Implementing Evolutionary Optimization to Model Neural Functional Connectivity

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ABSTRACT

Computational models are crucial in understanding brain function. Their architecture is designed to replicate known brain structures, and the behavior that emerges is then compared to observed fMRI and other imaging techniques. As the models become more complex with more parameters, they can explain more of the observed phenomena, and may eventually be used for diagnosis and design of treatments of brain disorders. However, those parameters need to be carefully optimized for the models to work, which becomes intractable as the models grow. In this preliminary work, CMA-ES has been configured to optimize continuous parameters of a functional connectivity model, resulting in a better fit to empirical data than manually selected parameters in all trial runs. This approach will be combined with other EC techniques to optimize other parameters. The techniques will be scaled up to more detailed structural and functional data and local parameters.

CCS CONCEPTS

• **Computing methodologies** → **Continuous space search**; • **Applied computing** → *Biological networks.*

KEYWORDS

evolutionary computation, genetic algorithm, computational neuroscience

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1 INTRODUCTION

Brains have evolved into the most complex natural system, containing billions of neurons as nodes and trillions of synapses as connections. However, even with such complexity, the patterns of activity over space and time are not random, even at cognitive rest. Previous empirical studies have shown that the functional connectivity (FC), which is the correlation of dynamic neural activity over space between regions, is related to the structural connectivity (SC), which is the strength of anatomical circuitry between regions [3]. Accurate models that simulate FC from known SC can then be matched to individual patients, and then used to diagnose pathologies and design treatments, such as Transcranial Magnetic Stimulation (TMS) protocols [1].

Neural activity models, while a simplification of the much more complex natural system, still have to be large and complex. Their parameters determine how it functions, defining values like the time constants of the interactions. Given that only a handful of parameters can be optimized manually, automated methods of optimization are crucial. Evolutionary computation (EC) techniques are well suited for this in large, high-dimensional, and deceptive search spaces, even with 2270 states and 1B variables [2, 6, 9]. They find solutions based on high-level fitness, such as how well the model FC matches a patient FC, even when gradient ascent and other standard techniques cannot be used.

The Dynamic Mean Field (DMF) model separates the cortical surface into local function-based areas, approximates the activity in each region as a simplification of a spiking model using a system of nonlinear stochastic linear equations, then calculates the FC from pairwise correlations of the dynamic activity time series per region [3]. The system of equations used for modeling activity are:

$$\frac{dS_i(t)}{dt} = -\frac{S_i}{\tau_s} + (1 - S_i)\gamma H(x_i) + \sigma v_i(t) \tag{1}$$

$$H(x_i) = \frac{ax_i - b}{1 - \exp(-d(ax_i - b))} \tag{2}$$

$$x_i = wJ_N S_i + GJ_n \sum_j C_{ij} S_j + I_0. \tag{3}$$

In these equations, S_i is the synaptic gating variable for region i and is correlated with the activity in that region. τ_s and γ denote kinetic factors both in seconds. σ is the noise amplitude of $v_i(t)$, which is Gaussian additive noise. $H(x_i)$ denotes the population firing rate for region i. a, b, and d are constants in newtons per Coulomb, Hertz, and seconds, respectively. w is the local excitatory recurrence. J_N is the synaptic coupling factor in Nanoamperes. G is the coupling strength, and is the only value varied by Deco et al. C_{ij} is the connectivity between the i^{th} and j^{th} regions from the SC matrix derived previously. I_0 is the overall effective external output.

DMF was previously shown to achieve a correlation of up to 0.46 with empirical resting state brain activity recorded by fMRI. In order to get this result, the global continuous model parameters, only loosely based on average physical properties, had to be hand-selected. Their interactions are nonlinear, so there is no gradient,

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and complete exhaustive search is too inefficient. As a result, exhaustive search has only been applied to a single such parameter in previous studies.

The Covariance Matrix Adaptation Evolution Strategy (CMA-ES) is a well-known EC optimization method in continuous spaces[5]. In CMA-ES, the population is described by a covariance matrix for a multi-variate normal distribution. Individuals in each generation are sampled from this distribution, and their resulting fitnesses are used to adapt the covariance matrix toward more successful individuals before selecting the next generation of individuals. By adapting the full covariance matrix, all pairwise dependencies between variables are considered. CMA-ES is therefore a good match with the multi-dimensional continuous parameter optimization problem of DMF, where fitness is the correlation coefficient of the model-generated FC to the empirically measured FC.

2 METHODS

CMA-ES was applied to evolve nine global parameters of the DMF model: $a, b, d, \gamma, \tau, w, J_N, I_0$, and G. Because these parameters are based on physical approximations and have different units and upper and lower bounds, they were each normalized. The initial mean for each parameter was set to its respective value for the best set of parameters found previously. A sigmoid was used to increase sensitivity of the parameter values to changes around their previous best value. A unique sigmoid normalization function for each parameter allowed the normalized value of all parameters be centered on a mean of 0 and a range of [-10,10].

Most default CMA-ES hyperparameters, including population size and weighting scheme, were used for this application. In the default configuration, these are computed based on the upper and lower bounds of the normalized values. This resulted in a population size of 110 individuals per generation. The only adjusted parameter was the initial step size, which was reduced by 2 orders of magnitude to 0.003 times the range of possible parameter values.

The fitness function to maximize was the correlation coefficient of the model-generated FC to previously empirically measured FC. The governing equations of the model are listed above as Equations (1)-(3). These equations are simulated for all 66 brain areas using the individuals denormalized parameters, empirically measures structural connectivity matrix. This is computed using Euler's method for 100000 time steps, with 1 ms per time step and 10 intermediate steps between each time step for downsampling, to be consistent with previous model studies. The resulting modeled activity time series are computed into a functional connectivity matrix by taking all pairwise correlations. This is repeated 10 times, and the resulting functional connectivity matrices are averaged and denormalized. The result is then correlated with the denormalized empirical functional connectivity matrix used in the previous study to yield a single fitness value of the individual.

Since the DMF model is non-deterministic due to the noise term in Equation (1), the fitness of the previous best set and the fitness of the best set found in each trial run were all measured 100 times each so they could be tested for statistically significant difference.

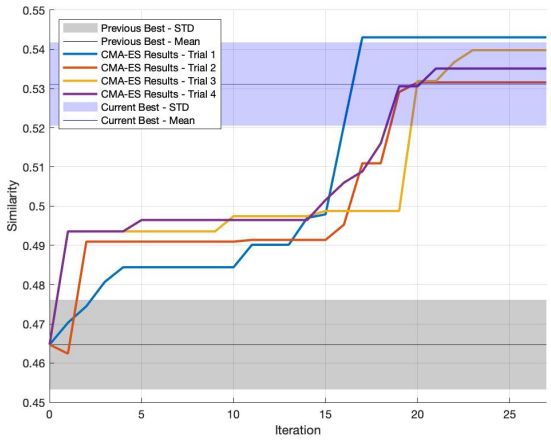

Figure 1: CMA-ES trial results. The best fitness seen after each generation of CMA-ES for each trial is plotted against the mean fitnesses of the previous best set and our best set found. The 95% confidence interval for the true interval of each set is shown. All four trials of CMA-ES found a parameter set that has a significantly better fitness than the previous best set.

3 RESULTS

Four trial runs of the CMA-ES algorithm were run. The CMA-ES algorithm was able to find a statistically significantly better set of parameters in all of these trial runs of the algorithm. The best fitness seen so far for each generation for each trial is shown in Figure 1. The parameter set yielding the best fitness in each trial is shown in Table 1.

4 DISCUSSION

The results from the preliminary experiments show that the EC optimization approach is feasible and potentially powerful beyond human design. Following experiments will focus on developing the methods that make it possible to scale up to full computational and scientific power.

CMA-ES is a stochastic algorithm, due to the random sampling occurring in every generation. Thus, different runs of the algorithm may result in different local optima being discovered. The distribution of optima will be further investigated.

The fitness function used is also stochastic. Evaluating each individual more to get a more confident measure of the true fitness is more computationally expensive, but will allow the individuals in each generation to be more accurately assessed.

Efficiency is a crucial factor. The original code for evaluating the model was previously written in MATLAB. Evaluating a single individual is completed on a time scale of minutes with no optimization or parallelization. Thus, the initial trials, which require 110 fitness evaluations per generation ran on a scale of days. This algorithm is a good candidate for increased efficiency via parallelization, as evaluating individuals within a population are independent calculations, as are the trials within a single fitness evaluation. Each

Table 1: Fitness and parameter values of previous best parameter set and resulting best parameter set of all trials of CMA-ES.

Parameter Set	Fitness	Parameters								
		a	b	d	γ	τ	w	J_N	I_0	G
Previous Best	.4647 ±.0114	270.0	108.0	.154	.641	100.0	.6	.2609	.33	2.4
CMA-ES: Trial 1 Best	.5205 ±.0102	225.0	107.3	.1255	.5329	91.01	.5233	.2736	.3641	3.153
CMA-ES: Trial 2 Best	.5255 ±.0093	139.5	63.44	.1252	.6654	119.4	.6224	.2616	.2629	4.278
CMA-ES: Trial 3 Best	.5329 ±.0105	67.60	14.45	.1623	.3498	60.24	.2458	.4609	.1485	7.537
CMA-ES: Trial 4 Best	.5321 ±.0097	167.7	73.94	.0367	.1792	50.68	.0006	.4467	.2738	9.496

individual has 10 functional connectivity matrices computed, so another potential speed up would be to evaluate the initial matrices to determine the likelihood that individual will have a high fitness value, so only the promising individuals are fully evaluated. Another potential speed up is to build a look-up table or surrogate model, such as a neural network, of past fitness evaluations. Both of these approaches would use past fitnesses to decrease CMA-ES time at the cost of additional memory and/or offline computation time.

The preliminary experiment was based on the default configuration of CMA-ES. The next step is to configure it for the brain model optimization specifically. This work includes adjusting the initial standard deviation, step size, sampling method, stochastic fitness evaluation, and other hyperparameters, as well as optimizing groups of interacting parameters in an incremental evolution process [4].

While the DMF model is a good initial target, the next generation of models for predicting FC from SC is still in development [8]. They are based on improving the quality of the SC data and making the empirical FC used for fitness testing more accurate. These models are expected to be more powerful especially when scaled in size and complexity by allowing different parameter settings for each individual region, and allowing them to change over time. In turn, such scaling is possible only through automated methods, leading to essential synergy of the two streams of research.

The CMA-ES algorithm is designed to only evolve continuous parameters. However, some of the parameters of the DMF model and similar brain models are discrete or categorical, which require a different approach. For instance, Estimation of Distribution Algorithms (EDAs) use Bayesian networks (instead of a covariance matrix) to capture dependencies between categorical variables [7]. The second step is thus to develop a new EC method, possibly a hybrid of CMA-ES and an EDA, to optimize solutions in heterogeneous spaces.

The ability to map SC to FC accurately and in a larger scale is an important stepping stone to addressing larger questions in brain science. In particular, such models can be fit to individual patient's imaging data to diagnose pathologies. It may then be possible to predict response to treatment protocols such as TMS and optimize them automatically.

5 CONCLUSION

The presented work provides a basis for utilizing evolutionary computation to optimize neural activity models. Statistically significant optimization has already been achieved with a relatively simple approach. With the discussed directions for future work, the optimization potential should continue to increase. This will further our understanding of the human brain and bring the field of neurology closer to personalized medicine.

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