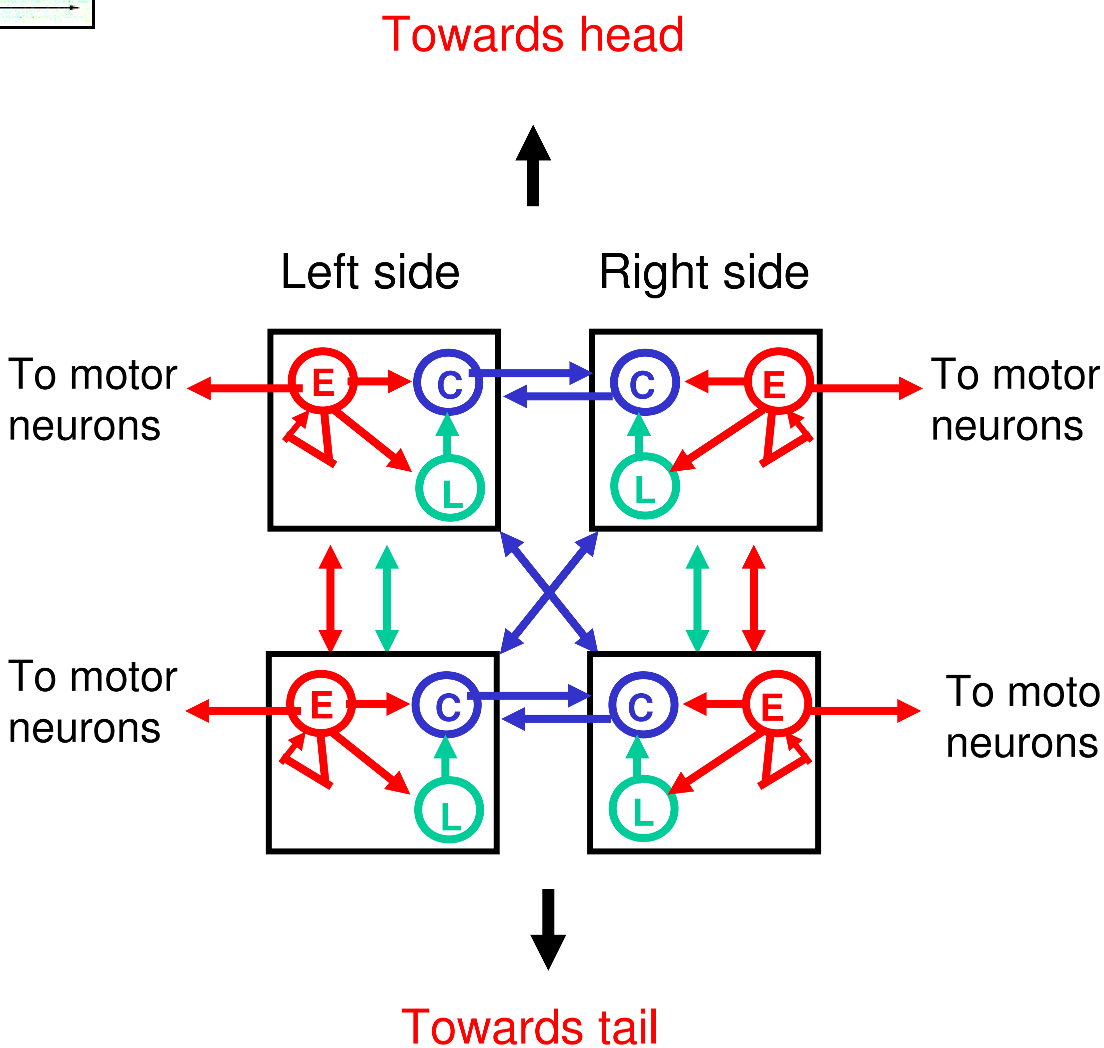
Spatially organized oscillatory neural activities in the spinal neural circuit generate oscillatory muscle action for swimming.

The nervous system survives under in vitro conditions for days for well controlled experimental study: fictive swimming.

A textbook model system to study motor control, neural circuit (network), and central pattern generator (CPG).



Two segments in the spinal cord neural circuit (the CPG):



Three types of neurons:

E (excitatory),
C (cross-caudal inhibitory),
L (inhibitory)

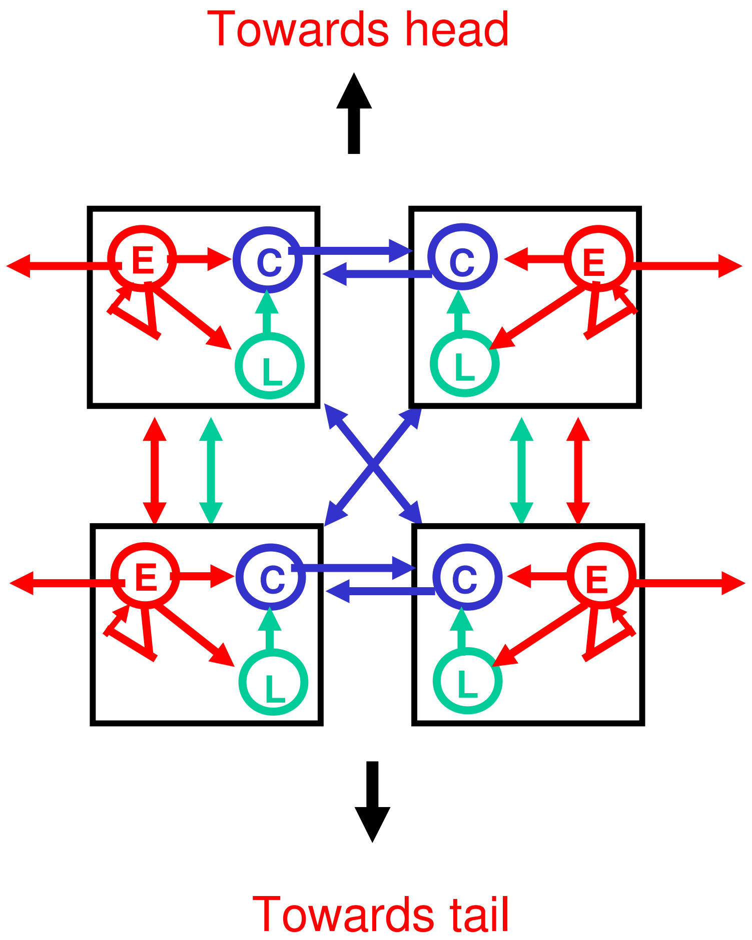
Experimental data in literature:

Spontaneous oscillations occur in decapitated sections with a minimum of 2-3 segments, from anywhere along the body.

E and C neurons: shorter range connections (a few segments), L: longer connections. Approx. 100 segments for whole body

Head-to-tail (rostral-to-caudal) descending connections dominate

E and L oscillate in phase, C phase leads.



Representative Previous works

More biological details

Grillner, Lansner, Hellgren, Kozlov, Brodin, Ekeberg, Wallen, etc:
Simulation of CPG with detailed cellular properties.

Our Work: analytical study of the neural circuit.

- How do oscillations emerge when single segment does not oscillate? --- {no previous studies}
- How are inter-segment phase lags determined by connections --- {not yet fully understood in previous works}
- How can the same network do both forward and backward swimming? how is it controlled?

More abstract

Kopell, Ermentrout, Cohen, Holmes, etc: Mathematical model of CPG simplified as a chain of coupled abstract phase oscillators.

$$d/dt\ \theta_i = \omega_i + \Sigma_j f_{ij} (\theta_{i,}\ \theta_j)$$

Neurons modeled as leaky integrators

$$\frac{d}{dt}\begin{pmatrix}E_L\\ L_L\\ C_L\end{pmatrix} = -\begin{pmatrix}E_L\\ L_L\\ C_L\end{pmatrix} + \boxed{\begin{pmatrix}J & 0 & -K\\ W & 0 & -A\\ Q & -H & -B\end{pmatrix}\begin{pmatrix}g(E_L)\\ g(L_L)\\ g(C_R)\end{pmatrix}}$$

+ external inputs from outside CPG

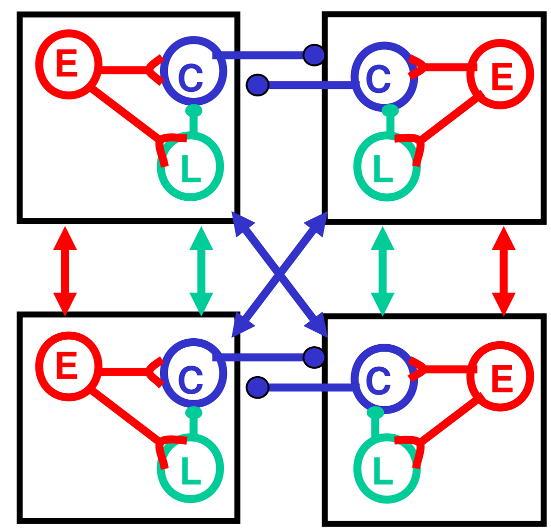
Membrane potentials

Decay (leaky) term

Connection strengths

Firing rates

Inputs from other neurons within CPG



Neurons modeled as leaky integrators

$$\frac{d}{dt}\begin{pmatrix} E_L \\ L_L \\ C_L \end{pmatrix} = -\begin{pmatrix} E_L \\ L_L \\ C_L \end{pmatrix} + \begin{pmatrix} J & 0 & -K \\ W & 0 & -A \\ Q & -H & -B \end{pmatrix}\begin{pmatrix} g(E_L) \\ g(L_L) \\ g(C_R) \end{pmatrix} + \text{external inputs}$$

Membrane potentials

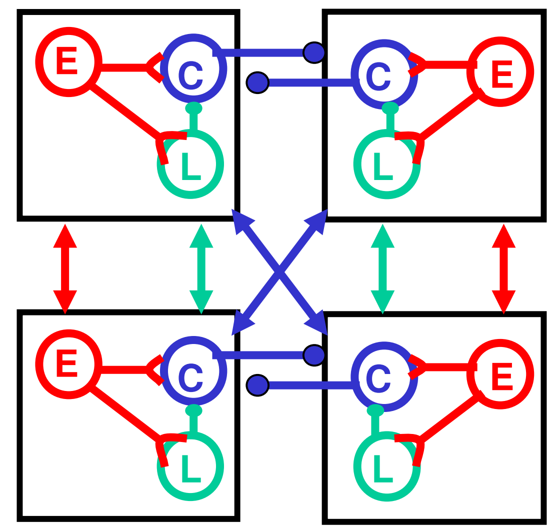
Decay (leaky) term

Connection strengths

Firing rates

Contra-lateral connections from C neurons

Left-right symmetry in connections



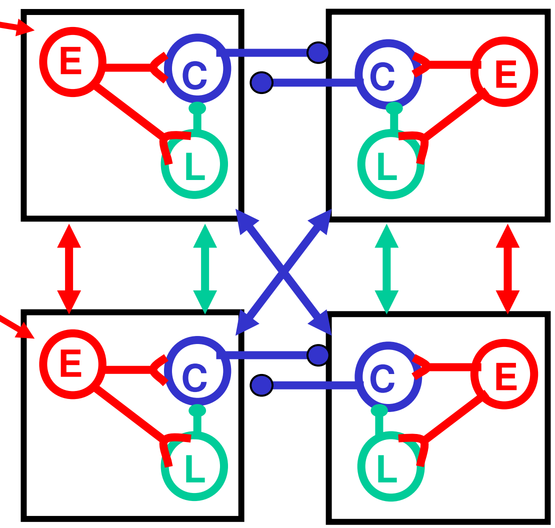
Neurons modeled as leaky integrators

$$\frac{d}{dt}\begin{pmatrix} E_L \\ L_L \\ C_L \end{pmatrix} = -\begin{pmatrix} E_L \\ L_L \\ C_L \end{pmatrix} + \begin{pmatrix} J & 0 & -K \\ W & 0 & -A \\ Q & -H & -B \end{pmatrix}\begin{pmatrix} g(E_L) \\ g(L_L) \\ g(C_R) \end{pmatrix} + \text{external inputs}$$

Membrane potentials

Connection strengths

E,L,C are 100 component vectors: $E_L = \begin{pmatrix} E^1_L \\ E^2_L \\ E^3_L \\ \vdots \end{pmatrix}$



$\begin{pmatrix} E_L \\ L_L \\ C_L \end{pmatrix}$ is an 300 component vector

Neurons modeled as leaky integrators

$$\frac{d}{dt}\begin{pmatrix}E_L\\ L_L\\ C_L\end{pmatrix} = -\begin{pmatrix}E_L\\ L_L\\ C_L\end{pmatrix} + \begin{pmatrix}J & 0 & -K\\ W & 0 & -A\\ Q & -H & -B\end{pmatrix}\begin{pmatrix}g(E_L)\\ g(L_L)\\ g(C_R)\end{pmatrix} + \text{external inputs}$$

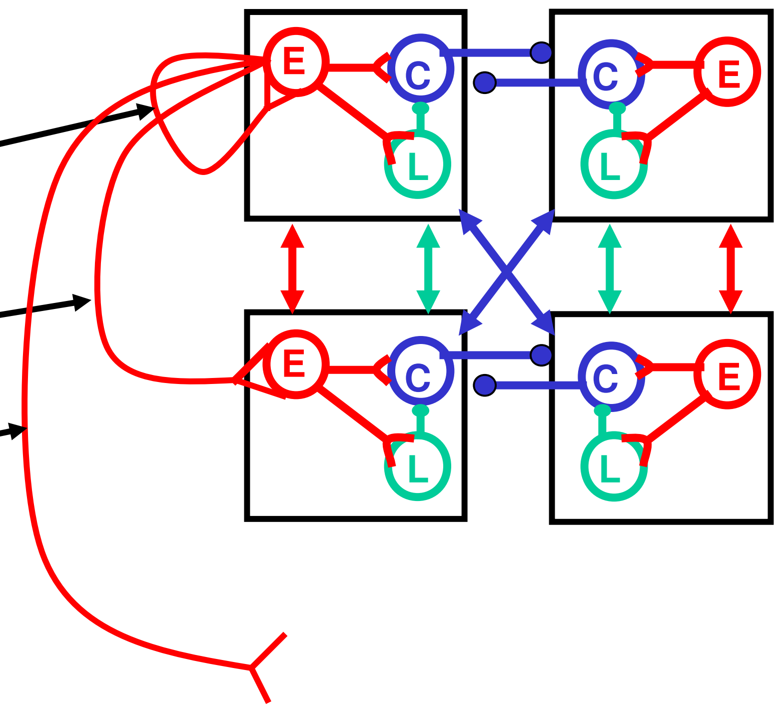
Membrane potentials

Connection strengths

J,K,etc are 100x100 matrices:

$$J=\begin{pmatrix}J_{11} & J_{12} & J_{13} & \cdot\\ J_{21} & J_{22} & \cdot & \cdot\\ J_{31} & \cdot & \cdot & \cdot\end{pmatrix}$$

Near-diagonal matrix



Neurons modeled as leaky integrators

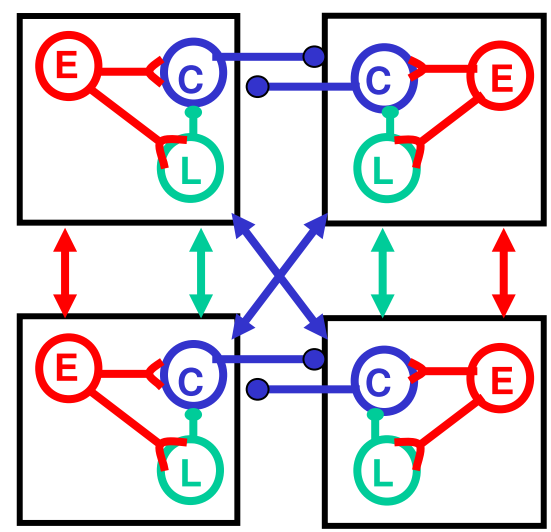
$$\frac{d}{dt}\begin{pmatrix} E_L \\ L_L \\ C_L \end{pmatrix} = -\begin{pmatrix} E_L \\ L_L \\ C_L \end{pmatrix} + \begin{pmatrix} J & 0 & -K \\ W & 0 & -A \\ Q & -H & -B \end{pmatrix}\begin{pmatrix} g(E_L) \\ g(L_L) \\ g(C_R) \end{pmatrix} + \text{external inputs}$$

Membrane potentials

Connection strengths

This is a 300 x 300 matrix

Equations still too complex, Need simplification!!!



Methods used in the simplification/analysis:

1. Linear approximation
   to reduce to a low-dimensional system (mode)
   using various real and approximated symmetries.

2. Using physiological data to arrive at another additional
   simplification to a 2-dim system

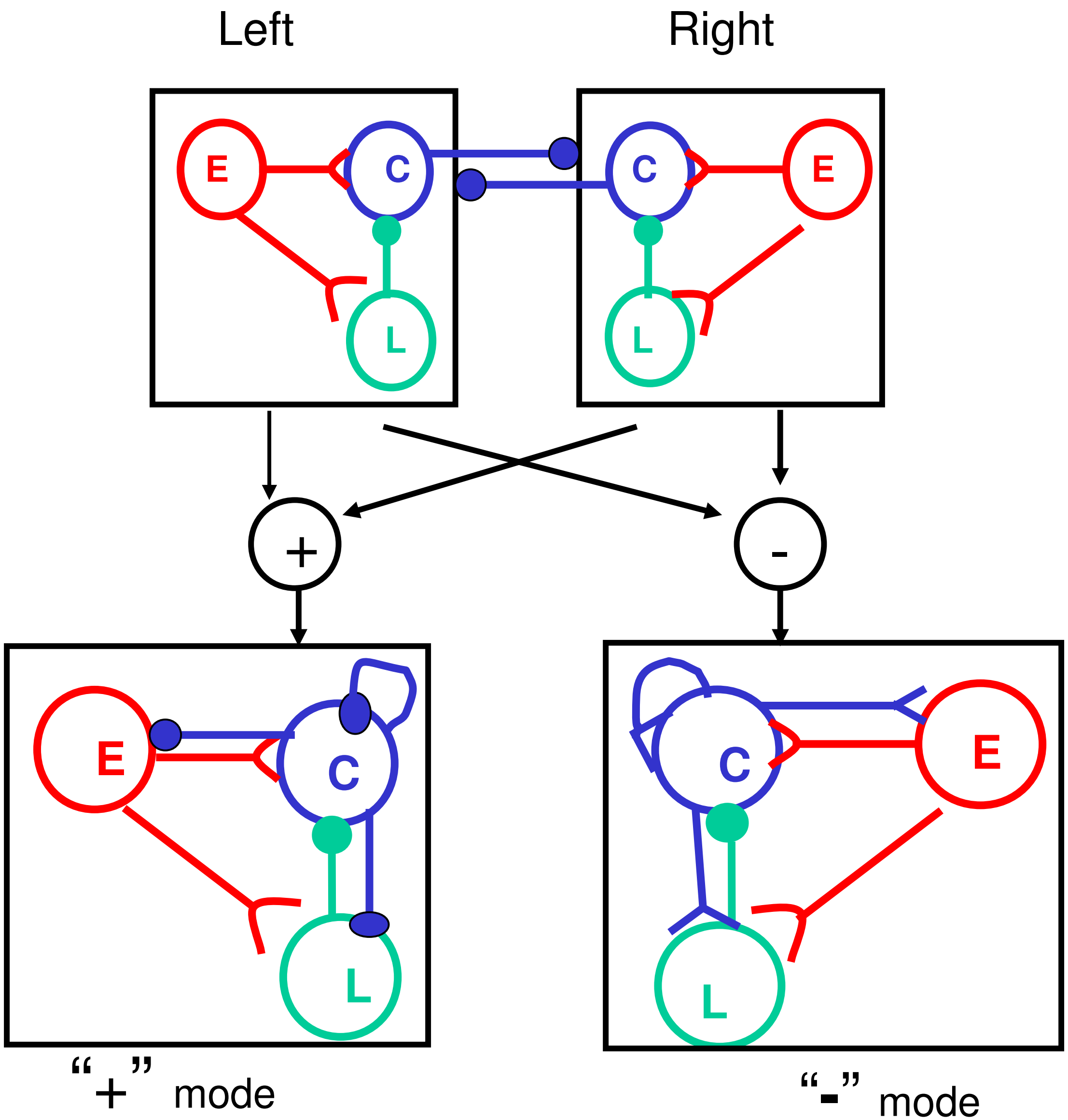
3. Computer simulation confirming the validity of the approximation

4. Nonlinear analysis --- to study coupling between modes and stability

5. Coupled oscillator analysis for boundary conditions

Left and right sides are coupled

$$\begin{pmatrix} E_+ \\ L_+ \\ C_+ \end{pmatrix} = \begin{pmatrix} E_L \\ L_L \\ C_L \end{pmatrix} + \begin{pmatrix} E_R \\ L_R \\ C_R \end{pmatrix}$$



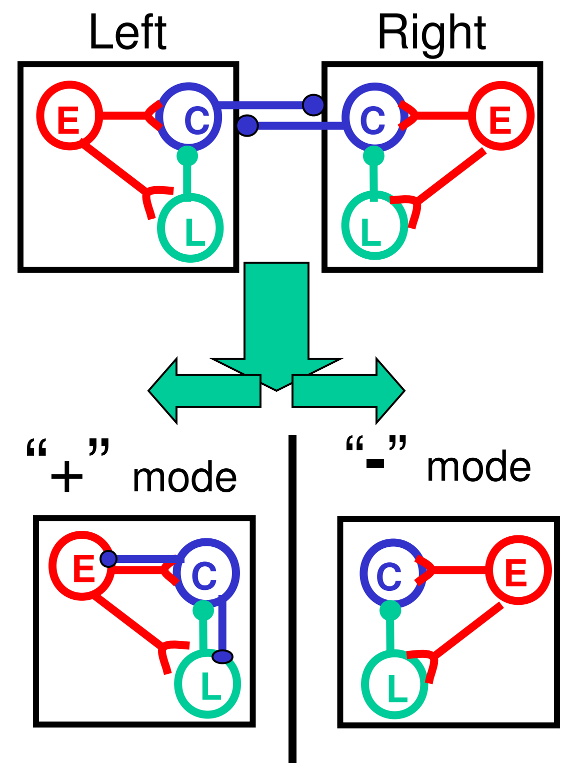
$$\begin{pmatrix} E_- \\ L_- \\ C_- \end{pmatrix} = \begin{pmatrix} E_L \\ L_L \\ C_L \end{pmatrix} - \begin{pmatrix} E_R \\ L_R \\ C_R \end{pmatrix}$$

The swimming mode !!

Now decoupled!

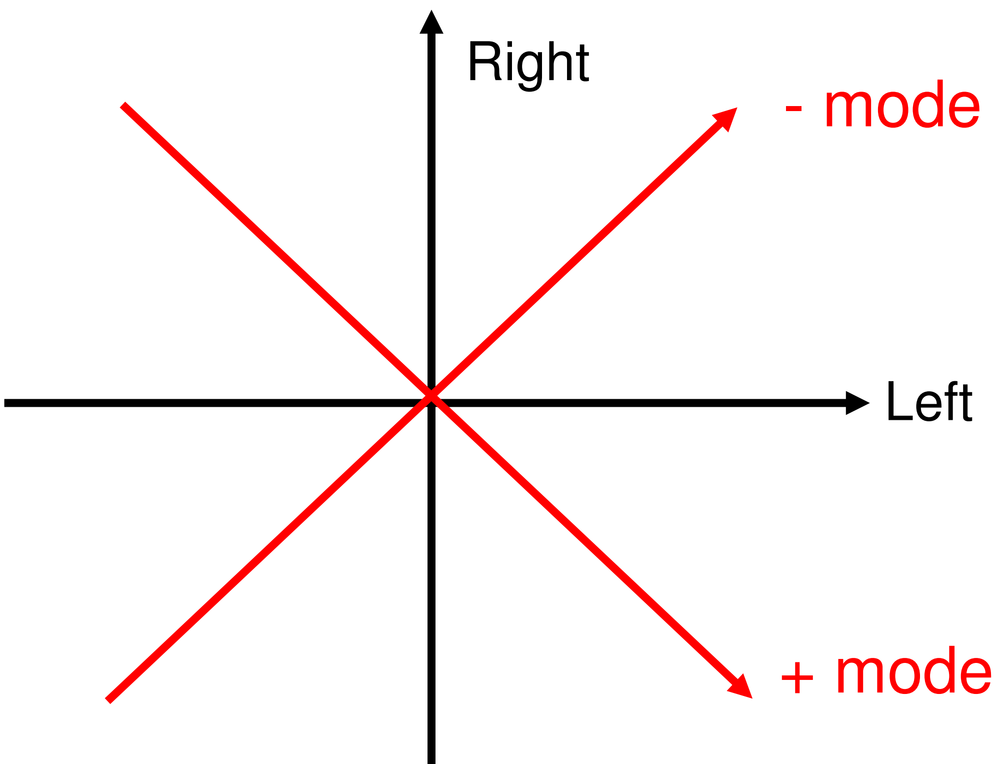
Mathematically:

$$\frac{d}{dt}\begin{pmatrix} E_L \\ L_L \\ C_L \end{pmatrix} = -\begin{pmatrix} E_L \\ L_L \\ C_L \end{pmatrix} + \begin{pmatrix} J & 0 & -K \\ W & 0 & -A \\ Q & -H & -B \end{pmatrix}\begin{pmatrix} g(E_L) \\ g(L_L) \\ g(C_R) \end{pmatrix} + \text{external inputs}$$



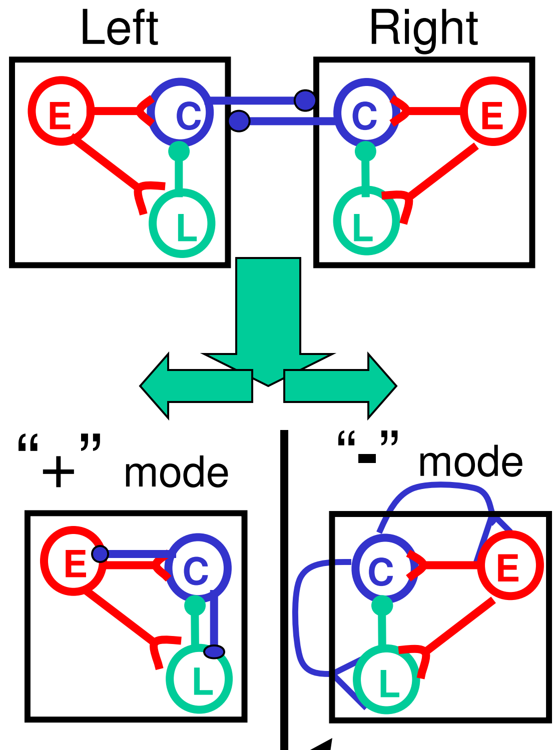
Linear approximation leads to decoupling

$$\begin{pmatrix} E_{\pm} \\ L_{\pm} \\ C_{\pm} \end{pmatrix} = \begin{pmatrix} E_L \\ L_L \\ C_L \end{pmatrix} \pm \begin{pmatrix} E_R \\ L_R \\ C_R \end{pmatrix}$$



Mathematically:

$$\frac{d}{dt}\begin{pmatrix} E_L \\ L_L \\ C_L \end{pmatrix} = -\begin{pmatrix} E_L \\ L_L \\ C_L \end{pmatrix} + \begin{pmatrix} J & 0 & -K \\ W & 0 & -A \\ Q & -H & -B \end{pmatrix}\begin{pmatrix} g(E_L) \\ g(L_L) \\ g(C_R) \end{pmatrix} + \text{external inputs}$$



Linear approximation leads to decoupling

$$\begin{pmatrix} E_\pm \\ L_\pm \\ C_\pm \end{pmatrix} = \begin{pmatrix} E_L \\ L_L \\ C_L \end{pmatrix} \pm \begin{pmatrix} E_R \\ L_R \\ C_R \end{pmatrix}$$

$$\frac{d}{dt}\begin{pmatrix} E_+ \\ L_+ \\ C_+ \end{pmatrix} = -\begin{pmatrix} E_+ \\ L_+ \\ C_+ \end{pmatrix} + \begin{pmatrix} J & 0 & -K \\ W & 0 & -A \\ Q & -H & -B \end{pmatrix}\begin{pmatrix} E_+ \\ L_+ \\ C_+ \end{pmatrix} + \text{external inputs}$$

$$\frac{d}{dt}\begin{pmatrix} E_- \\ L_- \\ C_- \end{pmatrix} = -\begin{pmatrix} E_- \\ L_- \\ C_- \end{pmatrix} + \begin{pmatrix} J & 0 & +K \\ W & 0 & +A \\ Q & -H & +B \end{pmatrix}\begin{pmatrix} E_- \\ L_- \\ C_- \end{pmatrix}$$

The connections scaled by the gain g'(.) in g(.), controlled by external inputs.

Swimming mode
C_- becomes **excitatory.**

Swimming mode always dominant!

Dynamics for the left-right antiphase (swimming) mode

$$\frac{d}{dt}\begin{pmatrix} E_- \\ L_- \\ C_- \end{pmatrix} = -\begin{pmatrix} E_- \\ L_- \\ C_- \end{pmatrix} + \begin{pmatrix} J & 0 & +K \\ W & 0 & +A \\ Q & -H & +B \end{pmatrix}\begin{pmatrix} E_- \\ L_- \\ C_- \end{pmatrix}$$

All connections J, W, Q, H, K, A,B are approximately that, e.g., connections J_{ij} depend only on segment difference

$x = i - j.$

Fourier Transform

$k=2\pi m/N$

$$\text{So } J_{ij} \longrightarrow J(x) \longrightarrow \mathcal{J}(k)$$

$$E_1, E_2, E_3 \ldots \longrightarrow E(x) \longrightarrow \mathcal{E}(k)$$

Amplitude of spatial waves $E(x) = \cos(kx+\varphi)$

$$J_{ij} E_j \longrightarrow J(x-x')E(x') \longrightarrow \mathcal{J}(k)\, \mathcal{E}(k)$$

Different waves k decouple from each other:

Fourier Connections

$$\frac{d}{dt}\begin{pmatrix} E(k) \\ L(k) \\ C(k) \end{pmatrix} = -\begin{pmatrix} E(k) \\ L(k) \\ C(k) \end{pmatrix} + \begin{pmatrix} J(k) & 0 & K(k) \\ W(k) & 0 & A(k) \\ Q(k) & -H(k) & B(k) \end{pmatrix}\begin{pmatrix} E(k) \\ L(k) \\ C(k) \end{pmatrix}$$

Solution:

$$\begin{pmatrix} E(k) \\ L(k) \\ C(k) \end{pmatrix} \exp[-t + \lambda(k) t]$$

eigenvector

Eigenvalue of

Fourier Connections

$$\begin{pmatrix} J(k) & 0 & K(k) \\ W(k) & 0 & A(k) \\ Q(k) & -H(k) & B(k) \end{pmatrix}$$

$-\mathrm{Im}(\lambda)$

$$\begin{pmatrix} E(k) \\ L(k) \\ C(k) \end{pmatrix} \exp[-t + \mathrm{Re}(\lambda)\, t \; - i\, \omega\, t]$$

Spatial waves, oscillating

at fr

Connection structure decides which wave k has **Re(λ(k)) > 1**

ding

Oscillation phase

$$\mathbf{E} \sim \exp[-t + \mathrm{Re}(\lambda)\, t \; - i\, (\omega\, t - k\, x + \Phi_E)]$$

$$\mathbf{L} \sim \exp[-t + \mathrm{Re}(\lambda)\, t \; - i\, (\omega\, t - k\, x + \Phi_L)]$$

$$\mathbf{C} \sim \exp[-t + \mathrm{Re}(\lambda)\, t \; - i\, (\omega\, t - k\, x + \Phi_C)]$$

k<0, phase descending from head to tail

Wave unsustainable unless Re(λ) > 1

Summary 1:

100x3x2 coupled neurons in a neural circuit of spinal cord

Left-right symmetry

100x3 coupled units in the swimming mode only

Translation symmetry

3 coupled units

Experimental data on phase pattern allow simplification

2 coupled units related to harmonic oscillator

Nonlinearity allows dominance of a single mode.

Selected mode controlled by neural connection patterns and external input --- testable predictions