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Beats-to-Beats Estimation of Blood Pressure During Supine Cycling Exercise Using a Probabilistic Nonparametric Method

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This work involved human subjects or animals in its research. Approval of all ethical and experimental procedures and protocols was granted by the Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee, and performed in line with the Declaration of Helsinki.

\section*{ABSTRACT}
Blood pressure (BP) is an important clinical vital sign that varies from beat-to-beat. Nevertheless, these variations cannot be captured by the conventional cuff-based BP monitors. This study proposes and evaluates novel cuffless frameworks to continuously estimate the 10-beat averaged systolic BP (SBP) and diastolic BP (DBP) during dynamic exercise by fusing information from multiple biosensors using five machine learning algorithms. Over 100 thousand beats of data were collected from 62 subjects (aged 59 \(\pm\) 10 years), each underwent a maximal exercise stress test. The average length of recording for each subject was 35 minutes. The BP ranges were 75-280 mmHg for SBP and 36-157 mmHg for DBP respectively. Multiple physiological parameters were measured continuously and used as inputs to five machine learning algorithms for estimating the 10-beat SBP and DBP averages before, during and after the cycling exercise. The mean absolute error (MAE) of Gaussian process regression (GPR) model was 4.8 mmHg and 3.4 mmHg for SBP and DBP, respectively. The MAE of multiple linear regression (MLR), regression tree (RT), ensemble of trees (ETs), and support vector machine (SVM) models varied from 6.1 mmHg to 17.6 mmHg and from 4.0 mmHg to 9.7 mmHg for SBP and DBP, respectively. The GPR model outperformed the other four models and showed promising results in estimating the 10-beat averages of both SBP and DBP without a cuff in a general elderly population under dynamic conditions.

\section*{INDEX TERMS}
AI-doscopist, cuffless blood pressure, machine learning, big data analytics, wearable sensing, sensor network.

\section*{I. INTRODUCTION}
Hypertension remains one of the leading causes to global morbidity and mortality for over half a century [1]. Hypertension is treatable by improving awareness of lifestyle and promoting health behaviors. Diagnosis rate of hypertension is, however, as low as 46\%, and only about a third of those diagnosed are adequately controlled [2].

The associate editor coordinating the review of this manuscript and approving it for publication was S. M. Rezaul Hasan\textsuperscript{5}.

According to the Systolic Blood Pressure Intervention Trial (SPRINT) [3], ambulatory blood pressure (BP) monitoring will help improve the awareness and management of hypertension. Nevertheless, existing ambulatory BP monitors are mostly developed by the oscillometric approach, which operates based on the inflation and deflation of a brachial cuff. These devices can only provide a snapshot of BP. Although continuous BP can be obtained noninvasively by tonometry and volume-clamp methods, these methods are relatively cumbersome. Tonometry requires frequent calibration.
as well as appplanation the artery using a probe which has been
proven difficult; while volume-clamp methods used inflatable
cuffs in the design and are disruptive during ambulatory mon-
toring, especially during sleeping [4]. A recent study devel-
oped a smartphone-based device based on the oscillometric
technique for cuff-less and calibration-free monitoring of BP,
however, it can hardly be applied to long-term continuous BP
or nighttime BP measurements as it requires human finger
pressing during measurement [5].

Alternatively, pulse transit time (PTT) or its reciprocal –
pulse wave velocity (PWV) has been investigated extensively
as a surrogate of BP for continuous and wearable cuff-less
BP measurement over a decade [6]. PTT is the time delay
for a pressure wave to propagate between two arterial sites
(typically between a proximal site and a distal site). Governed
by the wave propagation theory, PWV is determined by
the arterial elasticity which depends on BP. Thus, PTT is
versely related to BP mathematically. PTT can be estimated
from different biosensors, e.g. electrical, optical, mechanical,
bioimpedance, magnetic and radar [4]. In practice, one of
the most widely used methods for PTT measurement (i.e.,
pulse arrival time, PAT) is by calculating the time interval
between the R-peak of the electrocardiogram (ECG) and
a characteristic point (i.e. foot or peak) of the peripheral
photoplethysmography (PPG) in the same cardiac cycle. PAT
contains a pre-ejection period (PEP), which is a confounding
factor influencing relationship between PAT and BP [7], [8].
Nevertheless, PAT methods are still commonly used for cuf-
less BP estimation attributed to its great convenience.

The BP-PTT relationship depends on the mechanical
property of the arterial wall comprising elastin, collagen
fibers and smooth muscle cells (SMCs). Innervated by the
autonomic nervous system (ANS) and regulated by the
neuro-humoral factors, SMCs can actively contract/dilate to
alter the elasticity of arterial wall and the BP-PTT relation-
ship. Therefore, vascular tone which represents the activation
level of SMCs, is another essentially important factor that
influences PTT-based BP estimation in addition to PEP. Our
previous study showed that PTT can be used to estimate
24-hour ambulatory blood pressure [9], but clearly demon-
strated a hysteresis phenomenon against SBP during dynamic
exercise [10]. It was recently suggested that this is partly
because the derivations based on the Moens–Korteweg (MK)
and Hughes equations relied on assumptions that do not
hold for human arteries and that the artery hyperelastic
model should be used to describe the relationship between
BP and PWV [11]. Moreover, as peripheral arteries contain
more smooth muscles than central arteries, these influences
become even more prominent when using peripheral pulses
to calculate PTT or PAT [4].

Although biophysical models were important to under-
stand the basic underlying mechanism, these models often
felt short in describing the system under a complex situation
when the parameters of different submodules were inter-
related and the relationship between different submodules
were not completely known. On the other hand, a recent
direction is to incorporate machine learning (ML) techniques
and pulse wave analysis for BP estimation [12]. In particular,
since the waveform of a peripheral pulse obtained by PPG
depend on multiple factors of the cardiovascular system, such
as BP, contractile force of the heart, and elasticity of the
arterial wall [13], PPG waveform features have been often
used together with PTT for estimating BP using ML tech-
niques. Various ML regression techniques have been investi-
gated [14]–[17], nevertheless, most of these studies were
conducted in static conditions, while studies on estimating
BP in dynamic conditions, e.g. during exercise when BP of
each subject varied greatly, were quite limited.

In this study, we aim to evaluate novel frameworks to
estimate beats-to-beats SBP and DBP by fusing information
from multiple biosensors using five ML techniques: multiple
linear regression (MLR), regression tree (RT), ensemble of
trees (ETs), support vector machine (SVM) and Gaussian
process regression (GPR). Specifically, we focused on the
complex relationship between BP and features from wearable
sensors (i.e. PTT and PPG waveform features) on elderly
subjects during maximal exercise stress test. The physio-
logical conditions was chosen based on the fact that abnor-
mal BP responses during and after exercise are associated
with heightened cardiovascular risk that may be unnoticed
by conventional resting BP screening methods. In addition
to its prognostic value, continuous monitoring of BP
during exercise is also desirable as it can be important exter-
nal trigger of cardiovascular events, especially in elderly
whose arteries are often stiffer and less able to absorb BP
surges [18].

II. METHODOLOGY
A. SUBJECTS
Sixty-two subjects (aged 59 ± 10 years) participated in the
experiment. Amongst them, 22 were healthy, 16 were with
different cardiovascular risk factors (i.e., hypertension), and
24 were diagnosed with different CVDs, demonstrating
large differences in CVD status in the population. Figure 1
shows the clinical characteristics of these subjects. The
study was approved by the Joint Chinese University of
Hong Kong – New Territories East Cluster Clinical Research
Ethics Committee. Each subject signed the informed consent
before participating in the experiment.
B. EXPERIMENT PROTOCOL

The experiment was conducted at least 1 hour after meal in a standard patient room with temperature kept at 25 °C. Specifically, each subject underwent a maximal stress test in supine posture in a bed with his/her feet putting on a bicycle ergometer. A mercury sphygmomanometer was connected to an automatic auscultative BP meter (GE Case 8000, Germany) by a Y-tube. The cuff BP was taken by a registered nurse every 2 minutes on the right arm of the subject. Continuous ECG and cardiac output (CO) were obtained by an impedance cardiographic device (Physio Flow PF-05, Macheren, France) from the subject’s chest. Continuous BP was measured by Finometer (Finapres Medical System, Netherlands) from the left arm. Continuous PPG was acquired from the left index finger by using an in-house made acquisition device. Details of the specifications of the in-house system can be found in [19]. All data during the whole experiment were sampled at 1 kHz by a data acquisition system (DI220, DATAQ Instruments WinDaq, USA) and stored for further analysis.

After a 10-min rest, the bed was tilted towards the left-hand side of the subject by 20°–30° in order to avoid potential hypotension due to compression of the inferior vena cava. The subject was asked to start riding the bicycle at workload that began at 25W and increased by 25W every 2 minutes until it reached the tolerant limit of the subject. The workload was then kept at the tolerant limit until the subject reached his/her target heart rate (HR) \[85\% \times (220 - \text{Age})\] or exhaustion. Then, the subject stopped riding and lie still on the bed to recover. The recovery phase lasted until CO returned to the baseline or at most for 15 min. The experimental protocol is presented in Figure 2.

The detailed protocol has been reported in [10]. Nonetheless, the subject pool included in this study was slightly different since subjects with Finapres BP failure or subjects whose PPG features cannot be extracted were excluded in the following analysis.

C. SIGNAL PROCESSING

Continuous ECG, PPG and Finapres BP were used in this study. To remove noise and artifacts, the acquired ECG were filtered by a zero-phase low-pass filter with cutoff frequency at 30 Hz. PPG and Finapres BP were processed by the same type of low-pass filter at 16 Hz. The raw and filtered signals were presented in Figure 3. The 1st and 2nd derivatives of PPG were obtained by applying a finite impulse filter (FIR) differentiator on the PPG and 1st PPG derivative, respectively. Beat-to-beat SBP and DBP were extracted from the peaks and foots of Finapres BP respectively.

D. FEATURE EXTRACTION & SELECTION

The subjects were required to perform a lower body cycling exercise whilst signals were acquired from their chest and fingers simultaneously. The signal quality was generally good, but occasionally affected by motion. Therefore, the noisy episodes were manually removed after visual inspection. Outliers of each feature were also removed by thresholds. Around 72% of data were used in this study.

As shown in Figure 3 and 4, characteristic points of the waveforms of ECG, PPG, as well as the 1st & 2nd derivatives...
of PPG were identified, from which a set of features were calculated. The peaks of the 2nd derivative of PPG were extracted based on the definition in [20]. Peaks a and b were defined as the first peak and first valley of 2nd PPG derivative, and peak e was identified as the highest peak after peak b in the same cardiac circle. Peaks c and d, which were defined as the first peak and valley following peak b respectively [20], were unobvious in this dataset and hence were not used in this study.

SBP, DBP and all extracted features were averaged for every 10 non-overlapping beats of data. An additional feature – RRIV were calculated by the standard deviation (SD) of RRI of the 10 beats. To test the significance of features relating to BP, correlation analysis was performed between each extracted feature and SBP, DBP respectively. Features that had correlation with BP lower than 0.1 were discarded and were not used in further analysis. Five personal demographic parameters including age, weight, height, body mass index (BMI) and gender of subject were added in the feature set. As gender is a categorical parameter, it is defined as 1 for male and −1 for female. All selected features were then standardized to have zero mean and unit standard deviation before the next stage of analysis.

E. MACHINE LEARNING MODELS

Five ML regression methods were under investigation. Selected features served as inputs, while BP was considered as the targets. All algorithms were implemented in MATLAB.

- Multiple linear regression (MLR): MLR attempts to model the relationship between two or more variables and a response variable by fitting a linear equation to observed data. It has the advantage of displaying a weight for each feature showing its contribution [21].
- Regression tree (RT): RT is interpreted by building a tree structure. It sub-divides or partitions the space into small regions to deal with nonlinear and complex datasets. The problem is that they may create over-complex structures that do not generalize well [14].
- Ensemble of Trees (ETs): it is a model consisting of a weighted combination of multiple regression trees which aims to create a strong leaner by pulling together a set of weaker learners. Boosted and bagged methods were considered in this study.
- Support vector machine (SVM): SVM is one of the most powerful ML algorithms for its capability of creating strong models with reasonable training effort and high noise tolerance [14]. Different kernels including linear, quadratic, cubic and Gaussian functions were tested to obtain optimal performance.
- Gaussian Process Regression model (GPR): GPR is nonparametric kernel-based probabilistic model and has recently been evaluated in cuffless BP estimation task [15]. In this study, 4 kernel functions: rational quadratic, squared exponential, Matern 5/2 and exponential functions were investigated in the study.

Five-fold cross validation was used to test the performance of the above regression models. Specifically, all data points were randomly divided into 5 equal folds. For each regression method, a model was built on 4-folds of data and tested in the remaining 1-fold of data. The process was iterated for 5 times and the averaged results were reported. To avoid possibly overfitting the training data in each fold, a heuristic procedure was adopted to determine the hyperparameters of each model [22]. Figure 5 shows the workflow of the study.

Unpaired student’s t-test was employed to test the significance of differences in physical parameters between the two groups in Table 1. The mean absolute error (MAE), mean error (ME), standard deviation (SD), as well as squared correlations ($r^2$) between reference and estimated BP were used as metrics for evaluating the different models.
TABLE 1. Demographic description of all subjects.

<table>
<thead>
<tr>
<th></th>
<th>Healthy</th>
<th>Risk Factor</th>
<th>CVD</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects (Male/Female)</td>
<td>22 (16/6)</td>
<td>16 (9/7)</td>
<td>24 (22/2)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>60±8</td>
<td>57±14</td>
<td>61±10</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>164.4±8.5</td>
<td>161.6±12.1</td>
<td>161.8±8.2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>63.0±8.7</td>
<td>69.6±23.3</td>
<td>69.8±14.7</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.3±2.2</td>
<td>26.1±5.8</td>
<td>26.5±4.3**</td>
</tr>
<tr>
<td>Rest SBP (mmHg)</td>
<td>134±20</td>
<td>138±16</td>
<td>136±18</td>
</tr>
<tr>
<td>Rest DBP (mmHg)</td>
<td>78±10</td>
<td>78±11</td>
<td>81±11</td>
</tr>
</tbody>
</table>

BMI: body mass index; SBP: systolic BP; DBP: diastolic BP; **: indicates P < 0.01 between Healthy and CVD group.

III. RESULTS

Table 1 summarizes the demographic characteristics of the sub-groups of subjects. There were no significant differences in age, height, weight and resting SBP & DBP between the three subject groups while BMI was significantly larger in the CVD patients than in the healthy subjects.

The average length of recording for each subject was 35 minutes. Average time taken for reaching target HR since the start of exercise was 16.5 minutes, and average duration of recovery was 13.8 minutes. The BP ranges were 75-280 mmHg for SBP and 36-157 mmHg for DBP respectively. Totally 101,270 beats of data were collected from all subjects. The distributions of the 10-beat averaged SBP and DBP were shown in Figure 6. Details of the features and correlation between each feature and SBP and DBP were listed in Table 2. Two features (e_aR and ea_Lag) were discarded for the estimation of SBP and three features (DC_Amp, fp_Lag and ba_Lag) were discarded for the estimation of DBP due to their low correlations with SBP and DBP respectively. Therefore, 20 and 19 features were used for SBP and DBP regression respectively.

Table 3 compares the performance of the 5 models in estimating SBP with the criteria set out by the AAMI standard. “Gaussian” and “rational quadratic” kernel worked best

TABLE 2. Description of features extracted from ECG, PPG and 1st & 2nd derivatives.

<table>
<thead>
<tr>
<th>Sources</th>
<th>Feature</th>
<th>Definition</th>
<th>Correlation with SBP</th>
<th>Correlation with DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG</td>
<td>RRI</td>
<td>Interval between R peaks of two consecutive ECG waveforms</td>
<td>-0.30</td>
<td>-0.36</td>
</tr>
<tr>
<td></td>
<td>RRIV</td>
<td>Standard deviation of RRI of 10 beats</td>
<td>-0.13</td>
<td>-0.12</td>
</tr>
<tr>
<td>ECG &amp; PPG</td>
<td>PATp</td>
<td>Interval between ECG R peak and peak of PPG in the same cardiac cycle</td>
<td>-0.23</td>
<td>-0.25</td>
</tr>
<tr>
<td></td>
<td>PATm</td>
<td>Interval between ECG R peak and peak of 1st PPG derivative in the same cardiac cycle</td>
<td>-0.51</td>
<td>-0.27</td>
</tr>
<tr>
<td></td>
<td>PATf</td>
<td>Interval between ECG R peak and foot of PPG in the same cardiac cycle</td>
<td>-0.52</td>
<td>-0.15</td>
</tr>
<tr>
<td>PPG</td>
<td>DC_Amp</td>
<td>Amplitude of DC component</td>
<td>0.20</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td>AC_Amp</td>
<td>Amplitude of AC component</td>
<td>-0.41</td>
<td>-0.36</td>
</tr>
<tr>
<td></td>
<td>PIR</td>
<td>Photoplethysmogram intensity ratio: the ratio of the PPG peak intensity to PPG valley intensity of one cardiac cycle as defined in [20].</td>
<td>-0.24</td>
<td>-0.15</td>
</tr>
<tr>
<td></td>
<td>AreaR</td>
<td>S2/S1; S1: shaded area between foot and the diastolic notch of PPG; S2: shaded area between diastolic notch and foot of next beat of PPG</td>
<td>-0.25</td>
<td>-0.14</td>
</tr>
<tr>
<td></td>
<td>fp_Lag</td>
<td>Interval between foot and peak of PPG</td>
<td>0.11</td>
<td>0.00</td>
</tr>
<tr>
<td>1st PPG derivative</td>
<td>pos_Amp</td>
<td>Amplitude of the most positive peak of 1st PPG derivative</td>
<td>-0.41</td>
<td>-0.37</td>
</tr>
<tr>
<td></td>
<td>neg_Amp</td>
<td>Amplitude of the most negative valley of 1st PPG derivative</td>
<td>-0.34</td>
<td>-0.27</td>
</tr>
<tr>
<td></td>
<td>np_Lag</td>
<td>Interval between most positive peak and most negative valley of 1st PPG</td>
<td>0.14</td>
<td>-0.12</td>
</tr>
<tr>
<td>2nd PPG derivative</td>
<td>b_aR</td>
<td>Ratio between amplitude of b and a peak of 2nd PPG</td>
<td>-0.33</td>
<td>-0.19</td>
</tr>
<tr>
<td></td>
<td>e_aR</td>
<td>Ratio between amplitude of e and a peak of 2nd PPG</td>
<td>0.03</td>
<td>0.18</td>
</tr>
<tr>
<td></td>
<td>ba_Lag</td>
<td>Interval between b and a peak of 2nd PPG</td>
<td>-0.20</td>
<td>-0.09</td>
</tr>
<tr>
<td></td>
<td>ea_Lag</td>
<td>Interval between e and a peak of 2nd PPG</td>
<td>0.04</td>
<td>-0.21</td>
</tr>
</tbody>
</table>
TABLE 3. Performance of the 5 models in estimating SBP and DBP.

<table>
<thead>
<tr>
<th></th>
<th>SBP</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MAE</td>
<td>ME ± SD</td>
<td>r²</td>
<td>ME</td>
<td>ME ± SD</td>
<td>r²</td>
</tr>
<tr>
<td><strong>MLR</strong></td>
<td>17.6</td>
<td>0.0 ± 22.7</td>
<td>0.56</td>
<td>9.7</td>
<td>0.0 ± 12.6</td>
<td>0.42</td>
</tr>
<tr>
<td><strong>RT</strong></td>
<td>7.9</td>
<td>0.1 ± 12.1</td>
<td>0.87</td>
<td>4.9</td>
<td>-0.0 ± 7.2</td>
<td>0.82</td>
</tr>
<tr>
<td><strong>ETs</strong></td>
<td>6.9</td>
<td>-0.0 ± 9.8</td>
<td>0.92</td>
<td>4.3</td>
<td>-0.0 ± 6.1</td>
<td>0.87</td>
</tr>
<tr>
<td><strong>SVM</strong></td>
<td>6.1</td>
<td>-0.1 ± 9.3</td>
<td>0.93</td>
<td>4.0</td>
<td>0.2 ± 5.8</td>
<td>0.88</td>
</tr>
<tr>
<td><strong>GPR</strong></td>
<td>4.8</td>
<td>0.0 ± 6.9</td>
<td>0.96</td>
<td>3.4</td>
<td>0.0 ± 4.9</td>
<td>0.91</td>
</tr>
<tr>
<td><strong>AAMI standard</strong></td>
<td>-</td>
<td>≤5 ± 8</td>
<td>-</td>
<td>-</td>
<td>≤5 ± 8</td>
<td>-</td>
</tr>
</tbody>
</table>

Remark: units for MAE, ME and SD are mmHg.

for SVM and GPR model respectively. “Bagged” method showed better results than “Boosted” method for the ETs model. The MAE, ME, and SD of the estimation differences, as well as the squared correlations between the estimated and reference BP were presented. GPR model achieved the lowest MAE and SD, as well as the highest correlation between the estimated and reference values for both SBP and DBP.

Bland-Altman plots and scatter plots for GPR model were shown in Figure 7. Figure 8 shows the evaluation of the GPR model under the IEEE standard for wearable cuffless blood pressure measuring devices (IEEE Standard P1708) [23]. Absolute mean differences vs. standard deviation of differences between the reference and estimated BP were shown for each subject. Figure 9 shows the best case and the worst case scenarios for the estimation of SBP by the GPR model.

**IV. DISCUSSION**

Continuous and ubiquitous BP measurement has been a popular research topic for the last two decades. PTT/PWV based approaches enable cuff-less and wearable measurement of BP. Most of the previous studies focused on deriving the
mathematical models between PTT and BP, and estimating BP mainly from PTT.

Nevertheless, the PTT-BP relationship exhibits high non-linearity and complexity [10]. Influences of confounding factors such as PEP and vascular tone must be taken into account in order to ensure accurate measurement in dynamic situations. Under these situations, the traditional mechanism-based models are insufficient to describe the complex system and realize reliable BP estimation. Due to the increasingly powerful computational resources, data-driven cuff-less BP measurement based on ML techniques as presented in this study is achievable nowadays. Beats-to-beats estimation of BP without a cuff is possible.

A. ML BASED CUFFLESS BP ESTIMATION DURING EXERCISE

Different ML techniques have been studied for estimating cuffless BP from ECG and/or PPG sensor features, including regularized linear regression [14], decision tree regression [14], and adaptive boosting [14], ridge linear regression [16], multilayer perceptron neural network [16], SVM [14], [16], random forest [14], [16], Deep Belief Network [24], and artificial neural network (ANN) [17]. These studies attempted to estimate BP using data collected either from subjects under relatively stable conditions in caring centers of hospitals [16], [24] or from a public physiological database (i.e. MIMIC II) [14], [17].

Measuring BP during exercise is challenging but important, as exercise can be an important trigger of cardiovascular events. Moreover, accurate and continuous tracking of BP in dynamic conditions can provide novel opportunities for research and clinical assessment [25]. Studies that examined ML-based continuous BP estimation during exercise were few. One study [26] examined cuffless BP estimation before and after rope skipping exercise using MLR and SVM; however, the accuracy was low during follow-up experiments. Another study [21] estimated cuffless SBP by MLR during physical exercise, using PPG and ECG sensor features collected at rest for calibration. Both studies were conducted on healthy young subjects with exercise intensities that were much smaller than our study. To our best knowledge, our work is the first study to investigate ML-based approaches for the continuous beats-to-beats estimation of cuffless BP during physical exercise on a general elderly population. These subjects were more susceptible to develop cardiovascular events than the healthy, young subjects when their cardiovascular system were stressed.

B. CHALLENGES IN THE EXTRACTION OF PPG FEATURES

PPG contour analysis provides valuable information about the cardiovascular system. For example, time interval and amplitude ratio between the first and second PPG peaks are related to arterial properties and vasomotor tone [13], [27]. PPG AC amplitude is determined by the cardiac synchronous changes in the blood volume with each heartbeat, while its DC amplitude is influenced by respiration, sympathetic nervous system activity and thermoregulation. Both parameters were able to partly reflect the regulation of the cardiovascular system during exercise. On the other hand, the PPG waveform is also affected by temperature and sensor-contact force [28]. In this study, PPG signal was collected from the subjects’ finger which was kept still during the experiment in order to minimize the influence of contact force. Finger temperature reflected thermoregulation, which is weakly related to SBP [29] and confirmed in the correlation analysis shown in Table 2.

Features related to the second peak of PPG were not included in this study in spite of their physiological meaning. We observed that the PPG morphology evolved along with the progression of graded exercise. The PPG waveforms of the same subject have either one significant peak, multiple peaks or no obvious peak at diastole during different phases of exercise. In fact, it is well accepted that PPG includes three elements, i.e., main forward wave and two reflection waves, i.e. a tidal wave and a dicrotic wave. The observation may due to the unnoticeable first reflection wave and highlighted second reflection wave, and reduced PWV caused by muscle vasodilation and decreased muscle vascular resistance during exercise in response to increased demand of oxygen and other nutrients for muscle. Meanwhile, motion artifacts may also contribute to the phenomenon. Therefore, only features from PPG and its derivatives that were relatively stable and robust during the whole process were used.

Around 28% of data were discarded due to waveform distortions caused by motion in one of the signals, revealing challenges of feature extraction in such a condition. To address this question, sensor design and other features that represent the waveform, such as PPG spectral characteristics, can be investigated in the future. Other methods such as a genetic algorithm-based feature selection method can also help in identifying the most appropriate features for cuffless BP estimation [26].

C. POTENTIAL OF THE PROBABILISTIC NONPARAMETRIC MODEL

Five ML regression models were investigated in this work. The performance of MLR, RT and ETs were unsatisfactory, indicating that the relationship between BP and the wearable sensor features were non-linear. The differences between the reference and estimated DBP using RT, ETs, SVM were within 5 ± 8 mmHg; however, the estimation differences were above 5 ± 8 mmHg for the estimation of SBP using these models. On the other hand, the probabilistic nonparametric GPR model fully complied with the AAMI standard in terms of both ME and SD and also outperformed the other four models in terms of MAE for the estimation of both SBP and DBP. In fact, GPR can be interpreted as a Bayesian version of SVM. It is therefore not surprising that SVM with Gaussian kernel obtained the second best results in this study. Specifically, being a probabilistic nonparametric ML approach, GPR did not attempt to fit the data by using a fixed class of function. GPR can avoid errors induced by
the inappropriate assumption on the underlying functions used by the parametric methods like MLR or SVM with linear kernels. Instead, GPR considers an infinite number of functions by assuming a prior over them. As practical problems normally ask only for properties of functions at a finite number of data points, GPR is computationally tractable. Moreover, GPR presents great flexibility in the functions when additional observation arrives [30].

**V. CONCLUSION**

The main objective of this study is to evaluate five ML techniques in modeling the complex relationship of BP and wearable sensor features during supine cycling exercise in a cohort of elderly subjects. The results suggested that the probabilistic nonparametric GPR method has the potential to describe this relationship and achieve an estimation difference that is acceptable by both the AAMI and IEEE Standard for BP measuring devices. The estimation differences (MAE, ME ± SD) for the GPR models were (4.8, 0.0 ± 6.9 mmHg) and (3.4, 0.0 ± 4.9 mmHg) for the 10-beat SBP and DBP averages, respectively. None of the other four methods can model the estimation of SBP to an estimation difference that is acceptable by the AAMI or IEEE Standard. The work is fundamental for the future development of cuffless BP estimation systems, particularly in selecting the optimal estimation models for these devices.

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