2005 American Control Conference
June 8-10, 2005. Portland, OR, USA

Fusion of Hard and Soft Control Strategies for Left Ventricular Ejection Dynamics Arising in Biomedicine

D. Subbaram Naidu* and Vidya K Nandikolla

***Abstract*— A model of left ventricular pumping ejection dynamical process of the circulatory system arising in biomedicine is considered with the objective of minimizing the energy requirements of the heart as the sum of the potential energy stored in the tissues and muscles of the heart and that required for pumping the blood through the circulatory system. The resulting third-order, dynamic model is described in terms of state variables of left ventricular volume, rate of blood flow ejected out of the left ventricle, and blood pressure in the aorta and one input or control variable of left ventricular pressure. Using optimal control theory, a *closed-loop* optimal control technique is developed for the system with *fixed* boundary conditions and a performance index consisting of *mixed* state and control functions leading to an inverse matrix differential Riccati equation (IMDRE). Further, to improve the closed-loop performance, a soft control strategy such as an adaptive neuro-fuzzy inference system (ANFIS)-based intelligent technique is used leading to the fusion of hard control such as optimal control and soft control such as ANFIS. The application of this synergetic or hybrid (hard and soft) control strategy to the circulatory system shows a good agreement between the experimental data compared with the proposed, hybrid-control based theoretical results.**

I. INTRODUCTION

Heart is the main pump for circulation of blood through human body. It contracts in rhythmic motions that allow the blood to flow through the vascular system. First, venous blood flows through the right atrium and then into the right ventricle, after that it goes through oxygenation process where carbon dioxide is removed and finally blood flows from the left atrium to left ventricle. The amount of energy supplied to the heart is calculated by the mechanical work done by the heart, which is an integral of the product of the left ventricular pressure and the ventricular output. The production of the mechanical energy is very important to heart as it compensates the dissipation of energy as heat in the circulation system. There are three mechanisms to control the arterial blood pressure: stroke volume, heart rate and vasomotor control.

The cardiovascular dynamics is modeled as an electrical circuit. Note that the mechanical work is not the only energy factor involved in the pumping process but also the potential energy stored in the tissues and muscles are converted into useful work, which is later dissipated into heat. So in our study the performance index is the sum of stored potential energy and mechanical work [1].

The authors are with Measurement and Control Engineering Research Center, College of Engineering, Idaho State University, Pocatello, Idaho 83209-8060, USA. * The corresponding author naiduds@isu.edu

The *open-loop* optimal control problem for the circulatory system is described by Noldus [2] where the solution is obtained by solving a tedious, two-point boundary value problem (TPBVP) involving states and costates and compared with experimental results available for rabbits and dogs [2], [3], [4], [5]. These results for ventricular pressure, and ventricular volume based on open-loop optimal control have similar tendencies compared to experimental results although the results for the rate of blood flow are not in close agreement with those of the experimental results. Further, the *open-loop* optimal control scheme is well-known for its inability to compensate for any changes in the dynamical process and the more complicated and expensive hardware implementation of the controller.

The main aim of this paper is to determine the best control force strategy to eject a given amount of blood out of the left ventricle of the circulation system. The left ventricular pressure acts as the external driving force in the system which is optimized on the basis of reasonable performance index which relates to the energy expenditure of the left ventricular ejection system. The model obtained, provides fundamental philosophy of circulation biophysics and a logical explanation of the working of ventricle [1], [6].

In this paper, the left ventricular pumping ejection dynamical process of the circulatory system arising in biomedicine is modeled as an electrical circuit and the corresponding third-order dynamical equations are obtained in terms of state variables of left ventricular volume, rate of blood flow ejected out of the left ventricle, and blood pressure in the aorta and one input or control variable of left ventricular pressure. The objective function or performance index is chosen to minimize the energy requirements of the heart as the sum of the potential energy stored in the tissues and muscles of the heart and that required for pumping the blood through the circulatory system. Using optimal control theory, a *closed-loop* optimal control technique is developed for the system with *fixed* boundary conditions and a performance index consisting of *mixed* state and control functions leading to an inverse matrix differential Riccati equation (IMDRE). Further, to improve the closed-loop performance, a soft control strategy such as an adaptive neuro-fuzzy inference system (ANFIS)-based intelligent technique is used leading to the fusion of hard control such as optimal control and soft control such as ANFIS. The application of this hybrid (hard and soft) control strategy to the circulatory system shows a good agreement between the experimental

0-7803-9098-9/05/$25.00 ©2005 AACC

data compared with the theoretical results.

Special Features/Contributions of this Paper:

1) In this paper, theory of closed loop optimal control for *fixed-end* point problem with *mixed* state-control functions in the performance index is developed leading to the inverse matrix differential Riccati equation, whereas the work so far focused on performance index with quadratic functions in state alone and control alone.
2) The previous work (E. J. Noldus [2]), focused on *open-loop* optimal control of left ventricular ejection dynamics whereas in the present work we developed a *closed-loop* optimal control scheme which has the advantages of simplification of hardware implementation of the controller and of taking care of any process parameter variations.
3) Finally, in the present work, the integration or fusion of soft control technique such as adaptive network fuzzy inference system (ANFIS) and hard control technique such as closed-loop optimal control is to improve the performance compared to previous results.

In Section II, the dynamical ejection process is presented in the form of an electrical network, the various relations are obtained for the states and the performance index is formulated. Next, Section III contributes to the general theoretical development of closed-loop optimal control technique for *fixed* initial and final conditions and for *mixed* state and control quadratic functions in the performance index leading to an inverse matrix differential Riccati equation (IMDRE) and a vector differential equation (VDE). The application of the closed-loop technique to the circulatory system with simulations is shown in Section IV. Next, in Section V, the neuro-fuzzy controller is designed to improve the closed-loop optimal control results. The paper ends with some conclusions and discussions.

II. MODELING AND PROBLEM STATEMENT

A ventricular pump model as an electrical analog is shown in Figure 1 [2], [6]. The dynamical equations of this model are given as

$$\frac{dx_1(t)}{dt} = -x_2(t) \quad (1)$$

$$\frac{dx_2(t)}{dt} = \frac{u(t) - x_3(t) - R_2x_2(t)}{L} \quad (2)$$

$$\frac{dx_3(t)}{dt} = \frac{-x_3(t)}{R_1C} + \frac{x_2(t)}{C} \quad (3)$$

where,
$x_1(t) = V(t)$, $x_2(t) = i(t)$, $x_3(t) = P_a$, $u(t) = P(t)$,
$V(t)$ is left ventricular volume,
$V_o(t)$ is the ventricular volume at the beginning of ejection,
$P(t)$ is the left ventricular pressure,
$P_a(t)$ is the blood pressure in the aorta,
$i(t)$ is the rate of blood flow ejected out of left ventricle,
R_1 and C are the peripheral resistance and compliance of a lumped arterial windkessel load,
R_2 is the aortic valvular resistance, and
L is the inertia of the blood.
The boundary conditions are given as [9]

$$x_1(0) = V_o, \quad x_1(t_f) = V_e = V_o - V_s,$$
$$V_s = a + (c - d * P_a)V_o, \quad x_2(0) = x_2(t_f) = 0,$$
$$x_3(0) + x_3(t_f) = 2P_a. \quad (4)$$

The performance index, to minimize the energy requirement of the heart as the sum of the potential energy stored in the tissues and muscles of the heart and that required for pumping the blood through the circulatory system, is formulated as

$$J = \int_0^{t_f} \left[u^2(t) + \alpha u(t)x_2(t)\right] dt, \quad (5)$$

where α is a positive quantity.

III. CLOSED-LOOP OPTIMAL CONTROL

Let us now express the previous model (1)-(3) and performance index (5) in general terms so that the necessary theory is developed for obtaining closed-loop strategy. Thus, the state equation is,

$$\dot{\mathbf{x}}(t) = \mathbf{A}\mathbf{x}(t) + \mathbf{B}\mathbf{u}(t) \quad (6)$$

with *fixed* boundary (initial and final) conditions

$$\mathbf{x}(t = t_0) = \mathbf{x}_0, \qquad \mathbf{x}(t = t_f) = \mathbf{x}_f, \quad (7)$$

and the performance index is

$$J(\mathbf{u}) = \frac{1}{2}\int_{t_0}^{t_f} [\mathbf{x}'(t)\mathbf{Q}\mathbf{x}(t) + 2\mathbf{x}'(t)\mathbf{S}\mathbf{u}(t) + \mathbf{u}'(t)\mathbf{R}\mathbf{u}(t)]\, dt. \quad (8)$$

Here, $\mathbf{x}(t)$, $\mathbf{u}(t)$ are n- and m- dimensional state and control vectors, respectively and $\mathbf{A}$, $\mathbf{B}$ are system and input matrices of appropriate dimensionality. Also, the performance index matrices $\mathbf{Q}, \mathbf{S}$, are *positive semidefinite* matrices and $\mathbf{R}$ is a *positive definite* matrix of appropriate dimensions. Note the *mixed* state $\mathbf{x}(t)$ and control $\mathbf{u}(t)$

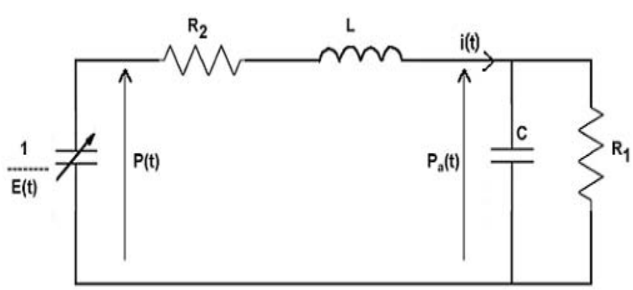

Fig. 1. Electrical Analog of the Left Ventricle System

quadratic functions associated with $\mathbf{S}$. Using optimal control theory [7] for the previous general system (6) along with *fixed* boundary conditions and the general performance index (8), an inverse matrix Riccati differential equation (IMDRE) and an associated vector differential equation (VDE) are developed leading to the closed-loop optimal control $\mathbf{u}^*(t)$ in terms of the optimal state functions $\mathbf{x}^*(t)$. Let us develop the procedure under the following steps [7]:

- *Step 1: Formation of Hamiltonian*

$$H = \frac{1}{2}\mathbf{x}'(t)\mathbf{Q}\mathbf{x}(\mathbf{t}) + \mathbf{x}'(t)\mathbf{S}\mathbf{u}(t) + \frac{1}{2}\mathbf{u}'(t)\mathbf{R}\mathbf{u}(t) + \boldsymbol{\lambda}'(t)[\mathbf{A}\mathbf{x}(t) + \mathbf{B}\mathbf{u}(t)]. \quad (9)$$

- *Step 2: Optimal Control*

$$\frac{\partial H}{\partial \mathbf{u}(t)} = 0 \longrightarrow \quad (10)$$

$$\mathbf{S}'\mathbf{x}^*(t) + \mathbf{R}\mathbf{u}^*(t) + \mathbf{B}'\boldsymbol{\lambda}^*(t) = 0, \quad (11)$$

which gives optimal control $\mathbf{u}^*(t)$ as

$$\mathbf{u}^*(t) = -\mathbf{R}^{-1}[\mathbf{S}'\mathbf{x}^*(t) + \mathbf{B}'\boldsymbol{\lambda}^*(t)]. \quad (12)$$

- *Step 3: State and Costate System*
Obtain the optimal state and costate equations as

$$\dot{\mathbf{x}}^*(t) = \frac{\partial H}{\partial \boldsymbol{\lambda}(t)} \longrightarrow \quad (13)$$

$$\dot{\mathbf{x}}^*(t) = \mathbf{A}\mathbf{x}^*(t) + \mathbf{B}\mathbf{u}^*(t), \quad (14)$$

$$\dot{\boldsymbol{\lambda}}^*(t) = -\frac{\partial H}{\partial \mathbf{x}(t)} \longrightarrow \quad (15)$$

$$\dot{\boldsymbol{\lambda}}^*(t) = -\mathbf{Q}\mathbf{x}^*(t) - \mathbf{A}'\boldsymbol{\lambda}^*(t) - \mathbf{S}\mathbf{u}^*(t). \quad (16)$$

- *Step 4: Closed-Loop Optimal Control*
The development is based on a transformation $\mathbf{M}(t)$ between the state $\mathbf{x}^*(t)$ and costate $\boldsymbol{\lambda}^*(t)$ as

$$\mathbf{x}^*(t) = \mathbf{M}(t)\boldsymbol{\lambda}^*(t) + \mathbf{v}(t) \quad (17)$$

taking the derivative of which leads to,

$$\dot{\mathbf{x}}^*(t) = \dot{\mathbf{M}}(t)\boldsymbol{\lambda}^*(t) + \mathbf{M}(\mathbf{t})\dot{\boldsymbol{\lambda}}^*(t) + \dot{\mathbf{v}}(t). \quad (18)$$

Using the previous state (14), costate (14), and control (12) relations, we finally obtain the inverse matrix differential Riccati equation (IMDRE) in $\mathbf{M}(t)$ as

$$\dot{\mathbf{M}}(t) = \mathbf{A}\mathbf{M}(t) + \mathbf{M}(t)\mathbf{A}' + \mathbf{M}(t)\mathbf{Q}\mathbf{M}(t) - [\mathbf{M}(t)\mathbf{S} + \mathbf{B}]\mathbf{R}^{-1}[\mathbf{S}'\mathbf{M}(t) + \mathbf{B}'] \quad (19)$$

and the vector differential equation (VDE) in $\mathbf{v}(t)$ as

$$\dot{\mathbf{v}}(t) = [\mathbf{A} - \mathbf{B}\mathbf{R}^{-1}\mathbf{S}' + \mathbf{M}(t)\mathbf{Q} - \mathbf{M}(t)\mathbf{S}\mathbf{R}^{-1}\mathbf{S}']\mathbf{v}(t). \quad (20)$$

The boundary conditions for solving the previous IMDRE and VDE equations depend on the given *fixed* boundary conditions (7).
Case 1: At t = t_0, the relation (17) becomes

$$x^*(t_0) = \mathbf{M}(t_0)\boldsymbol{\lambda}^*(t_0) + \mathbf{v}(t_0). \quad (21)$$

Since $\boldsymbol{\lambda}(t_0)$ is arbitrary, the above equation becomes $\mathbf{M}(t_0)$ = 0, therefore $\mathbf{v}(t_0)$=$x(t_0)$.
Case 2: At t = t_f, the relation (17) becomes

$$x^*(t_f) = \mathbf{M}(t_f)\boldsymbol{\lambda}^*(t_f) + \mathbf{v}(t_f). \quad (22)$$

Since $\boldsymbol{\lambda}(t_f)$ is arbitrary, the above equation becomes $\mathbf{M}(t_f)$ = 0, therefore $\mathbf{v}(t_f)$ = $\mathbf{x}(t_f)$. The above $\mathbf{M}(t)$ and $\mathbf{v}(t)$ equations can be solved using either the initial or final conditions.
The optimal state is obtained as

$$\dot{\mathbf{x}}^*(t) = [\mathbf{A} - \mathbf{B}\mathbf{R}^{-1}(\mathbf{S}' + \mathbf{B}'\mathbf{M}^{-1}(t))]\mathbf{x}^*(t) + \mathbf{B}\mathbf{R}^{-1}\mathbf{B}'\mathbf{M}^{-1}(t)\mathbf{v}(t) \quad (23)$$

and the optimal control is obtained as

$$\mathbf{u}^*(t) = -\mathbf{R}^{-1}(\mathbf{S}' + \mathbf{B}'\mathbf{M}^{-1}(t))\mathbf{x}^*(t) + \mathbf{R}^{-1}\mathbf{B}'\mathbf{M}^{-1}(t)\mathbf{v}(t) \quad (24)$$

The above set of closed loop optimal control equations are used to solve the circulation problem with general boundary conditions.

IV. APPLICATION OF CLOSED-LOOP OPTIMAL CONTROL

From the problem statement discussed in Section II, the values for the state-space matrices $\mathbf{A}$, $\mathbf{B}$, $\mathbf{Q}$, $\mathbf{R}$, and $\mathbf{S}$ are computed as follows:

$$\mathbf{A} = \begin{bmatrix} 0 & -1 & 0 \\ 0 & -R_2/L & -1/L \\ 0 & 1/C & -1/R_1C \end{bmatrix}; \quad \mathbf{B} = \begin{bmatrix} 0 \\ 1/L \\ 0 \end{bmatrix}$$

$$\mathbf{S} = \begin{bmatrix} 0 \\ 2\alpha \\ 0 \end{bmatrix}; \mathbf{F} = 0, \ \mathbf{R} = 2, \mathbf{Q} = 0, \alpha = 3.78. \quad (25)$$

The data used in the simulation is given below [2].

$$R_1 = 1.0, \quad R_2 = 1.9, \quad L = 0.003, \quad C = 1.9,$$
$$x_1(0) = 200, \quad x_1(t_f) = 133.4, \quad x_2(0) = 0,$$
$$x_2(t_f) = 0, \quad x_3(0) + x_3(t_f) = 200, \quad t_f = 0.18. \quad (26)$$

The optimal solutions are shown in the following figures. Figure 2 shows the optimal volume $x_1^*(t)$ in the left ventricular system. Figure 3 represents the optimal rate of blood flow $x_2^*(t)$ in the left ventricular system. Figure 4 depicts the optimal arterial pressure $x_3^*(t)$ in the left ventricular system. Figure 5 represents the optimal pressure $u^*(t)$ in the left ventricular system. The primary peak in Figure 5 represents the slope of the discontinuity at the beginning of the ejection. It indicates that the pressure curve is only calculated during ejection. The secondary peak in Figure 5 is due to the beginning of the last quarter of the systolic phase. The model accurately predicts the shape of the left ventricular pressure wave, which is a function of arterial pressure and end-diastolic volume [13], [14], [15].

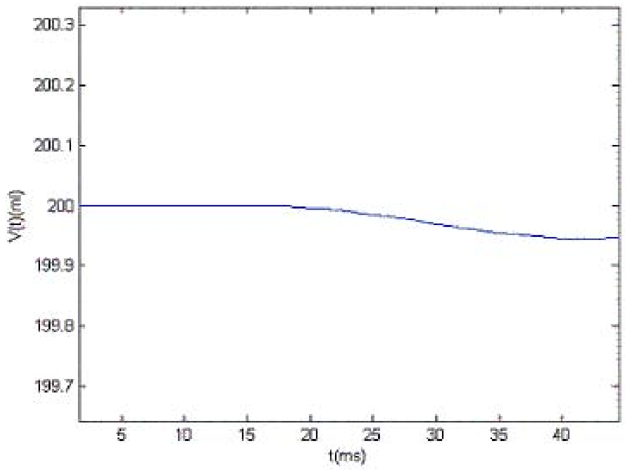

Fig. 2. Left Ventricular Volume $x_1^*(t)$

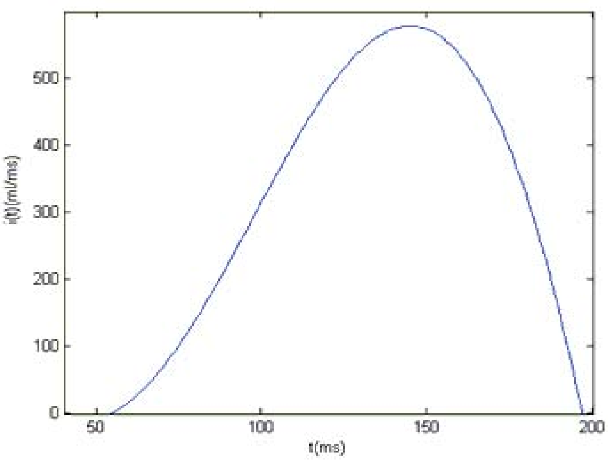

Fig. 3. Rate of Blood Flow $x_2^*(t)$

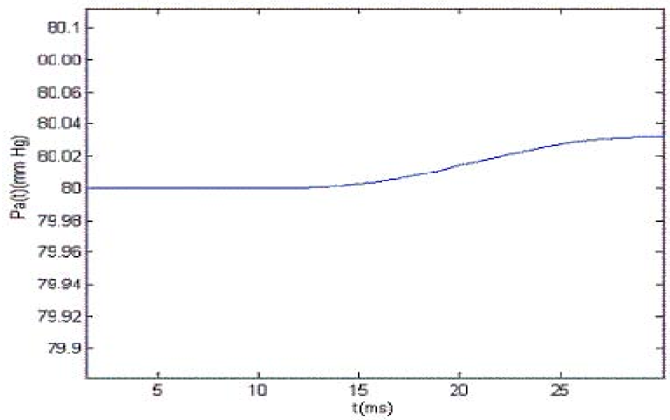

Fig. 4. Arterial Pressure $x_3^*(t)$

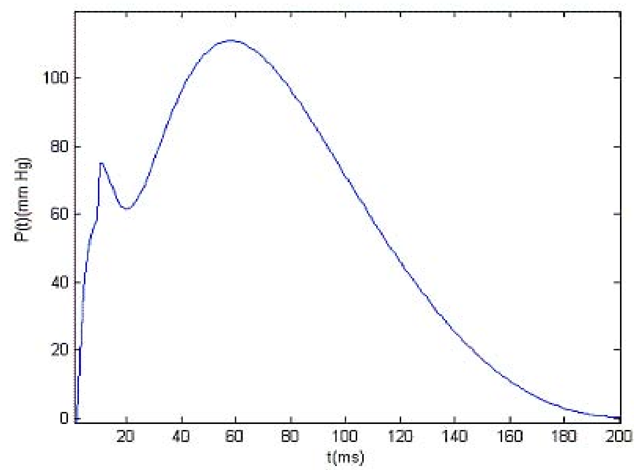

Fig. 5. Left Ventricular Pressure $u^*(t)$

V. ADAPTIVE NEURO-FUZZY INFERENCE SYSTEM

First of all, let us note that the soft control (SC) techniques involving neural networks (NN), fuzzy logic (FL), genetic algorithms (GA) etc. have the following attractive features or advantages [8], [10]:

1) SC incorporates human knowledge and experience in the form of fuzzy logic rules and membership functions.
2) Derivative-free optimization technique such as genetic algorithms based on genetic evolution and selection or survival is a part of SC.
3) Model-free learning and fault tolerance are some other special features of SC, where due to intensive parallel computational structure, the failure of a single neuron or a single IF-THEN rule does not destroy the system completely.
4) Finally, the techniques of NN, FL, and GA are not competing with but complementing each other.

On the other hand, hard control, using optimal, robust and adaptive control techniques,

1) is straightforward and is based on precise theory and results,
2) has solutions for stability and performance which are more predictable, and
3) the overall computational burden is moderate.

Thus, the fusion or integration of soft control (SC) and hard control (HC) methodologies has the following desired features [10], [16]:

1) The SC and HC are potentially complementary methodologies.
2) The fusion could solve problems that cannot be solved satisfactorily by using either methodology alone.
3) Novel synergetic combinations of SC and HC lead to high performance, robust, autonomous and cost-effective solutions.

The basic principle of fusion of hard and soft control strategies is shown in Figure 6. In the present work, we use a synergy of hard control technique such as closed-loop optimal control and a soft control technique such as

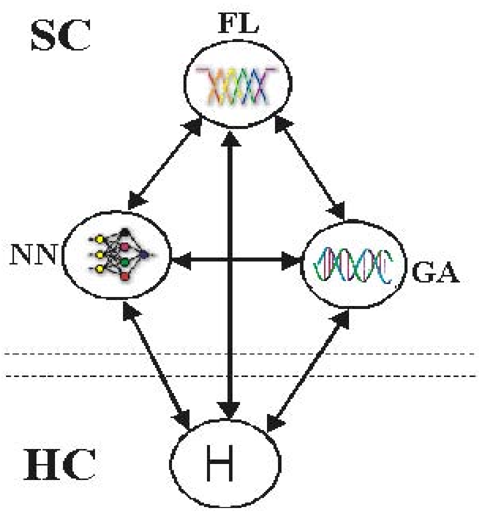

Fig. 6. Fusion of Hard Control(HC) and Soft Control(SC)

adaptive neuro-fuzzy inference system (ANFIS). ANFIS is an fuzzy inference system which is implemented in the framework of adaptive networks which provides the best optimization tool to find parameters that best fits the data. It applies two techniques, premise parameters and consequent parameters. Premise parameters define membership functions, and consequent parameters define the coefficients of each output equations. ANFIS uses gradient descent to tune the membership function and uses the least-squares method to identify the coefficients.

In this section we propose an ANFIS controller to reduce the error between the optimal solutions and experimental data. The proposed ANFIS controller constructs an input-output mapping based on human knowledge in form of fuzzy if-then rules and input-output data. The ANFIS parameters are updated to reduce the system's output error. The error is defined by the difference between the system's output and desired output. The block diagram of the hybrid controller is shown in Figure 7[8], [9], [10], [11], [12]. For

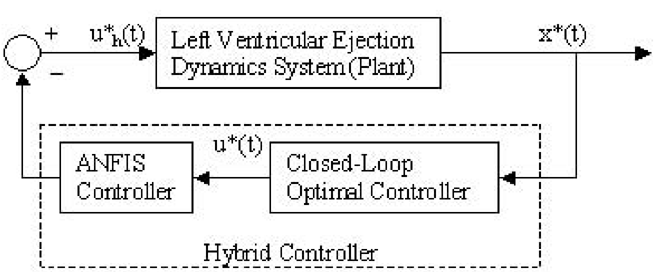

Fig. 7. Block Diagram of the Hybrid Controller for the Left Ventricular System

training ANFIS, the optimal control strategy $u^*(t)$ shown in Figure 5, is reformatted for the purpose of simulation as shown in Figure 8, suitable as the input to ANFIS controller. The membership functions are shown in Figure 9.

We can change the characteristics of membership functions for better approximation. Figure 10 describes the ANFIS surface after the training. Figure 11 shows the performance of the ANFIS controller after training with 50 epoches. The error between the hybrid optimal and experimental results is shown in Figure 12. Our simulation was based on off-line

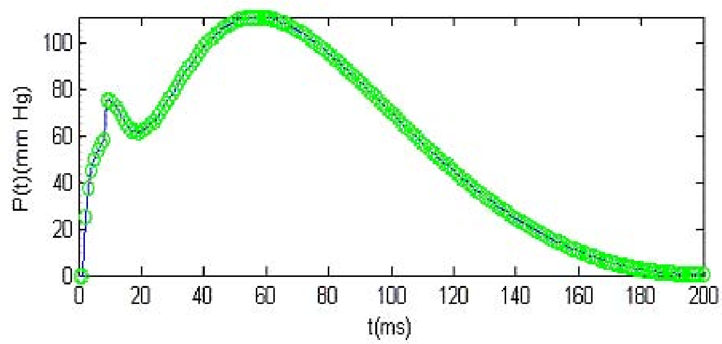

Fig. 8. Plot of Ventricular Pressure $u^*(t)$ for Training

learning but it is possible to turn on the on-line learning with time varying plant dynamics. In our simulation the ANFIS controller achieves a good performance with considerable reduction in the error between the experimental and theoretical results.

VI. CONCLUSIONS/DISCUSSIONS

In this paper, based on the model for left ventricular pumping ejection dynamical process with the objective of minimizing the energy requirements of the heart as the sum of the potential energy stored in the tissues and muscles of the heart and that required for pumping the blood through the circulatory system, a *closed-loop* optimal control strategy is developed for the system with *fixed* boundary conditions and a performance index consisting of *mixed* state and control functions leading to an inverse

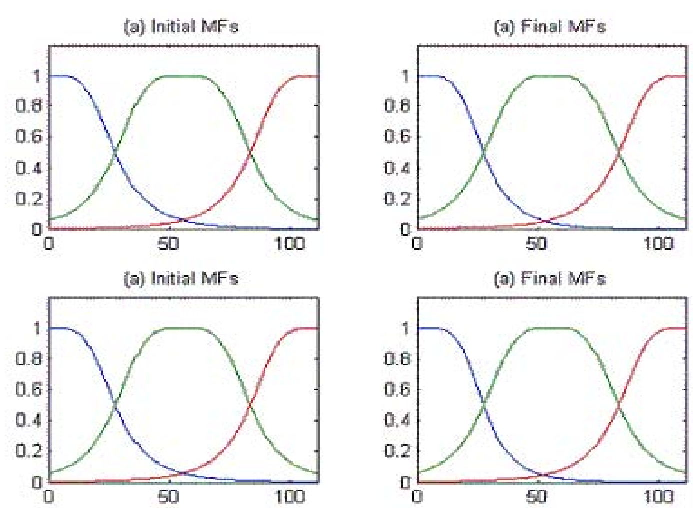

Fig. 9. Plot of the Membership Functions

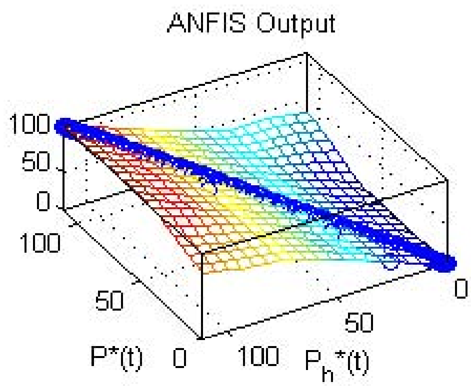

Fig. 10. ANFIS Surface after Training

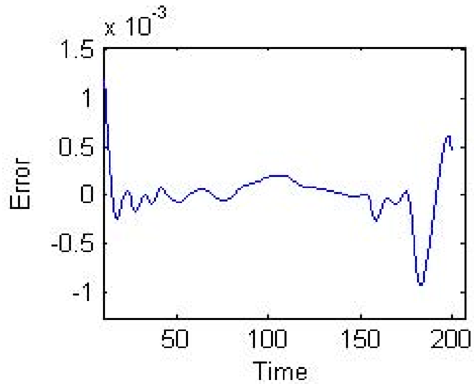

Fig. 12. Plot of the Error after Training

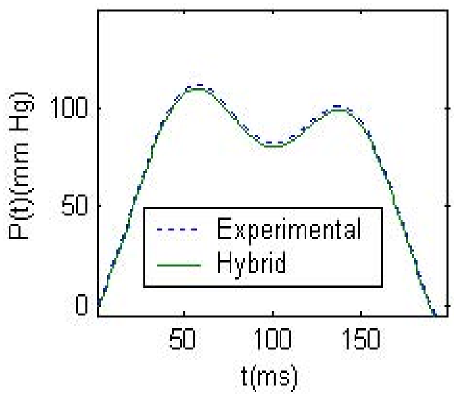

Fig. 11. Experimental and Hybrid Optimal $u_h^*(t)$

matrix differential Riccati equation (IMDRE) and a vector differential equation (VDE). Since the results with the hard control technique using IMDRE and VDE alone are not satisfactory compared to the experimental results, a soft control technique such as the adaptive neuro-fuzzy inference system (ANFIS)-based on intelligent technique was integrated with the hard control strategy. The application of this hybrid (hard and soft) control strategy to the circulatory system showed a good agreement between the experimental data and the hybrid control results. Further investigations are being directed towards hardware implementation of the hybrid control strategy.

ACKNOWLEDGMENT

The authors would like to thank the Office of Research at Idaho State University (ISU), Pocatello, ID for supporting the second author in awarding a graduate research assistantship.

REFERENCES

[1] A. C. Burton, *Physiology and Biophysics of the Circulation*, Year Book Medical Publishers, Inc, Chicago, 1970.

[2] E. J Noldus, "Optimal Control Aspects of Left Ventricular Ejection Dynamics", *Journal of Theoretical Biology*, Vol. 63, pp. 275-309, 1976.

[3] H. Suga, "Time course of Left Ventricular Pressure-Volume Relationship under Various Enddiastolic Volume", *Japanese Heart Journal*, Vol. 10, pp. 509-515, 1969.

[4] H. Suga, "Time course of Left Ventricular Pressure-Volume Relationship under various Extents of Aortic Occlusion", *Japanese Heart Journal*, Vol. 11, pp. 373-378, 1970.

[5] H. Suga, "Theoretical Analysis of a Left-Ventricular Pumping Model Based on the Systolic Time-Varying Pressure/Volume Ratio", *IEEE Transaction Biomedical Engineering*, Vol. 18, pp. 47-55, 1971.

[6] G. W. Swan, *Application of Optimal Control Theory in Biomedicine*, Marcel Dekker, Inc., New York and Basel, 1984.

[7] D. S. Naidu, *Optimal Control systems*, CRC Press, Boca Raton, FL, 2003.

[8] J-S.R Jang, C-T Sun, E. Mizutani, *Neuro-Fuzzy and Soft Computing*, Prentice-Hall, Upper Saddle River, NJ, 1997.

[9] H. L. Tsoukalas, R. E. Uhrig, *Fuzzy and Neural Approaches in Engineering*, John Wiley and Sons, Inc, New York, NY, 1997.

[10] D. S. Naidu and M. P. Schoen, MCE 646: *Intelligent Control Systems, Graduate Course Class Notes*, Measurement and Control Engineering Research Center, Idaho State University, Pocatello, Idaho, Spring 2003.

[11] H. T. Nguyen, N. R. Prasad, C. L. Walker and E. A. Walker, *A First Course in Fuzzy and Neural Control*, Chapman and Hall/CRC,Boca Raton, FL, 2003.

[12] H. Ying, *Fuzzy Control and Modeling: Analytical Foundations and Applications*, IEEE Press in Biomedical Engineering, New York, NY, 2000.

[13] J. G. Defares, H. Hara, J. Osborn and J. Mcleod, "Theoretical Analysis and Computer Simulation of the Circulation with Special Reference to the Starling Properties of the Ventricles", In Circulatory Analog Computers (A. Noordergraaf, ed.), Amsterdam: North-Holland Publ. Co, pp. 91-121, 1963.

[14] J. G. Defares, J. Osborn, and H. Hiroshi, "Theoretical Synthesis of the Cardiovascular System", *Acta Physiol. Pharmacol. Neerl*, Vol. 12, pp. 189-265, 1964.

[15] M. E. Greene, J. Clark, D. Mohr and H. Bourland, "Mathematical Model of Left Ventricular System", *Medical and Biological Engineer*, Vol. 11, pp. 126-134, 1973.

[16] S. J. Ovaska, H. F. VanLandingham, and A. Kamiya, "Fusion of soft computing and hard computing in industrial applications: An overview", *IEEE Transactions on Systems, Man, and Cybernetics - Part C: Applications and Reviews*, Vol. 32(2), pp. 72-79, May 2002.