Sensory Encoding of Smell in the Olfactory System of Drosophila

(reviewing “Olfactory Information Processing in Drosophila” by Masse et al, 2009)

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Smell Drives Our Behavior...

FOOD

SEX

and...
Food Aversion!
This Week

- Today:
  - Olfactory coding in drosophila

- Thursday:
  - Olfactory coding in mammals
  - Explore a bit (taste? pheromones? memory?)
Why Drosophila

• You can poke 'em for real cheap!
• We're REALLY good at controlling their genetics,
  - And olfaction is ALL about controlling your molecular chemistry!
• Olfactory Receptors (ORs) are highly preserved
• Processing stages through first two neurons are functionally similar with mammals
• Because flies are cute:
Today

- Gross anatomy of drosophila olfactory system
- Transduction (chemistry = bad)
- Basic Sensory Coding
  - glomeruli
- Downstream Transformations
  - Projection neurons
  - Kenyon cells
- Smells!
Gross Anatomy

Fig. 1 from Masse et al (2009)

Keene & Waddel (2007)
Gross Anatomy of Coding

- **Antenna**
  - Olfactory Receptor Neurons (ORNs)

- **Antennal lobe**
  - Glomeruli
  - Projection Neurons (PNs)
  - Local Neurons

Keene & Waddel (2007)
Cytoarchitecture of Coding

- **Antenna**
  - Olfactory Receptor Neurons (ORNs)

- **Antennal lobe**
  - Glomeruli
  - Projection Neurons (PNs)
  - Local Neurons
1\textsuperscript{st} Order Neurons: ORNs

- Located in antennae and maxillary palps (~1300 per)
  - ORs are transmembrane molecules in cilia
  - Use G protein second-messenger signaling
    - Influx of Na\textsuperscript{+}, K\textsuperscript{+}, Ca\textsuperscript{+}
    - Outflux of Cl\textsuperscript{-}

- 50 “classes”
  - Express one specific set of ORs (usually OR83b PLUS 1-3 receptors)
  - Each “class” respond typically

Firestein & Menini (1999)
Tuning Curves of ORNs

2\textsuperscript{nd} Order Neurons: Projection Neurons

- Live in antenna lobe (~200 per)
- Receive input from \textbf{ALL ORNs of a single class} (~50; ~25 from each side)
- Despite convergent input, show \textit{broader} odorant tuning than ORNs
- Project out to “higher centers”: mushroom body & lateral horn
Between 1\textsuperscript{st} and 2\textsuperscript{nd} Order: Glomeruli

- In Antenna Lobe, one per odorant “class” (50)
- Consist of:
  - Axons of ORNs
  - Dendrites of projection neurons
  - Neurites (axons and dendrites) of local neurons
- ORN inputs all from same “class”, come bilaterally
- PNs tend to innervate ONLY one glomerulus

Kandel, Jessel, Schwartz (2000)
Glomeruli: Local Neuron Connectivity

- Interglomerular EXCITATORY
  - Input from ORNs
  - Output to PNs
  - Strengths “non-uniform”

- Interglomerular (and intraglomerular) INHIBITORY
  - Input from ORNs, PNs
  - Output to ORNs, PNs
  - Interglomerular scales with ORN output strength

- “Probably all permutations exist”

Fig. 2 from Masse et al (2009)
Coding: From Odor to Behavior

- 50 odorant receptor classes to detect
- Hundreds of odorants
- Combinatorial explosion of smells (combination of odors)
- Must be population / ensemble encoding

- From odor → spikes → ensembles → behavior

3 types of cones, TrueColor displays > 16M colors
Coding: From Odor to Spikes

- Not well understood
- Each odorant has many molecular properties
- Interaction between molecular properties and spiking behavior not well understood

Fig. 3 from Masse et al (2009)
Coding: Single ORN to Ensembles

- ORNs respond to many odors
- Some ensemble firing patterns will represent odors
- **Focus of paper:** from individual ORN activity to *ensemble* PN activity

Fig. 3 from Masse et al (2009)
Coding: Ensemble Spiking to Behavior

- Not well understood
- Correlational study
  (Riffel et al, 2009)
  - Only a few odorants are necessary and sufficient to produce behavior
  - Mean firing and synchronous firing both correlate with elicitation of natural behavior

Riffel et al (2009)
Transformation I: Increasing SNR

• How?
  – Big Idea: Averaging (woo!)
  – Small Idea: Strong, reliable synapses

• Advantages: fewer synapses, faster decisions
Transformation II: Variable Gain

• Now THIS is cool!

• 200-300 spikes/s can represent 8 orders of magnitude in concentration

• *Per-glomerulus* control!

• How?
  
  − Short-term synaptic depression
  
  − Local neuron inhibition
    
    − Interglomerular: coordinate gain control across glomeruli
    
    − Intraglomerular: scale according to concentration

Fig. 5 from Masse et al (2009)
Transformation II: Variable Gain

Fig. 5 from Masse et al (2009)
Issues in Gain Control

• Low gain (high concentration): can measure changes?
  – Multiple ORNs active at high concentration
  – Variability in ORN sensitivity

• What to adjust gain-based connectivity on?
  – Most probable smells?
  – Most behaviorally relevant smells?
  – Ex. pheromone vs $\text{CO}_2$: gain control on pheromones, not $\text{CO}_2$

• Interglomerular inhibition: masking smells?
  – Strong fruit smell inhibiting pheromone scent

• Representing concentration...?
  – Changes in firing of PNs due to concentration are different for each odorant (in locust, at least...)
Decorrelation?

- ORNs responses are highly correlated
- Gain control histogram-equalizes
  - Each neuron uses its dynamic range better
  - But not all of coding space is used, due to spike correlations

- How to decorrelate?
  - If ORNs respond together, use global signal to decorrelate
  - If ORNs are more pairwise correlated, more complex lateral connections needed
    - Role for lateral excitatory cxns?
Mushroom Body and Kenyon Cells

- 150-200 PNs **diverge** to 2500 Kenyon cells
- Highly odor-specific
- Sparse coding
  - Spiking studies
  - Calcium influx
- Respond much more strongly than PNs

Keene & Waddel (2007)
Sparse Coding in Kenyon Cells

- IN THE LOCUST
  - PNs (columns) respond to most odorants; KCs (columns) respond to very few
  - “Population sparseness” - % of cells that do NOT respond to an odor (rows)
How Do Locust KCs Become Sparse?

- High convergence (400:1, 50% of PNs!)
- Weak unitary synaptic connections
- Synaptic integration in (oscillatory) time windows
- Voltage-gated channels amplify coincident spikes
- High spiking threshold (50-100 coincident PNs)
- Loss of oscillations in bees → no “fine” discriminations

Fig. 7 from Masse et al (2009)
How Do Drosophila KCs Become Sparse?

- Low convergence (10:1, 5% of PNs!)
- Strong unitary synaptic connections
- Non-oscillatory decoding
- Probably cannot sustain oscillations with 10 input neurons
- ? Integrator model / Hebbian learning?
Summary

- Drosophila olfactory system similar to mammalian
- Odorant receptor neurons (antennae) broadly tuned
- Projection neurons (antenna lobe) broadly tuned
- Glomeruli (antenna lobe) mediate SNR, gain control, and (perhaps) decorrelation, output via PNs
- Kenyon cells create sparse (oscillatory?) representations of odors
Higher Centers

• Lateral horn:
  • Sensory-motor integration
  • No MB: still discriminate
  • PN inputs highly stereotyped across animals
  • Spatial map of behaviorally relevant odorant types?

• Mushroom Body:
  • Needed for associative learning
  • Few output neurons, far from motor control
  • Perhaps useful for oscillations (but what about drosophila?)
  • Decorrelate inputs via output cell cross-inhibition?
Olfactory Generator Potentials

- **Odorant** binds to the **odor receptor**
- **Odor receptor** changes shape and binds/activates an “olfactory-type” **G protein**
- **G protein** activates the **lyase - adenylate cyclase (LAC)**
- **LAC** converts ATP into **cAMP**
- **cAMP** opens cyclic nucleotide-gated **ion channels**
- Calcium and sodium ions to enter into the cell, depolarizing the ORN
- Calcium-dependent Chlorine channels contribute to depolarization as well
Confusing Jargon

• “Transmembrane receptors … whose membrane topology is inverted compared with the … receptor superfamily that includes vertebrate odorant receptors”
  – The receptors are inverted (inside-out or upside-down?) compared to those in vertebrates!

• “Or83b … heterodimerises with other odorant receptors, is required for their trafficking to the dendrites and may act as a co-receptor”
  – Or83b may bind to other odorant receptors to improve the function of that receptor, or may help get the receptor proteins to the sensory cilia of the ORN.