April 8, 2013
Disease Presentation
Simulation
Introduction to Remote
Control of Neuronal Activity
Monitoring Behavior
Maggot Neurobiology

Childhood Absence Epilepsy
Symptoms:
• onset 4-10 yrs, peak 5-7 yrs
• short lasting (~10 s) seizures
• sudden impairment of consciousness
• interruption of ongoing activity
• upward blank stare

Prognosis: most patients “grow out” of it
Hypothesized Cause:
• genetic mutations alter T-type calcium channel properties (e.g., lower voltage activation)
• found often in thalamus
• open near resting potential
• create low-threshold spikes after EPSPs
• depolarized beyond threshold for Na-dependent APs

Drug:
• Zarontin (ethosuximide)
  • Prevents absence seizures
  • Although debated, commonly believed to be T-type channel blocker

Characteristic 3Hz spikes
Mark and Dinan

Remote Control of Neuronal Activity
Electrical stimulation
Problems?: precise stimulation low yield tedious
Remotely Stimulate
Record Neural Activity or Behavior

What ways can we alter neuronal activity or behavior?

What people have used:
Long Term?:
• Toxins
• Gene Knockouts
• Gene over-expression

Big Problem??:
• Homeostatic compensation
**What people have used:**

Short term:
- Temperature sensitive - Shibere synaptic mutants
- Insect neuromodulators linked with K channels
- Light-activated channels

![Optogenetic excitation and inhibition](image)

**Shibere**, a temperature sensitive fly mutant, vesicle recycling is blocked

Depression correlates with depleted vesicles

**Maggot Neurobiology**

Channelrhodopsin - cation channel
Halorhodopsin - Cl channel
Archaerhodopsin - proton pump (H+)
Light-activated G proteins
Bacterial second messenger activation

![Maggot life cycle](image)
Monitoring Behavior; Examples of behavioral components of male fly aggression

Wing threat  Lunge  Hold

Tussle  Box

Example Behavior: Aggression in male fly aggression

http://www.hms.harvard.edu/bss/neuro/kravitz/movie/flymoviewithmusic.mov

Table 1: Ethogram of offensive and defensive actions of male flies during agonistic encounters

<table>
<thead>
<tr>
<th>Component Description</th>
<th>Offensive actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approach</td>
<td>One fly lowers body, then advances in the direction of the other</td>
</tr>
<tr>
<td>Low-level fencing</td>
<td>Both flies extend one leg and tap opponent's leg</td>
</tr>
<tr>
<td>High-level fencing</td>
<td>One or both flies face each other, extend leg forward and push opponent</td>
</tr>
<tr>
<td>Chasing</td>
<td>One fly runs after the other</td>
</tr>
<tr>
<td>Lunging</td>
<td>One fly rears up on hind legs and snaps down on the other</td>
</tr>
<tr>
<td>Holding</td>
<td>One fly grasps the opponent with forelegs and tries to immobilize</td>
</tr>
<tr>
<td>Boxing</td>
<td>Both flies rear up on hind legs and strike the opponent with forelegs</td>
</tr>
<tr>
<td>Tussling</td>
<td>Both flies tumble over each other, sometimes leaving food surface</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Component Description</th>
<th>Defensive actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walk away</td>
<td>Loser turns and retreats slowly from advance of winner</td>
</tr>
<tr>
<td>Defensive wing threat</td>
<td>Loser flicks wings at 45° angle while facing away from opponent</td>
</tr>
<tr>
<td>Run away</td>
<td>Loser runs away quickly from advance of winner</td>
</tr>
<tr>
<td>Fly away</td>
<td>Loser flies off food surface</td>
</tr>
</tbody>
</table>

Within each category the order of the components is roughly in increasing levels of intensity.

Quantitative description of male fly aggression

This week's ethograms

http://www.hms.harvard.edu/bss/neuro/kravitz/movie/flymoviewithmusic.mov

Forward locomotion  anterior exploration
anterior movement

Blue light
Larval electrophysiology preparation

Larvae pinned dorsal side up

- Head (dark mouthparts)
- Tail (dark spiracles)

Dorsal surface (two large silver tracheae running in parallel, under the skin)

Larval neuromuscular system is a model preparation

Nervana2-gal4; UAS-GFP (Salveterra et al. 1999)

Synaptic Physiology at larval NMJ

Larval electrophysiology preparation

Filleted maggot

- Head
- Brain
- Motor Nerves
- Body Wall Muscles
- Synapse
Synaptic Physiology at larval NMJ

Close-up of anti-HRP stained neuromuscular junction

This week’s lab

Remote activation of synapses

Facilitation with light pulses- New Results 4910 2010