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Novel Cuffless Blood Pressure Estimation Method Using a Bayesian Hierarchical Model

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***Abstract* — Continuous blood pressure (BP) monitoring is important for the prevention and early diagnosis of cardiovascular diseases. Cuffless BP estimation using pulse arrival time (PAT) via a mathematical model which enables continuous BP measurement has recently become a popular research topic. In this study, simultaneous biomedical signals from ten healthy subjects were acquired by electrocardiogram (ECG) and photoplethysmogram (PPG) sensors and the continuous reference BP data were collected by a cuff-based Finometer PRO BP monitor. A hierarchical model was applied to estimate the parameters of a nonlinear model which in turn is used to estimate systolic blood pressure (SBP) using PAT with few calibration measurements. The mean absolute difference (MAD) between the estimated SBP and reference SBP is 4.35±1.43 mmHg using the proposed hierarchical model with three calibration measurements and is 4.36±1.17 mmHg with a single calibration measurement.**

***Index Terms*—Cuffless blood pressure estimation, pulse arrival time, hierarchical models**

I. INTRODUCTION

Blood pressure (BP) is the pressure exerted by blood on the artery walls as the blood circulates through the body. It is considered as one of the most important physiological parameters in the evaluation of human health. Uncontrolled high blood pressure increases the risk of serious health problems, including heart attack and stroke [1].

A number of continuous cuffless BP measurement methods have been developed over the last decade and most of them have employed PAT and PTT (pulse transit time) which can be approximated by the time differences between ECG R peaks and different landmarks of PPG waveforms. Several BP estimation models were introduced and their performances for BP estimation using PAT which is the time difference between ECG R peak and the point with maximum gradient on the rising edge of the PPG were compared in [2]. This research indicated that nonlinear models are better than a linear one in continuous BP estimation. In our previous work [3], a new time interval which is the time difference between ECG R peak and ballistocardiogram (BCG) J peak was employed for SBP estimation with an exponential model, and the SBP estimation based on this new time interval was more accurate than the SBP estimation obtained using PAT. However, most of the related studies employed the least squares method to optimize the model parameters which makes it difficult to estimate BP for a group of subjects with a generalized model. Also, it performs poorly on a small dataset and does not provide uncertainties of estimations.

In hierarchical (multilevel) Bayesian regression modelling, the regression coefficients are themselves given a model, whose parameters are also estimated from data. Compared with classical regression, hierarchical modeling is almost always an improvement, as shown for example in the prediction of home radon levels in U.S. counties [4]. In this study, the SBP which is a more frequent cardiovascular risk factor than diastolic blood pressure (DBP) [5] will be estimated using a one-level hierarchical model by optimizing the parameters of the nonlinear relationship between PAT and SBP at both individual level (each subject) and group level (between subjects). The feasibility of estimating SBP with few calibrations (three calibration points and one calibration point) using a hierarchical model was verified.

This paper is organized as follows. Section 2 describes the study population, experimental protocol, instrumentation, and signal pre-processing approaches. In Section 3, a nonlinear model which was used to express the relationship between BP and PAT is introduced, and the methodologies of model parameter optimization using a hierarchical model are described. Section 4 shows the performance of SBP estimation using a hierarchical model in comparison against the ordinary least squares (OLS) method. Finally, conclusions and future work are presented in Section 5.

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II. MATERIALS & METHODS

2.1 Study population and experimental protocol

The aim of this work is to estimate SBP using PAT via a hierarchical model. Ten healthy subjects (5 males and 5 females, 28.3±8.3 years' old) without known cardiovascular diseases or hypertension participated in the study. For each participant, ECG, PPG and continuous reference BP were recorded simultaneously for 10 minutes. The performance of cuffless BP measurement was evaluated with the subjects at rest and while performing the Valsalva maneuver (VM), which is known to induce dynamic BP changes, at pre-defined time points. Specifically, participants were required to perform one VM every 2 minutes for a total of 5 to 6 VMs performed during 10 minutes' data collection. The experimental protocol was approved by the University of Ottawa Research Ethics Board.

2.2 Signal acquisition system

The ECG signal was collected from both left and right index fingers using a pair of Lead I ECG dry electrodes. An optical PPG sensor was placed on the left wrist above the ulnar artery. The reference beat-to-beat BP was collected by a continuous Finometer PRO BP monitor (Finapres Medical System BV, The Netherlands) using a cuff placed on the middle finger. The ECG and PPG signals were digitized at 2000 Hz using a DAQ card (National Instrument USB 6002, 16 bits). A LabVIEW program (LabVIEW 2016, National Instruments) displayed the digital biomedical signals in real time and saved them for subsequent analysis. The signals were processed and the BP estimation model was developed in Python (3.8.3) with two main libraries PyMC3 (3.8) and ArviZ (0.6.1) for probabilistic programming.

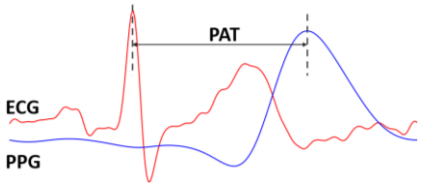

Figure 1. Morphological definition of PAT

2.3 Signal pre-processing and PAT extraction

Since the ECG and PPG signals were collected using one personal computer and beat-to-beat reference BP waveforms were collected using Finometer, all these three waveforms were synchronized by checking timestamps and extracting intersections from the dataset before further processing. A 60 Hz notch filter was applied to remove power-line noise. A third-order Butterworth bandpass filter with passband of 0.5-25 Hz was applied on ECG and 0.5-7 Hz on PPG signal.

In this study, the beat-to-beat PAT is extracted by calculating the time difference between ECG R peaks and PPG systolic peaks for every cardiac cycle as shown in Figure 1. PAT outliers were removed (Z-score>3 or Z-score<-3) along with corresponding SBP values. Similarly, SBP outliers were removed along with corresponding PAT values, and a median filter was applied to smooth the simultaneous PAT and SBP data.

III. CUFFLESS BLOOD PRESSURE ESTIMATION

3.1 Cuffless BP estimation model

PTT is related to pulse wave velocity (PWV) which is further related to BP. The theoretical relation is expressed by Moens-Korteweg equation [6] which models the relationship between PWV and the incremental elastic modulus of the arterial wall or its distensibility.

$$PWV = \frac{L}{PTT} = \sqrt{\frac{E \cdot h}{2r\rho}} \tag{1}$$

where L is the pulse transit distance, PTT is the pulse transit time, ρ is the blood density, r is the inner radius of the vessel, h is the vessel wall thickness, and E is the elastic modulus of the vascular wall. There exists an empirical exponential relation between elastic modulus E and BP [7].

$$E = E_0 \cdot \exp\left(\kappa \cdot (BP - BP_0)\right) \tag{2}$$

where κ is a constant, E_0 and BP_0 are nominal values of the Young's modulus and blood pressure, respectively. A logarithmic dependency between BP and PTT can be extracted from (1) and (2) by assuming all other parameters are constant. Thus, the relationship between PTT and BP can be expressed by:

$$BP = \alpha + \beta \cdot \ln(PTT) \tag{3}$$

The coefficients α and β are optimized based on the acquired simultaneous BP and PTT. In this study, we approximated the PTT with PAT and therefore the SBP values can be estimated by applying the extracted coefficients in $SBP_{est} = \alpha + \beta \cdot \ln(PAT)$ for new PAT measurements.

3.2 Cuffless BP estimation using classical estimates

The regression between the PAT and SBP can be extracted by considering all PAT and SBP measurements from all subjects as a whole (complete pooling), or it can be optimized for different individuals (no pooling) which is commonly employed for cuffless BP estimations. However, both methods have drawbacks. At one extreme, the complete pooling method neglects the individual differences such as arterial stiffness and blood density and gives identical estimates for all subjects. At the other extreme, the no-pooling model can cause overfitting on a small dataset. Therefore, the hierarchical model which is a middle ground to both of these extremes is more reasonable for this application.

3.3 Cuffless BP estimation using a hierarchical model

There are several ways to optimize the parameters for the proposed nonlinear model (3). One commonly used method is known as least squares fitting which returns the values of α and β yielding the lowest average quadratic error between the observed BP and the predicted BP. An alternative to optimization is to generate a probabilistic model which can obtain the best values of α and β together with an estimation

of the uncertainty about the parameter's values [8].

In this study, the nonlinear model (3) can be probabilistically expressed as follows:

$$SBP \sim \mathcal{N}(\mu = \alpha + \beta \cdot \ln(PAT), \epsilon) \quad (4)$$

That is, the data vector SBP is assumed to be distributed as a normal distribution with a mean of $\alpha + \beta \cdot \ln(PAT)$, and a standard deviation of the measurement noise ϵ.

The probabilistic model and the OLS method should have similar performance in optimizing model parameters on a large dataset. However, the parameters α and β are unbounded when the dataset is extremely small, for example, only one data point. This can be solved by selecting strong priors for the unknown parameters α and β. Another way to convey information is by defining hierarchical models, since hierarchical models allow information to be shared between subjects, shrinking the plausible values of the estimated parameters [8].

In a hierarchical model, the parameters can be estimated directly from the data by placing shared priors over them, instead of fixing the parameters of our priors to some constant numbers. These higher-level priors are known as hyperpriors and their parameters are hyperparameters, and informative priors will be assigned based on the fact that the hyperpriors will be shared between subjects and their posteriors will shrink to the group mean. The α and β derived from each subject's PAT and SBP values are -1 ± 30.85 and -116.35 ± 32.24 using OLS method. Thus, the graphical representation of the one-level hierarchical model for this study with the definition of the parameters and priors for each level is shown in Figure 2.

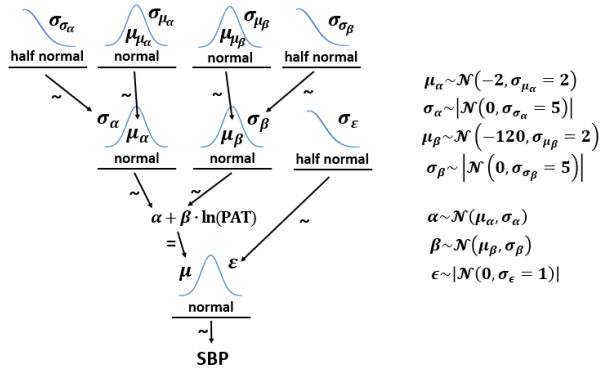

Figure 2. The Kruschke diagrams of the proposed hierarchical model and the selection of the hyperpriors.

As shown in Figure 2, the parameters α and β that mainly determine the distribution of BP have their priors in normal distributions. The hyperparameters μ_α and μ_β have their hyperpriors in normal distributions and the hyperparameters σ_α and σ_β have their hyperpriors in half-normal distributions. The model parameters of interest are estimated using posterior distributions which are determined by analytical integration. The Markov chain Monte Carlo (MCMC) method was employed for parameter estimation and No U-turn Sampler (2000 samples for each channel with 1000 tuning samples) was used to evaluate the posterior distributions.

IV. Results

In this study, we aim to evaluate the feasibility of the proposed hierarchical model in cuffless BP estimation via a nonlinear model, and a real-world application which is to estimate BP for a new subject with some calibration measurements of PAT and BP is demonstrated. For example, there is a PAT and BP database which is collected from a number of different subjects available for cuffless BP estimation. A new user collects ECG and PPG signals using a wearable device and measures the BP using a cuff-based device several times, and the averaged PAT values for each measurement and the corresponding BP values can be considered as calibration measurements. With the database and the new calibration measurements, the hierarchical model will be trained and the parameters for the nonlinear model (3) will be optimized and then the BP can be estimated with new PAT measurements for this user.

4.1 Cuffless BP estimation with three calibrations

In this study, a ten-fold cross validation was employed to evaluate the generalization of the hierarchical model in SBP estimation. For each fold, the collected data were split into a training set which includes nine subjects' beat-to-beat PAT and SBP values (database) and three PAT and SBP measurements (new user's calibration measurements) of one remaining testing subject to train the hierarchical model. The mean SBP (normal BP), maximum SBP (increased BP) and the minimum SBP (decreased BP) with their corresponding PAT values of the testing subject's first fifty measurements were selected as three calibrations. SBP estimations of the testing subject are validated against a testing set which is the rest of that subject's PAT and SBP measurements. Also, the OLS method was applied for testing subject's calibration points as a comparison of SBP estimation accuracy. The optimized parameters α and β, mean absolute difference (MAD) between the estimated SBP and reference SBP for the testing subject obtained using both OLS method and hierarchical model are shown in Table I. The extracted regressions obtained by applying hierarchical model and OLS method on the subject 7's calibration measurements with the true regression line of the testing set are shown in Figure 3 (a) as an example.

4.2 Cuffless BP estimation with a single calibration

In this section, we will assume an extreme condition that the new subject only conducts a single calibration. As before, a ten-fold cross validation was applied. For each fold, the training set includes nine subjects' beat-to-beat PAT and SBP values (database) and the mean PAT and SBP values of the remaining one subject's first fifty measurements (new user's calibration measurement) to train the hierarchical model, and the testing set is the rest of that subject's PAT and SBP measurements. The MAD between the estimated SBP and reference SBP for the testing subject obtained using hierarchical models are shown in Table II. The extracted

regression obtained by applying hierarchical model on the subject 7's calibration measurement and the real regression line of the testing set are shown in Figure 4 (a) as an example.

Table I. The optimized parameters α and β, MAD between the estimated SBP and reference SBP using OLS method and hierarchical model with three calibration measurements.

Subject #	OLS method			Hierarchical model		
	α	β	MAD (mmHg)	α (mean ± std)	β(mean ± std)	MAD (mmHg)
1	-573.89	-675.57	16.72	-3.5±10.00	-119.2±9.75	4.52
2	-244.87	-355.19	4.65	-9.1±9.82	-113.5±10.12	2.89
3	-214.78	-364.78	8.28	3.4±9.94	-127.5±10.74	6.12
4	-70.98	-189.30	3.54	-5.1±8.02	-118.4±8.56	2.94
5	-121.22	-201.76	3.70	-12.6±10.09	-104.5±9.16	4.31
6	-136.66	-274.03	3.49	7.1±10.27	-129.0±10.35	3.23
7	-263.08	-334.97	6.12	-8.7±10.96	-114.1±9.55	3.62
8	-426.16	-618.08	8.12	14.4±9.57	-130.5±10.52	4.29
9	-410.47	-501.61	6.49	-8.7±9.97	-114.6±9.67	3.91
10	-63.33	-185.31	8.73	0.2±9.75	-122.3±9.70	7.68
mean±std	-252.54±161.05	-370.06±166.73	6.98±3.77	--	--	4.35±1.43

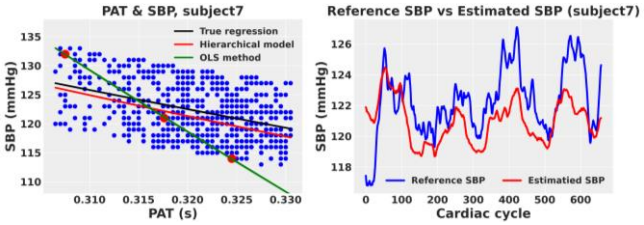

Figure 3. (a) Regression curves for one subject for the case when only 3 PAT-SBP pairs are used as a training set (red dots). The remaining PAT-SBP pairs (testing set) are not used for calibration and are shown as blue dots. Regression curves include the green line obtained using only red points based on OLS (OLS method), red line obtained using only red points based on the hierarchical model (Hierarchical model) and black line obtained using blue points using OLS (True regression); (b) the estimated SBP trend (red) using the hierarchical model and the reference SBP trend (blue) of the testing set.

V. Conclusion and Future Work

As shown in Table I, the SBP estimations using a hierarchical model are almost always better than using OLS method with three calibration measurements. It can be observed from Figure 3 (a) that the regression line extracted from three calibrations of subject 7 using the hierarchical model is almost parallel to the true regression line derived from testing set using the OLS method. As shown in Figure 3 (b) and Figure 4 (b), the hierarchical model can also track the BP trend which is derived by averaging BP values using the moving average with the window length of 30 beats. As shown in Table II, the SBP estimations using a hierarchical model with only one calibration measurement are almost identical to the SBP estimation using three calibration measurements and the estimation performance is expected to be improved with more calibrations performed in different scenarios (rest, exercise, sleep etc.). Furthermore, the estimated regression using the hierarchical model with one calibration is parallel to the true regression extracted from the testing set, which means the hierarchical model can estimate BP accurately with few calibrations. Additional limitation in using hierarchical models is that it is necessary for the training of the model to have a subset of subjects for whose beat-to-beat PAT-SBP measurements are obtained.

In the future, we will include DBP and MBP for estimation and also quantify the prediction uncertainty. A larger dataset including more subjects and longer data collection durations will be employed, for example, the MIMIC-III clinical database [9].

Table II. The MAD between the estimated SBP and reference SBP using a hierarchical model with one calibration measurement (unit: mmHg)

	Subject #										
	1	2	3	4	5	6	7	8	9	10	mean±std
MAD	4.90	3.24	4.61	2.92	5.16	3.56	3.78	4.32	3.89	7.20	4.36±1.17

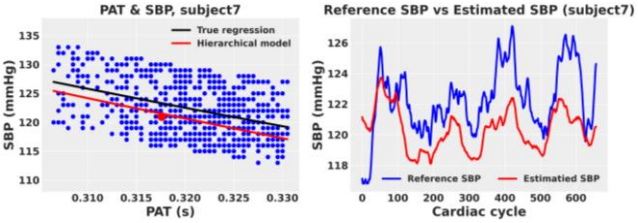

Figure 4. (a) Regression curves for one subject for the case when only 1 PAT-SBP pair is used as a training set (red dot). The remaining PAT-SBP pairs (testing set) are not used for calibration and are shown as blue dots. Regression curves include the red line obtained using only red point based on the hierarchical model (Hierarchical model) and black line obtained using blue points using OLS (True regression); (b) the estimated SBP trend (red) using the hierarchical model and the reference SBP trend (blue) of the testing set.

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