A Plan for the Comparative Analysis of Optimization Algorithms on a Synthetic Biological Model

1.0 Objective

The objective is to conduct a rigorous and reproducible comparison of five distinct optimization algorithms representing diverse search strategies:

- **Bayesian Optimization (BO):** A surrogate-model-based approach for sample-efficient optimization.
- **Covariance Matrix Adaptation Evolution Strategy (CMA-ES):** An advanced evolution strategy that adapts the geometry of its search distribution.
- **L-SHADE:** A state-of-the-art adaptive differential evolution algorithm.
- **Particle Swarm Optimization (PSO):** A canonical swarm intelligence heuristic serving as a robust baseline.
- **DIviding RECTangles (DIRECT):** A deterministic global optimization algorithm based on systematic space partitioning.

The analysis will evaluate their performance on a parameter estimation problem for a synthetic gene circuit model. The goal is to identify which algorithmic strategy is most effective at recovering known ground truth parameters from noisy synthetic data.

2.0 Experimental Design

The experiment is a controlled computational study using a known ground truth to allow for objective evaluation of algorithm performance.

2.1. Ground Truth Model and Data Generation

- **Ground Truth Parameters:** The comparison will use a single, known set of ground truth parameters as specified in the synthetic.py script.
- **Benchmark Suite:** A benchmark suite of 3 distinct datasets will be generated.
- **Dataset Composition:** All 3 datasets will originate from the same clean simulation trace derived from the ground truth parameters. Each of the 3 datasets will contain 3 unique replicate noisy traces. The noise for each replicate will be generated independently, ensuring different noise profiles across the datasets.

2.2. Objective Function

Each optimization algorithm will seek to find a parameter set that minimizes the Sum of Squared Errors (SSE). The SSE is calculated between the model's simulated trace and the average of the 3 noisy replicate traces within a given dataset.

2.3. Experimental Protocol

- **Execution Runs:**
  - For the four stochastic algorithms (BO, CMA-ES, L-SHADE, PSO), a minimum of 3 independent runs will be performed for each of the 3 datasets to account for statistical variance. Each run will use a different random seed.
  - For the deterministic algorithm (DIRECT), a single run will be performed for each of the 3 datasets.
- **Computational Budget:** A fixed computational budget of 5,000 function evaluations will be strictly enforced for every run of every algorithm. Runs will be terminated upon reaching this budget. This ensures all algorithms are compared based on identical computational effort.
- **Initialization:** To ensure a fair comparison, the initial sampling for all algorithms will be performed using a Latin Hypercube Sample (LHS) strategy.

3.0 Performance Metrics and Analysis

Algorithm performance will be assessed based on accuracy, goodness of fit, robustness, and convergence speed. The analysis will also interpret performance differences to characterize the problem's fitness landscape.

- **Parameter Accuracy:** The primary metric, measured as the Mean Squared Error (MSE) between the final parameters found by the optimizer and the known ground truth parameters. A lower value is better.
- **Goodness of Fit:** The final SSE value between the simulation from the found parameters and the averaged noisy data trace.
- **Robustness:** An algorithm's performance consistency across the 3 datasets (and across multiple runs for stochastic methods) will measure its robustness to noise.
- **Convergence Speed:** The profile of the best objective function value versus the number of function evaluations will be recorded to analyze search efficiency.

4.0 Data Visualization

Results will be presented through plots designed for clear performance comparison.

- **Box Plots:** To compare the distribution of final Parameter Accuracy and Goodness of Fit for each algorithm across the 3 datasets. For stochastic methods, these plots will summarize the results of all independent runs.
- **Convergence Curves:** A plot of the best objective function value versus the number of function evaluations for each algorithm to compare optimization efficiency.
- **Parameter Error vs. Goodness of Fit Scatter Plot:** A 2D plot to visualize performance trade-offs. Each algorithm will be represented by points corresponding to its performance on each dataset.
    - **X-Axis:** Parameter Accuracy (MSE)
    - **Y-Axis:** Goodness of Fit (SSE)