

Non-invertibility of basal ganglia network calls for new biomarkers

Arash Golmohammadi¹, Revathi Appali^{1,3}, Jan Philipp Payonk¹, Ursula van Rienen^{1,2,3}, Timon Merk⁴, Wolf-Julian Neumann⁴

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

D1

GPi

THALAMUS

Interneuron

STRIATUM

CORTEX

STN

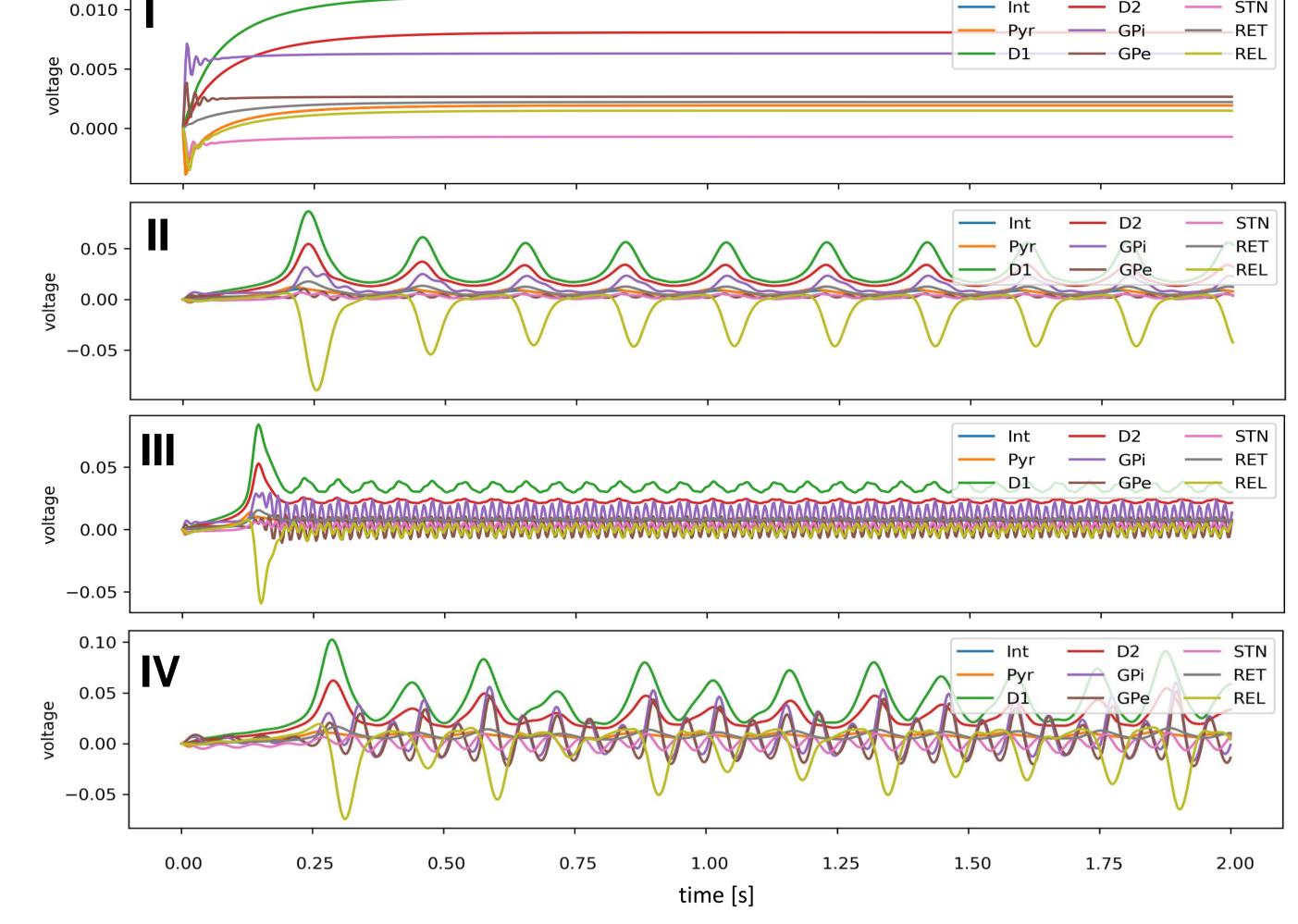
RETicular

RELay

Brainstem

D2

GPe

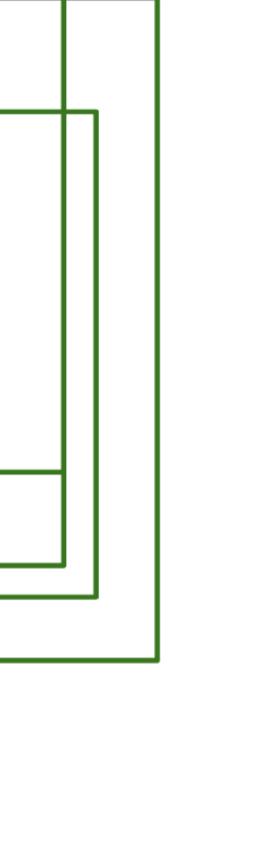


 May be discerned based on number of modes, peak frequency, or additional biomarkers (e.g. cross-correlation)

Beta Power ratio

Utilizing brain recordings is necessary to extract parameters

B. Multitude of P-conformal parameter regions



Pyramidal

Mean-field model

Basal Ganglia

Glutamatergic

GABAergic

Input

Excitatory

Population

Inhibitory

Population

- Spatially homogeneous neural field
- Exponential synapses
- Axonal pulse attenuation without delay
- Noise-free input from brainstem

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)
- Investigate the pathological to healthy beta power ratio
- Parameters consistent with the beta excess biomarker (ratio >1) are marker as "P-conformal"

P-conformal =
$$\left(\frac{P_{\beta}^{parkin}}{P_{\beta}^{healthy}} > 1\right)$$

$$P_{\beta} = \int_{12 \, Hz}^{30 \, Hz} PSD(f)df$$

RESULTS

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

I. Steady-state

→ [1,2], this work

II. Unimodal oscillation

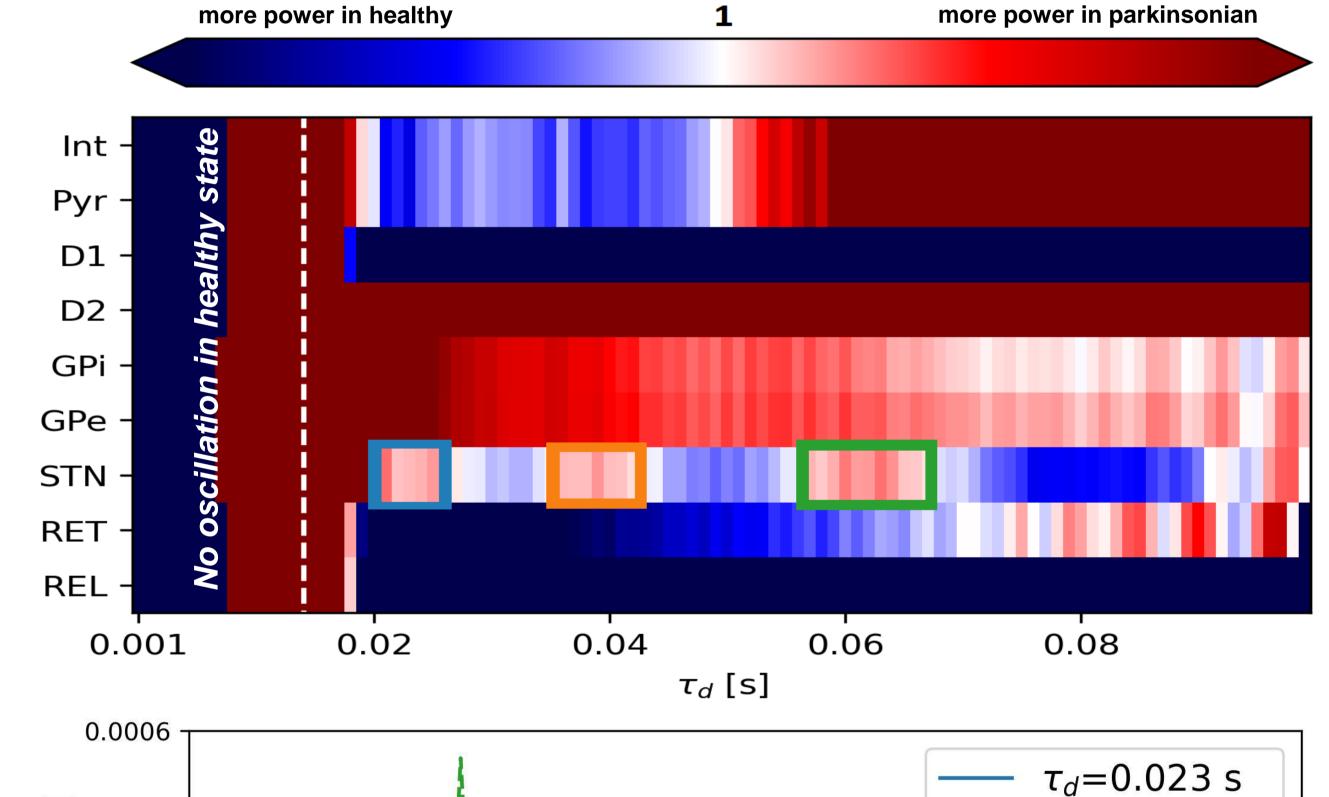
→ [3], this work

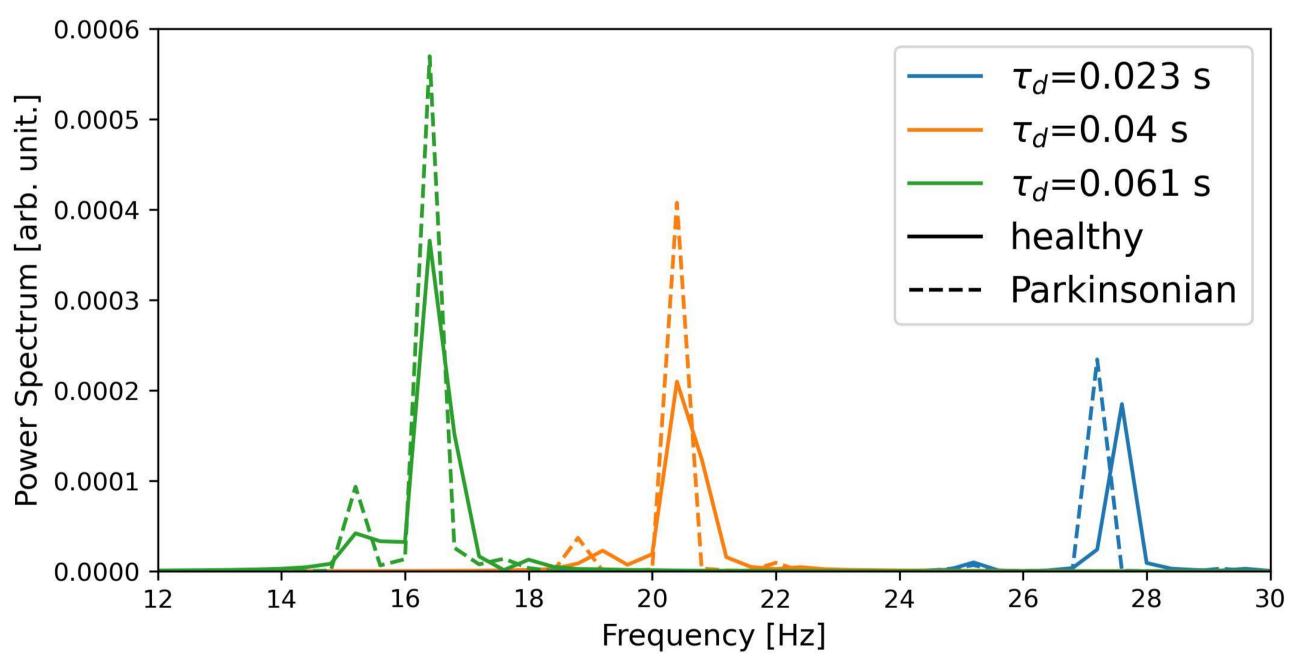
III. Multimodal oscillation

→ this work

IV. Chaotic

→ this work





FUTURE WORK & ACKNOWLEDGMENT

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

This work was funded by DFG via CRC 295 RETUNE (424778381)

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.
- 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.
- 1.Institute of General Electrical Engineering, Faculty of Computer Science. and Electrical Engineering, University of Rostock, Germany
- 2.Department Life, Light & Matter, University of Rostock, Germany
- 3.Department Ageing of Individuals and Society, University of Rostock, Germany
- 4. Movement Disorder and Neuromodulation Unit, Department of Neurology, Charité Universitätsmedizin Berlin, Germany



