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Parameter Identification of the Arterial System Using the Tube-load Model and Neural ODE Methodology

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Abstract

Fluid resuscitation, the primary treatment of acute circulatory failure (ACF) affecting 30%-80% of intensive care unit (ICU) patients in ~50% of cases, fails. Recent studies demonstrated that model-based methods can be used to assess the fluid resuscitation outcome, but the development of model-based diagnostic methods requires the central arterial pressure curve, which can be only measured by invasive methods. This study aims to develop a parameter-identification method for the Tube-load model-based transfer function connecting the clinically available femoral arterial pressure and central arterial pressure curve by using the so-called Physics-informed Neural Network methodology, namely the Neural ODE method. The study presents an extension of the Tube-load model using an additive neural network term. Five different procedures are presented that aim to identify the extended model's parameters, and the results using these procedures are evaluated.

1 Introduction

1.1 Acute circulatory failure

Acute circulatory failure (ACF) is a clinical syndrome when the heart and circulatory circulation cannot provide adequate blood supply to meet the metabolic needs of the organs. ACF affects 30%-80% of intensive care unit (ICU) patients. Fluid resuscitation is the primary treatment of ACF. However, it fails in $\sim 50\%$ of cases due to lack of clinically feasible non-invasive perfusion markers to assess the efficacy of the fluid therapy. Unsuccessful fluid therapy negatively affects patient outcomes, increasing ICU length of stay (3 days on average) and thus costs [1].

1.2 Model-based Decision Support of Fluid Therapy

Due to the potentially adverse and deleterious effects of inappropriate fluid administration [2, 3, 4, 5, 6, 7, 8], fluid therapy should only ever be administered if a significant ($> 10\%$) increase in CO is expected [9]. This requires clinicians to predict the likelihood of a positive response, prior to treatment, by determining the preload responsiveness of a patient (fluid responsiveness). Current methods of assessing fluid responsiveness require extensive prerequisites for proper application and may fail to adequately capture a patient's responsiveness state [10, 5]. This can lead to several risk factors associated with fluid therapy being overlooked [11, 4].

Model-based methods for supporting decisions during fluid therapy can provide clinicians with advanced diagnostic tools and more accurate metrics for assessing the state of a patient's cardiovascular system (CVS) compared to the traditional indices of fluid responsiveness. The CVS is a dynamic entity, and single measurement often fails to capture the complex factors influencing preload responsiveness [11]. Simplified CVS models are able to extract additional information from clinical measurements otherwise inaccessible when considering measurements in isolation [12, 13, 14, 15, 16]. By integrating multiple patient measurements into a model, the complex determinants of fluid responsiveness can be better understood. These models utilize available measurements to identify clinically relevant, patient-specific parameters, offering clinicians advanced tools for guiding decision-making during fluid therapy.

However, the identification of CVS models often requires central (aortic) pressure, which is not

routinely measured due to the highly invasive, time-consuming and risky procedures required. Peripheral pressure measurements are typically used as surrogates to guide treatment. Unfortunately, pressure waveforms undergo augmentation as they travel towards the periphery, thus peripheral arterial pressure measurements differ significantly in both magnitude and overall contour to measurements taken in the central arteries. Pressure waves generated through ventricular contraction travel toward the periphery encountering changes in the geometric and mechanical properties of the blood vessels resulting in wave reflections [17, 18, 19]. The reflected waves travel back towards the heart and the superposition of the forward travelling and reflected waves yield the pressure waveforms measured at any point in the arterial system. These wave reflections significantly alter the peripheral pressure waveform, resulting in a narrowing and amplification of systolic pressure, and augmentation or elimination of the diastolic notch. Overall the augmentation of the waveforms makes peripheral pressures unsuitable as direct surrogates when identifying CVS models. In order to accurately identify CVS models clinically, methods for estimating the unavailable central arterial pressure waveforms from routinely measured peripheral pressure are required.

This paper presents an extension of the Tube-load model using an additive neural network term. Five different procedures are presented that aim to identify the extended model's parameters, and the results using these procedures are evaluated. The advantages of using an additive neural network term are twofold. The additive term improves the simulation accuracy and also improves the identification of the original parameters of the Tube-load model.

2 Methods and Data

2.1 Data

2.1.1 Physiological data set from model animal experiments

The experimental dataset was obtained from a series of animal studies conducted at the Centre Hospitalier Universitaire de Liège (Reference Number 14-1726). A total of seven pure Piétrain pigs, with body weights ranging from 18.5 kg to 29.0 kg, were included in the study. The animals were initially sedated and placed under general anaesthesia. Anaesthesia and sedation were sustained through a continuous infusion of pharmaceutical agents, specifically sufentanil, Thiobarbital, and Nimbex, administered via a superior vena cava catheter. The pigs were subjected to mechanical ventilation throughout the experiment.

To monitor blood pressure, high-fidelity pressure catheters were inserted into the proximal aorta (P_{ao}), femoral artery (P_{abd}), and vena cava (P_{cv}). Additionally, left ventricular pressures (P_{LV}) and volumes (V_{LV}) were recorded. Aortic flow (Q_{ao}) was assessed using an aortic flow probe positioned on the proximal aorta near the aortic valve. Once the probe was correctly placed, the thorax was temporarily closed with clamps. All recorded data had a sampling frequency of 250 Hz and were stored in a single Notocord data file, ensuring comprehensive data collection for model validation.

During the measurement process, the pigs underwent various haemodynamic interventions. Throughout mechanical ventilation, multiple respiratory recruitment manoeuvres were executed for each pig, involving stepwise increases in positive end-expiratory pressure (PEEP) by 5 cmH₂O increments. Increasing PEEP leads to a reduction in systemic venous return to the right atrium and elevates pulmonary vascular resistance. To augment circulatory volume and ventricular preload, multiple intravenous infusions of saline solution were administered at a delivery rate of 500 mL over 30 minutes.

Additionally, an endotoxin infusion (E. Coli lipopolysaccharide) was administered at a dosage of 0.5 mgkg⁻¹ over 30 minutes to induce a septic shock-like condition characterized by inflammation, capillary leakage, reduced afterload, hypovolemia, tissue hypoxia, and eventual cardiac dysfunction. The sequence of these interventions is depicted in Figure 1.

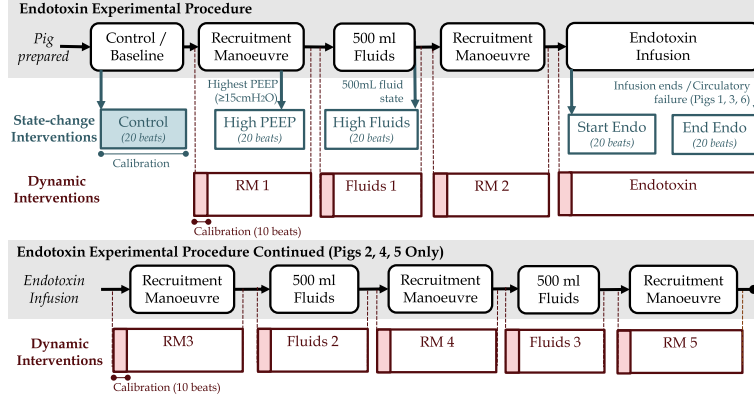


Figure 1: The schedule of interventions performed on the examined pigs [20].

2.1.2 Benchmark data set: pressure curves without dicrotic notch

The dicrotic notch (DN) is a small downward deflection of the arterial pressure waveform during the downstroke after the systolic peak resulting from the closure of the valve [21]. The dicrotic notch in the pressure curve of the aorta is considered noise from the aspect of parameter identification of the Tube-load model, as the Tube-load model describes only the waveform of the forward and reflected waves. Thus, a "denoised" reduced dataset was constructed in which the dicrotic notch was manually removed from the waveform. The beginning and end of the dicrotic notch were visually identified on the aortic pressure curve in the descending dicrotic limb and connected with a straight line. The beginning of the notch is considered to be the change in slope before the negative peak, and the end is the peak after. Figure 2 presents one such section. The manually modified waveforms are referred to as no-notch data.

2.2 Tube-load model

The Tube-load model describes the arterial system as an arbitrary number of parallel uniform lossless tubes, representing the large conduit arteries, in series with loads, representing peripheral blood vessels, as shown in Figure 3. [22].

The impedance of distal arterial beds (Z_{load}) is modelled in the frequency domain as a single

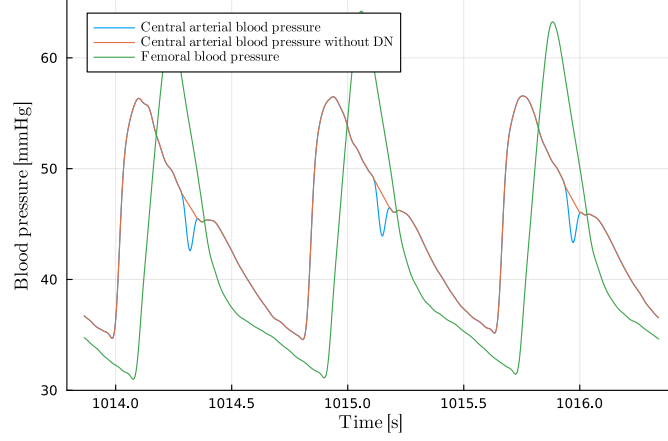


Figure 2: A section of femoral arterial and central arterial blood pressure measurements (shown by blue line); and the manually modified arterial blood pressure waveform (shown by brown line) without the dicrotic notch. The femoral pressure is shown by a green line to allow comparison of the pressure signals used in this study.

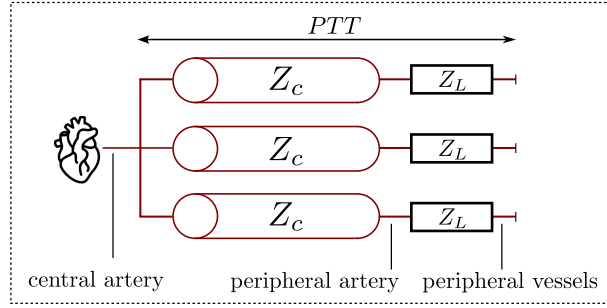


Figure 3: The schematic figure of the Tube-load model [22].

pole and zero, characterized by parameters A , B , with a gain factor Z_c :

$$Z_{load}(\omega) = Z_c \frac{j\omega + B}{j\omega + A}, \quad (1)$$

where $(0 < A < B)$, and Z_c is the impedance of the corresponding tube, ensuring pressure wave reflections are positive, stable, and become negligible at high frequencies. As the frequency becomes very large, the peripheral load tends to Z_c , and the tube and load are impedance matched, so there are no reflections.

Thus, the Tube-load model can be used to create transfer functions between central and peripheral pressures and flows in the frequency domain. Thus, $P_{ao,est}$, and $Q_{ao,est}$ are calculated using measured P_{fem} and PTT [23, 24, 25]:

$$\frac{P_{ao,est}(\omega)}{P_{fem}(\omega)} = \frac{\left(\frac{B+A}{2} + j\omega\right) e^{j\omega PTT} + \left(\frac{B-A}{2}\right) e^{-j\omega PTT}}{j\omega + B} \quad (2)$$

where A , B are the gain factors introduced in Equation (1), and PTT is the pulse transit time, the time it takes for pressure waves generated by the left ventricle to travel through the large arteries to the periphery.

The transfer function can be represented in the continuous time domain describing the transfer function with parameters A , B and PTT :

$$\begin{aligned} \dot{P}_{ao,est}(t) + BP_{ao,est} &= \dot{P}_{fem}(t + PTT) + \\ &+ \frac{B+A}{2}P_{fem}(t + PTT) + \frac{B-A}{2}P_{fem}(t - PTT). \end{aligned} \quad (3)$$

Solving Equation (3) for the derivative of aortic pressure yields a differential equation enabling calculation of the aortic pressure based on the initial value of the aortic pressure and femoral pressure data:

$$\begin{aligned} \dot{P}_{ao,est}(t) &= -BP_{ao,est} + \dot{P}_{fem}(t + PTT) + \\ &+ \frac{B+A}{2}P_{fem}(t + PTT) + \frac{B-A}{2}P_{fem}(t - PTT). \end{aligned} \quad (4)$$

A new parameter set of the model was introduced in [26], which uses physiologically interpretable variables as parameters. The Γ and Θ parameters are the gain and cutoff frequency of the reflection

coefficient. The model can be equally described using these parameters instead of A and B :

$$\Gamma = \frac{B - A}{B + A} \quad (5)$$

$$\Theta = \frac{B + A}{2} \quad (6)$$

$$\begin{aligned} \dot{P}_{ao,est}(t) + \Theta(1 + \Gamma)P_{ao,est} &= \dot{P}_{fem}(t + PTT) + \\ &\Theta P_{fem}(t + PTT) + \Theta \Gamma P_{fem}(t - PTT). \end{aligned} \quad (7)$$

Solving Equation (7) for the derivative of aortic pressure yields a similar form of the differential equation than Equation (4):

$$\begin{aligned} \dot{P}_{ao,est}(t) &= -\Theta(1 + \Gamma)P_{ao,est} + \dot{P}_{fem}(t + PTT) + \\ &\Theta P_{fem}(t + PTT) + \Theta \Gamma P_{fem}(t - PTT). \end{aligned} \quad (8)$$

As it has been mentioned before, this research aims to develop a Neural ODE-based parameter identification method to identify Γ and Θ used in Equation (8).

2.3 Neural ODE

Neural Ordinary Differential Equations (Neural ODEs) represent a novel class of deep learning models that integrate differential equations with artificial neural networks [27]. This integration is intuitive, as both fields aim to describe arbitrary nonlinear transformations. In neural networks, such transformations are realized through linear weights and nonlinear activation functions at each layer, while in differential equations, they are defined by specifying the derivative of the variable of interest, utilizing prior structural knowledge of the system.

As machine learning models continue to grow in complexity and demand larger datasets, differential equations have emerged as a compelling tool for encoding nonlinearities in a learnable yet constrained manner [28]. Neural ODEs exemplify one such fusion of ODEs and artificial neural networks (ANNs).

A foundational concept in this field is the Residual Neural Network (ResNet). ResNets are

characterized by identity skip connections, as illustrated in Figure 4.

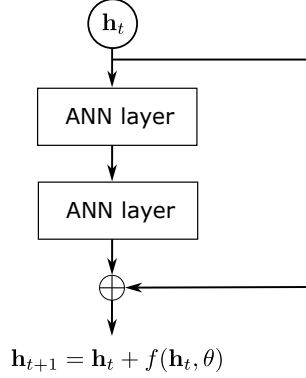


Figure 4: Architecture of a residual neural network

The output of a layer in a ResNet is given by the sum of the input state and the layer’s output:

$$\mathbf{h}_{t+1} = \mathbf{h}_t + f(\mathbf{h}_t, \theta) \quad (9)$$

where $t \in 0 \dots T$, h_t represents the state variable vector at the t^{th} layer of the network ($\mathbf{h}_t \in \mathbf{R}^D$), and θ denotes the network parameters.

Equation (9) can be interpreted as an Euler discretization of a continuous transformation. By increasing the number of layers and reducing step sizes, the discrete model transitions into a continuous one, ultimately leading to an ODE representation:

$$\frac{d\mathbf{h}(t)}{d(t)} = f(\mathbf{h}(t), t, \theta) \quad (10)$$

Starting from an initial input state $h(0)$, the final output $h(T)$ corresponds to the solution of this ODE at time T . A black-box ODE solver can compute this solution by evaluating the hidden unit dynamics $f(\cdot)$ as needed to achieve the desired level of accuracy. Figure 5 highlights the relationship between ResNets and Neural ODEs ([27]).

One of the primary challenges in training continuous-depth networks is computing gradients efficiently, a key step in backpropagation. The authors of the Neural ODE framework address this by treating the ODE solver as a black box and employing the adjoint sensitivity method, which is

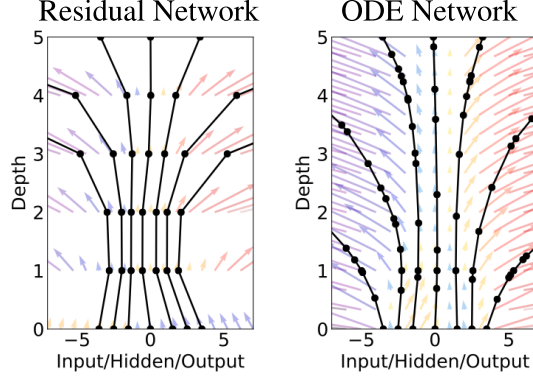


Figure 5: Comparison of ResNets and Neural ODEs [27].

compatible with all ODE solvers. This method computes gradients by solving an auxiliary ODE in reverse time, offering advantages such as linear scalability with problem size, reduced memory overhead, and precise numerical error control [27].

2.4 Enhancing the Tube-load Model Using Additive Neural Network Term

The Tube-load model describes the arterial system using three parameters (Γ , Θ , PTT). This simple model is capable of capturing the reflections of blood pressure waves in the arteries. However, another significant feature of the central arterial pressure wave, the dicrotic notch, is not described by the model.

Using the Neural ODE approach, an additional additive term in the differential equation governing the Tube-load model is proposed to account for the effects of the disturbances unmodelled by the original ODE model. The most significant disturbance is the dicrotic notch, which is the effect of the aortic valve closing the left ventricle.

Introducing this additive term has two main benefits. Firstly, it can enhance the output waveform when simulating the model. Secondly, assuming the additive term describes the effect of the dicrotic notch, it facilitates more accurate identification of the physiological parameters of the ODE model, and the target waveform will be accurately described by the augmented model.

Augmenting the Equation 8 with an additive term $F_{ao,nn}(t)$ yields to the following Neural ODE

model:

$$\begin{aligned}\dot{P}_{ao,est}(t) = & -\Theta(1 + \Gamma)P_{ao,est}(t) + \dot{P}_{fem}(t + PTT) + \\ & \Theta P_{fem}(t + PTT) + \Theta \Gamma P_{fem}(t - PTT) + F_{ao,nn}(t).\end{aligned}\tag{11}$$

Let's introduce $F_{ao,ode}(t)$, representing the right side of the differential equation of the original Tube-load model, as follows:

$$F_{ao,ode}(t) = -\Theta(1 + \Gamma)P_{ao,est} + \dot{P}_{fem}(t + PTT) + \tag{12}$$

$$\Theta P_{fem}(t + PTT) + \Theta \Gamma P_{fem}(t - PTT).\tag{13}$$

Equation (11) will be simplified as:

$$\dot{P}_{ao,est}(t) = F_{ao,ode}(t) + F_{ao,nn}(t).\tag{14}$$

The parameter identification process aims to identify the parameters of the Tube-load model in an iterative process based on the difference between the measurement and model output.

The neural network used as an additive term features a dense hidden layer with 10 units using the ReLU activation function and has a 1-element output layer. Let's call the parameters of the neural network, $F_{ao,nn}(t)$, $\mathbf{p}_{nn}$, and the parameters of the ODE model, Equation 7, $\mathbf{p}_{ode}$:

$$\mathbf{p}_{ode} = param(F_{ao,ode}(t))\tag{15}$$

$$\mathbf{p}_{ode} = [\Gamma, \Theta, PTT]\tag{16}$$

$$\mathbf{p}_{nn} = param(F_{ao,nn}(t))\tag{17}$$

$$\mathbf{p}_{nn} = \mathbf{W}_{nn} = [w_1, w_2, ..., w_k]\tag{18}$$

$$\mathbf{p} = [\mathbf{p}_{ode}, \mathbf{p}_{nn}]\tag{19}$$

where $\mathbf{p}$ is the vector of all the parameters identified.

The cost function used for the parameter identification is defined as the L2 norm of the simulated output and the measurement, noted as $P_{ao,mes}(t)$:

$$\Phi_{ao}(\mathbf{p}) = \sqrt{\sum_{t=1}^N \left(P_{ao,est}(t) - P_{ao,mes}(t) \right)^2} \quad (20)$$

Thus, the parameter identification problem is written in the form as follows:

$$\mathbf{p}_{ao} = \arg \min_{\mathbf{p}} \Phi_{ao}(\mathbf{p}). \quad (21)$$

2.4.1 Parameter identification procedures

To improve the parameter identification accuracy and still receive physiologically valid ODE parameters when using the additive term implemented by the neural network, the additive term must be enforced to model only the noise of the measurement, mainly the dicrotic notch, as the ODE model parameters describe the characteristic features of the blood pressure wave.

To develop the identification method effectively ensuring the enforcement, five parameter identification procedures are defined and compared. The definitions of the five identification procedures are as follows:

- **Method A):** Identification of $\mathbf{p}_{ode}$ using no-notch data for training.

The result of this identification procedure is considered as a reference of the ODE model parameters. The identified model parameters are likely close to their physiological value as removing the notch from the measurement curves, the effect of the most important unmodelled disturbance is eliminated.

- **Method B):** Identification of $\mathbf{p}_{ode}$ and $\mathbf{p}_{nn}$ using measurement data for training.

This identification method is a naive approach and assumes that without additional methodological effort, the ODE term will model the forward and reflected pressure waves and the neural network will model the unmodelled disturbances by the ODE model, in our case, the dicrotic notch.

- **Method C)**: Identification of $\mathbf{p}_{ode}$ using measurement data for training.

This identification method is used to estimate the noise on the identified parameter values due to the dicrotic notch when only the ODE model is identified without the additive term. This method was used in [29] and [26].

- **Method D)**: An identification process with three subsequent phases.
 - First, the identification of $\mathbf{p}_{ode}$ with $P_{ao,nn}(t) = 0$ using no-notch data for training;
 - Second, the identification of $\mathbf{p}_{nn}$ using the fixed trained parameters of $P_{ao,ode}(t)$ ($\mathbf{p}_{ode}$) and the measurement data for training.
 - Third, the identification of $P_{ao,ode}(t)$ using the fixed trained parameters of $P_{ao,nn}(t)$ ($\mathbf{p}_{nn}$) and the measurement data for training.

This identification procedure represents the identification process when the ODE model parameters are identified - assumingly - to the physiologically correct values because, in the first phase, the "denoised" no-notch data set is used for the parameter identification of the ODE model. In the subsequent phase, the neural network parameters are identified using the measurement data to let the model represent the unmodelled disturbance, the dicrotic notch. In the last phase, the ODE model parameters are identified in order to see whether the loss function would modify the previously identified parameters.

This identification method assumes the existence of the no-notch data set, which does not exist on the bedside.

- **Method E)**: The identification sequence *D)* except for using the measurement data for all the phases of the identification process.

This identification procedure is a simplified version of **Method D)** which uses only measurement data available on the bedside.

The specifications of the proposed identification methods are summarized in Table 1 and illustrated in Figure 6. The identification procedures differ from each other in three aspects:

1. **The applied model: Either Equation 8 or Equation 14 is used for the identification.**

In Figure 6, the application of the equations is visually illustrated by a grey (unused) and

green/white (used) background.

2. **The identified parameter set: Only $\mathbf{p}_{ode}$, only $\mathbf{p}_{nn}$, or both of them are identified.**

Figure 6 illustrates the identified model parameters with grey (not identified) and green (identified) background. In the case when the given parameter set was identified in a previous phase of the identification process, and the parameters are fixed and the background is white.

3. **The data used for training, specifically the data used to calculate the loss function:**

Either the measured central arterial pressure or the no-notch benchmark data is used for the network training. Figure 6 illustrates the usage of the measurement and benchmark data sets a blue (measurement) and orange (no-notch, benchmark) signal.

The identification was performed on three-heartbeat-long sequences, shifted by one heartbeat for the subsequent sequence. For consistency and comparability, 500 learning epochs and 0.1 learning rate were used for all methods.

Method ID	$\mathbf{p}_{ode}$	$\mathbf{p}_{nn}$	Training dataset
Method A) <i>Phase 1</i>	identified	not used	no-notch
Method B) <i>Phase 1</i>	identified	identified	measurement
Method C) <i>Phase 1</i>	identified	not used	measurement
Method D) <i>Phase 1</i> <i>Phase 2</i> <i>Phase 3</i>	identified fixed identified	not used identified fixed	no-notch measurement measurement
Method E) <i>Phase 1</i> <i>Phase 2</i> <i>Phase 3</i>	identified fixed identified	not used identified fixed	measurement measurement measurement

Table 1: The specifications of the proposed identification methods in terms of identified parameters and the applied data set in various phases of the identification method.

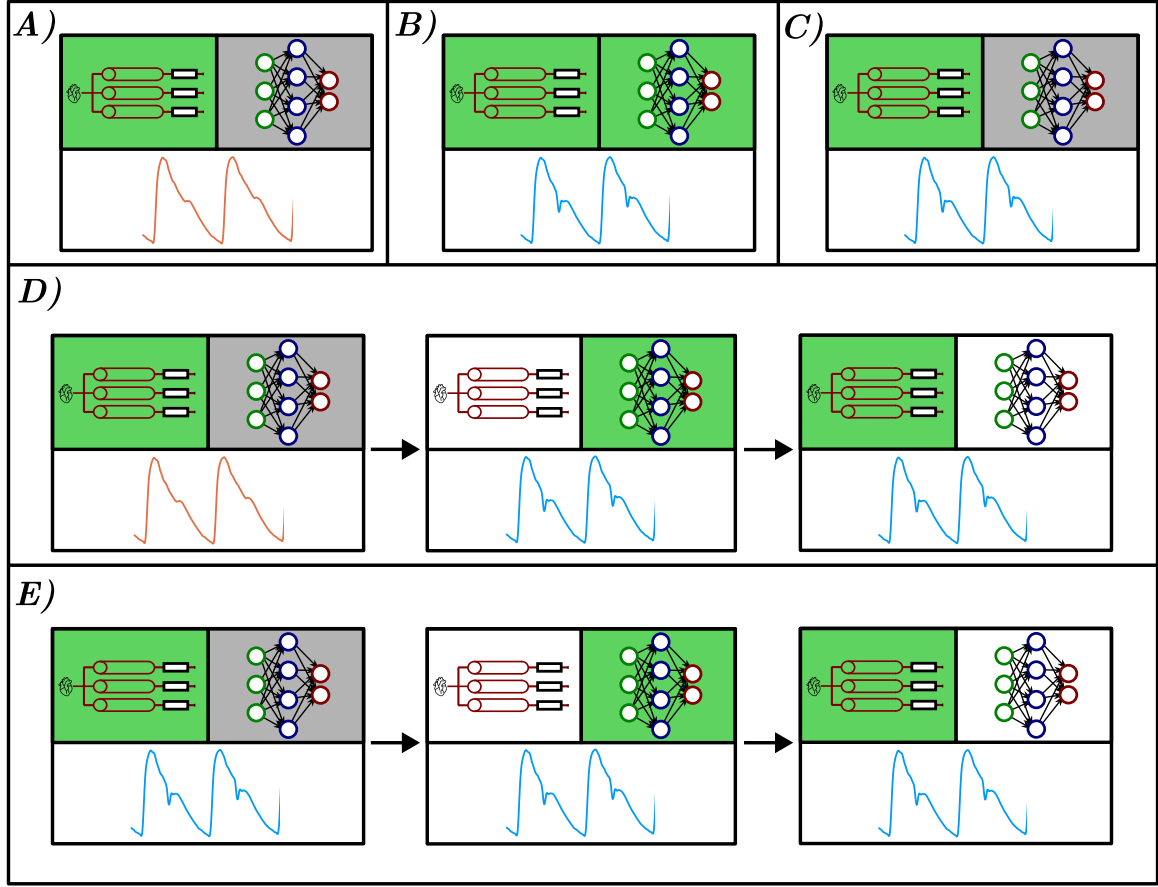


Figure 6: Five different parameter identification methods were applied. *A)* Identification of $P_{ao,ode}(t)$ using no-notch data for training. *B)* Identification of both $P_{ao,ode}(t)$ and $P_{ao,nn}(t)$ simultaneously using measurement data for training. *C)* Identification of $P_{ao,ode}(t)$ using measurement data for training. *D)* A sequence of identifications. First, the identification of $P_{ao,ode}(t)$ with $P_{ao,nn}(t) = 0$ using no-notch data for training; then the identification of $P_{ao,nn}(t)$ using the fixed trained parameters of $P_{ao,ode}(t)$ and the measurement data for training. Finally, the identification of $P_{ao,ode}(t)$ using the fixed trained parameters of $P_{ao,nn}(t)$ and the measurement data for training. *E)* The identification sequence *D)* except for using the measurement data for all identifications.

3 Results

The physiologically valid reference value in the analyzed heartbeats of Γ parameter – the output of **Method A)** –, shown as the blue line in Figure 7. It stays in the range of 0.395 ± 0.005 during the 45 heartbeats analysed. In contrast, the Γ parameter identified by **Method B)** appears to deviate substantially, varying between 0.1 and 0.5 with relatively large variations. This substantial deviation

is also visible in the error values shown in Table 4 showing the statistics of absolute error of Gamma parameter calculated for each heartbeat by different identification methods. The correlation between Γ parameters identified by *Method A)* and *Method B)* over a sequence of heartbeats, shown in Table 2, also indicates negative correlation saying that the identified values by the two methods are uncorrelated.

	<i>Method B)</i>	<i>Method C)</i>	<i>Method D)</i>	<i>Method E)</i>
COR	-0.283	0.854	0.768	0.71

Table 2: The correlation (COR) between the identified curves of the Γ parameter using *Method A)* and other identification methods.

Despite the large differences in the identified Γ parameter values and the negative correlation between the values identified by *Method A)* and *B)*, the pressure curves calculated using the parameters identified by the methods are largely consistent and fits relatively well to the measurement, as can be seen in Figure 8, where the black curve shows the measurement, the orange curve the pressure values calculated from the parameters of *Method B)*, and the black curve the pressure values calculated from the parameters of *Method A)*. The root mean square error calculated between the two curves, shown in the second column of Table 3, confirms that the calculated distance between the curves is relatively small compared to the absolute value of the signal. These results mean that *Method B)* identified physiologically invalid parameters and outline the importance of developing an identification method ensuring physiologically interpretable parameters.

	<i>Method A)</i>	<i>Method B)</i>	<i>Method C)</i>	<i>Method D)</i>	<i>Method E)</i>
RMSE [mmHg]	3.11	1.37	3.08	1.01	0.99

Table 3: The root mean square errors of the model simulations using the identification results of different methods compared to the measurement data (RMSE = measurement - simulation of the identified model). RMSE is a pressure measured in millimetre of mercury (mmHg).

The bottom subfigure of Figure 7 illustrates the identified values of Γ using the identification methods but *Method B)*. This enables a more effective visual comparison of the four methods. Methods *C)*, *D)* and *E)* remain in close proximity of the reference Γ parameter curve. The values identified using *Method C)* are marginally elevated in comparison to the reference curve, however, they follow a similar trend. *Method D)* incorporates the reference method, as its first phase, therefore, producing similar results in the figure, as it remains closest to the results of *Method A)*.

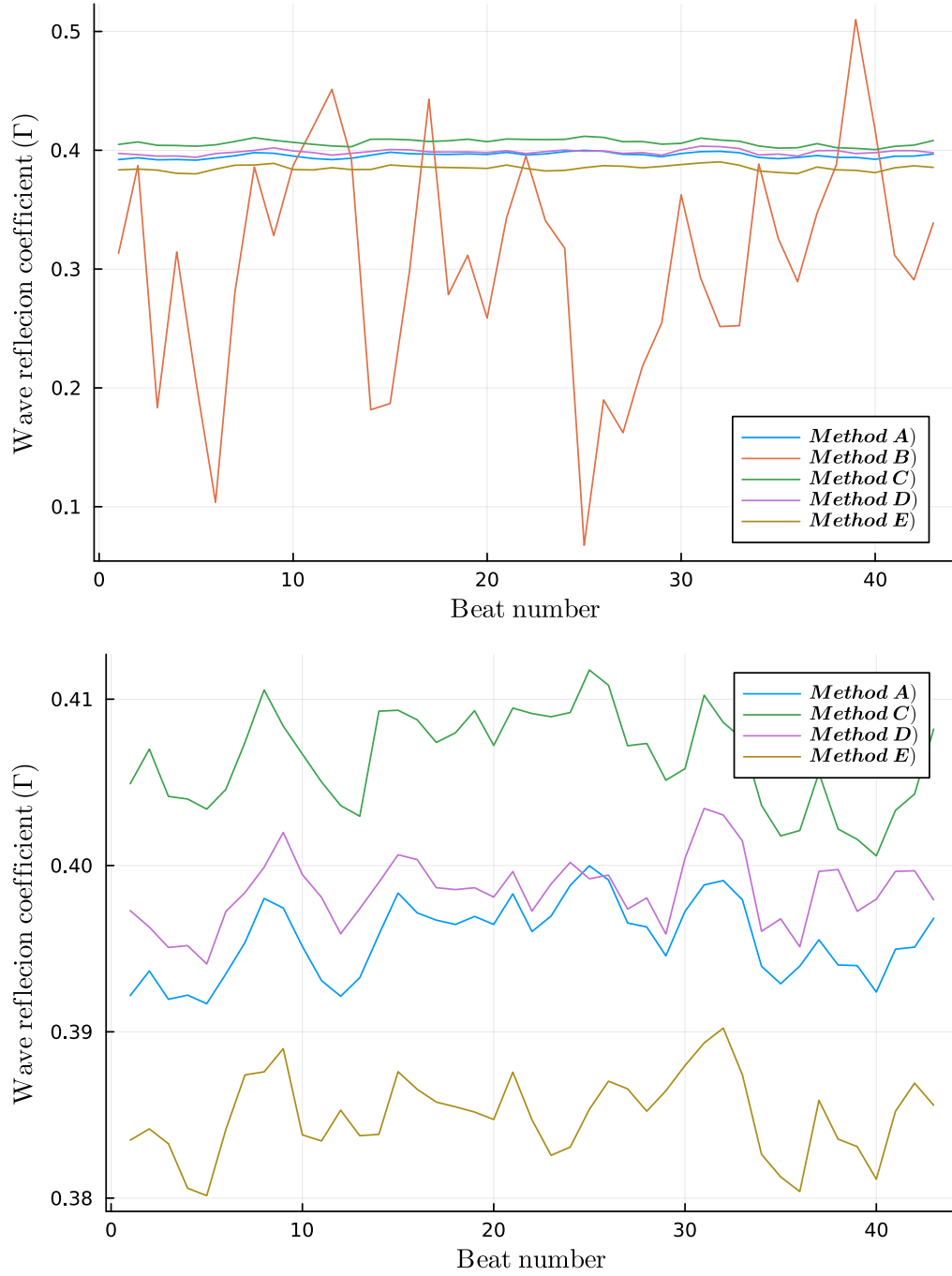


Figure 7: On the top of the figure, the identified values of Γ in a selected section of the measurement using all of the proposed identification methods are shown. On the bottom **Method B**) is omitted to enable the visual comparison of other methods. The scale on the vertical axes is enlarged in the corresponding region of the Γ parameter.

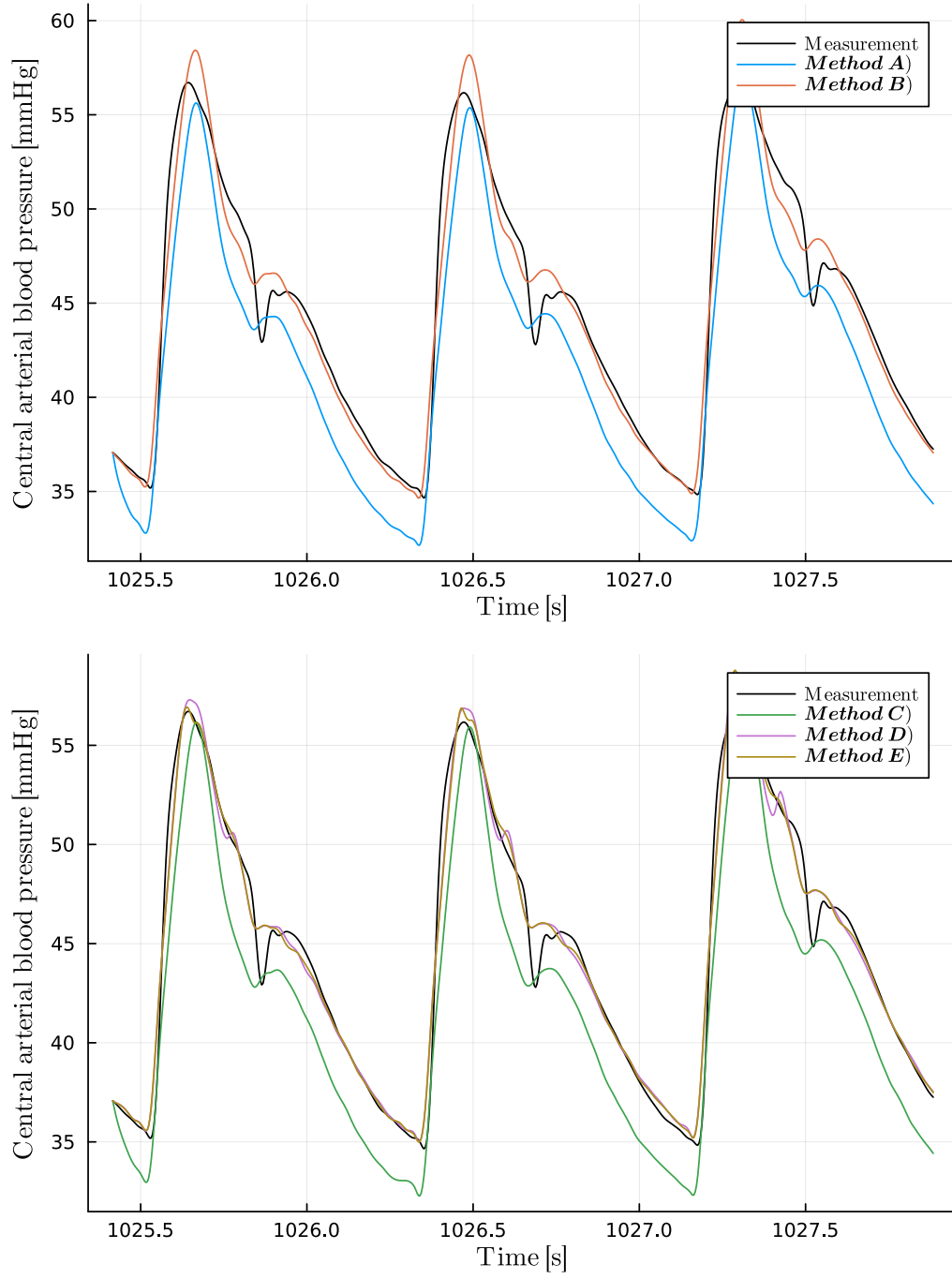


Figure 8: On the top, the simulated heartbeats using results of the identification methods **A)** and **B)**, on the bottom the simulated heartbeats using results of the identification methods **C)**, **D)** and **E)** are shown. The measured central arterial blood pressure curve is plotted for comparison.

	Mean	Median	IQR	5th Percentile	95th Percentile
Method B)	0.102	0.083	0.095	0.006	0.232
Method C)	0.011	0.011	0.002	0.008	0.013
Method D)	0.003	0.003	0.002	0.001	0.005
Method E)	0.011	0.011	0.002	0.008	0.014

Table 4: The descriptive statistic of absolute errors of Γ of the results using different identification methods compared to **Method A)**.

	Mean	5th Percentile	Median	95th Percentile	IQR
Method B)	25.8	1.4	21.1	58.6	24.0
Method C)	2.7	2.1	2.8	3.3	0.5
Method D)	0.7	0.2	0.8	1.3	0.6
Method E)	2.7	2.1	2.7	3.6	0.5

Table 5: The descriptive statistic of relative errors of the identified Γ parameter using different identification methods compared to **Method A)**.

Finally, the brown curve, which illustrates the identified values of Γ using **Method E)**, follows a trend similar to the reference; however, it remains lower than the blue line. Quantitative comparison of the identified Γ parameter by the proposed identification methods is given in Table 4 and 5 showing the statistics of the absolute and relative difference of **Method B)**, **C)**, **D)**, and **E)** from **Method A)** calculated on heartbeat basis.

All identification methods determine the optimal values of the parameters Γ and Θ . Figure 7 illustrates the identified values of Γ , while Figure 9 presents the results of the identification of Θ , the cutoff frequency of the model. Based on its absolute value, the green curve corresponding to **Method C)** is an outlier, as it remains in the range of 17 ± 1 , whereas the other curves - including the curve corresponding to the reference curve generated by **Method A)** - are in the range of 22 ± 2 . Based on trends, the curves can be divided into three groups. The results of **Methods A)** and **C)** follow similar trends, while the results of **Method D)** has a trend similar to the one of **Method E)**. The naive solution presented in **Method B)** can be considered an outlier as its trend does not approximate the others. Table 4 and 5 provide quantitative comparison of the identified Θ parameter by the proposed identification methods presenting the statistics of the absolute and relative difference of **Method B)**, **C)**, **D)**, and **E)** from **Method A)** calculated on heartbeat basis.

The presented results of the identification methods were applied to simulate the corresponding models and so generate central arterial blood pressure curves. Figure 10 illustrates three heartbeats

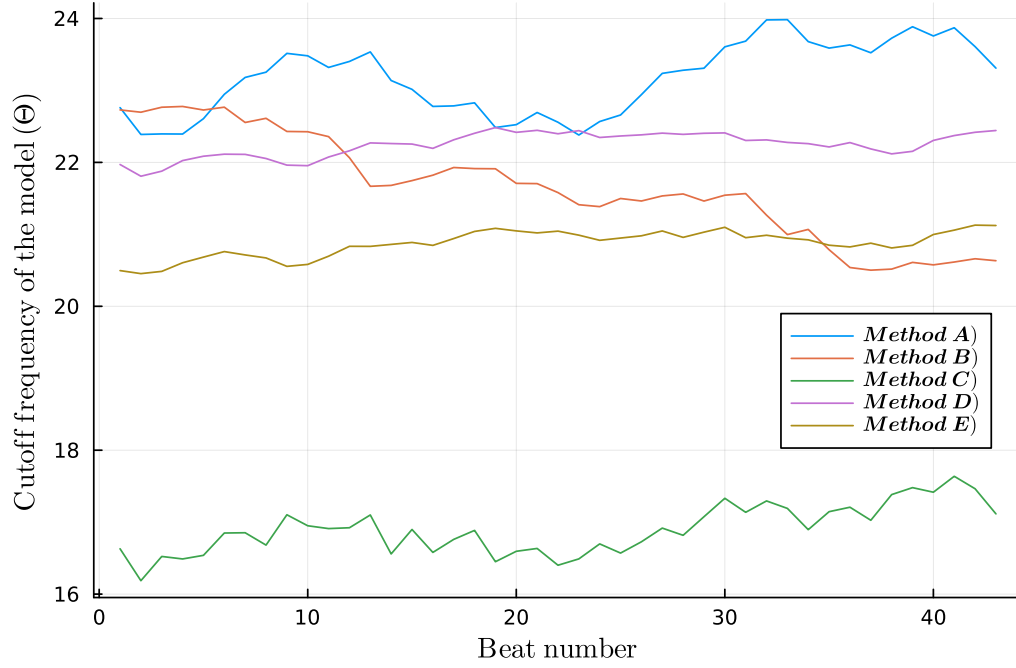


Figure 9: The identified values of Theta in a section of the measurement data using the five presented methods.

	Mean	Median	IQR	5th Percentile	95th Percentile
<i>Method B)</i>	1.6	1.3	1.8	0.2	3.2
<i>Method C)</i>	6.3	6.2	0.3	5.9	6.7
<i>Method D)</i>	0.9	0.9	0.8	0.1	1.7
<i>Method E)</i>	2.3	2.3	0.8	1.5	3.0

Table 6: The descriptive statistic of absolute errors of **Theta** of the results using different identification methods compared to *Method A)*.

	Mean	5th Percentile	Median	95th Percentile	IQR
<i>Method B)</i>	6.7	0.8	05.5	13.5	7.3
<i>Method C)</i>	27.1	26.0	26.9	28.3	1.0
<i>Method D)</i>	4.0	0.5	3.8	6.9	3.5
<i>Method E)</i>	9.9	6.6	10.0	12.6	3.1

Table 7: The descriptive statistic of relative errors of the **Theta** parameter using different identification methods compared to *Method A)*.

Absolute error	<i>Method B)</i>	<i>Method C)</i>	<i>Method D)</i>	<i>Method E)</i>
Gamma	0.102	0.011	0.003	0.011
Theta	1.577	6.271	0.928	2.297

Relative error [%]	<i>Method B)</i>	<i>Method C)</i>	<i>Method D)</i>	<i>Method E)</i>
Gamma	25.8	2.7	0.7	2.7
Theta	6.8	27.1	4.0	9.9

Table 8: The mean values of the absolute and relative errors of the results of different methods compared to *Method A)* collected from Tables 4, 5, 6, and 7.

of the measured central arterial blood pressure curve in black and the results of the simulations using the models, and identified parameter values of *Method A)* in blue, *Method B)* in orange, *Method C)* in green, *Method D)* in pink, and *Method E)* in brown. The green and blue curves differ from the others because these curves correspond to simulations using only the ODE model as described in Equation 8. The curves corresponding to *Methods B)*, *D)* and *E)* illustrate simulations of the model using an additive neural network term; therefore, these approximate the measurement better. These findings from the observation of the figure are confirmed by Table 3, which provides a quantitative comparison of the magnitude of the error between the simulation curves and the measurement. Based on the root mean square error calculated on the entire measurement (Table 3), the ODE-only model results in significantly higher errors than the enhanced model.

For an easier comparison of the four identification methods, the mean values of the Γ and Θ parameters are collected into Table 8 from Tables 4, 5, 6, and 7.

Method E) is executed in different sections of measurement representing different physiological states of the model animal. 45 heartbeats are selected from each section of the experiment. Table 9 presents the statistics of the root mean square error between the measurement and the simulated pressure curve using the parameters identified by *Method E)*. The error is calculated on a heartbeat basis.

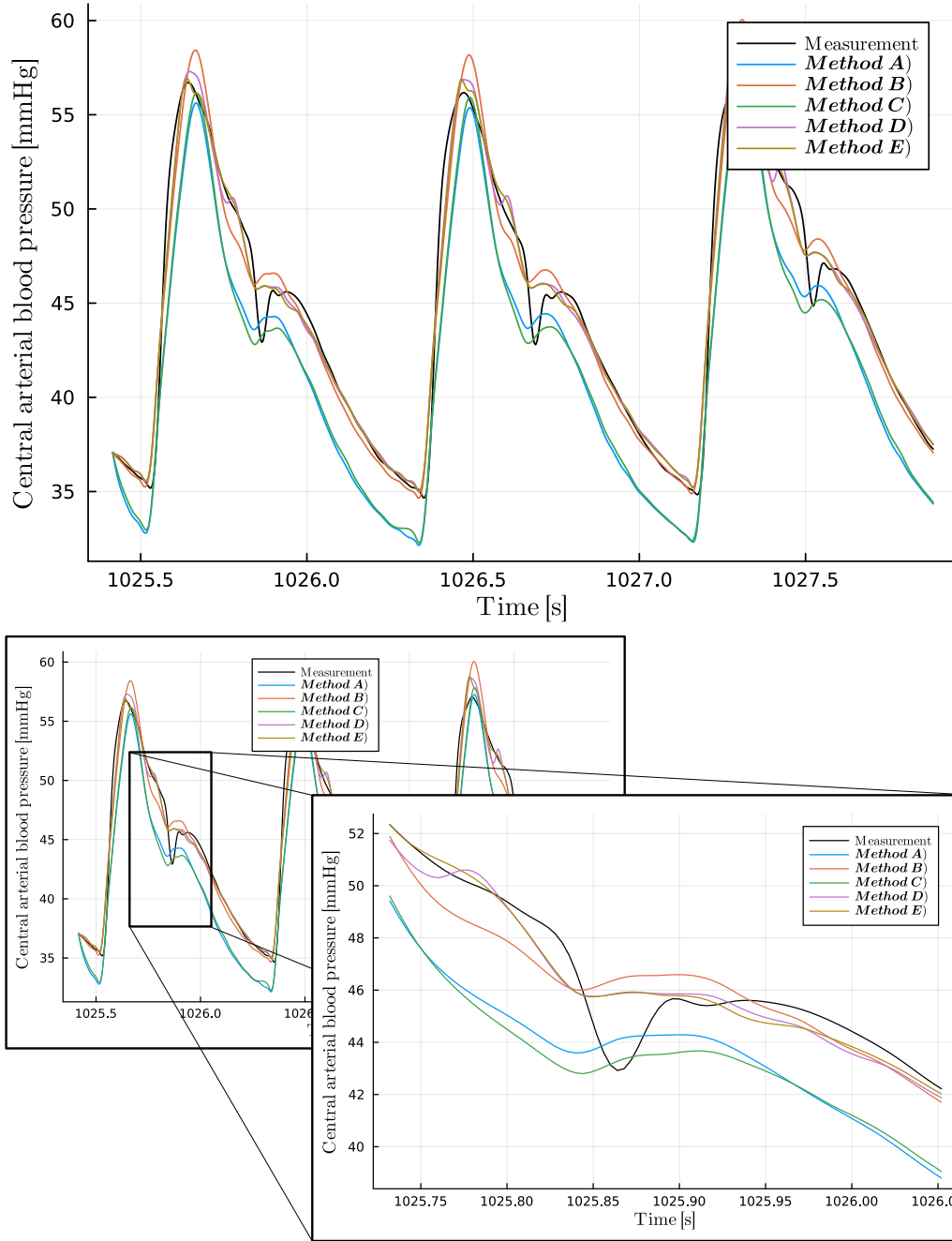


Figure 10: On the top, the simulated heartbeats using the results of the performed identification methods are shown, on the bottom, the area of the diastolic notch is enlarged to help illustrate the effect of the noise introduced by this feature. The measured central arterial blood pressure curve is plotted for comparison.

Experiment section	RMSE_MEAN	RMSE_STD
pig7_01_rm1	1.4	0.3
pig7_02_base1	1.3	0.2
pig7_03_fluid1	1.1	0.0
pig7_04_pause1	8.9	0.1
pig7_05_rm2	14.9	3.6
pig7_06_endotoxin	5.4	3.7
pig7_07_pause2	0.9	0.0
pig7_08_rm3	1.0	0.1
pig7_09_fluid2	0.9	0.0
pig7_10_pause3	6.2	0.1
pig7_11_rm4	6.6	1.0
pig7_12_fluid3	5.7	0.3
pig7_13_pause4	6.4	1.1
pig7_14_rm5	3.8	0.2
pig7_15_fluid4.300ml	2.1	1.1
pig7_17_rm6	10.2	1.3
pig7_18_rest	14.0	2.5

Table 9: The mean (RMSE_MEAN) and standard deviation (RMSE_STD) of the root mean square errors (RMSE) of the model simulations using the model parameters identified by **Method E**) compared to the measurement data (RMSE = measurement - simulation of the identified model). The error is calculated for the first 45 heartbeats of each measurement section separately. RMSE is a pressure measured in millimetre of mercury (mmHg).

4 Discussion

The identified parameter values using **Method A**) are assumed to be close to their physiological value. Therefore, this method is considered the baseline, and the other identification methods are analysed in comparison to **Method A**).

4.1 Method B)

Method B) is a naive approach that employs the model described by Equation 11. New random initial weights were assigned to the neural network in the additive term of the equation for every identified heartbeat. The solution, illustrated in Figures 8 and 10, approximates the measurement well. The neural network has the capacity to learn complex representations; therefore, the simulation of the model using the identified neural network weights and $\mathbf{p}_{ode}$ parameter values results in low error. However, the other goal of the identification is to produce physiologically correct values for the parameters in $\mathbf{p}_{ode}$.

The identified values of Γ are presented in Figure 7. The naive approach results in a considerable variance in the identified values of Γ . The neural network is not constrained to learn only the noise – including the diastolic notch – but all features simultaneously as $\mathbf{p}_{ode}$ is identified. Figure 9 illustrates the identified values of Θ . The values identified using *Method B)* fall into the same range as those identified by *Method A)*.

The naive approach employed in *Method B)* results in low error of the simulation outcome compared to the measurement. However, the identified values of Γ do not represent the physiology of the measurement subject; the error of the identified Γ values, shown in Table 8, is a magnitude higher than in the case of the other methods compared to the identification result of *Method A)*.

4.2 *Method C)*

The additive term using the neural network is not utilised in *Method C)*, as the model employed is instead the one represented by Equation 8. This method has been employed by [29] and [26]. The identified values of the parameters are visualised in Figure 7 and Figure 9. These figures and the results presented in Table 8 demonstrate that the method produces values of Γ with low error, however values of Θ with high error compared to *Method A)*. Additionally, the simpler model, excluding the additive term, is not capable of accurately modelling the central arterial pressure, as illustrated in Figure 10.

Method C), while offering a straightforward implementation, results in a high error in the identified values of Θ compared to *Method A)* and is unable to precisely reproduce the central arterial blood pressure measurement.

4.3 *Method D)*

A complex, three-phase solution is employed in *Method D)*. In contrast to the naive approach applied in *Method B)*, the neural network is forced to learn the representation of the features that the Tube-load model does not include. The outcomes demonstrate that the identified values exhibit the lowest error when compared to *Method A)*.

The findings demonstrate that the identification approximates *Method A)* well. The method produces central arterial blood pressure values that approach the measurement. However, it should

be noted that this method relies on no-notch data, which is not readily available in clinical settings. *Method E)* has been developed to achieve a comparable outcome without the necessity for such data.

4.4 *Method E)*

The initial phase of *Method E)* is equivalent to *Method B)*. The subsequent phases are focused on enhancing the efficacy of the identification process. In the second phase, a neural network is trained to learn the features of the measurement that are not modelled by Equation 8. Finally, in phase three, the values of $\mathbf{p}_{ode}$ are identified once more. However, in this phase, the trained neural network and the extended model described by Equation 11 are utilised.

The simulation, illustrated in Figure 10, results in a central arterial blood pressure curve that approximates the measurement well. As demonstrated in Figure 7 and Figure 9, the identified values of the Γ and Θ parameters lie close to the results obtained using *Method A)*. Table 8 presents the quantitative evaluation of the identification compared to *Method A)*. *Method E)* results in identified values of Γ with a lower error than *Method B)*, higher than *Method D)* and similar to *Method C)* compared to *Method A)*. In case of Θ , *Method E)* has lower error than *Method C)*, but higher than *Methods B)* and *D)*.

This complex identification method aims to outperform *Method B)*, which was applied in previous research methods [29] [26]. The model produces a similar error in the case of Γ , however, it outperforms *Method B)* in the identification of Θ .

Thus, *E)* is capable of identifying physiologically valid ODE parameters ($\mathbf{P}_{ode}$) and identifying the neural network parameters ($\mathbf{P}_{nn}$) which will then model the dicrotic notch. The identification experiment with measurements from different physiological states of the model animal presented in Table 9 suggests that using *E)* the identified model is capable of describing various states of the cardiovascular system. However, the identification accuracy depends on the physiological state of the subject, indicating the need for a more detailed analysis of these aspects of the Tube-load model-based parameter identification.

5 Conclusions

The Neural ODE method-based parameter identification method provided physiologically plausible results. The most complex identification method, *Method E*) is capable of identifying the Tube-load model parameters and identifying the model of the additional disturbances, the dicrotic notch, by using the neural network. The proposed method directly uses the raw measurement signal enabling the detailed analysis of the physiological parameters in different physiological and pathological situations in the ICU treatment. *Method E*) can be used to define a detailed model of the dicrotic notch supporting the development of signal processing methods for filtering the disturbances of the arterial pressure curve.

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