Quantifying the Optokinetic Reflex in Zebrafish Models of Neurodegenerative Disorders Caused by *SLC25A46* Recessive Mutations

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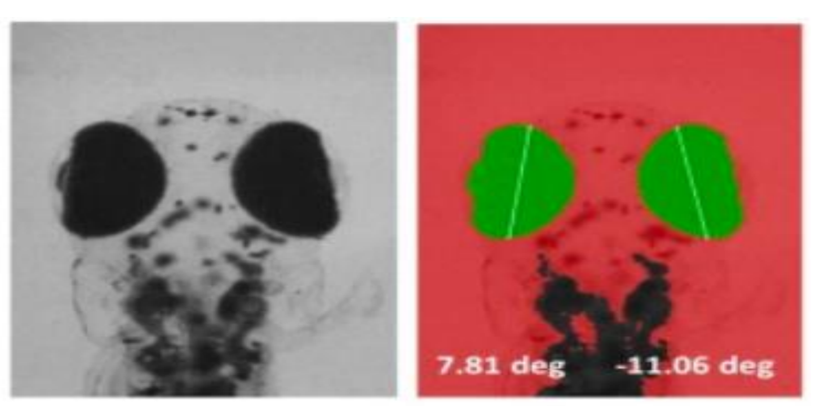
Background:

Neurodegenerative disease optic atrophy has been linked to recessive mutations in *SLC25A46* gene. This disorder is characterized by progressive vision loss and optic nerve degeneration.

(Abrams et. al, 2015) Affected Unaffected

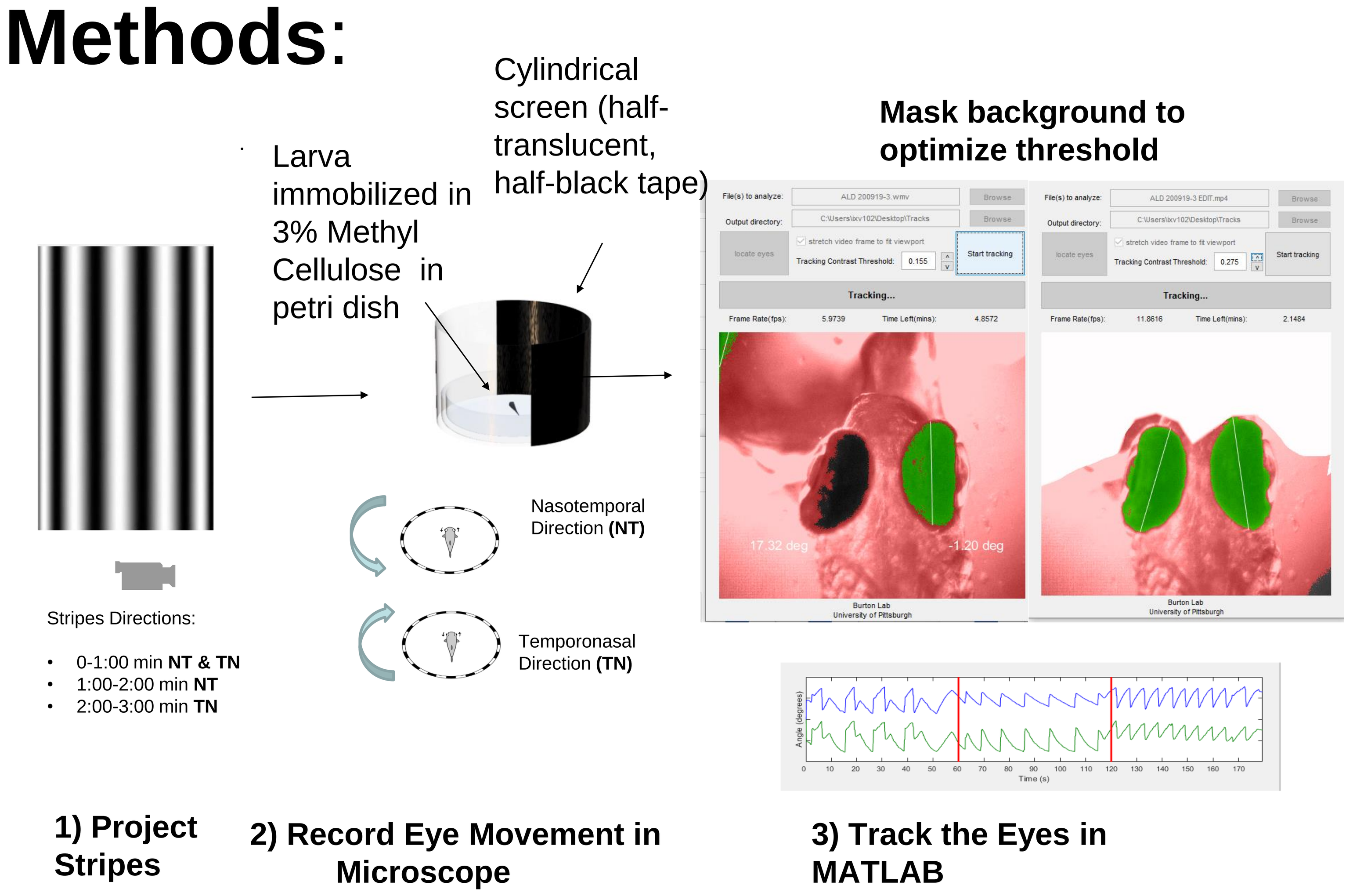
A measure of the optic nerve is the **optokinetic reflex**, the eye's tracking response to moving landscape. A code for quantifying this reflex was created in the Burton Lab at the University of Pittsburg.



(Sheetz et, al 2018)

This project aims to quantify this response in zebrafish model (*Danio rerio*) of neurodegenerative disease. We hypothesize that establishing parameters for this reflex in *slc25A46* mutants could provide an early indication of neurodegeneration in optic atrophy.

Methods:



Results

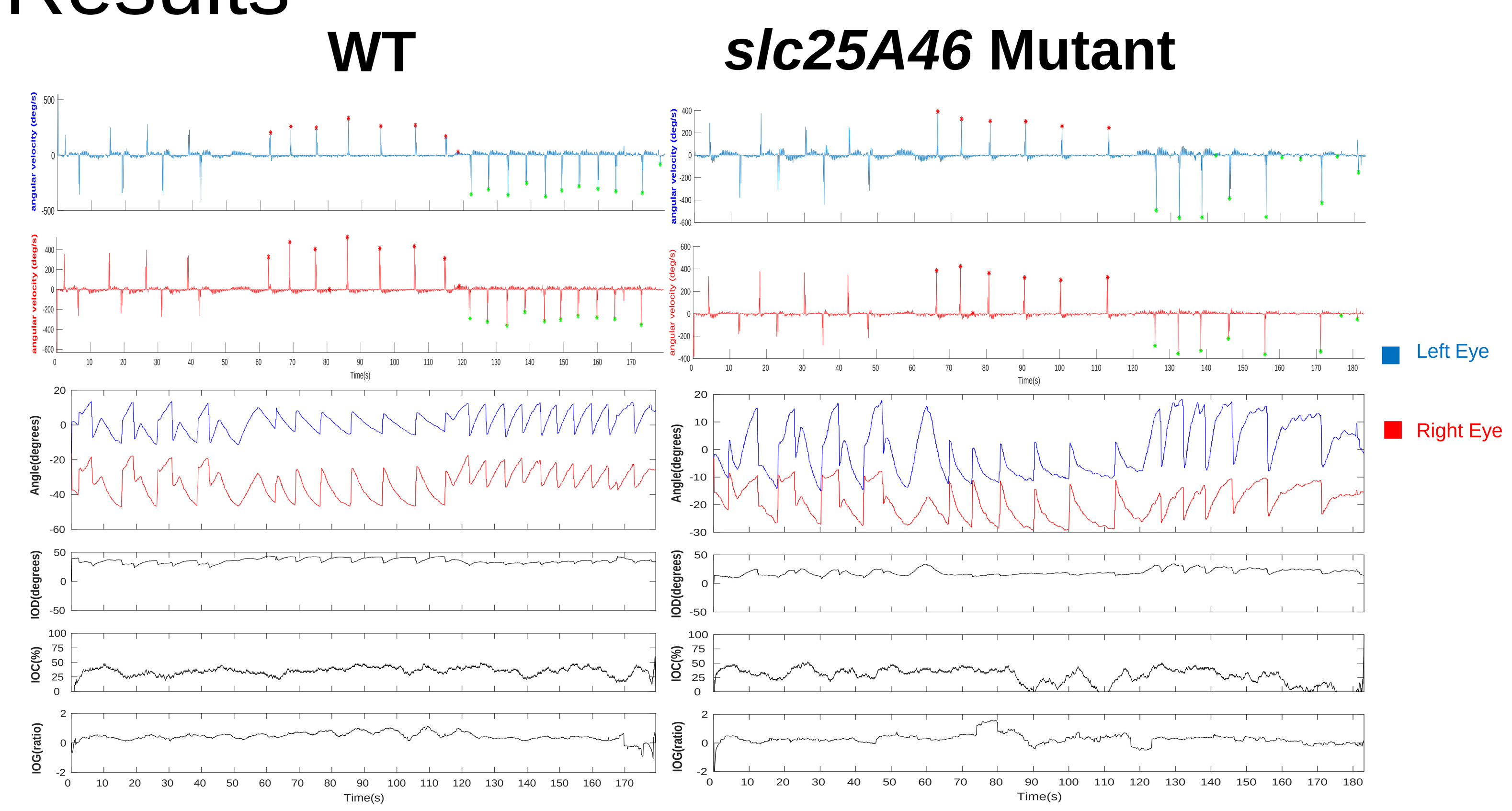


Fig1. Tracking behavior of a representative zebrafish from the wild type (WT) and *slc25A46* mutant group is depicted here. Figures measure the following parameters: Ocular angle, interocular concordance (IOC), interocular gain (IOG), and interocular difference (IOD).

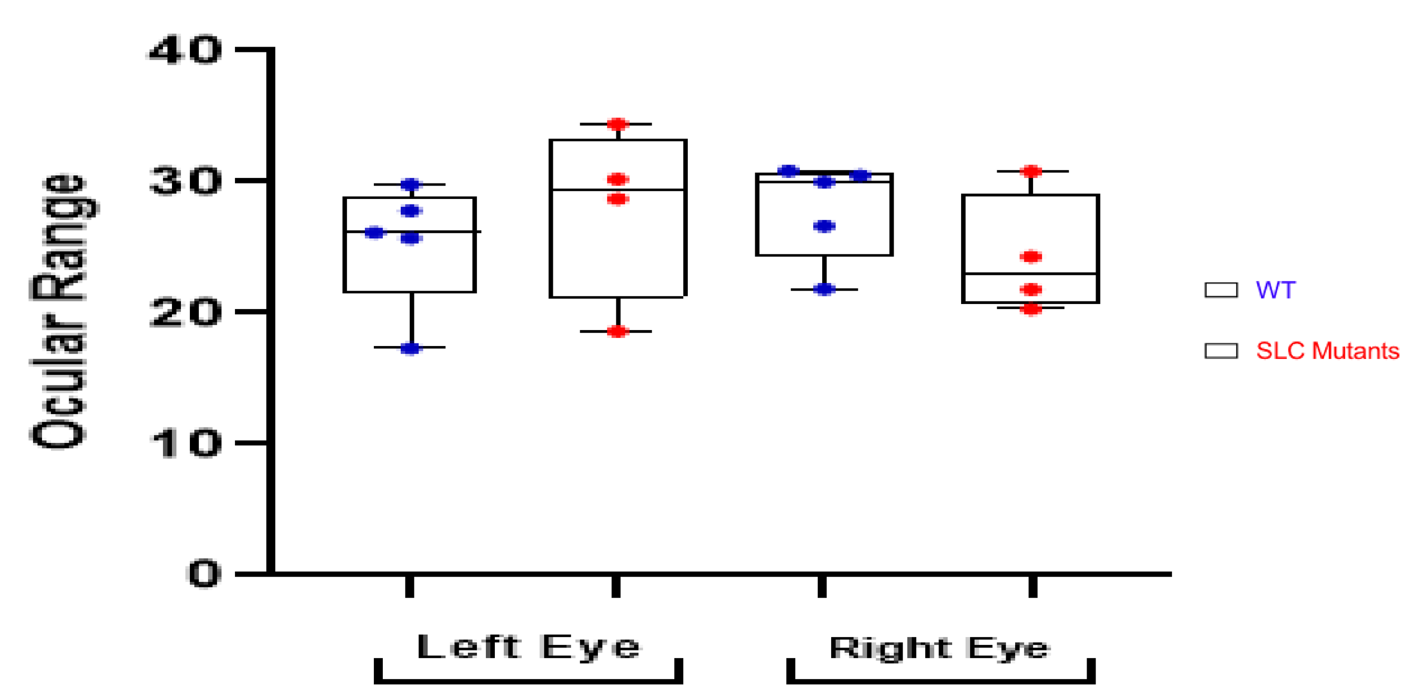


Fig2. Ocular angle is shown for wildtype (n=5) and *slc25A46* mutants (n=4) with no significant difference in the left and right eyes (p=0.2857)

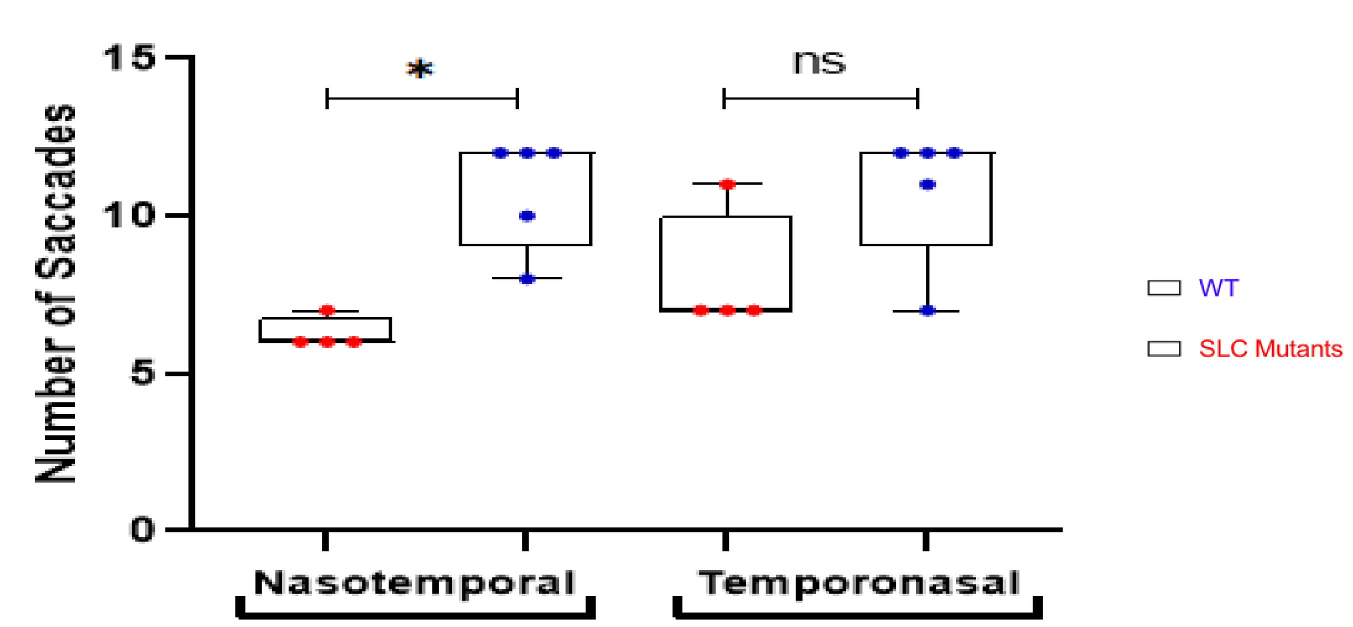


Fig3. Number of saccades in nasotemporal (NT) and temporonasal (TN) in ipsilateral eye is shown for wildtype (n=5) and *slc25A46* mutants (n=4) with a significant difference in the NT direction and an insignificant one in the TN direction (p=0.0159,p=0.1111 respectively)

Conclusions

- ❖ The optokinetic reflex appears intact in 5 dpf *slc25A46* mutants, but fewer saccades indicate that mutants do not track lines as consistently as WT larvae.
- ❖ Early signs of neurodegeneration were evident in differences in tracking behavior graphs, specifically in the NT direction.
- ❖ Overall ocular range in both eyes did not appear to be greatly affected in these stages.

Future Directions:

- ❖ Run experiment with a minimum of 30 larvae from both groups to confirm reliability and establish more concrete parameters.
- ❖ Elicit OKR (optokinetic reflex) at different speeds to produce significant differences between *slc25A46* mutants and WT larvae.
- ❖ The next step is to fix and stain for pERK (neuronal activity proxy) to determine neural circuit basis for altered OKR in *slc25A46* mutants.

Acknowledgments

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- The Bridge to the Baccalaureate Program (5R25GM050083-13)
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References

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Webcam Kinematics Recording System for Brain Machine Interface Studies

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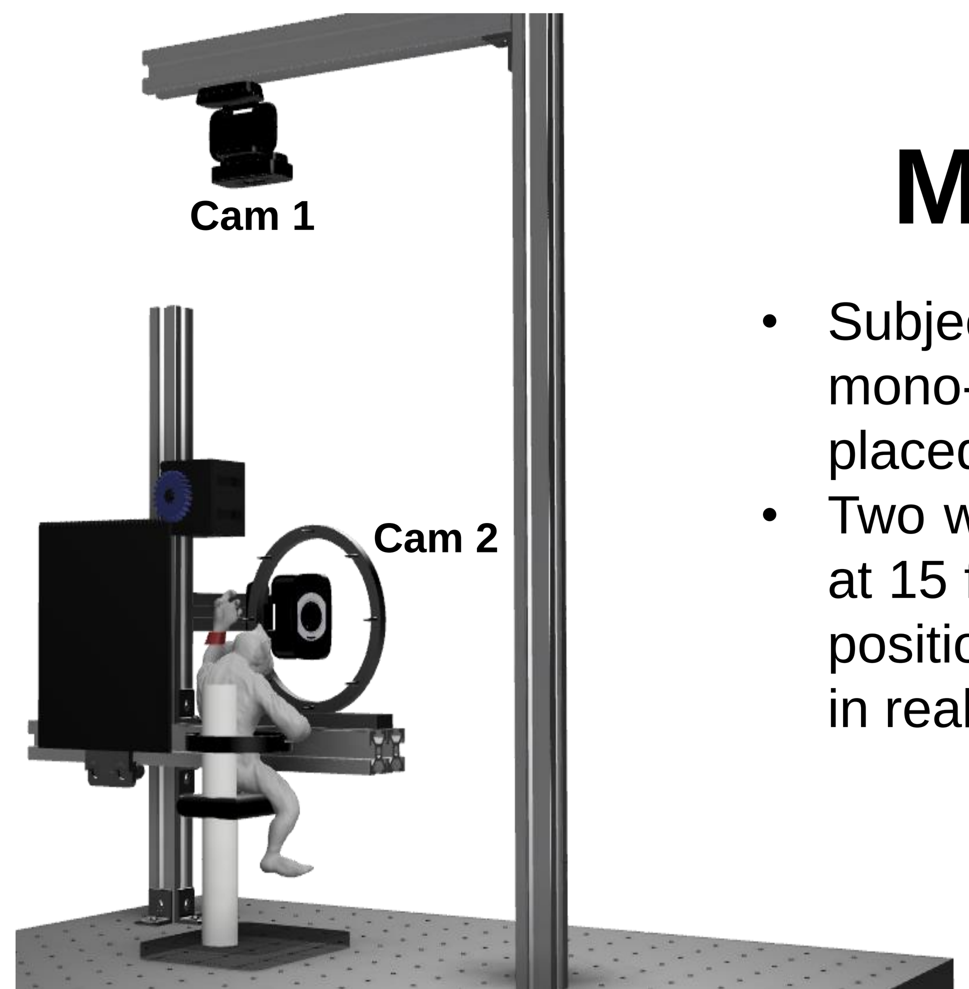
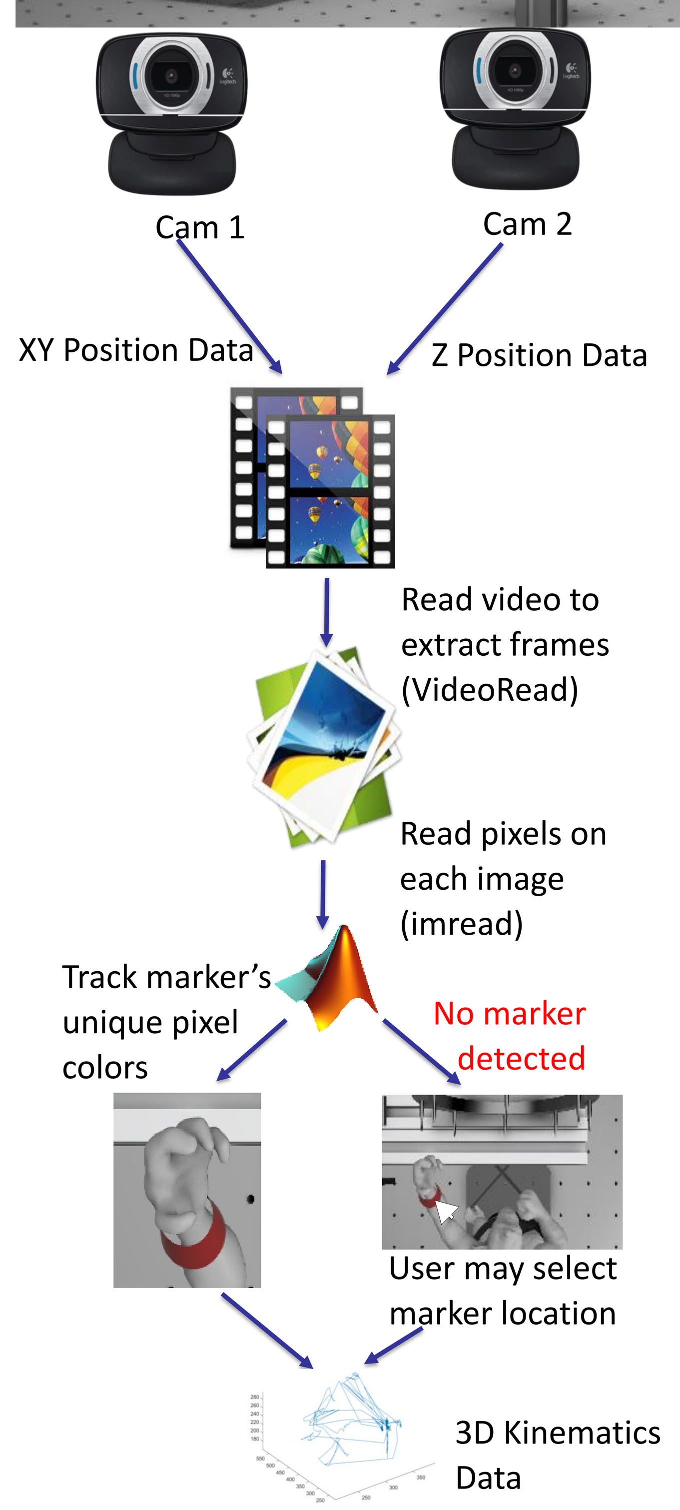
Background

- It is critical to match neural data with motion data in order to assess the mapping of neural data to the behavior.
- Given that neural recordings are susceptible to electromagnetic interference signals, my project aims to replace a magnetic kinematics system (TrakSTAR).
- By implementing a new system, consisting of two webcams simultaneously recording motion of the subject's upper limb, we hypothesize that accurate motion data can be acquired without compromising neural recordings.



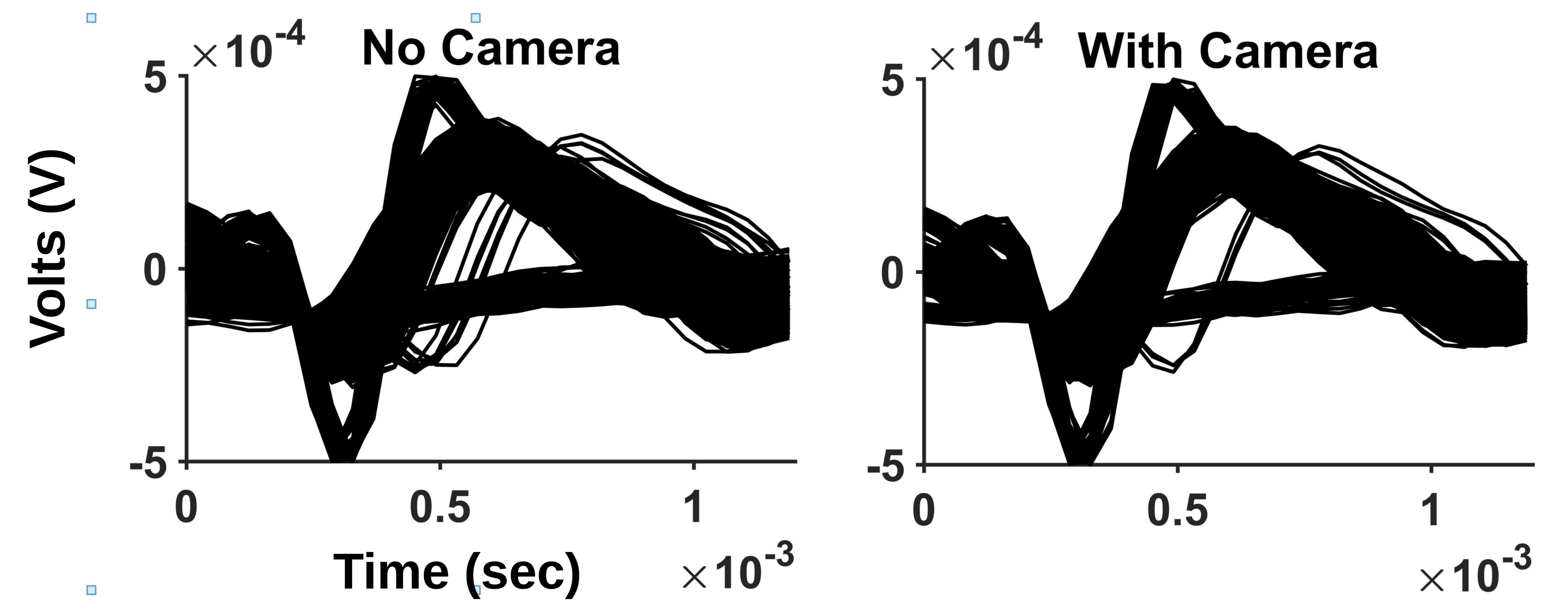
Methods

- Subjects will have one mono-color marker placed at the wrist
- Two webcams streaming at 15 fps will capture 3-D positions of the markers in real time.

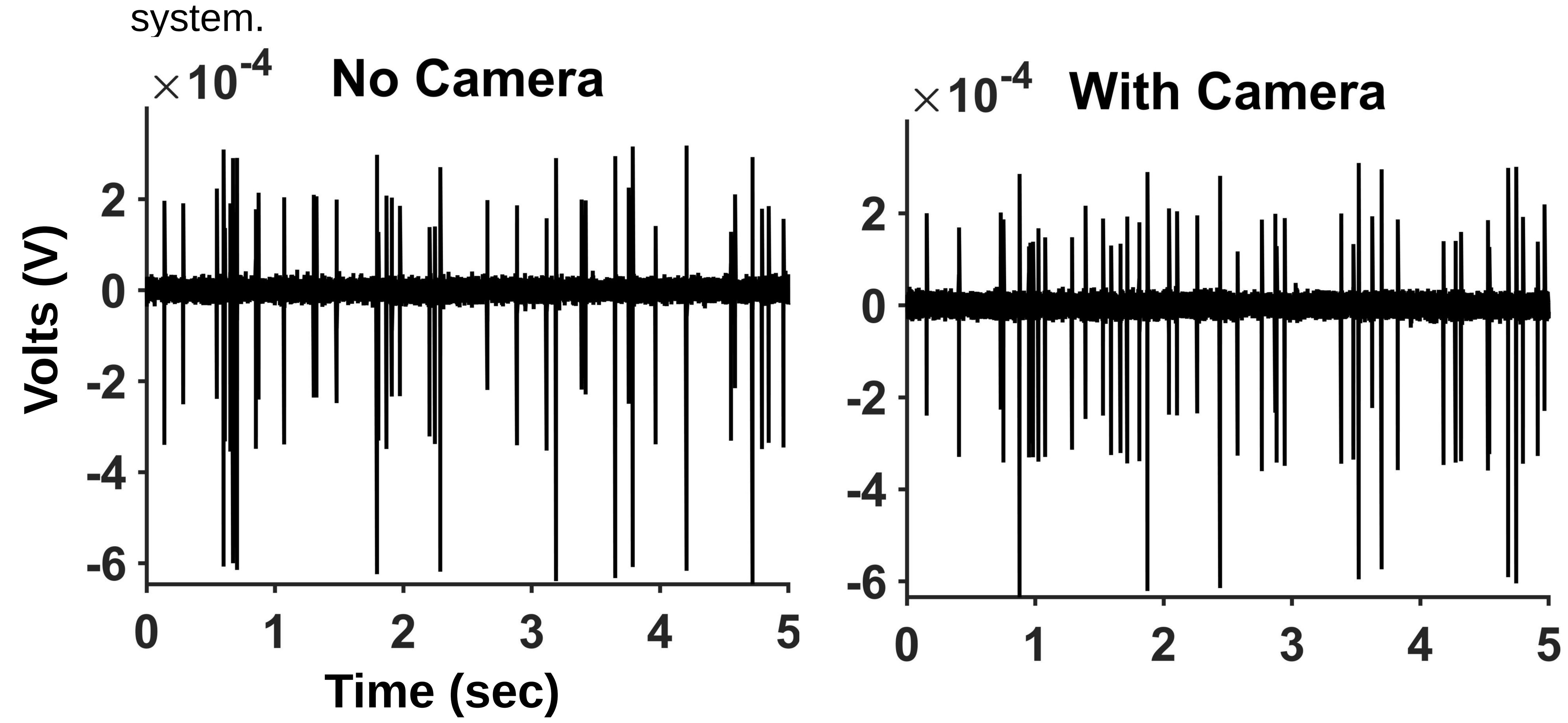


- One camera captures the X,Y position. The other camera captures Z position.
- Images are read through MATLAB and markers are tracked.
- Effects on recorded signals assessed through use of a neural simulator (FB128, TDT, Alachua, FL).

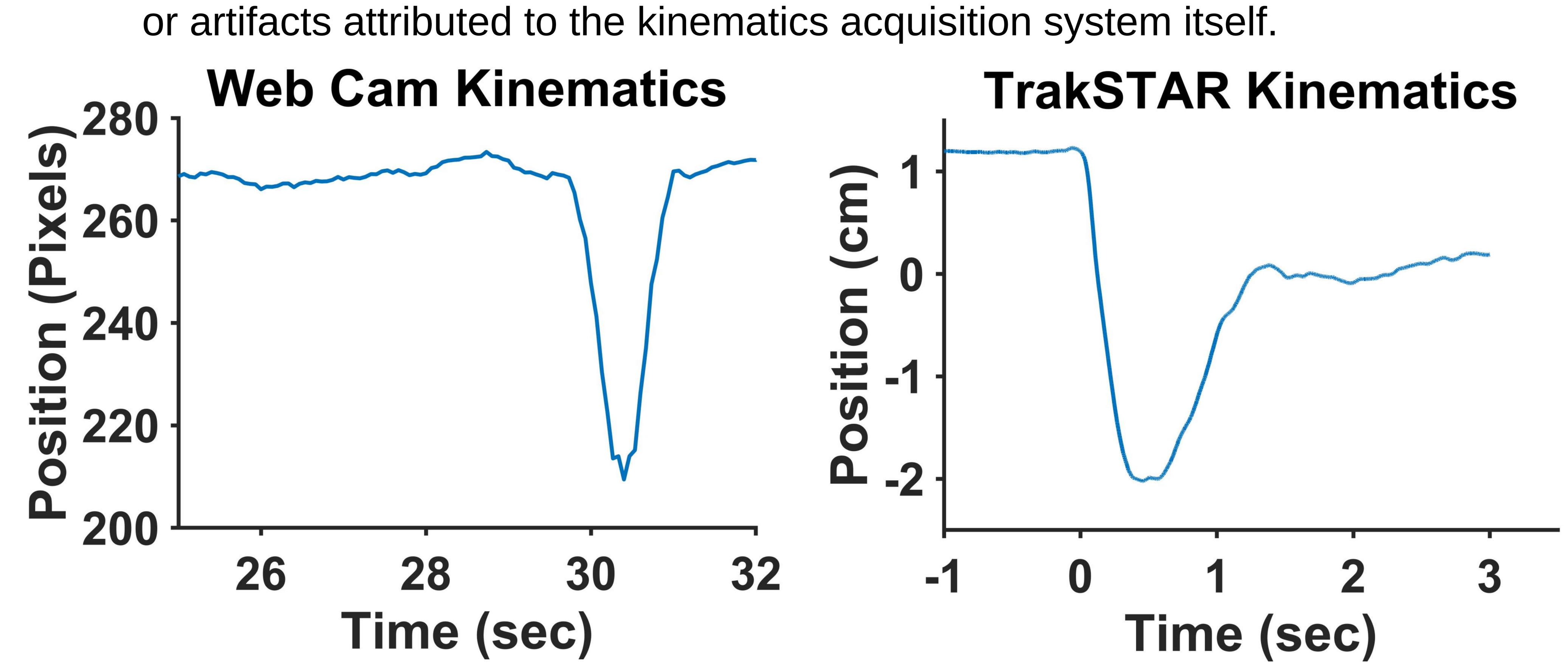
Results



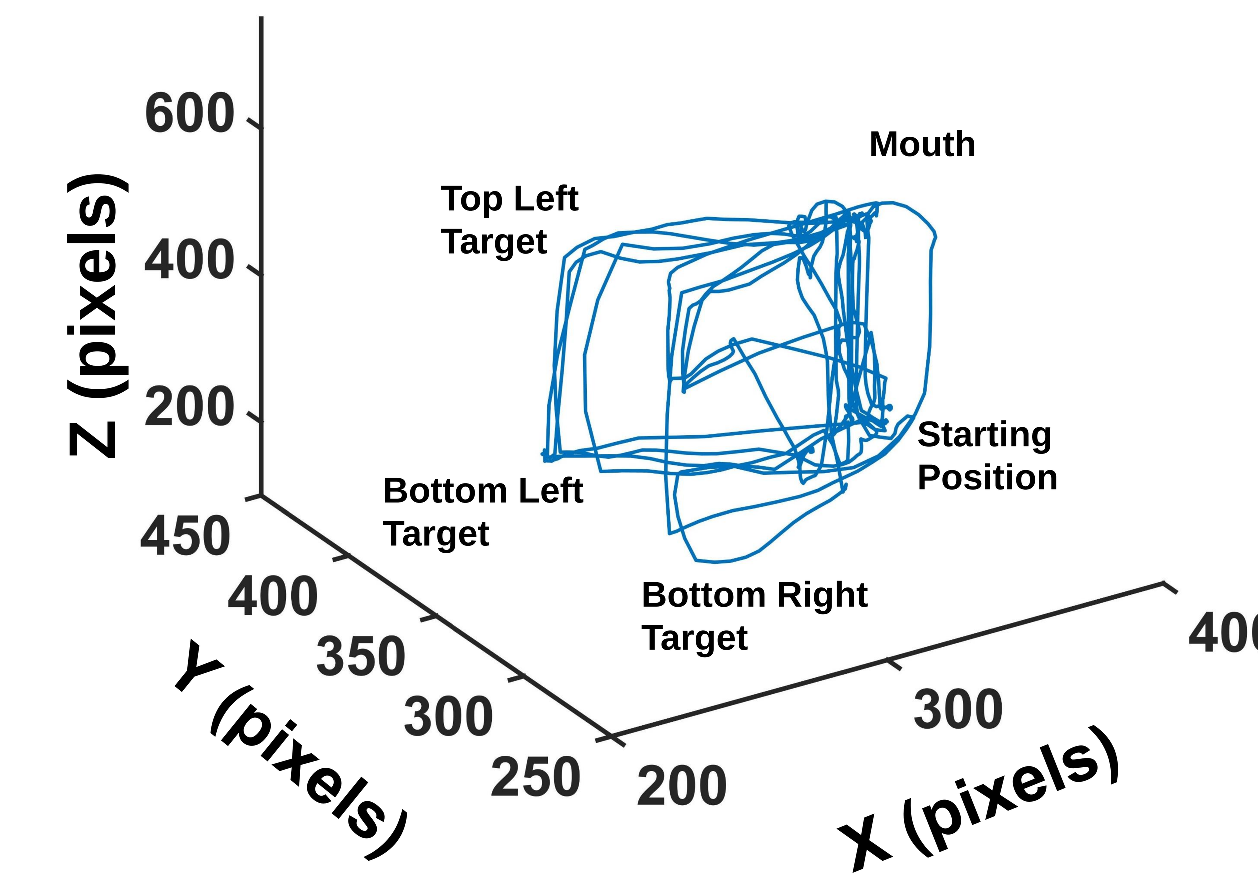
- Simulated spike data from Synapse (1) under a controlled experimental environment and (2) while the cameras were operating.
- No significant deviations in sorted spikes during operation of new kinematics system.



- 5 seconds of simulated spiking activity with (1) no camera and (2) with camera system running illustrate no significant change in noise floor of recorded signal or artifacts attributed to the kinematics acquisition system itself.



- Z-axis movement data of wrist marker (1) from tracking a yellow marker with the webcam system and (2) with the TrakSTAR system.



- Continuous 3D kinematics data obtained tracking a red marker to test tracking accuracy for 1 minute at 15 frames per second.

Conclusions

- The Webcam Kinematics Recording System did not introduce any noise in the neural recordings.
- It successfully tracked upper limb motion despite the low sampling rate, 15 fps, of the cameras used.
- It allows for tracking of any color, which can be selected based on the experimental set up.

Future Directions

- Higher frame rate on the camera system.
- The program used to obtain motion data will store information of the colors for specific markers.
- The position of the cameras will be optimized to prevent blind spots in the recording. Such improvements will help facilitate the analysis of neural data from neural interfaces.

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