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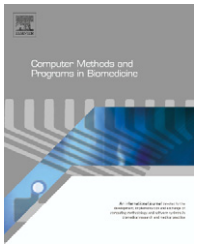

Model-based cardiac diagnosis of pulmonary embolism

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ABSTRACT

A minimal cardiac model has been shown to accurately capture a wide range of cardiovascular system dynamics commonly seen in the intensive care unit (ICU). However, standard parameter identification methods for this model are highly non-linear and non-convex, hindering real-time clinical application. An integral-based identification method that transforms the problem into a linear, convex problem, has been previously developed, but was only applied on continuous simulated data with random noise. This paper extends the method to handle discrete sets of clinical data, unmodelled dynamics, a significantly reduced data set theta requires only the minimum and maximum values of the pressure in the aorta, pulmonary artery and the volumes in the ventricles. The importance of integrals in the formulation for noise reduction is illustrated by demonstrating instability in the identification using simple derivative-based approaches. The cardiovascular system (CVS) model and parameter identification method are then clinically validated on porcine data for pulmonary embolism. Errors for the identified model are within 10% when re-simulated and compared to clinical data. All identified parameter trends match clinically expected changes. This work represents the first clinical validation of these models, methods and approach to cardiovascular diagnosis in critical care.

1. Introduction

Cardiac disease state is highly patient specific and difficult to accurately diagnose due to the limited measurements available. In addition, the body's natural reflex responses try to restore circulatory equilibrium, which can often mask the underlying symptoms [1,2]. Successful diagnosis and treatment often rely on the experience and intuition of clinical staff. Thus, a physiological, identifiable and validated computer model offers several potential advantages in diagnosis and therapy selection, by aggregating diverse patient data into a compact, patient specific, clinically relevant and potentially real-time assessment of circulatory status.

There are many CVS models in the literature ranging from very complex finite element models [3–6] to relatively simpler pressure volume approaches [7–9]. However, the focus is often on only specific areas of CVS dysfunction. Although there are full CVS models, patient-specific parameter optimization is either not considered or restricted to small subsets of the overall much larger parameter set (e.g.[10,11]). This restriction to specific CVS aspects can dramatically limit the range of CVS disturbances that can be detected, thus prohibiting use as a broader diagnostic tool for patients with unknown condition. For relatively larger, more complex system models computational cost and feasibility can also become a major issue.

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This research employs a physiologically validated minimal model [12–15] capable of capturing patient dynamics commonly seen in an ICU, while using a relatively small number of physiological variables. A highly efficient solution method [16] provides the necessary simplicity, flexibility and rapid forward simulation that is required in a clinical environment. An integral-based parameter identification method has been also been developed and shown, in simulation, to rapidly and accurately identify virtually the entire parameter set in the presence of significant measurement noise [17]. However, a relatively large measured data set was assumed, including continuously measured pressure and flow waveforms. Such measurements might not always be clinically available.

In this paper, the integral method is extended to allow discrete sets of clinical data and is shown to be robust to unmodelled dynamics and measurement noise. The measurements utilized are also reduced from prior work to a more clinically feasible set. The use of integrals in the formulation is shown to be critical for stability, even with locally smoothed curves, as compared to numerical derivative-based identification approaches. The method is initially tested on simulations of pulmonary embolism that capture all the physiologically expected responses. The CVS model and integral method are then clinically validated on a porcine model of pulmonary embolism.

2. Methodology

2.1. CVS model

The CVS model is a lumped parameter model [19], where the left and right ventricle chambers are characterized by the flow in and out of the chamber, the pressure up- and downstream and the resistances of the valves, and inertia of the blood. An overview of the model is given in Fig. 1. To add flexibility and better match waveform shape as well as peak values, the model is extended from [19] to allow a slightly non-linear pressure–volume relationship in the aorta and pulmonary artery. The equations for the left ventricle are defined:

$$V_{pcd} = V_{lv} + V_{rv} \tag{1}$$

$$P_{pcd} = P_{0pcd} \cdot (e^{\lambda_{pcd}(V_{pcd} - V_{0pcd})} - 1) \tag{2}$$

$$P_{peri} = P_{pcd} + P_{th} \tag{3}$$

$$V_{lvf} = V_{lv} - V_{spt} \tag{4}$$

$$P_{lvf} = \mathrm{dri}L \cdot E_{eslvf} \cdot V_{lvf} + (1 - \mathrm{dri}L) \cdot P_{0lvf} \cdot (e^{\lambda_{lvf} V_{lvf}} - 1) \tag{5}$$

$$P_{lv} = P_{lvf} + P_{peri} \tag{6}$$

$$P_{pu} = E_{pu} \cdot V_{pu} + P_{th} \tag{7}$$

$$\dot{V}_{ao} = Q_{av} - Q_{sys} \tag{8}$$

$$Q_{sys} = \frac{P_{ao} - P_{vc}}{R_{sys}} \tag{9}$$

$$P_{ao} = E_{ao} \cdot V_{ao}^{f} \tag{10}$$

$$\dot{V}_{lv} = Q_{av} - Q_{mt} \tag{11}$$

$$\dot{Q}_{mt} = H(H(P_{pu} - P_{lv}) + H(Q_{mt})) \cdot \frac{(P_{pu} - P_{lv} - R_{mt} \cdot Q_{mt})}{L_{mt}} \tag{12}$$

$$\dot{Q}_{av} = H(H(P_{lv} - P_{ao}) + H(Q_{av})) \cdot \frac{(P_{lv} - P_{ao} - R_{av} \cdot Q_{av})}{L_{av}} \tag{13}$$

where H is the Heaviside function, f is a non-linear factor ranging from 0.8 to 1.4, and all other variables are as shown in Fig. 1. Similar equations are used for the right ventricle and pulmonary/systemic circulation. For a more detailed description see [19,16,12–14]. The parameter f in Eq. (10) provides more flexibility to capture the shape and peak of P_{ao} seen in clinical data. Definitions of the parameters in the model are given in Table 1.

2.1.1. Activation function

The electrical activation of the left and right ventricles are described using a driver function and time varying elastance to model cardiac muscle activation [19,7]. For clinical validation on the porcine data, separate driver functions are chosen for the left and right ventricles:

$$\mathrm{dri}_L = A_L \cdot e^{(-b_L \cdot (t - (\mathrm{period}/c_L))^2)} \tag{14}$$

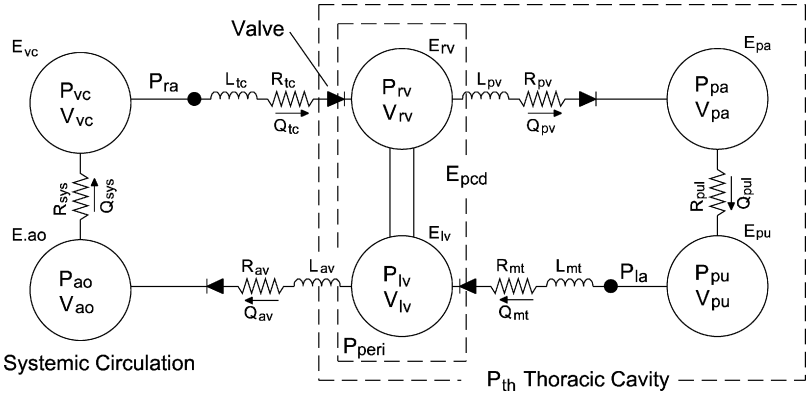

Fig. 1 – Minimal CVS model overview. The model is made up of elastic chambers connected by resistors and conductors in series. Each elastic chamber simulates the pressure–volume relationship in a particular area of the circulation.