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A New Real-time Parameter Estimation for Virtual Cardiovascular Model using ECG Signal

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Abstract

This research presents a new approach for real-time simulation of heart dynamics where the real-time electrocardiogram (ECG) measurements are used as external activation. The model uses lumped mass nonlinear differential equations to capture the coupled mechanical and physiological actions of the heart chambers, valves, pulmonary and systemic blood circulation loops. The model parameters are estimated online from the ECG features. The model was implemented in Matlab/Simulink environment and tested using signals in MGH/MF Waveform Database from Physionet. The results show that the model was able to discern the effect of variations in the time and frequency patterns of central venous pressure, pulmonary blood pressure, and respiratory impedance. The model-derived signals correlated well (R^2 ~0.78) with the actual hemodynamic signals. These findings support the suitability of developing a virtual instrument platform where the model-derived signals (presented appropriately) can be used for clinical diagnosis in lieu of expensive instrumentation.
Keywords:model parameter estimation, activation functions, cardiovascular model, virtual instrument cardiovascular healthcare.

1. Introduction:

Cardiovascular diseases are presently the primary cause for human mortality, accounting for 33.6% (813 ,804 out of 2,423,712) of all deaths in 2007[1]. According to American Heart Association [1] the nation spends approximately $286.3 billion towards diagnostics and treatment of these disorders. Typical medical instrument suite for cardiovascular diagnosis costs from $18,000 to $27,000 per patient. A virtual instrument along the lines of that used in engineering system (e.g., SCADA) would immensely address this healthcare cost and affordability issues.

Thrusts towards virtual instrument have enhanced the impetus for quantitative understanding of the complex interactions among electrical, mechanical and chemical processes taking place at cellular through systematic levels constituting the cardiovascular dynamics. The present study uses a lumped parameter model to relate the state of the cardiovascular system with the online ECG signal. Analogous to mechanical system analysis, it uses a single channel of ECG to generate a diverse set of virtual heart signals (e.g., other ECG leads, pressure, volume, respiratory impedance). The model combine Guyton's seminal workand heart valve dynamics model of Korakianitis and Shi [2] with real-time ECG signal events as the activation functions.

The contributions of the present approach emerge from the method used for the development of activation functions that relate the measured ECG signals with the functions of various aspects of cardiovascular processes. The earlier investigations have focused on capturing the qualitative, group characteristics of elastance. In this research, the elastance e(t) is developed based on the individual ECG signal. As ECG can express cardiac features that are unique to an individual's cardiovascular system [3], the elastance functions developed from ECG can capture the effects of physiological differences among individual cardiovascular systems in the model. The temporal events of the recorded ECG and ECG-extracted respiratory signal of every individual were used to estimate the elastance function in real-time. The ECG-based activation function then was used to drive the cardiovascular model. In addition, the paper suggests a model adaptation and parameter estimation method to capture the various mechanisms of heart dynamics so that real-time rendering of the heart signals from the measured ECG is facilitated. The experimental investigations suggest that the model can capture the salient time and frequency patterns of the measured hemodynamic signals. The remainder of the paper is organized as follows. Section 2 presents the formulation of the activation functions, parameter tuning procedure, and the mathematical model of the cardiovascular system. Section 3 describes the implementation of the heart model, results of parameter estimation, and the comparisons of model outputs with measured data. Further discussions on the model and its applications, as well as conclusions are presented in Sections 4 and 5.

2. Research approach:

Fig.1 presents our approach to formulate the activation function and develop ECG-driven lumped parameter model of cardiovascular dynamics. The model captures the coupled dynamics of the heart chambers, heart valve, pulmonary and systemic circulation using activation function derived from the measured ECG signals. The modeling approach consists of the following modules: (1) Data collection, (2) ECG-based activation function, (3) Parameter estimation, (4) Heart model.

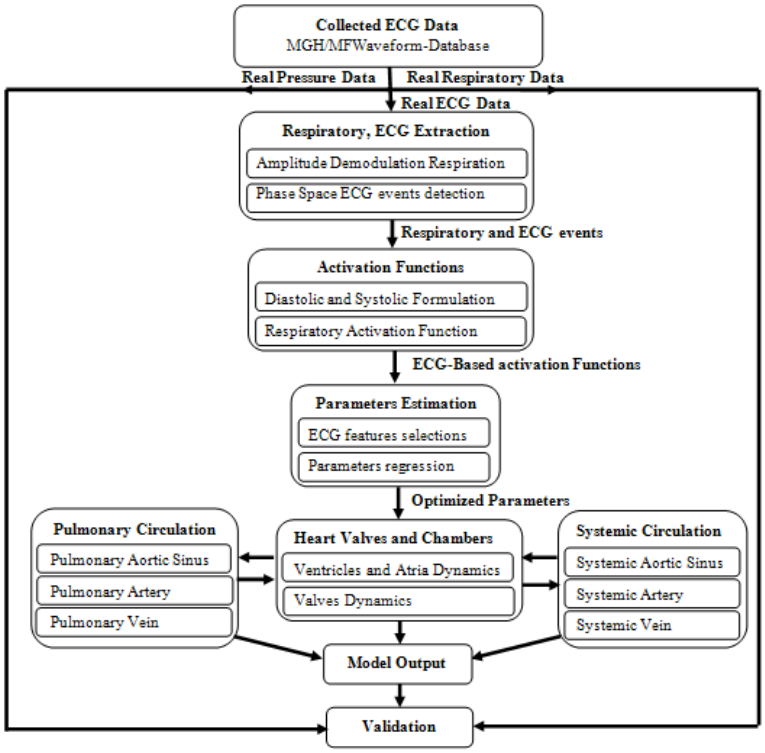

Figure 1: Summary of the virtual simulation cardiovascular model

The details of the modeling method including the generation of activation functions, model parameter estimation, and the development of the simulation model are provided in the following sections.

2.1. ECG-based activation function:

First a band-pass filter with a pass-band in the range of 0.06-40Hz was employed to remove the identified noise, artifacts, base-line wandering and kept the critical features for ECG fiducial point extraction. Next, anamplitude demodulation method [4] was implemented to extract the respiration signal from ECG. The phase space method [5] was used to extract fiducial points of P, T waves and QRS complex in an ECG signal. The phase space method tends to be robust for extracting the critical points including the peaks, onset and offset of P, T, QRS complex of ECG signal under both steady and transient conditions [6].

The present cardiovascular model uses the combination of atrial and ventricular activation to describe the elastance, known as the nature of relationship between the pressure *(P)* and volume (*V*) of the four heart chambers. According to Chung *et al.*[7], a curvilinear relationship exists between *P* and *V* at end-diastolic volume (EDV) and end-systolic volume (ESV) events. Therefore, the elastance can be approximated by trigonometric functions at the EDV and ESV events. The EDV event time is taken as the Q peak and ESV as the S peak of ECG signal. Thus, the ECG fiducial points can be used to formulate the activation functions for the ventricular and atrial dynamics follows.

$$\text{DiaAct}\,(t)=\begin{cases}0 & 0\le t\le T_1\\ \sin\left(\frac{\pi(t-T_1)}{(T_2-T_1)}\right) & T_1\le t\le T_2\\ 0 & T_2\le t\end{cases} \tag{1}$$

$$\text{SysAct}\,(t)=\begin{cases}0 & 0\le t\le T_3\\ \sin\left(\frac{\pi(t-T_3)}{(T_4-T_3)}\right) & T_3\le t\le T_4\\ 0 & T_4\le t\end{cases} \tag{2}$$

$$\text{VenFunc}(t) = \text{SysAct}(t) + \alpha\,\text{Resp}(t) \tag{3}$$

$$\text{AtrFunc}(t) = \text{DiaAct}(t) + \alpha\,\text{Resp}(t) \tag{4}$$

Where T_1 is the instant at the onset of P peak in measured ECG, T_2 the Q peak, T_3 the R peak,T_4 the offset of T and Resp(t) is the extracted respiratory signal from ECG.

2.2. Cardiovascular Model:

Four sets of differential equations were used to capture the dynamics of the four heart chambers formed by right (pulmonary) and left (systemic) sides of ventricular and atrial parts of a heart, respectively. For example, the dynamics of left ventricle volume (V_{lv}) and pressures (P_{lv}) are given by:

$$\frac{dV_{lv}}{dt} = CQ_{ao}\,N_{ao}\sqrt{|P_{lv,0}+e_{lv}(V_{lv}-V_{lv,0})-P_{sas}|} \tag{5}$$

$$P_{lv} = P_{lv,0} + e_{lv}(V_{lv} - V_{lv,0}) \tag{6}$$

Where N_{ao} is used to define the blood flow rate and valve interaction effect and decided by the angular position of the aortic valve leaflets as:

$$N_{ao} = \frac{(1-\cos\theta_{ao})^2}{(1-\cos\theta_{max,ao})^2} \tag{7}$$

The elastant functions for the ventricles and atria are given based on the ECG-derived activation functions Eq. (3) and Eq. (4) as:

$$e_{lv}(t) = e_{rv}(t) = \text{VenFunc}(t) \tag{8}$$

$$e_{la}(t) = e_{ra}(t) = \text{AtrFunc}(t) \tag{9}$$

Aortic valve dynamics is expressed as:

$$\frac{d^2\theta}{dt^2} = \begin{cases}(P_{lv}-P_{sas})K_{p,ao}\cos\theta - K_{f,ao}\frac{d\theta}{dt} + K_{b,ao}Q_{ao}\cos\theta - K_{v,ao}Q_{ao}\sin\theta, & Q_{ao}\ge 0\\ (P_{lv}-P_{sas})K_{p,ao}\cos\theta - K_{f,ao}\frac{d\theta}{dt} + K_{b,ao}Q_{ao}\cos\theta - K_{v,ao}Q_{ao}\cos\theta, & Q_{ao}<0\end{cases} \tag{10}$$

The systemic pressures and flowrates are given by:

$$\frac{dP_{sas}}{dt} = \frac{Q_{ao}-Q_{sas}}{C_{sas}} \tag{11}$$

$$\frac{dQ_{sas}}{dt} = \frac{P_{sas}-P_{sat}-R_{sas}Q_{sas}}{L_{sas}} \tag{12}$$

$$\frac{dP_{sat}}{dt} = \frac{Q_{sas}-Q_{sat}}{C_{sat}} \tag{13}$$

$$\frac{dQ_{sat}}{dt} = \frac{P_{sat}-P_{svn}-(R_{sat}+R_{sar}+R_{scp})Q_{sas}}{L_{sat}} \tag{14}$$

$$\frac{dP_{svn}}{dt} = \frac{Q_{sat}-Q_{svn}}{C_{svn}} \tag{15}$$

$$Q_{svn} = \frac{P_{svn}-P_{ra}}{R_{svn}} \tag{16}$$

The pulmonary loop is developed similarly to that of the systemic loop with change in values of system parameter values. Altogether, the cardiovascular process dynamics was expressed in terms of deterministic nonlinear different equations with the parameters and activation function determined from the measured ECG signals.

3. ECG-based parameter estimator:

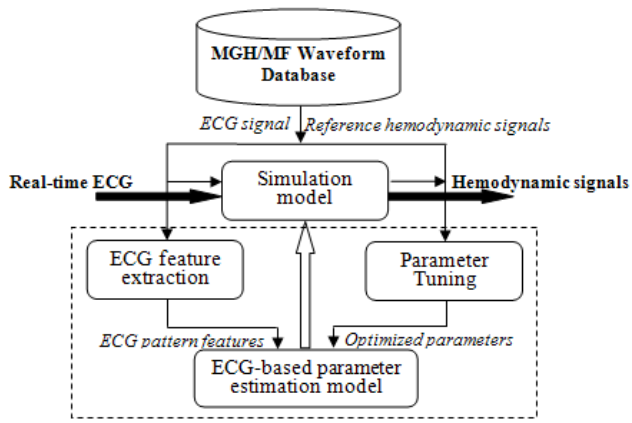

Figure 2: Summary of ECG-based parameter estimation method for virtual cardiovascular model

Physiological parameters in the cardiovascular system are very difficult to measure and verify due to the complex invasive measuring procedures and the physiological differences of individuals. To improve the model accuracy we developed a parameter estimation method that uses the ECG features as the predictor variables. Compared to conventional parameter selection methods [8-9], this method adaptively estimates the model parameters responding to the real-time changes in ECG signals. The parameter estimation procedure shown in Fig. 2 consists mainly of parameter tuning and ECG parameter estimation.

3.1. Parameter tuning:

The purpose of tuning of the model parameters isto determine an optimized model parameter set that minimizes the mean square error between thesimulation model outputs and the reference signals. Here, the model estimated pulmonary vein pressure (P_{pvn}), left atrium pressure (P_{la}) and right atrium pressure (P_{ra}) are referenced to the measured respiratory signal, pulmonary pressure, and central venous pressure, respectively. A global optimization-based pattern search algorithm is used to find a set of parameters which minimize the mean square error between the model output and the real measurements.The optimization problem for pattern search is formulated as follows: $\min f(x)_{x\in\Omega}$ where $f: \boldsymbol{R}^n \to \boldsymbol{R}$ with $\Omega = \{x\epsilon \boldsymbol{R}^n : l \leq \mathrm{Ax} \leq u\}$ where $\mathrm{A}\epsilon\mathbf{Q}^{mxn}$ is a rational matrix, and $l < u$. Pattern search algorithms for constrained minimization generate a sequence of iterates$\{x_k\}$ in $\boldsymbol{R}^n$ with objective function values f_Ω. Each iteration consists of two phases: an optional search and a local poll. In the search step the objective function is evaluated at a finite number of points on a mesh $\Delta_k > 0$. If $f_\Omega(x_{k+1}) < f_\Omega(x_k)$then the search is successful and x_{k+1} is set to be an improved mesh point and the mesh coarsened to start a new search; otherwise the poll step is invoked. The objective function at the neighboring mesh points are evaluated to see if a lower function value can be found there. If no improved mesh point is found the mesh is refined as $\Delta_{k+1} = \tau\Delta_k$ where $\tau > 1$. The poll set now is updated as $M_x = \{x_k + \Delta_{k+1}d : d \in D\}$

where D is the positive spanning set in$\boldsymbol{R}^n$. If the search and the poll step can find an improve mesh point $f_\Omega(x_{k+1}) < f_\Omega(x_k)$ then increase mesh size $\Delta_{k+1} > \Delta_k$, otherwise, set $\Delta_{k+1} < \Delta_k$, increase $k \leftarrow k + 1$and continue with the search and poll steps. The pattern search algorithm would ultimately converge to a global optimum [10-11].

3.2. ECG-based parameter estimation model:

Empirical multiple regression model for prediction of cardiovascular system model parameters is developed. Ascertain ECG expressed cardiac features that are unique to individual, we used these features to derive the cardiovascular parameters that characterize for the physiological basics of the cardiovascular system. Here, The ECG events were extracted via phase space analysis. The other 15 ECG features include the means of P, QRS, T wave amplitude, the sample averages and standard deviations of RR, PR, ST, QT intervals, ST profiles, and systolic-diastolic differences. It may be noted that components that comprise the ECG waveform represent the sequences of depolarization and repolarization resulting from the action potential propagation through the cardiac muscle cells. The P wave amplitude is the measurement of electrical potentials generated when the atria are depolarized and the QRS complex comprises the potentials generated when ventricles depolarize. The duration between the beginning of a P wave and the beginning of the QRS complex represents the time interval between of atrium and ventricular excitations. After depolarized, the heart returns to a rest stage through the repolarization process marked by T wave in the ECG signal. The amplitudes and the intervals between P, QRS and T features characterize for the atrial and ventricular contraction levels known as the major affects causing the changes of pressure and volume within the heart chambers and blood vessels [12]. In addition, the interval difference of ST-PR, QT-PR are extracted to estimate the difference between diastole and systole, necessary for tracking the elastance changes of the heart chambers,.

We consider a multiple linear regression model $Y = X\beta + \epsilon$, where Y is an n x 1response variable vector (model parameters), X is an n x p full-column rank matrix predictors (ECG features) , β is a p x 1 vector of unknown coefficients to be estimated, and $\epsilon$is an independent random variables. It may be noted that many of the features contain redundant information, and each of the model parameters tends to more sensitive to a different set of the ECG features. In order to address this redundancy and diversity of the relationships between the model parameters and ECG features we used principal component analysis (PCA) followed by a stepwise regression process for parameter estimation.The estimates of β minimize the sum squares of the deviations of the observed Y from the values $\hat{Y}$ predicted by the model. The predicted value coefficient values were estimated as $\hat{\beta} = (X^T X)^{-1} X^T Y$, with the variance $\mathrm{var}(\hat{\beta}) = \sigma^2 (X^T X)^{-1}$, and $\hat{Y} = X\hat{\beta}$. In a regression model, we often have$\mathrm{more}X$'s than needed for predicting Y. Some of them may be redundant and can be discarded. Backward stepwise approach [13] is used for variable selection. The selection procedure begins with considering all variables in the model and deletes sequentially one at a time. The partial F-test for each variable in the presence of the others is conducted, and the variable with the least$F$value is eliminated. The overall regression hypothesis testing can be expressed as $H_0: \beta = 0$with the test statistic $F = \frac{(\hat{\beta} X^T Y - n\bar{Y}^2)/p}{Y^T Y - \hat{\beta} X^T Y/(n-p-1)}$following the distribution$F_{p,n-p-1}$. We reject H_0 if p-value of the $F_{p,n-p-1}$< 0.05. The stepwise procedure is continued until the smallest F with p-value < 0.05 is reached.

4. Implementation Details and Results:

The model was implemented in Matlab/Simulink environment. The implementation consisted of four main subsystems: heart chambers, valves, systemic circulation and pulmonary circulation.The heart chambers included left ventricle, right ventricle, left atrium and right atrium, which were activated by the ECG-based activation functions. The heart valves were considered as concentrated components and governed by the derivations of various forces acting on the valve leaflets. The systemic and pulmonary circulation loops were separated into 3 blocks including veins, aortic sinuses and the arteries. Venous blocks comprised of veins, arterioles and capillaries. Two ECG-based activation functions VenFunc(t) in Eq. (3) and AtrFunc(t) in Eq. (4) excite the ventricles and the atria. The activation function values

determined from recorded ECG data, along with the corresponding time stamps were input to the simulation model as the signal source blocks. The sample time of the signal sources and the model were matched so that the outputs of the model were synchronized with the input ECG signal. The simulation runtime was 60 seconds and the model reached steady state after 7 seconds. Therefore, we studied the data statistics after a 10 sec "initial warm-up". The outputs of the model included the profiles of the pressure, volume, flow rate from heart chambers, pulmonary and systemic circulations.

Principal component analysis (PCA) was performed to reduce the statistical redundancy between the high dimensional ECG features without significant loss of information of total.The first four components could explain 78% of the data variance and were considered for further study. Table 1 shows the contributions of each feature in the four loading principal components. The larger the coefficients the higher the contribution of that feature to the variation along that eigen direction. It is evident that all except RR standard deviation and ST-PR have contributed to one of the leading components. These 13 significant ECG features were used for stepwise regression.

Table 1: Contribution of ECG features to the first four principle components

No	Feature	Comp1	Comp2	Comp3	Comp4
1	R AmpAvg	-0.0287	0.3599	-0.1023	0.2739
2	PAmpAvg	-0.2561	0.2574	0.0030	-0.4099
3	TAmpAvg	-0.0971	0.3538	-0.0828	0.3729
4	RRAvg	0.3102	0.1509	-0.2517	-0.0062
5	PRAvg	-0.0970	0.1178	-0.0409	-0.4485
6	STAvg	0.4195	0.0492	0.0685	-0.2110
7	QTAvg	0.4193	0.0344	0.1101	-0.2358
8	RRStd	-0.0280	0.1631	0.0853	-0.2737
9	PRStd	0.2783	0.1705	-0.1158	0.3995
10	STStd	0.0452	-0.1076	-0.6487	-0.1122
11	QTStd	0.0482	-0.1040	-0.6511	-0.1061
12	ST-PR	0.2324	-0.0178	0.0840	0.0465
13	QT-PR	0.4405	-0.0232	0.1229	-0.0102
14	STArea	-0.0070	0.5390	0.0509	-0.0170
15	STAreaStd	0.0556	0.5191	-0.1036	-0.0604

Next, the pattern searching method was used to tune the parameters retaining to elastance (Elvs, Elvd, Ervs, Ervd), offsets and gains of chamber pressures (ResGain, ResOff, PatGain, PatOff, CVPGain, CVPOff) and the coupling α to capture the respiration effect on cardiovascular dynamics. The tuned parameters were regressed with ECG features so that real-time adaptation can be facilitated. The Table 2 shows the significant predictive variables and the coefficient vector of the parameter estimation model. All p-value were $<10^{-3}$.

Table 2: Regression coefficients of the parameter estimation model

No	ECG Features	Intercept	R AmpAvg	P AmpAvg	T AmpAvg	RR Avg	PR Avg	ST Avg	QT Avg	ST Std	PR Std	QT Std	QT-PR	ST Area	STAreaStd	R^2
1	PatGain	9.34					-2.16			-0.22	0.7					0.94
2	PatOff	2.25		0.38	0.39	0.68										0.88
3	ResOff	-0.48					0.25		-1.51							0.89
4	CVPGain	-3.55						0.81			-0.08	0.71		5.41		0.95
5	CVPOff	10.51	1.14										-7.26			0.85
6	ResCof	5.48			0.416							1.87		0.248	-1.48	0.94
7	Elvs	0.57				1.77			2.36					0.15	0.24	0.96
8	Ervs	1.81				8.79			1.29			0.94		1.86		0.9
9	Elvd	0.62		0.17							1.31		-0.27		0.41	0.95
10	Ervd	0.06	0.14	0.005							0.17		-0.13			0.89

Subsequently, we compared the salient features of the cardiovascular systems extracted from the model outputs with the real measurements. The following combinations of signals were compared:

i) Heart chamber pressure and volume with ideal profiles [12] ii) Right atrium pressure (P_{ra}) from the model with the central venous pressure (CVP) from real measurement iii) Pulmonary blood pressures from the model (P_{pat}) and from real measurement (PAP) iv) Pulmonary vein pressure from the model (P_{pvn}) with the respiratory impedance from the real measurement.

Figs.3 shows the absolute values of pressure (plot (a) of the figures) and volume (plot (b) of the figures) of left chambers and right chambers, respectively. The figures indicate that the absolute value profiles match well with the geometric features of ideal profiles [12]. For the left ventricle (Fig.3), the pressure ranges from 0 to 125 mmHg and volume varies from 70 to 130 ml which are in the normal range of heart pressure and volume. Furthermore the shape of the pressure and the volume were comparable with those of ideal profiles [12].

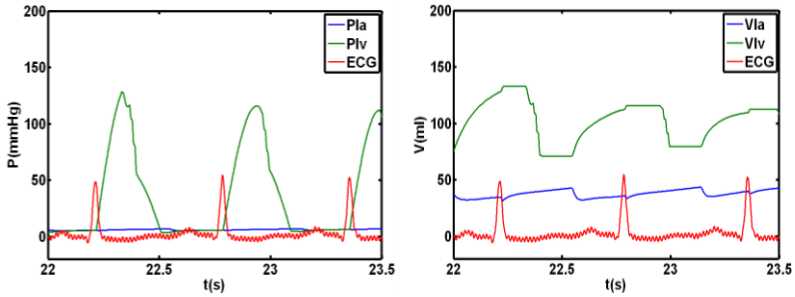

Figure 3: Pressure (P) and Volume (V) of left atrium (la) and left ventricle (lv).

Fig. 4 describes the central venous pressure and the right atrium pressure in time domain and frequency domain respectively. It is observed that the model output agree well with the measurement. In time domain, the right atrium pressure output captures the signal shape variations and trends of the recorded central venous pressure signals. In frequency domain, right atrium pressure is compatible with the spectrum of right atrium pressure in both frequency and power spectrum. Comparison of the pulmonary pressures, respiratory impedance and pulmonary vein pressure are shown in Fig.5

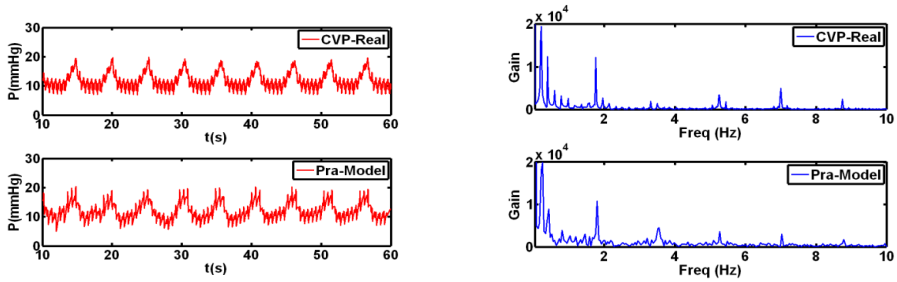

Figure 4**:** Central Venous Pressure (CVP) and right atrium pressure (P_{ra})in time and frequency domain

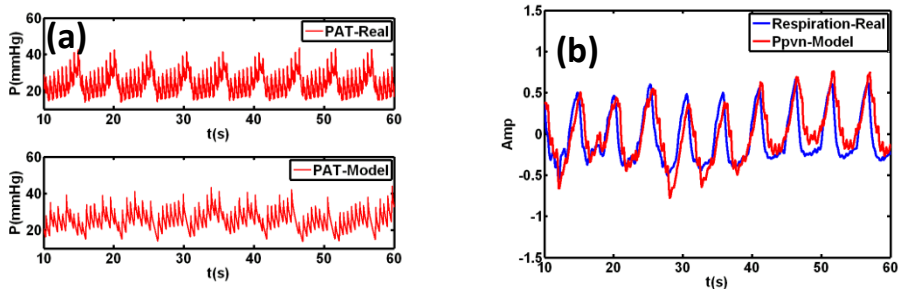

Figure 5: Pulmonary arterial pressure (a) and respiratory impedance vs pulmonary vein pressure (b)

To have a quantitative assessment on the correlations between the signals from the model and from the real measurements (pulmonary vein pressure VS respiratory signal, pulmonary pressure VS pulmonary arterial pressure, right atrium pressure VS central venous pressure) the correlation coefficient and R square are calculated. Cross validation has been used to test the accuracy of the model. We

randomly partitioned the dataset into 10 subsets. For parameter estimation, we removed one subset of the data for testing and use nine training subsets to build the parameter regression model. For model validation, the ECG features of the removed subset are used to estimate the parameters to run the model. This process is repeated 20 times and Table 4 shows the mean correlation coefficient and R square of the outputs from model and the signals from the real measurements. By using cross-validation technique we can access the accuracy of the model with an independent data set.

Table 4: Comparison between model output and real measurement

Signals	Correlation Coefficient	R^2
Pulmonary vein pressure Respiratory signal	0.76	0.78
Pulmonary pressure Pulmonary pressure	0.58	0.61
Right atrium pressure Central venous pressure	0.65	0.68

5. Conclusions:

This paper has presented an approach for real-time simulation of heart dynamics using a single channel ECG as the input. The outputs of the model including right atrium pressure (P_{ra}), pulmonary artery pressure (P_{pat}) and the pulmonary vein pressure (P_{pvn}) were consistent with the actual recordings in both time and frequency domains.

The output of the models can be used to analyze the dynamics of the hearts by solely using ECG input. In this paper, only ECG signals were used to generate the outputs of the model. The heart parameters such as atrium pressure, chamber volume or the opening angle of the heart valve require invasive or expensive medical instruments. The model serves as a virtual instrument where outputs, including the pressure, volume, blood flow rates, and heart valve opening angles from the model can approximate the real measured values. Such real-time model can offer the advantages of cost efficiency and time saving.

The research is among the initial efforts to use-ECG to form the activation functions for cardiovascular dynamic models. The close matching of the time and frequency domain characteristics of the model outputs and the real data suggests the viability of ECG as the activation source for the cardiovascular model development. The model helps us gain some quantitative assessment of underlying couplings between heart dynamics and ECG signal.

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