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P 64 – Computational modelling and imaging in DBS . **E-mail: arash.Golmohammadi@uni-rostock.de**

Non-invertibility of basal ganglia network calls for new biomarkers

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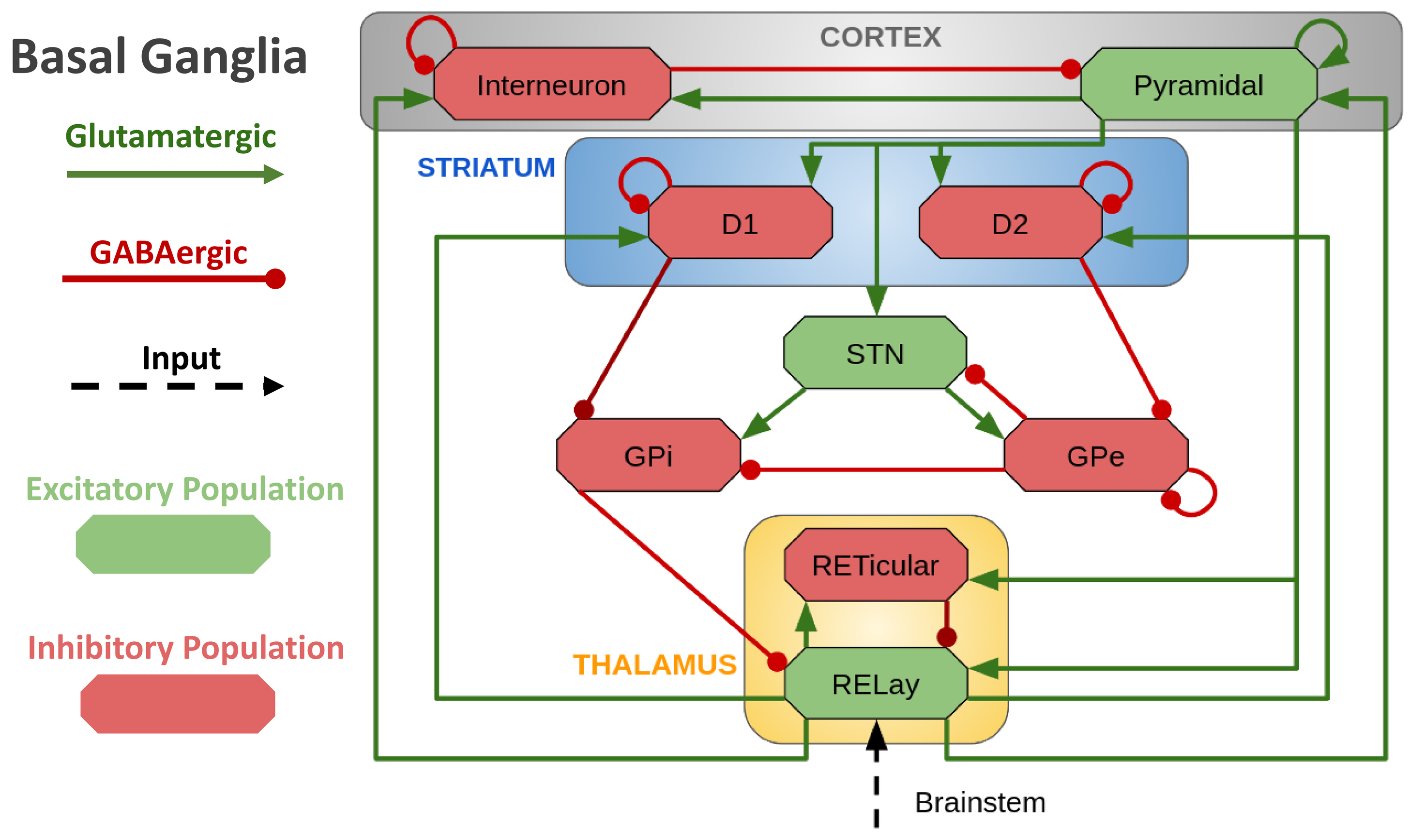
INTRODUCTION

- 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

MODEL



Mean-field model

Solved for voltage $V_k(t)$ and field $\phi_k(\boldsymbol{r},t)$ for each population k

$$\tau_r\tau_d\frac{d^2V_k}{dt^2}+(\tau_r+\tau_d)\frac{dV_k}{dt}+V_k=\sum_i \nu_{ki}\,\phi_i(t-\delta_{ki})+I_k^{ext}$$

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

- Synaptic rise time τ_r and somatic decay time τ_d
- Axonal pulse attenuation with damping rate γ_a
- Spatially homogeneous neural field ($r_a^2\nabla^2\phi_k=0$)
- Axonal pulse attenuation without delay ($\delta_{ki}=0$)
- Sigmoidal activation function with threshold θ_k, steepness r_k, and maximum firing rate of $Q_k^{\max}$
- Noise-free input I_k^{ext} from brainstem to k=thalamus

Parameters

- set according to physiological steady-state firing rates
- Parkinsonian state defined by varying connectivity and thresholds

Study

- Sweep the decay time scale (τ_d) to find *P-conformal* regions using the integral of power spectral density (PSD):

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

RESULTS

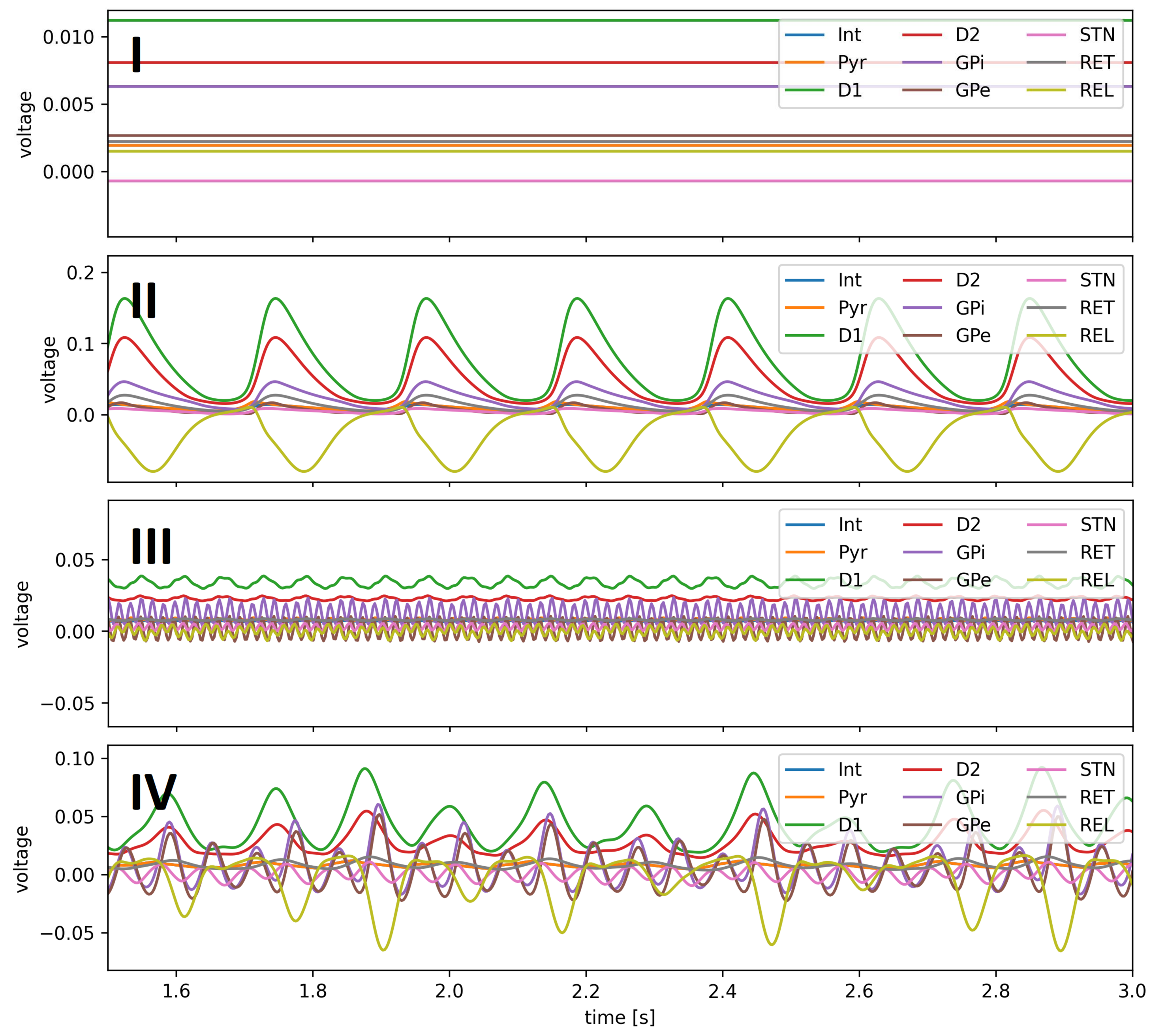


Figure 1: Canonical response types of the model

RESULTS

- Model exhibits dynamically different response types (Fig.1)
  I. Stationary steady-state → [1,2], this work
  II. Uni-modal oscillation → [3], this work
  III. Multi-modal oscillations → this work
  V. Chaotic → this work

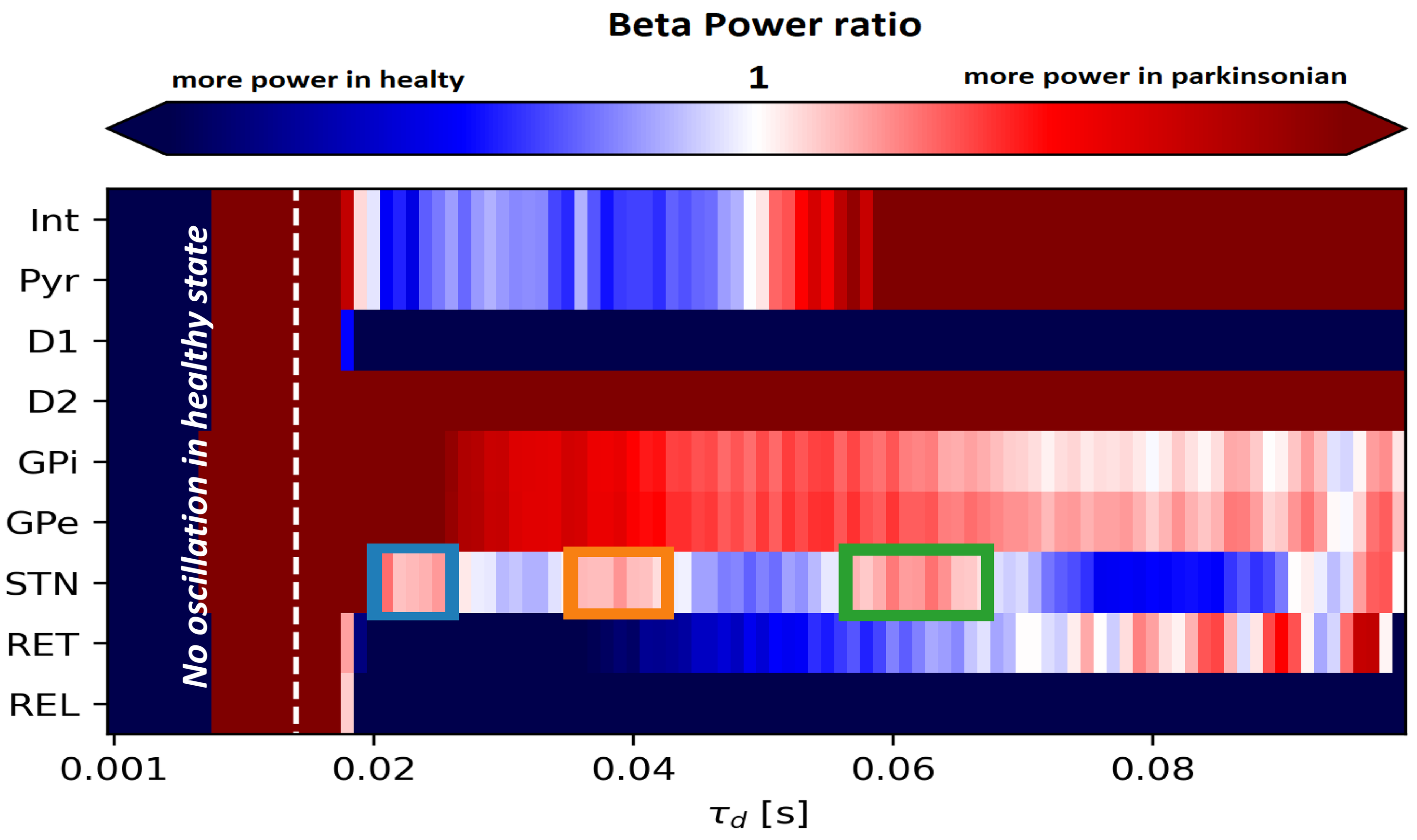


Figure 2: Multitude of P-conformal parameter regions. Some STN windows are marked in blue, orange and green

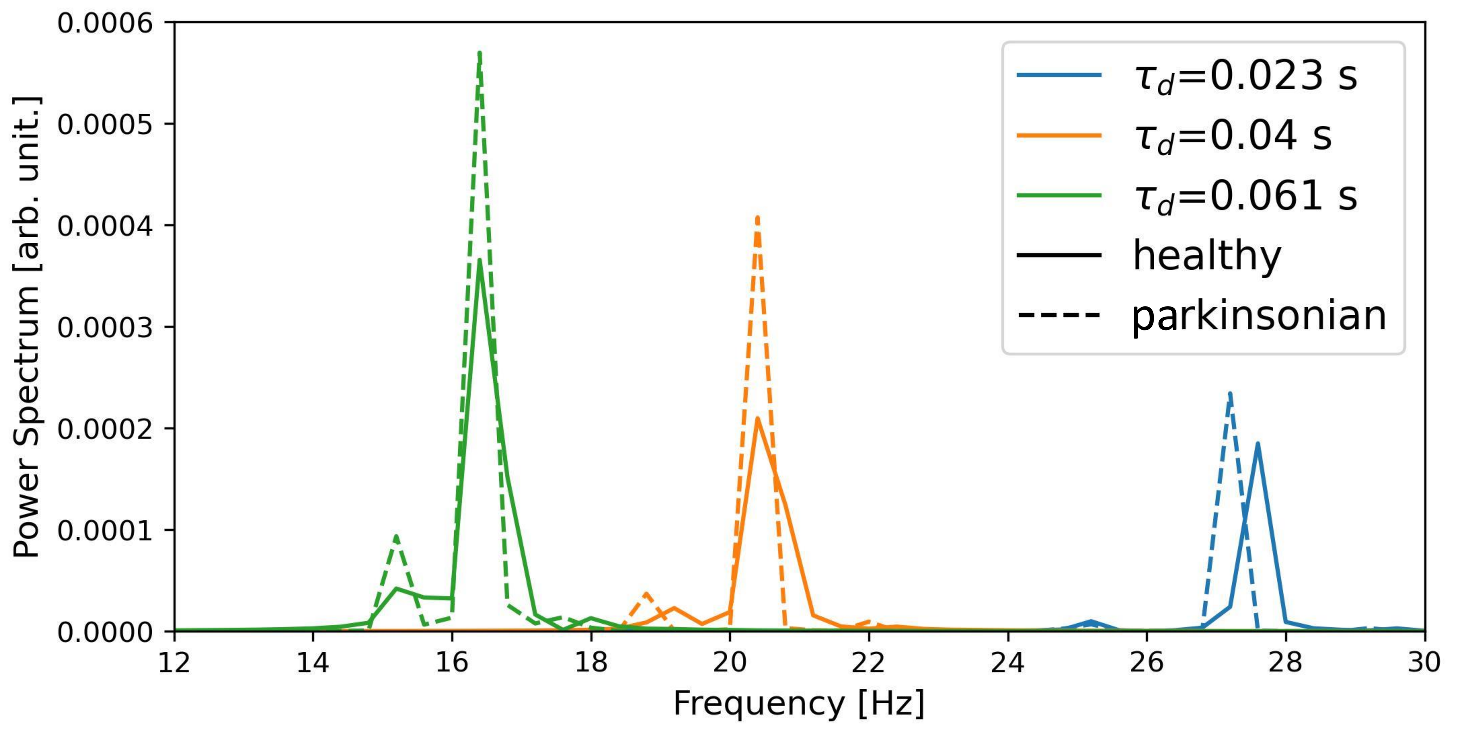


Figure 3: STN power spectral density of the windows marked in Fig. 2 in beta frequency range

DISCUSSION

- Several physiologically plausible parameter sets exhibit parkinsonian-like responses
- Computational models provide tests to discern these parameter sets using the response's dynamical type (number of modes, peak frequency, cross-correlations)
- Such tests must be validated against additional biomarkers or monitors in the brain

CONCLUSION

- Network can show varieties of dynamical responses depending on the parameters and the inputs
- Single biomarker is not enough to fully parametrize the computational model of healthy or parkinsonian state
- Model parameters must be systematically estimated using EEG/ECoG/LFP recordings and Bayesian inversion

FUTURE WORK

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

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[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 Computational Biology*, *14*(5), e1006217. https://doi.org/10.1371/journal.pcbi.1006217

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