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A Computational Model of Cardiovascular Physiology and Heart Sound Generation

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Abstract— **A computational model of the cardiovascular system is described which provides a framework for implementing and testing quantitative physiological models of heart sound generation. The lumped-parameter cardiovascular model can be solved for the hemodynamic variables on which the heart sound generation process is built. Parameters of the cardiovascular model can be adjusted to represent various normal and pathological conditions, and the acoustic consequences of those adjustments can be explored. The combined model of the physiology of cardiovascular circulation and heart sound generation has promise for application in teaching, training and algorithm development in computer-aided auscultation of the heart.**

I. Introduction

A computational model of the physiology of heart sound generation would provide a framework for testing theories about the production of heart sounds in health and disease. Such a model would make explicit the relationships between physiological parameters, hemodynamic variables and acoustic characteristics of heart sounds and murmurs. Such excellent descriptions of the process of heart sound production as that of Harris, Sutton & Towers [1] could be translated into a comprehensive computational model that would express in quantitative terms the relationships between blood pressure, flow, velocity, vessel compliance, inertance, and cross-sectional areas involved in the generative process and frequencies, amplitudes and durations of heart sounds. The model would support controlled manipulation of cardiovascular variables and demonstrate the hemodynamic consequences and heart sounds resulting from changes in cardiovascular condition. Consequently, a computational model would provide an excellent environment for instantiating, testing, replicating, sharing and evaluating theories of heart sound generation.

Models of heart sound generation are also highly useful for teaching auscultation. The ingenious early photoelectric synthesizer of Abe Ravin [2] shows the pedagogical value of being able to generate realistic examples of a wide range of sounds by controlling the amplitude, timing and spectral properties of constituent sounds that are reflective of various pathophysiological conditions. More deeply, a solid understanding of the physiology of heart sound generation is foundational to achieving excellence in auscultation of the heart. For that reason, a computational model of cardiovascular physiology and heart sound generation would provide an excellent tool for learning both cardiac physiology and auscultation of the heart. A well-designed model would support interactive adjustment of model parameters through a graphical user interface and the ability to see and hear the heart sounds and changes in heart sounds resulting from the model adjustments.

Moreover, in the context of the development, verification and validation of medical devices for computer-aided auscultation of the heart, a physiological model of heart sound production allows for the generation of an unlimited number of heart sounds under physiologically realistic conditions. Physiological variables can be instantiated over a range of values either singly or jointly to cover the space of patient conditions, whether normal or pathological, as densely as desired. In general, it would be extremely challenging to duplicate this coverage among live patients due to the statistical nature of the sampling process that is involved in any realistic clinical protocol. Consider the difficulty of finding subjects with varying degrees of mitral regurgitation as measured in cross-sectional area of the regurgitant orifice, regurgitant volume and fraction and pulmonary venous pressure. Moreover, the precise, repeatable nature of synthetic heart sounds enables quantitative measures of algorithm performance in terms of basic independent variables. Even the synthesis of extreme cases facilitates "stress-testing" of algorithms with beneficial effects on robustness of performance.

II. Lumped-Parameter Cardiovascular Model

Following Clark and colleagues [3-10], we represent the cardiovascular system as a lumped-parameter model comprised of the heart, pericardium and systemic and pulmonic circulatory systems. As shown in Figure 1, we extend the Clark model to represent the systemic circulation as separate upper/lower body circuits returning to the heart via the inferior and superior vena cavae and the pulmonary circulation as separate left and right circuits.

A. Heart model

The heart is modeled as four chambers with associated valves. The myocardial chambers are represented as time-varying compliances which give rise to pulsatile flow that becomes directional due to the action of the heart valves.

Myocardial contraction is modeled as a time-varying activation function that controls the weighted combination of an end-systolic and an end-diastolic pressure-volume relationship for each chamber. The end systolic P-V relationship is scaled by a parameter that represents

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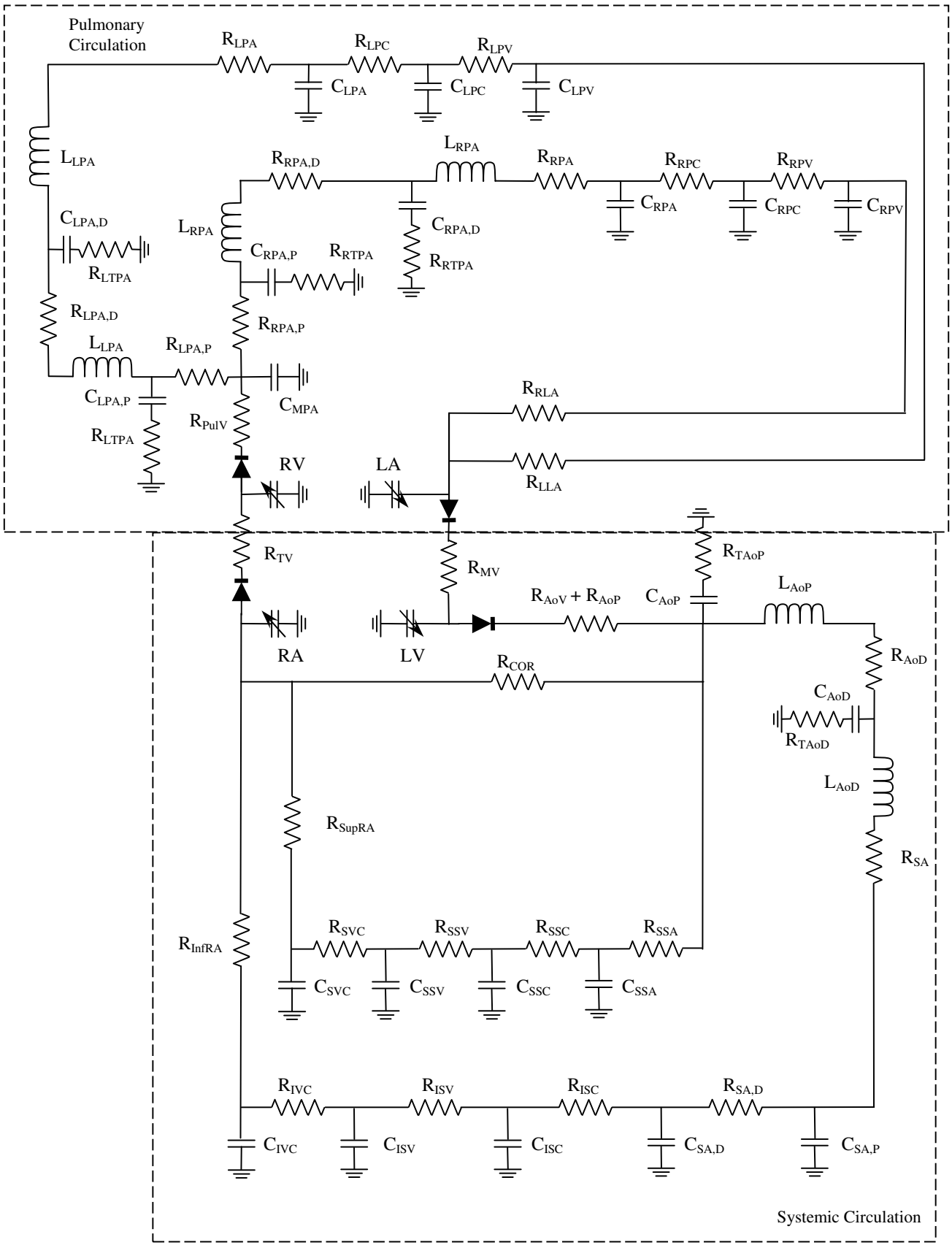

Fig. 1. Architecture of lumped parameter model of cardiovascular circulation with superior and inferior systemic circulation and left/right pulmonary circulation.

contractility. The time-compression/expansion of the activation function is also parameterized by contractility to reflect more or less vigorous contraction. The contractility parameter is related to the HR through sympathetic and vagal processes that are described in [7]. For our purposes, the relationship between heart rate and contractility (as well as vasomotor tone) is controlled independently using physiologically realistic values.

The heart valves were originally modeled as anti-parallel diodes to allow forward and backward resistances to be represented. The valve state of open/closed is determined by the transvalvar pressure, and the forward flow resistance in the open state captures the pressure drop across the valve during forward flow. Regurgitant flow is prevented in the normal case by a virtually infinite back resistance, which can be reduced appropriately to model valvular insufficiency.

Subsequently, the valve model was modified based on the simplified Bernoulli equation to compute the transvalvar flow from the product of the velocity, derived from the pressure gradient, and the valvular cross-sectional area, whether the area of open valve during forward flow or the area of the regurgitant orifice if present. This approach allowed valve stenosis and regurgitation to be modeled in terms of aperture size.

The electrophysiological generation of heart beats is modeled by synchronizing the activation functions of the four heart chambers with appropriate conduction delays with respect to a pace-making fiducial point which is derived from the specified heart rate. The cardiac electrical cycle is assumed to begin with the sino-atrial (SA) node from which activation of the left and right atria begins after specified SA-LA and SA-RA delays. The propagation of the atrial depolarization to the atrio-ventricular (AV) node is modeled as a simple time-delay, from which the activations of the left and right ventricles begin after specified AV-LV and AV-RV delays. These delays are initialized to heart-rate appropriate values and can be modified to reflect various conduction diseases. The regularity of the fiducial point itself can also be modified to represent various cardiac arrhythmias.

Following [7], the pericardium is modeled as a passive variable compliance that exerts pressure on the heart chambers in proportional to the total pericardial volume, comprised of total cardiac and pericardial cavity volumes.

B. Systemic circulation

The systemic circulation includes the aorta and inferior and superior circuits, which are comprised of arterial, arteriolar, capillary, venous and vena caval resistance-compliance segments. The aortic structure is represented by proximal and distal sections, each with a series flow resistance and inductance inertial mass, along with a shunt compliance and viscoelastic resistance. A coronary supply and return is represented by a single shunt resistance which originates from the proximal aorta and terminates in the right atrium. The cerebral circulation is represented by a single shunt resistance which arises similarly from the proximal aorta and returns to the vena cava. The parameter values for the systemic circulation were adapted from Lu [7] and Luo [10], corrected and adjusted to balance the inferior and superior circulation.

The wall compliance and axial resistance of systemic arteries and arterioles are significantly affected by vasomotor tone. Following Lu [7], the wall compliance is modeled as an active and a passive P-V relationship, the actual P-V relationship being the sum of these relationships weighted by a parameter reflecting the degree of vasoconstriction. The volume-dependent axial resistance of the systemic arteries also contains a vasoconstriction-dependent offset term.

C. Pulmonic circulation

Following Lu [7], the pulmonary circulation is modeled as sections representing the pulmonary artery, arterioles, capillaries and veins. The pulmonic artery is represented by proximal and distal sections, each with a series flow resistance, inductance, shunt compliance and viscoelastic resistance. We extended the model by representing the left and right pulmonary circuits separately, and adjusting the model parameters so that the impedance of the left path mirrored the right with the same combined impedance. We also inserted a section representing the main pulmonary artery trunk between the right ventricle and the left/right branch pulmonary arteries.

The pulmonary arterioles, capillaries and veins are modeled by series resistances and shunt compliances culminating in a series resistance connecting each pulmonary circuit to the left atrium.

The respiratory process is modeled as an independent input to the cardiovascular system, in which the respiratory rate, amplitude and phase with respect to the heart rhythm are variable parameters. The appropriate relationship between heart rate and respiratory rate must thus be maintained outside of the model. Respiration is modeled as a sinusoidal variation in intra-thoracic pressure, which affects in turn the pericardial pressure, ventricular pressure and venous return.

III. HEART SOUND GENERATION

A. First heart sound

The first heart sound is a composite of the acoustic consequences of mitral and tricuspid valve closures at the onset of ventricular systole. The respective component sounds are generated as the contracting ventricle accelerates the ventricular blood volume toward the corresponding atrium and the valve is forced closed as the blood catches the underside of the valve leaflets and presses them into apposition. The closure of the valve causes a reverberation as the chordae tendinae become tensed and transmit energy through the papillary muscles which causes the entire cardiohemic mass to vibrate.

This process can be modeled by representing the blood volume as a mass that is accelerated by the force corresponding to the net pressure between ventricle and atrium applied to the closed valve area. This force is transmitted via the tendinae to the papillary muscles and myocardium which provide a spring-like counter-force proportional to displacement. We include a damping factor to represent the dissipation of energy via the absorption of the myocardium. The equation of motion is thus:

$$(P_{LV} - P_{LA})\, A_{mitral} = \rho V_{LV} \ddot{x} + D\dot{x} + K(x - x_0)$$

where P_{LV} = left ventricular pressure, P_{LA} = left atrial pressure, A_{mitral} is the effective cross-sectional area of the closed mitral valve, ρ is the density of blood, D is the damping coefficient, x_0 is the relaxed displacement of the mitral valve surface, K is the aggregate spring constant, and x is the displacement of the mitral valve surface. This equation can be solved beginning from the point of valve closure, with the initial conditions of relaxed mitral position $x=x_0$ and an initial velocity that reflects the initial reversal of flow that accompanies valve closure. Note that the atrial and ventricular pressures are generated by the cardiovascular model and vary with time. During isovolumic contraction, when the first sound is generated, the ventricular volume is constant.

From the characteristics equation, we can determine that oscillatory solution will occur when $D^2 < 4K\rho V_{LV}$, with a fundamental frequency of:

$$f = \frac{1}{2\pi \rho V_{LV}} \sqrt{K \rho V_{LV} - \frac{D^2}{4}}$$

and a damping time constant of:

$$\tau = \frac{2\rho V_{LV}}{D}$$

This equation can be solved beginning from the point of valve closure, with the initial conditions of relaxed mitral position $x=x_0$ and an initial velocity that reflects the initial reversal of flow that accompanies valve closure.

The passive opening of the mitral valve in diastole can also be modeled by an analogous approach so that the valve leaflets are reposition for the subsequent systolic onset.

B. Second heart sound

The constituents of the second heart sound can be similarly modeled using the gradients between aortic and left ventricular pressures on the left side (A2), and pulmonary artery and right ventricular pressures on the right side (P2) as the driving force, and analogous spring and damping constants, cross-sectional areas and blood volumes. Respiratory variations in ventricular filling affect the relative timing of the aortic and pulmonic components of the second sound.

C. Third and fourth heart sounds

Following Kovacs, et. al [11,12], third [11] and fourth [12] heart sounds on both left and right sides can be generated from the ventricular filling velocities and accelerations based on a damped oscillatory system that includes ventricular compliance and dissipation. The amplitude, frequency and damping time-constant of the third and fourth sounds are determined by the spring and damping coefficients.

D. Heart murmurs

Heart murmurs are produced by turbulent blood flow across an open valve, backwards through a partially closed valve, past a point of occlusion or constriction or through a pathological aperture.

We assume that the acoustic energy of the murmur is proportional to the kinetic energy of the turbulent flow; that is $|x(t)|^2 \propto mv^2(t)$. From which we infer that the envelope of the murmur is proportional to the velocity times the square root of the mass. To reflect the contribution of the square root of the mass, we include the diameter of the aperture in the proportionality: $e(t) = k\, D\, v(t)$.

The frequency characteristics of heart murmurs are determined primarily by the velocity of flow. For fluid flow in a pipe, the Reynolds number ($R = \rho v D/\eta$) gives a measure of the likelihood of turbulent flow, where the diameter D and velocity v are hemodynamic variables, and density ρ and viscosity η are properties of the blood. We assume a stationary isotropic turbulence and design a bandpass filter with corner frequencies determined by the peak velocity to approximate the Kolmogorov spectrum[13]. We then generate the murmur by passing white noise through this filter and modulate the result with the velocity-based envelope.

IV. RESULTS

The cardiovascular model was configured with parameter values and initial conditions appropriate to a subject with mild mitral regurgitation. An example of the model output is shown in Figure 2 which depicts the transvalvar flows across each valve along with aortic and pulmonary artery flows. Other plots show the blood pressure, volume and flow at each point in the model along with variable compliance and resistance values for the given modeling parameters.

The model of mitral closure was separately implemented using selected physiological values for spring and damping constants in Table 1. The spring constant was derived from typical elastance values for left ventricle, assumed to be spherical. We obtain an oscillatory frequency of 108 Hz and a damping time constant of 13 ms.

The model was tested using a simulated pressure waveform that consisted of a parabolic pressure wave with a peak pressure of 90 mmHg and a width of 300 ms.

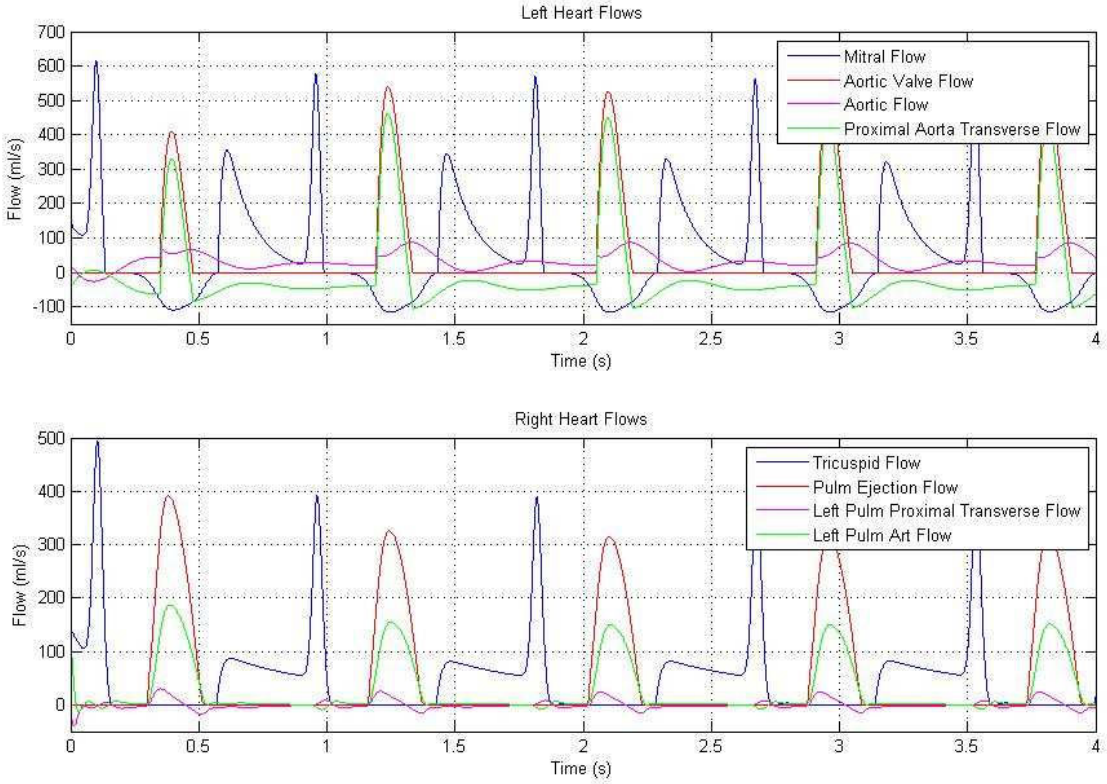

Figure 2 Transvalvular flows for cardiovascular model with mild mitral regurgitation

The results of the model are depicted in Figure 3, which shows the displacement of the mitral valve leaflet in response to ventricular systole. Simulations appropriate to the tricuspid valve with a peak pressure of 15 mmHg yielded similar results

TABLE I
PARAMETERS FOR MITRAL VALVE CLOSURE SOUND

Parameter	Symbol	Value	Units
Displacement	x_0	2	cm
Velocity	$\dot{x}_0$	0.2	cm/s
Spring constant	K	6×10^7	g/s^2
Damping const.	D	2×10^4	g/s
Volume LV	V_{LV}	120	ml
Blood density	ρ	1.06	g/cm^3
Area MV	A_{mitral}	5.5	cm^2

The validation of this model awaits comparison with phonocardiographic recordings but the modeled M_1 sounds plausibly like the mitral component of the first heart sound.

The valve leaflet displacement model can be integrated into the cardiovascular model by augmenting the state variable vector appropriately.

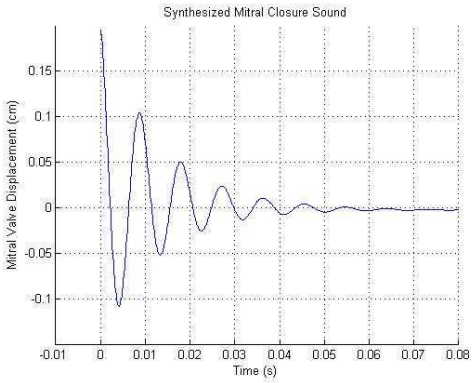

Fig. 3. Displacement of mitral valve leaflets at closure.

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