Quantitative measurements of olfactory perceptual thresholds in *Drosophila*

Introduction

A large body of work has revealed the molecular, genetic, and circuit substrates for odor-driven behaviors in *Drosophila melanogaster* (Wilson, 2013). However, quantitative measurements of the performance limits of odor-driven behaviors in flies are comparatively rare, and are a necessary step towards understanding the neural codes underlying behavior. For this project I will be investigating the perception of odor in *Drosophila* and more specifically making quantitative measurements of the threshold for odor detections and discrimination. I will be using *Drosophila* as the subject of my investigation as they have a numerically compact brain, and a sophisticated genetic toolbox for manipulating circuit functions. Most olfactory neurons are also stereotyped in Drosophila, and one can find neurons with the same connectivity and physiology in every individual brain. *Drosophila* also have genetic labels for specific neurons and these labels can be used to target specific neurons for electrophysiological measurements.

Previous work (Parnas *et al.*, 2013) has shown the ability of *Drosophila* to discriminate between two different smells, and to show an innate bias towards a specific odor. However, this work did not address the thresholds for odor detection and discrimination as a function of the firing rate of the primary olfactory receptors. This information is critical to understanding odor processing in the fly antennal lobe.

In *Drosophila* odor is detected and then processed by the primary olfactory center, the antennal lobe (Tanaka *et al*., 2012). The antennal lobe has a glomerular structure, where each glomerulus receives input from a certain type of olfactory receptor neuron (ORN), creating a map of the odor quality. Output projection neurons (PNs) innervate the antennal lobe to take information to higher brain regions. This organization of the antennal lobe allows for parallel processing of olfactory input by many parallel coding channels, each of which can be genetically identified.

Objectives

The goals of this project are to make quantitative measurements of olfactory perceptual thresholds in Drosophila, and to investigate the rules by which the presence of sustained odors in the environment (background odors), affect odor detection. We would like to measure olfactory behavioral performance as a function of spike rates of the relevant olfactory receptor neuron classes. This will allow us to quantify odor perception in *Drosophila* and will help answer the following questions. How is odor detection affected when there is a constant background odor present? If so, then does the change in detection threshold depend on the identity of the background odor? Can we reduce the detection threshold by giving the target and background odor independent temporal dynamics? Does fly olfaction obey Weber's law which states that the smallest discriminable difference between stimuli scales linearly with stimulus intensity?

Approach

We will adapt existing behavioral assays from the literature and apply them to measuring olfactory perceptual thresholds in individual flies. We will build a long chamber with two ends, at which odor will be able to be pumped into the chamber in vapor form. We will mix the odor to a specific concentration in mineral oil solvent sealed in a vial, and then pump air through the headspace of the vial to deliver the odor into the chamber.

First we will use positive or negative associative conditioning to “clamp” the motivation of the flies and maximally motivate the flies to detect the target odor. Briefly the target odor will be presented in close temporal association with an innately appetitive (i.e. sugar) or aversive (i.e. electric shock) unconditioned stimulus to maximally motivate the animals to respond to the target odor. This should allow the flies to easily discriminate all odor pairs at the concentrations presented, and thus enable our measurements of perceptual threshold.

We will then perform a series of trials with *Drosophila* inside the chamber with fixed concentrations and combinations of odor on either end of the chamber. We will quantify odor preference index as the percentage of decisions in favor of the chosen odor during a testing interval of four minutes. A decision will be counted every time the fly enters and exits the choice zone between the two odors on each side of the chamber (Claridge-Chang *et al.*, 2009).

We will then proceed to record neural firing rates from olfactory receptor neurons that are known to respond to the odors used. This would allow us to understand how behavioral performance quantitatively relates to neural firing rates.

After collecting both the preference index data and the olfactory receptor neuron firing rates for each of the odors, I will perform a thorough MATLAB analysis on these results. I hypothesize that the presence of sustained background odors will increase the threshold for detection of the target odor (background odor suppression). Since background odor suppression is thought to arise from global gain control, I also hypothesize that the identity of the background odor should not affect background odor suppression, as long as it is an odor that broadly activates a large proportion of the primary olfactory receptor neurons

Timeline

- Design and manufacture of chamber to run trials in: 2-3 weeks.
- Conditioning of *Drosophila:* 1-2 weeks.
- Recording preference index: 2-3 weeks.
- Data analysis: 1-2 weeks.
- Olfactory receptor neuron firing rate recordings and analysis 2-3 weeks.
- Proposed work period: June 14th 2016 – August 19th 2016 (10 weeks).

Personal Statement

Not only do I believe that this project is the perfect fit for me, I believe that I am the perfect fit for it. I am extremely interested in this project because it combines both behavioral observations with molecular studies, to answer an important question: how can we quantify perception? Whilst this particular project focuses on quantifying odor detection in *Drosophila* this is really just the beginning of the implications of this study. If we are able to quantify odor detection in *Drosophila* then maybe we can apply similar methods the quantify other forms of perception such as vision in mammals such as mice.

I believe that I am the perfect undergraduate to work on this project. I was originally a physics major (and am now finishing off my minor in physics at MIT) and spent the past two years working in an experimental physics laboratory. Thus I have plenty of experience when it comes to building equipment and performing rapid data analysis. Therefore I will be able to complete these parts of the project more quickly than students who may need to learn how to do this; and focus more of my time over the summer on actually recording odor detection in *Drosophila*.

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