# Mutually Exclusive Multi-Modal Approach for Parkinson's Disease Classification

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Keywords: Parkinson's Disease, Multi-Modal, Classification, Siamese Network, Deep Learning.

Abstract: Parkinson's Disease (PD) is a progressive neurodegenerative disorder that affects the central nervous system and causes both motor and non-motor symptoms. While movement related symptoms are the most noticeable early signs, others like loss of smell can occur quite early and are easy to miss. This suggests that multi-modal assessment has significant potential in early diagnosis of PD. Multi-modal analysis allows for synergistic fusion of complementary information for improved prediction accuracy. However, acquiring all modalities for all subjects is not only expensive but also impractical in some cases. This work attempts to address the missing modality problem where the data is mutually exclusive. Specifically, we propose to leverage two distinct and unpaired datasets to improve the classification accuracy of PD. We propose a two-stage strategy that combines individual modality classifiers to train a multi-modality classifier using siamese network with Triplet Loss. Furthermore, we use a Max-Voting strategy applied to Mix-and-Match pairing of the unlabelled test sample of one modality with both positive and negative samples from the other modality for test-time inference. We conducted experiments using gait sensor data (PhysioNet) and clinical data (PPMI). Our experimental results demonstrate the efficacy of the proposed approach compared to the state-of-the-art methods using single modality analysis.

## 1 INTRODUCTION

Parkinson's Disease, an incurable central nervous system disorder, affects approximately 8.5 million individuals worldwide, gradually impairing motor activity. Early symptoms encompass rigidity, tremors, slowed movement, gait difficulties, and behavioral changes, with intensification in later stages. The disorder's etiology remains elusive, prompting researchers to investigate commonalities among PD (Emamzadeh and Surguchov, 2018; Makarious et al., 2022) patients. Advanced stages present with manifestations such as muscle stiffness, olfactory loss, rapid eye movement, and sleep disturbances, significantly impacting daily life. Subtle early symptoms often go unnoticed, leading to a progressive neurodegenerative condition. Challenges in diagnosing the disease at its early stage arise from its diverse manifestations, requiring extended observation to discern symptoms.

Recent advancements in machine learning and deep learning techniques show promise in assisting the diagnosis of Parkinson's disease. Researchers have initiated investigations into the symptomatology of the disease. Initially, the focus centered on identifying commonalities among patients. Subsequently, it was observed that various factors impact the diagnostic process. Single-symptom experiments provide accuracy for specific data types, disregarding potential co-occurring symptoms. To address this, a proposed framework for differential PD identification takes into account multiple symptoms in characterizing individuals as either Parkinson's Disease (PD) or Healthy Control (HC) subjects. However, achieving the required high accuracy remains challenging in healthcare. Clinical diagnosis relies on tests, patient responses, and neuroimaging, contributing to detection errors. Early detection poses an additional challenge, marked by brain structural changes preceding subtle symptoms. Notably, the impact of Parkinson's Disease on the substantia nigra and basal ganglia is evident in brain images, reflecting dopaminergic effects preceding motor symptoms. Timely identification facilitates intervention with neuroprotective medication. Machine learning techniques (Archila J., 2022; Pahuja G., 2022), increasingly popular over the past decade, aid in pattern recognition within clinical data and images. In this context, gait sensor data, along with motor and

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Chaudhuri, A., Sambyal, A. and Bathula, D.
Mutually Exclusive Multi-Modal Approach for Parkinson's Disease Classification.
DOI: 10.5220/0012376100003657

In *Proceedings of the 17th International Joint Conference on Biomedical Engineering Systems and Technologies (BIOSTEC 2024) - Volume 1*, pages 236-243
ISBN: 978-989-758-688-0; ISSN: 2184-4305

non-motor symptom data, is employed to classify PD patients.

Given a comprehensive understanding of the aforementioned challenges, we propose the development of a multi-modal framework that utilizes various data sources to improve disease classification. Our goal is to integrate gait analysis data and clinical data to enhance the accuracy of categorizing Parkinson's disease. Furthermore, we have implemented a robust cross-validation technique to address over-fitting complexities within the machine learning model. Our contributions can be summarized as follows:

- We proposed a novel approach to jointly train two mutually exclusive datasets within a multi-modal framework. Additionally, we suggested an innovative inference method utilizing embedding with a triplet loss function.
- We conducted a comprehensive evaluation of the training and inference framework using a variety of metrics and compared it with state-of-the-art (SOTA) approaches.
- Our approach demonstrated a significant reduction in error rates and an improvement in accuracy for the diagnostic process.

## 2 LITERATURE SURVEY

Research studies that are based on machine learning techniques have been done until now a can be categorized into three parts. Those are summarized in the following:

**1. Studies to Discriminate PD and HC Using Machine Learning Techniques –** Combining diverse data modalities, including images and clinical data, while accommodating varying measurement scales, has emerged as a promising avenue. (Prashanth et al., 2016) advocate for a comprehensive analysis, integrating cerebrospinal fluid (CSF), non-motor attributes, and images, enhancing preclinical PD diagnosis. Likewise, (Glaab E et al., 2019) establish the value of merging blood sample data with PET images, enhancing the distinction between PD and healthy controls. (H. Hirschauer et al., 2015) propose an innovative methodology, utilizing neuro-pathological brain data alongside motor and non-motor symptom data within an enhanced probabilistic neural network. Impressively, this approach surpasses classical machine learning algorithms, yielding significantly higher accuracy than previous experiments. These endeavors collectively underscore the potential of multi-modal data fusion in advancing PD diagnosis and classification accuracy.

**2. Studies on Different Diagnoses of PD Using Machine-Learning Techniques –** Variability within Parkinson's disease (PD) necessitates distinct treatment approaches, prompting recent investigations. Leveraging Dopaminergic images, structural MRI, functional MRI, and diffusion tensor images, machine learning techniques like SVM and logistic regression effectively differentiated PD categories. However, the amalgamation of multi-modal features emerges as a promising avenue for classification. This approach is exemplified in recent studies, such as (Cherubini A and et al., 2014), who integrated DTI and voxel-based morphometry using support vector machines to distinguish PSP and PD patients. This experiment highlights the potential of automated pattern recognition for PSP and PD detection. Moreover, (Du G. and et al., 2017) demonstrated the utility of apparent transverse relaxation rate and DTI images as critical markers for PD differential identification. These findings collectively underscore the viability of multi-modal data fusion in enhancing PD variation differentiation.

**3. Experiments on the Initial Phase Identification of PD Using ML Techniques –** Numerous investigations have converged on the integration of image and clinical data to enhance initial PD diagnosis. (Long D. and et al., 2012) notably harnessed structural and resting-state functional magnetic resonance imaging (rsfMRI) data, extracting diverse characteristics encompassing ALFF, RFCs, ReHo, as well as cerebrospinal fluid (CSF), gray matter (GM), and white matter (WM). Employing a two-sample t-test in conjunction with a Support Vector Machine (SVM), they achieved an impressive 87% accuracy in early PD patient classification, surpassing the efficacy of single-source image data. Another study by (Oliveira et al., 2018) delved into SPECT imaging data, extracting seven features from each brain hemisphere and leveraging classical machine learning techniques. Strikingly, by combining all features, they attained a remarkable classification accuracy of 97%, outperforming previous studies that employed individual features. These collective investigations underscore the potential of multi-modal data integration in substantially enhancing early PD diagnosis and classification accuracy.

The preceding discussions reveal notable challenges. Clinical diagnosis data's error susceptibility warrants caution for PD patient classification. Consequently, unsupervised techniques are proposed to unveil data patterns, while handling image data encounters feature extraction limitations. Machine learning's

opaque nature conflicts with evidence-based medicine principles, emphasizing the need to identify disease-specific features. Over-fitting poses a significant concern, with models excelling in training but struggling in testing. Recent studies underscore the impact of excessive data heterogeneity on generalizability, even with a single source. Addressing this entails augmenting data quantity and rigorous validation to enhance model generalization a comprehensive, aware approach is pivotal for robust PD classification and understanding.

# 3 DATASETS

The two mutually exclusive or unpaired datasets chosen for this work are described below:

## 3.1 Gait in Parkinson's Disease

This dataset by PhysioNet (Goldberger and et al., 2000) includes multi-channel gait sensor data collected from 93 patients with PD (mean age: 66.3 years; 63% men), and 73 healthy controls (mean age: 66.3 years; 55% men). The dataset captures vertical ground force measurements as subjects walk normally for approximately 2 minutes on flat terrain. Eight sensors beneath each foot record force over time at a sampling frequency of 100 Hz. Additionally, demographic information, measure of disease severity and other related measures are also included.

## 3.2 Parkinson's Progression Markers Initiative (PPMI)

This dataset has been captured by in-person clinical assessments, covering people with a confirmed diagnosis of PD, people who exhibit PD risk factors but have not yet been diagnosed with PD, and healthy controls. This repository contains data from more than 1500 participants of which, 423 participants exhibit PD and 196 are healthy individuals. The clinical data collection spanned 12 visits including clinical motor assessment at three-month intervals during first year, transitioning to six-month intervals thereafter. Behavioral and cognitive diagnoses are conducted annually for all participants. 24-month visits for SWEDD participants, and baseline recordings for healthy controls. Blood sample collection followed a scheduled three-month interval during the first year, then transitions to six-month intervals. Fourth, Cerebrospinal fluid (CSF) data are collected at 6-month and 12-month intervals. And lastly, Urine testing was administered at 12-month intervals for all participants. As some of this information is available only for a subset of the participant population, we used data from initial visit along with visits 2, 4, 6, 8, 10 and 12 for our analysis. This generated a pool of 476 subjects with data in all these visits.

# 4 METHODOLOGY

Given the constraints of mutually exclusive datasets, our primary focus lies on expanding our sample size to facilitate effective training of our proposed model. The following section provides a detailed view of the techniques employed for generating supplementary data samples from our available dataset. This is followed by an in-depth elucidation of our proposed framework.

## 4.1 Data Generation and Pre-Processing

This section is structured to enhance clarity by delineating two pivotal steps which is also described in Figure 1. We commence by streamlining gait sensor data, simplifying its format for seamless integration with PPMI data.

**Data Separation Step –** Initially, we apply seven fundamental statistical techniques to each sensor data column, including Minimum, Maximum, Mean, Median, Standard Deviation, Skewness, and Kurtosis. Subsequently, we consolidate the complete time series data for each subject into a unified row, resulting in 126 features (each attribute is transformed into seven additional columns). In the case of the PPMI dataset, we encompass data from seven visits, including the baseline, capturing motor and non-motor symptoms, thereby yielding a cumulative total of 1595 features. As detailed in the dataset description, gait data comprises records from 93 PD patients and 73 HC patients, while the PPMI dataset encompasses 294 PD patient records and 154 HC patient records. Before amalgamation, data from both sources are stratified based on class distribution.

**Cross-Merging Step –** The generation of the merged dataset is accomplished through a cross-merging operation involving corresponding class data from both datasets. More precisely, it combines the features of a single sample from the gait dataset with the features of a corresponding sample from the PPMI dataset, both belonging to the same class. For model training, 50% of the merged data is used and

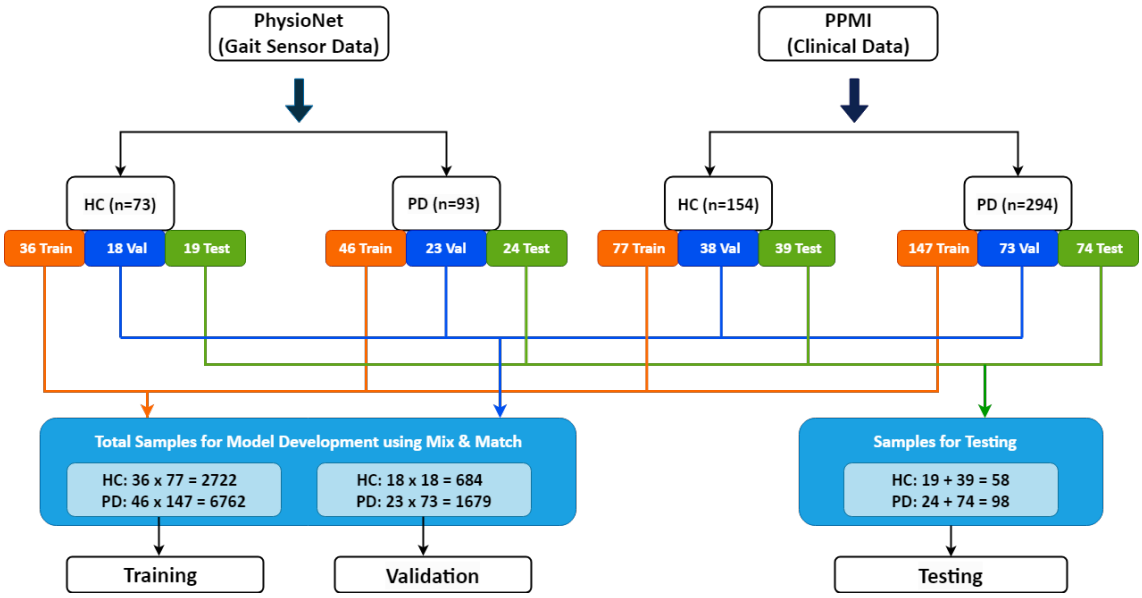


Figure 1: Data Generation Diagram. Each cohort is separated into two classes (mainly Parkinson's Disease (PD) and Healthy Control (HC)) and each class data of each cohort has been divided into 50%, 25% and 25% for the use of training, validation and test. The orange line depicts the training data flow, whereas the blue and green data flows are for validation and test. The first blue-colored block is responsible for generating data for model development whereas the second one is for generalization. Same colored block data coming for training or validation are crossed between same class (Exp: Orange colored cohort 1 HC data is crossed with orange colored cohort 2 HC date and same for PD data also.) This process has been repeated for blue colored types of data.

the remaining 50% is equally assigned to validation and testing. As a result of these post-splitting and cross-merging operations, the dataset comprises 9484 records for training, 2363 for validation, and 2517 for testing, encompassing a total of 1721 features.

## 4.2 Proposed Mutually-Exclusive, Multi-Modal Framework

Multi-modal analysis helps improve the accuracy of machine learning algorithms by leveraging the complementarity of heterogeneous data. However, acquiring all modalities for all samples might not only be expensive but also practically infeasible in some conditions. Consequently, we propose an unpaired multi-modal learning strategy that learns to extract benefits from mutually exclusive modalities. Our proposed two-stage process along with training and inference mechanisms are described below.

**Individual Modality Networks.** In stage one, we used simple multi-layer perceptrons (MLPs) or fully connected networks (four layers) for Parkinson's disease prediction using individual modalities of gait and clinical data. Each of the individual networks were trained and optimized for best PD classification accuracy with one modality using categorical cross-entropy. Once trained, the weights of these networks were frozen and the output or features extracted from the penultimate layer is considered as the latent space representation of corresponding modalities.

**Multi-Modal Network.** In stage two, the feature vectors encompassing the distinct attributes of gait and clinical data modalities are concatenated and used as input to train a multi-modal network. While we use similar architecture with four fully connected layers, we utilize it in a siamese network with Triplet loss function. As siamese networks are designed to compare pairs of feature embeddings rather than make a prediction, they are suitable for small datasets. Furthermore, the Triplet loss function helps the model to recognize the similarity or differences between classes.

**Triplet Loss.** The objective of the triplet loss function is to learn from the distributed representation of data points in a high-dimensional vector space. It ensures that similar data points are projected closer together, while dissimilar ones are pushed farther apart. The loss function is defined as:

$$\mathcal{L} = max(d(a,p) - d(a,n) + margin, 0)$$

where '$a$' represents the *anchor* sample, '$p$' and '$n$' denote the *positive* and *negative* samples respectively.

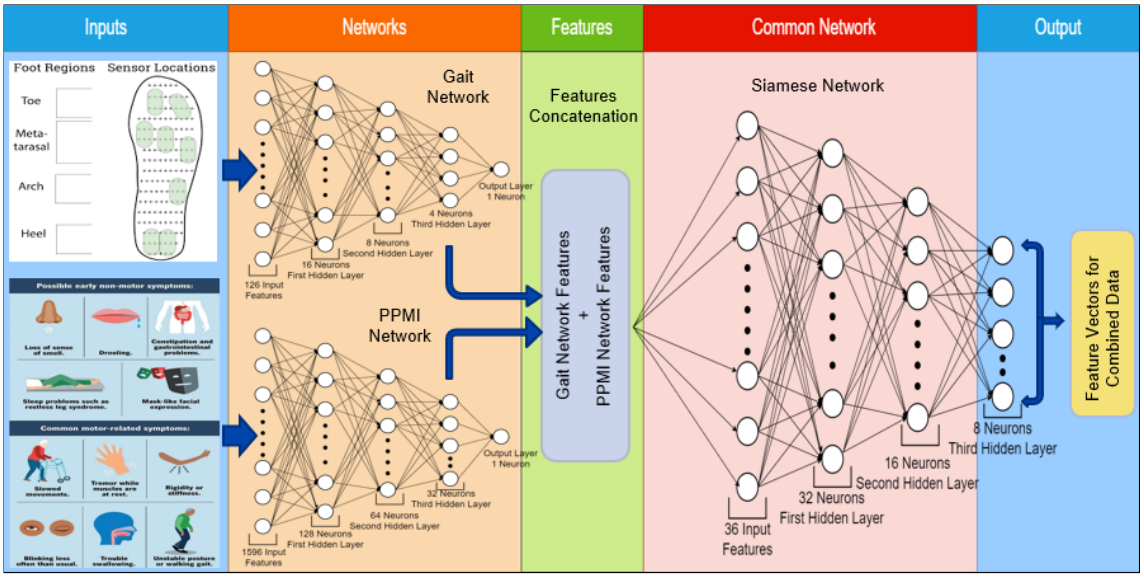


Figure 2: Siamese Network Architecture. Complete pipeline to generate embedding using combination of gait and PPMI data. The input block is used for send the data to baseline models. Network section contains two previously used baseline networks (Gait and PPMI Network) which will take gait and PPMI data individually and will generate feature matrices (Blue arrow in between network and features section the diagram) corresponding to each data. In features section, these two feature matrices are combined into single matrix. The common network section (Siamese Network) takes the combined feature matrix as input and generates embedding output in the output section.

Notably, the similarity between "$a$" and "$p$" should exceed that between "$a$" and "$n$." An additional hyper-parameter termed "margin" is integrated into the loss function. This parameter dictates the degree of dissimilarity required, aiding in the efficient discrimination of distinct samples.

Consequently, we compute gradients, which in turn facilitate the adjustment of biases and weights within the siamese network. Throughout the training phase, we gather an anchor sample along with random positive and negative samples to compute loss and update the network's gradients.

**Training Multi-Modality Network.** As the two datasets are mutually exclusive, there is no paired data to train the multi-modal network. We address this difficulty by pairing each sample of a particular class in one dataset with every sample of the same class in the other dataset. For instance, $s_1$ samples of PD in gait dataset and $s_2$ samples of PD in PPMI dataset generates a total of $s_1 \times s_2$ PD samples for training the multi-modal network. This approach not only captures the variance in the modalities but also provides implicit data augmentation. Such pairing is repeated for samples of all classes and given the same label.

At each training step, triplets are composed by first randomly selecting a sample to represent the anchor. Next, another sample from the same class is randomly chosen as the positive sample and a sample from different class is randomly chosen to be the negative sample. All the samples are first processed using individual modality networks to extract modality specific features. Features extracted for each sample are concatenated to create input feature vectors to the siamese network. The network operates by independently processing the anchor, positive, and negative losses, generating distinct embedding vectors for each sample. Employing the triplet loss function, the model computes the Euclidean distance between the anchor and positive embedding, as well as between the anchor and negative embedding. These computations facilitate the update of gradients within the siamese network, thereby refining the network's performance.

**Proposed Inference Technique.** Conventional inference approaches are unsuitable due to the absence of a modality. Therefore, we propose a novel method for predicting the label of a test instance, employing a combination of the max-voting approach and mix-and-match pairing. During inference, we utilize triplets of *anchor, positive, negative*.

*Anchor*: We first generate a test sample in the required format for inference by combining a gait test sample with five positive and five negative instances from the PPMI training dataset. This process yields ten anchor instances and removes the missing modality issue.

*Positive and Negative*: Each anchor instance is then paired with one PD and one HC instance from the out-

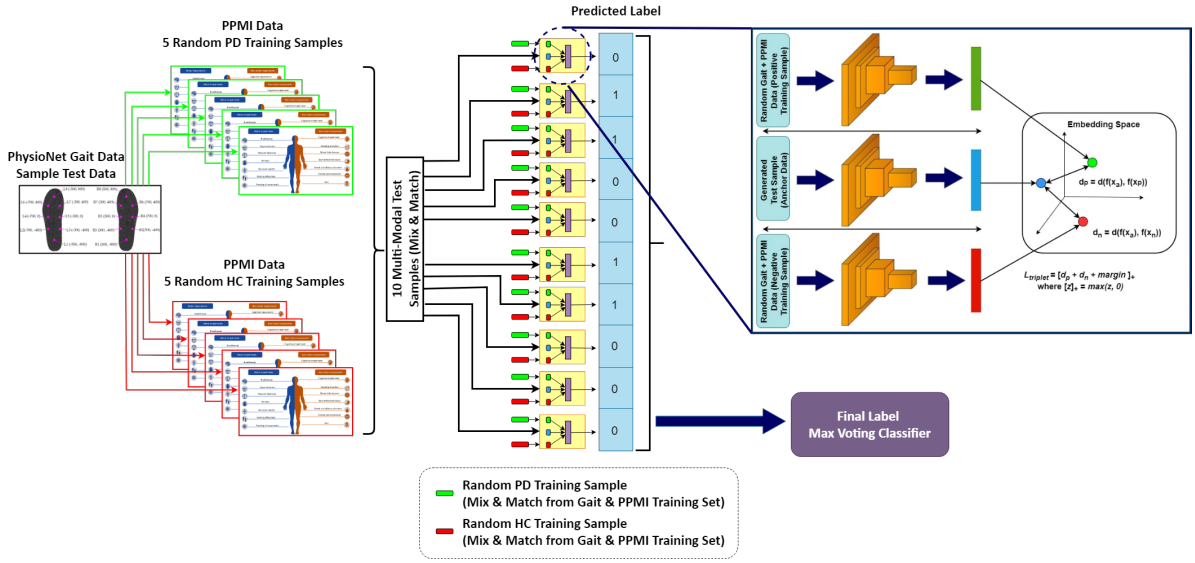


Figure 3: Model Inference Flow Diagram. The approach in the figure explains the classification of gait test sample. Gait test sample is combined with 5 random positive (PD) and 5 random negative (HC) samples of PPMI data from training set. The curated samples are then used as an input to proposed multi-model. The output will be aggregated using max voting technique and compared with the actual class label to measure accuracy.

Table 1: Performance comparison of Single modal vs. Multi-modal approach (Higher is better).

| Model | Dataset | Accuracy (%) | Precision | | Recall | | F1-Score | | Kappa | AUC |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | HC | PD | HC | PD | HC | PD | | |
| Single-Modality | Gait | 83.33 | 1.00 | 0.77 | 0.61 | 1.00 | 0.76 | 0.87 | 0.64 | 0.81 |
| | PPMI | 92.03 | 0.81 | 1.00 | 1.00 | 0.88 | 0.90 | 0.94 | 0.83 | 0.94 |
| Multi-Modality | Gait | 99.20 | 1.00 | 0.98 | 0.97 | 1.00 | 0.97 | 0.98 | 0.98 | 0.97 |
| | PPMI | 99.12 | 1.00 | 0.99 | 0.97 | 1.00 | 0.99 | 0.99 | 0.98 | 0.97 |



put of the cross-merging step, serving as positive and negative samples, respectively. The generated triplet is then inputted into the triplet loss, predicting one of the two classes (PD/HC). Applying a max-voting strategy allows us to determine the final prediction. Figure 3 illustrates the operation of the proposed inference method.

## 5 RESULT

The multi-modality approach generally outperforms single-modality for classification, but it hasn't been much explored for Parkinson's disease tasks. In single-modality, we individually trained the gait network and PPMI network (Figure 2) using separate datasets. Our proposed multi-modality framework (Figure 2) combines features from both models, gait and PPMI, along with the inference technique described in Section 4.2. In our experiments, we evaluated both single-modality and multi-modality on the test set using various performance metrics such as accuracy, precision, recall, F1-score, Kappa, and AUC. Table 1 shows that the multi-modality approach achieves $\approx$ 13% higher average accuracy compared to its single-modality counterpart, also significant improvement in other metrics like precision and recall affirms the correctness and reduction in false negatives which is essential in healthcare domain, making it preferable for classification tasks. Similar trends of multi-modal superiority over single-modality are observed in other performance metrics as well.

**Comparison with SOTA Methods –** To further analyze the effectiveness of our proposed method, we compared it with various methods in the literature using both the gait and PPMI datasets. Our goal is to assess the method's ability to classify data without specific modalities. Table 2 and Table 3 describe the comparisons for the PPMI and gait datasets, respectively. In Table 2 for the PPMI dataset, our method significantly outperforms established accuracy benchmarks, as well as other performance measures such as AUC, Kappa Score, sensitivity, and specificity. For gait dataset in Table 3, recent studies have achieved accuracy levels exceeding 99%, leaving limited room

Table 2: Performance comparison of the proposed approach with SOTA on PPMI dataset. (Higher is better).

| Studies | Model | Accuracy (%) | Sensitivity (%) | Specificity (%) | AUC | Kappa |
|---|---|---|---|---|---|---|
| (Prashanth et al., 2016) | Support Vector Machine (SVM) [non-motor, CSF and imaging markers] | 96.40 | 97.03 | 95.01 | 0.98 | NA |
| (Leger C, 2020) | Generalised Additive Model (GAM) [Baseline Evaluation with non-motor clinical and biomarker features] | 89.80 | 92.30 | 85 | 0.94 | 0.77 |
| (MS Hema and et al., 2023) | Random Forest [Motor, Non-Motor, Mental Health, Semantic Features] | 94.50 | 93.40 | 89.20 | 0.97 | NA |
| Ours | Multi-Modal Siamese Network (motor and non-motor) | $99.12 \pm 0.62$ | $99 \pm 0.007$ | $97.43 \pm 0.02$ | $0.97 \pm 0.01$ | $0.98 \pm 0.014$ |

Table 3: Performance comparison of the proposed approach with SOTA on gait dataset. (Higher is better).

| Studies | Model | Accuracy (%) | Sensitivity (%) | Specificity (%) | F1 Score |
|---|---|---|---|---|---|
| (Zeng W and et al., 2016) | Radial Basis Function (RBF) Neural Networks | 98.8 | 98.92 | 98.63 | NR |
| (Acici K and et al., 2017) | Random Forests | 98 | 99.1 | 95.7 | 0.98 |
| (Asuroglu T and et al., 2018) | Locally Weighted Random Forest (LWRF) | 99 | 97.8 | 99.5 | NR |
| (Zhao et al., 2018) | Long Short-Term Memory (LSTM) and Convolutional Neural Network (CNN) | 98.61 | NR | NR | NR |
| (Veeraragavan S and SA., 2020) | Artificial Neural Network (ANN) | 97.7 | 97.05 | 97.41 | 0.97 |
| (Xia Yand Yao Z and N., 2020) | Long Short-Term Memory (LSTM) and Convolutional Neural Network (CNN) | 99.07 | 99.1 | 99.01 | NR |
| (Priya SJ and N., 2020) | Logistic Regression | 98.82 | NR | NR | NR |
| (Ghaderyan and Fathi, 2021) | Sparse NNLS coding Method | 97.22 | 98.22 | 95.86 | NR |
| (Liu et al., 2021) | Long Short-Term Memory (LSTM) and Convolutional Neural Network (CNN) | 99.22 | 98.04 | 100 | 0.99 |
| (Tong J and S., 2021) | Support Vector Machine (SVM) | 99.23 | NR | NR | NR |
| Ours | Multi-Modal Siamese Network | $99.20 \pm 1.13$ | $98.20 \pm 0.01$ | $99 \pm 0.02$ | $0.99 \pm 0.01$ |

for further improvement. Nonetheless, our method demonstrates similar accuracy performance. When comparing other metrics such as sensitivity, specificity, and f1-score, we gain a deeper and more comprehensive understanding of the model's actual performance. Our method also shows improvement across the majority of metrics when compared to other approaches in the literature.

## 6 CONCLUSION

We proposed a novel technique that uses mutually exclusive multi-modality training and inference approaches for classifying Parkinson's disease (PD) in scenarios with missing modalities. Our method involves fusing features from a multi-modal network into a combined feature vector, pairing reference modality samples with positive and negative samples from other modalities during inference, and using a voting scheme for final classification. Comparing our multi-modal approach to a single-modality approach, we observed significant performance improvements. Our method also outperformed existing approaches on both PPMI and gait datasets. This research has broader implications for addressing other disease detection scenarios with missing modalities, enhancing prediction precision, and reducing the need for exhaustive datasets.

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