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Feedback linearization based computer controlled medication design for automatic treatment of parturient paresis of cows

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ABSTRACT

Based on an existing model for calcium homeostatis (dynamics) and taking the help of feedback linearization philosophy of nonlinear control theory, two control design (medication) strategies are presented for automatic treatment of parturient paresis (milk fever) disease of cows. An important advantage of the new approach is that it results in a simple and straightforward method and eliminates the necessity of a significantly more complex neural network based nonlinear optimal control technique, as proposed by the author earlier. As an added advantage, unlike the neural network technique, the new approach leads to 'closed form solution' for the nonlinear controller. Moreover, global asymptotic stability of the closed loop system is always guaranteed. Besides theoretical justifications, the resulting controllers (medication strategies) are validated from numerical simulation studies of the nonlinear system as well. Moreover, from a numerical study about the robustness of the algorithms with respect to parametric uncertainty, it was observed that the optimal control formulation is a better option over the dynamic inversion formulation.

1. Introduction and background

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 as well [1]. A mathematical model for the calcium homeostatis (dynamics) of cows was first developed by Ramberg et al. [2]. The one-dimensional model was modified to a two-dimensional model by El-Samad et al. [3]. Besides describing the Ca homeostatis problem in healthy cows, this model also explains 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.

From a system theoretic point of view, the parturient paresis problem of dairy cows can be thought of as follows (see Fig. 1). 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. [4], a common

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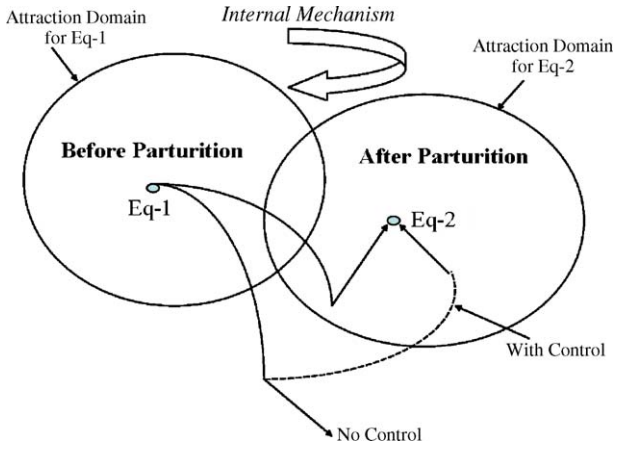

Fig. 1 – System theoretic view of parturient paresis.

treatment strategy for such patients is the intravenous infusion of Ca salt.

The model in [3] has been refined further by the author of this paper along with his co-author (Padhi and Balakrishnan) in a recent paper [5]. In this reference, the authors have also come up with an on-line medication (feedback control) strategy for automatic treatment of the disease. It was based on automatic infusion of the Ca salt into the blood pool of the animal. The controller was designed based on a neural network approach, which finds out the optimal controller (in a state feedback form) taking the help of approximate dynamic programming philosophy, after extensive offline training of the neural network. An interested reader is referred to [5] for more details.

However, the approach presented in [5] suffers from the following limitations: (i) it is a complex technique and usually demands an expert for synthesizing the controller through neural networks (one reason for that is the need to come up with a 'good guess' for the domain for the closed loop states and their histories, prior to control design), (ii) it does not lead to a closed form expression for the controller, (iii) the controller synthesized is valid only in the domain for which the networks are trained and hence the result is not global, and (iv) even though numerical results are promising, coming up with a mathematical proof for stability (even local stability) is difficult (such a proof is not given in [5]).

In this paper two alternative nonlinear control synthesis approaches are presented for the same purpose; i.e. for administering the drug for automatic treatment of the parturient paresis (milk fever) disease of cows. Both of them rely on the key technique of feedback linearization [6]. For simple interpretation, the controller can be thought of having two additive components. One component cancels out the nonlinear dynamics and leads to a residual linear system. The other component is then designed based on linear control synthesis techniques to drive the states (of the residual linear system) to origin, there by achieving the overall goal. The difference between the two controllers synthesized in this paper arises because of the way the linear controllers are synthesized. One is based on the classical control idea (namely PID control), whereas the other one takes the help of linear optimal control theory (linear quadratic regulator formulation). Both of the resulting nonlinear controllers do not suffer from any of the limitations of the neural network approach as pointed out earlier [5]. The applicability of the synthesized controllers (drug infusion strategies) is validated from numerical simulation studies of the nonlinear system as well.

After obtaining satisfactory results for nominal case, a numerical study about the robustness of the algorithms with respect to parametric uncertainty was carried out. A 5% uncertainty was assumed in parameter values and 2% uncertainty was assumed in control efficiency factor. From a large number of repetitive runs (5000 runs, to be specific), it was observed that the optimal control formulation is a much better option over the dynamic inversion formulation in the sense that the dynamic inversion controller could recover the patients in 53.14% cases, whereas the optimal control formulation could recover the patients in 99.8% cases.

Rest of the paper is organized as follows. In Section 2, a description of the problem is outlined, with appropriate mathematical equations. In Section 3, taking the help of the concept of feedback linearization, two control design approaches are presented. In Section 4, a clear medication strategy is presented, exploiting the mathematics presented in Sections 2 and 3. A Status report (which essentially contains the numerical results obtained) is presented in Section 5, with appropriate detail analysis of the results. The lessons learned are summarized in Section 6 and the future plans are outlined in Section 7.

2. System description

A mathematical model of the Ca homeostatis (dynamics) of cows was first developed by Rabmerg et al. [2]. The model has recently been modified to a two-dimensional model by El-Samad et al. [3], which was further refined by Padhi and Balakrishnan [5]. In this section, a summary of this refined model is outlined.

The Ca homeostatis of cows is governed by the following coupled differential equations:

$$\dot{x}_1 = \frac{1}{\mathrm{Vol}}\begin{bmatrix} A_1 \tanh\left\{-K_p x_1/A_1\right\} + f(z_1^0 + x_1) \\ \times A_2 \tanh\left\{(z_2^0 + x_2)/A_2\right\} - V_{cl} \end{bmatrix} + \eta u,$$
$$\dot{x}_2 = -K_l x_1 \tag{1}$$

where x_1 and x_2 represent deviations of z_1 and z_2 from z_1^0 and z_2^0, respectively; i.e. $[\,x_1 \quad x_2\,]^T \triangleq [\,(z_1 - z_1^0) \quad (z_2 - z_2^0)\,]^T$. z_1^0 and z_2^0 represent natural equilibrium values for z_1 and z_2 respectively and are given by

$$\begin{bmatrix} z_1^0 \\ z_2^0 \end{bmatrix} = \begin{bmatrix} r \\ A_2 \tanh^{-1}(V_{cl}/A_2) \end{bmatrix} \tag{2}$$

Here z_1 is the Ca concentration (g/L) in the blood plasma, z_2 the rate (g/day) at which Ca is supplied to blood plasma from intestine, $\dot{z}_1$, $\dot{z}_2$ are the rates of change of z_1 and z_2 respectively, with respect to time t, Vol the total plasma volume (L), V_{cl} the total Ca clearance from the plasma (g/L), r the set point for Ca

concentration regulation (g/L), K_p the constant for the internal proportional block (L/day), and K_I is the constant for the internal integral block (L/day^2). A_1 and A_2 represent saturation values for $K_p(r - z_1)$ and z_2, respectively. $f(z_1^0 + x_1) = f(z_1)$ is a multiplicative reduction factor, which reflects the effect of plasma Ca concentration on rate of Ca supply from intestine and is given by

$$f(z_1) = \begin{cases} \frac{1}{12}(\alpha_1 + \alpha_2 z_1)(\alpha_3 + \alpha_4 z_1), & z_1 < r \\ 1, & z_1 \geq r \end{cases} \quad (3)$$

where $\alpha_1 = 5.29$, $\alpha_2 = 92$, $\alpha_3 = 0.23$, $\alpha_4 = 9$ are constants, fixed after numerous experimental studies [3]. Note that A_1, A_2, K_p, K_I act as system parameters which are typically patient dependent (see Section 5.1 for numerical values). η is the efficiency of external control u, which is the rate of external Ca infused per unit volume of the blood plasma. Note that the actual rate of Ca infusion (g/day) by time $t > t_0$ is given by $u_a = \text{Vol} \cdot u$. For more details about this model, an interested reader can refer to [3,5].

3. Design considerations: feedback linearization based nonlinear control synthesis

As in [5], the aim for the control design in this study is to regulate the system about its equilibrium point; i.e. $[x_1 \quad x_2]^T \to 0$ as $t \to \infty$. As mentioned earlier, the key technique used here is feedback linearization [6], followed by linear control design techniques. Note that meeting the goal as $t \to \infty$ is mentioned only for mathematical compatibility. In practice, the goal will be met within a meaningful finite time by appropriate selection of design parameters.

The first step of feedback linearization process is to define an output. Here at the first sight of Eq. (1), one is tempted to take x_1 as the output since one of the goals is $x_1 \to 0$ and the control variable u appears in the $\dot{x}_1$ equation. However, upon a close look it is evident that in such a formulation $x_1 \to 0$ may happen before $x_2 \to 0$ and in that case, it is clear from Eq. (1) that $\dot{x}_2 \to 0$ (instead of $x_2 \to 0$). In such a situation, x_2 will approach a steady-state value other than zero, and hence, the goal for the problem will not be met. On the other hand if we assure $[\dot{x}_2 \quad x_2]^T \to 0$, from the $\dot{x}_2$ equation it is clear that $[x_1 \quad x_2]^T \to 0$. Hence, we can define the output as x_2 and aim to synthesize a controller that will assure $[\dot{x}_2 \quad x_2]^T \to 0$ as $t \to \infty$. For better clarity, however, we carry out rest of the discussions in this section in an alternative manner than what is found in the standard feedback linearization theory [6].

It can be observed from Eq. (1) that $\dot{x}_2$ equation is already in a linear form. However the $\dot{x}_1$ equation is in the nonlinear form and can be written as follows:

$$\dot{x}_1 = f_1(X) + c + \eta u \quad (4)$$

where $X \triangleq [x_1 \quad x_2]^T$, $c \triangleq -(V_{cl}/\text{Vol})$ and $f_1(X)$ is appropriately defined. Note that because of the constant c, standard linearization technique [7] will not be a good approximation of the system dynamics as the effect of c will be lost while taking the derivatives. Probably this is the reason why the linearized system does not lead to a good control design for this problem [5].

Next, we split the controller into two parts; i.e.

$$u(t) = u_0(t) + \tilde{u}(t) \quad (5)$$

Moreover, we add and subtract $A_{1_0}X$ in Eq. (4) and write it as

$$\dot{x}_1 = f_1(X) - A_{1_0}X + c + A_{1_0}X + \eta(u_0 + \tilde{u}) \quad (6)$$

where $A_{1_0} = [a_{11} \quad a_{12}] \triangleq [\partial f_1/\partial X]_{X=0}$. Note that $A_{1_0}X$ acts like a linear term for the x_1 dynamics. At this point, we design $u_0(t)$ such that it cancels out the nonlinear dynamics. This leads to

$$u_0(t) = -\frac{1}{\eta}[f_1(X) - A_{1_0}X + c] \quad (7)$$

Substituting Eq. (7) in Eq. (6) and observing the $\dot{x}_2$ equation from Eq. (1), we can now write the following linear dynamics:

$$\begin{aligned} \dot{x}_1 &= A_{1_0}X + \eta\tilde{u} \\ \dot{x}_2 &= -K_I x_1 \end{aligned} \quad (8a)$$

Alternatively, we can write Eq. (8a) as

$$\dot{X} = AX + B\tilde{u}, \quad \text{where } A \triangleq \begin{bmatrix} A_{1_0}(1) & A_{1_0}(2) \\ -K_I & 0 \end{bmatrix}, \; B \triangleq \begin{bmatrix} \eta \\ 0 \end{bmatrix} \quad (8b)$$

At this point it is quite clear from Eqs. (8a) and (8b) that one can design $\tilde{u}(t)$ by using any of the linear control design techniques. Here two such techniques are outlined, which have been used in this study. Recall that the goal of the control was to make sure that $[x_1 \quad x_2]^T \to 0$ or, alternatively, $[\dot{x}_2 \quad x_2]^T \to 0$ as $t \to \infty$. Note that even though the problem formulation facilitates using linear control design techniques to design $\tilde{u}$, the resulting controller $u = u_0 + \tilde{u}$ is a nonlinear controller and is valid globally. This is because, unlike linearization, no part of the original nonlinear system dynamics is thrown away by the algebraic manipulations in Eqs. (5)–(8).

In the first method, we aim to achieve the objective $[\dot{x}_2 \quad x_2]^T \to 0$ as $t \to \infty$. Taking the help of standard second order linear system theory, namely PID control synthesis approach [8], we aim to design $\tilde{u}(t)$ such that the following second order error equation will be satisfied:

$$\dot{x}_2 + 2\varsigma\omega_n\dot{x}_2 + \omega_n^2 x_2 = 0 \quad (9)$$

where $0 < \varsigma \leq 1$ is the damping ratio and $\omega_n > 0$ is the natural frequency. Taking the help of Eq. (8a) and carrying out the necessary algebra with respect to Eq. (9), we arrive at

$$\tilde{u}(t) = -(1/\eta)\left[A_{1_0}X + 2\varsigma\omega_n x_1 - \frac{\omega_n^2 x_2}{K_I}\right] \quad (10)$$

Finally, combining the results in Eqs. (5), (7) and (10), we arrive at

$$u(t) = u_0(t) + \tilde{u}(t) = -(1/\eta)\left[f_1(X) + c + 2\varsigma\omega_n x_1 - \frac{\omega_n^2 x_2}{K_I}\right] \quad (11)$$

Satisfying Eq. (9) essentially guarantees $[\dot{x}_2 \quad x_2]^T \to 0$ as $t \to \infty$ [8]. Moreover, this is true globally. Note that even though the underlying philosophy followed is the feedback linearization technique, the controller (medication scheme) essentially guarantees $[x_1 \quad x_2]^T \to 0$ as $t \to \infty$. Hence, the concern of unstable "internal dynamics" [6] does not arise in this case. From a system theoretic interpretation, this happens since the 'relative degree' of the problem is same as the state dimension. In other words, the approach presented not only yields a 'closed form solution' of the controller in state feedback form, but at the same time it assures 'global asymptotic stability' of the system as well [6]. Note that the solution in Eq. (11) closely resemble the technique commonly known as "dynamic inversion" [9]. For this reason, we denote the solution in Eq. (11) as "*dynamic inversion control*" in rest of the paper.

In the second (alternate) method, the aim is to achieve the objective $[x_1 \quad x_2]^T \to 0$ as $t \to \infty$ somewhat more directly. To achieve this objective, we aim to design $\tilde{u}(t)$ by minimizing the following quadratic cost function:

$$J = \frac{1}{2}\int_0^{t_f \to \infty} (X^T Q X + r\tilde{u}^2)\, dt \tag{12}$$

subjected to the constraint of the linear system dynamics in Eq. (8b). In Eq. (12), we restrict ourselves to choose $Q > 0$ (a positive definite matrix) and $r > 0$.

This formulation essentially leads to an optimal control formulation known as "linear quadratic regulator"; the solution for which is well established [7,11]. Note that because $t_f \to \infty$, it leads to solving the algebraic Riccati equation for the constant Riccati matrix S. Finally the control solution is given by

$$\tilde{u} = -KX \tag{13}$$

where the gain matrix $K = r^{-1}B^T S$ (see [7,11] for more details on this technique). Note that the linear quadratic regulator (LQR) theory demands that $Q \geq 0$ (a positive semi-definite matrix) and $r > 0$ for a regular solution to exist, in addition to the requirement that the pair $\{A, B\}$ be controllable [7,11].

Combining the results in Eqs. (5), (7) and (13), we arrive at the control solution as

$$u(t) = u_0(t) + \tilde{u}(t) = -\left(\frac{1}{\eta}\right)[f_1(X) - A_{1_0}X + c] - KX \tag{14}$$

This optimal control formulation and the associated solution also guarantees asymptotic stability of the system, i.e. $X = [x_1 \quad x_2]^T \to 0$ as $t \to \infty$. This can be proved by following a Lyapunov approach (see page 523 of [7]). Moreover, this result is globally valid as well. Hence, this approach also leads to a medication strategy which yields a 'closed form solution' and, at the same time, assures 'global asymptotic stability' as well. For convenience, we denote the solution in Eq. (14) as "*optimal control*" for rest of the paper.

Note that the optimal control formulation outlined here is different from the optimal control approach followed in [5]. The differences appear because here (i) the formulation is with respect to a linear dynamics and (ii) in the cost function only a part of the controller $\tilde{u}$ appears. Because of these, there is no one-to-one analogy of the two formulations.

4. Medication strategy

As pointed out by Oetzel et al. [4], the milk fever can be categorized as stages I, II or III, depending on the Ca concentration in blood. Stage I milk fever has blood Ca concentration in the range of 0.055–0.075 g/L, stage II in the range of 0.035–0.065 g/L and stage III can have as low as 0.01 g/L. Stage I milk fever, considered to be a milder disease, is treated either with oral Ca supplement or intravenous Ca salt infusion. Cattle in stage II or III require immediate treatment with intravenous Ca salt. In [4] it is also pointed out that the intravenous Ca should always be administered "slowly", to prevent sudden cardiac arrest due to hypercalcemia. In some sense that justifies the feedback control proposed approach in this paper, to facilitate slow (yet precisely monitored) automatic infusion of the drug. Note that in this work the parameters for a typical animal are assumed to be known and both states are assumed to be measurable.

Before the details of the proposed medication strategy is explained, the following points are worth noting: if the Ca concentration in the blood pool is 0.05 g/L or higher, the milk-fever problem falls under stage I and is not considered serious. Since the value at the new equilibrium point is 0.08 g/L, this essentially translates to (deviation from equilibrium) $x_1 \geq -0.03$. When $x_1 < -0.03$, the animal runs into the danger of stages II–III milk fever and hence, our goal should be to assure that the deviation of the Ca concentration level (from the new equilibrium point) never drops below −0.03 g/L after stopping the medication. Moreover since most of the milk fever cases have been observed to occur within a day or two of the parturition [4], medication is important at this early period after calving. Based on the above observations, we propose the following medication strategy:

(i) Monitor the condition of an animal after parturition, showing the sign of milk fever; i.e. keep measuring the Ca concentration in the blood pool. Note that the parameters for a typical animal are supposed to be known and assumed to remain fixed.
(ii) If x_1 value drops below a specified level, say −0.03, bring the sick animal under the medication scheme.
(iii) The medication is carried out for a fixed amount of time, say for 1 h. During that period, the following steps are carried out:
   - At any time step t_k the control magnitude $u_k = u(t_k)$ is computed on-line, using one of the methods discussed in Section 3.
   - If the computed control $u_k < 0$, we forcefully make $u_k = 0$, since a negative infusion rate is impossible to implement. However, $u_k < 0$ essentially indicates that the blood pool already contains more Ca than necessary and hence there is no requirement of additional intravenous infusion. For this reason, forcefully making $u_k = 0$ will not lead to any catastrophic consequence.
   - The Ca infusion process is continued at a rate u_k until the next time step $k + 1$.

(iv) At the completion of Step (iii), the condition of the patient animal is projected for some specified future time, say for a week (which is normally required for an animal to restore the Ca regulation internally [3]). This is done using the homogeneous part of the system dynamics. Note that even we propagated the system for a week in our simulation studies, we plotted the results in Section 5 only for 2 days, to maintain clarity of the pictures.

(v) If the projected states show $[\,x_1 \quad x_2\,]^T$ develop towards the origin (i.e. the patient recovers without further medication) and x_1 trajectory never enters the region $x_1 < -0.03$, STOP medication. Otherwise, go to Step (iii) and continue medication for another fixed amount of time (in this case, an hour).

Note that as in [5], this paper too does not deal with any new drug development. Rather, it attempts to make use of the advanced control theory concepts to use the available drug much more efficiently.

5. Status report: numerical results

5.1. *Selection of control design parameters*

For numerical experimentation, first the values for parameters r, V_{cl_0}, V_{cl}, Vol were chosen as in [3,5], i.e. $r = 0.08$ g/L, $V_{cl_0} = 20$ g/day (before parturition), $V_{cl} = 70$ g/day (after parturition), Vol = 30 L. Guided by the range of values in [3], we selected $K_p = 2050$ L/day, $K_I = 2150$ L/day^2, $A_1 = 60$ g/day, $A_2 = 90$ g/day. We carried out our numerical studies assuming a drug having 20% efficiency, i.e. $\eta = 0.2$. Note that these values serve as 'nominal values', which are fixed from a number of experimental studies [3]. First we used these values in our control design and simulation studies. Later we carried out a robustness study of our control design approach with respect to the errors in these values for realistic patients (i.e. with respect to parametric uncertainty).

For designing the controllers (medication strategies), after a few trial-and-error studies, we finally selected the following parameters. In the dynamic inversion method, we selected $\varsigma = 0.6$ and $\omega_n = 0.8$. In the optimal control method, we selected $Q = \mathrm{diag}(1.1, 1.9 \times 10^{-3})$ and $r = 0.099$. For the discritization purpose (both for state propagation and control update), we fixed $\Delta t = 30$ s. The state equation was integrated using the fourth-order Runge–Kutta method (with constant step size).

5.2. *Analysis of numerical results*

To begin our numerical studies, we fixed the initial condition for x_1 as $x_1(0) = 0$ (which is the case at parturition). Next, we computed a minimum value for x_2 as $x_{2\,\min} = A_2[\tanh^{-1}(V_{cl_0}/A_2) - \tanh^{-1}(V_{cl}/A_2)]$. However, we selected an actual value for the initial condition for x_2 as $x_2(0) = \mathrm{random}(0.8, 1.1)x_{2\,\min}$. In this way, we could account for a range of possible initial conditions for our simulations.

Starting with an initial condition as outlined above, the homogeneous system was propagated, until x_1 dropped below $x_{1\mathrm{cut}}$, a known value (we took it as -0.03). Then the corresponding value of x_2 at that time was collected. The values of the state at that time were taken as the initial condition for the initiation of control (drug infusion). At that point, the time was also reinitialized to zero. Moreover, as pointed out in Section 4, all the simulation plots are given only for 2 days (48 h). This is to have a magnifying effect near parturition, to clearly see the effect of control.

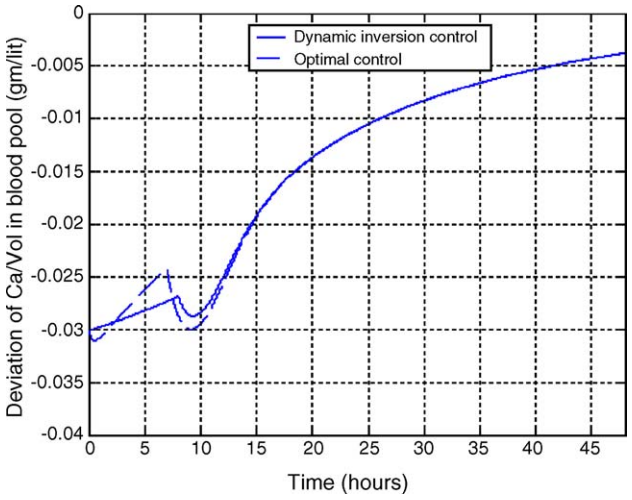

Fig. 2 – Deviation of Ca/Vol in blood pool.

Figs. 2–5 show the results for a typical case. First, note that the discontinuity in the plots indicate termination of the control application, since at that time it was sensed that there is no need of further control application to recover the patient animal (see Section 4 for details).

From Fig. 2, it is clear that the medication strategy coming out of both the dynamic inversion as well as the optimal control formulations work fine in recovering the patient. However, the dynamic inversion controller seems to work slightly better because the x_1 trajectory always remain above the danger level of -0.03 and after the termination of the controller, it does not drop much. However, quantitatively this is a very minor advantage. More important, it should be noted that the

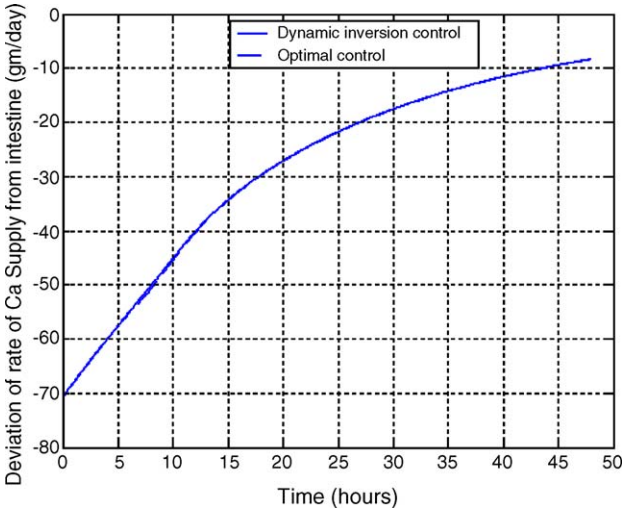

Fig. 3 – Deviation of Ca absorption rate in intestine.

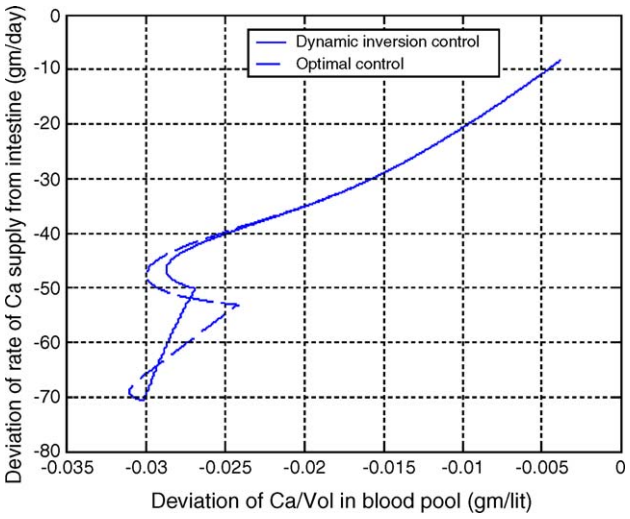

Fig. 4 – Phase plot for the system trajectory.

x_1 trajectory never goes to the positive side (for both the controllers), which leads to a similar major advantage as in [5], in the sense that the medication strategy avoids the danger of hypercalcemia and the associated danger of cardiac arrest.

Fig. 3 depicts the trajectory of the rate of Ca resorption from intestine. The two plots (one using dynamic inversion and the other using optimal control) are quite close to each other. It indicates that both the medication schemes lead to quite similar behavior in the rate of Ca absorption in intestine. The phase plot for this case is as in Fig. 4. It shows how the deviation trajectories develop towards the origin (even after stopping the medication) and that justifies the medication scheme proposed in Section 4.

Fig. 5 shows the drug requirement (rate of Ca needed to be infused) histories. Here, one can clearly notice that the drug requirements are quite comparable in both the dynamic inversion and optimal control approaches. However, their histories are slightly different and the advantage here is in favour of the optimal control approach. This is because of two reasons. First, it starts with a lower value and then builds up. Second,

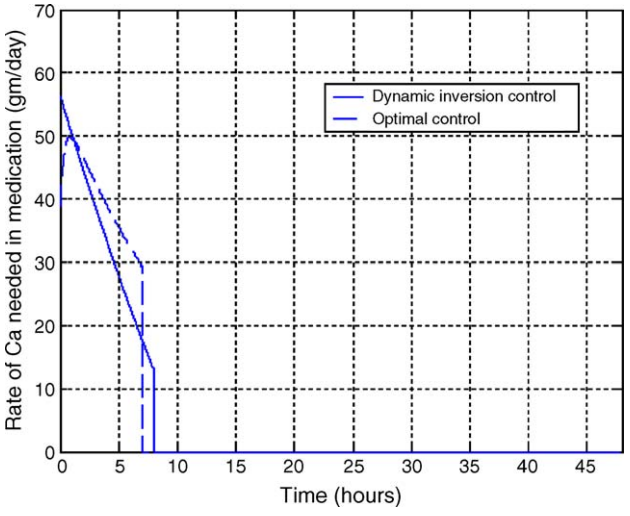

Fig. 5 – Rate of Ca needed in medication.

duration of the drug infusion turns out to be 1 h shorter. Both of these are good advantages from control implementation (drug application) consideration. These advantages were observed to be true in our numerous simulation studies, starting from randomly selected initial conditions. Hence, even though both of the control synthesis techniques were found to be working well, probably the author would recommend using the optimal control approach. However, a better justification for recommending the usage of optimal control approach comes from a robustness study, which is discussed next.

A numerical study about the robustness of the two approaches with respect to the issue of parameter variation in the model was carried out. In this exercise, realistic patients were assumed to have 5% uncertainty in the parameters V_{cl}, V_{cl_0}, Vol, K_p, K_I, A_1, A_2 over their nominal values. It was also assumed that the control efficiency factor η has an uncertain value of 2% over its nominal value of 20%. With these assumptions, these parameters were randomly selected and the program was run 5000 times. Note that only nominal parameter values were used in the controller design, whereas randomly selected parameter values were used for the system simulation. In this study, the following two assumptions were made to decide whether the controller is a success or a failure:

(i) The control application time should not cross 24 h. This was based on the observation that for nominal cases (without parametric uncertainly), it typically takes about 8–10 h to recover the patients. Moreover, it is also probably not practically feasible to administer (infuse) the drug on a continuous basis for a very long duration of time.
(ii) The condition $x_1(t) \geq -0.04$ should be valid for all time. Otherwise, the patient may suffer unrecoverable damage during the transition, even though computer simulation would show stabilizing nature after the transient behavior. Note that if the $x_1(t)$ values is too low and approaches -0.08 (indicating $z_1(t) \to 0$), the patient may even die!

From this robustness study it was found that the optimal controller out performs the dynamic inversion controller. It was observed that out of the 5000 random cases, the dynamic inversion controller was successful in recovering the patients in 2657 cases, i.e. the percentage of success was 53.14%. However, the optimal controller performed much better in the sense that it was successful in recovering the patients in 4990 cases, i.e. the percentage of success was 99.80%. The result of this study is compatible with the established facts the dynamic inversion formulation is sensitive to modeling inaccuracies [9,10], whereas the LQR formulation is fairly robust to this issue. In fact the LQR formulation has infinite gain margin and 60° phase margin [7,11]. This robustness study (with respect to parametric uncertainty in the model) clearly indicates that the optimal control formulation is a better approach and hence should be preferred over the dynamic inversion approach.

However, it should be noted that even though the controllers are capable of recovering the patients with parametric uncertainty, the response of the system with different parameter values will not be the same as the response of the system with nominal parameter values. To have a pictorial idea of the actual response, we have included the response of a particular

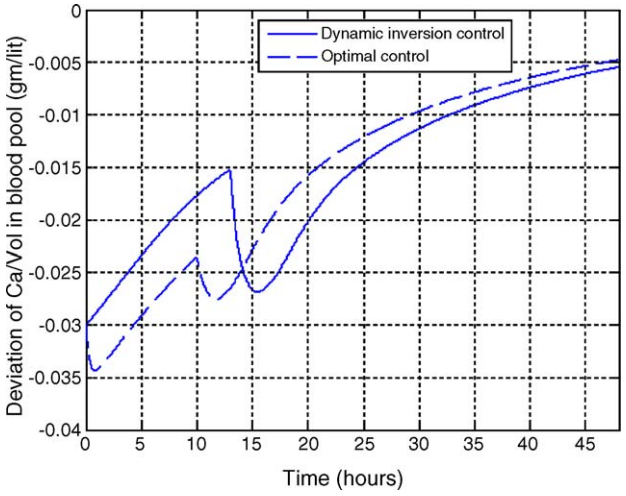

Fig. 6 – Deviation of Ca/Vol in blood pool with parameter variation.

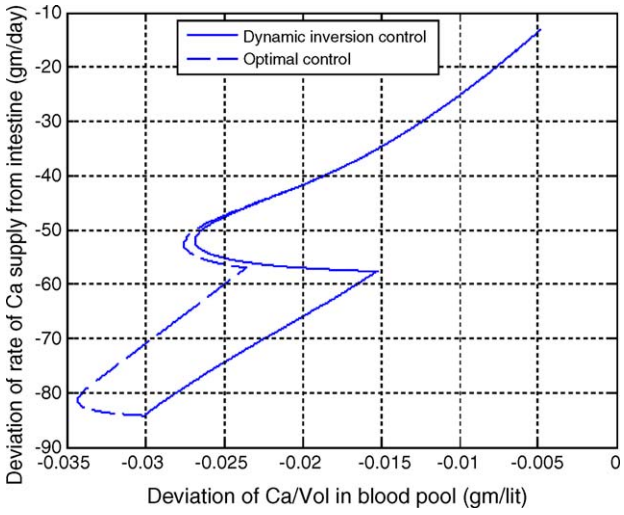

Fig. 8 – Phase plot for the system trajectory with parameter variation.

case in Figs. 6–9, where both dynamic inversion as well as the optimal controller was successful in recovering the patient. In this case, the parameter values (randomly selected) turned out to be $V_{cl} = 70.0782$ g/day, $V_{cl_0} = 20.2590$ g/day, Vol = 29.1603 L, $K_p = 2152.2$ L/day, $K_I = 2238.4$ L/day^2, $A_1 = 86.3937$ g/day, $A_2 = 86.3937$ g/day and the control efficiency factor turned out to be $\eta = 19.79\%$. The randomly selected initial value of x_2 for propagating the homogeneous system (to check whether medication is required before starting it) happened to be -85.4865 g/day. One can clearly see that the response natures in this case in Figs. 6–9 are clearly different from the corresponding ones in Figs. 2–5.

In this case one can notice that the dynamic inversion controller makes sure that x_1 value always remain higher than -0.03 g/L, whereas in the optimal controller case initially it dips a bit before recovering back. However, since the dip did not cross -0.04 g/day (beyond which it is unacceptable) and also since the dip is only for a short time, we can conclude

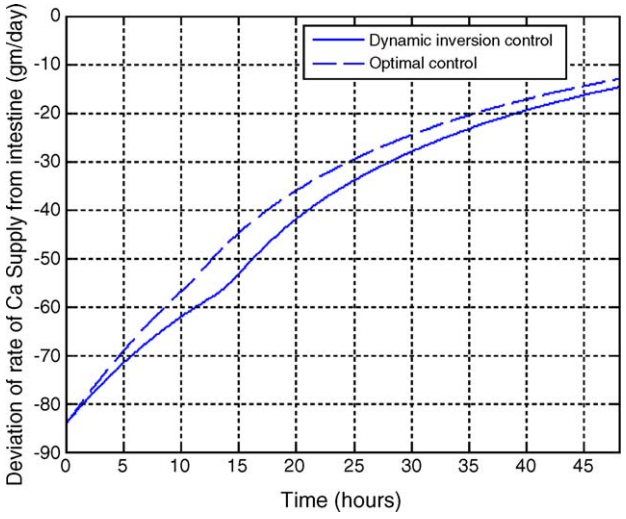

Fig. 7 – Deviation of Ca absorption rate in intestine with parameter variation.

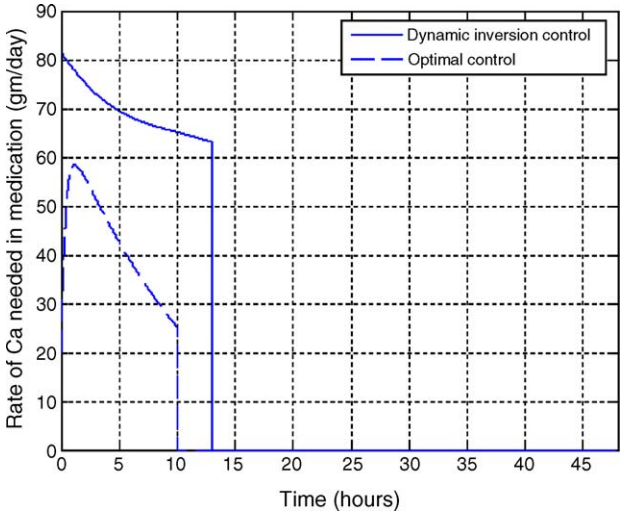

Fig. 9 – Rate of Ca needed in medication with parameter variation.

that the patient will most likely recover in reality, and hence, probably such a situation is acceptable. The advantages of the optimal controller, on the other hand, include a smaller magnitude of the control and gradual initial build up (rather than a jump start). The control application time is also smaller (see Fig. 9).

6. Lessons learned: summary

Taking the help of feedback linearization philosophy, two nonlinear controllers are synthesized for automatic treatment of the parturient paresis (milk fever) disease of cows. An important advantage of the new technique is that it results in a simple and straightforward approach and the resulting nonlinear controller is free from the drawbacks of a significantly more complex neural network based nonlinear optimal control technique, as proposed by the author earlier [5]. The new

approach leads to closed form solutions for the controller, and more important, global asymptotic stability of the closed loop system is always guaranteed.

The resulting nonlinear controllers are validated from simulation studies of the nonlinear system. The proposed computerized automatic medication scheme (with either of the feedback controllers) has been shown to work successfully to recover a patient animal. As in the previous work by the author [5], it was also found that both of the proposed new controllers do not lead to hypercalcemic problems, thereby avoiding the associated disastrous consequence of cardiac arrest.

From the simulation studies it was found that out of the two approaches presented in this paper, the advantage was found to be in favour of the optimal control approach. This is because (i) the drug infusion process starts with a lower value and then builds up (ii) duration of the drug infusion turns out to be shorter in general and, most important, (iii) it is substantially more robust to the issue of parameter uncertainty.

7. Future plans

In future, two important improvements of the technique presented are planned, which will make the medication process more realistic. First, one may notice that even though we have proposed a state feedback control design, it may not be possible to measure both of the state variables. Even though the calcium concentration can be measured by doing blood sample analysis, measuring the other state (i.e. the rate at which Ca is supplied to blood plasma from intestine) is not an easy task. To the best of the knowledge of the author, such an instrument is not available. Hence, there is a necessity to incorporate an observer [7]. Subsequently, an appropriate filter (e.g. Kalman filter [7]) can be incorporated for the same purpose, which can filter out the measurement noise, while estimating the states.

Second, even though we have carried out a study with the parametric uncertainty issue and the results were found to be in favor of the optimal control approach, for a better design a parameter identification algorithm [12] can be incorporated to make the medication tailored to the individual patients. Another alternative idea to address the same problem is to make the control synthesis process robust to parameter uncertainties (without identifying the parameters) by incorporating a recently developed model following neuro-adaptive control algorithm [13].

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