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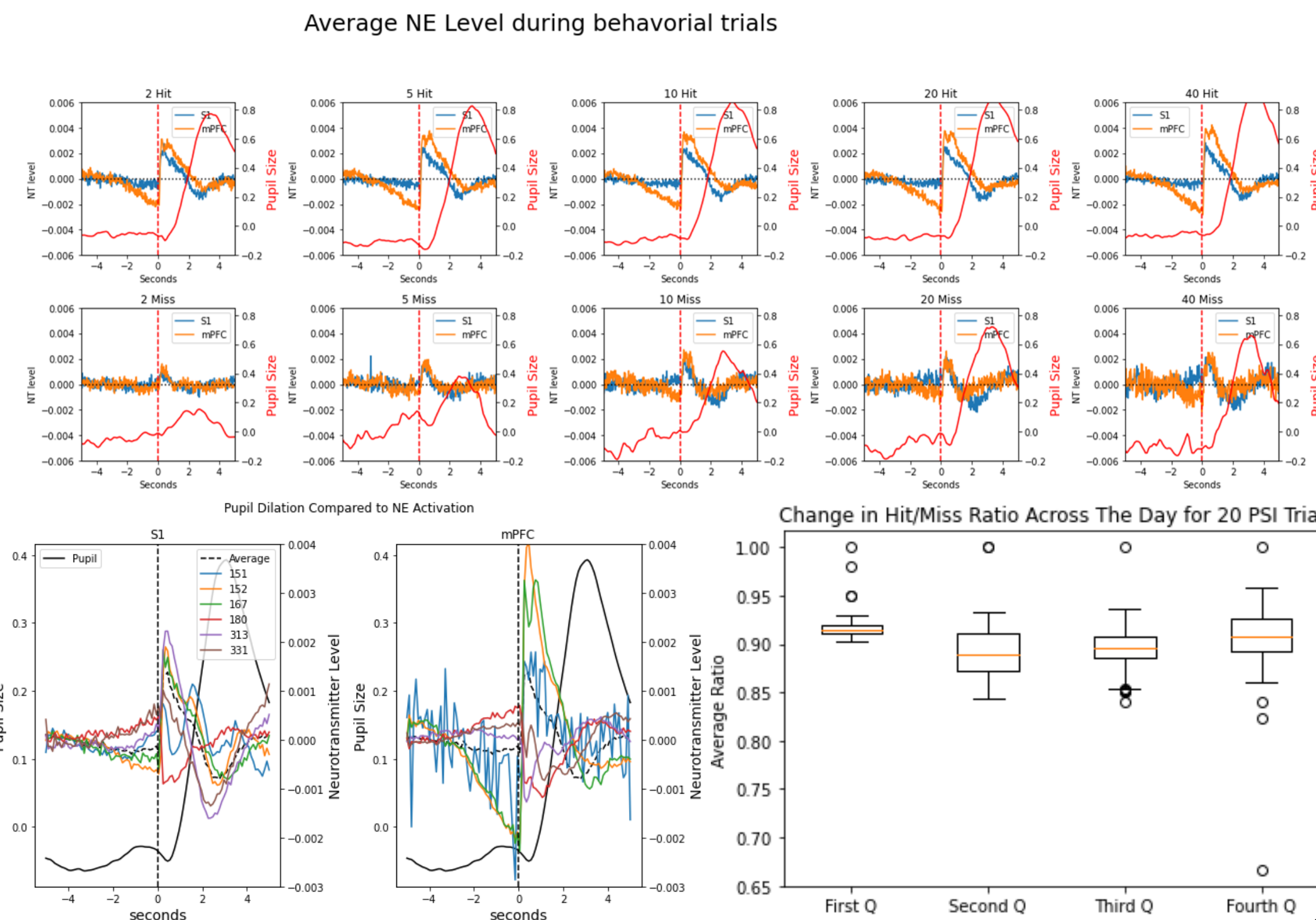
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Introduction

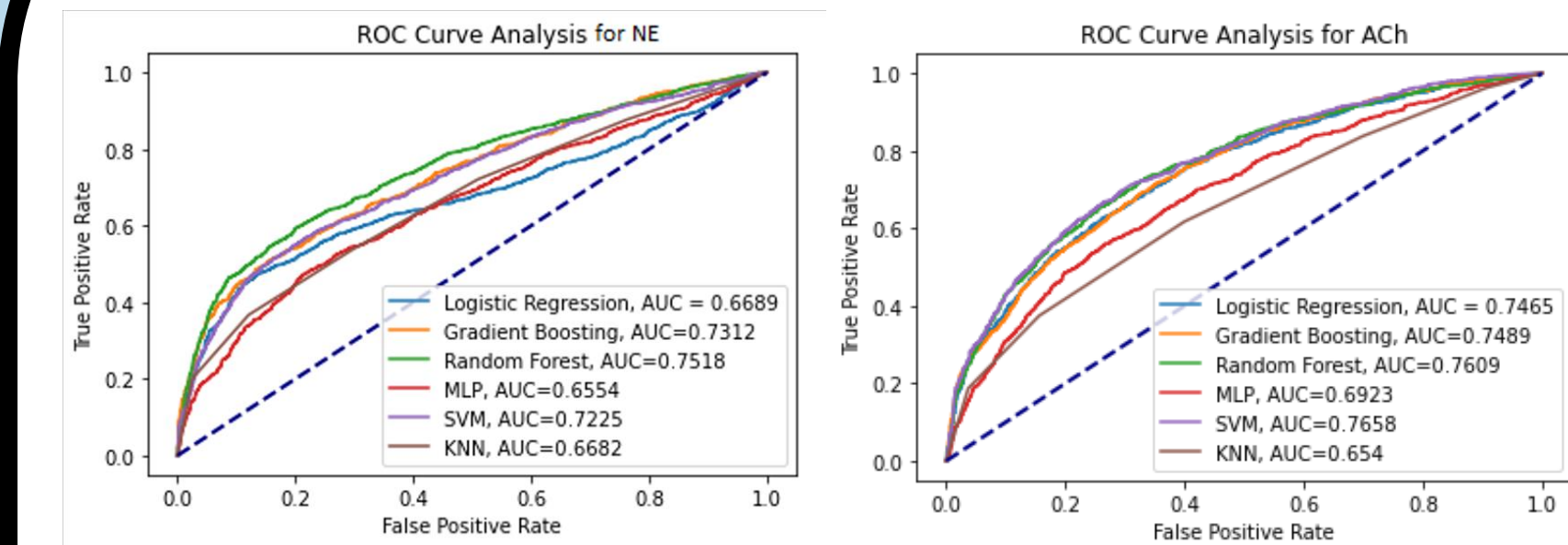
- Neuromodulator systems such as Norepinephrine (NE) and Acetylcholine (ACh) have predictable phasic patterns and play a critical role in sensory discrimination behavior.
- Future attempts to derive control systems for somatosensation will require an understanding of these neuromodulator dynamics.
- Prior evidence shows consistent pupil physiological responses prior to behavior and thus an indirect correlate to neuromodulator activity. We first hypothesized that neurotransmitter levels preceding stimulation could predict mice response.
- Additionally, given previous findings that GCAMP intensity was related to stimulation strength, we predicted data post stimulation would predict stimulation PSI.
- We expect more complex models will have greater performance due to their ability to extract non-linear features.

Behavior

- Across all animals there was not a significant decrease in performance throughout experimental days, however there was an increase in variability.
- As expected, neuromodulator activity (ACh then NE) lagged peak pupil size during stimulation.
- There was a large heterogeneity in neurotransmitter dynamics across all animals.
- There was also consistent dynamics between hit and miss trials with a clear difference in waveform.
- There was no difference in dynamics between trials with different PSIs besides a slight increase in peak amplitude.



Results



- When trained on individual animal's, logistic regression reached 88% accuracy at peak for logistic regression and 91% accuracy for MLP to predict behavior.
- When trained on all animals at once accuracy reached 76% at peak.
- Attempting to predict PSI failed with only 25% accuracy, compared to 16% random chance.
- Both LSTM and ESN models converged to minimal loss during training, however LSTM only reached 44% accuracy.
- ESN reached 88% accuracy at peak however due to a large variability it reached 68% accuracy on average.

Methods

Norepinephrine: Diagram of a neuron with GRAB sensors (green) and a GPCR-activation based NE and ACh fluorescent receptor (blue).

GRAB sensors: Diagram showing the location of S1 and mPFC in the somatosensory cortex and medial prefrontal cortex.

Experimental Setup: Diagram of a mouse in a body restraint box with a head fixation plate, piezo stimulator, and water spout.

Behavioral Protocol: Timeline showing Punishment & Restart, Random Waiting Period (2-8s), Distractor Puff, No Lick Period (2s), Opportunity Window (500ms), Lick, Air Puff, Sugar water reward (200ms), and Reward/Relax Window (5-7s).

- Mice expressed GPCR-activation based NE and ACh fluorescent receptors which enabled *in vivo* photometry recordings with high temporal resolution.
- Mice (n=10) had two-photon microscopy recording sites in somatosensory cortex (S1) and medial prefrontal cortex (mPFC) during which head was fixated and whiskers were stimulated with air puffs.
- 40,000 total trials were collected which consisted of a random onset time, followed by an air puff of 0, 2, 5, 10, 20, or 40 PSI and a 500ms window of opportunity to lick and retrieve a reward.

Models

Logistic Regression Predicting Outcome Prior to Stimulation: Diagram showing input x_1, x_2, \dots, x_m with weights w_1, w_2, \dots, w_m and bias b entering a net input function Σ , followed by a sigmoid function and a quantizer to produce output y .

Logistic Regression Predicting Outcome Prior to Stimulation using ACh: A line plot showing Accuracy vs Seconds Prior for ACh (blue) and NE (orange). ACh accuracy is higher, around 0.65.

Logistic Regression Predicting Outcome Prior to Stimulation using ACh: A line plot showing Accuracy vs Seconds Prior for mPFC (blue), S1 (green), Combined (red), and Pupil (orange). The Combined model shows the highest accuracy, around 0.65.

Echo State Recurrent Neural Network: Diagram showing an input layer $u(t)$ feeding into a reservoir of neurons with weights W_{in} and W_{out} . The reservoir output goes through a dimension reduction layer to a readout layer, which produces output $y(t)$.

- To predict animal response Hit/False Alarm trials were encoded as 1 and Miss/Correct Rejection trials were encoded as 0.
- Each data point for S1 and mPFC was a single feature: 2 seconds of photometry * 120 Hz sampling rate * 2 brain regions = 480-time dependent features.
- Logistic regression was used as a first pass simplistic model to determine if neurotransmitter dynamics could be fitted to a linear curve.
- 2 seconds of data prior to stimulation provided the highest model performance.
- Individually mPFC had a performance of 54% but when combined with mPFC, exceed mPFC alone.
- To fit nonlinear patterns MLP, RF, XGBoost, KNN, and SVC models were tested.
- To extract temporal dynamics Long Short-Term Memory (LSTM) and Echo State Networks (ESN) were used.

Conclusions/Directions

- These results show that individual mice's neurotransmitter dynamics immediately prior to behavior can be modeled with a linear S curve, however, to generalize across multiple animals requires deeper networks that incorporate nonlinear temporal filtering in RNNs.
- Even though prior data could predict action, it remains unclear why photometry data prior to stimulation is predictive of action when the trials should be randomized, therefore more research needs to examine the potential of animals learning/expecting stimulation over time.
- Deeper models could be attempted to reach higher generalized accuracy such as Multivariate CNNs, but more importantly more data should be used to optimize LSTM/ESN architecture and hyper parameters.

References / Acknowledgements

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