Closed-loop control of Mesoscale Cortical activity

Aditya Deole, Anna Li, Eric Shea-Brown, Mehran Mesbahi, Nick Steinmetz

University of Washington

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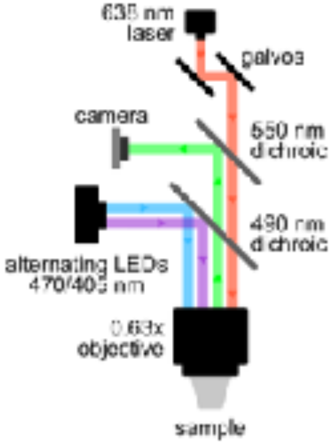
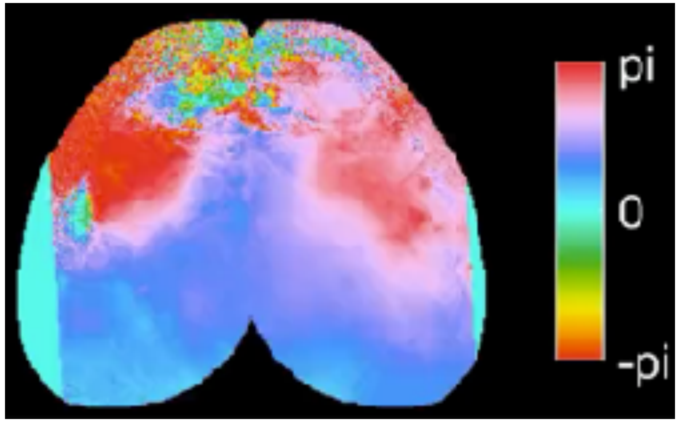
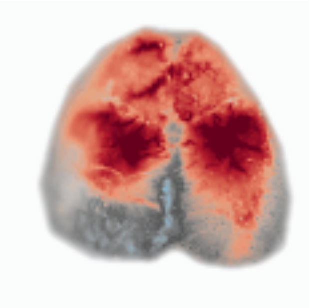
Simultaneous Recording and Stimulation







- Mesoscale cortical- dynamics measured using widefield imaging.

- Mesoscale activity relevant for behavior and perception (Zhiwen 26)

- Simultaneous ontogenetic stimulation of cortical regions (Matveev, Li 24)

Can we shape behavior using mesoscale cortical information ?

Motivation

- Targeted stimulation of cortex wide activity can help shape behavior.

We will design a control system !!

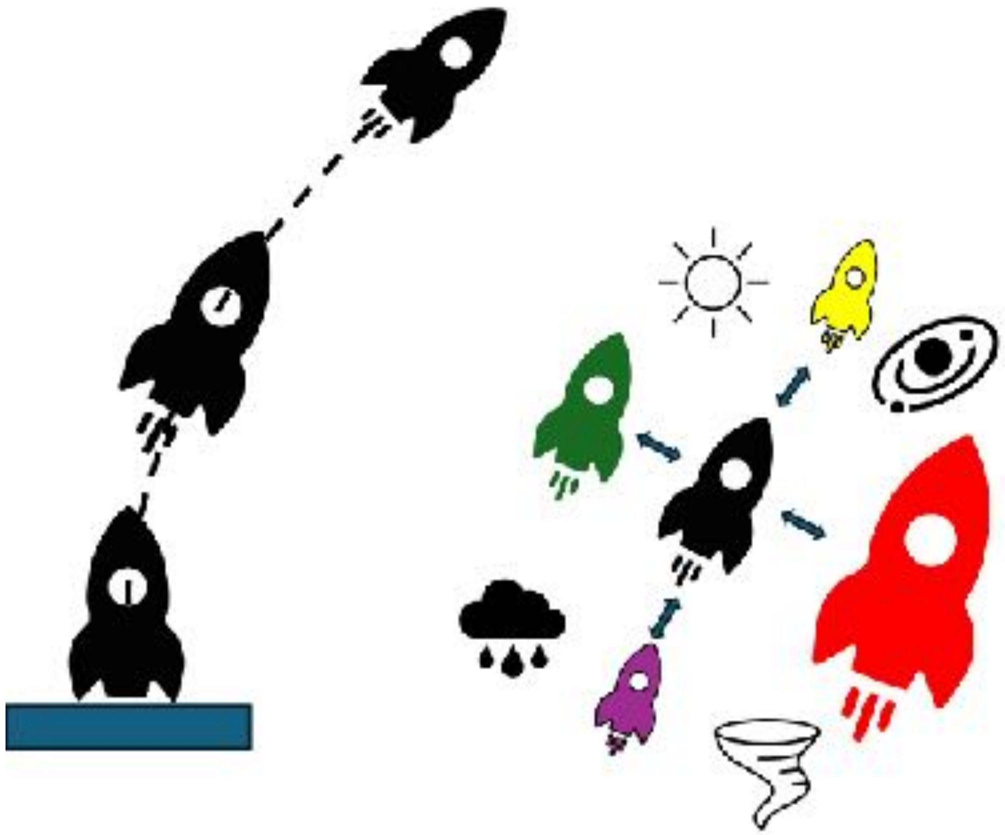
- Control theory :: robustness, safety guarantees and are energy optimality

- Reveals internal properties like state dependence and interactions

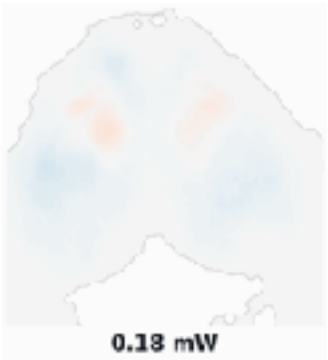
Variability: Uncertainty to a Control System and more

- Neuronal dynamics appear like a parameter varying, noisy
- Brain states change resonant frequencies
- Motion affects global activity
- Unknown stimulus
- Regional interactions

Can we control this system?

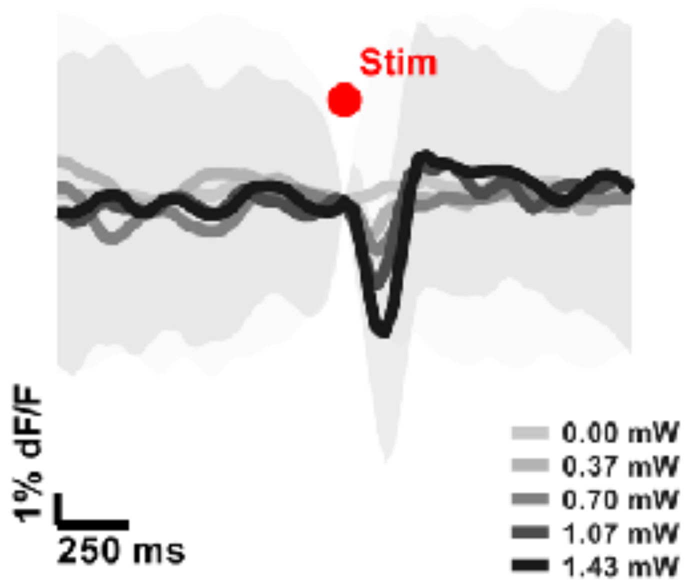


Input-Output Characterization

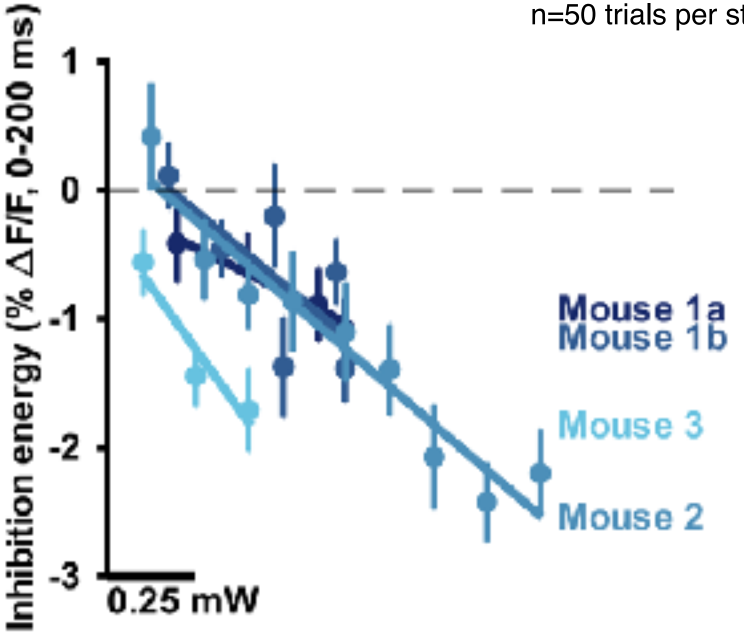


LTI systems explain the trial-averaged stim response.

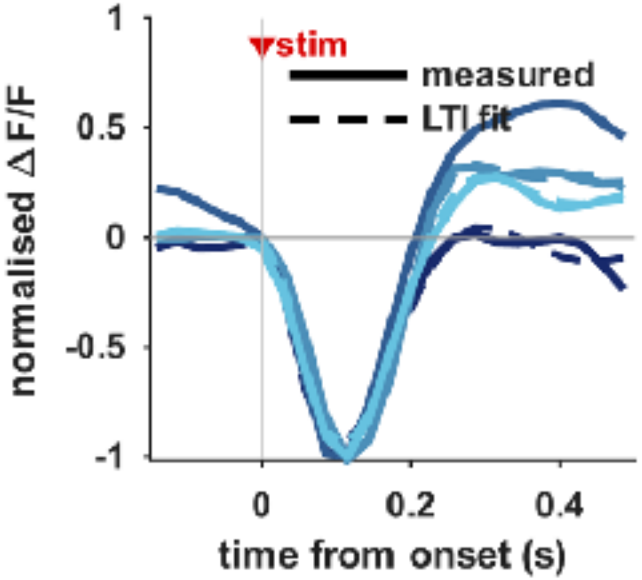
n=50 trials per stim



n=50 trials per stim

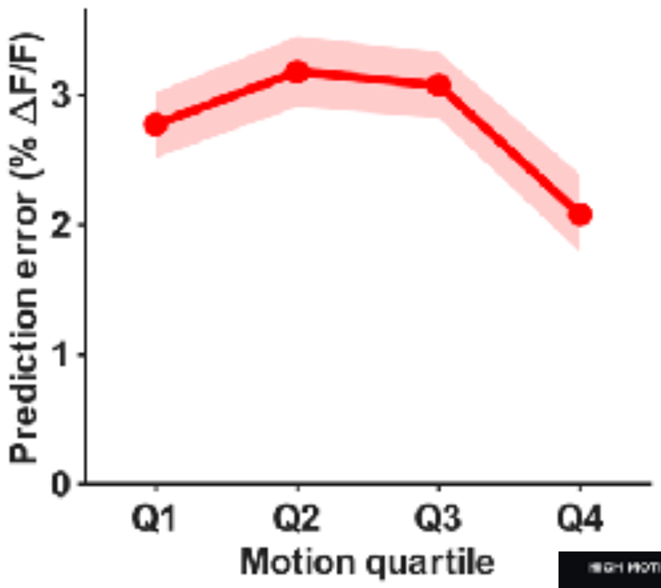


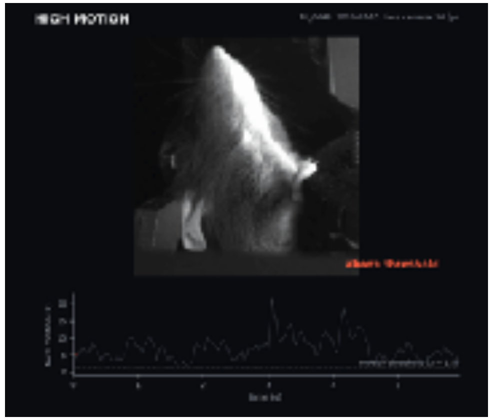
Cross validated

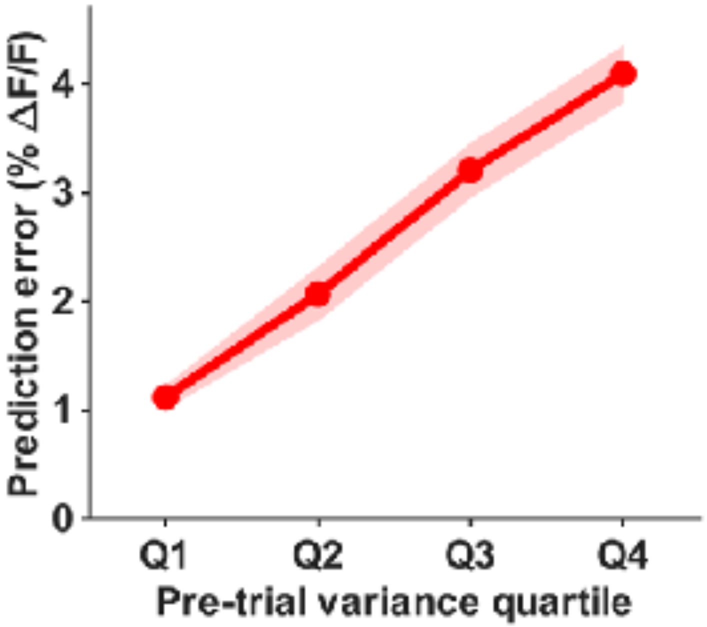


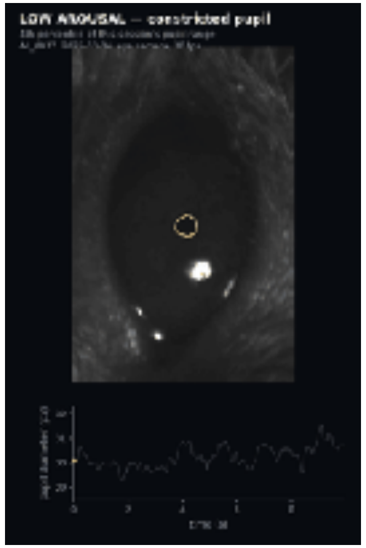
State Dependent Stim Response

The **predictability of stim responses depend on brain states,** namely motion and pre-stimuli variance



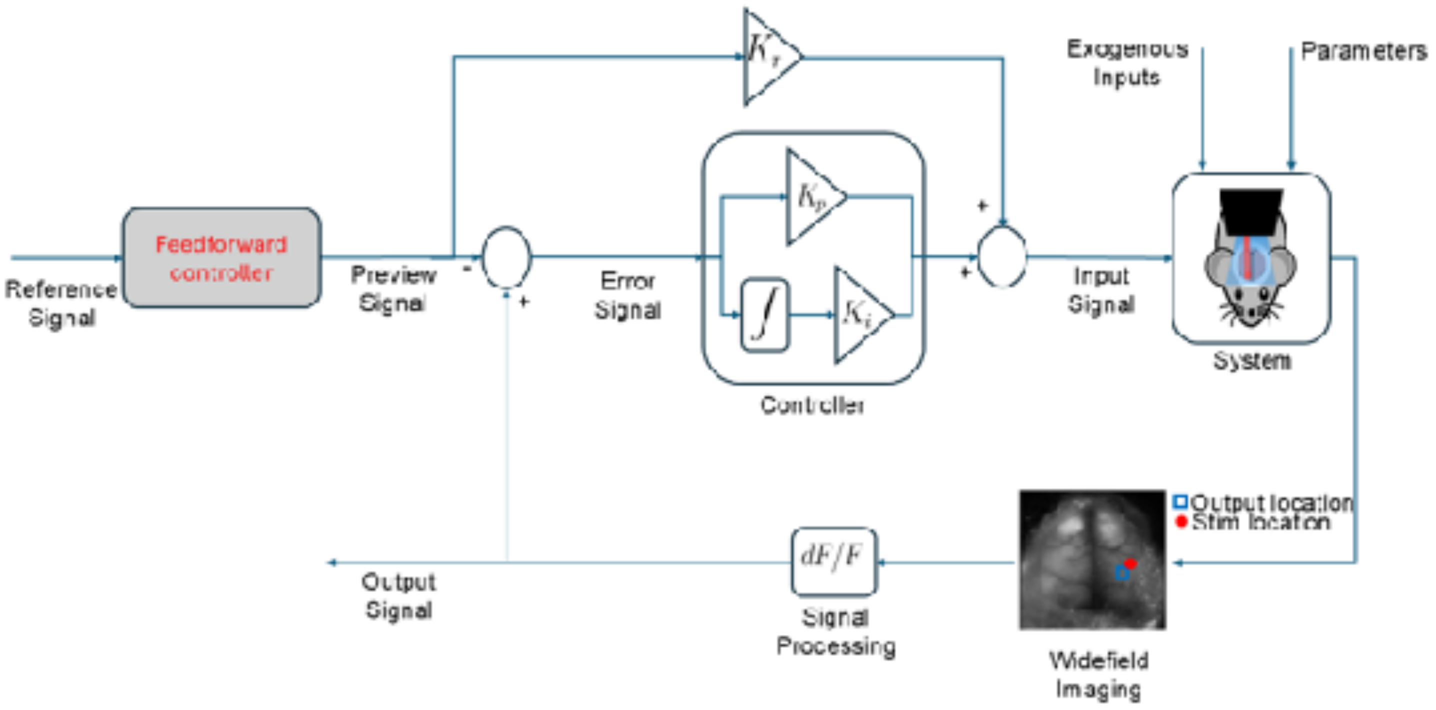






System Design

Assumption: A *trial-averaged dynamics are LTI.*



**Subject to Brain state

Non-linear system

Average

LTI

But trial-level activity is highly variable.

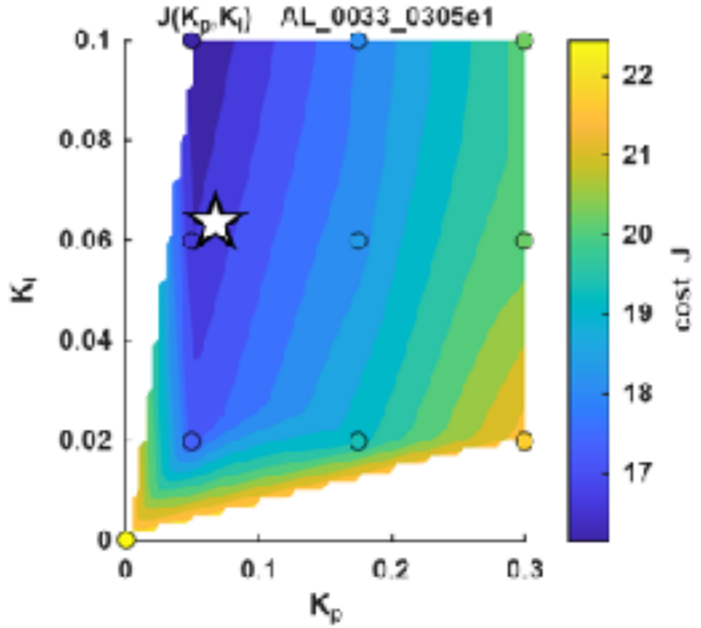
Solution: Proportional-Integral output-feedback controller

$$\boldsymbol{u}_t = K_r \boldsymbol{y}_{ref}(t) + K_p(\boldsymbol{y}(t) - \boldsymbol{y}_{ref}(t)) + K_i \sum_{i=0}^{t}(\boldsymbol{y}(i) - \boldsymbol{y}_{ref}(i))$$

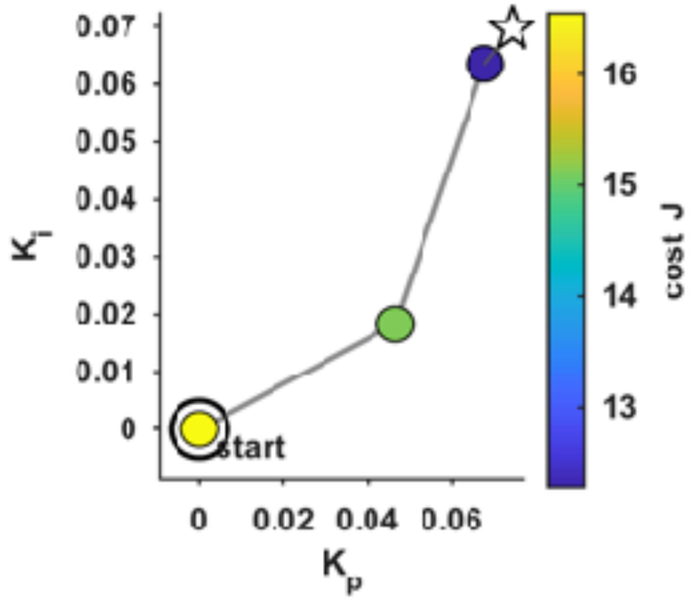
Controller Design

$$u_t = K_r y_{ref}(t) + K_p(y(t) - y_{ref}(t)) + K_i \sum_{i=0}^{t}(y(i) - y_{ref}(i))$$

Cost map across controller gains



Gains derived through optimization



Controller evaluation cost : $J(K) = \sum_{i=0}^{T} \|y(i) - y_{ref}(i)\|_2 + \|u(i)\|_2$

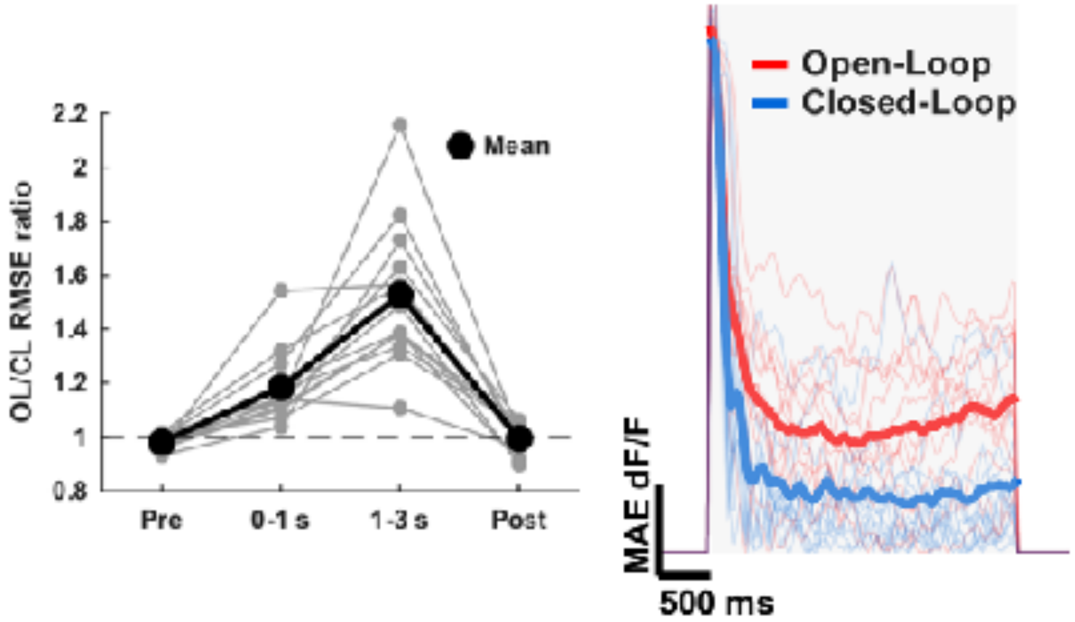
stationarity assumption must be true.

Real-time Implementation

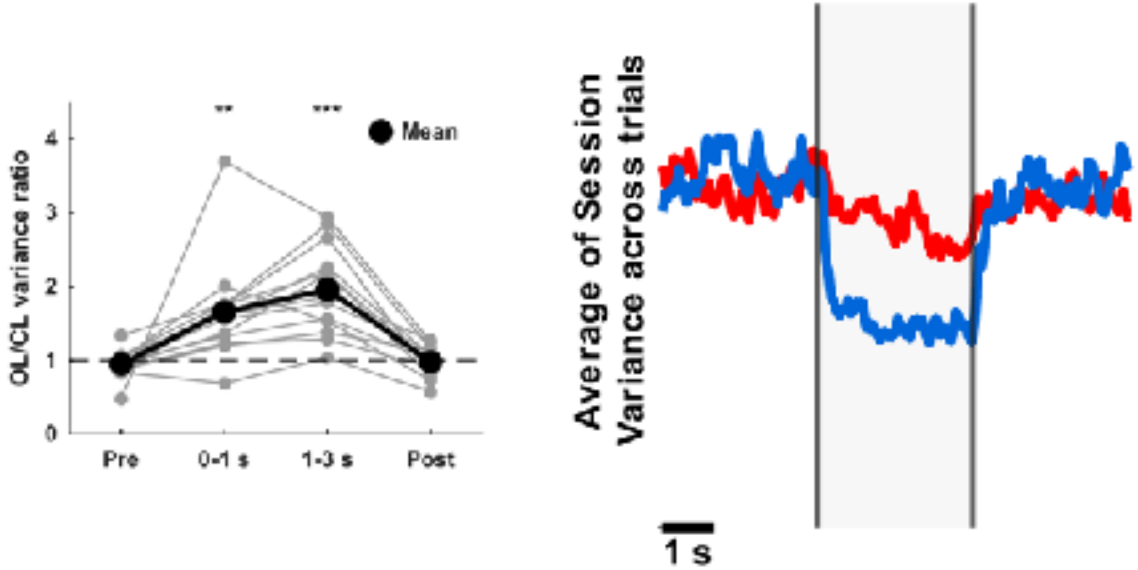
Targeted closed-loop optogenetic control of cortical dynamics

Performance

Closed loop controller improves tracking and rejects disturbance



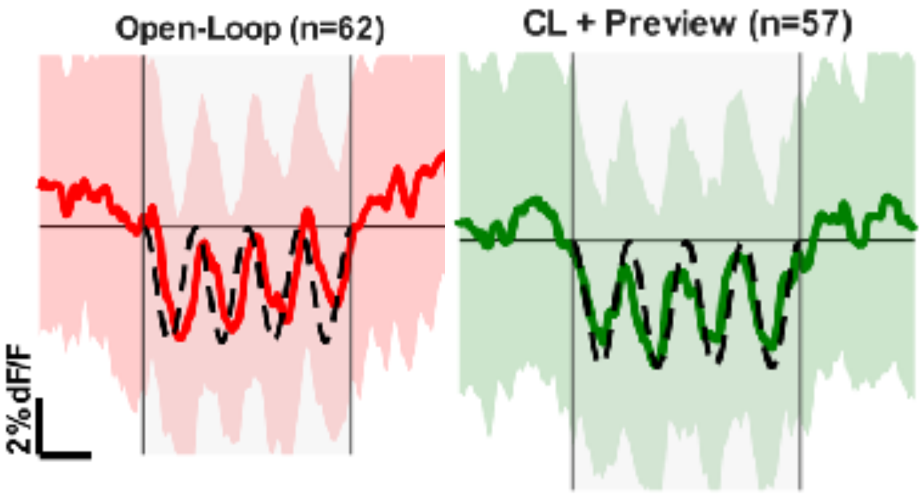
Trial-by-trial variability significantly reduces across sessions



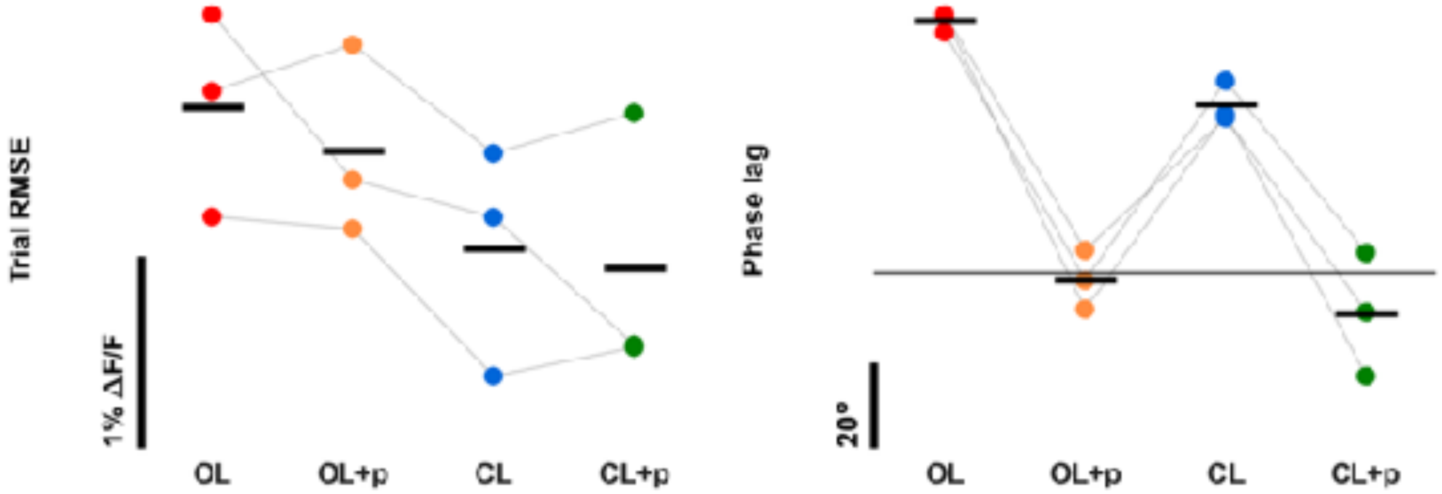
Performance

Feedforward Controller drives local activity close to moving reference

A controller with model knowledge drives activity (preview)



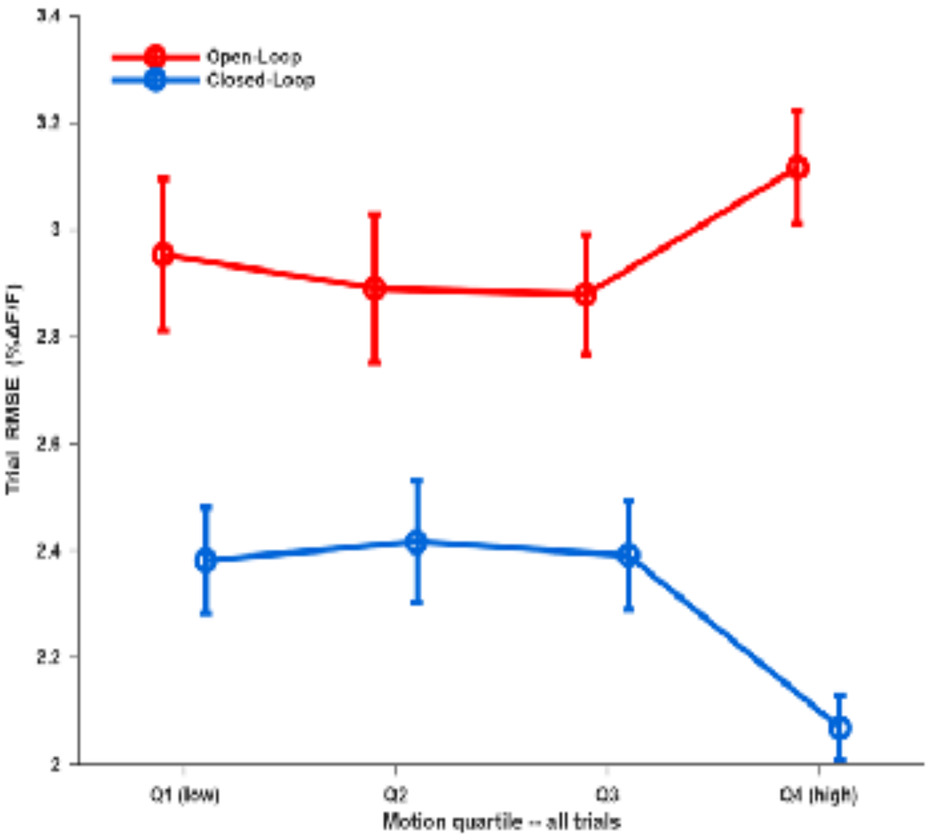
Model knowledge Improves tracking and tracks phase

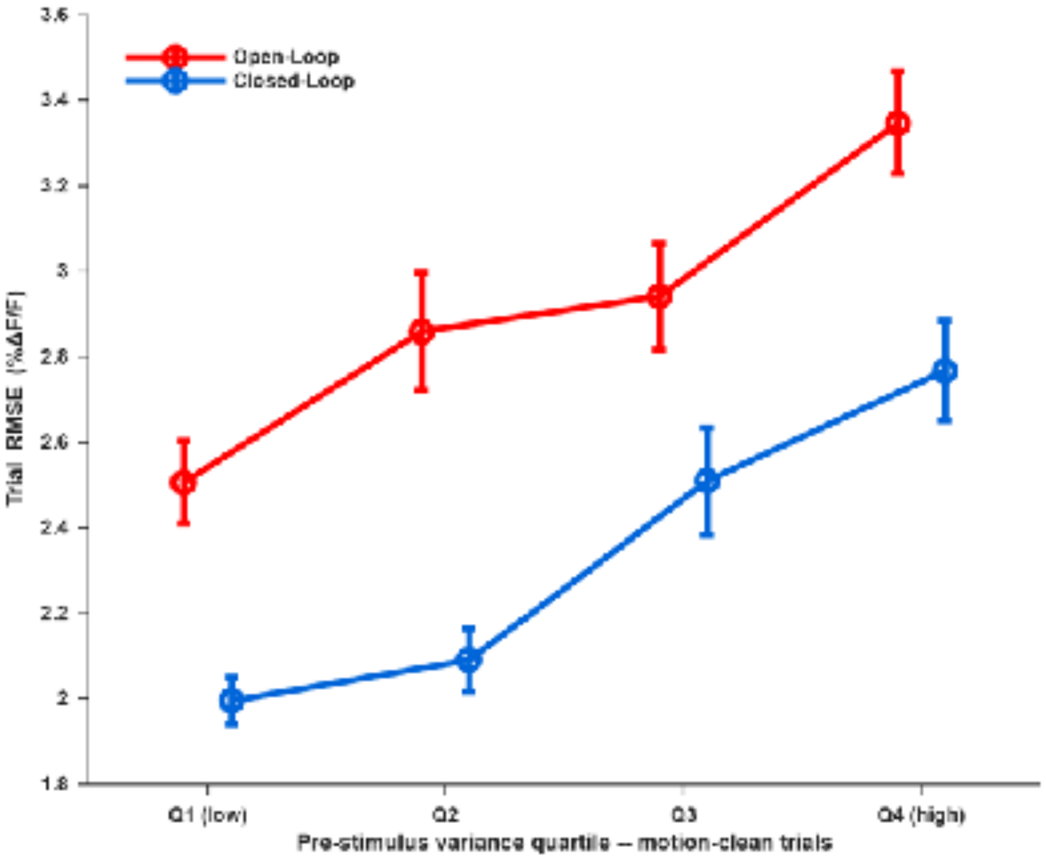


Internal Brain Model

Controller performance reveals system properties,

- Motion improves controllability, while synchronization degrades it





Conclusion

- We designed a Real-time Closed loop feedback system using LTI principles

- The closed loop controller can guide dynamics to desired trajectory and reduces trial to trial variability

- We found that brain states affect controllability of the closed loop system.

Future directions

- Disturbance rejection model
- Identifying relevant subspaces for optimum Observability and Controllability
- Multimodal Control that exploit multi-region interactions
- Behavioral Manipulation using Model Predictive Control

Thank you

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