Efficient validation of dynamical whole-brain models via mathematical optimization algorithms

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Introduction

- Experimentally discovered characteristics of resting-state brain dynamics may be simulated and studied via **mathematical whole-brain models**
- Optimally selected input parameters can put the models' output in **close correspondence with empirical observations**
- A **challenge**, however, is given by the **search for optimal model parameters**
- Increasingly many free parameters render a **systematic parameter space exploration** on a dense grid **intractable**

➢ **Aim:** To facilitate the process of model validation by suggesting some mathematical **optimization algorithms** as effective and resource-saving alternatives to an exhaustive grid search

Methods

Study design

- **105 subjects** from the Human Connectome Project [1]
- **Schaefer's functional brain atlas** [2] with $N = 100$ cortical regions
- **Subject-specific**, atlas-based empirical **structural and functional connectivity** (eSC and eFC, respectively)

Computational model

- Kuramoto model [3] of coupled phase oscillators
  → **simulated BOLD signals** → **simulated FC** (sFC)
- Phase dynamics of brain region $i \in \{1, \ldots, N\}$ [4]:

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

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	Natural frequency ($0.01 - 0.1$ 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

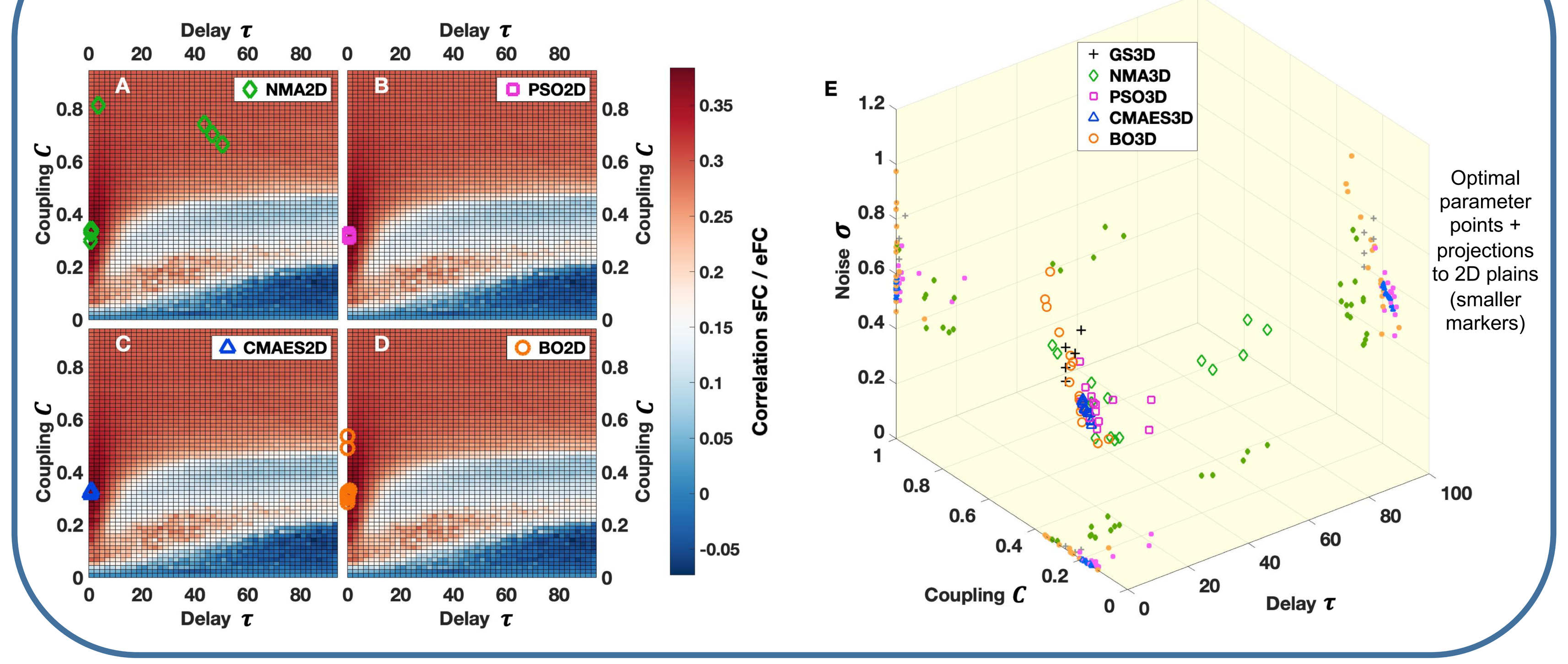
- Optimizing the subject-specific model parameters to **maximize the similarity** (Pearson correlation) **between sFC and eFC**
- Two different parameter spaces:
  I. Two-dimensional scenario (2D) with C and τ as free parameters ($\sigma = 0.3$ fixed)
  II. Three-dimensional scenario (3D) with C, τ and σ as free parameters
- **Brute-force approach:**
  ➢ **Grid search (GS):** Exhaustive parameter space scan for $64 * 48 = 3072$ parameter tuples (C, τ) in 2D and for $48 * 22 * 81 = 85536$ tuples (C, τ, σ) in 3D

- **Derivative-free optimization algorithms:**
  ➢ **Nelder Mead Algorithm (NMA)** [5]: Direct local search method with deterministic optimization procedure, replacement of the worst trial solution in every iteration step
  ➢ **Particle Swarm Optimization (PSO)** [6]: Population-based variant of global stochastic search strategies, swarm of particles exploring the parameter space collaboratively and exchanging information about discovered function values
  ➢ **Covariance Matrix Adaptation Evolution Strategy (CMAES)** [7]: 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)** [8]: Sequential design strategy for global optimizations of black-box functions, probabilistic surrogate model for the goal function, adjusted after every new function evaluation

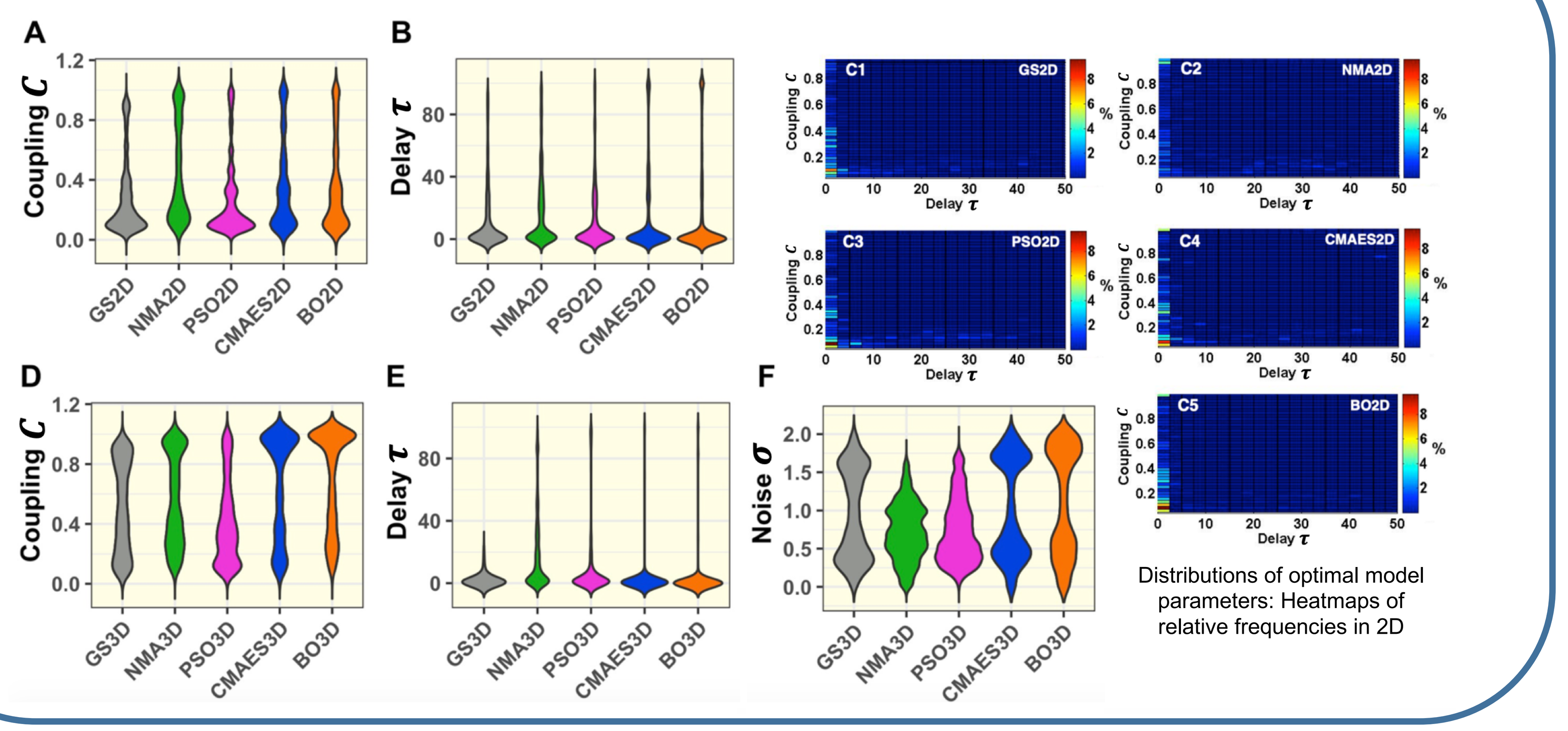
15 executions per subject

Results

Optimized model parameters in 2D and 3D (personalized simulations)

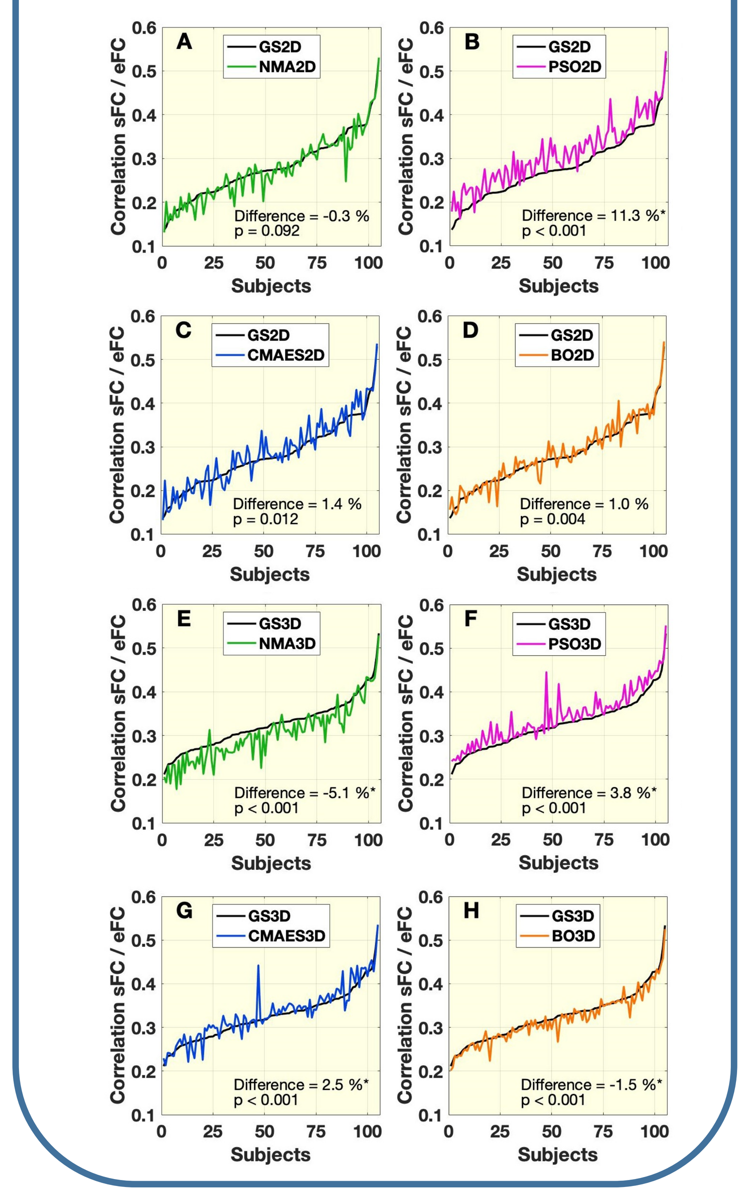


Optimized model parameters in 2D and 3D (group-level analysis)



Algorithms vs. Grid search

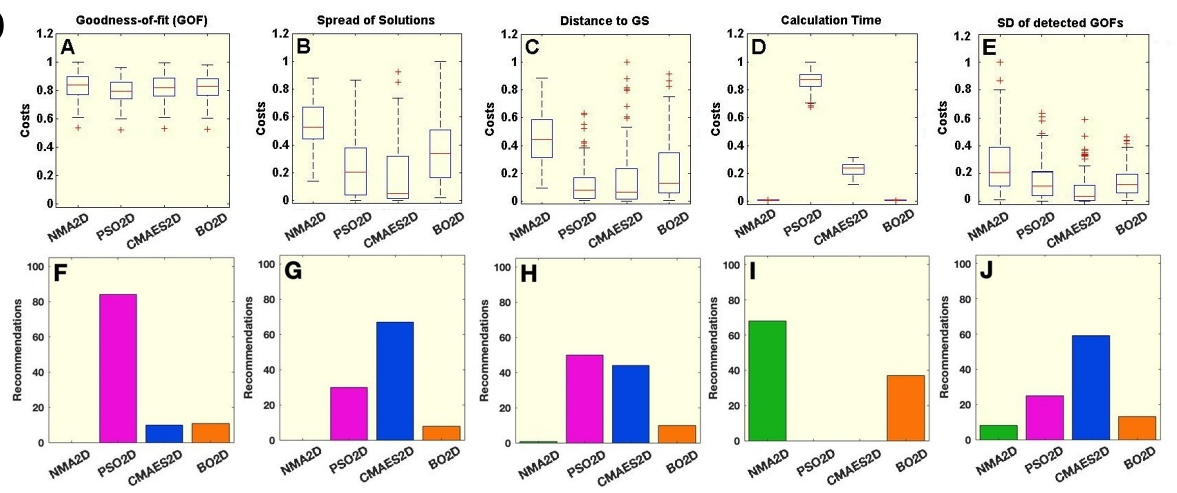
Subjects in ascending order according to grid search results
Statistical significance of median of relative difference assessed via Wilcoxon signed-rank test



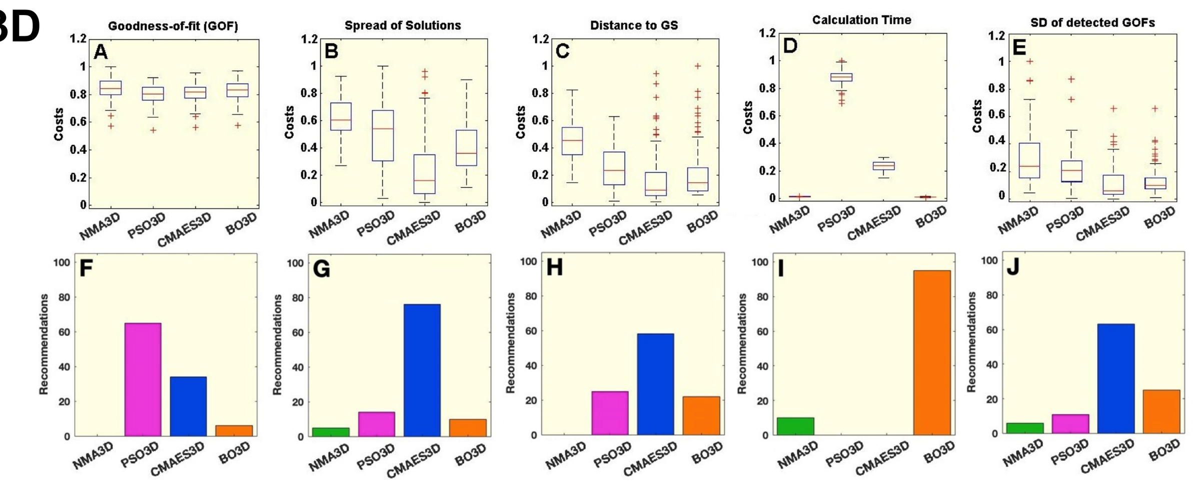
Comparison criteria

- ✓ Highest correlation sFC / eFC (goodness-of-fit)
- ✓ Spread of algorithm solutions in parameter space
- ✓ Distance to grid search solutions in parameter space
- ✓ Calculation time
- ✓ Standard deviation (SD) of detected goodness-of-fit values
  ➢ **Costs** (lower = better) and **Recommendations** (higher = better)

2D



3D



Conclusions

- Mathematical optimization algorithms can be an **efficient tool** to detect optimal model parameters
- The tested algorithms' results could compete with those of the grid search in terms of the highest detected correlation between sFC and eFC
- However, the optimization methods varied greatly regarding their overall convergence properties and, especially, the required computational resources
- **CMAES and BO** demonstrated the **most favorable** trade-off between the quality of the model validation and the necessary computation time

Outlook

- High-dimensional models properly validated bear a huge potential for more precise and personalized studies of human brain dynamics
- The location of optimal parameters might serve as an individual subject's personal profile

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