01 Jan 2001

An Optimal Control Based Treatment Strategy for Parturient Paresis Using Neural Networks

Radhakant Padhi

S. N. Balakrishnan
Missouri University of Science and Technology, bala@mst.edu

Recommended Citation

R. Padhi and S. N. Balakrishnan, "An Optimal Control Based Treatment Strategy for Parturient Paresis Using Neural Networks," *Proceedings of the 2001 IEEE International Conference on Control Applications, 2001*, Institute of Electrical and Electronics Engineers (IEEE), Jan 2001.
The definitive version is available at https://doi.org/10.1109/CCA.2001.973927

Proceedings of the 2001 IEEE International
Conference on Control Applications
September 5–7, 2001 • México City, México

AN OPTIMAL CONTROL BASED TREATMENT STRATEGY FOR PARTURIENT PARESIS USING NEURAL NETWORKS

RADHAKANT PADHI* S. N. BALAKRISHNAN**

Department of Mechanical and Aerospace Engineering and Engineering Mechanics
University of Missouri - Rolla, MO 65409, USA

Abstract. An optimal on-line feedback treatment strategy is developed for the parturient paresis of cows, based on nonlinear optimal control theory. A limitation in the development of an existing mathematical model for calcium homeostatis is addressed and the model is extended to incorporate control inputs. An optimal feedback controller is synthesized for the nonlinear system using neural networks. Though the main aim of this paper is to solve the bio-medical control problem, the methodology presented in this paper is a general computational tool, which can be applied to solve a fairly general class nonlinear optimal control problems.

Key Words: Calcium Homeostatis, Parturient Paresis, Optimal Control, Neural Networks, Adaptive Critic Design

1. INTRODUCTION

Calcium (Ca) has various crucial physiological roles in animals. Besides maintaining the integrity of the bone structure, Ca ions are involved in the activity of a large number of enzymes [Griffin]. A mathematical model for the calcium homeostatis problem of cows was first developed by Ramberg et. al. [Ramberg]. The one-dimensional model has recently been modified to a two-dimensional model by El-Samad et. al. [El-Samad]. This model clearly describes the Ca homeostatis problem in healthy cows. It also attempts to explain a disease with the onset of parturition (calving), commonly known as parturition paresis (milk fever), for some animals. This fever is caused by the hypocalcemia, which occurs when the complex internal control mechanism for maintaining calcium homeostatis fails, because of a sudden and severe outflow of calcium.

Except for very special class of problems (like the Linear Quadratic Regulator problems, for example), it is quite difficult to obtain a state feedback controller in an optimal control formulation. The method of dynamic programming handles this problem by producing a family of optimal paths [Bryson]. One great drawback of the dynamic programming approach, however, is that its solution warrants a prohibitive amount of computation and storage requirements. The main idea pursued in this paper is based on the model-based adaptive critic methodology for optimal control proposed by Balakrishnan & Biega [Balakrishnan]. The methodology synthesizes two sets of neural networks. One set of networks, named as the '*critic networks*', captures the relationship between the states and costates. The other set of networks, named as the '*action networks*', capture the relationship between states and control. After successful iterative off-line training between the action and critic networks, it results in a feedback form of the optimal controller. The methodology allows the philosophy of dynamic programming to be carried out without the need for excessive computation and storage requirements. An interesting discussion about the philosophy of the adaptive critic designs can be found in [Werbos]. The optimal control synthesis methodology described in this paper retains all the features of the adaptive-critic methodology. However, we have been successful in completely eliminating the 'action networks'. For that reason, we no longer require the iterative training loops between the action and critic networks. Consequently, the computation time in synthesizing the neural controller is reduced considerably and this paper can be viewed as a significant improvement of the model-based adaptive critic methodology.

From a system theoretic point of view, the milk fever problem of dairy cows can be thought of as follows. Before the onset of parturition, the internal Ca homeostatis mechanism operates at a stable equilibrium point. However after the parturition, due to the outflow of Ca, the equilibrium point shifts to a new value. With respect to this new equilibrium point, the earlier one can be thought of as an initial condition. Depending on the parameters, the dynamics may drive the system from this initial condition to the new equilibrium point (in which case, the animal is supposed to be normal) or, it may drive the system away from this new equilibrium point (in which case, the animal is supposed to suffer from the disease). As pointed out by Oetzel et. al. [Oetzel], a common treatment strategy for the milk fever patients is the intravenous infusion of Ca salt. The goal of this paper is to come up with an on-line feedback optimal control (medication) strategy based on this Ca salt infusion process. The controller is based on the nonlinear system dynamics of Ca homeostatis and is synthesized taking the help of neural networks.

2. CALCIUM HOMEOSTATIS IN COWS

2.1 Existing Model

A dynamic model for the Ca homeostatis problem was first developed by Rabmerg et. al. [Ramberg]. The model has recently been modified to the following two-dimensional model, by El-Samad et. al. [El-Samad].

$$\dot{z}_1 = \frac{1}{Vol}\left[Sat_1\{K_p(r-z_1)\} + f(z_1)Sat_2\{z_2\} - V_{cl}\right] \qquad (1)$$
$$\dot{z}_2 = K_I(r-z_1)$$

where, $z_1 \equiv$ Ca concentration (gm/L) in the blood plasma, $z_2 \equiv$ rate (gm/day) at which Ca is supplied to blood plasma from intestine, $\dot{z}_1$, $\dot{z}_2 \equiv$ rate of change of z_1 and z_2 respectively *wrt.* time (t), $Vol \equiv$ total plasma volume (L), $V_{cl} \equiv$ total Ca clearance from the plasma (gm/L), $r \equiv$ set point, for Ca

* Ph.D student **Professor, contact person

concentration regulation (gm/L), $K_p \equiv$ constant for the internal proportional block (L/day), $K_I \equiv$ constant for the internal integral block (L/day^2), $Sat_1(.)$, $Sat_2(.)$ are the saturation values, $f(z_1) = \begin{cases} \frac{1}{12}[(\alpha_1 + \alpha_2 z_1)(\alpha_3 + \alpha_4 z_1)], & z_1 < r \\ 1, & z_1 \geq r \end{cases}$ is a multiplicative reduction factor, reflecting the effect of plasma Ca concentration on rate of Ca supply from intestine, where $\alpha_1, \alpha_2, \alpha_3, \alpha_4$ are constants.

2.2 Modifications to the Model

Since biological systems are seldom prone to *hard-nonlinear* saturation functions, we propose to change the hard-nonlinear saturation functions to *hyperbolic tangent* functions. Towards the development of a mathematical model with external control term, we are primarily interested in a medication strategy with intravenous Ca infusion, which is infused directly to the blood plasma. Because of direct infusion, the *rate of change* of Ca ($\dot{z}_1$) in the blood plasma is assumed to be change *instantaneously* by the rate of external Ca infusion. However, the externally infused Ca is assumed to reflect in the blood plasma with efficiency η. With this observation, we can write

$$\dot{z}_1 = \frac{1}{Vol}\left[A_1 \tanh\left\{\frac{K_p(r - z_1)}{A_1}\right\} + f(z_1) A_2 \tanh\left\{\frac{z_2}{A_2}\right\} - V_{cl}\right] + \eta v \qquad (2)$$
$$\dot{z}_2 = K_I(r - z_1)$$

where, $A_1 \approx Sat_1$, $A_2 \approx Sat_2$. We consider A_1, A_2, K_p, K_I as system parameters and v is the external control. As an observation, In Eq.(1), the equilibrium point is given by $\begin{bmatrix} z_1^0 & z_2^0 \end{bmatrix}^T = \begin{bmatrix} r & V_{cl} \end{bmatrix}^T$, whereas in Eq.(2), the equilibrium point is given by $\begin{bmatrix} z_1^0 & z_2^0 \end{bmatrix}^T = \begin{bmatrix} r & A_2 \tanh^{-1}(V_{cl} / A_2) \end{bmatrix}^T$. Thus, in our modified model, the final equilibrium point after parturition is *parameter dependent*. Intuitively this makes more sense, since different animals are supposed to settle at different equilibrium points.

2.3 Reformulation for Control Development

Our main aim is to regulate the system, described in Eq.(2), about its equilibrium point. Hence, we re-write the system dynamics in terms of deviations from the desired (equilibrium) point. Towards this, we define $\begin{bmatrix} z_1 \\ z_2 \end{bmatrix} = \begin{bmatrix} z_1^0 \\ z_2^0 \end{bmatrix} + \begin{bmatrix} y_1 \\ y_2 \end{bmatrix}$, and re-write the system dynamics as

$$\dot{y}_1 = \frac{1}{Vol}\left[\begin{array}{l} A_1 \tanh\left\{\frac{-K_p y_1}{A_1}\right\} \\ + f(z_1^0 + y_1) A_2 \tanh\left\{\frac{z_2^0 + y_2}{A_2}\right\} - V_{cl} \end{array}\right] + \eta v \qquad (3)$$
$$\dot{y}_2 = -K_I y_1$$

Since our final aim is to synthesize a neural network based controller (described in Section-3, in detail), for faster convergence in the training process of the networks, it is a standard technique to input all the variables, in some sort of a normalized fashion. Towards this end, we define the new variables $x_1 = (y_1 / y_{1nom})$, $x_2 = (y_2 / y_{2nom})$, where, y_{1nom} and y_{2nom} are the *nominal values* of y_1 and y_2 respectively. The normalized system is given by:

$$\dot{X} = \begin{bmatrix} \frac{1}{Vol.\, y_{1nom}}\left[g_1(x_1) + \tilde{f}(x_1)\, g_2(x_2) - V_{cl}\right] + \eta u \\ -K_I (y_{1nom} / y_{2nom})\, x_1 \end{bmatrix} \qquad (4)$$

where, $X = \begin{bmatrix} x_1 & x_2 \end{bmatrix}^T$ and

$$u = \frac{v}{y_{1nom}}, \quad \tilde{f}(x_1) = f(z_1^0 + x_1 y_{1nom})$$
$$g_1(x_1) = A_1 \tanh\left\{\frac{-K_p x_1 y_{1nom}}{A_1}\right\} \qquad (5)$$
$$g_2(x_2) = A_2 \tanh\left\{\frac{z_2^0 + x_2 y_{2nom}}{A_2}\right\}$$

3. OPTIMAL CONTROLLER SYNTHESIS

3.1. Optimality Conditions

The discussion in this section is in the general framework. The discrete system dynamics considered in this paper is expressed as

$$X_{k+1} = F_k(X_k, U_k) \qquad (6)$$

where, the subscript k denotes the time step. $X_k \in R^n$ and $U_k \in R^m$ represent state and control vectors respectively at time step k. Similarly, we consider a general scalar cost function to be of the form.

$$J = \sum_{k=1}^{N-1} \Psi_k(X_k, U_k) \qquad (7)$$

where, N represents the number of discrete time steps. Note that when $N \to \infty$, Eq.(7) represents an infinite time problem. Following the above representation of the cost function, we denote the *cost function from time step* k as $J_k = \sum_{\tilde{k}=k}^{N-1} \Psi_{\tilde{k}}(X_{\tilde{k}}, U_{\tilde{k}})$. Then we can breakup and re-write $J_k = \Psi_k + J_{k+1}$ where, Ψ_k *and* $J_{k+1} = \sum_{\tilde{k}=k+1}^{N-1} \Psi_{\tilde{k}}$ represent the *utility function* at time step k and the *cost-to-go* from time step $k+1$ to N respectively. We define the $n \times 1$ *costate* vector at time step k as $\lambda_k \equiv \frac{\partial J_k}{\partial X_k}$ For optimal control, the necessary condition for optimality is given by $\frac{\partial J_k}{\partial U_k} = 0$. After some algebra, this leads to

$$\left(\frac{\partial \Psi_k}{\partial U_k}\right)+\left(\frac{\partial X_{k+1}}{\partial U_k}\right)^T \lambda_{k+1}=0 \qquad (8)$$

Similarly, the co-state propagation equation, on the optimal trajectory can be derived as

$$\lambda_k = \left(\frac{\partial \Psi_k}{\partial X_k}\right)+\left(\frac{\partial X_{k+1}}{\partial X_k}\right)^T \lambda_{k+1} \qquad (9)$$

We have used Eq.(6), (8) and (9) for the synthesis of the neural networks. We will consider a fairly general class of special cases, where Eq.(8) is explicitly solvable for U_k as a function of x_k and λ_{k+1}. The bio-medical problem of our study falls under this class.

3.2. Optimality Conditions for Calcium Regulation Problem

Assuming Δt to be the step size in time, the discretized state equation can be written as

$$X_{k+1}=X_k+\Delta t\begin{bmatrix}\frac{1}{Voly_{1nom}}\left[g_1(x_{1k})+\tilde{f}(x_{1k})\,g_2(x_{2k})-V_{cl}\right]+\eta u_k \\ -K_I\left(y_{1nom}/y_{2nom}\right)\,x_{1k}\end{bmatrix} \qquad (10)$$

It is clear that the medication problem falls under the class of *regulator problems*, the regulation being carried out about the equilibrium point $X=0$. Following the standard practice for regulator problems, we assume a quadratic cost function of the form

$$J=\frac{1}{2}\sum_{k=1}^{\infty}\left(X_k{}^T Q_D X_k + R_D\, u_k{}^2\right) \qquad (11)$$

where, $X_k=\begin{bmatrix}x_{1k} & x_{2k}\end{bmatrix}^T$ is the state vector. Using this expression for Ψ_k in the optimality conditions derived earlier Eq.(10) & (12), we arrive at the following equations for optimal control and costate dynamic equations.

$$u_k = -R^{-1}\begin{bmatrix}\eta & 0\end{bmatrix}\lambda_{k+1} \qquad (12)$$

$$\lambda_k=\lambda_{k+1}+\Delta t\left[QX_k+\left(\frac{\partial F^k}{\partial X_k}\right)^T\lambda_{k+1}\right] \qquad (13)$$

At each time step k the coupled equations (10), (12) & (13) have to be solved simultaneously, together with the boundary conditions (X_1 specified and $\lambda_N=0,\quad N\to\infty$), to obtain the solution for u_k. One can notice $Q_D=Q\Delta t$ and $R_D=R\Delta t$, to be compatible with continuous and discrete time formulations.

3.3 Procedure for Neural Network Based Controller Synthesis

The schematic of the controller synthesis procedure is outlined in Figure-1. This discussion is in the general framework as well.

State Generation for Neural Network Training

We follow the procedure outlined below to generate the states for training the networks.

Define, $S_i=\left\{\text{all } X_k:\ \|X_k\|_\infty \le c_i\right\}$, $i=1,2,3,\ldots$ where, c_i is a positive constant. Notice that for $c_1\le c_2\le c_3\le\ldots$, $S_1\subseteq S_2\subseteq S_3\subseteq\ldots$. Thus, for some $i=I$, S_I will include the domain of interest for initial conditions. Hence, to begin the control synthesis procedure, we fix a small value for the constant c_1 and train the networks for the states generated within S_1. Once the critic networks converge for this set, we keep on increasing the constant c_i this way till the set S_i includes domain of interest for the initial conditions. In this paper, we chose $c_1=0.05$, $c_i=c_1+0.01(i-1)$ for $i=2,3,\ldots$ and continued till $i=I$, where $c_I=1$. It should be noted that any other scheme to generate the training sets should also be fine.

Neural Network Training

We have assumed that the parameters of the problem (K_p, K_I, A_1, A_2) are not fixed and they can vary, within known minimum and maximum values. Thus, $K_p\in\left[K_{p\min},K_{p\max}\right]$, $K_I\in\left[K_{I\min},K_{I\max}\right]$, $A_1\in\left[A_{1\min},A_{1\max}\right]$ and $A_2\in\left[A_{2\min},A_{2\max}\right]$. We have assumed that the parameters remain constant for any particular animal and hence, for a typical state trajectory. In order to capture the relationship between X_k and λ_{k+1} with varying parameters, we construct an augmented vector X_k^{inp}, which serves as the input to the neural networks. However, since the individual elements of X_k^{inp} vary widely in magnitude, we construct a normalized vector, to serve as the input. In our bio-medical problem, we have $X_k^{inp}=\left[x_{1k}\quad x_{2k}\quad \frac{K_p}{K_{p\,nom}}\quad \frac{K_I}{K_{I\,nom}}\quad \frac{A_1}{A_{1nom}}\quad \frac{A_2}{A_{2nom}}\right]^T$, where $K_{p\,nom}, K_{I\,nom}, A_{1nom}$ and A_{2nom} are the normalizing values for K_p, K_I, A_1 and A_2 respectively.

One can notice that since U_k is a known function of X_k and λ_{k+1}, after successful training of the networks, we can directly calculate the associated optimal control U_k from Eq.(8). We synthesize the neural networks in the following manner [Figure 1]. Generate S_i, as described in Section 3.2.1. Construct X_k^{inp} Input X_k^{inp} to the networks to get λ_{k+1}. Let us denote it as λ_{k+1}^{a}. Calculate U_k, knowing X_k and λ_{k+1}, from *optimal control equation* [Eq.(9)]. Get X_{k+1} from the *state equation* [Eq.(6)], using X_k and U_k. Construct X_{k+1}^{inp}. Input X_{k+1}^{inp} to the networks to get λ_{k+2}. Calculate λ_{k+1}, form the *costate equation* [Eq.(8)]. Let

us denote this as λ^{t}_{k+1}. Train the networks, with all X^{inp}_{k} as input and all corresponding λ^{t}_{k+1} as output.

3.3.3. Convergence Condition

Fix c_i to the same values that have been used for the training of the networks. Generate a set S^c_i of states, exactly the same manner used to generate S_i. Fix a tolerance (tol) value (we have fixed $tol = 0.1$, for the bio-medical problem). By using the states from S^c_i, generate the target outputs, as described in Section-3.3.1. Say the outputs are $\lambda^{t_i}_1, \lambda^{t_i}_2, \ldots, \lambda^{t_i}_n$. Generate the actual output from the networks, by simulating the *trained* networks with the states from S^c_k. Say the values of the outputs are $\lambda^{a_i}_1, \lambda^{a_i}_2, \ldots, \lambda^{a_i}_n$. Check whether $\frac{\left\|\lambda^{t_i}_l - \lambda^{a_i}_l\right\|_2}{\left\|\lambda^{t_i}_l\right\|_2} < tol$, $\forall\, l = 1, \ldots n$. If yes, we assume that the networks have converged.

4. MEDICATION STRATEGY

At any time step k, the control magnitude U_k is computed on-line, using the using the neural networks synthesized off-line, outlined in Section-3. To address an implementation concern, if the computed control $U_k < 0$, we forcefully make $U_k = 0$, since a negative infusion rate is not feasible in practice. However, it should be noted that even though this condition was incorporated, it was never encountered in our simulations. The Ca infusion process is continued for an hour. The condition of the patient is projected for some specified future time, say for a week (which is normally required for an animal to restore the Ca regulation internally). This is done using the homogeneous system dynamics. If the projected states show $x_1 \to 0$ and $x_2 \to 0$ (*i.e.* the patient recovers without further medication), and x_1 trajectory never enters a predetermined region ($x_1\, y_{1nom} < -0.03$, in our case), STOP medication. Else, continue medication for another hour.

One should note that this paper does not deal with any new drug development. Rather, it attempts to make use of the advanced control theory concepts, to optimally use the available intravenous Ca infusion drug, thereby aiming to improve the effectiveness of the drug substantially.

5. NUMERICAL RESULTS

5.1 Numerical Values

For our numerical experimentation, we chose the values for parameters r, V_{cl0}, V_{cl}, Vol as used in [El-Samad]. However, for the parameters K_p, K_I, A_1, A_2 we carried out the simulations with various combinations of parameter values and plotted the phase plots [Figure 2]. From the qualitative nature of the phase plots, we fixed the parameter values for which the plots showed instability (indicating the onset of milk fever) for a number of initial conditions. The diagonal elements of the weighting matrix on the states in the cost function Q were chosen as $Q_{11} = 4/(0.01/y_{1nom})^2$ and $Q_{22} = 1/(50/y_{2nom})^2$, where, $Q = \begin{bmatrix} Q_{11} & Q_{12} \\ Q_{21} & Q_{22} \end{bmatrix}$. The off diagonal elements Q_{12} and Q_{21} were set at zero. The weighting value on the control R was chosen as $(\eta/20)^2 Q_{11}$. For the discritization purpose, we fixed $\Delta t = 30$ Sec. We synthesized our numerical results for two drugs, assuming $\eta = 20\,\%$ for one drug and $\eta = 30\,\%$ for the other. The nature of the results were similar and results for $\eta = 20\,\%$ are given in this paper.

5.2 Analysis of Simulation Results

As mentioned in [Oetzel], the current practice of Ca infusion to treat parturient paresis is to infuse 10.8 gm of Ca in 12 min. We refer to this as *impulse medication*. We attempted to compare our results with this medication scheme, which is currently in practice. For the numerical simulation with impulse medication, we assumed a constant rate of infusion (control) of (10.8gm/12min) for 12 minutes, and then assumed it to be zero for rest of the time.

We assumed $K_p = 2000$ lit/day, $K_p = 2100$ lit/day^2, $A_1 = 60$ gm/day and $A_2 = 90$ gm/day. These parameters lead to an unstable trajectory for the initial condition $x_1 = 0$, $x_{2\min} = \frac{A_2}{y_{2nom}}\left[\tanh^{-1}(V_{cl0}/A_2) - \tanh^{-1}(V_{cl}/A_2)\right]$, indicating a diseased animal. Starting with this initial condition, we first propagated the homogeneous system, till x_1 dropped below x_{1cut}, a known value. Then we collected the corresponding value of x_2 value at that time and considered the state values at that time as our initial condition for the application of control. Accordingly, in our simulation plots we set the initial time to zero. We have presented all the simulation plots only for two days (48 hours). This is to have a magnifying effect near parturition, to clearly see the effect of control.

Figures 2-4 show the results by assuming the control efficiency $\eta = 20\,\%$ and $x_{1cut}\, y_{1nom} = -0.05$. It is clear that both the continuous and the impulse medication work fine in recovering the animal. Moreover the actual amount of Ca infused to the system in the 6 hr. long medication is $m_a = 15.78$ gm, a comparable value to 10.8 gm. However, as seen in Figure-2, the trajectory of the deviated amount of Ca per unit volume of the blood pool from its equilibrium value enters the positive domain, which means the presence of extra Ca in the pool than necessary. This may lead to the potential threat of hypercalcemia [Oetzel]. Moreover, the same trajectory for the impulse medication again drops below -0.04 gm/lit, a sufficient low value, before recovering back. On the other hand, the continuous medication shows a much smoother trajectory. It never goes to the positive side. Moreover after termination of the medication, even though the trajectory drops a little before recovering back, it always remains well above the danger level of -0.03 gm/lit for all future time. Figure-3 depicts the trajectory of the rate of Ca resorption from intestine. The two plots for impulse and continuous control are quite close to each other. It indicates that by continuous control we did not do anything drastically wrong to the absorption in intestine. It operated as it would have operated under the impulse control. Figure-4 depicts the control trajectory

under the on-line optimal medication. At time $t = 6$ hrs, the control is purposefully terminated. Moreover one can notice, as compared to the impulse input of 10.8 gm in 15 min, which corresponds to 1036.8 gm/day, the control magnitude at any particular time in the continuous scheme is much lesser. Consequently the system is pulled towards the equilibrium point in a much smoother way. We also simulated the system with $x_{1cut} y_{1nom} = -0.03$. It was surprising to see that the impulse control did not work. It means the current practice of quick infusion works only after the condition of the patient becomes sufficiently bad. Before that the impulse infusion is ineffective. However, the on-line continuous scheme was successful in recovering the cow irrespective of its starting time.

One of our main aims was to see that the proposed methodology and the synthesized controller work from a variety of initial conditions, which is even more useful in a practical case. Towards this end, we assumed a large number of random parameter values and random initial states and simulated the system. Figures 5-8 show some of the simulated results, which clearly indicate that the proposed scheme works for all these cases. For clarity of the figures, only ten such cases are presented. However, similar results were obtained for a very large number of cases. In fact, in none of the large simulation cases the nonlinear neuro controller failed. Moreover, as another important observation, in *no case* the trajectory of Ca deviation per unit volume of blood pool was found to enter the positive domain , avoiding the hypercalcemic problem.

6. CONCLUSIONS

After suggesting a modification to an existing model for the calcium homeostatis of cows, we have successfully synthesized an on-line feedback optimal medication strategy for the parturient paresis problem. The proposed medication scheme improves the effectiveness of the drug substantially, as compared to the impulsive quick infusion process, currently in practice. It was found that whereas the current practice can be effective only after the condition of a cow deteriorates, the proposed continuous medication process could be initiated at any time. Moreover, the on-line continuous infusion never leads to the hypercalcemic problem. Further, whereas as the current practice of quick Ca infusion has a non-zero probability of failure for patient animals, the simulation studies shows that the probability of failure for the proposed on-line optimal continuous medication scheme is zero, for all practical purposes. In this paper, we have also come up with a systematic approach for the state feedback solution of optimal control problems associated with the nonlinear systems, for a fairly general class of problems, which can be viewed as a significant improvement of the existing adaptive-critic based optimal control design methodology.

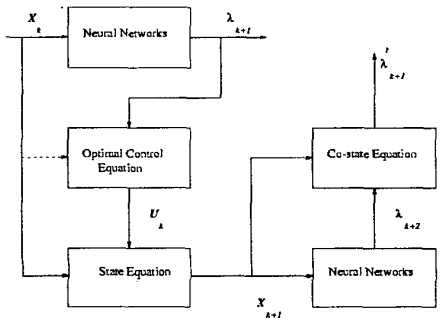

Figure 1: Schematic of optimal control synthesis using neural networks

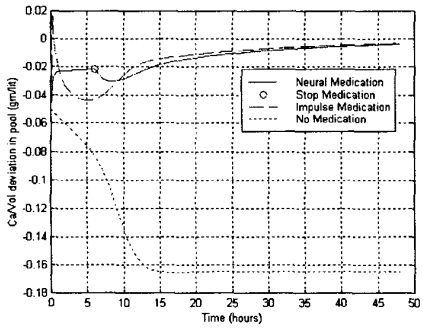

Figure 2: Calcium/Vol. deviation in the pool, with 20% control efficiency

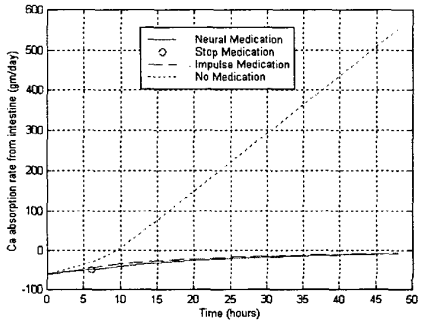

Figure 3: Calcium absorption rate in intestine, with 20% control efficiency

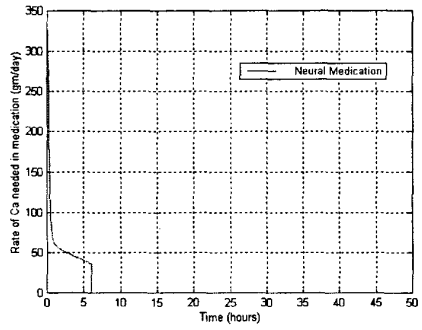

Figure 4: Rate of Ca needed in medication, with 20% control efficiency

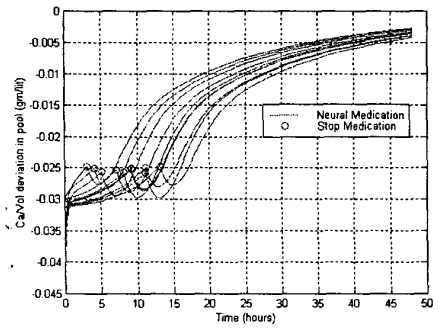

Figure 5: Calcium/Vol. deviation in the pool, with 20% control efficiency

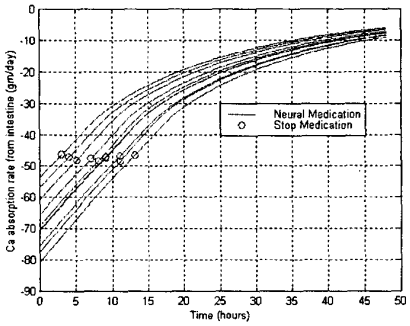

Figure 6: Calcium absorption rate in intestine, from various initial conditions

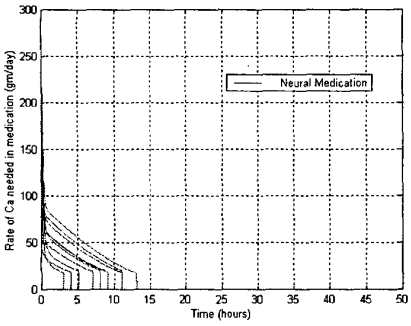

Figure 7 Rate of Ca needed in medication, from various initial conditions

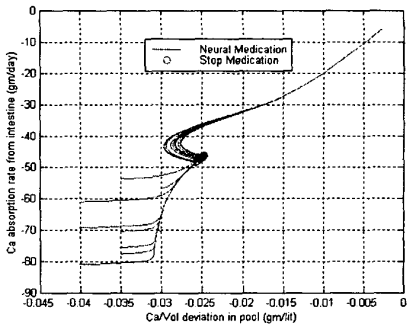

Figure 8: Phase plots from various initial conditions

Acknowledgement

This research was funded by NSF-USA grant ECS 9976588. The authors are thankful to NSF. The authors are also grateful to Hana El-Samad, graduate student, Iowa state university. Discussions with her were quite helpful and productive.

7. REFERENCES

1. Balakrishnan S. N. and Biega V., Adaptive-Critic Based Neural Networks for Aircraft Optimal Control, *Journal of Guidance, Control and Dynamics, Vol. 19, No. 4, July-Aug. 1996, pp. 893-898.*

2. Bryson A. E. and Ho Y. C., Applied Optimal Control, *Taylor and Francis, 1975.*

3. El-Samad H, Khammash M and Goff J., Calcium Homeostasis: a Feedback Control Point of View, *Proceedings of the American Control Conference-2000, pp. 2962-2966.*

4. Griffin J. E. and Odeja S. R., Textbook on Endocrine Physiology, *Oxford University Press, 1996.*

5. Hunt K. J., Neural Networks for Control Systems – A Survey, *Automatica, Vol. 28, No. 6, 1992, pp. 1083-1112.*

6. Oetzel G. R. and Goff P., Milk Fever (Parturient Paresis) in Cows, Ewes and Doe Goats, *Current Veterinary Therapy: Food Animal Practice,* Howard J. L. (Ed.), *W.B. Saunders Company, 1998, pp. 2962-2966.*

7. Ramberg C. F. (Jr.), Johnson E. K., Fargo R. D. and Kronfeld D. S., Calcium Homeostatis in Cows, with Special Reference to Parturient Hypocalcemia, *American Journal of Physiology, Vol. 246, 1984, pp. R698-R704.*

8. Werbos P. J., Neurocontrol and Supervised Learning: An Overview and Evaluation, in White D. and Sofge D. (Eds.), *Handbook of Intelligent Control, Van Nostrand Reinhold, 1992.*