Central Pattern Generating Neural Networks (CPGs):

Small, relatively simple neural systems with well-defined units, well-defined circuitry, and well-defined function

Such central pattern generators are believed to be responsible for practically all known muscle behaviour.
simple models for pattern generating networks

Wilson‘s model of the locust flight CPG (1961)

Delcomyn (1998)
Spinal Circuits for Generating Rhythm
**Postinhibitory rebound**: tendency of a neuron to fire a brief series of APs upon being released from inhibition, without any excitatory input.

Delcomyn (1998)
Rhythm generation in CPG circuits

Understanding CPG circuits:

Models of biological neural circuits generating self-sustained out-of-phase (or anti-phase) oscillations.

Figure with permission: A. Ayali
How do neuromodulators and neuromodulatory neurons reconfigure circuits so that the same group of neurons can produce a variety of behaviorally relevant outputs?
There are probably only few synapses which are not subject of some kind of modulation.

Marder, Thirumalai (2002)
Development of circuits that generate simple rhythmic behaviors in vertebrates

Martyn Goulding1 and Samuel L Pfaff2
Mathematical Modeling
Mathematical Analysis and Simulations of the Neural Circuit for Locomotion in Lampreys

Li Zhaoping,1 Alex Lewis,1 and Silvia Scarpetta2

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Experimental data

Spontaneous oscillations in decapitated sections with a minimum of 2-4 segments, from anywhere along the body.

Three types of neurons: E (excitatory), C (inhibitory), and L (inhibitory). Connections as in diagram

E, C neurons: shorter range connections (a few segments), L: longer range

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

E and L oscillate in phase, C phase leads.

Two segments in CPG
Neurons modeled as leaky integrators

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

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

\[J, K, \text{etc} \text{ are matrices:} \]

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

\[E_L, L_L, C_L \text{ are vectors:} \]

\[E_L = \begin{pmatrix} E^1_L \\ E^2_L \\ E^3_L \\ \cdot \cdot \cdot \end{pmatrix} \]
Left and right sides are coupled

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

Linear approximation leads to decoupling

\[
\begin{pmatrix} E_L \\ L_L \\ C_L \end{pmatrix} = \begin{pmatrix} E_R \\ L_R \\ C_R \end{pmatrix} \pm \begin{pmatrix} E_L \\ L_L \\ C_L \end{pmatrix}
\]

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

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

Swimming mode always dominant

Swimming mode becomes excitatory.
The swimming mode

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

Experimental data show E & L synchronize, C phase leads

\[
\frac{d}{dt} \begin{pmatrix} E \\ C \end{pmatrix} = \begin{pmatrix} J^{-1} & K \\ Q & -H & B^{-1} \end{pmatrix} \begin{pmatrix} E \\ C \end{pmatrix}
\]

Prediction 1: H > Q needed for oscillations!

Oscillator equation:

\[
\frac{d^2}{dt^2} E + (2-J-B) \frac{d}{dt} E + [(1-J)(1-B) + K(H-Q)] E = 0
\]

Damping

Restoration force
Oscillator equation: \[\frac{d^2}{dt^2} E + (2-J-B) \frac{d}{dt} E + [(1-J)(1-B) + K(H-Q)] E = 0\]

Single segment: \(J_{ii} + B_{ii} < 2\) → Self excitation does not overcome damping

An isolated segment does not oscillate (unlike previous models)

**Inter-segment interaction:**
\[\frac{d^2}{dt^2} E_i + a \frac{d}{dt} E_i + w_o^2 E_i = \sum_j F_{ij}\]

\(i\)th damped oscillator segment of frequency \(w_o\)

Driving force from other segments.

When driving forces feed “energy” from one oscillator to another, global spontaneous oscillation emerges.

**Coupling:** \(F_{ij} = (J_{ij} + B_{ij}) \frac{d}{dt} E_j + [B+J]_{ij} E_j - [BJ+K(H-Q)]_{ij} E_j\)
**Controlling swimming directions**

**Coupling:**

\[ F_{ij} = (J_{ij} + B_{ij}) \frac{d}{dt} E_j + [B+J]_{ij} E_j - [BJ+K(H-Q)]_{ij} E_j \]

- Feeds energy when \( E_i \) & \( E_j \) in phase
- Feeds energy when \( E_i \) lags \( E_j \)
- Feeds energy when \( E_i \) leads \( E_j \)

**Given** \( F_{ji} > F_{ij} \), (descending connections dominate)

- \( B+J > BJ+K(H-Q) \) → Forward swimming (head phase leads tail)
- \( B+J < BJ+K(H-Q) \) → Backward swimming (head phase lags tail)

**Prediction 2:** swimming direction could be controlled by scaling connections \( H \), (or \( Q \), \( K \), \( B \), \( J \)), e.g., through external inputs
More rigorously:

\[
\begin{align*}
\frac{d}{dt} \begin{pmatrix} E_- \\ C_-
\end{pmatrix} &= \begin{pmatrix} J^{-1} & K \\ Q^{-1} - H & B^{-1}
\end{pmatrix} \begin{pmatrix} E_- \\ C_-
\end{pmatrix}
\end{align*}
\]

Its dominant eigenvector \( E(x) \sim e^{\lambda t + ikx} \sim e^{-i(\omega t - kx)} \) determines the global phase gradient (wave number) \( k \)

For small \( k \), \( \text{Re}(\lambda) \approx \text{const} + k \cdot \text{function of } (4K(H-Q) - (B-J)^2) \)

+ve \( k \)  \hspace{1cm} forward swimming

-ve \( k \)  \hspace{1cm} backward swimming

Eg. Rostral-to-caudal \( B \) tends to increase the head-to-tail phase lag (\( k>0 \)); while Rostral-to-caudal \( H \) tends to reduce or reverse it (\( k<0 \)).

So, increasing \( H \) (e.g., via input to \( L \) neurons) \hspace{1cm} Backward Swimming
Simulation results:

Forward swimming

Increase H, Q

Backward swimming

Segment Number
Turning

Amplitude of oscillations is increased on one side of the body.

Achieved by increasing the tonic input to one side only (see also Kozlov et al., Biol. Cybern. 2002)
Summary

Analytical study of a CPG model of suitable complexity gives new insights into

- How coupling can enable global oscillation from damped oscillators
- How each connection type affects phase relationships
- How and which connections enable swimming direction control.

Further work:

Include synaptic temporal complexities in model → Control of swimming speed (oscillation frequency) over a larger range
Renshaw Cell
Motor neurons send collaterals to small interneurons.

Excitability of motor neurons was reduced following electrical stimulation of its peripheral axon.
Renshaw Cells: Spinal Inhibitory Interneurons

Renshaw cells produce ‘Recurrent Inhibition’.
Increase motor neuron firing causes increased inhibition via Renshaw Cell (also to inh\(^n\) of synergist muscles)

Acts to prevent large transient changes in motor neuron firing
Renshaw Cells: Spinal Inhibitory Interneurons

Renshaw cells ‘Dysinhibit’ antagonistic muscles

Recurrent inhibition of muscle & dysinhibition of antagonist acts to prevent large sudden movements

Descending Cortical Pathways modulate Renshaw Cells
Recurrent inhibition:
Renshaw cells control the degree of efferent signal sent to the muscle

Presynaptic inhibition
Interneurons mediate the afferent signal before it gets to motor neuron, influencing the signal sent back to the muscle
Evolutionary Training of a Biologically Realistic Spino-neuromuscular System
Stanley Gotshall
Results

With Renshaw Interconnections

Behavior with network *with* Renshaw interconnections

Fitness = -10.08
Results

No Renshaw Cells

Behavior with no Renshaw cells

Fitness = -114.51
Results

No Renshaw Interconnections

Behavior with *no* Renshaw interconnections

Fitness = -16.09
Results

Trainability
Average Best Fitness v. GA Iterations
75,000 GA Iterations

Interconnecting Renshaw Cells
Single Renshaw Cell Connection
Observations

• GA is successful in training controlled behavior.
• Removing Renshaw cell connections makes training difficult.
• GA takes advantage of more complex model.
Second Paper
Using Genetic Algorithms to Train Biologically Realistic Spino-neuromuscular Behaviors

- Introduction
- Experiments
- Results
- Conclusions
Introduction

• Uses more complex model
  – Train model with six muscle units and proxy afferent neurons.
  – Allow GA to evolve the strengths of each muscle unit.

• Hypotheses
  – The GA will find better solutions when training muscle unit strengths (force multipliers)
  – Adding a proxy afferent neuron will result in more realistic alpha-MN firing patterns.
New Network Model

Subnet Input

Inhibitory Connections to Other $\alpha$-Motoneurons

Synfire Chain

Alpha-MN

Renshaw Cell

Gamma-MN

Proxy Afferent Neuron

Contractile Element
Experiments

• Renshaw cells vs. no Renshaw Cells
• Training with Muscle Force Multipliers With and Without Renshaw Cells
• Training With Proxy Afferent Neurons
• Vary Forearm Mass With and Without Afferents
Renshaw cells vs. no Renshaw cells

- Fixed force force multiplier (0.8)
- Upward frequency 1 in 6
- Downward frequency 1 in 140

- Purpose
  - (confirm that results are consistent with first paper)
Results – Renshaw cells vs. no Renshaw cells

• Trends from first paper hold.

• This is a good thing!
Trained Muscle Force Multipliers With and Without Renshaw Cells

- 2 Configurations
  - Same parameters as first experiment
- Purpose
  - In biology, strengths of muscle units vary. So we add this flexibility to the model.
- No longer only training synaptic weights. Now we also train the strengths of the muscle units.
Results – Trained Force Multipliers With and Without Renshaw Cells

• Both cases show improvement when force multipliers are trained.
Results – Trained Force Multipliers With and Without Renshaw Cells

Renshaw cells become less relevant because GA uses force multipliers to compensate.
Results – Trained Force Multipliers With and Without Renshaw Cells

Sample Arm Behavior With Renshaw Cells and Trained Force Multipliers
Trained with Proxy Afferent Neuron

- Add proxy afferent neuron and gamma motoneuron
- 6 motor units up – 3 motor units down
- Upward frequency 1 in 6 (same)
- Downward frequency 1 in 12
  - Potentially smoother downward motion
  - The GA can train a given motion with different frequencies.
- Purpose (Observe effect of active feedback)
Results – Trained with Proxy Afferent Neurons \textit{and} Force Multipliers
Results – Trained with Proxy Afferent Neurons and Force Multipliers
Results – Trained with Proxy Afferent Neurons and Force Multipliers
Results – Trained with Proxy Afferent Neurons and Force Multipliers

Alpha-MN Recruitment with Afferents

0.2 Second Delay
Vary Forearm Mass With and Without Afferents

• Train 4 configurations
  – 0.55 kg / no afferents
  – 0.55 and 0.65 kg / no afferents
  – 0.55 kg / with afferents
  – 0.55 kg and 0.65 kg / with afferents

• Purpose
  – To test networks on parameters they weren’t explicitly trained on
Results – Vary Forearm Mass With and Without Afferents

- Training with multiple masses results in more robust solutions

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<th>0.45kg</th>
<th>0.50kg</th>
<th>0.55kg</th>
<th>0.60kg</th>
<th>0.65kg</th>
<th>0.70kg</th>
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<tbody>
<tr>
<td>1 mass / no aff.</td>
<td>-101.97</td>
<td>-88.95</td>
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<td>-137.97</td>
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<td>-67.64</td>
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<tr>
<td>2 masses / with aff.</td>
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<td>-15.33</td>
<td>-23.64</td>
<td>-78.52</td>
<td>-212.48</td>
</tr>
</tbody>
</table>
Conclusions

• Training with a GA is a reasonable method to model biologically realistic behaviors in neuromuscular systems.
  – GA is an effective training tool for the system
  – GA finds better solutions as the model gets more complex (Renshaw cells, variable muscle strengths)
  – Active feedback from the muscle results in more biologically realistic behavior.

• Model has promise for testing hypotheses regarding SNMS pathways and components.
Future Work

• Make so anyone can use
• Expand Model
  – Model intrafusal fiber
  – Triceps
  – Multiple joints
  – More spinal connections
The End
Group 1a Inhibitory Interneurons

1a Inhibitory interneuron produces reciprocal inhibition of antagonistic muscle
Group 1a Inhibitory Interneurons

Descending Cortical Pathways can counteract Reciprocal Innervation to produce Co-Contraction (stiffening of a joint).

Allows fine control of joint stiffness
1b Inhibitory Interneuron

1b Inhibitory Interneurons receive convergent input from Cutaneous and Golgi Tendon Organs

1b Inhibitory Interneurons inhibit homonymous muscle and excite antagonistic muscles

This is opposite to the innervation of 1a Inhibitory Interneurons
1b Inhibitory Interneuron

Cutaneous input reduces firing rate of motor neuron

Provides a spinal mechanism for fine control during exploratory movements

Descending inputs can modulate sensitivity of 1b afferent input
Summary

- The STNS of crustaceans - preliminary the STG -, serves as a model system to study the properties and the modulation of central pattern generators (CPGs).
- A CPG consists of a network of neurons and produces a repetitive output pattern, generally needed for stereotype movements (e.g. stomach movements, walking, flying, breathing etc.).
- The properties of a CPG depend on intrinsic properties of the individual neurons and their connectivity.
- Both, intrinsic properties and connectivity can be subject of modulation – which eventually allows flexibility of the output pattern.
- Activity of the STG circuits can be modulated by a large amount of neuromodulators, brought by projection neurons from other areas of the NS or hormonally.
- Co-transmission plays an important role in neuronal network modulation.
- Co-transmitters can act on different or on the same targets within cells.