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SCUOLA DI INGEGNERIA INDUSTRIALE E DELL'INFORMAZIONE

Executive Summary of the Thesis

End-to-end deep neural network and virtual sensing techniques: An Arterial blood pressure waveform reconstruction using Soundi® device

Laurea Magistrale in Biomedical Engineering - Ingegneria Biomedica

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1. Introduction

Arterial pressure is a physiologically significant parameter in monitoring human health. It provides crucial insights into the functioning of the cardiovascular system and can reveal pathological conditions such as hypertension, hypotension, and other related diseases. This is a key factor in preventing cardiovascular diseases. It is often referred to as a "silent killer" since it does not cause visible symptoms but can lead to premature death. According to the World Health Organization, hypertension represents a global public health crisis and more than 4 million people die of cardiovascular diseases every year only in Europe, and more than 17 million worldwide [4, 5]. Therefore, early detection and continuous monitoring of blood pressure can be essential in preventing cardiovascular diseases and saving lives. Significant efforts are being directed towards studying new techniques that allow for simple monitoring of these parameters due to the difficulties associated with traditional invasive and non-invasive monitoring methods. Traditionally, arterial pressure measurement has been performed using non-invasive devices, such as mercury manometers or sphygmomanometers. However, these methods show limitations in terms of practicality and the ability to continuously monitor pressure. In recent years, the advent of artificial neural networks and machine learning has opened up new perspectives in the non-invasive prediction and monitoring of arterial pressure [1, 6]. Deep Neural Networks (DNNs) are particularly suited to handle complex data and learn patterns from physiological signals. The use of deep learning has gained increasing relevance in modern medicine, especially in the field of medical imaging, where it has become a key tool for diagnostic support. In the present study, deep learning-based neural networks are employed, creating an end-to-end approach for arterial pressure monitoring using a set of signals recorded with Soundi ®. An example of CNN application in the medical field is the U-Net, used for analyzing magnetic resonance and CT images. By using a novel device called Soundi ®, various physiological and non-physiological signals are recorded, which are then utilized for reconstructing the arterial pressure waveform using a deep learning-based neural network. This procedure creates a virtual sensor, aiming to monitor a target signal, in this case, the physiological pressure signal, based on other signals recorded with a device that does not have the function of directly monitoring the ABP signal. Using the traditional mathematical model the PTT regression is computed, and compared with the deep neural network. These networks are capable of automatically extracting relevant information from the data, enabling accurate estimations of arterial pressure, without the use of preprocessing part for the mark of the fiducial point.

2. Material and Methods

2.1. Employed software

The presented study was fully implemented using Python 3.7 programming language. The use of a single High-level language allowed for a unified workflow for all the tools required by the project. Moreover, Python is an open-source language, widely supported by a range of libraries and modules, including Keras, TensorFlow, Scikit-learn, NumPy, Pandas, SciPy, Plotly, and Matplotlib, which were utilized in this project for machine learning and artificial intelligence procedures, high-performance data analysis and dataframe manipulation, advanced computing in signal processing and mathematics, as well as data visualization and interactive figure creation. Since the work was conducted in collaboration, GitHub was used for shared files and update management.

2.2. Finapres Finometer® PRO

The Finapres Medical Systems BV (NL) offers the Finometer Finapres PRO ®, a medically certified device that utilizes a finger cuff to estimate continuous signals of blood pressure in a pulsatile manner. The device employs the Volume-Clamp technique, originally developed by Penaz et All. [8], to reconstruct the blood pressure waveform. In the research study, the Finometer Finapres PRO Finometer® was used to collect reference blood pressure waveforms for training the deep network and validating model predictions. Along with blood pressure estimation, the device also provides various hemodynamic parameters such as stroke volume, total peripheral resistance, cardiac output, pulse rate variability, and baroreflex sensitivity analysis. To ensure accuracy, the reconstructed blood pressure was periodically calibrated against brachial measurements using an upper arm cuff [3].

Figure 1: Finapres® device for ABP monitoring

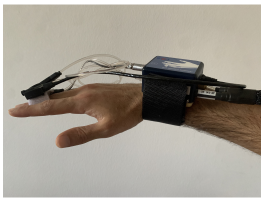

Figure 2: Cuff sensor for ABP finger acquisition by plethysmographic sensor

2.3. Soundi ®

The device is used for signal acquisition in this study is Soundi ®, a chest-worn sensor developed by Biocubica Srl (Milan, Italy) Figure 3. It is capable of simultaneously recording multiple physiological signals, including electrocardiographic, photoplethysmographic, acoustic, accelerometer, bioimpedance, and temperature (both body surface and ambient) for up to 24 hours. The device has a circular shape with a diameter of less than 6 cm and a thickness of approximately 1 cm, weighing no more than 40 grams. It is currently undergoing the CE marking procedure to become a certified medical device of class II, and it has been patented at the European level (Patent No. EP3248541A1). To ensure secure attachment to the chest during use, the device uses medically certified double-sided tape.

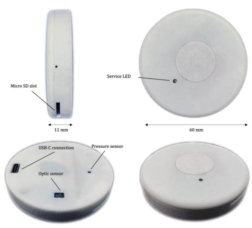

Figure 3: Soundi® device and its sensors.

2.4. Signals Processing

To create the dataset, it is necessary first to perform a signal analysis. These signals can be divided into two main blocks, those recorded with the Soundi ® sensors are:

- Acceleration signals;

acceleration signal				
signal	FilterType	Order	Low[Hz]	High [Hz]
A_x	Bessel	2	0.05	1
A_y	Bessel	2	0.05	1
A_z	Bessel	2	0.05	1
A_M	Bessel	2	0.05	1

Table 1: Filtering parameters adopted for Acceleration signals

- Plethysmographic signals;

acceleration signal				
signal	FilterType	Order	Low[Hz]	High [Hz]
Green	Bessel	2	0.05	10
Red	Bessel	2	0.05	10
Infrared	Bessel	2	0.05	10

Table 2: Filtering parameters adopted for PPG signals

- ECG and Bioimpedance;

acceleration signal				
signal	FilterType	Order	Low[Hz]	High [Hz]
ECG	Bessel	2	5	25
	Notch	2	36	/
BioImp	Bessel	2	0.05	10

Table 3: Filtering parameters adopted for ECG and Bio signals

- Phonocardiogram;

acceleration signal				
signal	FilterType	Order	Low[Hz]	High [Hz]
PCG	Butter	2	10	40

Table 4: Filtering parameters adopted for PCG signals

- Ambient temperature;
- Body temperature;

Those recorded by the Finapress are:

- Brachial ABP;

Signal	FilterType	Order	Low cut-on frequency	High cut-off frequency
ABP	Bessel	2	25	/

Table 5: Filtering parameters adopted for ABP Brachial signals

- Finger ABP;

Signal	FilterType	Order	Low cut-on frequency	High cut-off frequency
ABP	Bessel	2	25	/

Table 6: Filtering parameters adopted for ABP Finger signals

In addition, a mask is created to be used in training to exclude segments where the Finapress calibration is present. In this case, only the ABP signal acquired with the finger cuff is analyzed. Respiration signals are also added to these, derived respectively from the acceleration magnitude signal, the plethysmographic signal, and the acoustic signal. The first common operation for signals acquired through Soundi ® sensors (IMU, Acoustic sensor, ECG, PPG) is to extract and process the signals saved on the MicroSD. These signals are sampled at different frequencies depending on the sensor with which the signal is acquired, so they are interpolated around the central sampling frequency of 400 Hz. Since the Finapress has a sampling frequency of 1 kHz, it is also resampled at 400 Hz. Signals are processed and divided into 10-second windows without overlapping to be able to eliminate artifacts caused by the device. With the use of Jittering first, noise is added with a scale of 0.01 to the signal. Next, the signal was scaled and time-warped, effectively doubling the initial dataset by adding the newly processed signals. The *tsaug* library is used, which allows the application of the main algorithms previously described. The parameters used are shown in Table 7 [7].

type	Algorithm	Scale	max drift	drift point
Jittering	ts.AddNoise	0.02	/	/
Drift	tsaug.Drift	/	0.03	1

Table 7: **Tsaug** parameters for Data augmentation

Through a Labelling procedure, utilizing a simple interface developed in Python, chunks containing disturbances in the target signal or poor

PPG and ECG signals are eliminated. Upon completion of the signal acquisition procedure and labeling procedure, the dataset utilized to train the network is constructed. The subject metadata is presented in Table 8.

Item	Value
N° of subjects	25
Gender	
Woman	7 subjects
Man	18 subjects
Age	
Mean	26 years
STD	20 years

Table 8: Subjects Information

	Max (mmHg)	Min (mmHg)	Mean (mmHg)	STD (mmHg)
SBP	200.103	83.882	130.726	22.00
DBP	117.584	49.054	81.545	14.754
MBP	163.586	62.565	97.839	17.556

Table 9: Dataset description of all subjects enrolled

	Max (mmHg)	Min (mmHg)	Mean (mmHg)	STD (mmHg)
SBP	170.80	81.973	135.36	18.90
DBP	113.18	59.86	87.39	12.07
MBP	131.15	67.23	103.38	13.71

Table 10: Dataset description of Subject00

Table 9 presents the average values of systolic, diastolic, and mean pressures for the entire dataset, which include resting and pedaling measurements. These values have a high standard deviation. Table 10 provides the values specifically for Subject00, with six recordings totaling 134.5 minutes. The explained datasets are used for subject-independent and subject-dependent analysis. Notably, diastolic and mean pressure values have a low standard deviation, while systolic values show a significantly higher standard deviation. Some recorded values during the acquisition phase were outside the acceptable physiological range, especially for systolic pressure. This could potentially affect the performance of the proposed models.

3. Artificial Inteligence

The model consists of two distinct steps. The first step involves using one of the three proposed networks, taking the dataset's signal bank as input, and producing an intermediate arterial blood pressure (ABP) signal. The second step employs a ResNet that takes the signal predicted by the intermediate model as input and generates the final ABP signal as output. This second step helps the network in reassembling the temporal shift and reducing noise introduced by point-to-point prediction variability. The first proposed model for intermediate ABP calculation is a traditional U-Net, as shown in Figure 4. It is initialized with the parameters presented in Table 11. The model consists of a conventional yellow encoder module and a purple decoder module, connected by blue skip connections, with a red Bottleneck module.

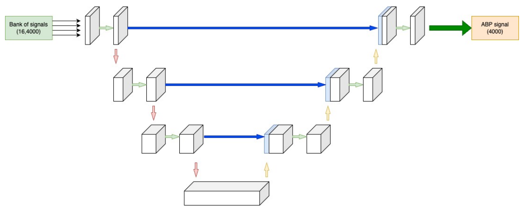

Figure 4: In this Figure is reported the classical architecture of U-Net

Models	Loss function	Optimizer	Initial Filter	Epochs	Batch size
U-Net	MSE	Adam	32	500	64

Table 11: U-Net Hyperparameters

The second model, illustrated in Figure 5, differs from the previous one by introducing a Gated Recurrent Unit (GRU) layer with a single unit positioned at the output of the decoder. The network is initialized with the parameters listed in Table 12.

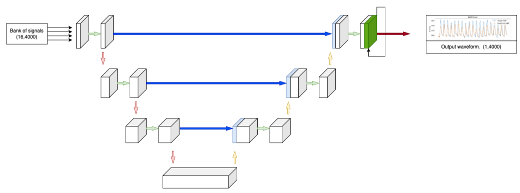

Figure 5: developed diagram of GRU-Net

Models	Loss function	Optimizer	Initial Filter	Epochs	Batch size
GRU-Net	MSE	Adam	32	500	64

Table 12: GRU-Net Hyperparameters

The third model, shown in Figure 6, features a specific characteristic developed specifically for the considered project. As illustrated in the encoder, there are three different branches designed to consider the frequency band of their respective input signals. In this case, the signal bank for each chunk is divided among the three branches based on its frequency content. The initial parameters of the network are listed in Table 13.

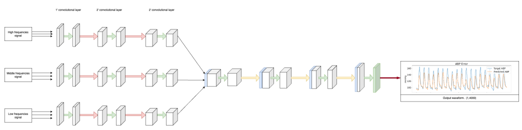

Figure 6: Developed diagram of 3GRU-Net

Models	Loss function	Optimizer	Initial Filter	Epochs	Batch size
3GRU-Net	MSE	Adam	32	500	64

Table 13: 3GRU-Net Hyperparameters

In the second step, the output calculated by the respective network used is fed as input to the ResNet, which is positioned in cascade with the first network. The model image of the ResNet is shown in Figure 7. It is noteworthy that, unlike the regular U-Net, this ResNet incorporates Residual Blocks in both the encoder and the decoder.

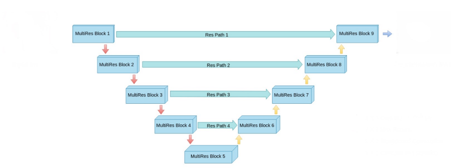

Figure 7: Proposed MultiResNet

Models	Loss function	Optimizer	Initial Filter	Epochs	Batch size
Res-Net	MSE	Adam	32	500	64

Table 14: Res-Net Hyperparameters

These blocks have a different structure from the blocks typically used in U-Net. They consist of convolutional layers with an increasing number of filters after each convolution. This design allows for a significant improvement in the overall performance of the model.

4. PTT Models

Many studies in the literature highlight the presence of three main models on Pulse Transit Time (PTT), as presented in the work at the 2019 5th Iranian Conference on Signal Processing and Intelligent Systems (ICSPIS) [2]. The three models are described as follows:

- **Linear Model**

$$\begin{cases} SBP = \alpha_s * PTT + b_s \\ DBP = \alpha_d * PTT + b_d \end{cases}$$

- **Inverse Model**

$$\begin{cases} SBP = \alpha_s * \frac{1}{PTT} + b_s \\ DBP = \alpha_d * \frac{1}{PTT} + b_d \end{cases} .$$

- **Quadratic Model**

$$\begin{cases} SBP = \alpha_s * \frac{1}{PTT^2} + b_s \\ DBP = \alpha_d * \frac{1}{PTT^2} + b_d \end{cases} .$$

4.1. Regression Models

A simple algorithm is implemented in Matlab for estimating the parameters α and b using the previously described linear, inverse, and quadratic models. Following the pipeline illustrated in Figure 8, a prediction is made for Diastolic and Systolic pressure values, and the mean absolute error is calculated to evaluate the accuracy.

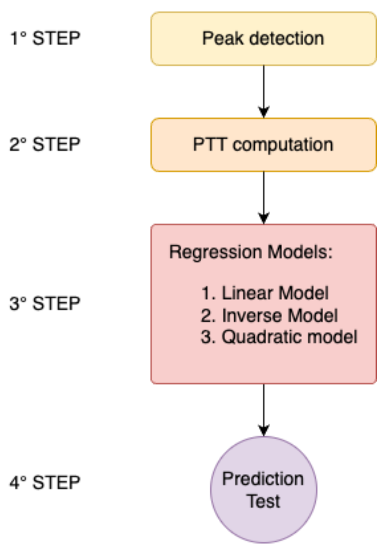

Figure 8: Description of Regression model pipeline

A total of 100 samples are selected, with 75 samples used for training the parameter estimation model and 25 samples for the test set, from which the accuracy and mean absolute error of the model are derived. Table 15 presents the average values of systolic, diastolic, and mean pressure for subject 00 in four out of the six recordings, on which manual feature selection was performed.

	Max(mmHg)	Min(mmHg)	Mean(mmHg)	STD(mmHg)
SBP	167.60	85.363	132.56	14.60
DBP	114.68	60.45	85.19	9.07
MBP	129.55	66.84	105.68	12.17

Table 15: Target value of input signals

5. Results

Table 16 provides a summary of the values for the three different models: U-Net, GRU-Net, and 3GRU-Net. As observed, the lowest values are obtained by the third model, indicating that it is more suitable for waveform reconstruction. In fact, the predicted waveforms obtained from the three models display that the U-Net introduces noise and temporal shift in the reconstruction while the GRU-Net, which, with the addition of a GRU memory layer, performs better in reconstruction and reduces noise. With the 3GRU net, the prediction is more accurate denoising the signal and reducing the temporal shift.

	Training set		Validation set	
Model	Loss value	MAE [mmHg]	Loss value	MAE [mmHg]
U-Net	193.34	9.80	257.90	11.55
GRU-Net	157.42	9.78	218.21	11.31
3GRU-Net	96.56	7.07	194.81	10.53

Table 16: Models metrics

A further evaluation is performed on the calculation of target parameters such as systolic, diastolic, and mean arterial pressure. Table 17 present the values of these physiological parameters. As observed, the most critical parameter is the systolic pressure, as all three models exhibit difficulties in predicting accurately. This issue may be related to the fact that the input dataset has a high standard deviation of systolic pressure, leading to high variability in the prediction. On the other hand, for other parameters such as diastolic pressure and mean arterial pressure (MAP), all three networks demonstrate robustness in their prediction. We observe relatively low MAE values for all three models.

	MAE + STD [mmHg]	MSE + STD [mmHg]	RMSE + STD [mmHg]
SBP	11.35 ± 8.71	204.88 ± 9.13	14.31 ± 8.60
DBP	4.68 ± 4.22	39.78 ± 5.36	6.30 ± 4.19
MAP	6.27 ± 5.33	67.78 ± 7.82	8.23 ± 5.40
STD	5.78 ± 3.15	43.37 ± 3.14	6.58 ± 3.24

Table 17: Parameters computation for 3GRU-Net over the Test set

The analysis of error distribution among the three models reveals that the 3GRU-Net model demonstrates lower mean values and a nearly Gaussian distribution for all parameters, indicating its robustness. The Bland-Altman plot demonstrates minimal differences between the Finapress method and the 3GRU model for mean arterial pressure (MAP) and diastolic values. However, the difference increases for systolic pressure, reflecting the previously described underestimation. The predicted waveform's standard deviation, which evaluates the shape of the predicted signal, is generally good, accurately approximating the peaks of systolic and diastolic pressure with slightly larger errors for systolic pressure. Figure 9 showcases the predicted signal for a specific test set chunk and analyzing the standard deviation of the signal, it can be observed that the model has excellent prediction capabilities for the waveform, closely approximating the target signal.

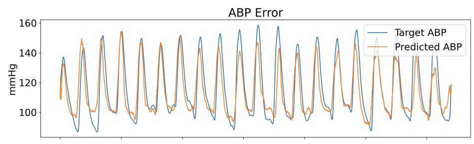

Figure 9: Prediction of ABP waveform with 3GRU-Net model

From the subject-dependent analysis, it is evident that the 3GRU-Net is the model that provides the best performance in predicting the arterial pressure waveform, as seen from the earlier analysis of the error in calculating the final parameters. This is further supported by the calculation of the BHS for the three models.

By using the 3GRU-Net cascaded with the Res-Net, a subject-independent analysis is conducted, utilizing the entire dataset described in the preceding section. Specifically, the values of the input systolic, diastolic, and mean pressure parameters are shown in Table 9. It can be observed that the standard deviation calculated on the input parameters is significantly higher compared to the subject00 input dataset in Table 10. This indicates a greater difficulty in predicting the target parameters. Table 19 reports the MAE and loss values of the network, and Table 18 provides the hyperparameters used. As seen here, the Adam optimizer is utilized, and there are 15 initial filters for each branch of the encoder and 5 filters for the ResNet.

Models	Loss function	Optimizer	Initial Filter	GRU Units	Epochs
3GRU-Net+ResNet	MSE	Adam	15/5	1	1200

Table 18: 3GRU-Net+ResNet initialization parameters for the complete model

3GRU-Net+ResNet			
Training set		Validation set	
Loss value	MAE [mmHg]	Loss value	MAE [mmHg]
303.419	14.593	366.035	15.583

Table 19: 3GRU-Net+ResNet parameters errors for the complete model

	MAE + STD [mmHg]	MSE + STD [mmHg]	RMSE + STD [mmHg]
SBP	22.59 ± 12.83	675.57 ± 15.50	25.99 ± 12.90
DBP	12.53 ± 8.73	233.31 ± 10.33	15.27 ± 8.58
MAP	9.34 ± 8.70	165.01 ± 12.83	12.84 ± 8.81
STD	10.98 ± 4.85	144.61 ± 4.90	12.02 ± 4.89

Table 20: Parameters computation for 3GRU-Net over the Test set for all subjects

Table 20 presents the error values calculated for the target parameters. It can be observed that the error for systolic pressure is relatively high compared to the other parameters: This can be explained by the fact that the standard deviation in the input dataset, as shown in Table 9, is high. Indeed, it is also evident from the prediction errors, their distribution, and the Bland-Altman plot of each parameter. Especially the Bland-Altman plot highlights a high mean difference of approximately 20.5 between the two methods. Additionally, an analysis of the standard deviation is provided, in which is possible to observe the prediction of the standard deviation, that exhibits a significant mean difference. This suggests that the reproduced waveform often displays greater variability compared to the target.

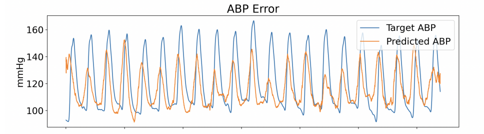

Figure 10: Prediction waveform example: in orange the predicted signal and in blue the target one

In Figure 10, an example of prediction on a chunk of the test set is shown. As observed, there is high variability in the signal and slight noise present. However, the prediction for some chunks appears to be very accurate, likely due to the high quality of the input signal.

6. Discussion and Conclusion

The analysis reveals that the developed models, especially the one with three branches corresponding to the frequency content of the input signals, perform well for subject-dependent analysis. However, achieving equally satisfactory results for subject-independent analysis on the entire dataset is challenging. To address this, the data is analyzed by combining both rest and pedaling phases to account for movement. This leads to an increased standard deviation of the pressure, and the Finapress device occasionally produces pressure values outside the clinical range. During the pedaling phase, certain PPG signals exhibit better quality, resulting in excellent prediction performance. Higher quality in the PPG and ECG signals leads to better prediction results. Although the model's predictions differ from the target, it accurately approximates the systolic pressure. The positioning of the plethysmographic sensor is critical for the Soundi ® device and can impact the signal quality. This master's thesis presents an "End-To-End" approach to continuously calculate arterial blood pressure waveform using three deep learning models. A regression model based on pulse transit time (PTT) is also developed using mathematical models. The goal of the project is to reconstruct arterial blood pressure waveform by utilizing a bank of physiological signals, without relying on a loss function that maximizes point-to-point prediction by the network. The study focuses on subject-dependent analysis and compares the results obtained with the best-proposed model with those from PTT regression models and literature that computes the BHS index. The findings demonstrate the good performance of the model for subject-dependent analysis, approaching clinical standards defined by the British Hypertension Society. Then thanks to the fact that the Soundi ® doesn't need the initial calibration phase, a subject-independent analysis was performed. In this case, the performance is lower compared to subject-dependent analysis, as the complete dataset exhibits high variability in input blood pressure, making it challenging for the model to make accurate predictions. Further ablation studies could be conducted to enhance the architecture's complexity and refine the selected hyperparameters. Enhanced performance could lead to the development of a monitoring model that utilizes key physiological and non-physiological signals for arterial blood pressure reconstruction. Given the ease of recording these signals, this could be a revolutionary aspect of non-invasive arterial pressure monitoring. Therefore, the development of a technique capable of calculating arterial pressure parameters through the creation of a regression model using a deep neural network, without the need for initial calibration like most techniques, is a major advantage as it enables rapid measurement once the network is trained. This is one of the key strengths of this end-to-end approach compared to conventional techniques for acquiring pressure through PPG, such as the Finapress, which requires initial calibration on the subject under analysis to calibrate the pressure. By refining and integrating the model with Soundi®, it is possible to monitor blood pressure without the need for device calibration, allowing measurements to be taken even during movement.

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