Modeling, Estimation and Control of Cardiovascular Systems with A Left Ventricular Assist Device

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Abstract

In this paper, a dynamic model is developed through theoretical analysis and numerical solutions to approximate the response of human cardiovascular circulatory system. This system model has one critical time-varying parameter, the resistance of blood vessels. A parameter estimation scheme is derived to estimate this parameter, and the parameter estimate is used to implement an adaptive observer to estimate the aortic pressure for physiologic control. An optimal adaptive controller is proposed to control the estimated aortic pressure to track a reference signal updated by a nonlinear function of the pump head to meet the physiologic need.

A Matlab simulation model and an experimental mock human circulatory loop are employed as test environments for human cardiovascular circulatory systems with a left ventricular assist device and their physiologic controllers. Different physiologic conditions, such as the variation of left ventricular failures, variation of activities, and left ventricular suction, are evaluated to test the designed physiologic control system. Simulation and experimental results consistently show that the aortic pressure estimation error is small, and that the abnormal hemodynamic variables of a congestive heart failure patient are restored back to the normal physiologic range.

Keywords: Cardiovascular circulatory system, estimation, feedback control, left ventricular assist device, modeling.

1 Introduction

Left ventricular assist devices (LVADs) are mechanical circulatory assist devices used to save the lives of congestive heart failure (CHF) patients. Heart disease is the leading cause of death in the United States. Nearly 5 million Americans suffer from congestive heart failure, and 550,000 new cases are diagnosed each year [1]. The traditional solution to end-stage CHF is heart transplantation. However, some patients are not eligible for a transplant because of age or health reasons. Even if the patients are eligible for a transplant, the severely limited supply of donor hearts can give only approximately 10% patients transplantation each year [2]. Therefore, mechanical circulatory assist devices, called artificial heart pumps

(AHPs), have been introduced to save some lives of end-stage CHF patients since the 1960s. AHPs have several advantages over heart transplants: they are less costly and not limited by the availability of heart donors, and they may provide treatment for patients not eligible for heart transplants, leading to possible recovery of the failed ventricle.

An AHP can be either used as a total artificial heart (TAH) when it replaces both ventricles, or as a left ventricular assist device when it aids the failed ventricle by supplying additional blood flow but does not replace the left ventricle. Since the left ventricle takes most of the working load for blood circulation, about 75% of heart failures are caused by predominant left ventricular failure. Therefore, LVADs are in increasing use for heart failure patients, whose development has become an important research topic of major interest.

There have been three generations of AHPs: pulsatile pumps since 1960s, rotary continuous flow pumps since 1980s, and magnetically levitated continuous flow pumps currently under development. In magnetically levitated CF pumps, the impeller is levitated by magnetic forces without any mechanical contact. There is no bearing wear or bearing seal so that there is no thrombosis factor. Moreover, this type of pumps are expected to have a long mechanical durability to work 10 to 20 years. The researchers at University of Virginia and Utah Artificial Heart Institute together, among other groups in the world, are developing a new magnetically levitated axial flow heart pump as an LVAD.

Currently, AHPs have been used successfully for short term (less than 2 years) as a bridge to heart transplant [3] with a constant pump speed. The long-term use of AHPs is expected to benefit end-stage CHF patients much more, especially those who are not eligible for a transplant. One key issue to be addressed in order to achieve this long-term use of AHPs is the development of an effective and efficient (robust and adaptive) physiologic control system.

In this paper, we give an overview of the recent research on the development of dynamic modeling of human cardiovascular circulatory systems and physiologic controllers for such systems with LVADs, and present some of our new analytical, simulation and experimental results on modeling and control of LVAD systems (as summarized in the abstract).

Figure 1: Circuit analog of circulatory systems with an LVAD.

2 Human Circulatory System Model

A lumped parameter model of human cardiovascular circulatory systems can be analogously represented by a 11th-order electric circuit shown in Figure 1. It consists of analog blocks for left ventricle, aorta, systemic artery, vein and right atrium, right ventricle, pulmonary artery, pulmonary vein and left atrium. Two parallel blocks for skeletal muscle and non-muscular peripheral organs respectively are placed between the blocks of systemic artery and systemic vein. Resistors represent the viscous property of blood flow, while inductances embody the inertia property of blood flow. Capacitors model the elastic property, or compliance of the vessel wall, and diodes are used to mimic the properties of one-directional valve. Muscular vascular resistance (R_{m1}) and pulmonary vascular resistance (R_{13}) are modeled as variable resistors to accommodate their variations in different activity levels.

With the muscle pump function represented by the intramuscular pressure P_{muscle} and venous valve D_m , the sudden increase of central venous pressure at exercise onset was successfully simulated, in agreement with experimental results reported in literature. Simulation results showed that the cardiac output without the muscle pump underestimates the cardiac output with the muscle pump by 10%. This discrepancy can be explained from the perspectives of cardiac function and peripheral circulation. In terms of cardiac function, the increase in central venous filling from the muscle pump function augments the right ventricular end-diastolic volume, thus increasing the stroke volume. On the other hand, the muscle pump function helps to decrease the effective resistance of the peripheral blood vessel, resulting in the increase of the peripheral blood flow, equal to the cardiac output in average.

Congestive heart failure (CHF) is a chronic condition in which the heart cannot pump blood at a rate which effectively supplies the body's tissues and organs [4]. Most heart failures are caused predominantly by depression of the left ventricular systolic function. When CHF becomes severe and life threatening, these patients with CHF are prime candidates for left ventricular assist devices (LVADs), and usually have decreased ejection fraction (EF), decreased cardiac output (CO), and elevated left ventricular end-diastolic pressure (LVPED).

Pulmonary edema, a symptom resulting from the elevated LVPED, is commonly observed in these patients. In this paper, the pressure and volume relation of ventricle is modeled as an exponential function during diastole and a scaled quadratic function during systole. Heart failure is modeled by the decrease of the scale of the quadratic function, and the increase of the coefficients of the exponential function [5].

3 Objectives of Physiologic Control

As a destination therapy device, modulation of the degree of ventricular assist and overall cardiac output based on physiologic needs are imperative for long term LVAD performance. To reverse the symptoms of CHF as explained above, and to avoid damage to the cardiovascular system, the main objectives for a physiologic control system are: (i) to produce adequate cardiac output to ensure tissue perfusion, (ii) to support native cardiac function (i.e., antegrade flow across aortic valve), (iii) to adjust cardiac output to compensate for increased physiologic need due to activity, (iv) to avoid left ventricular collapse due to mechanical suction from the pump, and (v) to provide sufficient pump speed to avoid retrograde pump flow from aortic-left ventricular pressure differential.

All five objectives of LVADs are related to either blood pressure or flow rate. To regulate these hemodynamic variables, they need to be detected first by corresponding sensors. In artificial heart pumps, the sensors for hemodynamic variables (blood flow, pressure) are not available, due to the constriction of volume, blood compatibility, and reliability issues. Long term available signals, such as pump head and motor signals, do not have direct physiologic meanings. Therefore, to meet these objectives, a state estimator, which can derive the hemodynamic variable (blood flow or pressure) from available feedback signals, is needed for the design and implementation of a physiologic control system for an LVAD.

4 Review of Control Designs

Control in the physiologic sense of CF LVADs presents major challenges because they create suction when the impeller speed, and thus flow, exceeds the venous return to the left ventricle. The level of blood flow assistance can become inadequate when the speed is too low, for example, there may be

a retrograde flow of blood through the rotating impeller, from the pressurized aorta into the left ventricle, during ventricular diastole [6]. Avoiding retrograde flow when the speed is too low, and suction when the speed is too high, establishes the upper and lower limits of the LVAD rotational speed. These limits will frequently change in the patient, and particularly when the patient's heart moves more into and out of failure or when the patient starts to exercise.

Many continuous flow (CF) LVADs are operated at constant speed, such as the Jarvik 2000 [7] and the DeBakey pump. DeBakey pump also allows the physician or trained personnel to manually adjust the pump speed until a perceived comfort level of perfusion is achieved. These constant speed settings or manual adjustment are adequate for short period usage of LVADs, but are likely to be insufficient for long-term applications. A physiologic control system, which automatically responds to various real-time physiologic demands, is imperative for a long term LVAD.

P/PI control. Parnis et al. used a P controller for the Jarvik 2000 VAD. The pump rotational speed was set as a linear function to the heart rate, which was obtained from the fundamental frequency of the motor current waveform [8]. Treadmill exercise and heart pacing studies were performed on a calf with the Jarvik 2000 VAD and no deleterious effects were detected within test durations in excess of 26 weeks [8]. However, a linear function between the heart rate and pump rotational speed has an obvious discrepancy. It has been found that the cardiac output of a healthy subject is not only determined by the heart rate but also by the contractility of the heart, and most importantly determined by the peripheral circulation [9]. Waters et al. designed a PI controller for an LVAD using one feedback signal, the differential pressure over LVAD [10]. The beating of the natural left ventricle was considered as a sinusoidal disturbance to the LVAD.

Fuzzy logic control. A fuzzy controller was employed to regulate the LVAD flow to track a desired flow rate [11]. The LVAD flow rate was estimated from the motor current and rotational speed. The desired LVAD flow rate was assumed proportional to the heart rate. This assumption ignored the influence of heart contractility, and most importantly, the effect of the peripheral circulation on the desired flow rate [9]. Choi et al. also implemented a PI type fuzzy controller to realize an LVAD pump flow rate pulsatility tracking [12]. A reference pulsatility level of 15 mL/sec was selected to allow the natural heart to produce some stroke volume without introducing ventricular suction. The LVAD pump flow rate was estimated from the motor current and rotational speed. Simulation results showed that the control output of this fuzzy controller produced a much smaller variation in the LVAD speed with regard to parameter variations than that of a PI controller. However, the constant setting of the reference pulsatility may be inadequate since the failure level of the natural ventricle during the long period of LVAD support may change, resulting in different abilities to generate flow rate pulsatility.

Optimal control. This type of controller is designed to minimize some predefined penalty functions. Giridharan et al.

designed an optimal controller with the structure of a PI controller [13]. The time varying coefficients of the PI controller were obtained from exhaustive, direct numerical searches to minimize a weighting function, which was the combination of the differential pressure across the pump and the variation rate of the rotational speed. Because of the huge computational effort involved in the process to find these coefficients, this procedure can be only done off-line. When the physical cardiovascular condition is different from the conditions used in the numerical searches, the optimality of this controller may not be guaranteed. A similar but more complex optimal controller was designed by Boston et al. to minimize a multi-objective penalty function $J(\omega) = \sum_{i=1}^3 \mu_i J_i(\omega)$ [14], where $J_i(\omega)$ was the penalty function of cardiac output, arterial pressure, left atrial pressure respectively, and $\mu_i \geq 0$ with $\sum_{i=1}^3 \mu_i = 1$. The LVAD motor speed was used as the feedback signal. This technique required simple and accurate predetermined mathematical models of cardiac output, arterial pressure, and left atrial pressure with respect to the motor speed.

5 Simplified System Model

To develop an effective robust and adaptive controller to meet the desired physiologic need, we consider a simplified cardiovascular system model shown in Figure 2 (as compared with the 11th-order model shown in Figure 1).

Figure 2: A simplified system model.

In this model, the system elements are: C_{LV} , left ventricle; C_A , aorta; C_V , systemic vein and right atrium; D_1 , aortic valve; D_2 , mitral valve; TPR , total peripheral resistance; L , blood inertia in peripheral circulation; R_{LV} , resistance of aortic valve; R_V , resistance of vein and left atrium; δ_m , the mean pressure disturbance generated by muscle pump function in exercise; δ_P , pressure disturbance generated by pulmonary circulation; and the system signals are: P_{LV} , left ventricular pressure; P_A , aortic pressure; P_V , central venous pressure; Q_{LV} , inflow to left ventricle; Q_{14} , flow rate from the vein to the left ventricle; Q , pump flow rate; Q_8 , flow rate from the left ventricle to the aorta; Q_A , inflow to aorta; Q_V , inflow to systemic vein and right atrium; TPF , total peripheral flow rate.

As in [5], the dynamic equations of this system model are

$$\dot{x} = A^d x + B_1^d Q + B_2 \delta_P + B_3 \delta_m, y = Cx, \text{ in diastole} \quad (5.1)$$

$$\dot{x} = A^s x + B_1^s Q + B_3 \delta_m + B_4 \delta_{LV}, y = Cx, \text{ in systole} \quad (5.2)$$

where $x = [x_1, x_2, x_3]^T$, $x_1 = P_{LV} - P_A$, $x_2 = P_V - P_A$, $x_3 = TPF$, $y = \Delta P = P_A - P_{LV}$,

$$A^d = \begin{bmatrix} -\frac{1}{C_{LV}^d R_V} & \frac{1}{C_{LV}^d R_V} & \frac{1}{C_A} \\ \frac{1}{C_V R_V} & -\frac{1}{C_V R_V} & \frac{1}{C_A} + \frac{1}{C_V} \\ 0 & -\frac{1}{L} & -\frac{TPR}{L} \end{bmatrix}$$

$$B_1^d = \begin{bmatrix} -\frac{1}{C_{LV}^d} - \frac{1}{C_A} \\ -\frac{1}{C_A} \\ 0 \end{bmatrix}, B_2 = \begin{bmatrix} \frac{1}{C_{LV}^d R_V} \\ -\frac{1}{C_V R_V} \\ 0 \end{bmatrix}, B_3 = \begin{bmatrix} 0 \\ 0 \\ \frac{1}{L} \end{bmatrix}$$

$$A^s = \begin{bmatrix} -\left(\frac{1}{C_{LV}^s(t) R_{LV}} + \frac{1}{C_A R_{LV}}\right) \Pi(x_1) & 0 & \frac{1}{C_A} \\ -\frac{1}{C_A R_{LV}} \Pi(x_1) & 0 & \frac{1}{C_A} + \frac{1}{C_V} \\ 0 & -\frac{1}{L} & -\frac{TPR}{L} \end{bmatrix}$$

$$B_1^s = \begin{bmatrix} -\frac{1}{C_{LV}^s(t)} - \frac{1}{C_A} \\ -\frac{1}{C_A} \\ 0 \end{bmatrix}, B_3 = \begin{bmatrix} 0 \\ 0 \\ \frac{1}{L} \end{bmatrix}, B_4 = \begin{bmatrix} -1 \\ 0 \\ 0 \end{bmatrix}$$

$$\delta_{LV} = \frac{V_{LV}}{(C_{LV}^s(t))^2} \dot{C}_{LV}^s(t),$$

and $C = [-1, 0, 0]$. The value of the unit step function $\Pi(x_1)$ in (5.2) can be considered to be 0 for an LVAD recipient [5]. This model converts the variation of left ventricular capacitance in systole to an extra input δ_{LV} .

In this model, the output y is the measured pressure difference, and the control input Q is the pump flow rate which can be calculated from the pump characteristic equation

$$\frac{Q}{\omega} = \alpha_2 \left(\frac{\Delta P}{\omega^2} \right)^2 + \alpha_1 \frac{\Delta P}{\omega^2} + \alpha_0 \quad (5.3)$$

for the pump speed ω and some constants α_2 , α_1 and α_0 .

The key parameter is TPR which changes as the exercise condition changes. This parameter needs to be estimated for the design of a state observer for the system state x , and for the design of a feedback controller to make the aortic pressure P_A to follow a desired trajectory. It is important to note that a state observer is needed, because the aortic pressure P_A is not available for measurement. The blood volume equation

$$\frac{P_{LV}}{C_{LV}} + \frac{P_A}{C_A} + \frac{P_V}{C_V} = V_s = \text{total stressed blood volume} \quad (5.4)$$

could be used to calculate the aortic pressure P_A if x_2 and x_3 were available (note that $x_1 = -y$ is available):

$$P_A = \frac{[-C_{LV}, -C_V, 0]x + V_s}{C_{LV} + C_A + C_V} \triangleq Hx + N. \quad (5.5)$$

Stability analysis. For this system model, the system matrix switches from A^d to A^s , when the system state changes

Figure 3: Waveform of aortic pressure during one heartbeat.

from diastole to systole. We have shown that the homogeneous part ($\dot{x} = Ax$) of this system is Lyapunov stable at $x_e = [0, 0, 0]^T$, by finding a common Lyapunov function: $V = x^T M x$ for a constant symmetric and positive definite matrix, such that $\dot{V} < 0$ for $\dot{x} = A^d x$ (diastole) and $\dot{V} \leq 0$ for $\dot{x} = A^s x$ (systole) [5] (it can be further shown to be asymptotically stable [5], and thus exponentially stable).

The response of the system (5.1)–(5.2), in the steady-state, is a stable oscillation. The typical waveform of the aortic pressure P_A over the time period of one heartbeat is shown in Figure 3, where the time interval for diastole is $[t_s, t_d]$ and the time interval for systole is $[t_d, t_s]$.

With the ensured stability, the system equation (5.1)–(5.2) can be approximated by a single-equation model

$$\dot{x} = Ax + B_1 Q + B_2' \delta_P + B_3 \delta_m, y = Cx \quad (5.6)$$

$$A = \begin{bmatrix} -\frac{1}{C_{LV}^d R_V'} & \frac{1}{C_{LV}^d R_V'} & \frac{1}{C_A} \\ \frac{1}{C_V R_V'} & -\frac{1}{C_V R_V'} & \frac{1}{C_A} + \frac{1}{C_V} \\ 0 & -\frac{1}{L} & -\frac{TPR}{L} \end{bmatrix}, B_2' = \begin{bmatrix} \frac{1}{C_{LV}^d R_V'} \\ -\frac{1}{C_V R_V'} \\ 0 \end{bmatrix},$$

and $B_1 = B_1^d$, where R_V' is an equivalent venous resistance. In particular, the circulatory system (5.1)–(5.2) and the system (5.6) have the same solution at $t = t_s$ [5]. The output of (5.6) at $t = t_s$ is equal to the pump head of the LVAD: $\Delta P = P_A - P_{LV}$, whose maximum value in each heartbeat occurs at $t = t_s$.

The proof that system (5.6) has the same solutions of states at t_s in each heartbeat as system (5.1)–(5.2) is very tedious [5], but can also be briefly explained. Systole and diastole are two opposing process. In diastole, state x_1 of human circulatory system tend to converge exponentially, while in systole, state x_1 tend to diverge towards the opposite direction because of the zero eigenvalues in matrix A^s and the huge input δ_{LV} . The states of human circulatory system (5.1)–(5.2) thus exhibits periodic-like trajectory because of the alternation of systole and diastole. The bottom envelop of the periodic-like trajectory actually converge exponentially due to the proven exponential stability of the system (5.1)–(5.2)

Figure 4: Physiologic control system structure.

in previous paragraph, at a slower speed than the state trajectory in diastole, which is dominated solely by equation (5.1). Therefore system (5.6), which has the same structure as equation (5.1) but a different value for venous resistance, was proposed to match the bottom envelop. The equivalent venous resistance R'_V in system (5.6) is much bigger than the corresponding venous resistance R_V in equation (5.1), and matches the slow converging speed of bottom envelop. The value of R'_V can be determined by the measurements in LVAD implantation surgery by a formula given in [5].

System (5.6) provides a linear system whose parameter estimator and state estimators are easy to design. Since states of human circulatory system (5.1)–(5.2) are equal to the states of system (5.6) at $t = t_s$, we can obtain the states of human circulatory system at t_s in each heartbeat. Furthermore, the average value of aortic pressure, which is determined more by the bottom envelop of states than by the instantaneous value of states, is of more interest than the instantaneous value of aortic pressure. The approximation of states of system (5.1)–(5.2) with the state estimate of system (5.6) can thus be extended to the whole heartbeat besides at $t = t_s$.

With the value for R'_V in system (5.6) found accurately, the approximation error can be very small. However, big fluctuation of input, variation of systole vs. diastole ratio, heart rate will increase the approximation error because the perfectly matched value for R'_V may change in these conditions [5].

Based on this single-equation description of the circulatory system, a state observer, a feedback controller, and a parameter estimator can be developed for physiologic control. From this system expression (the presence of the parameter C_{LV}^d), we see that the diastolic behavior is more dominant in the circulatory system response in a mean sense.

6 An Adaptive Optimal Controller

In this section, we present the detailed results of our adaptive optimal physiologic controller whose design consists of three parts: an adaptive parameter estimation scheme to estimate the total peripheral resistance TPR , an adaptive state observer using the estimate of TPR , and an optimal PI controller also using the estimate of TPR for controller parameter selection. This physiologic control system is shown in Figure 4.

Parameter estimation. From (5.6), it follows that

$$(s^3 + a_2s^2 + a_1s + a_0)y(s) = (b_2s^2 + b_1s + b_0)Q(s) + (b_2^P s^2 + b_1^P s + b_0^P)\delta_P(s) + (b_2^m s^2 + b_1^m s + b_0^m)\delta_m(s) \quad (6.1)$$

for some constants a_i and b_i (which depend on TPR), b_i^P and b_i^m , $i = 0, 1, 2$. The nominal value of δ_P can be set to 5 mmHg, and the low frequency component of δ_m is less than 5 mmHg [5]. A low-pass filter $H(s) = \frac{1}{\Lambda(s)}$ with $\Lambda(s) = s^3 + 15s^2 + 75s + 125$, can be used to remove the high frequency components of δ_m , so that the signal δ_m can be ignored for the parameter estimation of TPR , using such a filter.

Filtering both sides of (6.1) by $H(s)$ and arranging the resulting terms, we can derive the parametric equation

$$\theta^* \phi(s) = z(s) \quad (6.2)$$

for $\theta^* = TPR$ and some functions $\phi(s)$ and $z(s)$ whose denominators are $\Lambda(s) = s^3 + 15s^2 + 75s + 125$ and numerators are combinations of $y(s)$, $Q(s)$ and $\delta_P(s)$ (with δ_m ignored).

In the time-domain, we define the estimation error $\varepsilon(t) = \theta(t)\phi(t) - z(t)$, where $\theta(t)$ is the estimator of θ^* , and use the following adaptive law to update the estimate $\theta(t)$:

$$\dot{\theta}(t) = -\frac{\gamma \varepsilon(t) \phi(t)}{1 + \phi^2(t)}, \quad \gamma > 0. \quad (6.3)$$

In terms of the unknown parameter error $\tilde{\theta}(t) = \theta(t) - \theta^*$, we can express this adaptive law as $\dot{\tilde{\theta}}(t) = -\frac{\gamma \phi^2(t)}{1 + \phi^2(t)} \tilde{\theta}(t)$. In this case when $\theta(t)$ is a scalar parameter, the error $\tilde{\theta}(t)$ converges to zero, that is, $\lim_{t \rightarrow \infty} \tilde{\theta}(t) = 0$, if $\int_0^\infty \frac{\gamma \phi^2(t)}{1 + \phi^2(t)} dt = \infty$ (it is satisfied if the signal $\phi(t)$ does not vanish). In practice, due to modeling errors, parameter variations, and disturbances, this ideal property may only be met approximately. In our application, the parameter θ^* is varying between two values (from exercise to rest, or vice versa), the adaptive law is to provide an on-line estimate of this parameter.

State observer. The state observer structure for the estimate $\hat{x}$ of $x = [x_1, x_2, x_3]^T$ in (5.1)–(5.2) is a standard one, based on the equivalent model (5.6) with all parameters but TPR known and δ_m ignored. The adaptive estimate of TPR

obtained on-line from the above parameter estimation procedure is used, leading to an adaptive observer. The estimate of P_A is given as $\hat{P}_A = H\hat{x} + N$ (see (5.5)).

Optimal PI controller. The objective of physiologic control is to raise the aortic pressure to a certain level (95 mmHg as the nominal value). This objective is achieved by a feedback control design and a chosen reference signal $r(t)$.

The motor equation of an LVAD can be described by

$$J\dot{\omega} = K_t I - T_{load}, \quad L\dot{I} + RI + K_e \omega = V \quad (6.4)$$

where V is the applied voltage, ω is the pump rotational speed, I is the motor current, and $T_{load} = \frac{\Delta P Q}{\omega \eta}$ is the blood hydraulic torque on the pump impeller, with η being the pump efficiency. Since the motor inductance and the pump moment of inertia J are small, the motor equation is simplified as

$$V = \frac{\Delta P Q R}{\omega \eta K_t} + K_e \omega. \quad (6.5)$$

This relationship, together with that in (5.3), gives an expression of Q in terms of ΔP and V , which can be linearized as $Q = \beta_1 \Delta P + \beta_2 V$ for some parameters β_1 and β_2 [5]. The implication of such an expression is that the equation (5.6) can be re-expressed with V as the input signal [5]. The control objective now is to find a feedback control signal (voltage) V for the re-expressed (5.6) such that the aortic pressure P_A (through its estimate $\hat{P}_A$ from the adaptive state observer) tracks a reference signal $r(t)$ chosen to meet certain physiologic need.

For the control system shown in Figure 4, K_I is an integral gain, K is a feedback gain vector calculated from an optimal control design procedure [5] in which the estimate of TPR is used to replace the unknown TPR in optimal control and state observation, leading to an adaptive control scheme. To derive such a control scheme, we started with the linearized expression $Q = \beta_1 \Delta P + \beta_2 V$, to express the system (5.6) as

$$\dot{x} = (A + B_1 \beta_1 C)x + B_1 \beta_2 V + B_2' \delta_P + B_3 \delta_m, \quad \Delta P = Cx. \quad (6.6)$$

An adaptive state observer using system parameters and an adaptive estimate of TPR is constructed to generate an estimate $\hat{x}$ of x and an estimate $\hat{P}_A$ of P_A . The adaptive optimal controller uses $\hat{P}_A$ for feedback control.

In this physiologic control scheme, the reference signal r is generated from a design function f and an auxiliary signal r_m , using a precompensation algorithm: $r = r_m + f(\Delta P)$. The function f is a nonlinear function of ΔP , which is inversely proportional to ΔP . If the LVAD flow rate is lower than the venous return, ΔP is decreased, and in turn the reference signal r is elevated. If the pump flow rate is higher than the venous return, the reference signal r is lowered.

This is important because the body need for blood flow may vary a lot in the presence of physiologic state variation. In these variations, some parameter of the human circulatory system, like total peripheral resistance, may change a lot, and cause the variation of the venous return, in turn left ventricular pressure P_{LV} . As a result, the pump head of LVAD ΔP will exhibit a variation too [5]. The update of reference signal by the designed f function of ΔP can guarantee that the

Figure 5: Simulation results: P_{LV} : left ventricular pressure; P_A : aortic pressure; Err_{PA} : estimation error for aortic pressure; TPR : total peripheral resistance; TPF : total peripheral flow; r : reference value; V : the control output voltage.

body need can always be matched by the LVAD flow rate, and prevent the underperfusion and overperfusion of human body that may happen if constant reference value is used in the variation of physiologic states.

7 Simulation Study

The control system shown in Figure 4 was simulated using Matlab/Simulink, with the controller designed based on the reduced-order model (5.6) and applied the full-order system shown in Figure 1. Extensive simulation results for various healthy and CHF cases have been obtained, which validated our analytical work in modeling, estimation and control of human cardiovascular circulatory systems with a left ventricular assist device [5].

Figure 5 illustrates the simulation results from rest to exercise with the LVAD. The resistance of blood vessel (TPR) decreases dramatically in exercise, and the total peripheral flow

(TPF) increases significantly. The average estimation error for aortic pressure is maintained less than 1 mmHg in this activity variation. The value for reference signal r changes from 100 mmHg to 105.4 mmHg in exercise. The blood flow rate, the left ventricular end-diastolic pressure, and the average aortic pressure, are restored by the LVAD to: 5.6 L/min in rest and 9.8 L/min in exercise, 1.1 mmHg in rest and 2.3 mmHg in exercise, and 99.6 mmHg and 103.2 mmHg respectively. These values are close to the simulation results for a healthy person in rest and exercise conditions [5].

8 Experimental Study

A mock human circulatory loop was set up as an in vitro test rig for different versions of prototype LVADs, as shown in Figure 5, whose components mimic the key components of the human cardiovascular system, and can simulate different normal or pathologic states and activities of a cardiovascular system [15] (a small centrifugal pump MY2 was used in the place of an LVAD).

Figure 6: The mock human circulatory loop [15].

Figures 7 and 8 illustrate the experimental results of a mock human loop in different pathologic states without and with the MY2 pump respectively. Three different pathologic states, namely I, II, and III are reproduced exactly the same in the Figures 7 and 8. MY2 pump is controlled by a real-time controller board DS 1104 (dSPACE Inc., MA.). The average estimation error for aortic pressure was maintained less than 2 mmHg. The abnormal hemodynamic variables, such as the blood flow rate, the left ventricular end-diastolic pressure, and the average aortic pressure, are all restored to the normal physiologic range, 5-6 L/min, < 15 mmHg, and ~95 mmHg respectively, by the designed physiologic controller in the presence of pathologic state variations. The reference sig-

Figure 7: Experimental results (without MY2 pump): P_{LV} : left ventricular pressure; P_A : aortic pressure; P_V : venous pressure; TPF: total peripheral flow.

nal is set constant with the value of 95 mmHg without an on-line update in the experiment because the mock circulatory loop was unable to reproduce the relation between the left ventricular pressure P_{LV} and the venous return [5], thus invalidate the use of the f function to update the reference signal derived upon that relation.

9 Concluding Remarks

The design of a physiologic controller for a permanent LVAD is described in this paper. With the single-equation model (5.6) derived for the human circulatory system, the adaptive estimation and control methods has been applied in the controller design. Computer simulation and mock circulatory loop test consistently show good controller performance in the variation of physiologic states, in terms of aortic pressure estimation error, restoring abnormal hemodynamic variables back to normal range, etc. A series of animal tests, which replicate the human circulatory system more accurately than

Figure 8: Experimental results (with MY2 pump): P_{LV} : left ventricular pressure; TPF: total peripheral flow; Q_{pump} : LVAD flow rate; P_A (dashed): aortic pressure; $\hat{P}_A$ (solid): estimated aortic pressure; V: control output voltage; r: reference value.

the mathematical model and the mock circulatory loop, is an indispensable step to verify the designed LVAD physiologic controller performance.

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