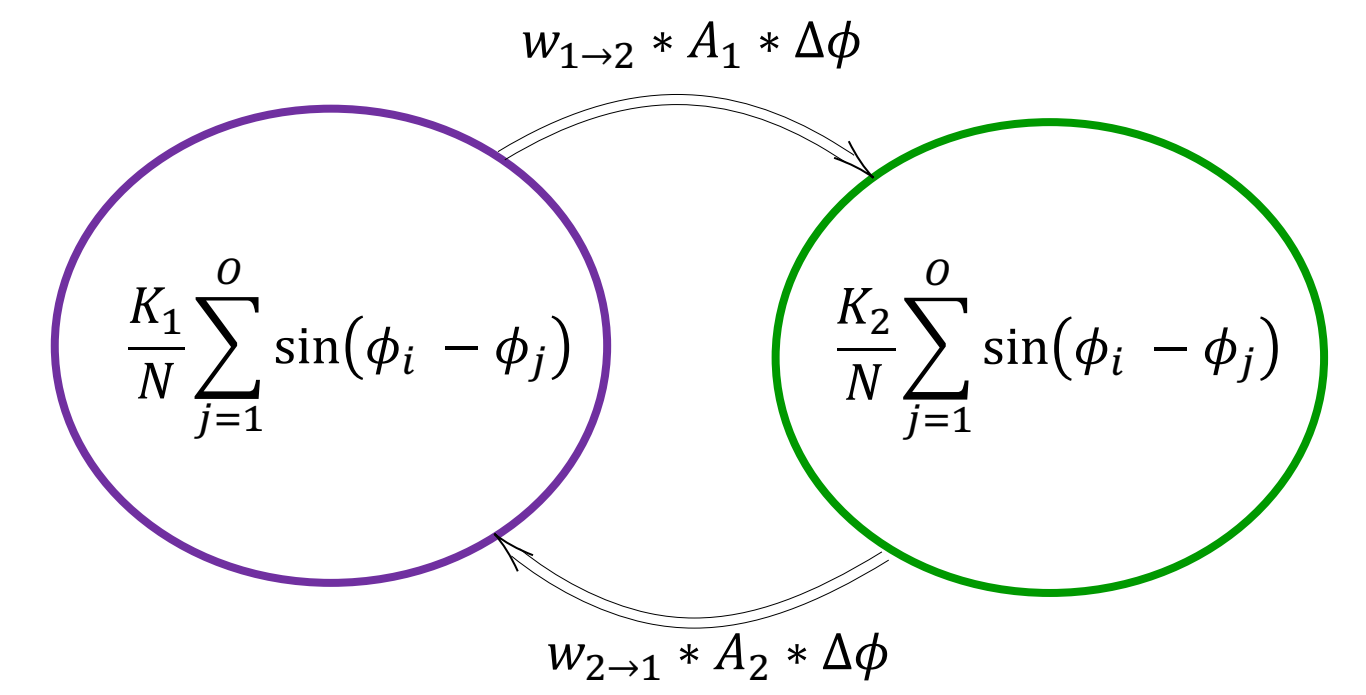


## Introduction

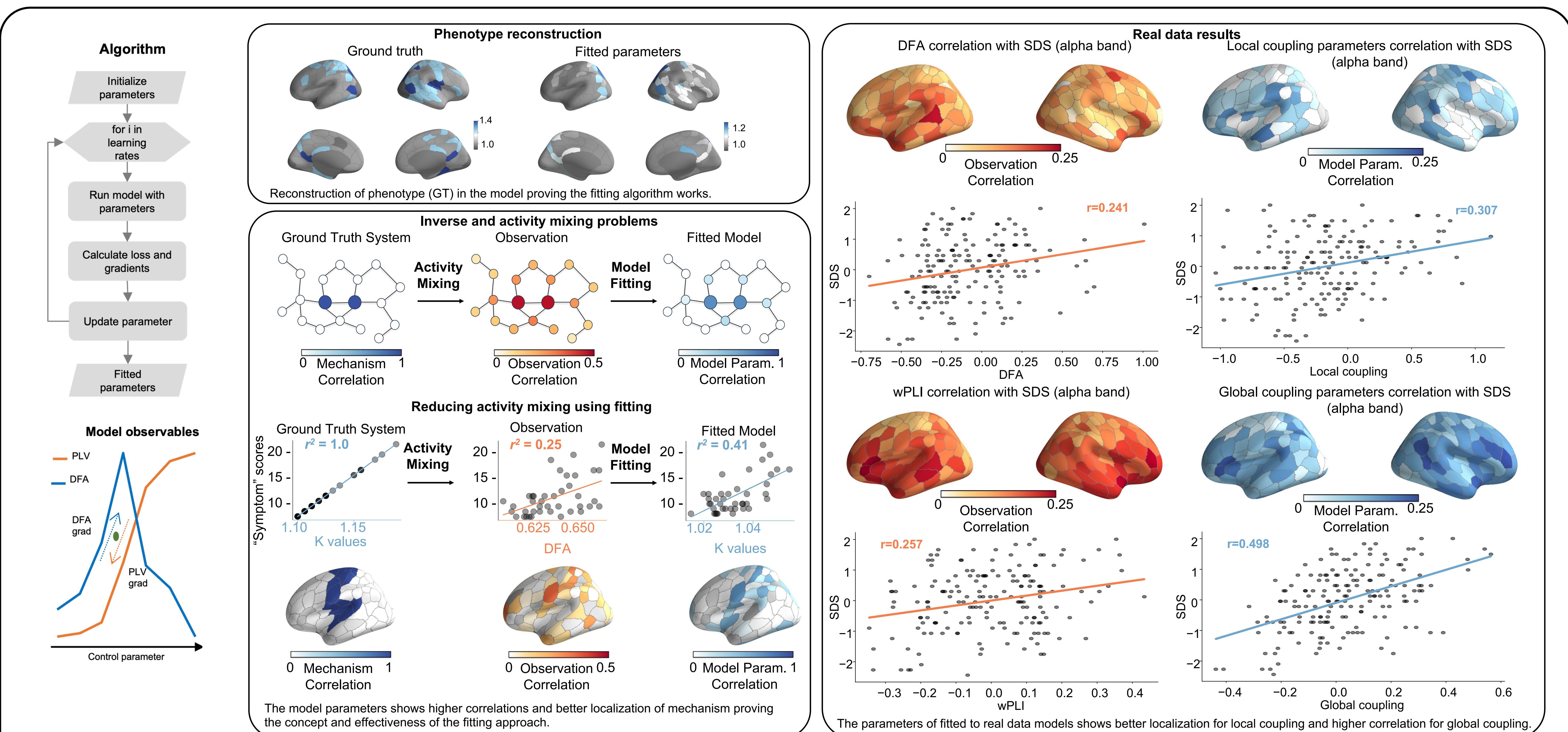
- The brain operates near a critical state regulated by excitatory and inhibitory neurotransmission. Disruptions in this balance are linked to various brain disorders, suggesting emergent dynamics as biomarker [1-2].
- In complex systems like the brain, identifying precise biomarkers is difficult because critical states create long-range correlations [3]. This causes "activity mixing," where localized mechanisms influence, and are influenced by, other network components, making dysfunctions hard to localize in observational data [4].
- We propose that fitting generative whole-brain models to individual data [5-6] can provide inverse solution to activity mixing. We fit the Hierarchical Kuramoto model aiming to reproduce dynamics similar to those in real data in terms of both functional connectivity and criticality.
- Using depression as a model system [6-7], we showed that the optimized model parameters correlated more strongly with depression symptoms than the raw neuroimaging data.

## Methods

- The Hierarchical Kuramoto model could be explained in three components:  
 $\theta_i = \text{Natural} + \text{Internal} + \text{External} + \text{Noise}$
- Where *Natural* is a central frequency of an oscillator, *Internal* describes the phase shift of the same node, and *External* describes nodes' interaction. In the model, two control parameters: local *K* and global *L*.
- Inter-areal phase synchrony was quantified with the calculated phase locking value (PLV) for the model and the weighted Phase Lag Index (wPLI) for MEG. We used Detrended Fluctuations Analysis (DFA) to measure long-range temporal correlations (LRTCs).
- Magnetoencephalography (MEG) and magnetic resonance imaging (MRI) were collected from *N* = 175 MDD patients.
- We used a multi-objective gradient optimization approach for fitting.



## Preliminary Results



### Phenotyping

- Several phenotypes were generated by alternating parameters such as the structural connectome or the vector of local coupling parameters *K*. Then model with default parameters was fitted to a simulated ground truth (GT) using these phenotypes. During the fitting steps, the correlation between the target metrics and the fitted metrics increased up to 0.8. The fitted parameters show similar changes as in the target areas.

### Fitting to the Real Data

- The model was fitted to real data FC and criticality metrics, such as wPLI and DFA. Then the fitted parameters were correlated with depression symptoms. Among these, the the Sheehan disability scale (SDS) symptom showed the stronger correlation with the read data metrics and the fitted parameters in alpha band.

## Conclusion

- The fitted parameters to the simulated phenotypes demonstrate alteration in the same subsystems as in the ground truth. The correlation coefficient between target and fitted metrics reaches 0.8.
- Using fitting to real data, we can study a mapping from structural to functional according to changes in model parameters. Overall, this research opens new avenues for understanding processes behind individual healthy and pathological dynamics.

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## Funding

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