PDMove: Towards Passive Medication Adherence Monitoring of Parkinson's Disease Using Smartphone-based Gait Assessment

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The medicine adherence in Parkinson's disease (PD) treatment has attracted tremendous attention due to the critical consequences it can lead to otherwise. As a result, clinics need to ensure that the medicine intake is performed on time. Existing approaches, such as self-report, family reminder, and pill counts, heavily rely on the patients themselves to log the medicine intake (hereafter, patient involvement). Unfortunately, PD patients usually suffer from impaired cognition or memory loss, which leads to the so-called medication non-adherence, including missed doses, extra doses, and mistimed doses. These instances can nullify the treatment or even harm the patients. In this paper, we present *PDMove*, a smartphone-based passive sensing system to facilitate medication adherence monitoring without the need for patient involvement. Specifically, *PDMove* builds on the fact that PD patients will present gait abnormality if they do not follow medication treatment. To begin with, *PDMove* passively collects gait data while putting the smartphone in the pocket. Afterward, the gait preprocessor helps extract gait cycle containing the Parkinsonism-related biomarkers. Finally, the medicine intake detector consisting of a multi-view convolutional neural network predicts the medicine intake. In this way, *PDMove* enables the medication adherence monitoring. To evaluate *PDMove*, we enroll 247 participants with PD and collect more than 100,000 gait cycle samples. Our results show that smartphone-based gait assessment is a feasible approach to the AI-care strategy to monitor the medication adherence of PD patients.

CCS Concepts: • **Human-centered computing** → *Ubiquitous and mobile devices*;

Additional Key Words and Phrases: Mobile Health, Parkinson's Disease, Medication Adherence Monitoring, Gait Analysis.

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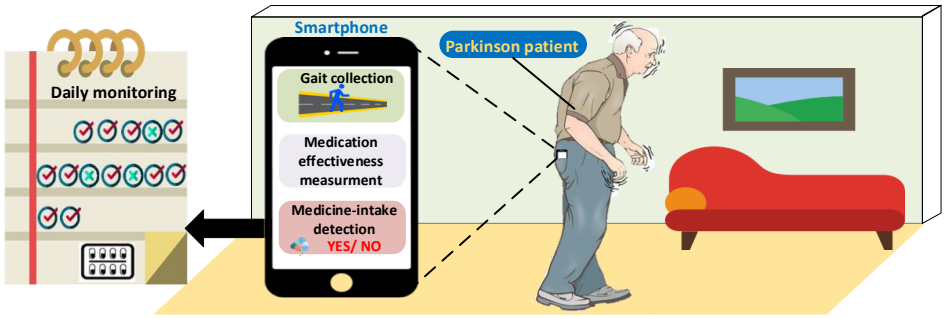

Fig. 1. **PDMove can continuously collect and analyze the gait of PD patients in a passive and non-disturbing manner to achieve medication adherence monitoring in daily life.**

1 INTRODUCTION

The diagnosis of Parkinson's disease (PD) initiates a long and periodic therapeutic exchange between the patient and physician. Once the treatment begins, the patients anticipate systematic improvement while physicians expect medication adherence. A dedicated medication adherence allows the physicians to accurately adjust the treatment based on the patient's clinical response. In contrast, non-adherence due to missed, mistimed or extra doses leads to increase in parkinsonism, *e.g.,* motor fluctuations. Several studies from NIH show that more than 40% of PD patients in the U.S., however, do not adhere to their assigned medication. This non-adherence in PD leads to significantly higher mean of yearly hospitalizations (2.3 vs. 1.8), office visits, and ancillary care visits [1]. Furthermore, non-adherence is associated with higher medical costs ($15,826 vs. $9,228 per subject per annum) despite lower prescription medicine costs [2], which can ultimately prevent the patients from affording proper medical treatment.

In real practice, achieving a high medication adherence among PD patients is a challenging task. Firstly, disease progressing is one relevant factor. In the early stage, patients are diligent in taking prescribed drugs 3∼4 times per day. However, as the treatment progresses, they are required to take drugs 6∼10 times per day. Greater regimen complexity is observed to profoundly impair medication adherence, which drops sharply with each incremental dose in daily life [3, 4]. Secondly, as a non-motor PD symptom, depression is considered as a significant risk factor for medication adherence. The non-adherence aggravates depression while depression fuels non-adherence [5]. Lastly, cognitive impairment, *e.g.,* dementia, affects at least 40% of PD patients [6]. Dementia impairs the patient's working memory and executive function, resulting in missed dose or overdosage in daily life [7, 8]. To summarize, the non-adherence caused by PD symptoms presents a knowledge gap between patients and physicians, *i.e.,* patients cannot recall or validate the medicine intake events due to which physicians cannot proactively suggest improvements in the treatment process.

A practical approach to facilitate medicine intake detection would serve as the first milestone for improving medication adherence. Existing methods in the clinical domain are primarily based on self-management strategy [9]. Considering most of the PD treatment happens outside the clinics, PD patients are encouraged to put effort into remembering their medicine intake periods. However, these self-management strategies do not possess specific measures to validate the intake events or improvement in adherence other than relying on the patient's verdict. Solutions offering timely reminders (*e.g.,* third-party phone call or alarm [10]) are inadequate for PD patients suffering from cognitive impairment [11], who are more likely to suffer from mistimed or severe overdosage. This raises a question. Once the physicians have assigned a drug schedule to the patients, how can they verify the day-to-day occurrences of medicine intake events?

We envision a novel AI-care strategy which can assist in the PD treatment by taking advantage of mobile technologies. The AI-care strategy relieves the daily burden from PD patients of remembering all medicine intake events. Specifically, it leverages a commercial off-the-shelf smartphone to monitor medication adherence without the user's awareness. The periods and frequency of intake activities are compared against the drug schedule assigned by the physicians to determine the mistimed, missed and extra doses. Afterward, the results from medicine intake detection, along with the medication effectiveness measurement, are transferred to the clinics automatically. In summary, we believe a practical solution should own three properties:

- **Continuous Monitoring**: PD is a chronic disease and most of the treatment happens outside the clinics. Therefore, continuous monitoring of medication adherence will allow the analysis of extended trends of patient's clinical response.
- **Passive Sensing**: Considering PD treatment is a long-term process, it would be ideal to passively assess the daily-life medicine intake without user participation or external supervision.
- **Non-adherence Alerting**: To be practical in real-world setups, the proposed solution should detect and remind the users any occurrence of non-adherence, including missed, mistimed, and extra doses.

Given the fact that gait impairments are among the most common PD symptoms and actively respond to medication, we aim to detect daily-life gait variability caused by medicine to achieve medication adherence monitoring. For evaluating the gait metrics, instead of asking the user to perform a test (*e.g.*, Timed Up and Go Test [12]), we hypothesize that gait variability can be effortlessly acquired by putting the smartphone in user's pocket, a common behavior in daily life. Considering that pocket is not the most sensitive body part to gait abnormality in comparison with other regions (*e.g.*, ankle, hip and low back [13]), we propose a deep learning-based method to automatically extract the features from raw data. These features vary from common-sense features (*e.g.*, speed and step length) and are highly correlated to PD symptoms. To validate the hypothesis, we design and implement *PDMove*, a smartphone-based passive sensing system for medication adherence monitoring as shown in Fig. 1. It comprises a smartphone end and a cloud-server end. At the smartphone end, *PDMove* leverages the built-in sensors, *i.e.,* accelerometer and gyroscope, to collect the gait and transmit the raw data to the cloud-server for further analysis. At the cloud-server end, the gait analyzer module first achieves the gait cycle segmentation and spectrogram representation in order to augment features in both the time domain and frequency domain. Afterward, the medication adherence detector consisting of a multi-view convolutional neural network facilitates medicine-intake detection. Finally, the cloud-server feedbacks the detection results to the user.

We collaborate with medical centers and enroll sufficient PD patients to evaluate *PDMove* in real life. Specifically, we develop an iOS application on the smartphone to collect raw gait data. We instruct the user to place the smartphone in the pocket and go strait some 20 steps before and after taking medication for PD treatment. Through a 3-month experiment, we totally enroll 247 PD patients (154 males and 93 females) and collect more than 100,000 samples of gait cycle. Results show that we can achieve a median accuracy of 83.4% and an average accuracy of 77.6%. We further validate the cross-patient generalizability of *PDMove* against three demographic factors (*i.e.,* age, gender and phone type) and two medical criteria (*i.e.,* severity and surgery) to demonstrate that *PDMove* is practical and can be applied in real-world scenarios without any additional components or design modifications. Our findings can drive future research on improving medication adherence in not only PD patients but across clinical domain.

We conclude our contributions as follows:

- To the best of our knowledge, we perform the first study to identify that medication-caused gait variability is an effective indicator of medicine intake events among the PD patients. We assess the gait patterns of PD patients before and after taking medication through the on-board sensors of the commercial off-the-shelf smartphone. The acquired gait patterns also provide valuable insights into medication effectiveness which can aid the physicians in designing future treatment routines.

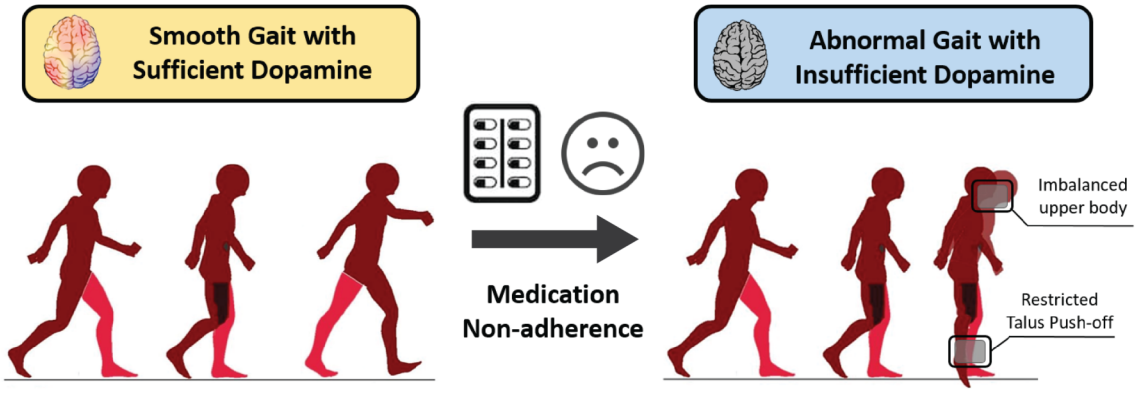

Fig. 2. **Medicine non-adherence introduces the gait variability of PD patients in daily life.**

- We design and implement *PDMove*, a passive-sensing system for continuous monitoring of medication adherence. We hypothesize that the gait variability of a PD patient can be effortlessly acquired in daily routine, such as placing the smartphone inside the pocket. To validate the hypothesis, we design and implement a deep neural network based approach, which automatically extracts high-level features that are highly correlated to gait variability, and can eventually predict whether the PD patient receives the medication care regularly. Thus, we can infer the medicine intake activity and notify the patient if necessary.
- We evaluate our proposed *PDMove* on a dataset collected from a daily-life scenario. Our results reveal that difference presented in gait before and after taking medication is an effective biomarker to detect medicine intake. This discovery paves the way for a new approach to PD medication adherence monitoring in daily life. Our system also paves the way for passive sensing in other related healthcare areas.

2 BACKGROUND

2.1 Gait Analysis: Definitions and Methods

Gait describes a particular manner of walking. Every person has his or her way of walking. Factors, such as aging, injuries, and chronic disease, can result in a slightly different walking styles, either permanent or temporary. For example, elders usually have a reduced range of hip motion at faster walking speeds and 5 degrees less hip extension than in their younger age. Gait analysis is a method for assessing biomechanical abnormalities in a gait cycle, which is usually defined as a period of movements, during which one-foot contacts the ground twice. One gait cycle consists of two phases *i.e.,* the stance phase and swing phase. The stance phase is a period when the foot contacts with the ground, and the swing phase is a period when the foot is not in contact with the ground. The stance phase can be further divided into several stages. It starts when the heel strikes and finishes when the foot toe leaves the ground. The stance phase is usually longer than the swing phase.

The approaches of gait analysis can be classified into three categories [14]. (1) *Vision sensor based*: In vision based approaches, gait data is collected by cameras. Then, some computer vision based algorithms, such as background segmentation, are adopted to extract the skeleton information. (2) *Floor sensor based*: In the floor sensor based approach, the sensors are placed along the floor (*e.g.,* on a mat) where gait data is measured when people walk across. (3) *Wearable sensor based*: In the wearable sensor based approach, people attach the sensors (*e.g.,* accelerometer and gyroscope) in different body positions for collecting gait information, such as waist, pockets, shoes and so forth. Our system belongs to the wearable sensor based approach. We utilize the smartphone to collect gait by putting it in the pocket.

2.2 PD-induced Gait Impairment

As a chronic disease caused by unclear reasons, PD affects the way a person walks. In the beginning, PD causes death of neurons in the substantia nigra areas. These neurons are responsible for producing dopamine, a chemical messenger transmitting signals from the substantia nigra to other parts of the brain. After the dopamine gets reduced, the signals controlling the movements cannot be fully carried to proper body regions. As a result, gait abnormality occurs.

The gait abnormality can be further divided into three phenotypes: (1) *Freezing of gait*: Freezing of gait (FOG) is considered as one of the most disabling motor symptoms in PD patients. It is characterized by a reduction of forwarding movement, or difficulties when initiating walking [15]. PD Patients report that they have difficulty in initiating muscle movements, when they either start walking or slow down. When the disease progresses, FOG can even lead to a fall and a loss of independence. (2) *Shuffling gait*: Clinical medicine defines shuffling gait as if a person is dragging his feet while walking. Specifically, the stride (step length) is short and the arm movement gets reduced. (3) *Festinating gait*: Festinating gait is defined if a PD patient owns a quick but short stride. Festinating gait is also called as Parkinsonian gait, which is the most commonly observed gait symptom in PD.

Clinical medicine nowadays leverages performance-based tests to observe and quantify different aspects of gait. These tests evolve from Unified Parkinson's Disease Rating Scale (UPDRS) [16], a standard clinical diagnosis for Parkinson's disease. For example, Timed Up and Go Test [12] can measure the functional mobility to provide information on transitions, gait metrics (*e.g.*, speed and stride length), and risk of falling. Levodopa and other antiparkinsonian drugs (*e.g.,* dopamine agonists and inhibitors of dopamine metabolism) are employed for alleviating PD symptoms. However, gait abnormality can occur when missed or mistimed dose happens (see Fig. 2). Given the fact that medication relieves gait symptoms and the non-adherence of medication induces gait abnormality, we are motivated to monitor such daily-life gait variability to achieve the detection of medicine intake.

3 PDMOVE

In this section, we present an overview of *PDMove*, including the application scenario and system diagram (see Fig. 3).

3.1 Application Scenario

PDMove builds on the fact that Parkinsonism gait abnormality responds to the medication. It works by putting a smartphone in the pocket with no special requirements, a universal behavior existing in our daily routine. A smartphone can continuously sense the gait information, and the active participation of the users is not required. In this way, *PDMove* enables passive sensing. The system consists of a smartphone end and a cloud-server end, where the smartphone collects and transmits the raw gait data to the cloud server, and the cloud-server is then responsible for analyzing the data and feeding back the results to the smartphone. Based on a drug schedule assigned by the healthcare provider, the smartphone reminds the user to take medicine or informs the next medication time. Through this method, *PDMove* helps the patients to avoid the missed, mistimed, or extra doses.

3.2 PDMove System Overview

Gait Collector: Data collection are conducted in a nonclinical daily-life environment (*e.g.,* at home or office). Our system utilizes the built-in inertial sensors (*i.e.,* accelerometer and gyroscope) of a smartphone to collect gait information which responses to medicine medication for PD patients. The detailed descriptions of the data collection are provided in Section 6.

Gait Preprocessor: We implement a gait preprocessor including the module of gait cycle segmentation and gait representation. To begin with, we are responsible for dealing with the raw data by removing the irrelevant

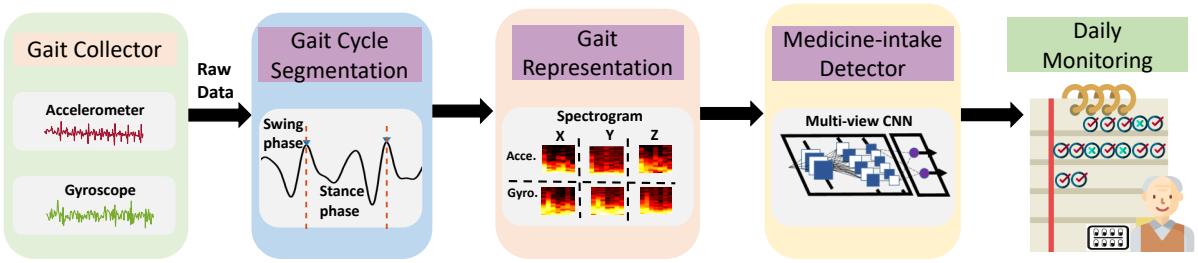

Fig. 3. **Our proposed *PDMove* framework consists of the smartphone end and the cloud-server end. In the former end, we passively collect the gait pattern in the user's daily activities. In the latter end, we develop a specialized deep-learning network to predict the medicine intake activity and notify the user if he/she doesn't follow the clinic's treatment properly.**

part and segmenting the data with a gait cycle. Then, spectrogram representation is adopted for two reasons. (1) Spectrogram helps augment the features in the frequency domain as well as in the time domain. (2) Spectrogram transforms the temporal data into the figure, which fits the input architecture of the following deep neural network.

Medicine Intake Detector: We implement a medicine intake detector to achieve the monitoring of medication adherence. To begin with, a concatenation layer is responsible for data fusion from different sensors. Afterward, a residual network consisting of convolutional layers and fully-connected layers achieves the medicine intake detection.

4 GAIT PREPROCESSOR

In this section, we introduce the design and implementation of the gait preprocessor, including gait cycle segmentation and gait representation.

4.1 Inertial Sensors in a Smartphone

Accelerometer and gyroscope are two types of built-in inertial sensors measuring the inertial dynamics in three directions, namely the X, Y and Z axis.

Accelerometer: The three-axis accelerometer is built on the basic principle of acceleration, and is used to measure the orientation of a smartphone's acceleration (including the gravity) related to the surface of the Earth. The accelerometer can gauge the orientation of a stationary item with respect to Earth's surface. In our study, the three-axis accelerometer measures the change of smartphone's linear velocity, and thereby reflects the movement of the PD patients.

Gyroscope: Although the accelerometer gauges the acceleration along with a particular direction, it provides little lateral orientation information with only the reference of gravity direction. Instead, the built-in three-axis gyroscope senses the angular velocity alone with one direction in the three-dimensional space. In our study, a PD patient generates both accelerations and rotations in different directions while walking. Correspondingly, gyroscope combined with accelerometer together provides us a powerful array of gait information.

4.2 Gait Cycle Segmentation

After collecting the gait data with built-in accelerometer and gyroscope, we are motivated to extract helpful information, *i.e.*, gait cycle, for further analysis. The reasons are two folds. First, the walking pattern of a human presents rhythmic, and an entire gait cycle contains all the helpful information (*i.e.,* the swing phase and the

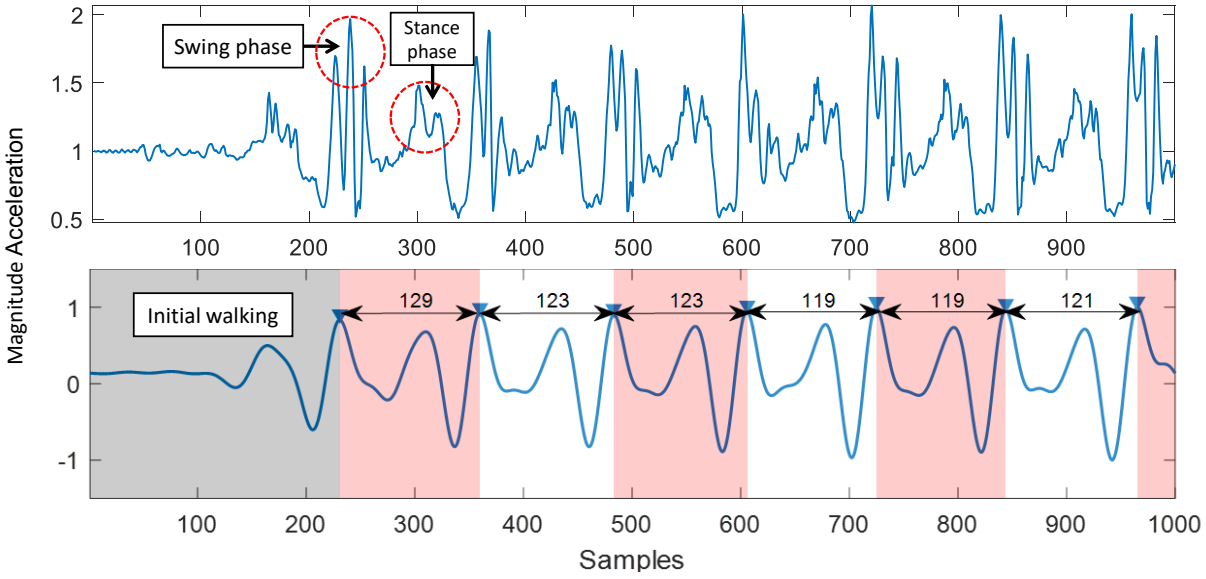

Fig. 4. **Top Figure: An example of magnitude acceleration. The gait curve presents a rhythmic pattern during walking. The swing phase achieves a higher acceleration than the stance phase. Bottom Figure: The proposed zero-phase FIR filter removes the high-frequency components. Red and white shades mark gait cycles.**

stance phase) we need. Second, the gait length is different from person to person and is varied even for the same subject in one day. Therefore, the gait cycle segmentation rather than blind segmentation presents the gait features better.

Before we introduce our solution, we first define a complete gait cycle as a time interval, which begins at the heel strike of one foot and continues until the heal strike of the same foot again. Without loss of generality, we adopt the data from the built-in accelerometer as a basis for gait cycle segmentation.

Calculation of Magnitude Acceleration: As a smartphone shows random postures when the user puts it in the pocket, neither axis can stably reflect the periodic pattern of the gait. Therefore, the first step is to calculate the magnitude signal to remove the orientation-related noise. Assuming that A_x, A_y, and A_z are values collected by a three-axis accelerometer, the magnitude signal A_0 can be calculated by:

$$A_0 = \sqrt{A_x^2 + A_y^2 + A_z^2}. \tag{1}$$

Fig. 4 shows the magnitude signal describing the acceleration of the smartphone in the pocket while walking. We can observe that the smartphone collects the rhythmic pattern. Along with the X-axis, the swing phase achieves a higher acceleration than the stance phase.

Removal of Motion Artifacts: To extract an entire gait cycle, our solution is to locate the local maximum in each cycle, which is the swing phase showing the highest acceleration. However, motion artifact can induce high-frequency burrs contained in the raw curve, which affects the precise segmentation (see Fig. 4). To address this problem, we filter out the high-frequency components. Traditional filters can induce phase distortion, which can bring bias in the phase of gait cycle segmentation. Therefore, we design and implement a zero-phase filter to eliminate this phase distortion [17]. To achieve a zero phase, we require that the frequency response of a filter should be a real function. According to the theory of Fourier transform, the frequency response of a filter is real

if its impulse response $h(n)$ is even. That is, it satisfies

$$h(n) = h(-n),\ n \in \mathbf{Z}. \tag{2}$$

Then, its frequency response can be presented as:

$$H(e^{j\omega t}) = \sum_{n=-\infty}^{\infty} h(n)cos(\omega nT) - j \sum_{n=-\infty}^{\infty} h(n)sin(\omega nT). \tag{3}$$

As the h is even and the *sine* function is odd, the sum over the second term is zero. Thereby, we have

$$H(e^{j\omega t}) = \sum_{n=-\infty}^{\infty} h(n)cos(\omega nT). \tag{4}$$

To construct an even sequence, the zero-phase filter leverages the information before and after the current gait signal point by prepending it the reflected piece of the signal onto the input, and carefully chooses the initial value.

Table 1. The List of FIR Filter Parameters in PDMove.

Name	Description
Filter Type	Band Pass
Filter Order	139
Stopband Frequency 1	0.5 Hz
Passband Frequency 1	0.75 Hz
Stopband Frequency 2	3 Hz
Passband Frequency 2	4 Hz
Design Method	Least Square
Sample Rate	100

Table 1 presents the detailed parameters while implementing the $h(n)$. Considering the average preferred walking speed is 1.4 m/s [18], we implement a bandpass filter with a passband from 0.75 Hz to 2.25 Hz to eliminate motion artifacts which are unrelated to gait cycles. We specifically choose the filter type of finite impulse response (FIR). Compared with infinite impulse response (IIR) filter, FIR can achieve faster transition attenuation by simply increasing the filter orders while keeping stability.

Algorithm 1 Gait Cycle Segmentation

Input: A_x, A_y, A_z ▷ Collected Accelerometer Data
Output: $\mathbb{H} = \{H_i | i = 1, \cdots, N\}$
1: **for** $i = 1 \rightarrow S$ **do**:
2: $A_0^{(j)} \leftarrow ComputMag(A_x^{(j)}, A_y^{(j)}, A_z^{(j)})$ ▷ Magnitude Acceleration to Remove Orientation Information
3: $A_0^{(j)} \leftarrow FiltFilt(A_0^{(j)})$ ▷ Filter Doubly to Remove High-Frequency Components
4: $\mathbb{H} \leftarrow PeakFind(A_0^{(j)}, \lambda)$ ▷ Segmentation Coordinates Calculation
5: **end for**
6: **return** $\mathbb{H}$;

Extraction of Gait Cycles: After removing the high-frequency burrs in the raw amplitude signal, the next step is to extract an entire cycle. For this purpose, our solution is to find each maximum local prominence in the filtered signal curve. Since the amplitude value of acceleration data can be different from person to person, we normalize the amplitude signal to a range of $[-1, 1]$ to eliminate the inter-person interference. Then, peak detection is adopted to get the coordinates for segmentation.
Algorithm 1 describes the procedure of gait cycle segmentation. $\mathbb{H} = \{H_i | i = 1, \cdots, N\}$ is a set containing the coordinates of gait segmentation. Segmentation is performed on each dimension of the raw data collected by accelerometer (*i.e.*, A_x, A_y, *and* A_z) and gyroscope (*i.e.*, G_x, G_y, *and* G_z). The bottom part of Fig. 4 is an example of gait segmentation. Each gait cycle starts with the current swing phase and ends with the next swing phase.

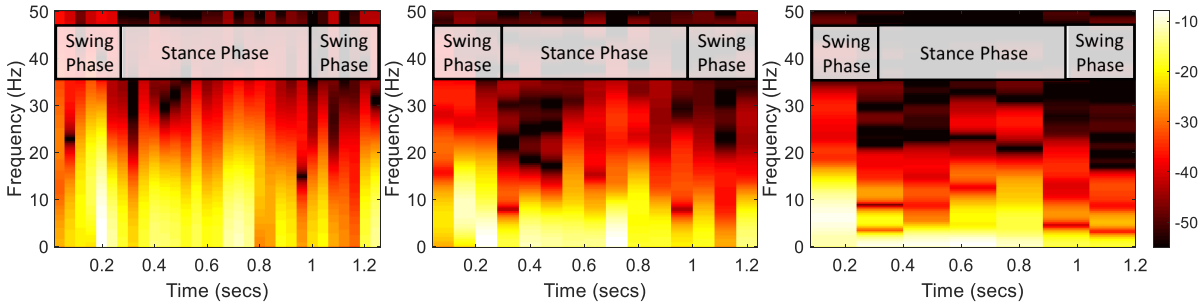

Fig. 5. **The examples of spectrogram. The X-axis shows the time dimension, and the Y-axis shows the frequency dimension. The third dimension shows the amplitude of a particular frequency at a specific time represented by the color. Moreover, the segmentation size of STFT is a trade-off metric between time-frequency resolution.**

4.3 Gait Representation

After segmenting the raw data, we now proceed to represent features for medicine intake detection. Since the data are time series, we adopt time-frequency analysis to extract features, which represents a signal in both the time and frequency domains simultaneously. We adopt spectrogram as a time-frequency analysis technique due to two reasons. First, spectrogram provides a high resolution in both time domain and frequency domain. Second, spectrogram has a low computational complexity which shows the potential for real-time implementation. The workflow of the calculation of spectrogram can be described as follows. After gait cycle segmentation, a one-dimensional time series will be represented as follows:

$$X(m, \omega) = \sum_{n=-\infty}^{\infty} x[n]w[n-m]e^{-j\omega n}, \tag{5}$$

where $x[n]$ is a time series of gait data and $w[n]$ is the window function. Accordingly, the spectrogram is an amplitude spectrum of $X(m, \omega)$:

$$\text{spectrogram}\{x(t)\}(m, \omega) \equiv |X(m, \omega)|^2. \tag{6}$$

Fig. 5 shows a couple of examples of the spectrogram of x-dimensional data in accelerometer. The X-axis shows the time dimension, and the Y-axis shows the frequency dimension. The third dimension shows the amplitude of a particular frequency at a specific time represented by the color. We observe that the swing phase contains more high-frequency components than the stance phase. We can also notice that increasing the segmentation size of

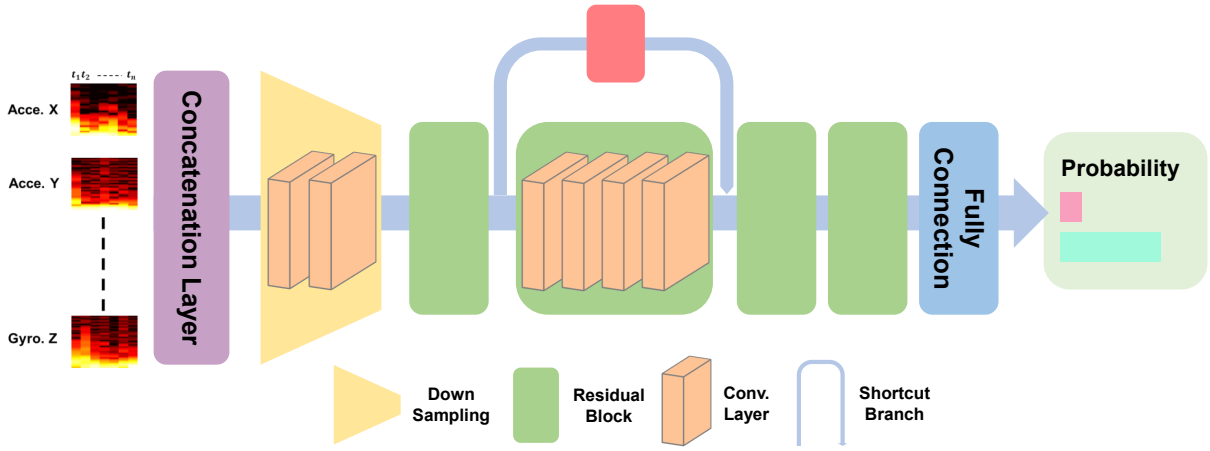

Fig. 6. **The medicine intake detection is achieved by our proposed multi-view CNN architecture. A concatenation layer carries out the data fusion from different sensors. A residual network consisting of four residual blocks achieves the feature extraction. A fully-connection layer and a Softmax activation function perform the prediction.**

short time Fourier transform (STFT) increases the resolution in the frequency domain, but reduces the resolution in the time domain. The influence of STFT segmentation size is evaluated in Section 7.1.

5 MEDICINE INTAKE DETECTOR

In this section, we introduce the design and implementation of our medicine intake detector, consisting of a multi-view deep neural network to achieve medicine intake detection.

5.1 Problem Formulation

We formulate the medication intake detection as a binary classification problem. Rather than quantifying multiple gait features (*e.g.*, speed, step length and variability) [19] from collected data, we investigate a deep learning-based approach for twofold reasons. First, deep learning provides us an end-to-end solution without heavy hand-crafted features engineering. It utilizes the vast parameters in its hidden layers to learn the data distribution automatically. In this way, deep neural network extracts some high-dimensional features, which are different from these common-sense features but highly correlated with PD symptoms. Second, deep learning utilizes some activation functions (*i.e.*, Sigmoid and ReLU) to provide the nonlinear ability. In this way, a deep neural network is considered to provide a better decision boundary than a traditional classifier.

In the case of *PDMove*, it is an underexplored problem which features are related to gait variability caused by medication non-adherence. Therefore, deep learning takes its advantages to differentiate the stages between before and after taking medication.

5.2 Multi-view Convolutional Neural Network

We introduce the architecture of medicine intake detector, which is a multi-view convolutional neural network (MVCNN) containing the modules of multi-view data fusion, feature extractor, and medicine intake predictor (see Fig. 6).

Multi-view Data Fusion: There are two solutions to handle the multivariate data [20]. One is called ensemble classifiers (EC). In this way, separate architectures designed for each sensing modality first learn sensor-specific information before their generated concepts are unified through representations. This concatenates across all the sensors later in the network. The other one is called feature concatenation (FC) that concatenates the steams of multiple sensors at the input of the neural network. According to this concatenation architecture, the EC concatenates the features in the high-dimensional space. In this case, the first half part of the neural network can learn the intra-sensor features, and the latter one learns the inter-sensor (across multiple modalities) features. Instead, hidden layers in FC architectures simultaneously learn intra-sensor and inter-sensor information. Referring to our system, accelerometer and gyroscope belong to the same sensing modality as both of them sense the movement of the smartphone. Therefore, we adopt the FC architecture to learn the intra and inter-sensor features simultaneously. During our implementation, concatenating layer is adopted to concatenate the spectrograms at the horizontal (time) dimension.

Feature Extractor: We adopt CNN as the feature encoder since CNN utilizes the layers with nonlinear filters to share weights among all the locations in the input. Compared with fully-connected layers, the convolutional layer is sparse, which contains fewer parameters and thereby facilitates depth hidden layers. The convolutional architecture has shown its superior capability for several content-related tasks (*e.g.*, Face Recognition, Scene Labelling, and Action Recognition [21]). Specifically, we choose a residual network, which has the shortcut connection to connect high-dimensional features with low-dimensional ones. The shortcut connections can be formulated as:

$$y = \mathcal{F}(x, \{W_i\}) + x, \tag{7}$$

where $\mathcal{F}(x, \{W_i\})$ represents the multiple convolutional layers, and $\mathcal{F}(x, \{W_i\}) + x$ represents element-wise addition. According to He *et al.* [22], shortcut connections make it easy for the network to learn the identity function. Specifically, our network contains four residual blocks, each of which contains four 3×3 convolutional layers. Shortcut connection is employed to connect the input and output of each residual block.

Intake Predictor: Given the output of feature extractor, we then adopt an activation function (*i.e.,* Softmax) to introduce the non-linearity and predict the medicine intake. Afterward, a cross entropy function is employed to calculate the loss between the predicted label and the ground truth. By minimizing the loss, we finally increase the confidence of the prediction.

5.3 Personalized Model in Real Life

Despite the powerful performance CNNs has, it requires sufficient data to work. Otherwise, the neural networks are either prone to underfitting or overfitting, which leads to unsatisfactory results. However, it is usually difficult to ask a PD patient to provide sufficient labeled data in real life. Thereby, how to train a personalized model with limited data becomes a critical problem for providing medication adherence monitoring. To address this challenge, we adopt the transfer learning, a technique that a model trained from one task is repurposed to another related task [23]. In this way, transfer learning allows a deep learning model to work with a small amount of data. According to existing studies, transfer learning allows the performance improvement when the two tasks are similar, and the features learned from the first task are general [24]. In our case, we first train our model on a base dataset consisting of multiple subjects. Then, we transfer the learned features to a target PD subject. Given the fact that two tasks are similar, the learned features from the base dataset can quickly transfer to an individual. We evaluate the significance of transfer learning in Section 7.1.

6 BENCHMARK PREPARATION

In this section, we introduce our benchmark preparation, including the data collection, neural network implementation, and evaluation metrics.

6.1 Data Collection

Participants Enrollment: Our study is approved by the WIRB. We collaborate with medical centers to enroll 247 PD patients from the U.S. to join our research. Professional medical centers confirm the PD onset. The ground truth is evaluated through the Unified Parkinson's Disease Rating Scale (UPDRS), a standard clinical diagnosis for Parkinson's disease, which requires each subject to take a series of tests, such as speech test, facial expression test, hand movement test, and gait analysis. Afterward, the physician diagnoses a subject as PD or non-PD according to the received scores. For each participant, we conduct a demographics survey to record confounding information such as gender, age, and smartphone usage. These PD patients are all above 50 years old. 154 PD patients are males, and the rest 93 PD patients are females. Fig. 7 shows the cumulative distribution function (CDF) of onset information. The year of onset is range from 1 to 47. The median number is five, and about 30% patients' onset time is less than or equal to three years. According to the conclusion from clinical medicine [25], PD patients are considered as early stages in PD if they are onset less than three years.

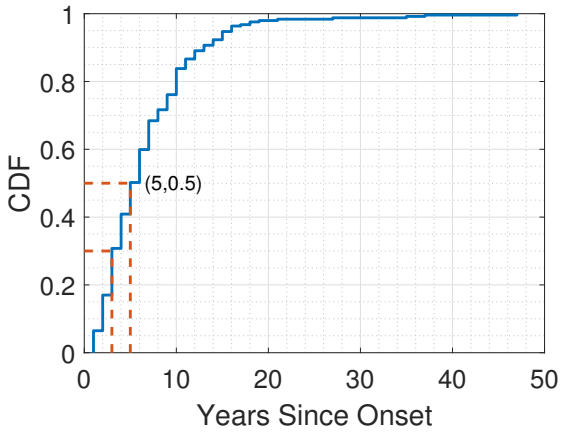

Fig. 7. **The CDF graph describes the "Years since Onset" for the PD patients in our dataset. About 50% of patients are onset longer than six years.**

Gait Collection: Data collection is conducted in an uncontrolled daily-life environment. Each participant is required to install our smartphone APP to collect gait data. Specifically, each participant needs to put the smartphone in the pocket and walks straight at least for 20 steps (see Fig. 8). During a three-month-long experiment, we collect 10623 recordings, of which 5507 recordings are collected before taking medication, and the rest 5116 recordings are collected after taking medication. Our gait cycle segmentation module totally extracts 125689 gait cycles. 65030 samples are labeled as "before taking medication", and the rest 60659 samples are labeled as "after taking medication".

6.2 Neural Network Implementation

Dataset Split: As we have mentioned in Section 5, the medicine intake detector contains the pre-training phase and the transfer learning phase. In the pre-training phase, we divide the PD patients into two person-independent subsets and acquire two pre-training models, respectively. In the transfer learning phase, we transfer the pre-training model from subset to all the PD patients from the other subset. In this way, we evaluate our system on every PD patient. For each PD patient, 80% data is used as training, and the remaining 20% data is used as testing.

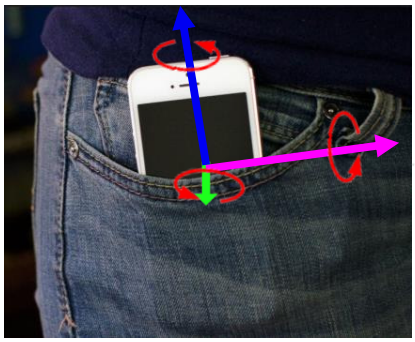

Fig. 8. **A PD patient is asked to put a smartphone in the pocket and walk straight for 20 steps.**

Network Implementation and Training Policy: We implement our neural network in PyTorch. We set up an initial learning rate of 0.1 when pre-training our model on a base set. We then drop the learning rate to 0.01 when training a model for each individual. We adopt stochastic gradient descent with momentum (SGDM) as the optimizer. Data augmentation methods are adopted in training, including random resize and crop, random horizontal flip, and color jitter.

6.3 Evaluation Metrics

We use the following metrics that are widely used in mobile health. We define the positive class as "after taking medication".

- Accuracy: Accuracy describes the fraction of samples that are correctly predicted. It is formulated as $accuracy = \frac{TP+TN}{TP+TN+FP+FN}$.
- Precision: Precision is defined as the fraction of predicted after medication samples that people truly take medicine, *i.e.,* $precision = \frac{TP}{TP+FP}$. It measures the robustness of our system against false positives. This value should be the higher, the better.
- Recall: Recall is defined as the fraction of "after taking medication" samples that are detected over the total amount of samples taking medicine, *i.e.,* $recall = \frac{TP}{TP+FN}$. It measures our system's ability in detecting all the samples of "after taking medication" without misses.

7 REAL-WORLD STUDY AND EVALUATION

In this section, we evaluate *PDMove* on our collected smartphone dataset.

7.1 Evaluation of Medicine Intake Detection

Medicine Intake Detection: Fig. 9 shows the average normalized confusion matrix of medicine intake detection on a total of 247 PD patients. The positive class is defined as the state after taking medication. The X-axis is the ground truth, and the Y-axis is the prediction results of our model. According to the formulation introduced in Section 6.3, *PDMove* can achieve an average accuracy of 77.6%, an average precision of 0.732, and an average recall of 0.894, respectively. The recall is higher than precision, showing that our system will be more likely to predict a given gait cycle sample as "after taking medication".

One reason is that medicine effectiveness can continue from the last medication time. In this case, gait samples collected before taking medicine can be predicted as "after taking medication". This issue can be addressed

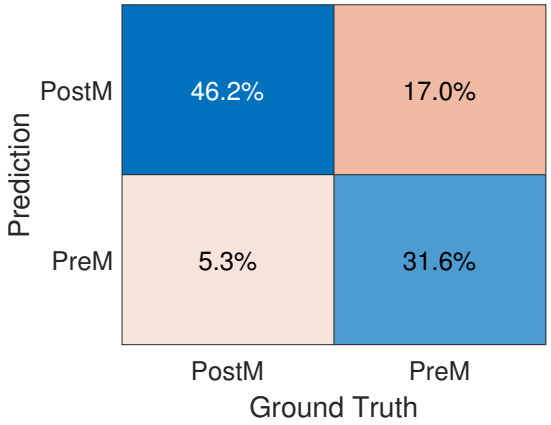

Fig. 9. **The normalized confusion matrix of medicine intake detection. The recall is higher than precision, showing that *PDMove* has a higher probability to predict a given sample as "after taking medication".**

by setting a time window in real-life usage. A healthcare provider can assign the time window. When a non-adherence event occurs (*i.e.,* a user forgets to take the medicine in this given window), smartphone reminds user the medicine intake. From another point of view, our results implicate that *PDMove* has the potential to achieve precise medicine. medicine metabolism is well known to vary from person to person, and *PDMove* shows the ability to monitor symptom fluctuation after medication continuously. With the help of *PDMove*, these healthcare providers can customize the precise drug schedule for each PD patient, including medication time and dosage. This customized drug schedule can further help a patient to reduce the side effects and improve their quality of life.

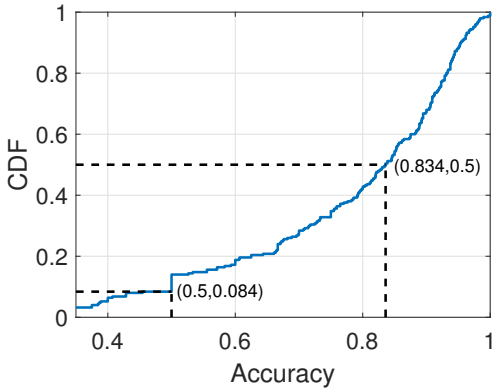

Fig. 10. **The CDF graph describes the accuracy of 247 PD patients. One set of the dotted lines show that about 50% of PD patients can achieve an accuracy higher than 83.4%.**

Scalability Study: We adopt a Cumulative Distribution Function (CDF) graph (see Fig. 10) to describe the accuracy distribution on a total of 247 PD patients. To better understand the results, we specifically plot two groups of dotted line in the figure. The first group describes the median value, showing that more than 50% of PD

patients achieve an accuracy higher than 83.4%. The second group describes the cases that our system achieves an accuracy of less than 50%, and we observe that about 8.4% of PD patients fall into this category. This means our medicine intake detector in *PDMove* is difficult to differentiate between before and after taking medication. The reasons are two folds. First, gait abnormality can vary from person to person. It is hard to differentiate between two stages when gait symptoms are not obvious. Second, medicines may have different effects on different people. It is hard to differentiate between these two stages when medicine effectiveness is weak.

Impact of Gait Data Segmentation: Considering that gait cycle segmentation achieves the feature alignment (*i.e.,* every sample contains a complete gait cycle from current swing phase to next swing phase), we further show interests to see how it benefits the medicine intake detection. We set up two groups. The first group implements the gait cycle segmentation as we introduced in Section 4. Besides, we prepare the second control group based on the blind segmentation, namely, segmenting the gait data with a fixed duration. Specifically, we evaluate different length by varying the segmentation size from 100 samples to 300 samples with an interval of 100. Every 100 samples mean one second in a real scenario since the sample rate is 100 Hz.

Fig. 11 compares the accuracy of medicine intake detection between the gait cycle segmentation and the blind segmentation. We observe that the gait cycle segmentation (see Fig. 11, bar with hatched shading) takes the advantage obviously, of which the average accuracy is about 4% higher than the best case of the blind segmentation (see Fig. 11, bars without hatched shading). The reason is that one gait cycle is already comprising all the useful information (*i.e.*, swing phase and stance phase), and therefore, the medication adherence detector module can effectively learn the gait variability caused by medication. On the contrary, the blind segmentation can either contain an incomplete gait cycle or non-integral cycles, which affects the convergence of our deep learning model.

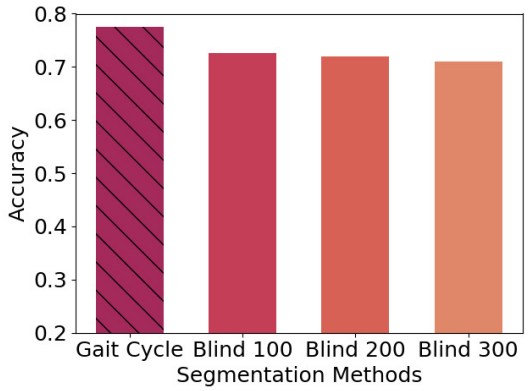

Fig. 11. **The comparison of accuracy between the gait cycle segmentation and the blind segmentation (*e.g.,* Blind 100 means to segment gait data every 100 samples). Gait cycle segmentation achieves a higher accuracy as the feature alignment facilitates deep learning model convergences. The variation of the blind segmentation length slightly affects the performance.**

Impact of STFT Segmentation: As we pointed out above, the segmentation size of short time Fourier transformation (STFT) is a trade-off metric between time-frequency resolution. Basically, the longer the segmentation size is, the higher the resolution is in the frequency domain and the lower resolution is in the time domain. This property motivates us to explore how this factor affects the performance of medicine intake detection. Specifically, we set up four groups, in which the segmentation size is configured as 8 samples, 16 samples, 32 samples, and 64 samples, respectively.

Fig. 12 shows the performance comparison among these four groups. We observe that smaller segmentation size helps achieve a higher accuracy of medicine intake detection. For example, the accuracy is 77.6% when segmentation size is 8. However, it drops to 75.3% when we increase segmentation size to 64. This indicates that it is the time domain resolution rather than the frequency domain that plays a significant role in gait features representation. The reason is that a gait cycle consists of multiple sub-phases, and high resolution in time domain allows a spectrogram to present more details about the gait features, which facilitates our deep learning model to have a more precise prediction.

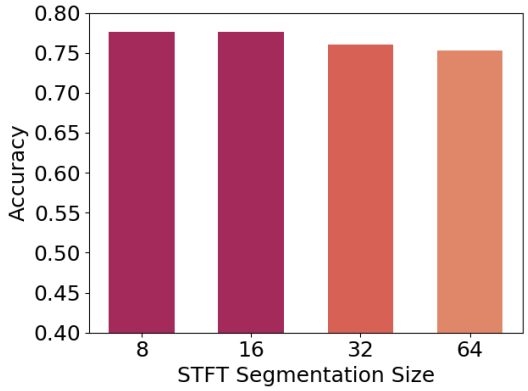

Fig. 12. **The impact of STFT segmentation size while implementing spectrogram representation. The longer STFT segmentation size indicates the higher resolution in the frequency domain but less resolution in the time domain. The high time domain resolution allows fine division of the walking phase, thereby achieving better performance.**

Impact of Transfer Learning: Fig. 13 is an example showing the significance of transfer learning for an individual. We totally collect 56 gait cycles. The X-axis describes the number of epochs. In each epoch, an entire set of data is passed both forward and backward through our model once. The Y-axis describes the testing loss, which is calculated every epoch using the criterion of the cross-entropy. The square-marker line describes the results of our model with the random initialization, and the triangular-marker line shows the results, of which we in advance pre-train our model on a base set. We observe that the loss without pre-training drops slowly and get saturated at the 25 epochs. Instead, the loss drops quickly if we pre-train our model on a base dataset in advance. Transfer learning works when the features from the first dataset are general, or these two tasks are correlated. In the case of our study, the two taskes are similiar. The weight distribution fits the gait data type after pre-training, and accordingly, it converges quickly on a specific individual.

7.2 Influence of Demographic Factors

In this section, we study the influence of demographic factors on medicine intake detection, including impact of age, gender, and smartphone, respectively.

Impact of Age: Human gait patterns inevitably change with the increase of age. The so-called aging effect may affect the detection accuracy of our system. Therefore, we are motivated to explore how age factor can influence the performance of our proposed medicine intake detection. As humans become increasingly frail and show significant degeneration after 75 years old [26], we set this age as a boundary to divide the collected dataset into two groups (age < 75 and age >= 75) and compare the performance.

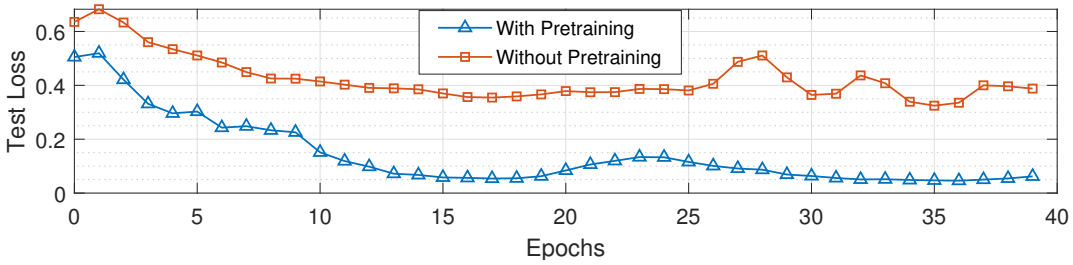

Fig. 13. **The comparison of test loss of an individual model between the case with and without pretraining on a base dataset. The model is hard to converge with the random initialization. On the contrary, transfer learning enables the convergence by repurposing the knowledge from one generalized model to a personalized one.**

Fig. 14 compares the accuracy of medicine intake detection between two prepared groups. The central mark indicates the median, and the bottom and top edges of the box indicate the $25th$ and $75th$ percentiles, respectively. The outliers are plotted individually using the "+" symbol. We observe that the middle-age group (age < 75) achieves a median accuracy of 83.8%, which is 11.3% higher than that of the old-age group (age >= 75). These results implicate that aging affects the medicine-intake detection. The reason is that aging impairs motor ability. When getting old, humans usually present reduced power in ankle joint that results in low walking speed [27]. Such aging-caused gait impairment can interfere with the medication intake detection. Form the perspective of our system, the gait features between before and after taking medication are close, and therefore our medicine intake detector can be more likely to misclassify a sample collected from an elder PD patient.

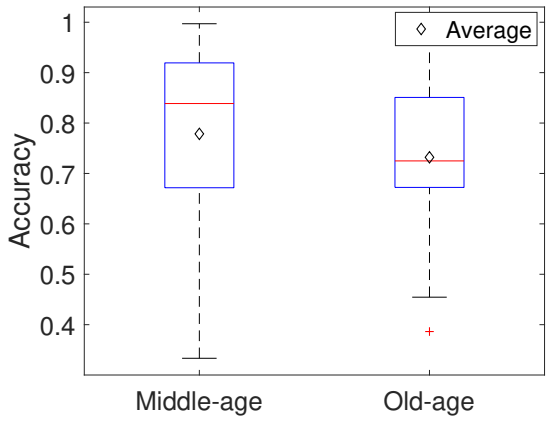

Fig. 14. **The comparison of accuracy of medicine intake detection between different ages. The middle-age group achieves higher accuracy, indicating that ageing-caused gait impairment can interfere with medicine intake prediction.**

Impact of Gender: Gender, as well as aging, can be another factor that affects the performance of medicine intake detection. According to previous research [28], females and males usually have a different walking pattern due to different skeleton structures. First, a female usually shows a higher walking cadence but shorter length of

stride than a male. Second, a female has less range of motion in the hip than a male. Such a difference motivates us to explore the impact of gender-induced variability on medicine intake detection.

Fig. 15 compares the accuracy of medicine intake detection between males and females. We can observe that our system is general to PD patients with different genders. First, males achieve an average accuracy of 77.7%, and females achieve an average accuracy of 77.2%. Second, the median accuracy of males is 84.5%, and this value is 81.3% for females. Our results implicate that gender is an independent biological factor. The reason is that gender-induced gait variability represented in the spectrogram is constant in both before and after taking medication. When differentiating between these two stages, back propagation enables our deep learning model to learn that gait-induced variability contributes little.

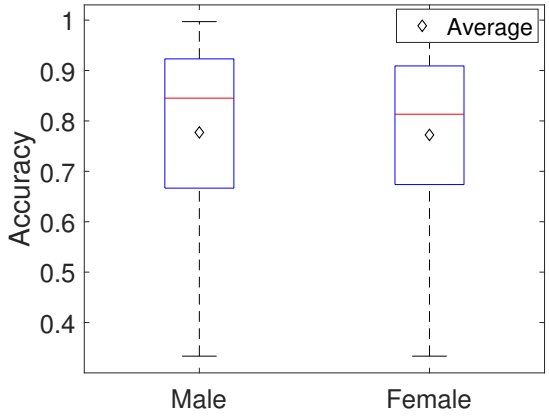

Fig. 15. **The comparison of accuracy of medicine intake detection between different gender. The performance (*i.e.*, median and average accuracy) is close, indicating that gender is an independent biological factor that does not contribute to the gait difference.**

Impact of Smartphone: Considering that the sensor type, sensor deployment, and sensor quality can be different in various smartphones, we further show interests to explore how phone model affects the medicine intake detection. In our collected dataset, participants mainly adopt iPhone 5 and iPhone 6. The iPhone 5 series consists of iPhone 5c and iPhone 5s, and the iPhone 6 series consists of iPhone 6 and iPhone 6 Plus, respectively. Table 2 presents the statistics of performance among different phone models, from which we observe that the gap between iPhone 5 and iPhone 6 is close. The average accuracy of the iPhone 6 series is 77.3%, which is only 0.7% lower than that of iPhone 5 series. This observation further shows that *PDMove* is a smartphone-independent system, providing its accessibility and scalability for serving different smartphone users in the real world.

7.3 Influence of Medical Confounding Factors

In this section, we further study the influence of medical confounding factors on medicine intake detection, including the impact of disease progression and deep brain stimulation (DBS) surgery.

Impact of Disease Progression: Considering that gait problems vary when the disease progresses, we show interests to understand whether *PDMove* can continuously monitor the medication adherence for patients in different stages. Previous study concludes that PD can be classified as the early stage and the mid-stage according to onset time [25]. The early stage usually refers to a PD patient who is onset within three years, while the mid-stage refers to a patient who is onset longer than three years.

Table 2. Impact of Smartphone Series on Medicine intake detection.

	iPhone 5 Series			iPhone 6 Series		
	iPhone 5c	**iPhone 5s**	**Average**	**iPhone 6**	**iPhone 6 Plus**	**Average**
Accuracy (%)	75.2	78.3	**78.0**	78.1	75.8	**77.3**
Precision	0.771	0.750	**0.750**	0.739	0.684	**0.721**
Recall	0.968	0.888	**0.892**	0.898	0.903	**0.899**

Fig. 16 shows the comparison of the accuracy, precision, and recall for PD patients between the early stage and mid-stage. In our evaluation, we group 76 PD patients into the early stage and rest 171 PD patients into the mid-stage. Both groups achieve similar results. The gap of accuracy is less than 1%, and the difference in scores in both recall and precision is less than 0.1. The close performance implicates that *PDMove* is not sensitive to changes ensuing with the degree of severity. Even though the disease severity can progress differently from person to person, gait impairment is one of the most common symptoms existing in all stages [19]. Our system can sense relative differences caused by medication. The results further implicate that *PDMove* can continuously monitor the medication adherence for a PD patient from the early to advanced stage.

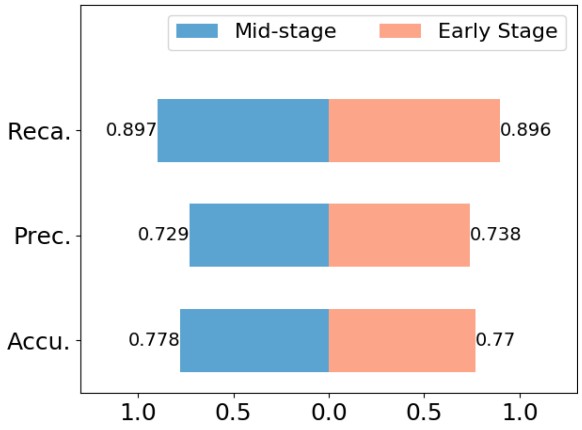

Fig. 16. **The bar graph compares the performance (*i.e.*, accuracy, precision, and recall) of medicine intake detection between early stages and mid-stage PD patients. The performance of the two groups is close, indicating that our system can continuously provide user the service of medication adherence when the degree of disease severity varies.**

Impact of Deep Brain Stimulation Surgery: With the progression of disease, PD symptoms can develop resistance to treatment. As a therapeutic approach, deep brain stimulation (DBS) is adopted to improve the medicine effectiveness. We are motivated to exploit the impact of DBS surgery on medicine intake detection. Fig. 17 shows that PD patients who take DBS can respond to medication better. The average accuracy of these PD patients is 87.8%, which is 10.4% higher than the group of patients without taking surgery. This observation is consistent with current clinic medicine. The reason is that DBS is responsible for enhancing the response of motor symptoms to dopaminergic treatment [29]. This kind of change makes it easy for our proposed deep

learning model to learn a decision boundary to differentiate between these two stages. Fig. 17 also shows that the prediction preference of our model gets altered. PD patients without taking surgery usually achieve a higher value in recall than precision. This result is, however, different from PD patients who take the DBS surgery. DBS helps to achieve a higher precision than recall. The precision for all the PD patients is 1.0, indicating that there exist no false positive samples.

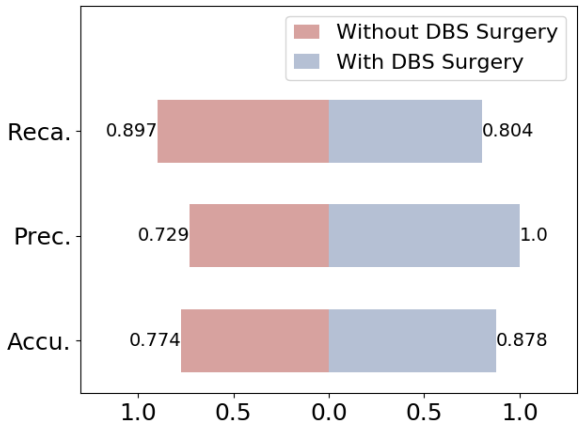

Fig. 17. **The bar graph compares the performance (*i.e.*, accuracy, precision, and recall) of medicine intake detection between patients with and without taking surgery. The patients who take the DBS surgery achieve the higher accuracy, indicating that DBS surgery improves medication response.**

8 RELATED WORK

Related work falls within two areas, including intake activity monitoring and Parkinsonism gait detection.

8.1 Wearable and Mobile Technologies for Intake Activity Monitoring

The intake activity monitoring has attracted much attention in recent years. AutoSense [30] developed a wearable sensor suite which focuses on detection of physiological signal for inferring onset, causality, and consequences of stress. Chun *et al.* [31] developed a wearable sensor to detect the eating activites by tracking the movements of jawbone. FluidMeter [32] adopted the smartwatch to guage the human daily fluid intake. Some work also focuses on how to increase the user adherence of medicine intake. Curci *et al.* [33] developed a wearable sensing system consisting of a smartphone and a RFID tag to detect the medicine intake activity. MoviPill [34] designed a mobile persuasive social game for improving the medication adherence for elders. Lee *et al.* [35] developed a self-management system consisting of an electronic pillbox and an ambient display to provide the real-time feedback of the medicine intake.

Our work, however, is different from existing work above. Considering the fact that medicine relieves the Parkinsonism gait, *PDMove* measures the daily-life gait variability to achieve the medication adherence monitoring.

8.2 Wearable and Mobile Technologies for Parkinsonism Gait Detection

PD detection using mobile technologies becomes a hot topic recently [36–39]. Gait analysis is one of the most conventional approaches. Moore *et al.* [40] adopted wearable sensors to achieve detection of Freezing of Gait (FOG). Mazilu *et al.* [41] achieved FOG detection with a smartphone-based system. Specifically, the smartphone

is adopted as a computing unit, and the external sensors achieve the gait data collection. Based on this work, Wang *et al.* [42] published an extension in which the smartphone is also viewed as a computing unit, and FOG measurement is finished by an accelerometer mounted on the back of the patient.

Most work focuses on detection of Parkinson's disease. The data is collected from both PD patients and healthy humans, and their objective is to screen the PD patients from healthy humans. Instead, our objective is to achieve medication adherence monitoring of PD patients by accessing the daily-life motor fluctuation using a smartphone.

9 IMPLICATION

In this section, we discuss the extension of *PDMove*, including medication effectiveness detection and precise medicine.

Medication Effectiveness Detection: As the disease progresses, drugs become less effective, and PD patients can progressively develop resistance to medicine. Once medicines lose effectiveness, they no longer relieve the PD symptoms while still causing side effects, such as involuntary twisting movements [43]. Existing studies find that "medicine lose effectiveness" widely exists, showing that about 40% of PD patients realize that the drugs are becoming less effective after several years of medication treatment [44]. Accordingly, patients are encouraged to frequently visit the clinics in order to understand their recovery conditions timely and adjust their treatments if necessary. However, resources, such as economic conditions, travel distance, and increasing disability, can prevent patients from frequent visits [43]. As a passive mobile sensing system, *PDMove* can continuously detect medication effectiveness and remind the user when drugs are losing effectiveness. Then PD patients can schedule an appointment with the physicians in good time.

Personalized Prescription and Precise Medicine: Due to the different physical condition and disease severity, the therapeutic effect can vary from person to person. Nowadays, clinical medicine agrees that doctors are responsible for adjusting the medicine type (*e.g.,* Levodopa, Dopamine agonists and MAO-B inhibitors) and treatment plan (daily dosage) for each individual. Improper medicine and unsafe doses will only aggravate motor symptoms, such as increasing the risk of falling [45], rather than provide relief. However, precise medicine in practice is actually challenging. First, PD progression varies among different individuals [46]. Second, everyone metabolism ability is different. The existing assessment usually relies on the clinical tests and self-report from patients, and thereby the prescription given by a doctor can exist bias with an occasional visit. Instead, *PDMove* can provide doctors the detailed information of the gait variability in daily, such as the medicine effectiveness and duration of efficacy, to assist doctors to optimize the prescription.

10 LIMITATION

PDMove marks a closer step towards passive medication adherence monitoring of PD in daily life. However, it exhibits some limitations. First, current data collection is active and each participant is instructed by an APP to walk twenty steps. This limitation can be addressed by deploying more experiments to understand its performance in real life in the future. Second, *PDMove* builds on the phenomenon that impaired gait responds to dopaminergic therapy. This performance may degenerate on subjects whose gait impairment are inconspicuous. We plan to explore the scalability of *PDMove* further, and develop a person-center protocol.

11 CONCLUSION

In this paper, we presented, *PDMove*, the first smartphone-based system that compares the different gait pattern, before and after taking medication, to facilitate the continuous medication adherence monitoring in daily life. It works by sensing gait through the built-in accelerometer and gyroscope, segmentation of gait cycle and detection via a convolutional neural network with a multi-view input architecture. *PDMove* demonstrates the significant

advantages and is a promising step in the real-world deployment of a passive-sensing protocol in the mobile system towards a large population in the future.

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