Non-invertibility of basal ganglia network calls for new biomarkers

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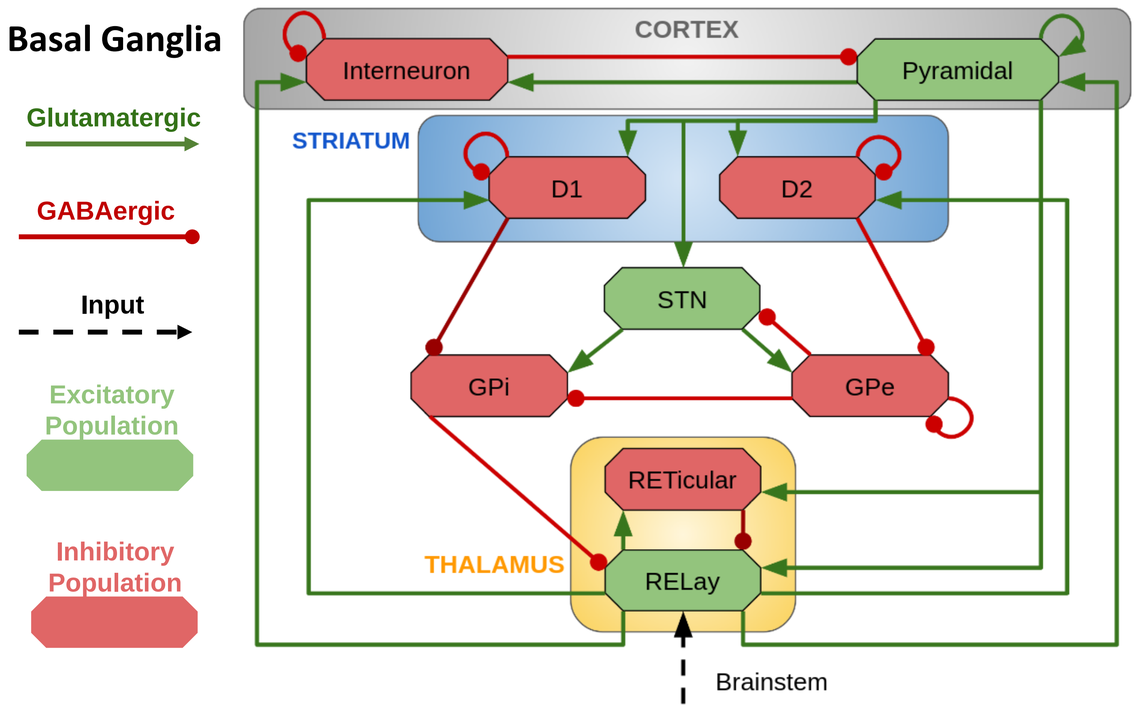
INTRODUCTION

- Mathematical models of the basal ganglia (BG) partition the parameter space based on the parkinsonian biomarkers into healthy and pathological (P-conformal)
- We show that biomarkers alone, do not constrain the high-dimensional parameters space of BG models
- Incorporation of new biomarkers or the brain recording data is a must for unique parameter extraction

MODEL



Mean-field model

- *Spatially homogeneous neural field ($r_a^2 \nabla^2 \phi_k = 0$)*
- *Axonal pulse attenuation without delay ($\delta_{ik} = 0$)*
- *Noise-free input from brainstem*

$$\left[\tau_r \tau_d \frac{d^2}{d^2 t} + (\tau_r + \tau_d)\frac{d}{dt} + 1\right] V_i = \sum_k \nu_{ik}\, \phi_k(t - \delta_{ik})$$

$$\left[\frac{1}{\gamma_a^2}\frac{\partial^2}{\partial^2 t} + \frac{1}{\gamma_a}\frac{\partial}{\partial t} + 1 - r_a^2 \nabla^2\right] \phi_k = \frac{Q_k^{max}}{1+\exp\left[-\frac{V_k - \theta_k}{r}\right]}$$

Parameters

- *Parameters set according to physiological steady-state firing rates*
- *Parkinsonian state defined by varying connectivity and thresholds*
- *Sweep decay time scale to find "P-conformal" regions*

Study

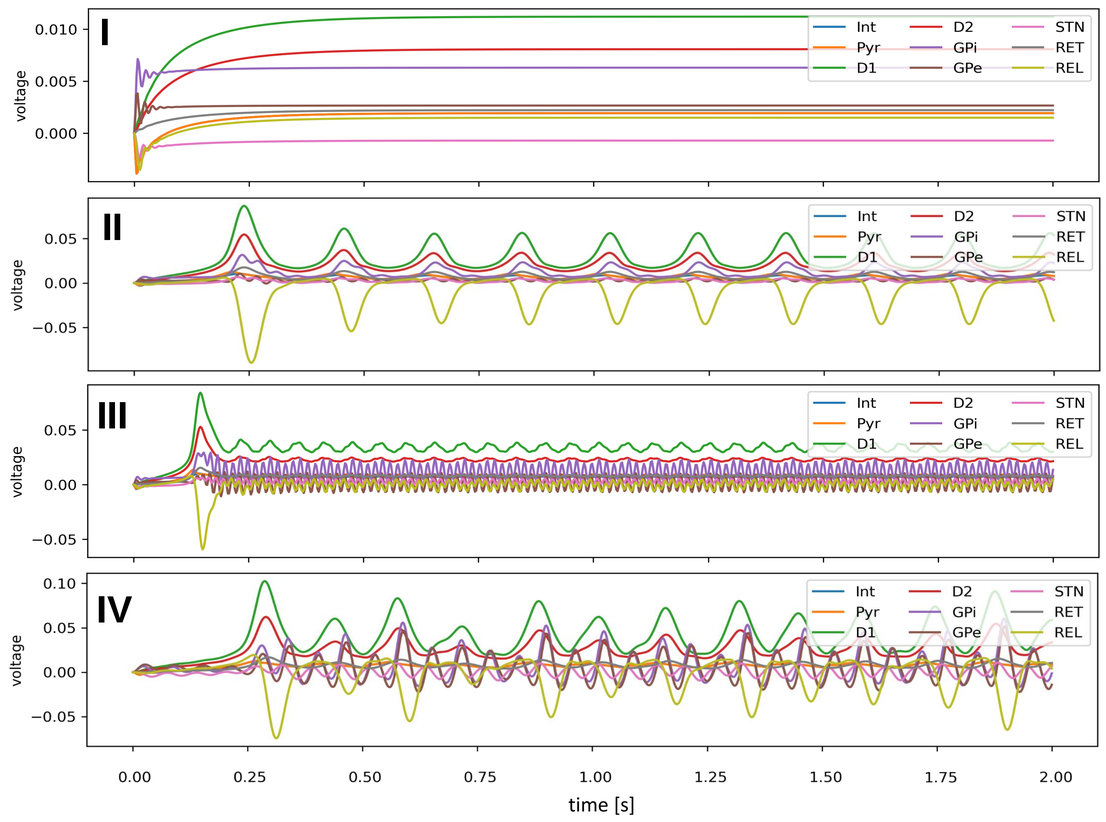
- *Sweep decay time scale (τ_d) to find "P-conformal" regions*

$$\textit{P-conformal} = \left(\frac{P_\beta^{parkin}}{P_\beta^{healthy}} > 1\right) \qquad P_\beta = \int_{12\ Hz}^{30\ Hz} PSD(f)\,df$$

RESULTS

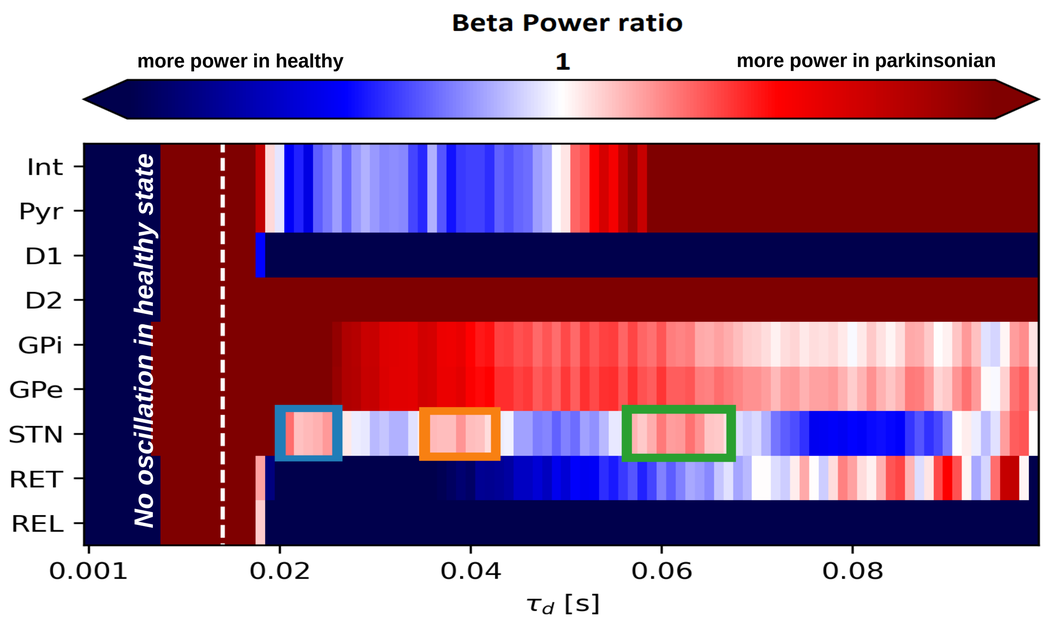
A. Existence of multitude of P-conformal parameters with dynamically different behavior

I. Steady-state → [1,2], this work
II. Unimodal oscillation → [3], this work
III. Multimodal oscillation → this work
IV. Chaotic → this work



B. Multitude of P-conformal parameter regions

- May be discerned based on number of modes, peak frequency, or additional biomarkers (e.g. cross-correlation)
- Utilizing brain recordings is necessary to extract parameters



FUTURE WORK & ACKNOWLEDGMENT

- Implementation of the axonal delays
- Use EEG/ECoG recordings and Bayesian inversion to estimate parameters systematically

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REFERENCES

1. *van Albada, S.J., Robinson, P.A., 2009. Mean-field modeling of the basal ganglia-thalamocortical system. I: Firing rates in healthy and parkinsonian states. Journal of Theoretical Biology 257, 642–663.*
2. *van Albada, S.J., Gray, R.T., Drysdale, P.M., Robinson, P.A., 2009. Mean-field modeling of the basal ganglia-thalamocortical system. II: Dynamics of parkinsonian oscillations. Journal of Theoretical Biology 257, 664–688.*
3. *Müller, E.J., Robinson, P.A., 2018. Quantitative theory of deep brain stimulation of the subthalamic nucleus for the suppression of pathological rhythms in Parkinson's disease. PLoS Comput Biol 14, e1006217.*

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