Optimizing Biophysically-Plausible Large-Scale Circuit Models With Deep Neural Networks

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1. Introduction

Large-scale biophysically plausible models of coupled brain regions are developed to provide insights into brain dynamics[1, 2, 3, 4]. Leveraging these models to extract biological insights requires parameter optimization[5, 6].

Traditional parameter optimization methods for biophysical neural models, including grid search[1, 7, 8], evolutionary algorithms[5, 6, 9], EM frameworks[10], and gradient-based approaches[11, 12], rely on time-consuming numerical integration to simulate time courses before computing objective functions.

To overcome the limitation, we proposed DELSSOME (DEep Learning for Surrogate Statistics Optimization in MEan field modeling), a deep neural network that directly predicts surrogate statistics of the objective function, bypassing explicit time-course simulations. By integrating DELSSOME with covariance matrix adaptation evolution strategy (CMA-ES) [13], we achieve significant computational speed-ups while maintaining accuracy. Compared to recent studies[14, 15], DELSSOME supports high-resolution simulations and requires simpler training by focusing directly on the objective function rather than full time series.

2. Results

We conducted our study using the feedback inhibition control (FIC) model[1], which is a neural mass model comprising ordinary differential equations (ODEs) that capture the dynamics of excitatory and inhibitory neuronal populations within each cortical region.

In our previous study[6], a FIC model was fitted to empirical fMRI data using CMA-ES. The optimized FIC model was then be used to generate an excitatory and inhibitory synaptic gating variable time courses S_E and S_I. The E/I ratio estimate was defined as the ratio of the temporal average of S_E and S_I (Figure 1), which is an important biomarker related to neurodevelopment[6].

2.1 Optimizing FIC model with numerical integration

To optimize the FIC model, CMA-ES samples 100 sets of candidate parameters from a randomly initialized 10-D Gaussian distribution corresponding to 10 parameters that need to be optimized. Each set of candidate parameters was then used to compute

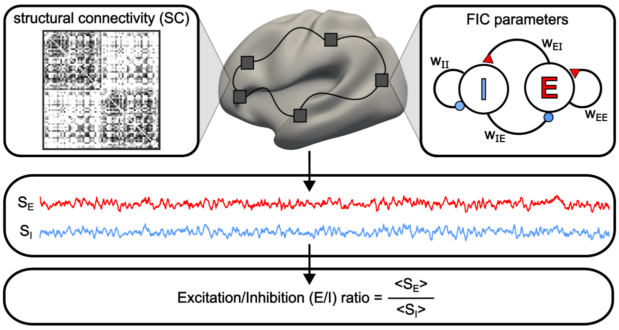

Fig. 1: Feedback inhibition control (FIC) model

an evaluation metric that measures the realism of the resulting FIC model. The 10 sets of candidate parameters with the best evaluation metric were then used to update the sampling distribution for the next epoch. These steps constitute one epoch of the CMA-ES algorithm.

For a given set of FIC parameters, neural and fMRI timecourses are simulated via numerical (Euler) integration of the FIC differential equations, which generally needs millions of steps and hence to be computationally expensive.

FIC parameters with simulated excitatory firing rate outside the physiologically plausible range were removed from further consideration. The remaining simulated fMRI time courses were then evaluated by computing a cost function that compared simulated and empirical functional connectivity (FC), as well as simulated and empirical functional connectivity dynamics (FCD)[16], which we will refer to as FC+FCD cost. The similarity of the static and empirical FC was computed based on Pearson's correlation between static and empirical FC (r) and absolute difference (d) between the means of them. Dissimilarity between the FCD matrices was computed using the Kolmogorov–Smirnov (KS) distance. The overall FC+FCD loss function was defined as $(1-r)+d+KS$. A lower FC+FCD cost indicates more realistic simulated fMRI time courses.

2.2 DELSSOME yielded over 2000× speed up for evaluating FIC model realism

To avoid computationally intensively numerical integration, we trained the DELSSOME within-range classifier to directly predict whether a set of FIC parameters will lead to within-range firing rates (Figure A1). For FIC parameters that survived the

DELSSOME within-range classifier, the DELSSOME FC+FCD cost predictor will predict the FC+FCD cost without numerical integration (Figure 2).

We divided Human Connectome Project (HCP)[17, 18] participants into training, validation and test sets. In the test set, the trained DELSSOME within-range classifier can reach 90% accuracy compared to chance accuracy 61% and the trained DELSSOME FC+FCD cost predictor can give a correlation between the predicted and ground truth loss at least 0.95. The evaluation speed of DELSSOME is over 2000$\times$ faster than Euler integration. (Figure A2)

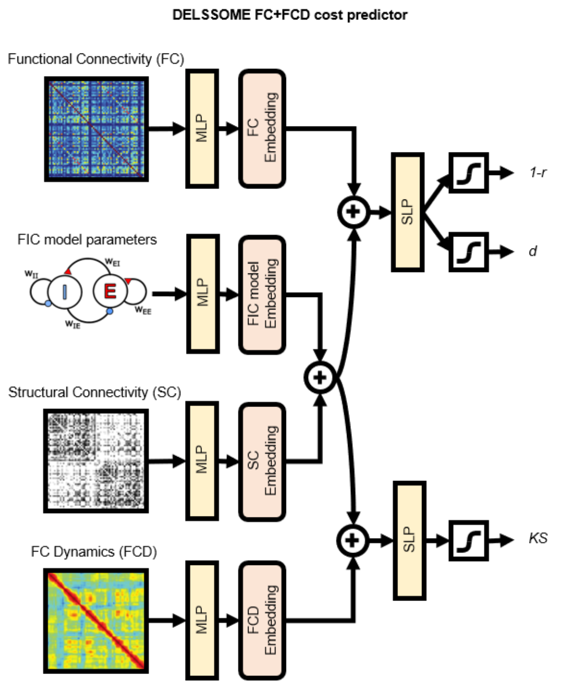

Fig. 2: DELSSOME neural network architectures

2.3 DELSSOME yielded 50$\times$ speed-up in the optimization of the FIC model

We tested whether DELSSOME models could replace Euler integration in the CMA-ES algorithm. We only considered the HCP test participants (previous section). The HCP test participants were further divided into the FIC model inversion training set, validation set and test set.

Euler CMA-ES was run on the FIC model inversion training set for 100 epochs. The best candidate parameter set from each epoch was collated, yielding 100 candidate parameter sets. The 100 candidate parameter sets were then evaluated in the FIC model inversion validation set. Finally, the top parameter set from the validation set was evaluated in the FIC model inversion test set. The same procedure was repeated with DELSSOME (replacing Euler integration) in the CMA-ES algorithm.

The results are shown in Figure 3. During the training phase, DELSSOME CMA-ES was more than 2000 times faster than Euler CMA-ES (42 minutes compared to 64 days). When we accounted for all phases, DELSSOME CMA-ES was around 50 times faster than Euler CMA-ES (33 hours compared to 65 days). On the other hand, FC+FCD costs between DELSSOME CMA-ES and Euler CMA-ES were similar.

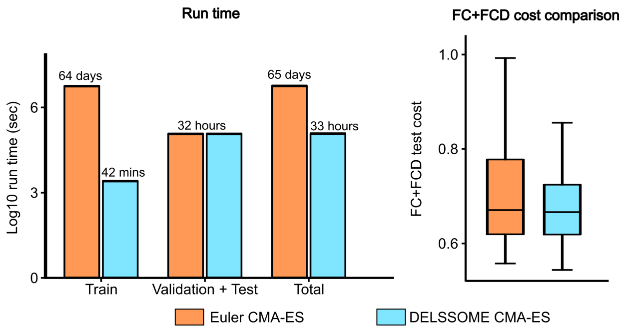

Fig. 3: Comparison of Euler CMA-ES and DELSSOME CMA-ES

2.4 DELSSOME generalized to a new dataset without further tunning

We replicated key findings of our previous study showing that E/I ratio decreases with age during neurodevelopment in a new dataset (the Philadelphia Neurodevelopment Cohort dataset; PNC)[6, 19, 20]. The DELSSOME models trained from the HCP dataset (previous section) were applied directly to PNC dataset without any further tuning.

The results are shown in Figure 4. DELSSOME CMA-ES was around 50 times faster than Euler CMA-ES. Consistent with the previous study[6], both DELSSOME CMA-ES and Euler EMA-ES revealed a decrease in mean cortical E/I ratio with age. Pearson's correlation between the 29 pairs of mean cortical E/I ratio was 0.88. The decrease in E/I ratio was also more pronounced in sensory-motor regions than association cortex for both DELSSOME CMA-ES and Euler CMA-ES.

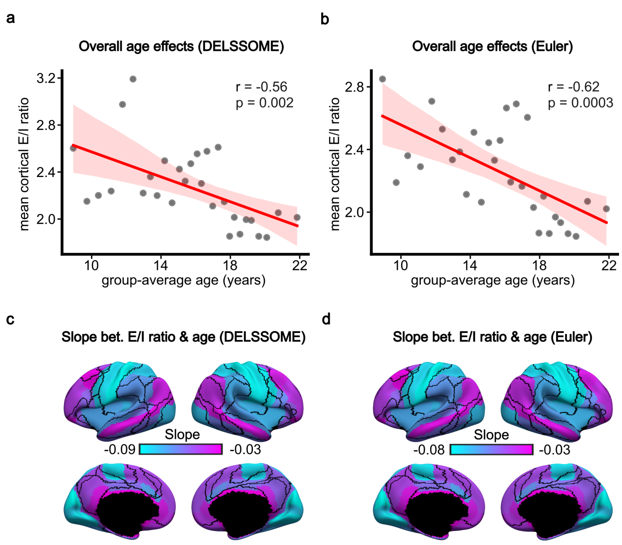

Fig. 4: DELSSOME CMA-ES generalized to PNC

Acknowledgments

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Appendix A. Supplementary figures

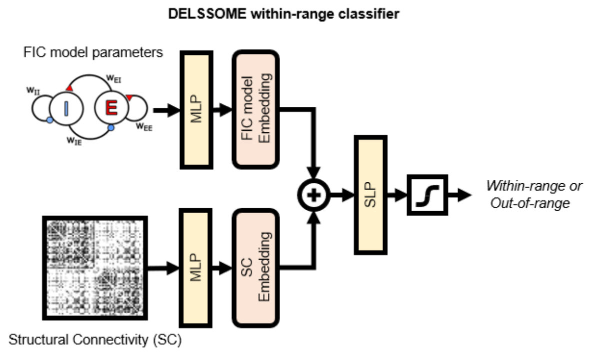

Fig. A1: DELSSOME neural network architectures

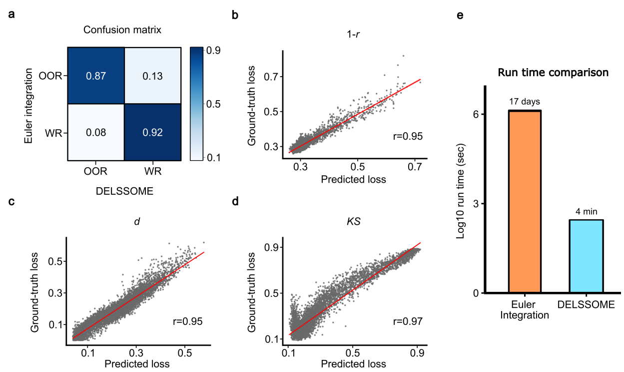

Fig. A2: Test performance of DELSSOME neural networks