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Simulating cardiac disorders with a lumped parameter synergistic model

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***Abstract*— A lumped parameter synergistic model of the human cardiovascular system (CVS) is proposed to integrate the heart's electrical activity with its mechanical activity. This model can represent the physiological condition of a patient in an effective way, whether it is considered normal or with some cardiac disorders. The electrical activity is coupled to the CVS model through electrocardiogram (ECG) signals in the suggested model. The variations in ECG morphology are detected by appropriate algorithms and changes parameters of the CVS model, such as systemic resistance and end-systolic pressure-volume relationship.**

***Clinical relevance*— It provides interpretation and analysis of physiological data of the cardiovascular system, both of electrical and mechanical cardiac behavior, evaluated together.**

I. INTRODUCTION

Cardiovascular diseases are considered the main cause of death globally, indicating a higher rate in low and middle-income countries [1]. In an attempt to minimize the mortality rate due to these diseases, advanced research is being directed to methods capable of providing the necessary support for treating these problems.

Lumped parameter models, also known as 0D models, are a widely used way to study the behavior of the human cardiovascular system (CVS), demonstrating a synthesized way of representing components of CVS using the analogy with electrical circuits. Simaan *et al.* [2] proposes a non-linear 5-th order model that reproduce the hemodynamics of the left side of the heart, simulating variables such as flow, pressure and volume. However, this model does not consider the coupling between the electrical and mechanical activities of the heart. Some authors suggest synergistic CVS models that allow the mechanical properties of the heart to be linked to electrical and chemical activity. However, this coupling to the chemical activity occurs at the cellular level, making the synergy implementation excessively complex [3]. Therefore, there is a need to develop a model that performs this coupling and that allows representing the physiological condition of a patient either in healthy clinical cases or to characterize extreme deficiencies, taking into account the reduced complexity of the 0D models.

In this paper, both electrical and mechanical activities are integrated into a CVS 0D model. In other words, the dynamic of the electrocardiogram signal (electrical activity) drives the behavior of the physiological variables corresponding to the mechanical activity. Moreover, changes in the ECG morphology are interpreted as physiological changes in the individual's condition and are reflected in the CVS model by changing some parameters.

II. SYNERGISTIC MODEL

The proposed synergistic model consists of choosing a lumped parameter CVS model based on the concept of time-varying elastance function to represent the mechanical behavior of the left ventricle. For the proof-of-concept, synthetic ECG signals were used to activate this function appropriately, either for healthy or pathological conditions.

A. Lumped Parameter Cardiovascular Model

The lumped parameter CVS model used in this work was developed in [2] and its representation shown in Fig. 1. This model allows the reproduction of the left side of the heart, the aortic pressure and flow as well as the systemic arterial system. Instead of using the left ventricular pressure, $P_{lv}(t)$, this model was adapted to use the left ventricular volume, $V_{lv}(t)$, as a state variable. This modification was made to avoid the use of a derivative $C(t)$, thus preventing numerical instabilities [4]. Thus, the five state variables are: $P_{ao}(t)$, the aortic pressure; $Q_{ao}(t)$, the aortic flow; $P_s(t)$, the systemic pressure; $P_{la}(t)$ that is the left atrial pressure and $V_{lv}(t)$.

In this model, left atrium is represented by the capacitor C_{la}; the mitral valve is represented by the resistor R_m and diode D_m; the aortic valve is represented by the R_a and D_a. The operation of these valves is represented by ideal diodes taking values of either one or zero, depending on if the valve is open or closed, respectively.

The aortic compliance is represented by C_{ao} and the systemic arterial system is modeled using a four-element Windkessel model comprising R_c, L_s, C_s and R_s. The compliance of the left ventricle (LV) is modeled by time-varying capacitor $C(t)$ which is the inverse of the ventricle's elastance function, $E(t)$ calculated as:

$$E(t) = 1/C(t) = (E_{max} - E_{min})E_n(t_n) + E_{min} \quad (1)$$

where $E_n(t_n)$ is the normalized elastance, $t_n = \text{mod}(t, 60/\text{HR})/T_{max}$ is the normalized time that is reset to 0 at each cardiac cycle, HR is the chosen heart rate and $T_{max} = 0.2 + 0.1555Tc$. The parameters E_{max} and E_{min} are used to describe the left ventricular condition [2].

The relationship between left ventricle pressure and volume is given by $E(t) = P_{lv}(t)/\left[V_{lv}(t) - V_o\right]$, where V_o is an empirical constant held over a wide range of intraventricular volume [5]. Using this relationship, $P_{lv}(t)$ might be easily calculated. All parameters of the CVS model, $\boldsymbol{\theta} = [R_s, R_c, R_m, R_a, C_{la}, C_s, C_{ao}, L_s, E_{max}, E_{min}]$, and their associated values are listed in Table I.

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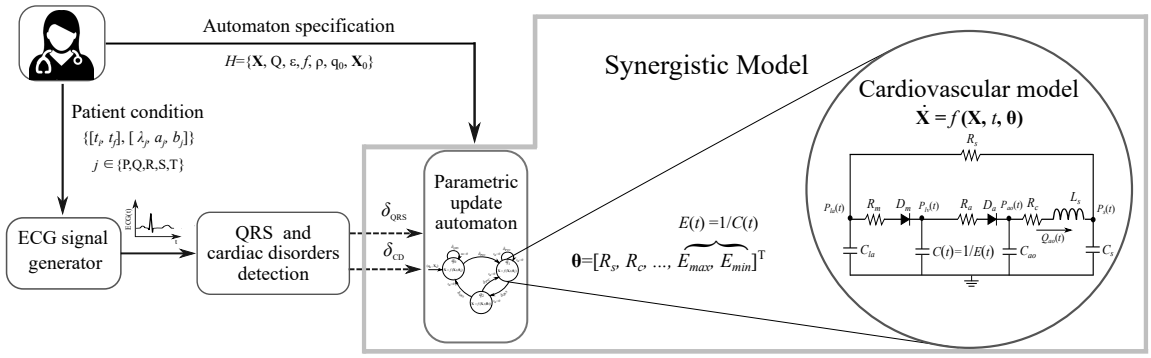

Fig. 1. The output of the "ECG signal generator" block is an ECG signal with or without cardiac disorders. The patient condition is defined by experts and is implemented by changing the "Automaton specification" and the parameters of the ECG generator: $[t_i, t_f]$ represent the beginning and the end of a cardiac cycle; the parameters λ_j, a_j and b_j represent the position, the amplitude and the duration of each ECG wave respectively; and $j \in \{P, Q, R, S, T\}$ indicates the respective ECG wave. The ECG signal is fed to the "QRS and cardiac disorders detection" block, which generates two independent discrete events as outputs: δ_{QRS} and δ_{CD} (dashed lines). These events are exogenous discrete events for the "Parametric update automaton". This hybrid automaton is responsible for updating the parameter values of the CVS model to properly simulate the patient condition.

TABLE I

EQUIVALENT CIRCUIT MODEL PARAMETERS.

Parameter	Value	Description
Resistances (mmHg s/ml)		
R_s	1.0000	Systemic vascular resistance
R_c	0.0398	Characteristic resistance
R_m	0.0050	Mitral valve resistance
R_a	0.0010	Aortic valve resistance
Compliances (ml/mmHg)		
$C(t)$	Time varying	Left ventricular compliance
C_{la}	4.4000	Left atrial compliance
C_s	1.3300	Systemic compliance
C_{ao}	0.0800	Aortic compliance
Inertances (mmHg s^2/ml)		
L_s	0.0005	Inertance of blood in aorta

B. Lumped parameter synergistic model

The proposed lumped parameter synergistic model (LPSM) makes the computation of $E(t)$ be simultaneous with occurrence of each QRS complex (δ_{QRS}) as proposed in [6]. This fact allows one to represent the excitation-contraction coupling phenomenon partially, but without the mechano-electric feedback [7]. This phenomenon is defined as a series of events occurring from generation of the action potential in the skeletal muscle fibers to the beginning of muscle contraction [8]. In this work, this series of electrical events is represented by δ_{QRS} and the muscle contraction by $E(t)$. To ensure the simultaneity of δ_{QRS} and $E(t)$, t_n in (1) is reset at each δ_{QRS} and the period of $E(t)$ is driven by the electrical activity. As a consequence of this, HR is now time-varying and depends on the δ_{QRS}. It is quite different from [2], where HR is chosen at the beginning of the simulation. Besides the reset of t_n, the vector $\boldsymbol{\theta}$ is also defined at each new cardiac cycle, allowing one to represent several physiological conditions.

The proposed synergy is implemented as described in the schematic shown in Fig. 1 (see area delimited by the gray line), disregarding δ_{CD} that will be discussed in the next section. An hybrid automaton (HA) used to update the $\boldsymbol{\theta}$ vector will also be treated later with a specific cardiac disorder and it can represents a patient without any cardiac disorder simply by removing states q_1 and q_2 in Fig.2.

1) Premature Ventricular Contraction: In this subsection, LPSM is evaluated by choosing the premature ventricular contraction (PVC) as the cardiac disorder. It is an early heartbeat followed by a compensatory pause between the PVC and the next normal heartbeat (prolonged diastole), which increases the left ventricle pressure compared with the regular beat preceding the PVC [9], [10].

Synthetic ECG signals [11], can be generated with one or more cardiac disorders [12], by adjusting the parameters according to the required disease. The parameters of synthetic ECG signal with PVC were determined using a Differential Evolution (DE) algorithm [13]. A fragment of a real ECG signal with PVC was extracted from record 114 of the MIT-BIH Arrhythmia Database [14] of Physionet [15]. The performance index Root Mean Square Error (RMSE) was used as a fitness function between the real signal and the signal generated with estimated parameters. The DE variant Best/1/Bin was executed for 1500 generations with parameters F (Recombination Constant) = [0.5,1.85), CR (Crossover Rate) = 0.7 and NP (Population Size) = 300. The exact method will not be explained due to a lack of space.

In the schematic of Fig. 1, one can see the block called QRS and cardiac disorders detection. This block generates two independent discrete events as outputs: one for each δ_{QRS}; and one for each cardiac disorders detection (δ_{CD}). Herein, the QRS detection was implemented using a wavelet-based approach with a sliding window of 1 second. The signal portion within the window is decomposed in 4 levels using the Maximum Overlap Discrete Wavelet Transform (MODWT) and then reconstructed using only the detail coefficients at levels 2 and 3. This fact creates a band-pass effect that emphasizes the QRS frequency components. After the reconstruction, the resulting signal is submitted to a thresholding process with an empirical threshold value of

8 times the magnitude average. This process is performed in real-time for each new sample of the ECG signal, and all points that exceed the defined threshold are deemed as detected QRS complexes. The PVC detection can be done with some real-time technique such as that in [16], which uses adaptive threshold methods and the the energy of the coefficients of the Redundant Discrete Wavelet Transform (RDWT) for PVC detection.

C. Parametric Update Hybrid Automaton

Events δ_{QRS} and δ_{CD} are exogenous to the HA that contains rules previously defined by experts for updating the parameters of CVS model (Fig. 2). This HA follows the formalism described in [17] and is defined as a 7-tuple $H = (\mathbf{X}, Q, \epsilon, f, \rho, q_0, \mathbf{X}_0)$ with the following components: $\mathbf{X} = \{P_{ao}(t), Q_{ao}(t), V_{lv}(t), P_s(t), P_{la}(t)\}$ is the continuous state space; $Q = \{q_0, q_1, q_2\}$ is the set of discrete states; $\epsilon = \{\delta_{\text{QRS}}, \delta_{\text{PVC}}\}$ is the finite set of exogenous discrete events; $f : Q \times X \rightarrow X$, defined as $f(\mathbf{X}, t, \boldsymbol{\theta})$, is the vector field describing the continuous dynamics; ρ is the reset function; q_0 is the initial discrete state; and $\mathbf{X}_0$ is the initial continuous state.

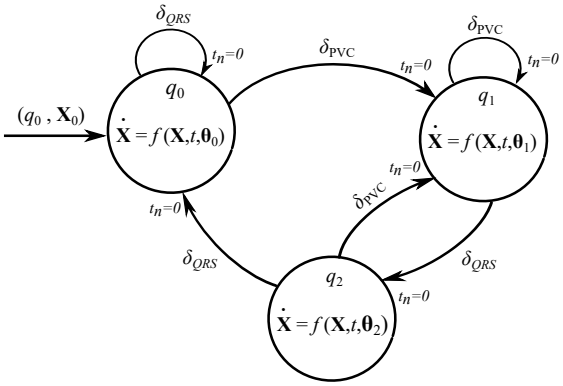

Fig. 2. Hybrid automaton used to simulate the LPSM with PVC.

Assuming the initial condition $(q_0, \mathbf{X}_0)$, in the first discrete state, q_0, the vector field is $f(\mathbf{X}, t, \boldsymbol{\theta}_0)$ and the continuous dynamics represents a normal heartbeat. If a new exogenous event δ_{QRS} takes place, the system remains in the same discrete state q_0 and a new cycle of $E(t)$ is started, i.e., a new normal heartbeat occurs. Moreover, a reset condition $t_n = 0$ is shown in all transitions, indicating that the variable t_n is reset whenever a new cardiac cycle occurs.

The transition to the discrete state q_1 occurs when an exogenous event δ_{PVC} takes place. Now, the vector field is $f(\mathbf{X}, t, \boldsymbol{\theta}_1)$ and the continuous dynamics represents the occurrence of a PVC. The difference between $\boldsymbol{\theta}_1$ and the previous one, $\boldsymbol{\theta}_0$, is the decreased value of E_{max} to simulate the weak premature contraction. If a new δ_{PVC} takes place, the system remains in q_1 and a new premature cycle of $E(t)$ is started with the same $\boldsymbol{\theta}_1$, i.e., a new premature heartbeat.

The transition to the discrete state q_2 occurs when a new δ_{QRS} takes place. Now, the vector field is $f(\mathbf{X}, t, \boldsymbol{\theta}_2)$ representing the occurrence of a new heartbeat with increased ejection pressure. The difference between $\boldsymbol{\theta}_2$ and the previous one, $\boldsymbol{\theta}_1$, is the increased value of E_{max} to simulate the high $P_{lv}(t)$ due to prolonged diastole. In the discrete state q_2, if a new δ_{PVC} takes place, the system returns to q_1 and a new premature contraction occurs. However, and still in q_2, if a new δ_{QRS} takes place, the system goes to q_0 and a new normal cycle of $E(t)$ is started with the first vector $\boldsymbol{\theta}_0$, i.e., a normal heartbeat.

III. RESULTS AND DISCUSSION

The hemodynamic behavior of a patient with PVC is represented in Fig. 3. The synthetic ECG signal used in the simulations lasts for 5 seconds and contains only one occurrence of PVC at approximately 1.7 seconds (Fig. 3-a). The parameters of both normal and premature heartbeat are listed in Table II.

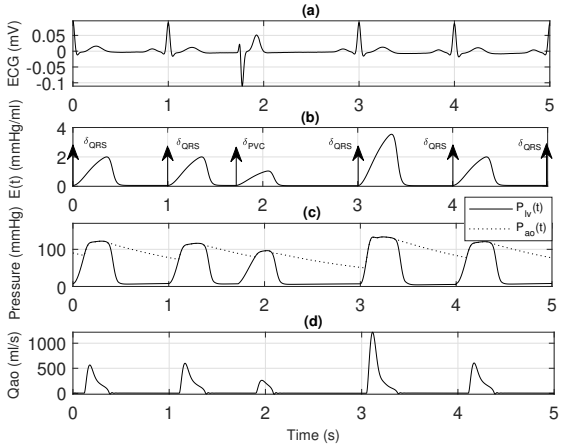

Fig. 3. Physiological variables involved in cardiac cycle events. (a) ECG signal; (b) $E(t)$ with indications of δ_{QRS} and δ_{PVC} events; (c) filled curve $P_{lv}(t)$ and dashed curve $P_{ao}(t)$; (d) aortic flow $Q_{ao}(t)$.

TABLE II
PARAMETERS OF ECG MODEL FOR BOTH NORMAL AND PVC.

	P	**Q**	**R**	**S**	**T**
λ_j	$-\frac{1}{3}\pi$	$-\frac{1}{12}\pi$	0	$\frac{1}{12}\pi$	$\frac{1}{2}\pi$
a_j	1.2	-5.0	30.0	-7.5	0.75
b_j	0.25	0.1	0.1	0.1	0.4
	$\mathbf{P}_{\text{PVC}}$	$\mathbf{Q}_{\text{PVC}}$	$\mathbf{R}_{\text{PVC}}$	$\mathbf{S}_{\text{PVC}}$	$\mathbf{T}_{\text{PVC}}$
λ_j	2.81	-1.55	-1.45	-1.38	-0.47
a_j	0.022	114.49	-191.20	-33.87	7.21
b_j	0.042	0.055	-0.053	0.102	0.222

The behavior of $E(t)$ function, as well as the indication of the events δ_{QRS} and δ_{PVC} are shown in the Fig. 3-b. The first two cardiac cycles are referred as normal heartbeats with $E_{\text{max}} = 2.0$ mmHg/ml. It can also be observed that the systolic and diastolic pressures in this period present values of approximately 120mmHg by 80mmHg (Fig. 3-c). The occurrence of a PVC at 1.7 seconds generates a weak and premature contraction, which was simulated with $E_{\text{max}} = 1.0$

mmHg/ml. Next, to represent high ventricular pressures duo to the prolonged diastole, $E_{\max} = 3.0$ mmHg/ml. After the adjustment cycle, around 4s, $E_{\max} = 2.0$ mmHg/ml again. The changes in the hemodynamic variables $P_{lv}(t)$, $P_{ao}(t)$ (Fig. 3-c) and $Q_{ao}(t)$ (Fig. 3-d) are in agreement with [10].

Another way to analyze the performance of this model is looking for the pressure-volume (PV) loops once there is a relevant change in LV pressure caused by the prolonged diastole. Three PV loops were simulated and can be viewed in Fig. 4, representing normal heartbeats, premature heartbeats occurring during the PVC and normal heartbeats occurring after PVC with increased LV pressure.

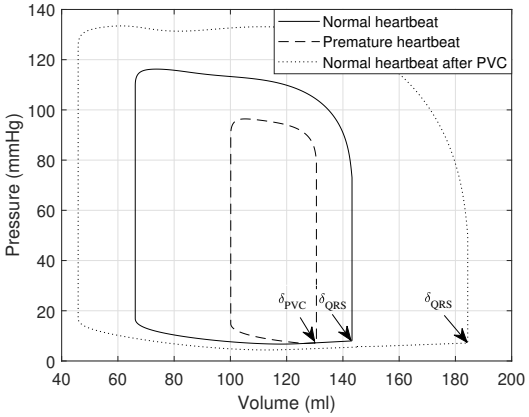

Fig. 4. PV-loop representing the cardiac behavior from a mechanical point of view. The filled curve corresponds to the normal heart rate; dashed curve represents premature beat; dotted curve is the compensatory pause period.

IV. CONCLUSIONS

A synergistic model of CVS that allows the study of the electrical and mechanical behavior is developed in this work. The synergy is implemented by coupling the ECG signals to a lumped parameter CVS model. The detection of QRS complexes and cardiac disorders generates discrete events used as exogenous inputs for a HA responsible for updating specific parameters of the CVS model. A synthetic ECG with PVC was simulated, as well as the implementation of the variable elastance function that is synchronized with each δ_{QRS} or δ_{PVC}. Synthetic signals were used to facilitate the implementation and test of the proposed solution. However, further research steps aim to use signals collected from patients or database ECG signals and explaining the relationship between the ECG signal and the CVS parameters and the vessel functions.

From the moment of the occurrence of a PVC, there were changes in $P_{lv}(t)$, $P_{ao}(t)$ and $Q_{ao}(t)$. In addition, mechanical behavior could also be assessed by analyzing the PV-loops since the amount of blood volume is reduced during the occurrence of a PVC. To varying the heartbeat to reproduce required diseases or change the level of physical activity, modifying parameters of the model, are actions that allow evaluating the effects in the implemented model and the effectiveness of the synergy.

In order to complete the Mecanoelectric Regulatory Loop, which allows modifications in a bidirectional way, we have also been working on Mecanoelectric Feedback, which is the electrical response from mechanics. Thus, the proposed approaches aim at improving the representation of CVS models with heart disease without increasing their complexity. There is no restriction to extend the CVS model to include the venous side of circulation and right atrial filling pressure. This method brings significant contributions, both in terms of teaching to understand better the functioning of the CVS and possible treatments and interventions.

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