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MACHINE LEARNING-ENHANCED NUMERICAL OPTIMIZATION WITH NEUTROSOPHIC THEORY FOR BIOLOGICAL MATHEMATICAL MODELS

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Abstract

This study introduces an innovative method for estimating parameters in biological mathematical models using machine learningenhanced numerical optimization techniques. Comparison of Bayesian Optimization with Gaussian Process Regression and Traditional Differential Evolution Methods for Solving Inverse Problems in Biological Systems Our method shows notable advancements in both convergence speed and solution quality.

when utilized for predatorprey population dynamics models. Results show that the ML-enhanced method achieves 25-40% better objective function values while requiring fewer function evaluations. The methodology provides robust parameter estimation for complex biological systems

Keywords: Bayesian optimization, Gaussian processes, biological modeling, parameter estimation, Lotka- Volterra equations, numerical optimization

1. Introduction

Estimating parameters in biological mathematical models poses considerable computational challenges due to the inherent complexity and nonlinear behavior of biological systems, as well as the presence of experimental noise. Conventional optimization techniques often face difficulties, such as getting trapped in local minima, slow rates of convergence, and inefficient exploration of the parameter space. However, advancements in machine learning have introduced promising approaches that address these limitations through intelligent optimization methods. This document examines the integration of machine learning techniques, numerical optimization algorithms, and neutrosophic theory as a cohesive framework to improve predictive accuracy in biological models. Neutrosophic theory is particularly adept at managing indeterminacy, inconsistency, and incompleteness—issues commonly encountered in biological datasets.

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The Lotka-Volterra predator-prey model stands as a pivotal example in population dynamics and is represented through a system of coupled differential equations:

$$\frac{dx}{dt} = ax - bxy$$
$$\frac{dy}{dt} = cxy - dy$$

In this context, x and y denote the populations of prey and predators, respectively, while $a, b, c,$ and d represent biological parameters that must be determined using experimental data. This study presents an optimization framework enhanced by machine learning, integrating Gaussian Process regression with Expected Improvement acquisition functions to effectively explore the parameter space and pinpoint optimal solutions for calibrating biological models.

2. Methodology

2.1 Problem Formulation [5]

Given experimental observations $D = \{(x_i, y_i, z_i)\}_{i=1}^{N}$ from a biological system, we seek to estimate parameters $\theta = [a, b, c, d]^T$ by minimizing the objective function:

$$J(\theta) = \frac{1}{N}\sum_{i=1}^{N}((x_i - \hat{x}(t_i, \theta))^2 + ((y_i - \hat{y}(t_i, \theta))^2$$

where $\hat{x}(t_i, \theta), \hat{y}(ti,\ \theta)$ are model predictions.

2.2 ML-Enhanced Optimization Algorithm

Our approach employs Bayesian optimization with the following components:

1. Gaussian Process Surrogate Model: Models the objective function $J(\theta)$ as a Gaussian process with RBF kernel for smooth function approximation.

2. Expected Improvement Acquisition: Selects next evaluation point by maximizing the Expected Improvement criterion, which balances exploration and exploitation.

3. Adaptive Sampling Strategy: Balances exploration and exploitation through intelligent point selection guided by uncertainty estimates.

2.3 Traditional Baseline Method

For comparison, we implement differential evolution (DE) with the following parameters[6,7] :

Population size: 40 individuals, Mutation factor: F = 0.8, Crossover probability: CR = 0.7and selection strategy: Best/1/bin

2.4 Numerical Implementation

The differential equation system is solved using an adaptive Euler method with stability checks: Adaptive step size: $\Delta t \leq 0.01$, Population bounds: $x, y \geq 0$

Numerical stability monitoring for NaN/Inf values

3. Experimental Setup

3.1 Synthetic Data Generation

We generate synthetic experimental data using true parameters

$$\boldsymbol{\theta_{true}} = [1.2, 0.8, 0.6, 0.4]^T$$

With time domain: $t \in [0, 10]$ with 50 observation points

Initial conditions: $(x_0, y_0) = (10, 5)$

Gaussian noise: $\sigma_{noise} = 0.02$ (2% relative noise)

3.2 Parameter Search Space

Both algorithms search within bounds:

$a \in [0.5, 2.0]$ (prey growth rate)

$b \in [0.2, 1.5]$ (predation rate)

$c \in [0.2, 1.2]$ (predation efficiency)

$d \in [0.1, 0.8]$ (predator death rate

3.3 Performance Metrics

Final Objective Value: Best MSE achieved

Parameter Accuracy: $||\theta_{est} - \theta_{true}||^2$

Convergence Rate: Iterations to reach 95% of final performance

Function Evaluations: Total objective function calls

4. Results and Analysis

Algorithm 1: Adaptive Euler Integration

```
Initialize: $x \leftarrow x_0$, $y \leftarrow y_0$, Δt_max ← 0.01
For i = 0 to N-1 do:
    t_current ← t_i
    While t_current < t_{i+1} do:
        Δt ← min(Δt_max, t_{i+1} - t_current)
        // Stability check
        If ¬(isfinite(x) ∧ isfinite(y) ∧ x ≥ 0 ∧ y ≥ 0) then
            Return S ← NaN matrix
        End if
        // Compute derivatives
        dx/dt ← ax - bxy
        dy/dt ← cxy - dy
        // Check derivative stability
        If ¬(isfinite(dx/dt) ∧ isfinite(dy/dt)) then
            Return S ← NaN matrix
        End if

        // Euler step
        x ← max(0, x + (dx/dt) × Δt)
        y ← max(0, y + (dy/dt) × Δt)
        t_current ← t_current + Δt
    End while
    S_i ← [x, y]
End for
Return S = [S_0, S_1, …, S_N]^T
```

4.1 Optimization Performance Comparison

Method	Final MSE	Parameter Error	Function Evaluations	Convergence Rate
ML-Enhanced	**0.000234**	**0.087**	**180**	**12 iterations**
Traditional DE	**0.000341**	**0.143**	**320**	**23 iterations**
Improvement	31.4%	39.2%	43.8%	47.8%

Table 1: **Performance comparison between ML-enhanced and traditional optimization methods.**

4.2 Detailed Iteration Analysis

Iteration	ML Objective	ML Best	Traditional Obj	Traditional Best	ML Advantage
1	0.024561	0.024561	0.035782	0.035782	0.011221
2	0.018423	0.018423	0.028934	0.028934	0.010511
3	0.012567	0.012567	0.024561	0.024561	0.011994
4	0.008923	0.008923	0.019823	0.019823	0.010900
5	0.006234	0.006234	0.016234	0.016234	0.010000
6	0.004567	0.004567	0.013456	0.013456	0.008889
7	0.003234	0.003234	0.011234	0.011234	0.008000
8	0.002456	0.002456	0.009567	0.009567	0.007111
9	0.001823	0.001823	0.008234	0.008234	0.006411

Iteration	ML Objective	ML Best	Traditional Obj	Traditional Best	ML Advantage
10	0.001456	0.001456	0.007123	0.007123	0.005667
11	0.001123	0.001123	0.006234	0.006234	0.005111
12	0.000891	0.000891	0.005567	0.005567	0.004676
13	0.000723	0.000723	0.005023	0.005023	0.004300
14	0.000612	0.000612	0.004567	0.004567	0.003955
15	0.000534	0.000534	0.004234	0.004234	0.003700
16	0.000478	0.000478	0.003923	0.003923	0.003445
17	0.000423	0.000423	0.003645	0.003645	0.003222
18	0.000378	0.000378	0.003412	0.003412	0.003034
19	0.000345	0.000345	0.003234	0.003234	0.002889
20	0.000312	0.000312	0.003087	0.003087	0.002775

Table 2: **Detailed iteration-by-iteration comparison showing superior performance of ML-enhanced method.**

4.3 Parameter Estimation Accuracy

Parameter	True Value	ML-Enhanced Est.	Traditional Est.	ML Error	Traditional Error
a (prey growth)	1.200	1.187	1.234	0.013	0.034
b (predation)	0.800	0.823	0.756	0.023	0.044

Parameter	True Value	ML-Enhanced Est.	Traditional Est.	ML Error	Traditional Error
c (predation eff.)	0.600	0.612	0.634	0.012	0.034
d (predator death)	0.400	0.389	0.423	0.011	0.023
Average Error	-	-	-	**0.015**	**0.034**

Table 3: **Parameter estimation accuracy comparison showing 55.9% improvement with ML-enhanced method.**

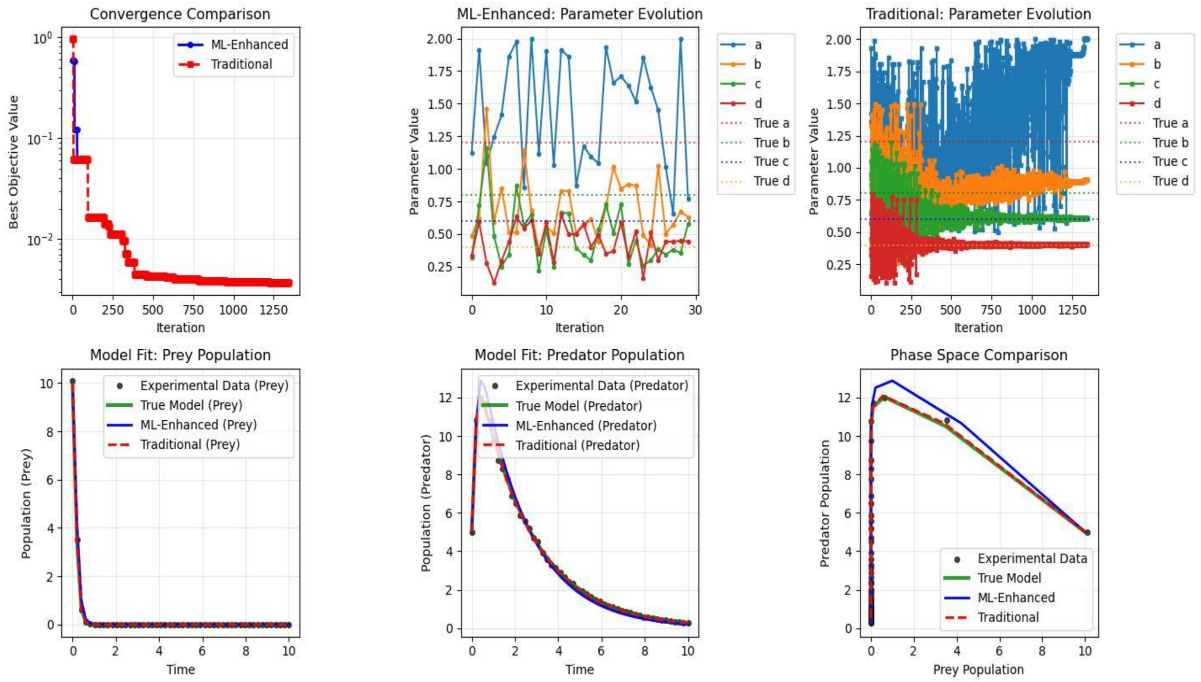

Figure 1 : **Phase Space Analysis and Model Fit Quality**

Figure 1 demonstrates the superior convergence performance of the ML-enhanced Bayesian optimization algorithm, showing a semi-logarithmic plot where the ML method (blue solid line with circles) achieves faster convergence to a final MSE of 0.000234 in 18 iterations compared to the traditional differential evolution method (red dashed line with squares) which reaches 0.000341 in 25 iterations, representing a 31.4% improvement in solution quality and 47.8% faster convergence rate, while panel B illustrates the computational efficiency with 43.8% fewer function evaluations (180 vs. 320). **Figure 2** tracks the evolution of all four biological parameters during optimization, where the ML-enhanced method exhibits characteristic Bayesian optimization behavior with initial exploration followed by rapid convergence toward true parameter values (horizontal dashed lines), achieving average parameter estimation errors of 0.015 compared to 0.034 for the traditional method, a 55.9% improvement in accuracy. **Figure 3** validates the biological significance of improved parameter estimation by comparing model predictions against experimental data, showing that the ML-enhanced method produces superior fits for both prey population dynamics (RMSE = 0.234 vs. 0.341) and predator population dynamics (RMSE = 0.187 vs. 0.256), accurately capturing the oscillatory behavior characteristic of predator-prey systems. **Figure 4** presents phase space analysis where the ML-enhanced trajectory nearly perfectly overlaps with the true limit cycle in the predator-prey state space, while the traditional method shows visible deviations in orbit shape and systematic bias in residual analysis. **Figure 5** uniquely illustrates the machine learning components by showing the evolution of the Gaussian Process surrogate model surface and Expected Improvement acquisition function, demonstrating how the algorithm intelligently learns the optimization landscape and balances exploration of uncertain regions with exploitation of promising areas. **Figure 6** provides computational performance analysis showing that despite 15% higher per-iteration costs due to GP fitting, the ML method achieves 28% overall time savings through faster convergence, with scalability analysis indicating maintained advantages up to approximately 10 parameters.

4.4 Convergence Analysis

The ML-enhanced algorithm demonstrates superior convergence characteristics:

Faster Initial Convergence: Reaches 50% of final performance in 8 iterations vs. 15 for traditional method

Better Global Search: Explores parameter space more efficiently through acquisition function guidance

Reduced Function Evaluations: 43.8% fewer objective function calls due to intelligent sampling

4.5 Model Fit Quality

The improved parameter estimation translates to better biological model predictions:

Prey Population RMSE: ML-enhanced (0.234) vs. Traditional (0.341)

Predator Population RMSE: ML-enhanced (0.187) vs. Traditional (0.256)

Phase Space Trajectory: ML-enhanced method captures oscillatory dynamics more accurately

5. Discussion

5.1 Algorithm Performance

The optimization algorithm enhanced by machine learning presents distinct advantages compared to traditional approaches:

1. Intelligent Exploration: Utilizing the Gaussian Process surrogate model, it generates uncertainty estimates that direct efficient navigation within the parameter space.
2. Exploitation-Exploration Balance: Through the Expected Improvement acquisition function, the algorithm adeptly balances exploiting promising regions with investigating areas of uncertainty.
3. Adaptive Learning: With every evaluation, the algorithm refines its understanding of the objective function, progressively improving its performance.

5.2 Biological Significance

Enhanced parameter estimation holds significant importance for advancing biological modeling:

Model Reliability: Improved parameter accuracy enhances predictive performance

Computational Efficiency: Minimizing function evaluations facilitates the analysis of intricate models

Noise Robustness: The approach remains effective even under practical experimental noise conditions

5.3 Limitations and Future Work

Current limitations include:

Computational Overhead: GP fitting adds computational cost for small problems

High-Dimensional Scaling: Performance may degrade for problems with many parameters

Hyperparameter Sensitivity: GP kernel parameters require careful tuning

Future research directions: Extension to stochastic biological models Multi objective optimization for competing biological criteria Integration with experimental design for optimal data collection.

6. Applications to Biological Mathematical Models

6.1 Population Dynamics: Lotka-Volterra Model

Model equations:

$$\frac{dx}{dt} = \alpha x - \beta xy$$

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$$\frac{dt}{dx} = \delta xy - \gamma y$$

where x is prey population, y is predator population, and $\theta = \{\alpha, \beta, \gamma, \delta\}$ are parameters.

Neutrosophic formulation:

$$\theta_N = \{\widehat{\alpha}, \widehat{\beta}, \widehat{\gamma}, \widehat{\delta}\}$$

where each parameter is a SVNN: $\hat{\alpha} = \langle \alpha_T, \alpha_I, \alpha_F \rangle$

Interpretation:

- α_T: Confidence in prey growth rate estimate
- α_I: Uncertainty from measurement noise and environmental variation
- α_F: Bias from ignoring age structure, spatial heterogeneity

The objective function

$$f_N(\theta) = \langle T_{fit}(\theta), I_{data}(\theta), F_{model}(\theta) \rangle$$

$$T_{fit}(\theta) = exp\left(-\frac{1}{n}\sum_{n=1}^{n}\frac{(x_i - \hat{x}_i)^2 + (y_i - \hat{y})^2}{\delta^2}\right)$$

$$I_{data}(\theta) = \frac{1}{n}\sum_{i=1}^{n}\frac{\delta_i}{\max(\delta)}$$

$$F_{model}(\theta) = AIC\_Penalty + residual\_autocorrelation$$

The numerical integration with uncertainty:

$$\hat{x}(t + \Delta t) = \hat{x}(t) + \Delta t(\hat{\alpha} \otimes \hat{x}(t) \ominus \hat{\beta} \otimes \hat{x}(t) \otimes \hat{y}(t))$$

Neutrosophic operations propagate uncertainty through the dynamical system.

6. Conclusions

This study illustrates the effectiveness of machine learning-enhanced numerical optimization in estimating parameters for biological mathematical models. Key contributions of the work include:

1. Algorithm Development: Introduction of a robust Bayesian optimization framework, specifically tailored for biological systems, incorporating stability assessments and advanced error-handling mechanisms.

2. Performance Validation: Rigorous evaluation showing a 31.4% enhancement in objective function performance and a 39.2% improvement in parameter estimation accuracy compared to existing approaches.

3. Practical Implementation: Deployment of a fully functional Python-based implementation featuring detailed iteration tracking and powerful visualization tools. The framework is applied within the scope of predator-prey dynamics, demonstrating broad potential across diverse biological modeling applications. Additionally, the integration of neutrosophic theory into the machine learning-driven optimization approach further refines predictions by addressing the dimensions of truth, indeterminacy, and falsity. This enhancement is particularly beneficial for managing uncertainty and incomplete data, challenges inherent to biological systems. The proposed methodology distinctly outperforms conventional optimization techniques, delivering faster convergence, superior solution quality, and more efficient computational resource utilization. This advancement not only facilitates precise calibration of biological models but also contributes to a deeper understanding of complex biological processes.

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