Validation of dynamical whole-brain models in high-dimensional spaces

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Kevin J. Wischnewski[1,2,3], Simon B. Eickhoff[1,2], & Oleksandr V. Popovych[1,2]

[1]Institute of Neuroscience and Medicine (INM-7: Brain and Behaviour), Research Centre Jülich, Jülich, Germany;
[2]Institute of Systems Neuroscience, Heinrich Heine University Düsseldorf, Düsseldorf, Germany;
[3]Institute of Mathematics, Heinrich Heine University Düsseldorf, Düsseldorf, Germany

Email: k.wischnewski@fz-juelich.de **Website:** www.fz-juelich.de/inm/inm-7

Introduction

- Simulating the resting-state brain dynamics via mathematical **whole-brain models** allows for describing a subject's brain activity by a set of **interpretable model parameters** and **simulated functional connectivity**.
- However, computational **challenges in parameter optimization** constrain high-dimensional model studies and their level of **model personalization**.
- We apply 2 **mathematical optimization algorithms** to explore high-dimensional parameter spaces at moderate computational costs, and validate **whole-brain models** by optimizing between 2 and 103 free model parameters simultaneously.

➢ **Aim:** To gain an insight into the behavior of high-dimensional whole-brain models and their potential utility for **personalized simulations** of human brain dynamics.

Methods

- **272 subjects** (Human Connectome Project [1]) with **individual** empirical **structural** and **functional connectivity** (eSC and eFC, resp.)
- **Brain atlases:** Schaefer 100 (Sch100) [2] and Harvard-Oxford 0% (HO0Thr) [3] atlases with $N = 100$ and $N = 96$ cortical regions, resp.
- **Computational model:** Kuramoto model [4] of coupled phase oscillators
- Phase dynamics of brain region $i \in \{1, \ldots, N\}$:

$$\dot{\theta}_i(t) = 2\pi f_i + \frac{C}{N}\sum_{j=1}^{N} k_{ij}\sin\left(\theta_j\left(t-\tau_{ij}\right) - \theta_i(t)\right) + \sigma\,\eta_i(t)$$

➡ **simulated BOLD signals** ➡ **simulated FC** (sFC)

Model variables	Description	Model variables	Description
$\theta_i(t)$	Phase of region i at time t	$\tau_{ij} = \frac{PL_{ij}}{< PL >}\tau$	Coupling delay (signal transmission time) between region i and j
f_i	**Free parameter** of natural frequency $(0.01 - 0.1\ \mathrm{Hz})$ of region i	PL_{ij}	Average fiber path length between region i and j
C	**Free parameter** of global coupling strength	τ	**Free parameter** of global delay
$k_{ij} = \frac{SC_{ij}}{< SC >}$	Relative coupling strength between region i and j	σ	**Free parameter** of noise intensity
SC_{ij}	Number of streamlines between region i and j in the eSC matrix	$\eta_i(t)$	Independent noise perturbation of region i at time t
$<.>$	Averaging operator	$\sin(\theta_i)$	Simulated BOLD signal of region i

Model validation:
Pearson Correlation (sFC,eFC) ❯ *MAXIMIZATION*

Detecting optimal, subject-specific model parameters:

- C and τ free, $\sigma = 0.3$ fixed, f_i from empirical BOLD: **2D**
- C, τ and σ free, f_i from empirical BOLD: **3D**
- C, τ, σ and f_i free: **103D (Sch100) / 99D (HO0Thr)**

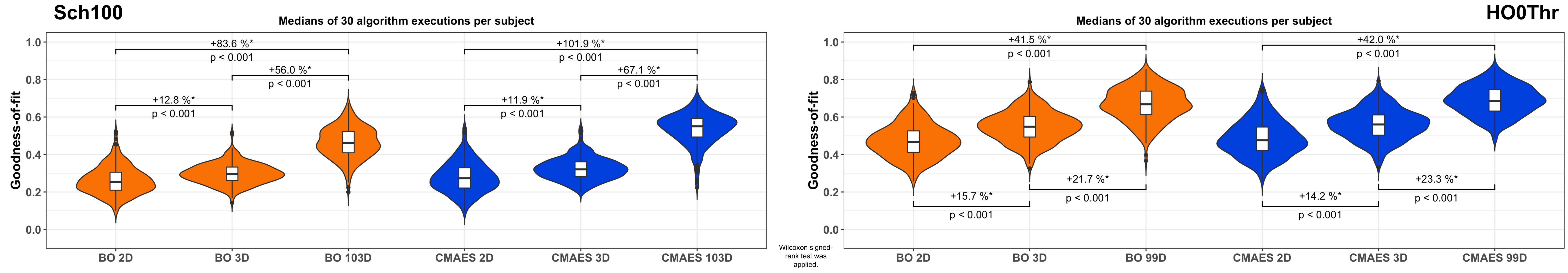
Optimization methods:

Covariance Matrix Adaptation Evolution Strategy (CMAES) [5]: Global population-based optimization technique, best trial solutions from every iteration (generation) are selected to form the distribution mean of the population for the next step

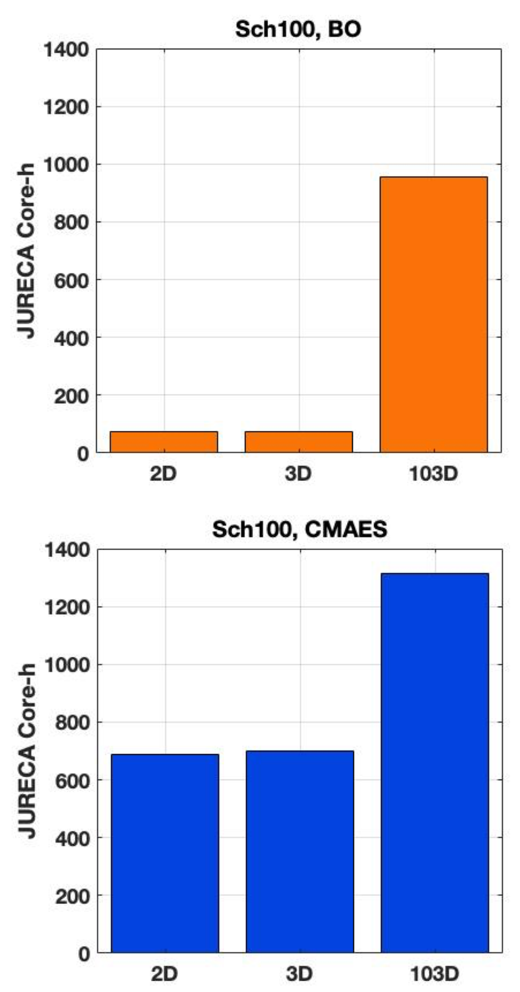
Bayesian Optimization (BO) [6]: Sequential design strategy for global optimizations of black-box functions, probabilistic surrogate model for the goal function, adjusted after every new function evaluation

Results

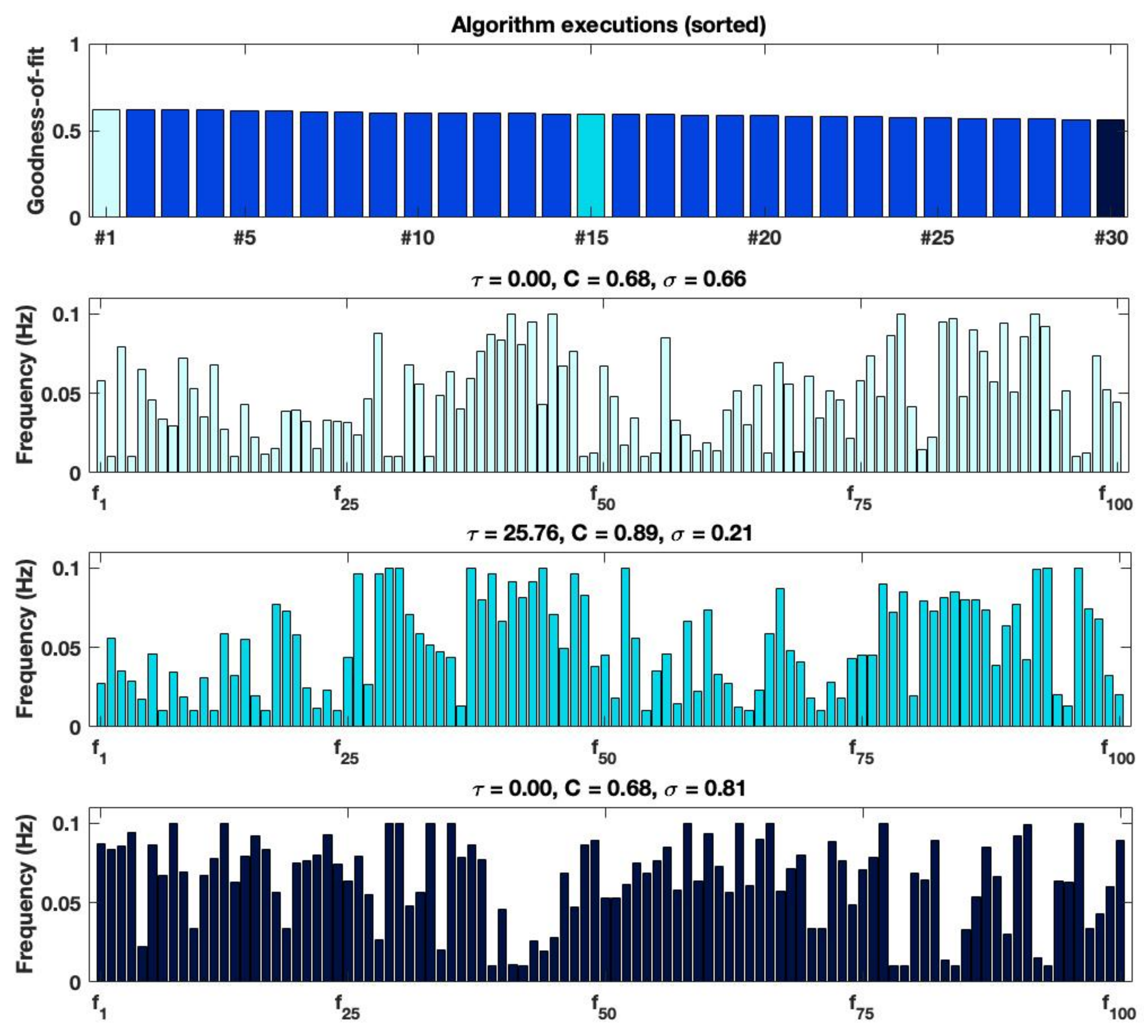
#1: Goodness-of-fit for personalized model simulations



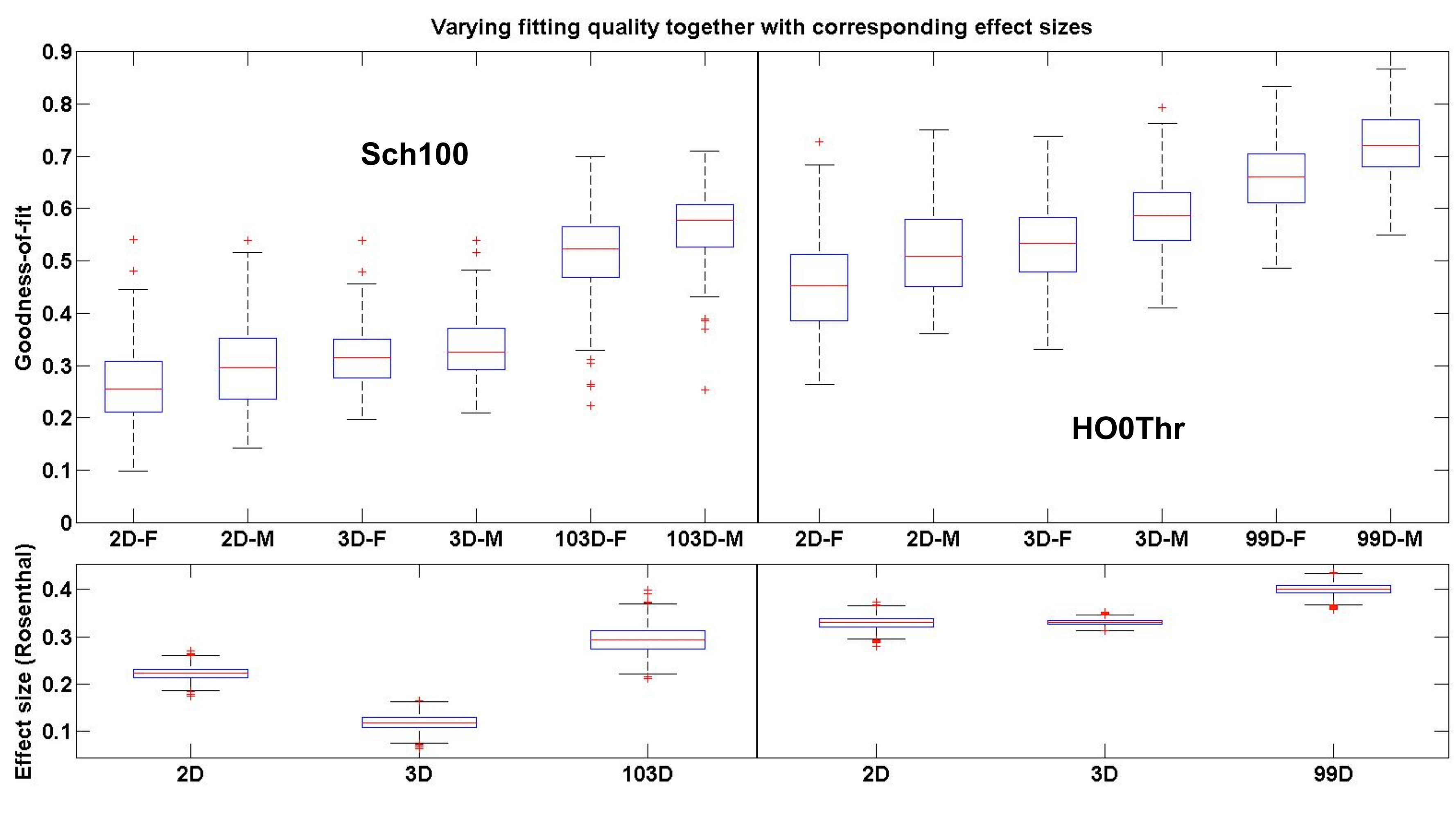
#2: Mean resource consumption per subject for 30 algorithm executions



#3: Example of high-dimensional simulation outcomes for one subject



#4: Differentiation between males (M) and females (F) on simulated data



128 males and 144 females. Effect sizes computed with Rosenthal's formula [7] for Wilcoxon rank-sum test.

Discussion

Summary:

- Empirical measurements can be much better replicated by high-dimensional models than by low-dimensional ones.
- A high goodness-of-fit can be obtained for **several configurations of "optimal" model parameters**, which are thus **less reliable** in high-dimensional cases.
- **Differences between males and females** appear to be **more pronounced** in data simulated by high-dimensional models.

Conclusions:

- New horizons for personalized brain modeling can be opened up by mathematical **optimization algorithms** which **enable the exploration of whole-brain models in high-dimensional parameter spaces**.
- Multiple algorithm executions per subject are necessary in view of the complexity of high-dimensional parameter spaces and the unfeasibility of a confirmatory grid search.

Outlook:

- High-dimensional brain models properly validated bear a huge potential for more precise and personalized studies.
- The manifold on which the optimal parameters seem to be located remains a hot topic for further investigations.
- The location of **optimal model parameters** might serve as an **individual subject's personal profile**.

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