Master's Thesis

Medical Informatics Master

Universität Heidelberg / Hochschule Heilbronn

in Cooperation with Taipei Medical University

Predicting Blood Pressure from Photoplethysmogram Waveform Data: A Signal Processing and Machine Learning Approach

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Affidavit

I hereby declare under oath that I have independently prepared the present work without using sources other than those indicated; any thoughts taken directly or indirectly from external sources (including electronic sources) are identified as such.

The work has not been submitted to any examination authority, either domestic or foreign, in the same or similar form, and has not been published.

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2 Introduction

2.1 Subject and Motivation

Cardiovascular diseases (CVDs) are the leading cause of death worldwide, according to WHO publishing statistics [32]. One of the main factors contributing to CVDs is Hypertension. It is the leading risk factor for mortality, and is ranked third as a cause of disability-adjusted life-years [13]. Currently, there is a significant need for continuous blood pressure (BP) monitoring due to various factors. Primarily, while hypertension is a manageable condition, the availability of accurate high BP detection remains scarce, especially in low-resource environments [5]. Additionally, blood pressure (BP) is subject to rapid fluctuations influenced by various factors, including stress, emotions, dietary intake, physical activity, and medication usage [35]. Continuous monitoring of blood pressure, rather than relying on isolated measurements, plays a vital role in the early detection and treatment of hypertension [11].

The current accurate methods for measuring BP continuously are either invasive or involving a cuff-mechanism. Catheterization is internationally recognized as the "gold standard" for obtaining the most accurate measurement of continuous blood pressure [39]. However, due to its invasive nature and limited applicability to hospital settings, this method requires medical intervention, which renders it inconvenient for everyday use.

While cuff-based devices are commonly utilized for this objective, it is worth noting that over 30% of home blood pressure monitors are found to be inaccurate, rendering continuous measurement unfeasible [26]. Moreover, this approach relies on the individual consciously and intentionally engaging in manual blood pressure monitoring, which poses limitations and might be often overlooked.

An ideal technology for measuring blood pressure should have the following attributes: non-invasiveness, cuffless operation, optical functionality, wearable design, and cost-effectiveness [11]. One approach satisfying these requirements is the estimation of BP from a single measurement PPG sensor. This approach, using two modes, reflectance and transmission, has gained an increasing amount of attention in the literature due its simplicity, and ability to provide continuous and cuffless measurement [11]. Typically, the photoplethysmography (PPG) technique has been traditionally employed in healthcare settings to measure heart rate [36] and blood oxygen saturation using a pulse

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oximeter [49].

Nevertheless, establishing a straightforward, distinct, and continuous relationship between these characteristics and blood pressure (BP) has proven to be challenging. To address this, the approach heavily depends on signal pre-processing techniques, extracting PPG features, and utilizing machine learning algorithms to estimate BP based on these features [11]. A recent scoping review by Knight et al. concluded that PPG can be successfully used to continuously measure BP, by evaluating latest publications and finding over 80% accuracy in detecting hypertension [21].

This study examines the current methods and aims to develop efficient approaches for the continuous and accurate measurement of blood pressure using PPG and addresses the following research questions:

1. **What is the relationship between PPG data and blood pressure among ICU patients?**

2. **Can PPG-based data be used to estimate blood pressure accurately?**

2.2 Tasks and Objectives

The tasks of the thesis are as follows:

1. Signal Processing: to find an optimal data fetching and filtering approach from available MIMIC Databases.

2. Likewise, to create a consistent algorithm for key feature extraction.

3. Machine Learning: to develop a model based on the resulting features from Signal Processing, to reliably predict BP from PPG.

2.3 Structure of the Thesis

This thesis is organized as follows:

In Chapter 3, the foundations of the used terms and prerequisites for the methods are explained. For example, in 3.1, the terms "Blood Pressure" (3.1.1) and "Photoplethysmography" (3.1.2) are discussed. Furthermore, the general structure of MIMIC databases is explained (3.1.3, 3.1.4). In addition, the essential information about the Computing part of this research is provided (3.2).

In Chapter 4, the methodology is explained.

Chapter 5 presents the results.

The focus of Chapters 6 and 7 is on summarizing the work. Here, both the future prospects for this research field and the next steps in relation to broader scope projects are presented.

3 Theoretical Background

3.1 Medical Background

3.1.1 Blood Pressure

Blood pressure (BP) is a physiological measure of the force exerted by circulating blood against the walls of the arteries [1]. It is highly dependent on blood flow, which refers to the movement of blood through a vessel, tissue, or organ. Blood circulation begins with the contraction of the heart's ventricles. This action generates a type of hydrostatic pressure, which is the force exerted by a fluid due to gravitational pull, typically against the walls of the container that confines it.

BP is a type of hydrostatic pressure, representing the force exerted by blood on the walls of blood vessels or the heart's chambers. While it can be assessed in various body regions, the term "blood pressure" without specific qualifiers commonly refers to systemic arterial BP. This denotes the pressure of blood within the arteries of the systemic circulation. In clinical settings, this pressure is measured in millimeters of mercury (mmHg) and is typically acquired using the brachial artery in the arm [4].

Measuring BP is crucial for assessing cardiovascular health and identifying potential risks. It allows for the early detection of conditions like hypertension and hypotension, enabling timely interventions to prevent serious cardiovascular events [31]. BP serves as a key indicator of the risk for heart attacks, strokes, and heart failure, guiding preventive measures and treatment strategies [12].

Various Types of Measurement

One of the most common BP measurement methods is one using a sphygmomanometer, also known as non-invasive blood pressure (NIBP), is typically recorded as numeric values at specific time intervals. The process involves inflating the cuff to temporarily stop blood flow and then gradually releasing the pressure to detect the sounds associated with the flow of blood through the brachial artery. The two primary values obtained are systolic pressure (maximum pressure during heartbeats) and diastolic pressure (min-

imum pressure between heartbeats). During the process of cuff inflation and deflation, each heartbeat generates characteristic sounds (Korotkoff sounds) that are detected by a stethoscope placed over the brachial artery. Systolic pressure is recorded when the first tapping sounds are heard, and diastolic pressure is recorded when the sounds disappear or change character. This beat-to-beat approach provides information about individual fluctuations in blood pressure [4].

While measuring blood pressure with a cuff using a sphygmomanometer is a common and convenient method, it has its limitations as it cannot be done continuously. This intermittent approach provides valuable insights into systolic and diastolic pressures at specific time intervals, but it may not capture the nuanced changes that occur between measurements. To address the need for continuous monitoring, other methods, such as arterial catheterization, are employed.

Arterial catheterization is commonly employed in critical patient care, serving dual purposes: continuous blood pressure monitoring and obtaining frequent blood gas measurements. Typically conducted at bedside, the procedure utilizes percutaneous methods like the Seldinger technique to cannulate arteries [9]. The resulting arterial blood pressure (ABP) is a dynamic parameter that can change with each heartbeat, and it is typically represented as a waveform rather than a single numeric value. The ABP waveform consists of two main components: systolic pressure and diastolic pressure. Such continuous monitoring of ABP is usually done in clinical settings, using an arterial line connected to a pressure transducer. The resulting waveform is displayed on a monitor in real-time. However, for ease of interpretation and documentation, numeric values are commonly extracted from the waveform at specific time intervals [16].

In situations where high temporal resolution is crucial, ABP can be recorded beat-to-beat, providing a value for each heartbeat. This is particularly important in situations where rapid changes in blood pressure need to be closely monitored, such as during certain medical procedures or in critically ill patients [25].

For routine monitoring and documentation, numeric values are often averaged over a specific time interval, such as every 1, 5, or 15 minutes. This averaged value may be reported as the mean arterial pressure (MAP), which is a weighted average of the systolic and diastolic pressures over a cardiac cycle [10] Some monitoring systems may also provide systolic and diastolic blood pressure readings at regular intervals.

Alternative approaches for measuring BP have emerged over the past years. Volume clamping [20] and tonometry [17] are some of the other methods. These non-invasive techniques offer continuous monitoring of blood pressure values. Volume clamping, which

involves the use of a small finger cuff and a PPG sensor, is one method for continuous blood pressure measurement. Tonometry, on the other hand, is a cuffless approach that utilizes a manometer-tipped probe pressed directly on an artery. The volume clamping approach allows for instantaneous and prolonged blood pressure measurement. However, it is associated with high costs and still necessitates the use of a cuff, which can be inconvenient and uncomfortable. Conversely, the tonometry method is sensitive to movement of the arm and probe, making it challenging to maintain accuracy in practical applications. Additionally, constant calibration with a cuff blood pressure device is required [33].

In conclusion, blood pressure serves as a critical physiological measure, representing the force exerted by blood on the walls of blood vessels. The conventional method of measuring blood pressure with a cuff and sphygmomanometer provides valuable insights into systolic and diastolic pressures but is limited by its intermittent nature. To address the need for continuous monitoring, arterial catheterization is commonly employed in critical care, offering real-time data through a dynamic waveform. Alternative non-invasive approaches like volume clamping and tonometry aim to provide continuous blood pressure monitoring, but they come with their own challenges and considerations. As technology advances, these methods contribute to a comprehensive understanding of blood pressure dynamics, facilitating improved patient care and risk assessment.

3.1.2 Photoplethysmography

Photoplethysmography (PPG) is an optical measurement technique designed to identify changes in blood volume within the microvascular bed of tissue [7]. Its clinical application is extensive, as the technology is integrated into commercially available medical devices, including pulse oximeters, vascular diagnostics, and digital beat-to-beat blood pressure measurement systems. The fundamental structure of PPG technology is straightforward, requiring only a few opto-electronic components: a light source for tissue illumination, usually a light-emitting diode (LED) and a photodiode (PD) to gauge slight variations in light intensity correlated with changes in perfusion in the catchment volume.

History

One of the first mentioned instances on the use of PPG were recorded in 1936 by Molitor and Kniazuk [30]. They outlined comparable devices employed for tracking alterations in blood volume in the rabbit ear under conditions of venous occlusion and the

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administration of vasoactive drugs. A pioneer who helped establish the PPG technique was Alrick Hertzman [15]. In his 1937 paper, Hertzman coined the term "Photoelectric Plethysmograph" etymologically meaning: photo - "light", plethora - "exess of body fluid, blood", graph - "something written". He detailed the application of a reflection mode system to assess alterations in blood volume within the fingers, particularly during the Valsalva maneuver [40], exercise, and exposure to cold. This contribution not only demonstrated the versatility of the technique but also underscored its potential clinical relevance.

Hertzman and Spealman [15] outlined two crucial features of the PPG pulse waveform. They categorized the pulse appearance into two phases: the anacrotic phase representing the ascending edge of the pulse, and the catacrotic phase representing the descending edge of the pulse. The initial phase primarily corresponds to systole, while the subsequent phase relates to diastole and wave reflections from the periphery. In individuals with healthy compliant arteries, a dicrotic notch is commonly observed during the catacrotic phase.

In the late 1970s, there arose a renewed interest in the PPG technology, driven by the demand for compact, dependable, cost-effective, and user-friendly noninvasive cardiovascular assessment techniques [50]. The progress in opto-electronics and clinical instrumentation has played a significant role in advancing PPG technology. Semiconductor advancements, particularly in LEDs, photodiodes, and phototransistors, have brought about substantial improvements in the size, sensitivity, reliability, and reproducibility of PPG probe design. A significant leap in the clinical application of PPG-based technology occurred with the introduction of the pulse oximeter [3]. This device revolutionized non-invasive monitoring of patients' arterial oxygen saturation, marking a major advancement in the field.

Other emerging technologies encompass PPG imaging technology, telemedicine, and remote monitoring. In 2005, Wieringa et al. detailed a contactless multiple-wavelength PPG imaging system designed primarily for remotely imaging the distribution of arterial oxygen saturation (SpO2) within tissue [47]. The system captures movies of two-dimensional matrix spatially resolved PPG signals at different wavelengths during respiratory changes. PPG was found to have substantial potential in telemedicine, particularly for remote/home health monitoring of patients. Miniaturization, user-friendliness, and robustness stand as pivotal design criteria for such systems. This is exemplified by finger ring-based PPG sensors for monitoring beat-to-beat pulsations ([37], [52]).

Most PPG devices these days either use the transmissive or reflective operating modes

(illustrated in Figure 1). Currently, the prevalent method is the transmissive mode, chosen for its notable accuracy and stability [24]. However, there is a growing interest in reflective-mode PPG due to its elimination of the need for a thin measurement site. This method proves versatile, applicable to various sites such as the feet, forehead, chest, and wrists. Especially when the wrist serves as the designated measurement site, PPG sensors can be conveniently employed in the form of a band or watch.
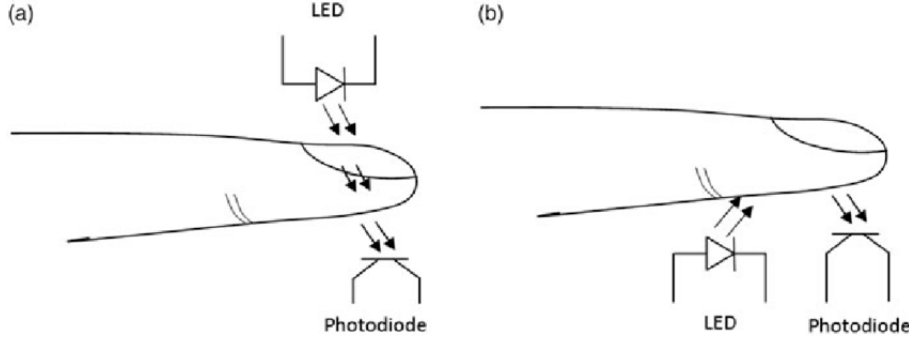

Figure 1: PPG Transmission (a) and Reflection (b) operating modes [29]

Working Principle

The PPG signal consists of pulsatile (AC) and superimposed (DC) components (see Figure 2). The AC component originates from variations in blood volume associated with heartbeats, while the DC component is influenced by factors such as respiration, sympathetic nervous system activity, and temperature regulation [2]. The AC component specifically illustrates changes in blood volume during phasic cardiac activity, representing both the systolic and diastolic phases. The systolic phase, also known as the "rise time", initiates with a valley and concludes at the pulse wave systolic peak. The pulse wave concludes with another valley at the end of the diastolic phase [46]. In most PPG waveform analyses including this one, the AC component in the form of a waveform signal is used.

Use Cases

PPG finds diverse applications in clinical settings, covering physiological monitoring (such as blood oxygen saturation and heart rate), vascular assessment (including arterial disease, aging and tissue viability), and autonomic function evaluations (such as thermoregulation, heart rate and other assessments of cardiovascular variability) [2]. Furthermore, the popularity of PPG technology as an alternative for monitoring heart rate has risen recently, primarily attributed to its ease of use, user-friendly wearing
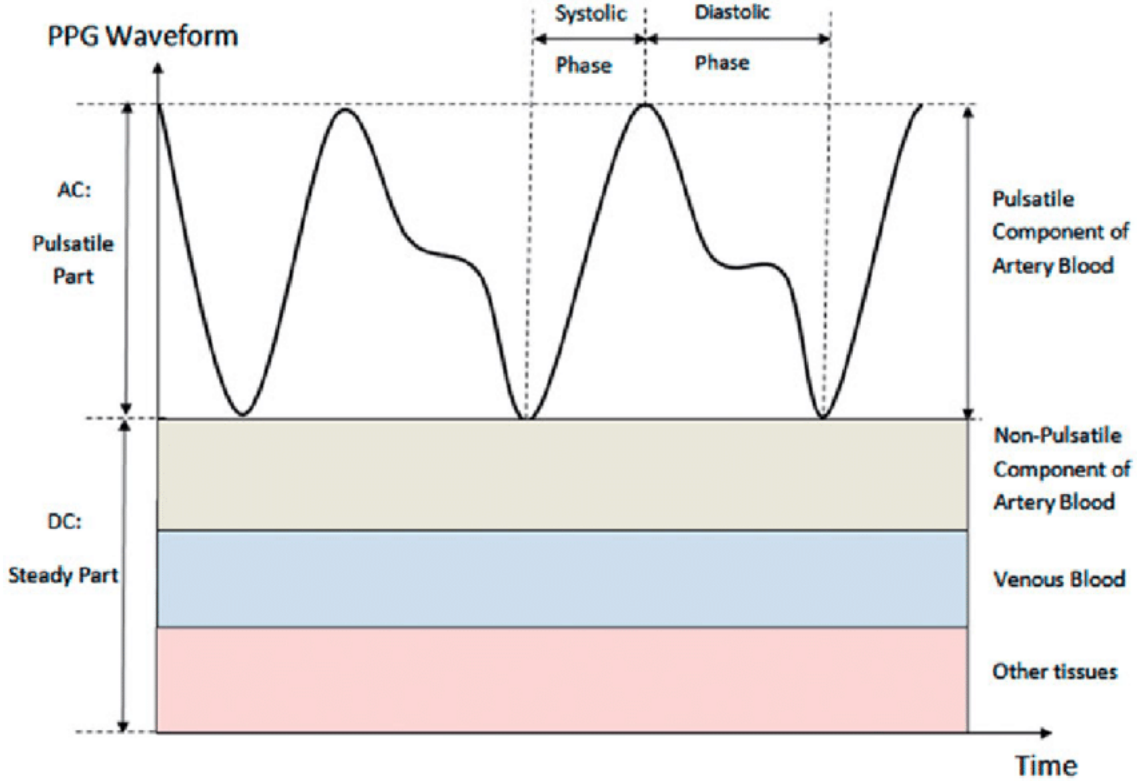
Figure 2: AC and DC components of the PPG signal [29]

comfort, and cost-effectiveness [43]. Nowadays, almost every wearable devices uses the PPG technology to track the user's heart rate and other extractable vital parameters [6]. PPG sensors in mobile and wearable devices typically feature red, green, or both light-emitting diodes. Most devices incorporate a green-light PPG sensor for continuous heart rate monitoring during daily activities. Some devices also include red-light PPG sensors, which are effective for measuring heart rate when a person is stationary, providing insights into hydration, muscle saturation, and total hemoglobin. While red-light PPG can penetrate tissue layers more deeply using near-infrared spectroscopy, it is susceptible to disturbance from ambient light. In contrast, green light, being less absorbed by the skin, minimizes the impact of ambient light noise on the heart rate signal. As a result, wearable devices commonly utilize green light rather than red-light PPG [34]. Different types of devices implement the PPG technology. It can be found in pulse oximeters, smartphones, smartwatches and other wearable devices (examples in Figure 3).

In conclusion, the PPG is an optical sensor, consisting of an LED paired with a PD, hence it is simple, inexpensive and can be easily build into a wearable device. The PPG waveform can be obtained using two modes, reflectance and transmission. This

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Figure 3: AC and DC components of the PPG signal [51]

waveform corresponds to the blood volume in blood vessels. Traditionally employed in healthcare for heart rate and blood oxygen saturation measurements, particularly with pulse oximeters, the PPG plays a pivotal role [2].

Additionally, peripheral volumetric changes exhibit correlation with BP [23]. Utilizing characteristic PPG features, machine learning functions can estimate Systolic BP (SBP) and Diastolic BP (DBP). However, establishing a simple, clear, and continuous relationship between these features and BP remains elusive. This method heavily relies on signal pre-processing, feature extraction, and the application of machine learning algorithms for BP estimation based on these features.

3.1.3 MIMIC-III

origin of MIMIC. When was it created? How is it structured?

3.1.4 MIMIC-IV

Multiparameter Intelligent Monitoring in Intensive Care IV (MIMIC-IV) [18].

1. How is the database structured?

2. Which patients and how many of them have both PPG and BP data?

3. Arterial Blood Pressue (ABP)

How does it differ from MIMIC3?

3.2 Computing Background

3.2.1 Signal Processing

1. What are the methods of signal processing for reading PPG?

   Approaches for processing the given PPG data in correlation to BP:

   Time (PTT) based on PPG & ECG - Inverse correlation between BP and PTT. PTT is the time delay for the pressure wave to travel between to sites on the body. It can be calculated as the time difference between proximal and distal waveforms indicative of the arterial pulse.

   Pulse Arrival Time (PAT) = PTT + pre-ejection period. It is defined as the time that takes the pulse wave to travel from the heart to a peripheral site e.g. finger, toe, etc. It can simply be estimated as the time delay between the R peak of the ECG waveform and a point on the rising edge of a distal PPG waveform.

   These methods require simultaneous measurement at two different sites on the body, hence two measurement sensors (ECG and PPG) are needed for recording the signals in order to estimate these parameters.

2. What are the different types of filters for processing the PPG signal?

   Signal filtering types include: Chebyshev filter, Butterworth filter [27].

   Savitzky-Golay (SG) filter [14]

   Second derivative & Age analysis [44]

   Hemodynamics and vascular age [8]

3.2.2 Machine Learning

1. What are the methods of machine learning for estimating BP from PPG?

Approaches for estimating BP from PPG:

BP estimation using ML techniques is data driven, unlike the traditional PTT/PAT only models. Several studies attempted to fit regression models, such as **multilinear regression, support vector machine and random forest**, for estimating BP using PTT/PAT based approach with some degree of success, but the results did not always satisfy the international standards.

Teng and Zhang [45] tried to fit a **linear regression** model to study the relationship between four PPG features and BP. It was reported that the diastolic time has higher correlation with SBP and DBP than the other features.

Suzuki and Oguri [42] used **AdaBoost** classifier for the estimation of BP. In this technique, SBP values were classified according to a threshold and afterwards the nonlinear machine learning model was employed for estimating SBP.

Ruiz-Rodriguez et al. [38] employed a probabilistic generative model, **Deep Belief Network Restricted Boltzmann Machine**, for predicting SBP, DBP and mean arterial pressure simultaneously. The results of this study were highly variable, and therefore was not reliable.

Kurylyak et al. [22] extracted 21 characteristic features from the PPG waveform. These features were used for estimating SBP and DBP using a **feed forward neural network**. The results were promising towards an accurate cuffless BP monitoring.

Xing and Sun [48] applied **Fast Fourier Transformation** for selecting frequency domain features from the PPG waveform followed by a **feed forward neural** network for BP estimation. However, the authors suggested that these features are not sufficient for effective BP estimation.

Liu et al. [28], added 14 features extracted from the PPG's second derivative, in addition to the 21 features used in Kurylyak et al. A **support vector machine (SVM)** was then applied for estimating SBP and DBP. The authors reported that these 14 features further improved the estimation.

The relationship between BP and PPG features is not always linear. Therefore, linear models are inappropriate and often fail to model the relationship between BP and PPG when tested on a large dataset collected from a diverse population. Other classical machine learning models, such as **SVM**, and **random forest**, provide better precision. Estimation using these models requires establishing one model per objective, hence, SBP and DBP are estimated separately. However, DBP strongly correlates with SBP and improve its estimation [49], thus should be modelled simultaneously using one model

architecture. This can be achieved using neural networks. **Neural network** models can leverage large amount of data faster and more accurately compared to classical machine learning models.

El-Hajj and Kyriacou proposed using **Bidirectional Long Short-term memory (Bi-LSTM) and Bidirectional Gated Recurrent Units (Bi-GRU) with attention mechanisms** [11].

In Su et al. [41], a four layers **LSTM** with bidirectional structure and residual connections has been employed for BP estimation using the PTT approach. The reported results outperform other PTT based BP regression models.

A study by Joung et al. [19] was conducted to evaluate a learning-based cuffless BP estimation system with calibration in challenging circumstances. A one dimensional CNN-based network was designed, that could efficiently extract BP from PPG signals using a comparative paired 1D-CNN structure with calibration.

To precisely design a learning-based BP estimation model such that its estimation accuracy obtained during the test is sustained after being built upon a practical cuffless BP monitoring system, the following delicate yet realistic experimental principles are applicable: i) the number of subjects should be sufficiently large, ii) subject independent training and test datasets are required, and iii) the intrasubject BP variation should be carefully scrutinized in the model design [19].

4 Methods

1. Data fetching and reading using WFDB and NumPy libraries.

   Get all available data from MIMIC-IV DB.

   This data is used as the validation dataset, since it is the one that's most up-to-date, most modern, and supposedly most reliable

   There are 198 subjects and 200 total studies in the DB (two subjects have two separate studies)

   The studies contain records with various signals (ECG, ABP, Pleth etc.) and are of different lengths

   A single record can contain various segments also of different lengths and signals

   Segments contain continuous values, that are used in this research

Only segments with at least 10 minutes of length are considered

These segments must also not contain "faulty" values

Faulty values: NaN, inf, negative values, for ABP values not below 30 and not above 250, for PPG only between 0 and 1

If a 10-minute part of the segment matches these criteria, it is saved to the ./validation directory, as 2 separate and synchronous ABP and PPG files

If a segment is longer than 10 minutes, then more 10 minute segments may be extracted (marked by a _ and a number representing the sequence)

Example of the files: `abp_80057524_0005_0`, `ppg_80057524_0020_18`

For MIMIC-IV data fetching, no limits on the total records and single study records are given. For MIMIC-III - 4 times the records of MIMIC-IV are fetched and a maximum of 100 segments per study is set, to avoid over-representation of single person or study data in the ML part of the research.

2. Digital signal filtering using Savitzky-Golay and Butterworth Lowpass filters.

3. Beat detection algorithms from MIMIC WFDB Tutorial used for primary estimation. Beat detection improved with manual implementation of SciPy library.

4. Fiducial Point calculation based on the algorithm provided in the MIMIC WFDB Tutorial.

5. Feature extraction with personally created code to extract time domain features, and NumPy library to extract frequency domain features (FFT). Median value calculation using NumPy library.

6. Machine Learning Model creation using PyTorch and Scikit-Learn libraries.

5 Results

5.1 Data Fetching

Data for Validation from MIMIC4: 5508 records each containing 37795 values corresponding to 605 seconds (fs=64.4725);

Data for Training/Testing from MIMIC3 (1st Iteration): 306 records each containing 75625 values corresponding to 605 seconds (fs=125);

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5.2 Data Processing

Same Signaling processing approaches were included (see 4.2) for both the MIMIC4 and MIMIC3 data.

5.3 Feature Extraction

CAVE: out of the 34 features, 2 (delta T and resistive index) depend on the accurate detection of the dicrotic notch. Significantly more values can be extracted if finding the dicrotic notch would not be necessary

FE from MIMIC4 for Validation: - For target reference Systolic, Diastolic and MAP values were extracted from the waveform data. - For Machine Learning, 34 features were extracted from the PPG waveform A total of **1,309,265** values were extracted, resulting in a 34 x 1,309,265 matrix. Total of **183,140** median values were extracted

FE 1st iteration from MIMIC3:

- For target reference ABP Systolic and Diastolic values were extracted from the waveform data. - For Machine Learning, 34 features were extracted from the PPG waveform A total of 161,269 values were extracted, resulting in a 34 x 161269 matrix. Total of 14,958 median values were extracted

The summarized results are displayed in Figure 4.

5.4 Machine Learning

6 Discussion

Limitations: - not knowing what devices were used - how they were calibrated - how accurate they are - pulse oximeter and arterial catheter parameters - sampling rates are different for every device (even between MIMIC 3 and 4)

Possible Improvements: - integrate both the ECG and PPG graphs for a more precise prediction - use further signal processing approaches - manually filter waveform graphics (e.g. faulty PPG signal) - expand on machine learning algorithms
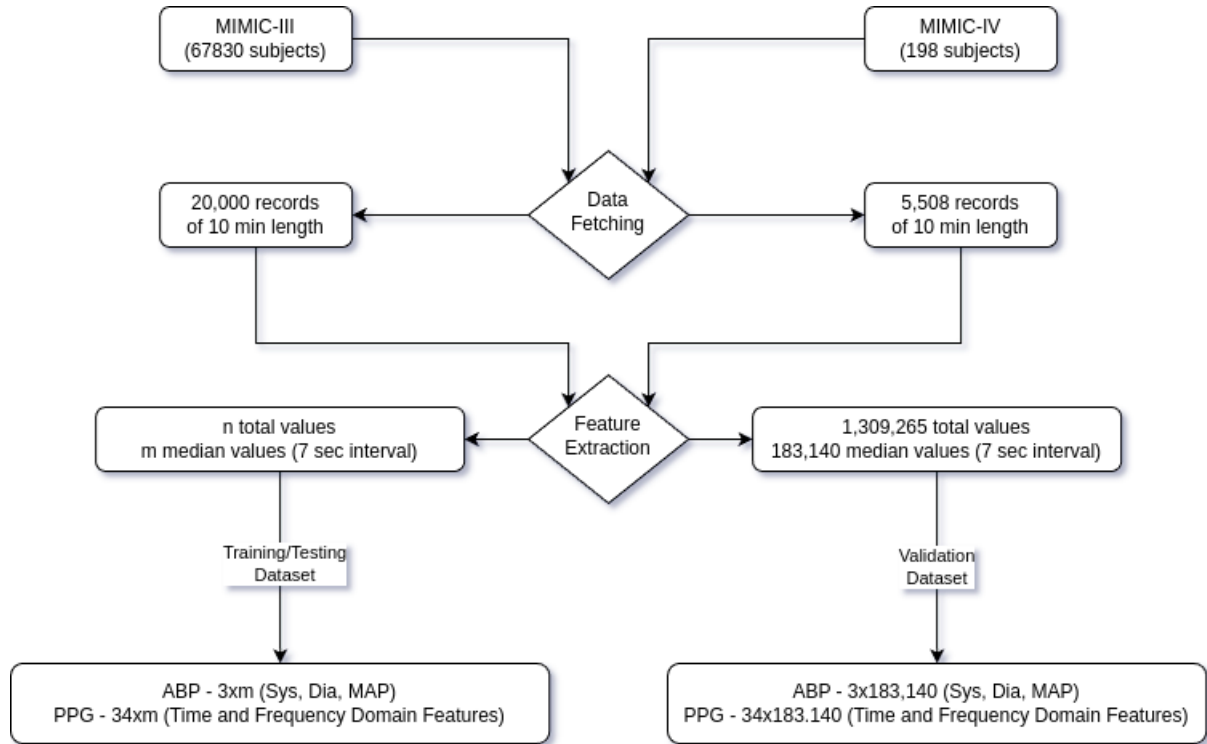
Figure 4: Flow Diagram presenting the Data Fetching and Processing

7 Conclusion

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