Conditional Neural ODE for Longitudinal Parkinson's Disease Progression Forecasting

Xiaoda Wang[1] Yuji Zhao[2] Kaiqiao Han[3] Xiao Luo[3] Sanne van Rooij[1]
Jennifer Stevens[1] Lifang He[4] Liang Zhan[5] Yizhou Sun[3] Wei Wang[3]
Carl Yang[1]

[1]Emory University [2]Illinois Institute of Technology [3]University of California, Los Angeles
[4]Lehigh University [5]University of Pittsburgh

Contact: xiaoda.wang@emory.edu j.carlyang@emory.edu

Summary

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by complex and heterogeneous changes in brain morphometry over time. Modeling these longitudinal trajectories is essential for understanding disease pathology, guiding treatment development, and enabling personalized "digital twin" simulations to forecast the evolution of PD under various hypothetical interventions. However, existing methods usually adopt recurrent neural networks and transformer architectures, which rely on discrete, regularly sampled data and struggle to handle the irregular and sparse magnetic resonance imaging (MRI) in PD cohorts. Moreover, these methods have difficulty in capturing individual heterogeneity including variations in disease onset, progression rate, and symptom severity, which is a hallmark of PD. To address these challenges, we propose CNODE (Conditional Neural ODE), a novel framework for continuous, individualized PD progression forecasting. The core of CNODE is to model morphological brain changes as continuous temporal processes using a neural ODE model. In addition, we jointly learn patient-specific initial time and progression speed to align individual trajectories into a shared progression trajectory. We validate CNODE on the Parkinson's Progression Markers Initiative (PPMI) dataset. Experimental results show that our method outperforms state-of-the-art baselines in forecasting PD progression, which can pave the way for deeper insights into PD dynamics and improved clinical decision support.

Framework

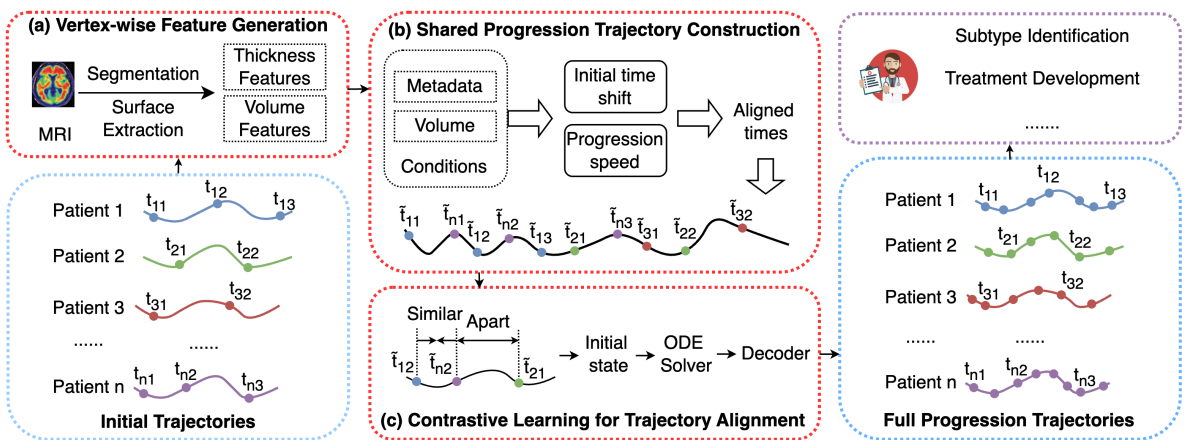


Figure: The overall framework of CNODE.

CNODE first extracts vertex-wise medial thickness from MRI scans, along with subcortical structure volumes and metadata. Then CNODE constructs a shared progression trajectory, aligning patient data through two neural networks that predict for individual start time τ_i and progression speed γ_i. And the aligned time $\tilde{t}_{i,k}$ for each visit $t_{i,k}$ in the shared trajectory is then computed as:

$$\tilde{t}_{i,k} = \tau_i + \gamma_i \cdot (t_{i,k} - t_{i,1}), \tag{1}$$

where $t_{i,1}$ is the first observed visit time for patient i. To ensure that visits with similar shape features are mapped closer in time, we integrate contrastive learning. This is achieved by computing feature-based similarity scores and optimizing a contrastive loss to refine the shared trajectory.

$$\mathcal{L}_{\text{contrast}} = -\sum_{i} \sum_{\substack{j: \\ y_{ij}=1}} w_{ij} \log \left(\frac{\exp\left(\text{sim}(\tilde{t}_i, \tilde{t}_j)/\tau\right)}{\sum_{k} \exp\left(\text{sim}(\tilde{t}_i, \tilde{t}_k)/\tau\right)} \right), \tag{2}$$

where $\text{sim}(\tilde{t}_i, \tilde{t}_j)$ is the cosine similarity, and τ is a temperature scalar. Next, we employ a Neural ODE [1] to model the continuous evolution of shape features. The model consists of an encoder that maps observed features to a latent space, an ODE solver that predicts latent state dynamics over time, and a decoder that reconstructs shape features from the latent representations.

Results

Dataset. We evaluate CNODE using the PPMI dataset [2], a comprehensive, multi-center study aimed at identifying progression markers for Parkinson's disease. For this study, we utilize T1-weighted MRI, which provides high-resolution anatomical details of the brain. The vertex-wise features were extracted from 68 sub-cortical brain regions using FreeSurfer. Our cohort includes 161 PD subjects, with 50 individuals having three visits and another 111 having two visits. The average visit interval is 1.11 years, with a maximum of 2.27 years and a minimum of 0.61 years.

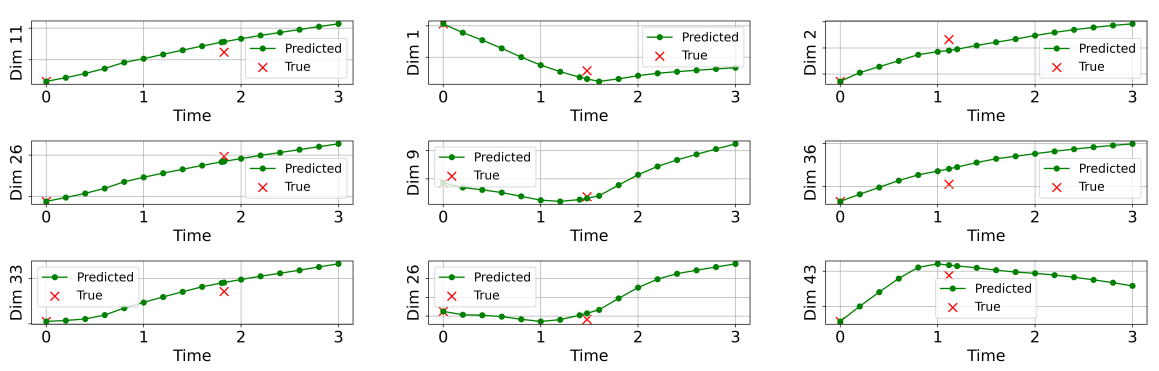
Experimental Results. We evaluated our model's performance in forecasting PD progression against several baseline models, including Recurrent Neural Networks (RNNs), Long Short-Term Memory networks (LSTMs), Gated Recurrent Units (GRUs), Neural Ordinary Differential Equations (Neural ODEs), Transformer, and LLMTime. Table shows that CNODE outperforms all baselines, achieving the lowest MSE, lowest RMSE, and highest R^2 score.

Table: Comparison of PD progression forecasting performance. All metrics are presented as averages with their standard deviations under 5-fold cross-validation. The best performances are in bold.

Model	MSE ↓	RMSE ↓	R^2 ↑
RNN	0.0305 ± 0.0027	0.1745 ± 0.0076	0.7947 ± 0.0179
LSTM	0.0292 ± 0.0019	0.1708 ± 0.0056	0.8037 ± 0.0130
GRU	0.0281 ± 0.0012	0.1675 ± 0.0036	0.8112 ± 0.0082
Transformer	0.0291 ± 0.0010	0.1705 ± 0.0030	0.8038 ± 0.0069
Neural ODE	0.0283 ± 0.0019	0.1632 ± 0.0043	0.7907 ± 0.0147
LLMTime	0.0282 ± 0.0105	0.1652 ± 0.0226	0.8041 ± 0.0739
w/o CL	0.0276 ± 0.0003	0.1662 ± 0.0010	0.8136 ± 0.0022
w/o PS	0.0278 ± 0.0006	0.1667 ± 0.0016	0.8126 ± 0.0037
Ours	$\mathbf{0.0258 \pm 0.0001}$	$\mathbf{0.1606 \pm 0.0003}$	$\mathbf{0.8260 \pm 0.0006}$

Ablation Study. We conduct an ablation study by comparing two model variants: (1) *CNODE w/o CL*, which removes contrastive learning, and (2) *CNODE w/o PS*, which excludes progression speed prediction and instead uses true time intervals.

Visualization of Parkinson's Disease Progression. To further demonstrate the interpretability of CNODE, we visualize the predicted disease progression trajectories for individual patients. It highlights CNODE's ability to generate biologically plausible progression patterns that closely align with real patient data. This interpretability is particularly valuable for identifying high-risk individuals and enabling timely interventions.



(a) Patient 1 (b) Patient 2 (c) Patient 3

Figure: Visualization of PD progression trajectory. The green curves denote the predicted progression trajectories, while the red crosses represent the true observed values.

Reference

[1] Chen, Ricky TQ, et al. "Neural ordinary differential equations." Advances in neural information processing systems 31 (2018).

[2] Marek, Kenneth, et al. "The Parkinson progression marker initiative (PPMI)." Progress in neurobiology 95.4 (2011): 629-635.