Effects of Optogenetic Stimulation of Mouse Olfactory Bulb on Odor Source Localization Behaviors

Taylor Kveragas[1,2], Andrew E. Papale[2], Annie Liu[3], Nathaniel N. Urban[1,2]

[1]Center for the Neural Basis of Cognition, Pittsburgh, PA; [2]Department of Neurobiology, University of Pittsburgh School of Medicine, Pittsburgh, PA; [3]Department of Surgery, Duke University, Durham, NC

Introduction

Successfully localizing foodborne odor sources is paramount to the survival of mice and many other species. Mice are able to successfully find odor sources on an open field spot-finding task. Despite the complex nature of a natural odor stimulus, behavioral strategies employed by mice are surprisingly consistent. But how do these behaviors change if we introduce additional "noise" to this navigation task? Here, we use randomly timed optogenetic stimulation of the olfactory bulb to perturb mouse behavior. Optogenetics is a powerful tool that can selectively activate specific types of neurons in the olfactory bulb using light pulses. We are interested in how this "optogenetic noise" introduced in the olfactory bulb changes behaviors during this task.

Methods

Heterozygous M72-CR RFP OMP mice (n = 3) were implanted with a 1.25 mm diameter optical fiber. We utilized stereotaxic coordinates, as shown in Figure 1, to ensure that the ferrule was placed centrally over the dorsal surface of the right olfactory bulb.

Figure 1A: (From mouse atlas) Stimulation of the dorsal olfactory receptor neurons will occur at the position marked by the red line.

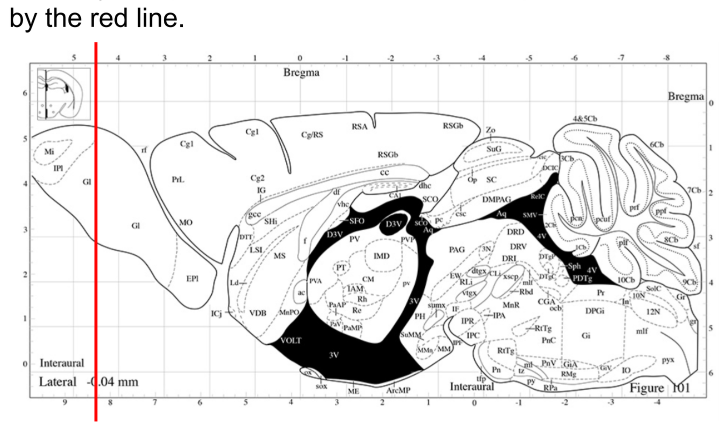
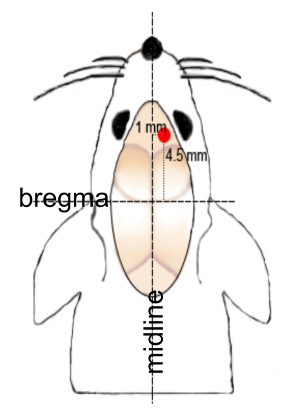


Figure 1B: (Dorsal view) Ferrule was implanted in a hole drilled in the skull at the position denoted by the red dot.



Mice located an odor spot on an open field surface based spot-finding task.

Figure 2A: Top View

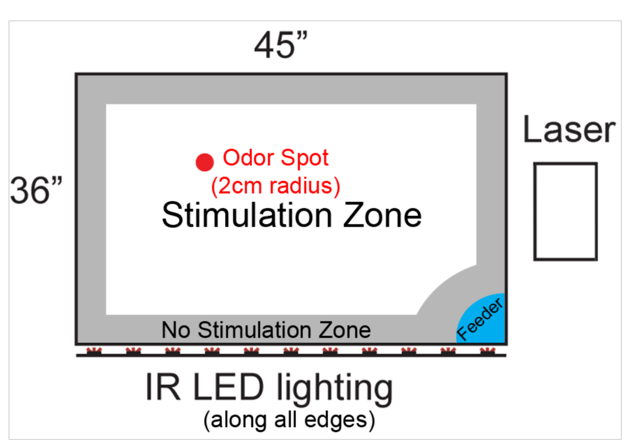


Figure 2B: Side View

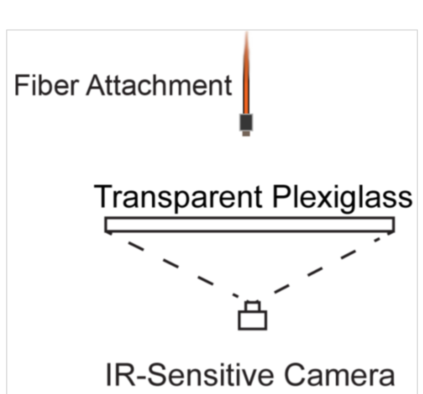
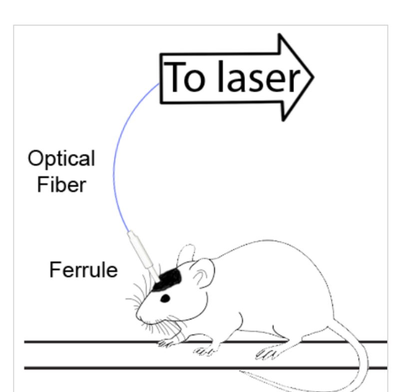


Figure 2C: Side View (Zoom)



We have developed a program to track body and nose positions in real time, automatically delivering a food reward when mice successfully locate the odor source. From recorded videos, we then extract more accurate position data samples using the deep learning program LEAP. The extracted positions are used to derive behavioral measures thought to be involved in olfactory navigation, such as changes in velocity and orientation.

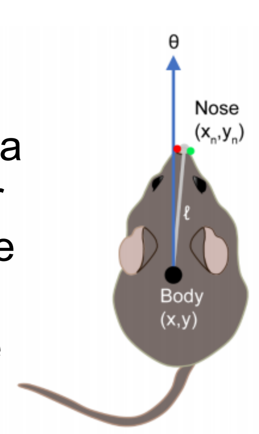


Figure 3A: Diagram of Mouse Geometry

Trial Types:

1. Mixed (0 mW & 10 mW laps, chosen randomly)
2. 0 mW only (control; 0 mW for all laps)

Laser parameters for Trials:

- Pulse duration fixed at 50 ms
- Stimulation frequency is between 0.5-3.0s, chosen randomly
- Stimulation occurred in "Stimulation Zone," as shown in Figure 2A

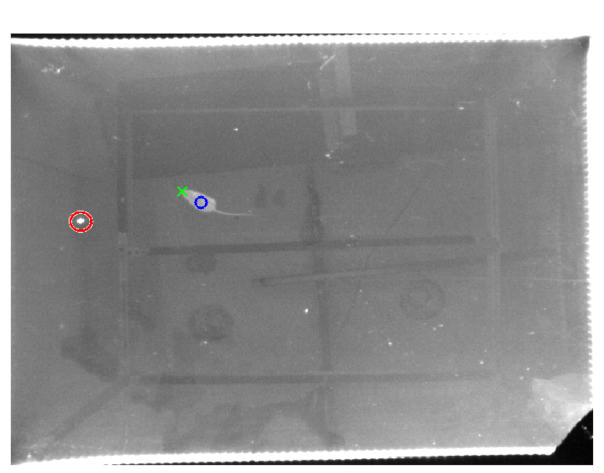


Figure 3B: View of our program tracking nose and body positions in real time, as well as the capture radius of the spot (shown in red)

Background

Distance From Spot Affects Velocity During Odor Source Localization

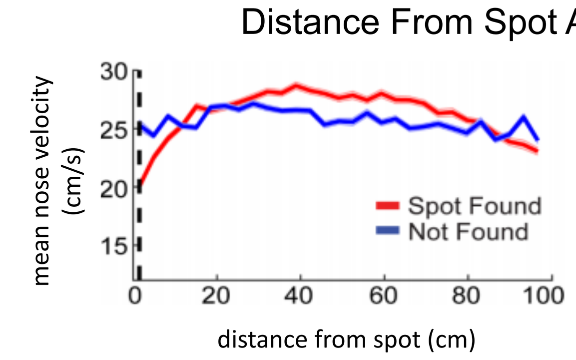


Figure 4: (Liu et al., BioRxiv)
In previous odor source spot localization experiments conducted by our lab, data suggests that during successful laps, nose velocity decreases within 20cm of the spot. This decrease is not observed during unsuccessful laps.

Results

Velocity Transiently Decreases following 10mW Stimulation

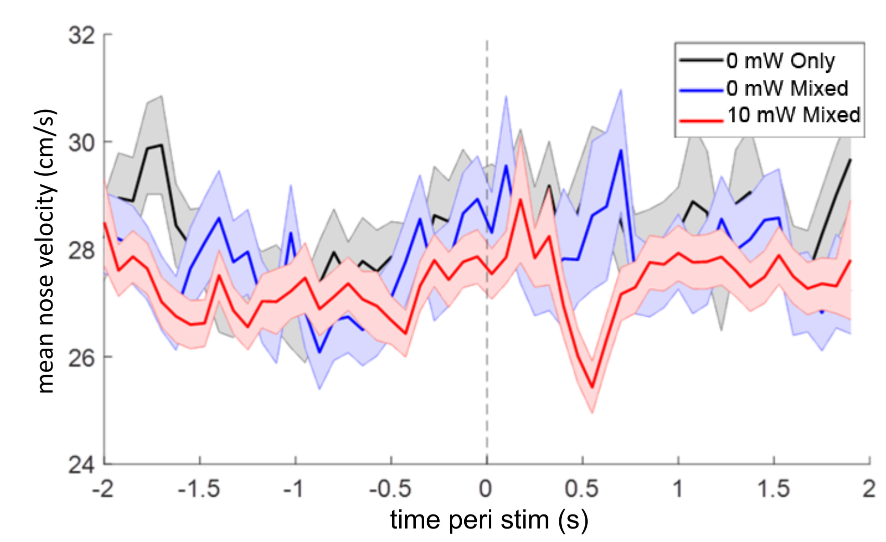


Figure 5A: During a 10 mW stimulus, we see a decrease in mean nose velocity. This effect is not observed for 0 mW stimulation during both mixed and 0 mW only trials.

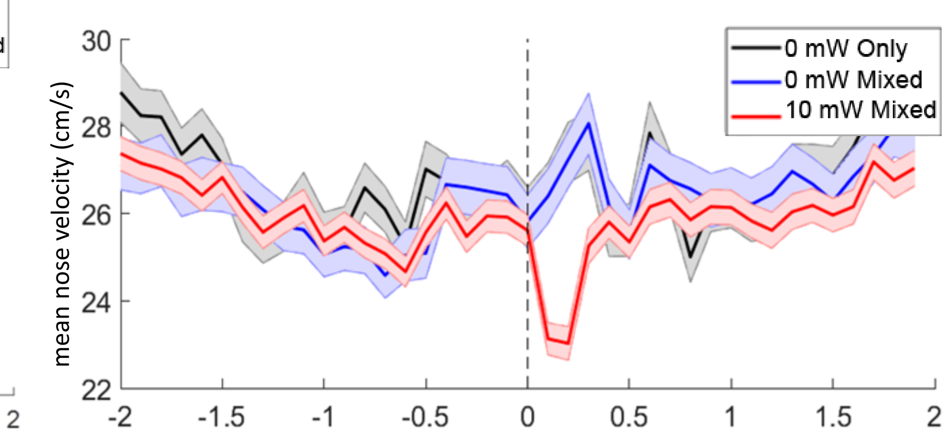


Figure 5B: The decrease in velocity during 10 mW stimulus is more pronounced when the mouse is farther away from the odor source. The effect is not observed during 0 mW stimulation. A subset of position data (greater than or equal to 50 cm distance from spot location) was used in this measure.

0 mW Only

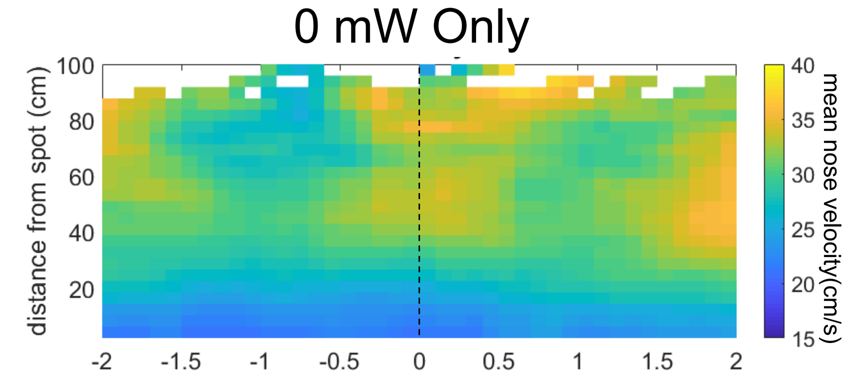


Figure 6A: During 0 mW only trials, no significant changes in mean nose velocity occur after 0 mW stimulation. Velocity overall decreases closer to the spot, which is consistent with Figure 4.

0 mW Mixed

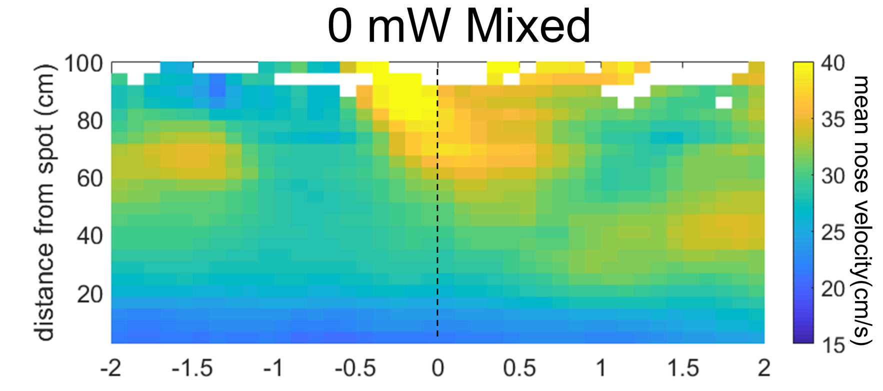


Figure 6B: During mixed trials, no significant changes in mean nose velocity occur after 0 mW stimulation.

10 mW Mixed

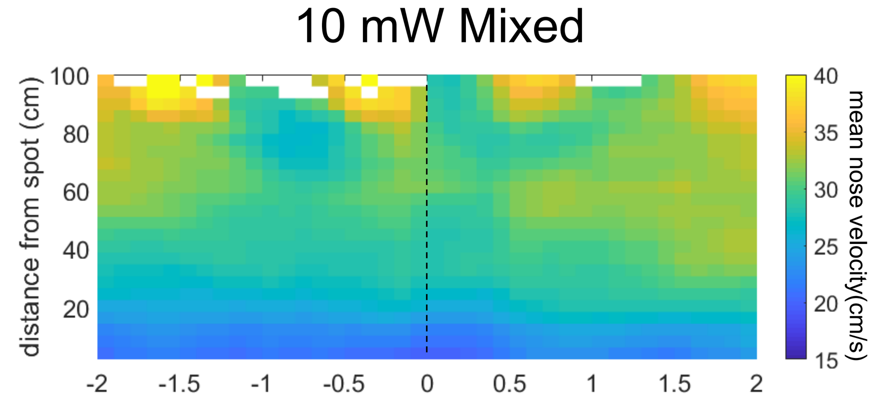


Figure 6C: During mixed trials, A decrease in velocity after 10 mW stimulation only occurs further away from the spot.

Subtraction: 10mW – 0mW Mixed

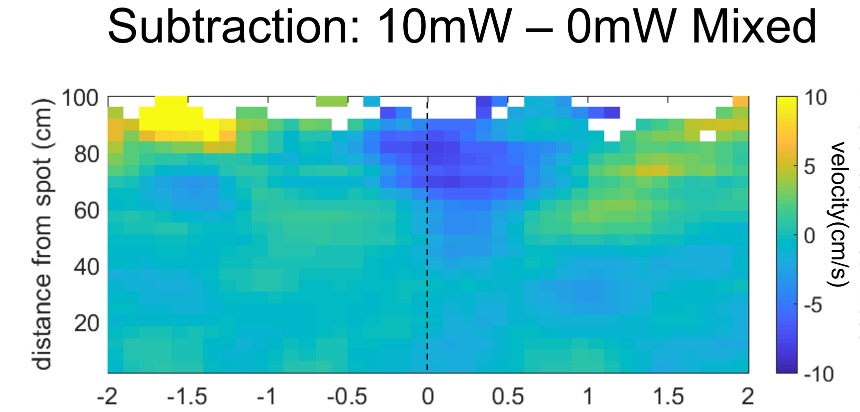


Figure 6D: We subtracted the 0 mW Mixed from the 10 mW Mixed to further illustrate that there is a significant difference in velocity change.

Exploration Ratio Varies by Spot Location

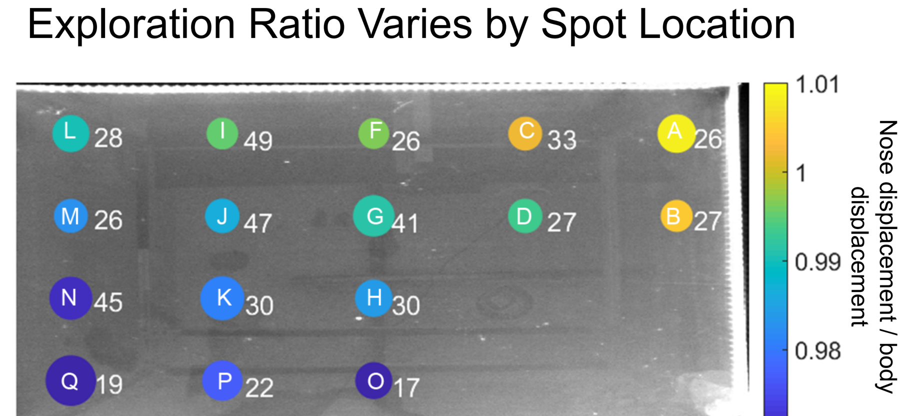


Figure 7: The "Exploration Ratio", or ratio of nose displacement to body displacement, varies according to the location of the spot. We hypothesize that this may be attributed to the tendency of mice to explore the field in counterclockwise patterns, and that lateral head movements relative to body position, or "casting", increase closer to the spot during successful trials (Liu et al., BioRxiv).

The numbers to the right of each spot denote the number of trials, n, collected for that spot. The size of each circle is proportional to the standard deviation.

Discussion

- As evidenced by Figure 7, the exploration ratio varies with spot location. This will need to be accounted for when investigating behavioral measures related to head movements and orientation, such as casting.
- A decrease in velocity is observed after 10mW stimulation, but not after 0mW. The effect seems to be greater further away from the spot (Figures 5 and 6). Prior work in our lab suggests that velocity decreases when close to the spot during a successful lap (Figure 4). Possibly, mice could be slowing down as a result of perceiving a local odor source during 10 mW stimulation, which may be context (i.e. distance) dependent.
- Our observations concerning velocity suggest that "Optogenetic Noise" has less of an effect when the mouse is close to the real odor source.
- More in depth analysis is needed to investigate complex behavioral measures, such as success rate or lateral head movements relative to body position.

Diagram of Exploration Ratio

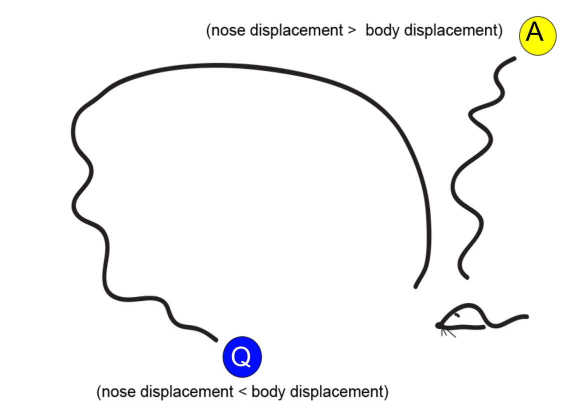


Figure 8: When Nose displacement is less than or equal to body displacement, mouse travels in a straighter trajectory. These example trajectories illustrate what an exploration ratio greater than and less than one might look like in the position data. Diagram is consistent with previous data showing that "casting" (see Figure 7) increases as mouse approaches the spot during successful localization laps.

Future Directions: "Virtual Spot"

After the completion of the "optogenetic noise" experiments, we wanted to see if mice could utilize a spatially-varying optogenetic stimulation gradient to navigate to a "virtual spot". This was achieved by varying stimulation amplitude as a function of distance from an odor source. We then tested the mice on trials in which there is no actual odor source, only the "virtual spot."

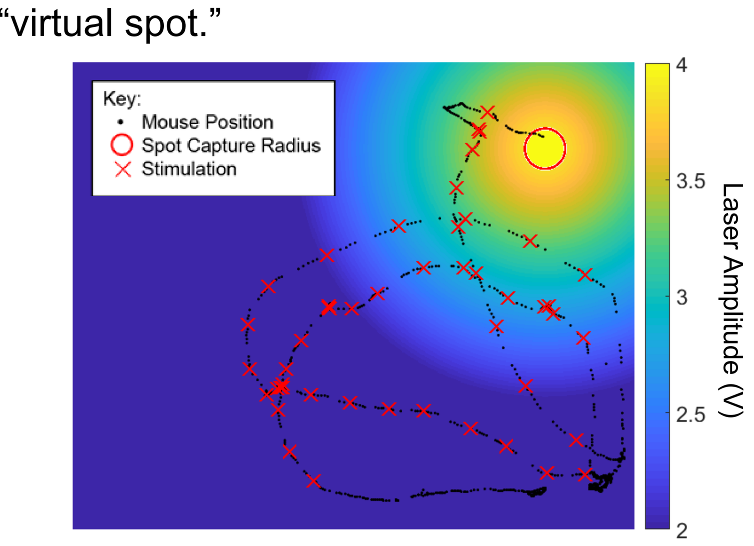


Figure 9A: An example trajectory from preliminary data of a mouse successfully navigating an optogenetic stimulation amplitude gradient to find a virtual spot. Note: no actual odor source is present.

Laser Power as a Function of Voltage

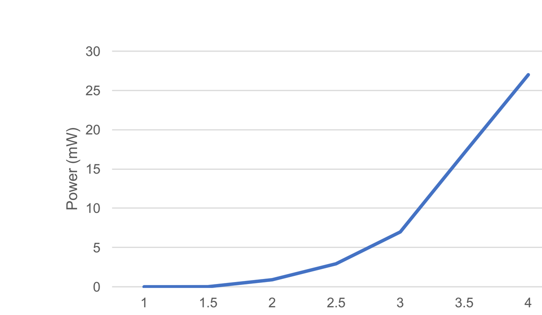


Figure 9B: We picked our amplitude range for Virtual Spot experiments based on the power distribution shown above.

We hypothesize that these changes in laser amplitude are being perceived by the mouse as changes in odor intensity. In analyzing the position data of these trials, we aim to provide insight about the behavioral measures of odor source localization and navigation through odor environments where the distribution of the salient stimulus is controlled.

References

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