

ARTICLE

Hybrid bio-inspired deep learning approach
for early detection and longitudinal analysis of
Parkinson's disease

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Abstract

Parkinson's disease exhibits complex temporal progression patterns, making accurate prediction of disease severity an important challenge. However, many existing models rely on stationary approaches that fail to capture temporal dependencies, while limited hyperparameter optimization further constrains predictive performance. To address these limitations, this study proposes a hybrid bio-inspired neuroevolutionary deep learning framework (HyBND-PD) integrating principal component analysis for feature reduction, long short-term memory networks for temporal modeling, and a genetic algorithm for hyperparameter optimization. Using Parkinson's telemonitoring data, the framework predicts motor and total Unified Parkinson's Disease Rating Scale scores. Experimental results demonstrate that HyBND-PD outperforms Metaheuristic-Inspired Optimization for Disease Analysis, Artificial Intelligence-based Parkinson's Evaluation and Review, and Classification and Evolutionary Parkinson's Identification Framework, achieving up to a 38% lower mean absolute error, 32% lower root mean squared error, and a 17% improvement in the R^2 score, indicating closer agreement with observed clinical measurements. These findings demonstrate the effectiveness of the proposed framework for longitudinal Parkinson's disease progression prediction and telemonitoring-based healthcare applications.

Keywords: Parkinson's disease; Bio-inspired optimization; Long short-term memory; Genetic algorithm; Unified Parkinson's Disease Rating Scale prediction

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1. Introduction

Motor deficits consist of tremors, stiffness, bradykinesia, and postural instability, and are accompanied by non-motor symptoms that progressively develop in Parkinson's disease (PD), a progressive neurodegenerative condition (A. Reddy *et al.*, 2024). To improve patient outcomes and enable timely intervention, early-stage detection of PD and continuous monitoring of disease progression are essential (Xie & Hu, 2022).

The temporal dynamics of PD are complicated, making it challenging to develop reliable prediction models (Govindu & Palwe, 2023). Conventional approaches to diagnosis and patient follow-up are based on subjective and potentially biased clinical assessments (He *et al.*, 2021). Telemonitoring has increased the availability of longitudinal data for timely patient assessment, making more accurate and data-driven models of PD development possible (Junaid *et al.*, 2023).

Machine learning (ML) and deep learning (DL) approaches for the analysis of PD data have been partially successful, yet most existing models do not adequately capture the dynamic nature of the symptoms (Loh *et al.*, 2021). Furthermore, the reliance of many systems on static architectures and manually tuned hyperparameters limits their ability to scale effectively to large patient populations (Doumari *et al.*, 2023). Biologically inspired genetic algorithms (GAs) and other optimization methods have demonstrated potential for automating hyperparameter tuning and improving model adaptability (Balaji *et al.*, 2021). Long short-term memory (LSTM) networks are particularly effective at modeling temporal dependencies by capturing temporal relationships in sequential data (Surguchov, 2021).

Considering the recent developments, this study introduces a hybrid bio-inspired neuroevolutionary DL framework (HyBND-PD) to monitor PD progression and identify early-stage progression (Magalhães & Lashuel, 2022). It utilizes LSTM networks to model temporal dependencies, reduce feature dimensionality, optimize model parameters with the help of GAs, and extract temporal patterns (Mughal *et al.*, 2022). Significant clinical outcomes, including motor and total UPDRS scores, are predicted using this hybrid architecture and longitudinal telemonitoring data (Leite Silva *et al.*, 2023).

Experimentally, HyBND-PD outperforms conventional bio-inspired techniques and conventional ML models in terms of prediction accuracy and correlation with the actual Unified Parkinson's Disease Rating Scale (UPDRS) scores (Abdullah *et al.*, 2023). The framework demonstrates strong potential for real-world clinical application, as it is capable of capturing not only temporal patterns but also disease progression trajectories (Saravanan *et al.*, 2022). This system can be applied to remote healthcare environments and is especially well suited because of its flexibility and automation, enabling proactive disease monitoring and personalized treatment planning (Kim *et al.*, 2024).

Existing studies have examined various combinations of dimensionality reduction, DL, and optimization techniques for predicting PD. However, most studies

have primarily focused on improving predictive accuracy without integrating these components into a unified framework for longitudinal disease progression analysis. The proposed HyBND-PD framework combines principal component analysis (PCA)-based feature compression, LSTM-based temporal dependency learning, and GA-based hyperparameter optimization into a unified neuroevolutionary architecture. The system also includes longitudinal UPDRS prediction and telehealth-enabled clinical decision support (CDS) for monitoring disease progression and supporting personalized intervention.

The proposed framework improves prediction accuracy while facilitating practical implementation for longitudinal PD monitoring in real-world clinical settings. The proposed framework is distinguished by its integration of PCA-, LSTM-, and GA-based optimization within a single architecture for longitudinal UPDRS prediction based on telemonitoring data, rather than employing these techniques as independent modules.

To address these research gaps, this study makes the following contributions:

- (i) The HyBND-PD framework is a hybrid proposal incorporating PCA for feature extraction, LSTM for learning temporal dependencies from sequential data, and GA for automated hyperparameter optimization, all within a single neuroevolutionary structure.
- (ii) The proposed framework is specifically designed to model longitudinal disease progression by continuously predicting motor and total UPDRS scores from telemonitoring data, rather than relying on traditional predictive models.
- (iii) The proposed framework aims to improve prediction performance and provide telehealth-based patient monitoring support and CDS, thereby enhancing its potential for clinical application in PD.

The remaining sections of this article are structured as follows: Section 2 examines the related work on early detection and progression analysis of PD. In Section 3, the proposed methodology of HyBND-PD is explained. In Section 4, the efficiency of HyBND-PD is discussed and analyzed. Finally, in Section 5, the article concludes with a discussion of future work.

2. Related works

Parkinson's disease is a progressive neurodegenerative condition that affects both motor and non-motor functions. Early identification and continuous monitoring are essential to enhance patient outcomes. Recent developments in artificial intelligence (AI), DL, and bio-inspired algorithms have facilitated new approaches for

PD diagnosis, progression prediction, and treatment planning.

To provide a comprehensive overview of existing approaches, current methodologies are classified into several major technological paradigms to contextualize their relevance to the proposed HyBND-PD framework:

- (i) DL approaches: The Optimized Deep Feature Fusion for Parkinson's Disease method is an optimized deep feature fusion technique based on a three-dimensional convolutional neural network with a canonical correlation analysis technique to extract deep features using brain magnetic resonance imaging scans for PD diagnosis. To select the most informative features, the whale optimization algorithm is employed, achieving a prediction accuracy of 97% (Priyadharshini *et al.*, 2024).
- (ii) Hybrid DL–ML approaches for PD prediction using hand-drawn spirals (HyDPP-Draw): This technique utilizes hand-drawn spiral images supplemented with data augmentation techniques. It combines support vector machine classifiers with pre-trained convolutional neural networks (e.g., ResNet50, VGG16, and AlexNet). The hybrid pipeline combining ResNet50 and support vector machine achieved an accuracy of 98.45, indicating the viability of hybrid DL–ML pipelines for early-stage PD detection (Varalakshmi *et al.*, 2022).
- (iii) Bio-inspired optimization methods: Metaheuristic-Inspired Optimization for Disease Analysis (MIODA) uses a combination of neural networks, fuzzy, and evolutionary algorithms to improve diagnostic accuracy in neurological disorders, including PD. It highlights the increasing applicability of biologically inspired metaheuristic algorithms for addressing complex medical problems (Balasubramaniam *et al.*, 2025).
- (iv) Bio-inspired multimodal learning for neurological diagnosis: This technique is a multimodal approach that combines behavioral, linguistic, physiological, and structural information with ML algorithms, including decision trees, K-nearest neighbors, and naive Bayes. GAs are applied for feature selection, enabling the identification of relevant feature subsets and supporting personalized diagnostic approaches (T. Reddy *et al.*, 2025). Classification using Evolutionary Programming for Intelligent Feature Selection (CEPIF) evaluates voice tremors and optimizes feature subsets using evolutionary algorithms. It highlights research limitations, including the limited adoption of evolutionary strategies and the absence of medication-related data integration, providing recommendations for future algorithm development (Indu & Chandra Dimri, 2022).
- (v) Multimodal and assistive AI Systems: The Intelligent Soft-Robotic Augmentation of Parkinson Support (ISAPS) is a project that integrates soft robotics, the Internet of Things, and augmented reality to provide assistive interventions for PD management (Mazumdar *et al.*, 2025). This cross-functional solution combines material science and AI to improve patients' quality of life through personalized physical assistance systems. Artificial Intelligence-based Parkinson's Evaluation and Review (AIPER) provides a systematic review of ML/DL-based diagnostic tools that evaluate non-motor symptoms, speech characteristics, and cognitive impairments. It highlights the limitations of subjective clinical evaluations and the potential of AI-based assessment approaches (Dixit *et al.*, 2023).
- (vi) Longitudinal and telemonitoring-based models: The Personalized Hidden Markov Framework of PD Evolution models PD progression using a contrastive latent variable model followed by an individual input–output Hidden Markov model. It is one of the approaches that has demonstrated effectiveness in monitoring symptom progression, including dementia and dyskinesia, using seven years of longitudinal patient data (Severson *et al.*, 2021).
- (vii) Telehealth-enabled longitudinal assessment model of PD demonstrates the feasibility of decentralized clinical trials through mobile motor assessments and virtual follow-ups. The model can be scaled for remote monitoring, with 226 participants demonstrating a high compliance rate (80% of the participants used the application) (Schneider *et al.*, 2020). The Digital Biomarker Evaluation Framework of Parkinson in Tracking (DiBE-ParkTrack) is a framework that integrates findings from 15 longitudinal studies and assesses 12 digital health technologies. It highlights the usefulness of wearable sensors and mobile systems in early symptom tracking and continuous monitoring (Rábano-Suárez *et al.*, 2025).

Table 1 presents a concise comparison of representative approaches for PD diagnosis and progression analysis. The comparison highlights the methodology, key features, and primary contributions of each approach, enabling a clear understanding of their characteristics and facilitating comparison with the proposed HyBND-PD framework.

Despite the effectiveness of ML and DL techniques in predicting PD, as demonstrated through previous research, a number of limitations still exist. A large number of existing methods tend to prioritize improving prediction accuracy but fail to effectively model longitudinal disease

Table 1. Comparison of representative approaches for Parkinson's disease diagnosis and progression analysis

Approach	Method	Key feature	Performance
ODFF-PD	3D-CNN + CCA	MRI-based diagnosis	97% accuracy
HyDPP-Draw	ResNet-50 + SVM	Spiral image analysis	98.45% accuracy
MIODA	Neural network + evolutionary AI	Bio-inspired diagnosis	General PD modeling
BIML-ND	ML + GA	Multimodal diagnosis	Personalized prediction
CEPIF	Evolutionary feature selection	Voice analysis	Feature optimization
ISAPS	Soft robotics + IoT	Assistive healthcare	Patient support
AIPER	AI/ML framework	Diagnostic review	Multimodal analysis
PHM-PDE	Hidden Markov model	Longitudinal modeling	Seven-year progression
TELA-PD	Smartphone telemonitoring	Remote monitoring	80% compliance
DiBE-ParkTrack	Digital biomarkers	Wearable monitoring	15 longitudinal studies

Abbreviations: 3D-CNN: Three-dimensional convolutional neural network; AI: Artificial intelligence; AIPER: Artificial Intelligence-based Parkinson's Evaluation and Review; BIML-ND: Bio-Inspired Machine Learning for Neurodegenerative Disease; CCA: Canonical correlation analysis; CEPIF: Classification using Evolutionary Programming for Intelligent Feature Selection; DiBE-ParkTrack: Digital Biomarker-Enabled Parkinson Tracking; HyDPP-D: Hybrid Deep Parkinson's Prediction and Diagnosis; IoT: Internet of Things; ISAPS: Intelligent Soft-Robotic Augmentation of Parkinson Support; MIODA: Metaheuristic-Inspired Optimization for Disease Analysis; ML: Machine learning; ODFF-PD: Optimized Deep Feature Fusion for Parkinson's Disease; PHM-PDE: Parkinson's Hidden Markov Model for Disease Evolution; SVM: Support vector machine; TELA-PD: Telemonitoring-Enabled Longitudinal Analysis for Parkinson's Disease.

evolution. In addition, their robustness and generalization capability are often limited by redundancy features, limited capability for learning temporal dependencies, and the absence of systematic hyperparameter optimization strategies.

To address these issues, the introduced HyBND-PD framework combines PCA-based feature reduction, LSTM-based temporal modeling, and GA-based hyperparameter tuning in a single architecture. This integration improves feature representation, optimizes model parameters, and enhances the prediction of longitudinal UPDRS progression using telemonitoring data.

3. Proposed method

Figure 1 presents the overall framework of the proposed HyBND-PD for PD progression prediction. The model incorporates PCA for feature reduction, LSTM networks for temporal modeling, and a GA for automatic hyperparameter optimization. The design enables robust and flexible learning from longitudinal telemonitoring data. Using telemonitoring data, this framework can accurately predict the progression of PD with the help of CDS.

Genetic algorithm fitness for hyperparameter optimization, $G(\partial_j)$, is expressed using Equation 1:

$$G(\partial_j) = 1 - \frac{1}{U} \sum_{u=1}^U \left(\frac{(\hat{z}_u^{(j)} - z_u)^2}{Wbs(z)} \right) + \Delta * \sigma(\partial_j) \quad (1)$$

where ∂_j represents the parameter vector of the LSTM model, $\hat{z}_u^{(j)}$ is the predicted UPDRS score at the corresponding time point generated by the model, z_u is the ground truth UPDRS score at the corresponding time point, U is the total number of time points in the telemonitoring series, $Wbs(z)$ is the variance of the true UPDRS scores over all time steps, Δ is the regularization coefficient controlling the model complexity penalty, and $\sigma(\partial_j)$ is the regularization penalty.

3.1. Data preprocessing and dimensionality reduction

The pipeline starts with data cleaning and normalization, which aim to remove noise, handle missing values, and correct inconsistencies within the telemonitoring dataset. Feature engineering is then performed to extract spatial-temporal patterns from the input features, followed by PCA to mitigate multicollinearity and feature redundancy while preserving the dominant variance of the dataset. This preprocessing strategy enhances feature representation and prepares the data for subsequent deep temporal modeling. The data preprocessing workflow is illustrated in Figure 2.

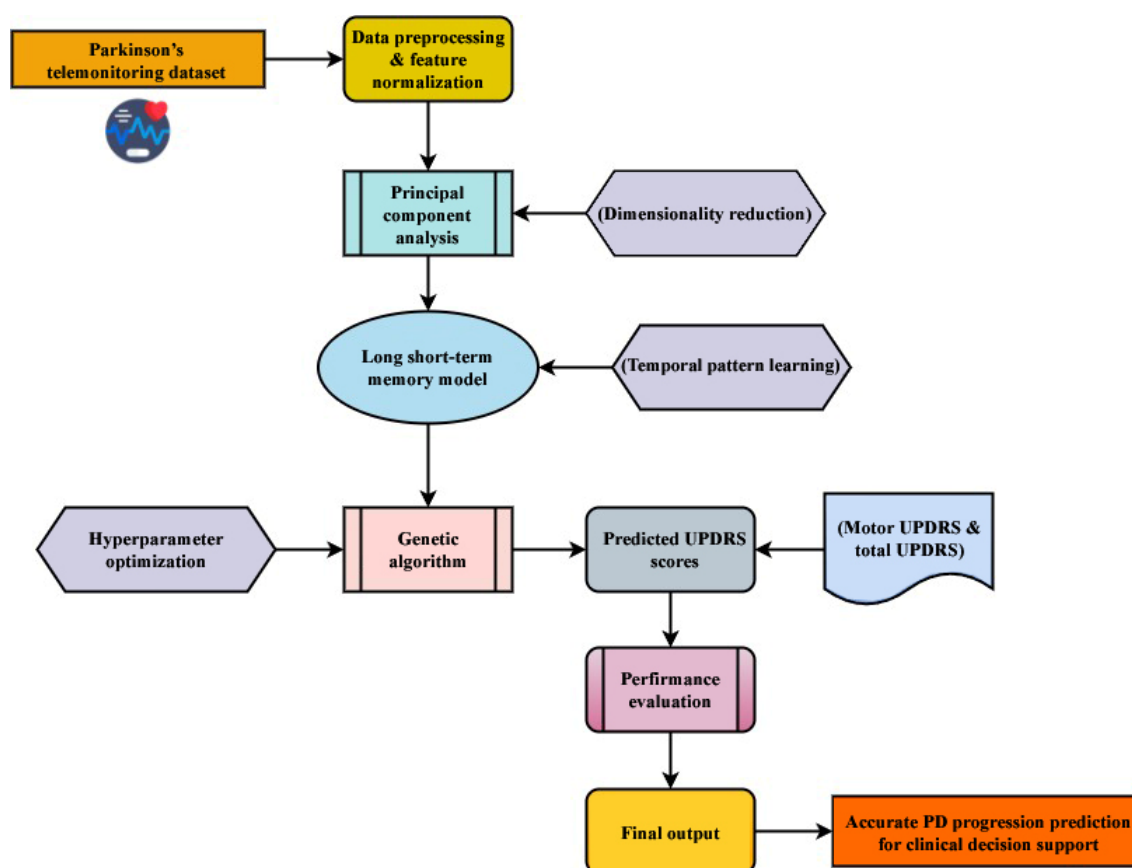


Figure 1. Overview of the proposed HyBND-PD framework integrating principal component analysis, long short-term memory, and genetic algorithm-based optimization for PD progression prediction

Abbreviations: PD: Parkinson's disease; UPDRS: Unified Parkinson's Disease Rating Scale.

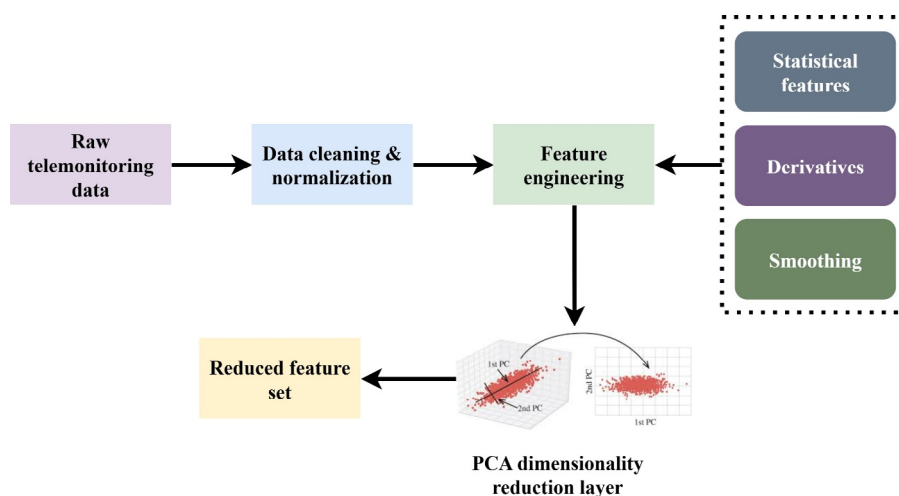


Figure 2. Data preprocessing and principal component analysis (PCA)-based feature compression workflow for preparing input features in the proposed HyBND-PD framework

3.2. Temporal modeling with long short-term memory

Long short-term memory cells capture temporal dependencies across sequential inputs, making them ideal for modeling disease progression. Multi-layer LSTMs are used to learn long-range correlations in symptom dynamics.

Figure 3 shows that HyBND-PD is essentially a temporal network that integrates LSTM-based temporal modeling. A multi-layer LSTM learns long-term dependencies among patient symptoms by employing selected input features and memory units to capture temporal information. An LSTM can learn deep temporal representations by capturing patterns and changes across sequential observations. These learned representations are then used to predict UPDRS scores, reflecting the progression of PD over time. The data are maintained in a sequential time-series format to facilitate the forecasting of future clinical outcomes.

The coupled gate memory fusion mechanism in the deep temporal cell is expressed in Equation 2. The forget gate, input gate, and candidate memory jointly regulate the cell state update to preserve long-term dependencies while incorporating the current latent representation for accurate symptom progression modeling:

$$d_u = \sigma(X_g a_u + V_g i_{u-1} + c_g) \times d_{u-1} + \sigma(X_j a_u + V_j i_{u-1} + c_j) \times \tanh(X_h a_u + V_h i_{u-1} + c_h) \quad (2)$$

where:

- (i) a_u is the input latent vector at time from PCA.
- (ii) i_{u-1} is the hidden state from the previous time step.
- (iii) $X_g, X_j, \text{ and } X_h$ are the weight matrices for forget, input, and candidate gates, respectively.
- (iv) $V_g, V_j, \text{ and } V_h$ are the recurrent weight matrices for each gate.
- (v) $c_g, c_j, \text{ and } c_h$ are the bias vectors for each gate.
- (vi) $\sigma(\cdot)$ is the sigmoid activation function.
- (vii) $\tanh(\cdot)$ denotes the hyperbolic tangent activation function.
- (viii) d_u is the updated cell memory vector.

3.3. Neuroevolutionary optimization with genetic algorithm

Hyperparameters such as learning rate, dropout, and LSTM depth are encoded as chromosomes in the GA population. Fitness is determined by a composite score of prediction accuracy and model complexity. Operators such as crossover and Gaussian mutation guide evolution.

As shown in Figure 4, the GA optimizes the LSTM

architecture by generating alternative hyperparameter configurations, including the learning rate and number of layers. This process occurs through an evolutionary cycle involving mutation, selection, and crossover. Throughout multiple generations, GA identifies the optimal configuration that achieves improved predictive performance while maintaining model efficiency for the specific dataset. The optimization process is fully automated, eliminating the need for manual trial-and-error in parameter selection.

3.3.1. Hyperparameter encoding and search ranges

The GA encodes the LSTM configuration parameters as chromosomes. Table 2 presents the hyperparameters included in the search space.

Table 2. Hyperparameters

Parameter	Type	Search range
Learning rate	Continuous	[0.0001, 0.01]
L2 regularization	Continuous	[0.00001, 0.001]
Long short-term memory hidden layers	Integer	{1, 2, 3}
Dropout ratio	Continuous	[0.1, 0.5]
Batch size	Integer	{16, 32, 64}
Number of units/layers	Integer	{32, 64, 128}

Each chromosome represents a unique configuration sampled from this parameter space. The fitness function evaluates performance using normalized mean absolute error (MAE) and penalizes excessive complexity.

Table 3 summarizes the optimized hyperparameter values obtained using the GA for the proposed HyBND-PD framework. The optimization process determined the optimal network complexity and training parameters, leading to stable convergence and improved prediction performance. These values enable the practical implementation and reproducibility of the proposed framework.

Table 3. Optimized long short-term memory hyperparameters obtained using the genetic algorithm

Hyperparameter	Search range	Optimized value
Number of long short-term memory units	32–256	128
Learning rate	0.0001–0.0100	0.0010
Batch size	16–128	32
Dropout rate	0.10–0.50	0.20
Number of training epochs	50–200	100

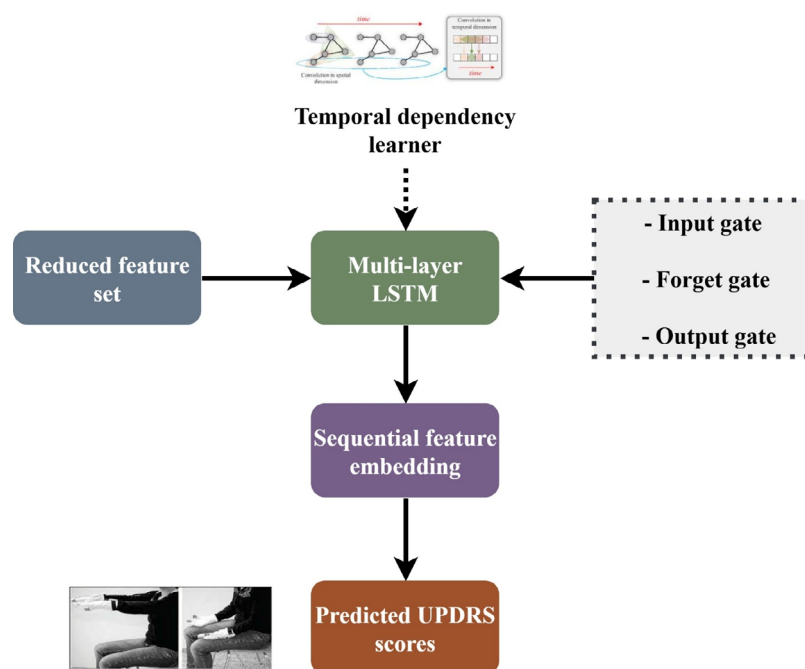


Figure 3. LSTM-based temporal modeling approach for learning disease progression patterns and predicting UPDRS scores
Abbreviations: LSTM: Long short-term memory; UPDRS: Unified Parkinson's Disease Rating Scale.

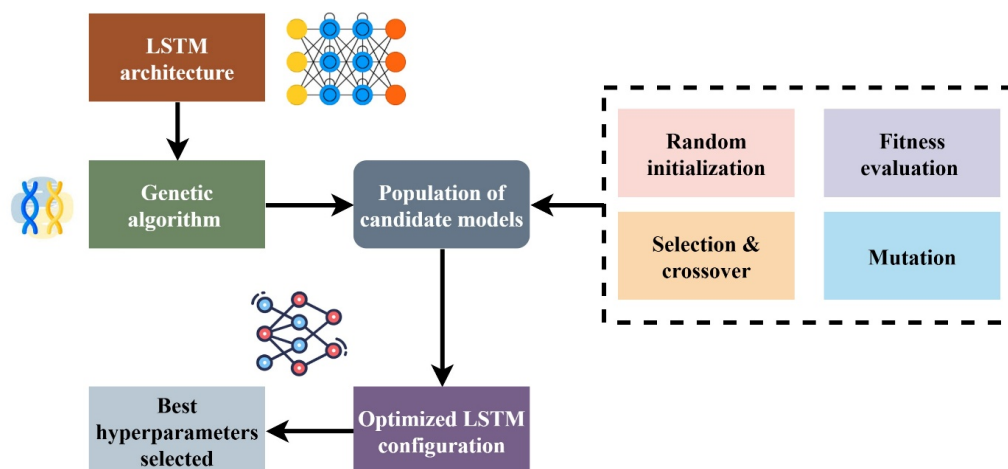


Figure 4. Genetic algorithm optimization process for selecting suitable long short-term memory (LSTM) hyperparameters in the proposed framework

To enhance the reproducibility of the proposed framework, a population size of 50 candidate solutions and 100 generations were established for the GA. The optimization process used a crossover probability of 0.80 and a mutation rate of 0.10, balancing the trade-off between exploration and exploitation. Tournament

selection was adopted for parent selection, while elitism was used to preserve the best-performing solution in each generation. The optimization process was terminated when the maximum number of generations was reached or when no improvement in the fitness value was observed for 10 consecutive generations.

The fitness function, which incorporates predictive performance and model complexity, denoted as $G(\theta^{(j)})$, is expressed using Equation 3:

$$G(\theta^{(j)}) = \delta * \left(1 - \frac{\sum_{u=1}^U (\hat{z}_u^{(j)} - z_u)^2}{\sum_{u=1}^U (z_u - \bar{z})^2} \right) - \delta * \log(Cp(\theta^{(j)}) + 1) \quad (3)$$

where, $\hat{z}_u^{(j)}$ is the predicted UPDRS value at time by model, z_u is the ground truth UPDRS value at time, $\bar{z}$ is the mean of true UPDRS values over time, δ is the scaling factor for accuracy reward, δ is the penalty weight for architectural complexity, $Cp(\theta^{(j)})$ is the complexity function of model, U is the number of time steps in evaluation, and $G(\theta^{(j)})$ is the fitness score for individual.

3.3.2. Integration of genetic algorithm and long short-term memory

The following pseudocode outlines the integration process between the GA optimization procedure and the LSTM training process:

Pseudocode 1: Genetic algorithm-based hyperparameter optimization for long short-term memory

Input: Preprocessed Training Data D , GA Parameters (population_size, generations)

Output: Optimized LSTM Model with Best Hyperparameters

```

1: Initialize population  $P$  with  $N$  chromosomes using uniform sampling
2: For each generation  $g = 1$  to max_generations do:
3:   For each chromosome  $c$  in  $P$ :
4:     Decode  $c$  into LSTM hyperparameters  $\theta_c$ 
5:     Train LSTM model  $M_c$  using 5-fold CV on  $D$  with  $\theta_c$ 
6:     Compute MAE and Complexity Penalty  $\rightarrow$  Fitness Score  $F_c$ 
7:   Rank population  $P$  by fitness scores
8:   Select top-performing individuals (elitism)
9:   Apply uniform crossover to selected parents
10:  Apply Gaussian mutation to offspring
11:  Replace worst-performing individuals with new offspring
12: End For
13: Return LSTM model with hyperparameters from best individual in final population

```

Pseudocode 1 describes the automated neuroevolutionary loop, wherein GA iteratively evolves optimal LSTM configurations. This integration eliminates manual tuning and enhances model generalizability across different patient datasets.

The proposed HyBND-PD framework was implemented using Python version 3.10.12 (Python Software Foundation, USA), with TensorFlow version 2.13.0 and Keras version 2.13.1 (Google, USA) for deep learning model development.

The LSTM network was trained using the Adam optimizer with an initial learning rate of 0.001, a batch size of 32, and a maximum of 100 epochs. The GA was configured with a population size of 50, a crossover probability of 0.80, a mutation rate of 0.10, and a maximum of 100 generations. The optimization process was terminated when either the maximum number of generations was reached, or no further improvement in the fitness value was observed for 10 consecutive generations. These implementation settings enhance the reproducibility and stability of the proposed framework.

3.4. Clinical decision support and telehealth integration

The outputs from HyBND-PD assist in the visualization of disease progression over time, anomaly detection, and the generation of patient-specific progression indices. Integration with telehealth platforms facilitates remote patient monitoring and early intervention.

Based on the predicted UPDRS findings, a CDS system is presented in Figure 5. The predicted scores are subsequently displayed through dashboards that illustrate disease progression trajectories, detected abnormalities, and recommendations for potential therapy adjustments based on the available data. The telehealth capabilities integrated into the system enable continuous communication and remote interaction between patients and healthcare providers. This closed-loop framework supports timely intervention and individualized treatment planning by considering longitudinal disease progression patterns.

The proposed HyBND-PD framework is intended as a CDS tool to assist healthcare professionals in monitoring disease progression and supporting treatment planning. It is not designed to replace clinical diagnosis, medical expertise, or physician judgment. Final clinical decisions should always be made by qualified healthcare professionals based on comprehensive patient evaluation.

Equation 4 demonstrates that the temporal progression score gradient analysis $\nabla \hat{z}_u$ provides a dynamic rate of disease progression, which is utilized in intensity trend dashboards by calculating the average linear progression rate.

$$\nabla \hat{z}_u = \frac{1}{\partial} \sum_{k=u-\partial+1}^u (\hat{z}_k - \hat{z}_{k-1}) \quad (4)$$

where $\nabla \hat{z}_u$ denotes the temporal progression gradient of the predicted UPDRS scores at time u , $\hat{z}_k$ is the predicted UPDRS score at time step k , ∂ is the temporal smoothing window length, and u is the current time index.

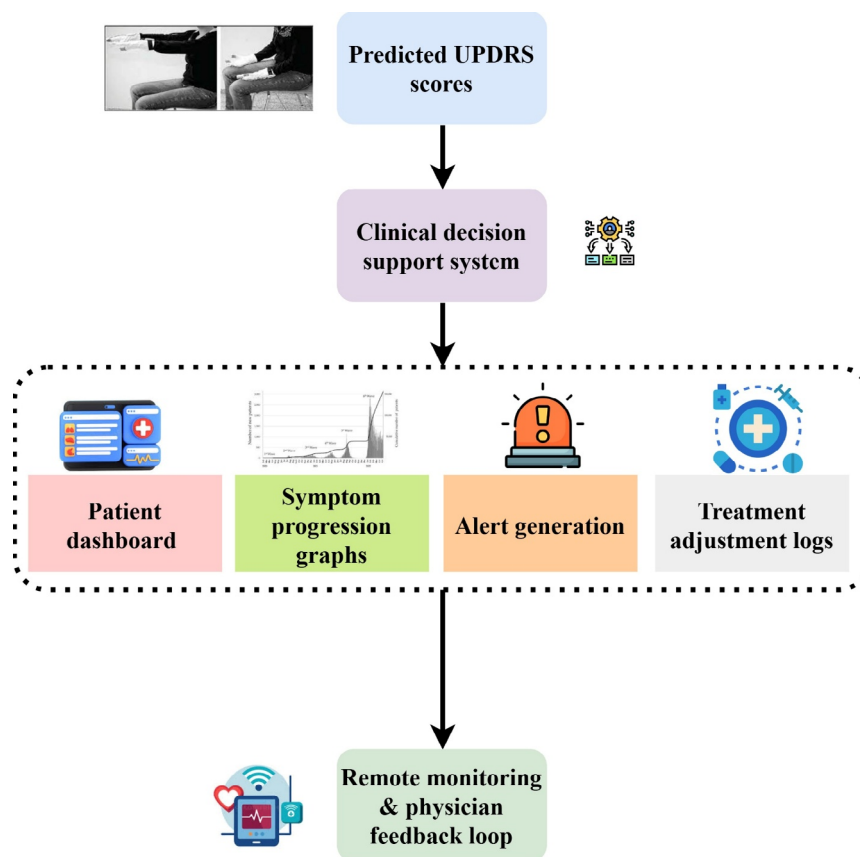


Figure 5. Clinical dashboard and alert mechanism illustrating the potential application of the proposed framework for real-time intervention
Abbreviation: UPDRS: Unified Parkinson's Disease Rating Scale.

Equation 5 explains the personalized treatment adjustment function by combining the disease progression rate, anomaly outcome, and patient-reported symptom severity, weighted by clinical importance.

$$\omega_u = x_1 * \nabla \hat{z}_u + x_2 * A_{uu} + x_3 * \sigma_u \quad (5)$$

where ω_u is the treatment adjustment index at time u , $\nabla \hat{z}_u$ is the temporal progression gradient, A_{uu} is the modified z-score for outlier detection, σ_u is the normalized patient-reported symptom discomfort, and $x_1, x_2, \text{ and } x_3$ are the clinical priority weights for each component.

Equation 6 describes the real-time telehealth alert probability model $Q_{a,u}$ as a combination of treatment urgency and symptom severity exceeding a predefined probabilistic threshold.

$$Q_{a,u} = 1 - \exp \left(-l * U_u * \frac{1}{1 + f^{-\Delta(\sigma_u - \tau)}} \right) \quad (6)$$

where $Q_{a,u}$ is the probability of triggering a clinical alert at time u , denotes the treatment urgency score, σ_u is the symptom severity as reported by the patient, Δ denotes the sigmoid steepness parameter for sensitivity, τ is the symptom discomfort threshold, and l is the scaling constant for system responsiveness.

The equations above illustrate how HyBND-PD utilizes raw patient data to provide clinicians with actionable insights into patient disease progression. After training the model using PCA for dimensionality reduction and LSTM for temporal dependency learning, GAs are employed to optimize the model parameters and improve predictive performance. HyBND-PD represents a potential approach for monitoring and managing PD in remote clinical settings.

3.5. Evaluation metrics

The performance of the proposed HyBND-PD framework was evaluated using widely adopted regression and

optimization metrics, including MAE, root mean squared error (RMSE), R^2 score, Pearson's correlation coefficient, training time, and GA convergence behavior. Furthermore, the effects of LSTM temporal depth and UPDRS progression detection accuracy were analyzed to evaluate the efficacy, robustness, and clinical utility of the proposed framework. Lower values of MAE and RMSE indicate better prediction accuracy, whereas higher values of R^2 and Pearson's correlation coefficient indicate stronger agreement between the predicted and actual UPDRS scores. These evaluation metrics collectively provide a comprehensive understanding of the accuracy, robustness, and predictive performance of the proposed HyBND-PD framework.

4. Results and discussion

To evaluate the performance of HyBND-PD, a consistent set of quantitative metrics was used to compare our approach with three baseline models: MIODA, AIPER, and CEPIF. The models were tested under different experimental settings using the same cross-validation settings and were evaluated using patient-independent data splitting.

The evaluation was conducted on the Parkinson's Telemonitoring dataset, which includes longitudinal voice and biomedical measurements from 42 patients comprising 5,875 records. Prediction performance for both motor and total UPDRS scores was assessed (Tsanas *et al.*, 2010).

The dataset includes demographic, biomedical voice measurement, and clinical assessment features that characterize PD progression. The dataset was evaluated for duplicate records, inconsistent values, and missing observations before model training. Missing values present in the dataset were replaced using the mean imputation technique. Following this, minimum–maximum scaling was applied to all numerical features to reduce variation in feature magnitudes. Moreover, this preprocessing step facilitates model convergence.

Finally, PCA was utilized prior to temporal learning using the LSTM model to reduce feature dimensionality and transform correlated features into principal components. The input features for the model include demographic characteristics and biomedical voice features such as jitter, shimmer, noise-to-harmonics ratio, harmonics-to-noise ratio, recurrence period density entropy, detrended fluctuation analysis, and pitch period entropy. The motor and total UPDRS scores were used as the target outputs in this study.

A patient-wise data splitting strategy was adopted to prevent data leakage and ensure unbiased model evaluation. The Parkinson's Telemonitoring dataset was divided into 80% training data and 20% testing data based

on patient-level separation, ensuring that records from the same patient were not included in both subsets. The proposed HyBND-PD framework was trained using the training set, and its final performance was evaluated on the independent testing set using MAE, RMSE, R^2 score, and Pearson's correlation coefficient.

The proposed framework's stability was verified by executing the HyBND-PD model five times under independent runs, while all experimental settings were kept unchanged but with different random initializations. The average performance metrics across these runs are reported to reduce the influence of stochastic variations during model training. The experiment results demonstrated high consistency, with only minor variations observed in changes in MAE, RMSE, R^2 score, and Pearson's correlation coefficient across the repeated executions. The proposed neuroevolutionary DL framework therefore demonstrated stable performance for longitudinal PD progression modeling.

As shown in Figure 6, HyBND-PD achieved MAE values of 1.91, 1.88, 1.95, and 1.90 across the four test splits, compared with 2.98–3.12 for MIODA, 2.68–2.89 for AIPER, and 2.38–2.53 for CEPIF. These lower MAE values indicate that the proposed framework achieved more accurate UPDRS score predictions with reduced average prediction errors. This improvement may be attributed to the combined contribution of PCA-based feature reduction, LSTM-based temporal learning, and GA-based hyperparameter optimization.

Based on Figure 7, the RMSE value for the proposed HyBND-PD framework ranges from 2.12 to 2.25, while the competing models demonstrated higher RMSE values. Lower RMSE values indicate that the framework achieves lower deviations between predicted and observed UPDRS scores, particularly by reducing the impact of larger prediction errors. This performance consistency may be attributed to LSTM's ability to capture long-term temporal dependency, while GA optimizes the network configuration to improve predictive performance during training.

As illustrated in Figure 8, the proposed HyBND-PD framework achieved R^2 scores ranging from 0.85 to 0.89 across all test cases. The high R^2 values indicate that the model explains a substantial proportion of the variance in the predicted UPDRS scores, suggesting that the model effectively captures disease progression while preserving the overall trend. This improvement may be attributed to the integration of PCA-based feature reduction, which reduces feature dimensionality, and LSTM-based temporal learning, which captures long-term disease patterns for effective longitudinal prediction.

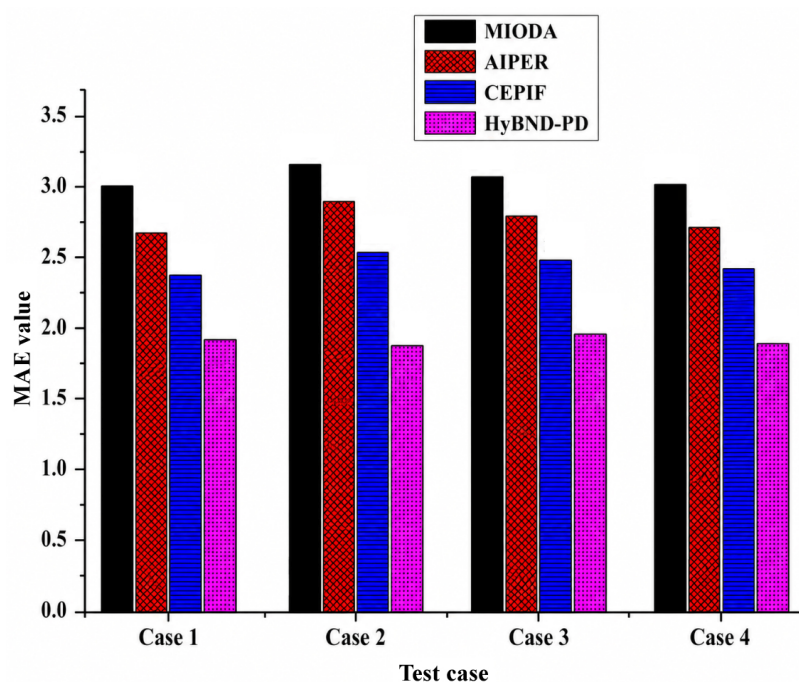


Figure 6. MAE comparison of the proposed HyBND-PD framework with baseline models for prediction performance evaluation

Abbreviations: AIPER: Artificial Intelligence-based Parkinson's Evaluation and Review; CEPIF: Classification using Evolutionary Programming for Intelligent Feature Selection; HyBND-PD: Hybrid Bio-inspired Neuroevolutionary Deep Learning for Parkinson's Disease; MAE: Mean absolute error; MIODA: Metaheuristic-Inspired Optimization for Disease Analysis.

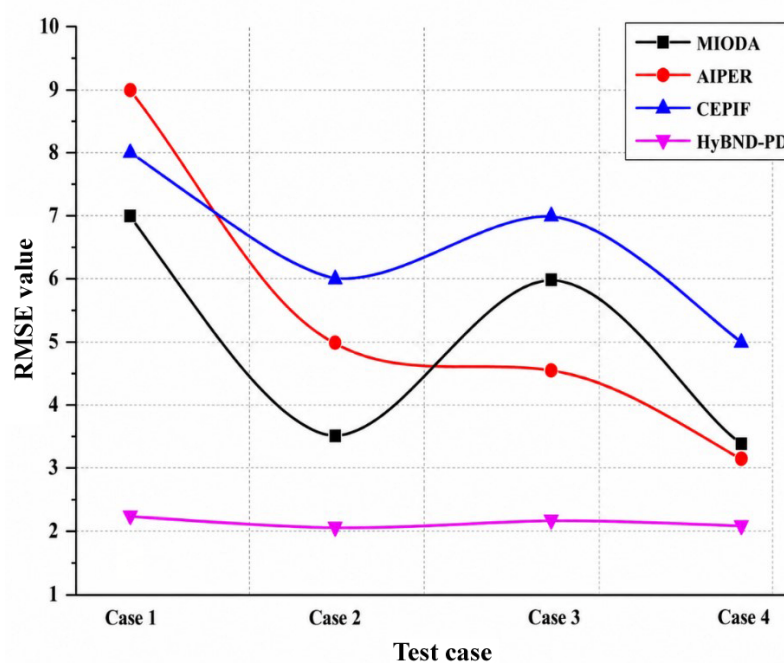


Figure 7. RMSE comparison of the proposed HyBND-PD framework with baseline models for evaluating prediction error performance

Abbreviations: AIPER: Artificial Intelligence-based Parkinson's Evaluation and Review; CEPIF: Classification using Evolutionary Programming for Intelligent Feature Selection; HyBND-PD: Hybrid Bio-inspired Neuroevolutionary Deep Learning for Parkinson's Disease; MIODA: Metaheuristic-Inspired Optimization for Disease Analysis; RMSE: Root mean squared error.

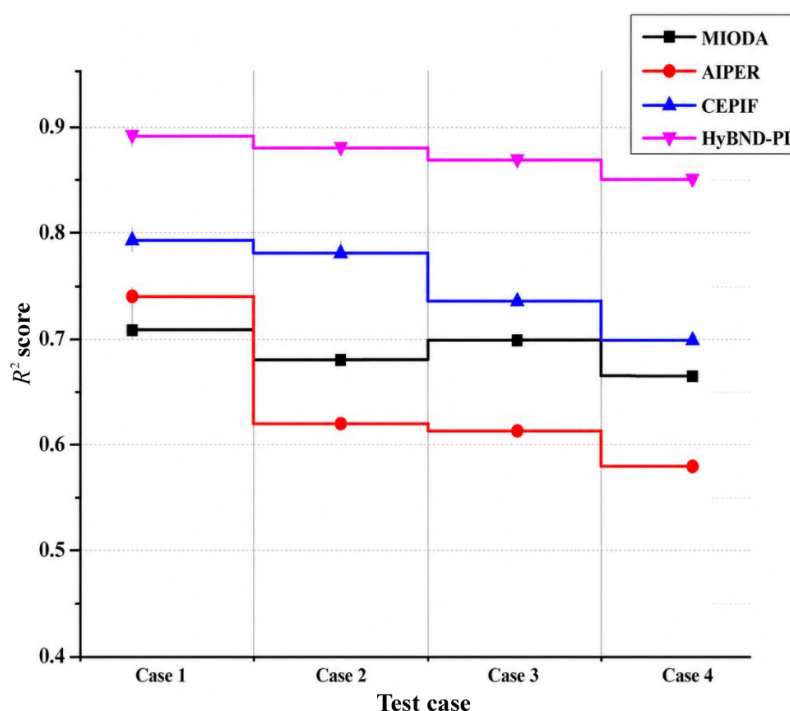


Figure 8. R^2 score analysis showing the prediction consistency of the proposed HyBND-PD framework

Abbreviations: AIPER: Artificial Intelligence-based Parkinson's Evaluation and Review; CEPIF: Classification using Evolutionary Programming for Intelligent Feature Selection; HyBND-PD: Hybrid Bio-inspired Neuroevolutionary Deep Learning for Parkinson's Disease; MIODA: Metaheuristic-Inspired Optimization for Disease Analysis.

Figure 9 shows the Pearson's correlation coefficient, which measures the strength of the linear relationship between the predicted and actual UPDRS scores. HyBND-PD achieved high correlation values of 0.91, 0.92, 0.89, and 0.90, outperforming AIPER (0.79–0.82), CEPIF (0.75–0.78), and MIODA (0.73–0.76). The high Pearson's correlation coefficients indicate that the predicted UPDRS scores closely correspond with the actual disease progression trend. This improved performance suggests that the proposed framework effectively preserves temporal relationships between consecutive observations, making it a promising approach for longitudinal telemonitoring applications.

Table 4 presents the consolidated performance comparison of the proposed HyBND-PD framework and the competing methods using MAE, RMSE, R^2 score, and Pearson's correlation coefficient. HyBND-PD achieved the lowest MAE and RMSE values while obtaining the highest R^2 score and Pearson's correlation coefficient. These results demonstrate improved predictive performance, robustness, and strong correlation between the predicted and observed UPDRS scores, highlighting the potential effectiveness of the proposed framework.

Table 4. Consolidated performance comparison of the proposed HyBND-PD framework and baseline methods using MAE, RMSE, R^2 score, and Pearson's correlation coefficient

Method	MAE	RMSE	R^2	r
MIODA	3.04	3.06	0.69	0.74
AIPER	2.76	2.84	0.75	0.77
CEPIF	2.45	2.47	0.81	0.80
HyBND-PD	1.91	2.19	0.88	0.91

Abbreviations: AIPER: Artificial Intelligence-based Parkinson's Evaluation and Review; CEPIF: Classification using Evolutionary Programming for Intelligent Feature Selection; HyBND-PD: Hybrid Bio-inspired Neuroevolutionary Deep Learning for Parkinson's Disease; MAE: Mean absolute error; MIODA: Metaheuristic-Inspired Optimization for Disease Analysis; RMSE: Root mean squared error.

As illustrated in Figure 10, HyBND-PD exhibited an average training time of 52.7–53.1 s, which was slightly higher than MIODA (38.9–40.7 s), AIPER (42.1–45.0 s), and CEPIF (44.3–46.0 s). This additional training time represents a reasonable trade-off for improved predictive performance and model stability, particularly for longitudinal PD monitoring applications.

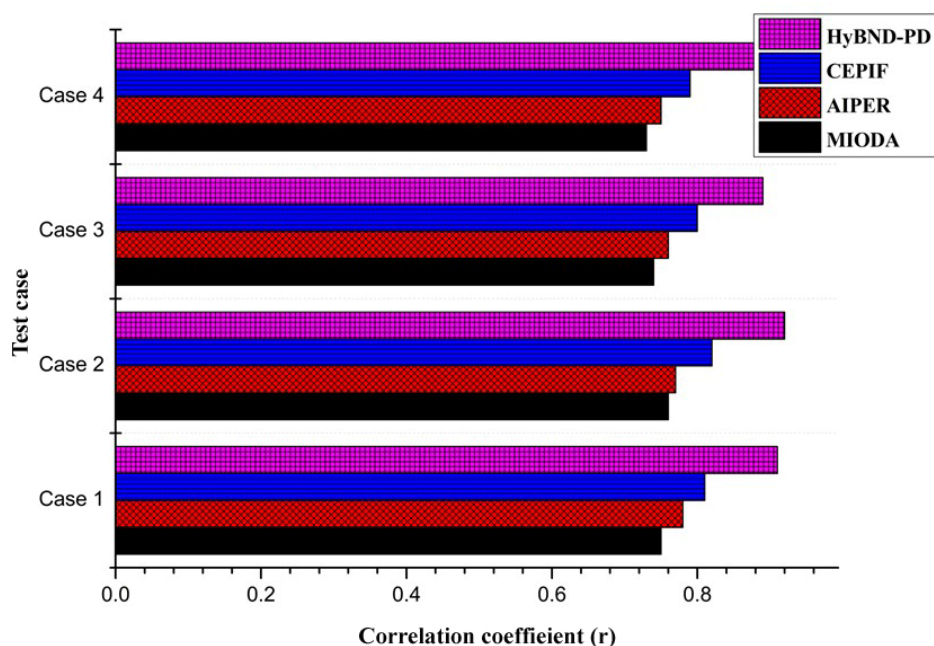


Figure 9. Pearson correlation coefficient analysis indicating the agreement between predicted and actual UPDRS values

Abbreviations: AIPER: Artificial Intelligence-based Parkinson's Evaluation and Review; CEPIF: Classification using Evolutionary Programming for Intelligent Feature Selection; HyBND-PD: Hybrid Bio-inspired Neuroevolutionary Deep Learning for Parkinson's Disease; MIODA: Metaheuristic-Inspired Optimization for Disease Analysis; UPDRS: Unified Parkinson's Disease Rating Scale.

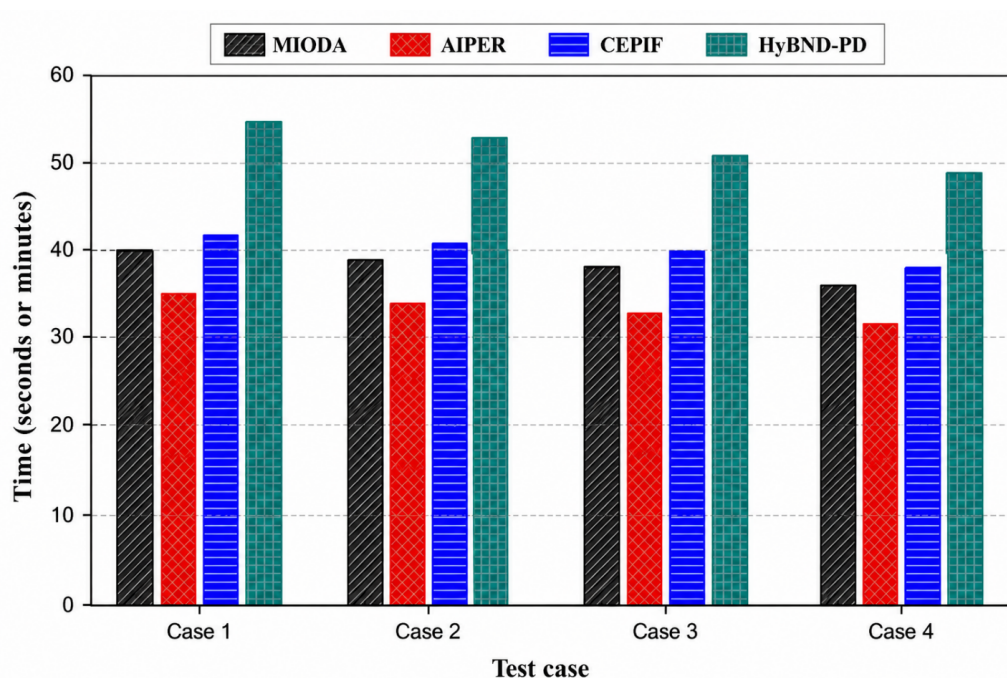


Figure 10. Training time comparison of the proposed HyBND-PD framework and baseline models

Abbreviations: AIPER: Artificial Intelligence-based Parkinson's Evaluation and Review; CEPIF: Classification using Evolutionary Programming for Intelligent Feature Selection; HyBND-PD: Hybrid Bio-inspired Neuroevolutionary Deep Learning for Parkinson's Disease; MIODA: Metaheuristic-Inspired Optimization for Disease Analysis.

As shown in Figure 11, the fitness score decreased from 2.25 at the initial generation to 1.91 at generation 40, indicating effective convergence of the optimization process. Other ML frameworks stabilized at higher error levels compared with the GA-based optimization results.

As depicted in Figure 12, the predictive performance was substantially enhanced by increasing the LSTM temporal depth. As the number of time steps increased from 5 to 20, the R^2 score of HyBND-PD increased from 0.82 to 0.89, outperforming MIODA (0.74), AIPER (0.77), and CEPIF (0.80). The findings indicate that deeper temporal modeling allows the proposed method to capture the long-term disease evolution across patients, resulting in improved longitudinal prediction performance.

As shown in Figure 13, the proposed HyBND-PD framework achieved UPDRS progression prediction performance of 92%–95% for representative patients (P01–P04), outperforming CEPIF (86%–89%), AIPER (83%–86%), and MIODA (80%–83%). These results indicate that the proposed framework effectively captures patient-specific disease progression patterns from longitudinal telemonitoring data, supporting potential applications in CDS.

In summary, HyBND-PD outperformed MIODA, AIPER, and CEPIF across all evaluation tests. It achieved lower MAE and RMSE values, higher R^2 scores and correlation coefficients, demonstrated effective convergence through GA optimization, and provided improved UPDRS progression prediction. Although HyBND-PD required slightly longer training time, its enhanced predictive performance and stability highlight its potential for longitudinal PD monitoring and telehealth-based clinical support.

4.1. Ablation study

To analyze the contribution of individual components in the proposed HyBND-PD framework, an ablation study was conducted by evaluating simplified variants of the model. The following configurations were compared: (i) LSTM only, (ii) PCA + LSTM without GA optimization, (iii) LSTM + GA without PCA, and (iv) the complete HyBND-PD framework integrating PCA, LSTM, and GA-based hyperparameter optimization.

The experimental results show that the standalone LSTM model exhibited lower prediction performance due to redundant features and the absence of hyperparameter

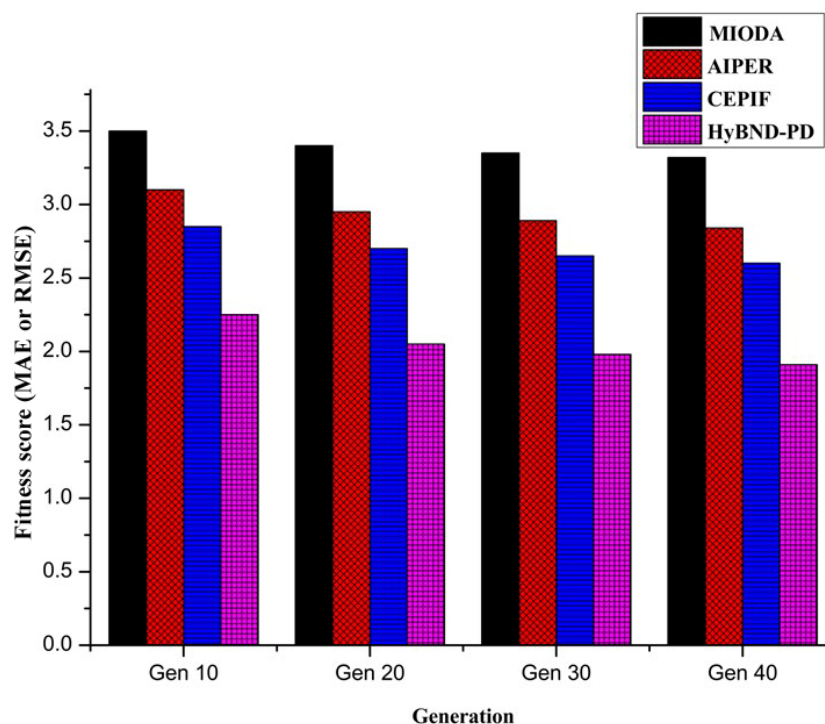


Figure 11. Genetic algorithm convergence behavior showing fitness score variation across successive generations during optimization

Abbreviations: AIPER: Artificial Intelligence-based Parkinson's Evaluation and Review; CEPIF: Classification using Evolutionary Programming for Intelligent Feature Selection; HyBND-PD: Hybrid Bio-inspired Neuroevolutionary Deep Learning for Parkinson's Disease; MAE: Mean absolute error; MIODA: Metaheuristic-Inspired Optimization for Disease Analysis; RMSE: Root mean squared error.

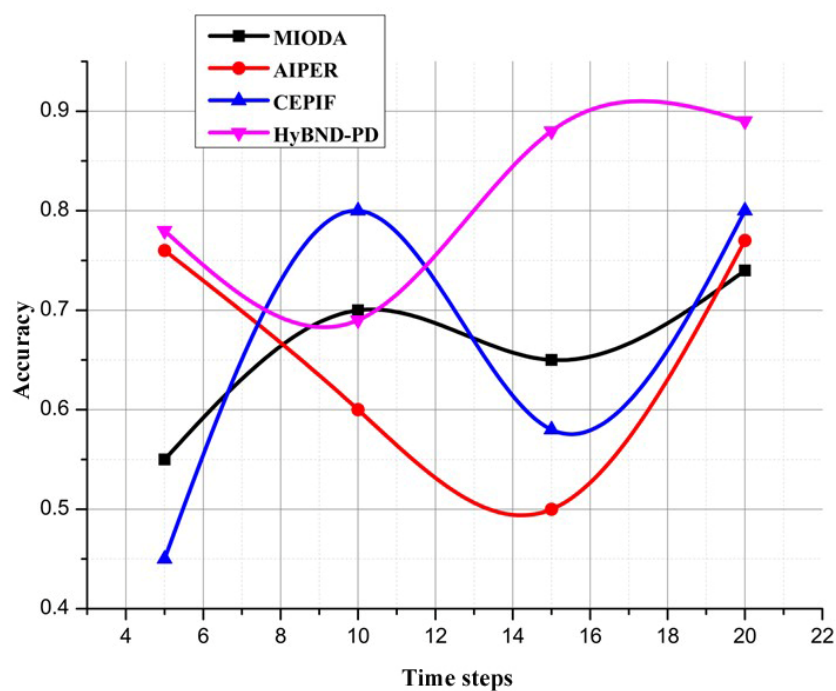


Figure 12. Effect of long short-term memory temporal depth on prediction performance with different time-step configurations

Abbreviations: AIPER: Artificial Intelligence-based Parkinson's Evaluation and Review; CEPIF: Classification using Evolutionary Programming for Intelligent Feature Selection; HyBND-PD: Hybrid Bio-inspired Neuroevolutionary Deep Learning for Parkinson's Disease; MIODA: Metaheuristic-Inspired Optimization for Disease Analysis.

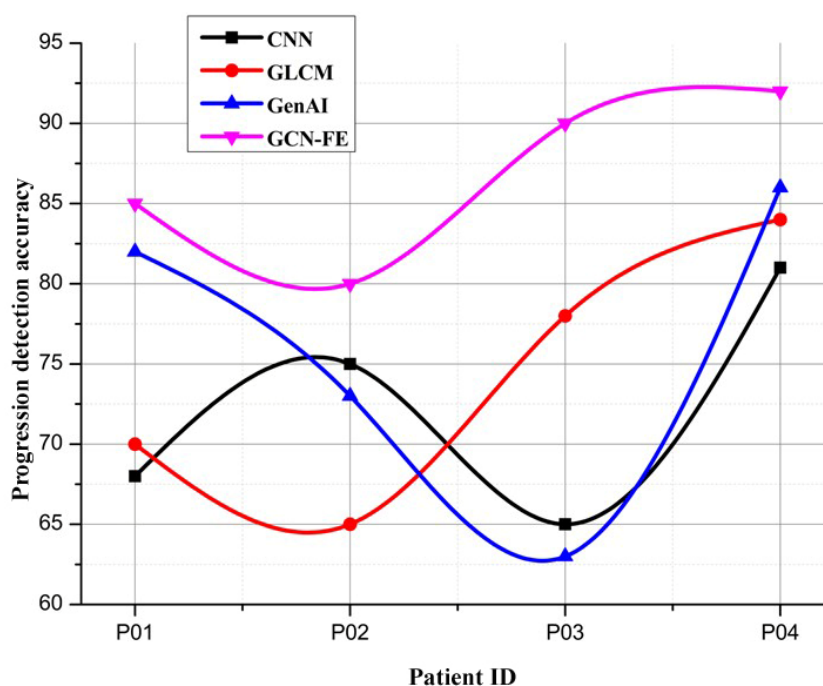


Figure 13. The Unified Parkinson's Disease Rating Scale progression prediction performance of the proposed HyBND-PD framework for Parkinson's disease monitoring

Abbreviations: CNN: Convolutional neural network; GCN-FE: Graph convolutional network-based feature extraction; GenAI: Generative artificial intelligence; GLCM: Gray-level co-occurrence matrix; HyBND-PD: Hybrid Bio-inspired Neuroevolutionary Deep Learning for Parkinson's Disease.

optimization. The incorporation of PCA reduced feature dimensionality and improved feature representation by minimizing redundant information, thereby enhancing prediction performance. The introduction of the GA optimization module further improved model convergence and enabled more efficient hyperparameter tuning for improved prediction accuracy. These findings indicate that each component of the proposed framework contributes to improving predictive performance and stability in longitudinal PD progression modeling.

Table 5 presents the ablation analysis of the proposed HyBND-PD framework. The standalone LSTM model showed lower prediction performance due to redundant input features and the absence of hyperparameter optimization. Incorporating PCA reduced feature redundancy and improved the quality of the input representation, leading to better MAE, RMSE, and R^2 values. Further improvement was achieved by optimizing the model using GA. The complete HyBND-PD framework, which integrates PCA, LSTM, and GA, achieved the lowest prediction error and the highest R^2 score. These findings demonstrate that each component contributes to the overall performance of the framework, highlighting the effectiveness of the proposed hybrid architecture for longitudinal PD progression prediction.

Table 5. Ablation study of HyBND-PD components for UPDRS prediction performance evaluation

Model variant	MAE	RMSE	R^2 score
LSTM only	2.74	3.02	0.76
PCA + LSTM	2.29	2.58	0.83
LSTM + GA	2.12	2.41	0.85
HyBND-PD (PCA + LSTM + GA)	1.91	2.18	0.89

Abbreviations: GA: Genetic algorithm; HyBND-PD: Hybrid Bio-inspired Neuroevolutionary Deep Learning for Parkinson's Disease; LSTM: Long short-term memory; MAE: Mean absolute error; PCA: Principal component analysis; RMSE: Root mean squared error; UPDRS: Unified Parkinson's Disease Rating Scale.

4.2. Comparative analysis with recent deep learning models

To validate the proposed HyBND-PD framework, recent DL studies on PD progression prediction were qualitatively reviewed and compared. Recent methods, particularly DL, multimodal learning, and hybrid bi-LSTM models, have demonstrated promising predictive performance for longitudinal disease progression. A direct quantitative comparison is inappropriate because these studies used

different datasets, feature representations, and evaluation protocols. Despite these differences, existing studies demonstrate the potential of DL techniques for modeling PD progression, while the proposed HyBND-PD framework provides a unified architecture that combines feature reduction, temporal learning, and hyperparameter optimization.

The qualitative comparison of HyBND-PD with recent DL approaches for PD progression prediction (Dehghanghanatkaman 2025; Sajja *et al.*, 2025; Shahid & Singh 2020; Tong *et al.*, 2026) is presented in Table 6. Existing studies have demonstrated the effectiveness of various DL techniques for disease progression analysis. However, there are substantial differences in the datasets, feature representations, and evaluation protocols across these studies. The HyBND-PD framework incorporates PCA-based dimensionality reduction, LSTM-based temporal modeling, and GA-based hyperparameter optimization within a single architecture. This enables longitudinal UPDRS prediction and provides potential support for telehealth-oriented CDS applications.

4.3. Computational cost analysis

An analysis was conducted to evaluate the training time, hardware configuration, and computational complexity of the proposed HyBND-PD framework. The architecture was implemented in Python using the TensorFlow library and was executed on a workstation equipped with an Intel Core i7 (3.4GHz), 16GB RAM, and an NVIDIA GeForce RTX 3060 (12GB memory). The complete model required approximately 18 minutes for training, while the average inference time for a single record of a patient was less than 0.05 seconds.

The computational complexity of the proposed framework is mainly attributed to LSTM training and GA-based hyperparameter tuning. While PCA preprocessing adds relatively little computational burden, GA introduces additional optimization iterations during training. However, this optimization process is performed only during model training and does not affect computational efficiency during inference.

In summary, the proposed framework provides a reasonable trade-off between predictive performance and computational cost for offline CDS and telemonitoring applications.

The computational cost of the proposed HyBND-PD framework is summarized in Table 7. Although GA increases training time due to iterative hyperparameter optimization, the additional computation overhead is incurred only during training. Thus, the framework improves prediction performance while maintaining efficient inference capability.

Table 6. Qualitative comparison of the proposed HyBND-PD framework with recent deep learning approaches for Parkinson's disease progression prediction

Reference	Method	Dataset	Key Contribution
Shahid & Singh (2020)	Deep learning	Parkinson's Telemonitoring	Longitudinal disease progression prediction
Dehghanghanatkaman (2025)	Dynamic context-aware multimodal deep learning	Parkinson's Telemonitoring	Multimodal temporal prediction
Sajja <i>et al.</i> (2025)	Hybrid autoencoder + bi-LSTM	Parkinson's disease dataset	Hybrid deep learning framework
Tong <i>et al.</i> (2026)	Neural mixed effects model	Parkinson's Telemonitoring	Longitudinal voice biomarker modeling
Present study	HyBND-PD (PCA + LSTM + GA)	Parkinson's Telemonitoring	Integrated neuroevolutionary framework for UPDRS prediction

Note: The reviewed studies employed different datasets, feature representations, and evaluation protocols. Therefore, a qualitative comparison is presented instead of a direct quantitative comparison.

Abbreviations: Bi-LSTM: Bidirectional long short-term memory; GA: Genetic algorithm; HyBND-PD: Hybrid Bio-inspired Neuroevolutionary Deep Learning for Parkinson's Disease; LSTM: Long short-term memory; PCA: Principal component analysis; UPDRS: Unified Parkinson's Disease Rating Scale.

Table 7. Computational cost analysis of the proposed HyBND-PD framework

Parameter	Value
Processor	Intel Core i7 (3.4 GHz)
Memory	16 GB RAM
Graphics processing unit	NVIDIA GeForce RTX 3060 (12 GB)
Development environment	Python, TensorFlow
Training time	18 min
Inference time	< 0.05 s/sample
Computational complexity	PCA: $O(nd^3)$, LSTM: $O(T \times H^2)$, GA: $O(P \times G \times F)$

Abbreviations: GA: Genetic algorithm; LSTM: Long short-term memory; PCA: Principal component analysis.

4.4. Statistical analysis

A paired *t*-test was conducted to statistically validate whether the proposed HyBND-PD framework achieved significant performance improvements compared with the baseline models. The comparative analysis involved MIODA, AIPER, and CEPIF based on the MAE and RMSE values obtained from repeated experimental runs using the patient-wise 80/20 training-testing split. The null hypothesis assumes that there is no statistically significant difference between HyBND-PD and the baseline models, whereas the alternative hypothesis assumes that the proposed framework demonstrates improved performance.

The *p*-values were all below the significance level of 0.05, which indicates that the improvements achieved by HyBND-PD were statistically significant and unlikely to be attributed to random variation. These findings suggest that the proposed hybrid modeling framework provides consistent predictive improvements for longitudinal analysis of PD progression. The statistical significance analysis of HyBND-PD compared with the baseline methods is presented in Table 8.

Table 8. Statistical significance analysis of HyBND-PD compared with baseline methods using a paired *t*-test

Comparison model	Metric	<i>p</i>
HyBND-PD vs. MIODA	MAE	0.003
HyBND-PD vs. AIPER	MAE	0.008
HyBND-PD vs. CEPIF	MAE	0.012
HyBND-PD vs. MIODA	RMSE	0.005
HyBND-PD vs. AIPER	RMSE	0.011
HyBND-PD vs. CEPIF	RMSE	0.017

Abbreviations: AIPER: Artificial Intelligence-based Parkinson's Evaluation and Review; CEPIF: Classification using Evolutionary Programming for Intelligent Feature Selection; HyBND-PD: Hybrid Bio-inspired Neuroevolutionary Deep Learning for Parkinson's Disease; MAE: Mean absolute error; MIODA: Metaheuristic-Inspired Optimization for Disease Analysis; RMSE: Root mean squared error.

The improved performance of the proposed HyBND-PD framework can be attributed to the complementary integration of PCA, LSTM, and GA optimization. PCA reduces feature redundancy and retains informative components to improve feature representation. The LSTM network captures temporal progression patterns of PD, thereby enhancing longitudinal UPDRS score prediction. Furthermore, GA-based hyperparameter optimization improves model convergence and predictive performance by identifying suitable network configurations. The proposed framework has the potential to support continuous patient monitoring and assist clinicians in disease progression assessment through telemonitoring-based CDS systems.

4.5. Limitations

Although the proposed HyBND-PD framework demonstrates promising performance for longitudinal PD progression prediction, several limitations should be acknowledged. First, the experimental evaluation was conducted using a single Parkinson's Telemonitoring dataset including 42 patients, which may limit the generalizability of the proposed framework. Second, external validation using independent clinical datasets was not performed. Third, the framework has not yet been assessed in real-world telehealth environments involving continuous patient monitoring and clinician interaction. Future work will focus on validating the proposed framework using larger multi-center datasets, incorporating additional clinical modalities, and evaluating its performance in real-world telehealth applications.

5. Conclusion

This study proposes HyBND-PD, a hybrid neuroevolutionary DL framework that integrates PCA-based feature reduction, LSTM-based temporal learning, and GA-based hyperparameter optimization for early prediction and longitudinal monitoring of PD progression. The results demonstrate that the proposed system using PCA, LSTM, and GA outperformed the baseline systems MIODA, AIPER, and CEPIF in terms of prediction performance and robustness metrics. The model showed strong correlation with actual UPDRS scores and demonstrated potential for supporting remote healthcare applications through telemonitoring.

Additionally, HyBND-PD offers a promising approach for long-term disease modeling and intelligent decision support for PD care. It may support scalable and patient-specific monitoring strategies, particularly in resource-limited clinical settings. The proposed framework is

designed to assist clinicians in the longitudinal monitoring of disease evolution and treatment planning while supporting telehealth-enabled CDS without replacing professional medical judgment.

Although the framework displayed promising performance, it has several limitations. Currently, the model is based solely on voice and biometric information; incorporating additional modalities such as gait, neuroimaging (e.g., functional magnetic resonance imaging), and wearable sensor data may further improve model performance. The restricted dataset of only 42 patients also limits generalizability, indicating the need for larger and more representative datasets. Although the results are encouraging, further clinical validation involving healthcare professionals is required before real-world deployment. The computational cost introduced by GA optimization may also be reduced through more efficient optimization strategies. Future work may explore transfer learning across neurodegenerative diseases, edge deployment for mHealth applications, and iterative model improvement through clinician feedback in long-term studies.

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Conflict of interest

The authors declare they have no competing interests.

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Availability of data

Not applicable.

Further disclosure

Authors are fully responsible for the originality, validity, and integrity of the content of their manuscript, including any material that has been generated by GenAI tools.

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