

GAP-FREE NEURAL CIRCUITS – CLASS #6: *C. elegans* olfaction and chemotaxis

OUTLINE:

- **Directed locomotion**
- **Chemical sensing**
- **Neural circuit for chemotaxis**

Directed locomotion

- SLIDES: Picture of worm chemotaxis behavior
- Strategies for chemotaxis
 - Klinokinesis: Biased random walk (e.g. bacteria)
 - Compare concentrations in time (e.g. is now better than before?)
 - If concentration is increasing, go straight (run)
 - If concentration is decreasing, randomly reorient (tumble)
 - Klinotaxis: Weathervane (e.g. maggots)
 - Compare concentrations in space (e.g. left/right)
 - If concentration is higher on one side, curve movement to that side
 - Worms do a bit of both
- SLIDES & VIDEO: klinokinesis vs. klinotaxis
- Movements for directed locomotion:
 - **Small angle turns** (~50°): forward with nose bending as a rudder
 - Medium angle turns (~100°): reverse followed by forward in a new direction
 - Large angle turns (~180°): omega bends / pirouettes
- SLIDES & VIDEO: locomotion patterns

Chemical sensing

- Cilium – organelle associated with sensory function
- 60 ciliated neurons (20% of all neurons)
- Principal head sensilla is the amphid, which includes 12 neurons (2 amphids per head)
- DRAW: head with sensilla
- 2 kinds of chemical sensing
 - Smell (olfactory) – molecules present in gases (volatile odorants)
 - Taste (gustatory) – molecules present in liquids or solids
- SLIDES
- Odortaxis = odorant-induced movement up an odor gradient
- Table of attractants

<i>Attractant</i>	<i>Smells like</i>	<i>Natural source</i>
Isoamyl alcohol (IA)	Banana	bacteria?
Benzaldehyde	Almonds	nuts, fruits
Butanone	Sweet	trees, fruits, vegetables
Diacetyl	Butter	fermentation

Pyrazine	Lots of things	foods
Trimethylthiazole	Chocolate	foods

Neural circuit for chemotaxis

What are the sensory neurons for these odors?

- Systematic ablation to identify neurons required for chemotaxis
 - AWC: benzaldehyde, butanone, isoamyl alcohol, trimethylthiazole
 - AWA: diacetyl, pyrazine, trimethylthiazole
- All can be distinguished from each other
- **How can single sensory neurons distinguish multiple odors?**
 - Adaptation: continuous stimulation is ignored while changing stimuli are not
 - Separate molecular pathways:
 - Sensory protein is usually 7-TM GPCR (DRAW) – 1000s in worm genome
 - GPCRs can use different G-alpha's, which can have different downstream effects
 - Different ion channels or different sets of the same ion channel may be used
- Different than mammals, where a single olfactory expresses only one olfactory receptor
- Olfactory receptors still unknown, except for diacetyl, which is sensed by ODR-10 in AWA
- SLIDES

How does AWC respond to odors?

- IA addition slightly reduces calcium
- IA removal significantly increases calcium! That's unexpected...
- Blocking synaptic release of glutamate from AWC blocks omega turns in response to odor removal
- So, AWC promotes chemotaxis by initiating turning when attractant is reduced (klinotaxis or klinokinesis)
 - Turns out omegas are not truly random but directed, so not a random walk
- SLIDES

What's happening downstream?

- Connectome shows AIY, AIA, and AIB downstream of AWC
- Following data shows correlation and necessity, but not acute sufficiency
- **AIA**
 - IA addition increases AIA calcium, suggesting inhibitory connection from AWC
 - AWC ablation blocks AIA response, so AWC upstream
 - Glutamate neurotransmission mutants (*eat-4*) is defective in chemotaxis and AIA response
 - Inhibitory glutamate receptor *glc-3* mutants are also defective in AIA response (partial)
 - AWC expresses *eat-4*

- Suggests that IA addition reduces AWC calcium which reduces inhibition on AIA, yielding a net increase
 - SLIDE
- **AIB**
 - IA removal increases AIA calcium, suggesting excitatory connection from AWC
 - AWC ablation blocks AIB response, so AWC upstream
 - Excitatory glutamate receptor *glr-1* mutants are defective in AIB response
 - So IA removal increase AWC glutamate which excites AIB via *glr-1*
 - SLIDE
- **AIY**
 - IA addition increases AIY calcium, suggesting inhibitory connection from AWC
 - AWC ablation blocks AIY response, so AWC upstream
 - Inhibitory glutamate receptor *glc-3* mutants are also defective in AIY response
 - So IA addition reduces AWC calcium which reduces inhibition on AIY, yielding a net increase
 - SLIDE

How does the activity of these interneurons lead to chemotaxis?

- SLIDE: Odors given at one phase of nose bend control turning
- Strategy: Use stimulation/inactivation to find neurons upstream and downstream of AIY
- **AWC**: stim causes turning in opposite direction
- **AIY**: stim causes turning in same direction
- **AIZ**: stim causes turning in opposite direction
- **SMB**: stim causes turning in same direction
- **RME**: stim causes turning in opposite direction
- Weakness: no ablation/inactivation analysis with activation to show ordering of neurons (instead rely entirely on connectome), so circuit as drawn is largely hypothetical

CONCLUSION:

Worm chemotaxis uses a serial inhibitory neural circuit that modulates dorsal vs. ventral bending to turn to the side with higher attractant. (klinotaxis)