

An Integrated Model of the Human Cardiopulmonary System

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Abstract—We have developed a mathematical model of the human cardiopulmonary system that is able to simulate the normal functions of the cardiovascular and pulmonary systems, as well as their coupled interactions. Included in the model are descriptions of atrial and ventricular mechanics, the hemodynamics of the systemic and pulmonic circulations, baroreflex control of arterial pressure, airway and lung mechanics, as well as, gas transport at alveolar-capillary membrane. With the suitable parameter set, the integrated cardiopulmonary model yielded pressure, volume and flow waveforms that agree well with published data. In addition, The model demonstrated stability under large amplitude perturbations of the physiological variables, such as Valsalva Maneuver.

Keywords – Cardiopulmonary modeling, ventricular interaction, closed-loop hemodynamics, baroreflex control, airway mechanics, gas exchange.

I. INTRODUCTION

The diagnosis and treatment of cardiopulmonary disease may be improved by using mathematical models of the cardiovascular and pulmonary systems. With this in mind, we have developed a model of the cardiopulmonary system that accurately describes various components of the system and simulates their normal behaviors in supine, resting human subjects. This integrated human cardiopulmonary model consists two main parts: (1) the circulatory model and (2) the airway/lung mechanics and gas exchange model.

The circulatory model used in our study is based on the multi-compartment model of the canine circulation that contains descriptions of heart, systemic circulation and pulmonic circulation [2,4]. We have added to this model the nonlinear descriptions of the venous system, and a description of how the baroreflexes influence heart rate, myocardial contractility and vasomotor tone. We based our baroreceptor control model on the work of Spickler et al [6] and Wesseling et al [8], and include descriptions of both parasympathetic (vagal) and sympathetic pathways.

The lumped airway mechanics and gas exchange model developed recently by our group describes ventilation, perfusion, mechanics and gas transport over the full range of normal lung volumes [3]. A modified version of this model is used in the current study. It characterizes the nonlinear resistive-compliant properties of the airways, and the nonlinear P-V characteristics of the lung. A distributed pulmonary circulatory model containing 35 contiguous capillary segments characterizes gas exchange at the

alveolar-capillary membrane, and yields good fits to expired O₂ and CO₂ data measured at the mouth.

II. MODEL DEVELOPMENT

The Circulatory Model

The general framework of our human circulatory loop model is similar to Olansen et al [4] (Fig.1) , with certain extensions and modifications. We have included the following components: (a) The heart model characterizes the atria, ventricles, interventricular septum, and the pericardial sheath. By incorporating the septum and pericardium, this heart model can conveniently mimic the ventricular interaction. (b) The lumped systemic and pulmonic circulatory loop consists of a group of resistive and elastic vessel segments. (c) The nonlinear pressure-volume (P-V) relationships describes the peripheral venous system. (d) A nonlinear collapsible description of the P-V relationship characterizes the vena cava. (e) The lumped characterizations of the baroreceptors and their reflex pathways control heart rate, heart contractility and vasomotor tone. There are four functional blocks that represent the baroreceptor, the central nervous system (CNS), the efferent pathways, and the effector organ, respectively.

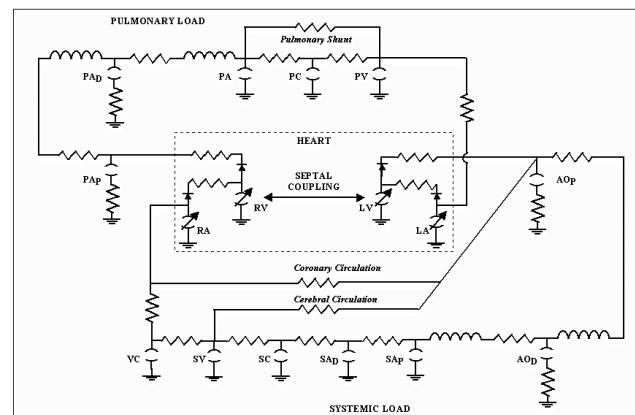


Figure 1. Hydraulic equivalent schematic of the closed loop circulatory model. (From: Olansen et al [4]).

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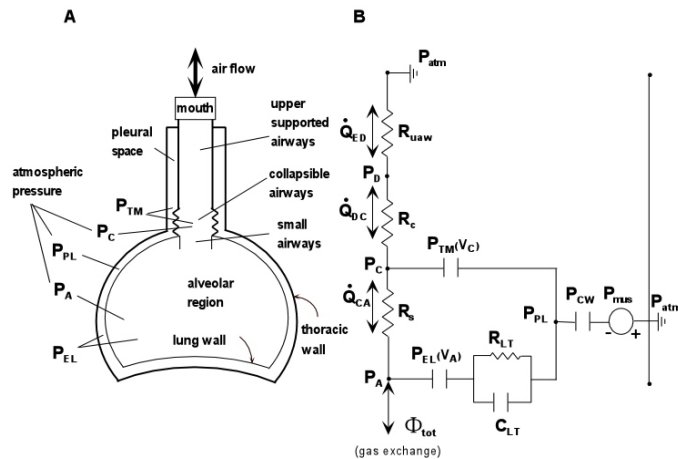


Figure 2. Airway/lung mechanics model. (Modified from: Athanasiades et al [1]).

The Airway/lung Mechanics and Gas Exchange Model

The pulmonary portion of our cardiopulmonary model combines two models previously developed. One focuses on airway/lung mechanics [1] and the other on gas exchange [3]. Figure 2 shows an equivalent pneumatic circuit model of the airways and lung of the normal human. The lung mechanics model includes nonlinear characterizations of airway resistance, airway and chest wall compliance, and lung tissue viscoelasticity (see Athanasiades et al [1] for details).

Gas exchange between air and blood occurs at the alveolar-capillary membrane. The empirical O_2 and CO_2 dissociation curves relate the content of each species with their corresponding partial pressures in blood. The diffusing capacity characterizes the gaseous diffusion across the alveolar-capillary membrane. O_2 is taken up by the blood, CO_2 is removed, and N_2 diffuses either way depending on the direction of their instantaneous partial pressure gradients.

The lumped pulmonary capillary is divided into 35 segments as in Liu et al [3]. Species molar balance is employed to describe the dynamics of the species blood concentration in each segment. The total flux rate of all gaseous species across the alveolar-membrane is thus computed as the sum of the individual fluxes in each of the segments.

III.COMPUTATIONAL ASPECTS

The complete model has 77 nonlinear differential equations and 116 parameters associated with its component models. In all, 149 outputs are generated simultaneously.

The model is programmed in C programming language and solved using the variable step-size Runge-Kutta-Merson algorithm with a maximum time step size of $2 \cdot 10^{-2}$ sec and an error tolerance of 10^{-6} . On average, it takes 20

minutes of CPU time on a Pentium II 333 MHz machine to simulate 35 seconds of cardiopulmonary events.

IV. RESULTS

Hemodynamics

The model predicted hemodynamics variables agree well with the typical human data. The left ventricular end-systolic pressure is 125 mmHg and the systolic duration is 0.3 second, or about one third of the cardiac cycle (0.8s). The aortic root pressure ranges from 80 to 120mmHg. The dirotic notch can be clearly seen in the simulation results. The left ventricular volume ranges from 150 ml (end-diastolic volume) to 70 ml (end-systolic volume), giving a stroke volume of 80 ml and an ejection fraction of 80/150 or 0.533. The volume added as the result of atrial systole is 30ml, about 20% of the end diastolic volume. The peak aortic flow rate is 750 ml/s and the peak pulmonary arterial flow rate is 400-500 ml/s.

The simulation showed that during inspiration, the stroke volume of left heart decreases, whereas the stroke volume of the right heart increases. During expiration, the stroke volume rises in the left heart and falls in the right heart. Our model helps explain the mechanism underlying this physiologic relationship.

Right and left ventricular volumes respond to pleural pressure because of both direct and series ventricular interaction. When pleural pressures are negative (e.g. with inspiration), an increase in venous return augments RV filling and RV stroke volume. The increased right ventricular filling causes the septum to encroach upon the left ventricle, because the pericardium limits total cardiac volume. As a result, left ventricular stroke volume is reduced. Simulations that ignore this ventricular interaction (rigid septum) underestimate the percentage fall in left ventricular stroke volume occurring during inspiration (2.5% vs. 5% with ventricular interaction). Without pericardial constraint, there is little respiratory variation in left ventricular stroke volume (1%). In addition, expiration causes a volume shift from the pulmonary to the systemic circulation. The blood pooling in the systemic vascular bed then increases left ventricular afterload with the next inspiration. Simulations show that both the end-systolic transmural pressure and volume of the left ventricle are highest at early inspiration, consistent with the increased afterload. Both the decreased filling and increased afterload decrease LV stroke volume during inspiration. The same mechanism explains why the two ventricles respond differently to elevated pleural pressures during expiration.

Airway Mechanics and Gas Exchange

During inspiration, subatmospheric pleural pressure is transmitted to the alveoli, facilitating air flow into the lungs. As this occurs, lung elastic recoil increases and the alveolar and atmospheric pressures equalize marking the

end of inspiration and the start of expiration. During expiration, the less negative pleural pressure and the resulting changes in lung elastic recoil cause positive alveolar pressure, pushing air from the lungs. The model predicts an average tidal volume of 500ml and a functional residual capacity (FRC) of 2.2L, which agree with measured values.

Inspiration fills the alveoli with O₂ enriched air, whereas expiration removes CO₂. The model-generated alveolar O₂ partial pressure (P_{O2}) varies from 95 mmHg to 105mmHg and CO₂ partial pressure (P_{CO2}) from 35mmHg to 40mmHg.

The model also predicted flux of O₂ and CO₂ at the alveolar-capillary membrane, which is modeled as 35 contiguous segments. For each segment, there is a gaseous flux waveform that pulsates with capillary blood flow. Most gaseous diffusion occurs at the initial capillary segments, but later diminishes when blood and alveolar gas content has equilibrated. Thus, the flux rates decrease exponentially from the first (entrance) to the last segment (exit).

We tested our model against the known changes that occur during the forced vital capacity and Valsalva maneuvers. The model demonstrated stability under these large amplitude disturbances and the model predictions agreed well with the available human data in both cases.

V. DISCUSSION

Our model of the human cardiopulmonary system combines several component models previously developed by our group. A nominal set of parameters provided reasonable fits to data obtained from studies of normal, supine, resting human subjects. The model accurately predicted the hemodynamic pressure, volume and flow waveforms, the airway pressure and volumes and the gaseous flux at the alveolar-capillary membrane. It also successfully simulated the large dynamic interactions between the cardiovascular and pulmonary systems that occur during the vital capacity and Valsalva maneuver. As such, it provides biophysical explanations of these large amplitude forcing maneuvers, that lends insight into their fundamental mechanisms. These preliminary results indicate that the model can be extended to characterize various cardiopulmonary disease states, and could be very helpful as a clinical tool when evaluating patients with suspected cardiac, pulmonary, or neurological disease.

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