Propofol anesthesia destabilizes neural dynamics across cortex

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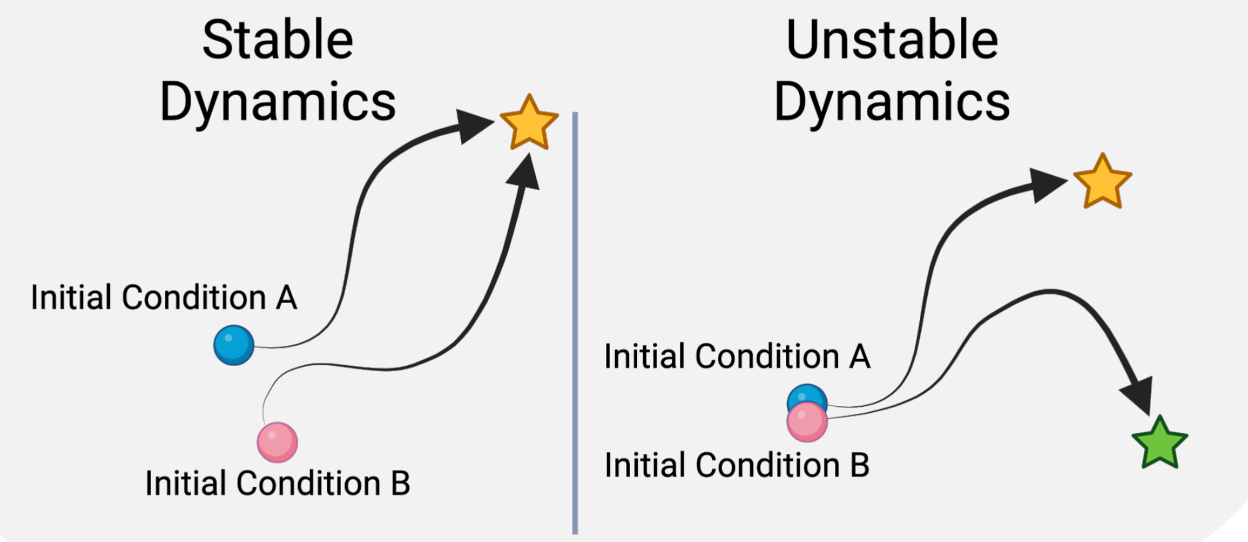
SCAN ME

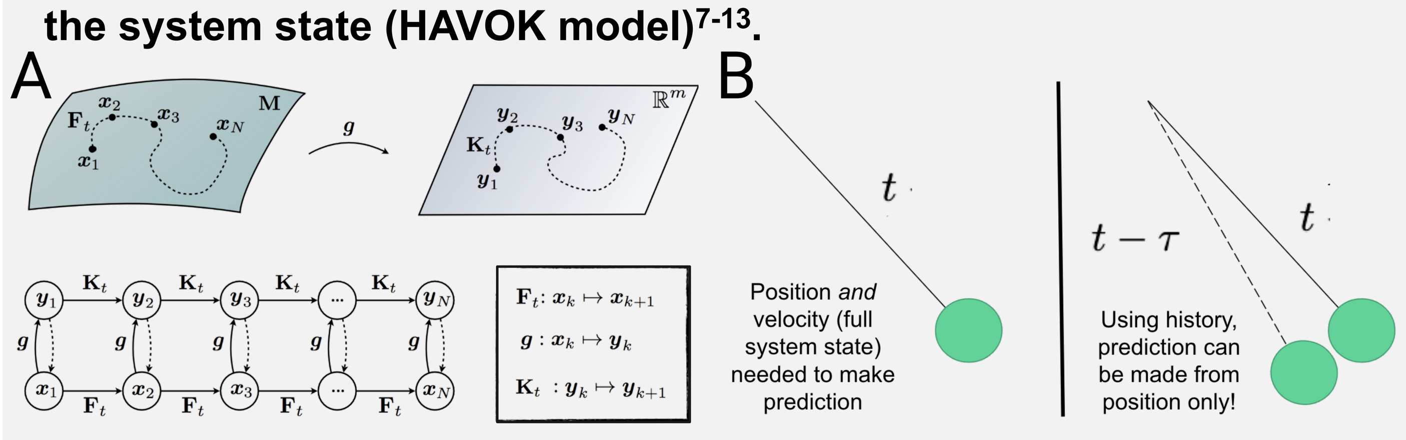
INTRODUCTION

- **The neural basis of consciousness is unknown** – anesthesia allows exploration of the transition between consciousness and unconsciousness.
- A prominent hypothesis suggests that **dynamic stability is critical to cortical function**[1-4]: awake brains are poised at a state that is sufficiently excitable for activity generation and propagation, yet controllable and stable.
- **Anesthesia could stabilize or destabilize neural dynamics.** Current approaches have not resolved this[5,6].
- We leveraged tools from dynamical systems theory.



METHODS
Model Building

By looking backwards in time, we can find a fully linear representation of the brain's complex nonlinear dynamics. **We can represent complex dynamics as simple linear ones based on a delay embedding of the system state (HAVOK model)**[7-13].



$$X \in \mathbb{R}^{n \times T}$$

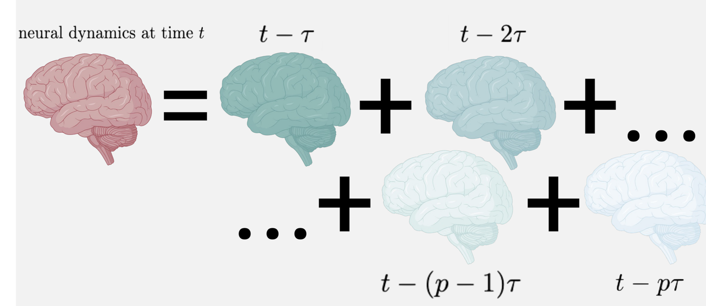
$$H = \begin{bmatrix} x_{p-1} & x_p & \dots & x_{T-1} \\ x_{p-2} & x_{p-1} & \dots & x_{T-2} \\ \vdots & \vdots & \ddots & \vdots \\ x_0 & x_1 & \dots & x_{T-p} \end{bmatrix} \in \mathbb{R}^{pn \times T-p}$$

$$H = U\Sigma V^*$$

$$A_v = \arg\min_{A_v} ||V_r^+ - A_v V_r^-||_F = V_r^+ V_r^{-\dagger}$$

METHODS
Stability Estimation

Using methods from linear delay differential equations (DDEs), we estimate stability by **discounting the impact of previous states on dynamics**[14,15].



Instability: mathematical definition

$$\vec{x}_t = \sum_{i=1}^{p} A_i \vec{x}_{t-i}$$

For a system of linear DDEs

$$y'(t) = A_0 y(t) + \sum_{j=1}^{m} A_j y(t-\tau_j) \quad \text{where } y(t) \in \mathbb{R}^n,$$

Stability is determined by roots of

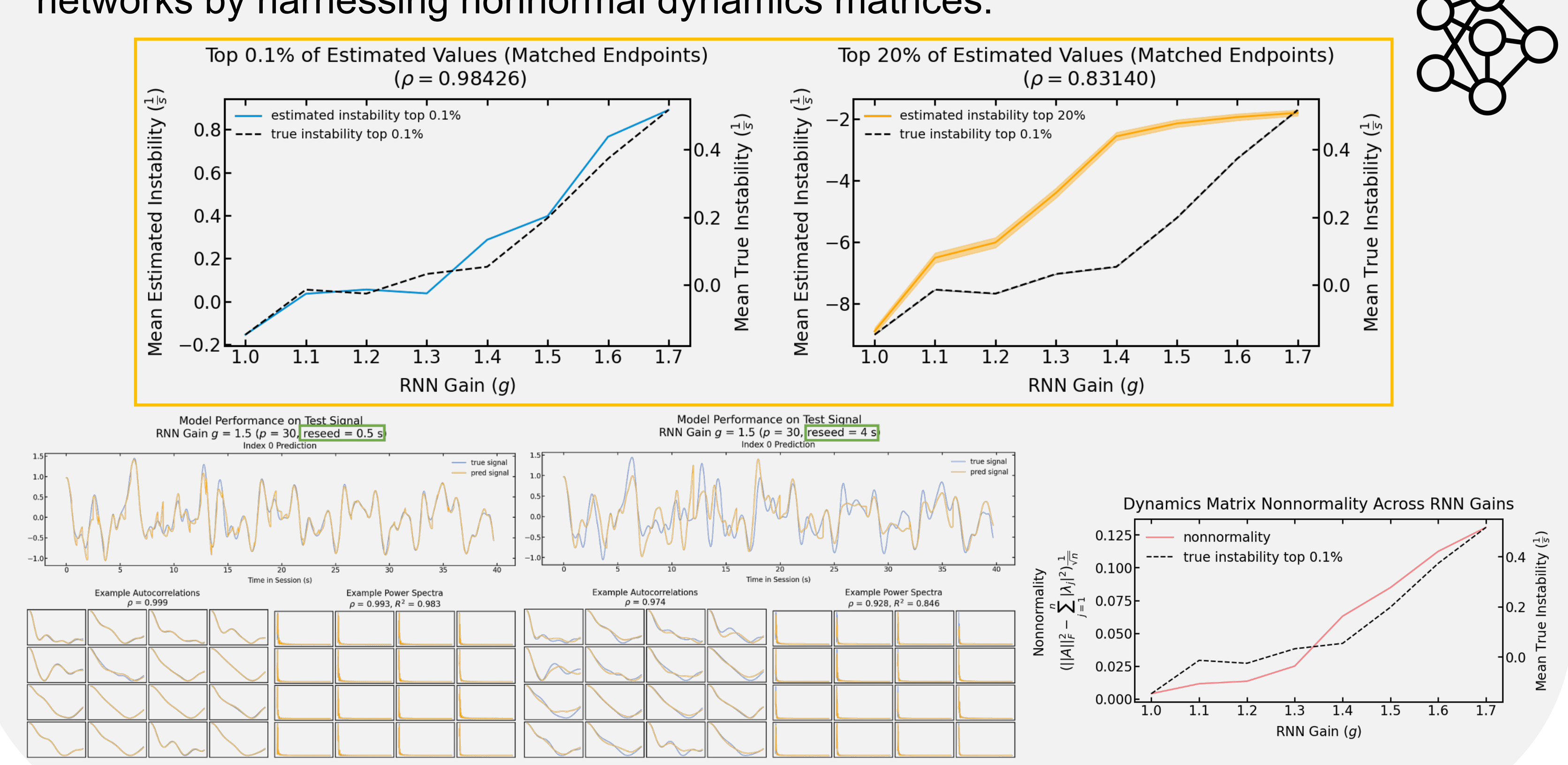
$$\det\left(\lambda I - A_0 - \sum_{j=1}^{m} A_j e^{-\lambda \tau_j}\right) = 0$$

(also true for linearizations of nonlinear systems)

*potentially infinite roots

RESULTS
Accurate stability estimation in simulation

We predicted relative changes in stability between RNNs (randomly connected networks with variance proportional to inverse square root of network size) using only partial observation (50 of 512 neurons observed). **The linear dynamical systems models also successfully capture the complex chaotic dynamics** in the simulated networks by harnessing nonnormal dynamics matrices.

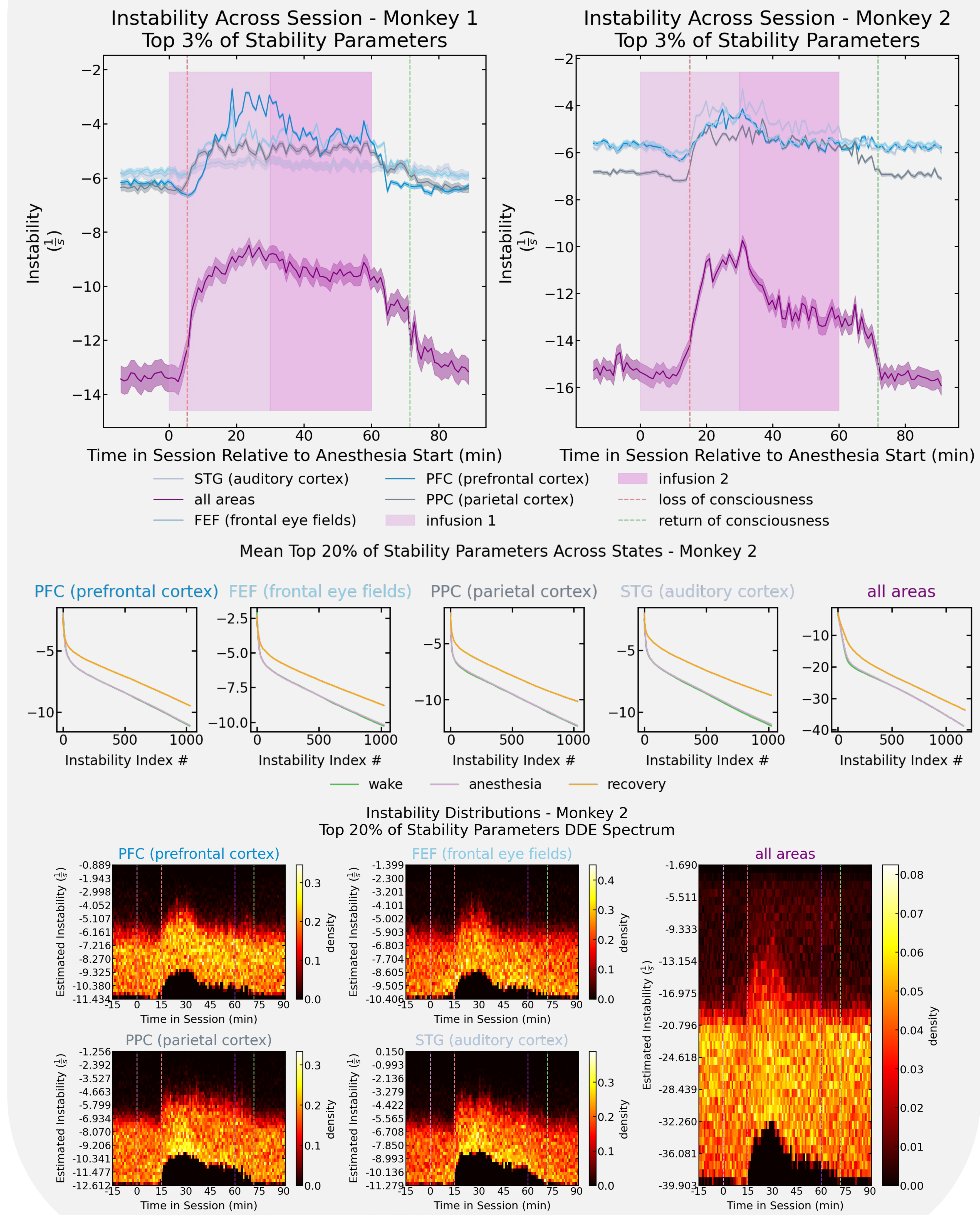


*10ms = 1 time step

RESULTS
Models capture nonlinear neural dynamics

*reinitialize with true state every 50 ms (50 time steps)

RESULTS
Propofol destabilizes neural activity



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