Conditional Neural ODE for Longitudinal Parkinson's Disease Progression Forecasting

Presented During: Poster Session 1
Wednesday, June 25, 2025: 01:15 PM - 03:15 PM

Presented During: Poster Session 2
Thursday, June 26, 2025: 01:45 PM - 03:45 PM

Poster No:

251

Submission Type:

Late-Breaking Abstract Submission

Authors:

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]

Institutions:

[1]Emory University, Atlanta, GA, [2]Illinois Institute of Technology, Chicago, IL, [3]University of California, Los Angeles, Los Angeles, CA, [4]Lehigh University, Bethlehem, PA, [5]University of Pittsburgh, Pittsburgh, PA

First Author:

Xiaoda Wang
Emory University
Atlanta, GA

Co-Author(s):

Yuji Zhao
Illinois Institute of Technology
Chicago, IL
Kaiqiao Han
University of California, Los Angeles
Los Angeles, CA
Xiao Luo
University of California, Los Angeles
Los Angeles, CA
Sanne van Rooij
Emory University
Atlanta, GA
Jennifer Stevens
Emory University

Atlanta, GA
Lifang He
Lehigh University
Bethlehem, PA
Liang Zhan
University of Pittsburgh
Pittsburgh, PA
Yizhou Sun
University of California, Los Angeles
Los Angeles, CA
Wei Wang
University of California, Los Angeles
Los Angeles, CA
Carl Yang
Emory University
Atlanta, GA

Introduction:

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by complex and heterogeneous changes in brain morphometry over time (Armstrong, 2020). 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 (Gratwicke, 2015). 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 (Lian, 2024). To address these challenges, we propose CNODE (Conditional Neural ODE), a novel framework for continuous, individualized PD progression forecasting as shown in Fig. 1. 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 (Marek, 2011). 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.

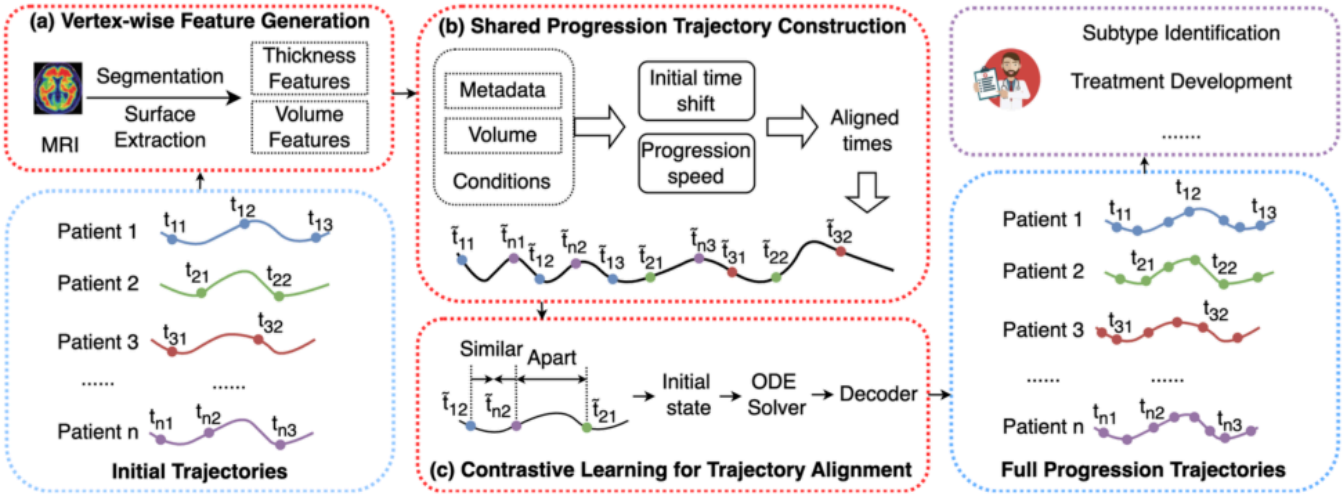


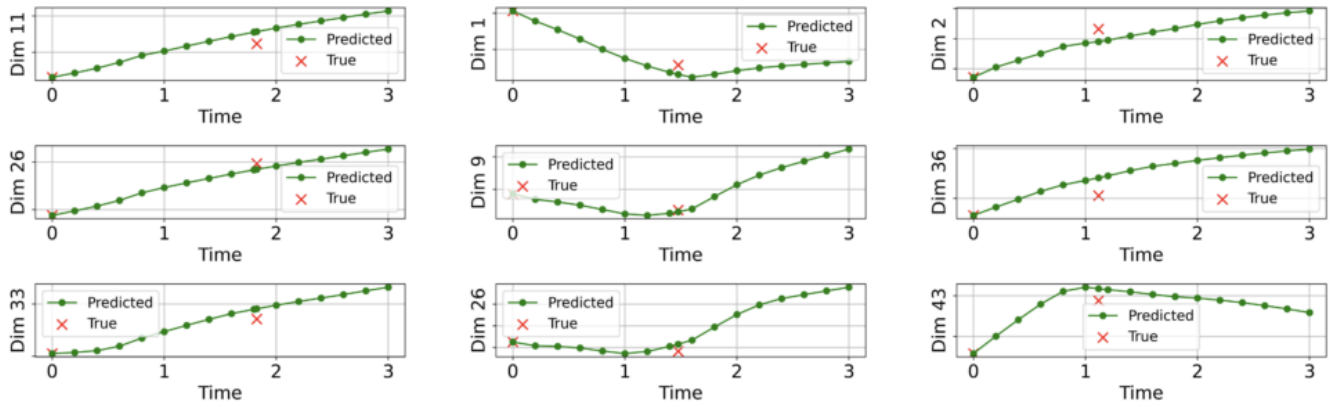
Fig. 1: Overview of CNODE. (a) Firstly, we extract vertex-wise *medial thickness* from MRI, with subcortical structure volumes. (b) Secondly, we construct a shared progression trajectory. (c) Then we employ contrastive learning to align time distributions. Finally, we model the continuous evolution with Neural ODE.

Methods:

CNODE first extracts vertex-wise medial thickness from MRI scans, along with subcortical structure volumes and metadata (Fischl, 2012). Then CNODE constructs a shared progression trajectory, aligning patient data through two neural networks that predict for individual start time and progression speed. To ensure that visits with similar shape features are mapped closer in time, we integrate contrastive learning (Oord, 2018). This is achieved by computing feature-based similarity scores and optimizing a contrastive loss to refine the shared trajectory. Next, we employ a Neural ODE (Chen, 2018) 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:

We evaluate our model using the PPMI dataset, leveraging T1-weighted MRI scans from 161 PD patients, 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. CNODE demonstrating superior performance in MSE, RMSE, and R^2 compared with RNN-based methods (Sherstinsky, 2020), Transformer (Vaswani, 2017) and LLMTime (Gruver, 2023). Ablation studies confirm the effectiveness of contrastive learning and progression speed alignment. To further demonstrate the interpretability of CNODE, we visualize the predicted disease progression trajectories for individual patients in Fig. 2. 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

Fig. 2: Visualization of PD progression trajectory. The green curves denote the predicted progression trajectories, while the red crosses represent the true observed values.

Conclusions:

In this work, we introduced CNODE that models continuous Parkinson's disease progression. By harnessing subcortical shape features and aligning patients within a shared progression trajectory, CNODE captures individualized disease dynamics while addressing common challenges such as missing timepoints and heterogeneous progression rates. Experimental results demonstrate the superiority of our proposed CNODE over state-of-the-art methods, highlighting its potential for personalized disease monitoring and therapeutic decision support.

Disorders of the Nervous System:

Neurodegenerative/ Late Life (eg. Parkinson's, Alzheimer's) [1]

Modeling and Analysis Methods:

Classification and Predictive Modeling [2]
Methods Development

Keywords:

Computational Neuroscience
Design and Analysis
Machine Learning
MRI
Other - Neural ODE; Parkinson's disease progression; Contrastive learning; Time series forecasting

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Please indicate which methods were used in your research:

Structural MRI
Computational modeling

Provide references using APA citation style.

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