Depth of Anaesthesia Control Investigation Using Robust Deadbeat Control Technique

Shahab Abdulla
Electrical, Electronic and Computer Engineering
University of Southern Queensland
Toowoomba 4350, QLD, Australia
Shahab.Abdulla@usq.edu.au

Peng Wen
Electrical, Electronic and Computer Engineering
University of Southern Queensland
Toowoomba 4350, QLD, Australia
peng.wen@usq.edu.au

***Abstract* - This paper investigates the depth of anaesthesia (DoA) control system using robust deadbeat technique. We propose to apply deadbeat control technique and develop a robust controller. The proposed robust control system with a deadbeat controller is evaluated in simulation. The performance is compared with that of a traditional control system with a PID controller and a control system with an internal model (IMC) controller. The results show that the proposed scheme has about 15% less overshoot, shorter settling time (about 1.5 minutes shorter) and more robust to disturbances caused by parameter changes. In addition, the proposed method is easy to design and impalement.**

Index Terms – Deadbeat control. Depth of anaesthesia.

I. INTRODUCTION

More recently, considerable efforts have been made to identify and control systems with uncertainty and nonlinearity in medical related control system. Dwayne (1997) developed a closed-loop PID controller to control the depth of anesthesia [1]. Sakai et al. (2000) employed a closed-loop PID control system for propofol administration using BIS (Bispectral Index) as the controlled variable. Both of them concluded that their systems provided intra-operative hemodynamic stability and a prompt recovery from the sedative-hypnotic effects of propofol [2]. Absalom et al. (2002) developed a similar closed-loop PID controller using BIS as the controlled variable, and a propofol targeting central plasma concentration-controlled infusion system as the control actuator [3]. The authors concluded that further studies were required to determine if control performance could be improved by changing the proportional gains of the PID controller or by using an effect-site-targeted propofol controlled infusion system. Later, they modified their control algorithm to a target-controlled infusion (TCI) system which regulated effect-site concentration, and proved it to be more efficient. However, the PID controller still faced some stability problems [4].

This study applies the deadbeat robust control technique to the depth of anaesthesia. First, a DoA model is build up based on our literature review. This model is a single-input-single-output (SISO) system with nonlinear component. Then, a PID-based robust deadbeat control scheme is applied to the SISO systems, and a deadbeat controller is designed. The robust deadbeat controller can tolerate system parameter's uncertainty for up to $\pm$ 50% [5]. The additions of the extra gains allow and permit the designer more flexibility of making any plant work with this method. This feature is used to deal with the uncertainty of the DoA model. The proposed method is implemented and evaluated in simulation. Comparing with other two different PID based control systems, the proposed method has less over and undershoot, shorter settling time and more robust to parameter change caused disturbances.

This paper is structured as follows. The DoA model is introduced in Mathematical Model of Anaesthesia section. The Deadbeat Control technique is explained in Method of Deadbeat Control for DoA section. The implementation and simulation study is providing in the Simulation and Results section. In this section we also analysed and compared the simulated results. Finally, the main findings of this paper are summarised in the Conclusion section.

II. MATHEMATICAL MODEL FOR DEPTH OF ANAESTHESIA CONTROL

First we consider the drug modeling approach and how the administered drug distributes within the body. This step leads to a pharmacokinetic model (PK) which can be used to predict the blood plasma concentration of the drug [6]. The second step is the mathematical expression relate to concentration to the drug effect itself. This expression is referred to as pharmacodynamic model (PD) [7].

A. Pharmacokinetics

Pharmacokinetics is the study of the absorption, distribution, metabolism and elimination of drugs by the body as shown in Fig. 1. The pharmacokinetic model of a drug is a mathematical term relating to the drug blood plasma concentration $C_p(s)$ to the administered dose $u(s)$. The aim of this section is thus to define the transfer function of $PK(s)$:

$$\boldsymbol{PK(s) = \frac{C_p(s)}{u(s)}} \qquad (1)$$

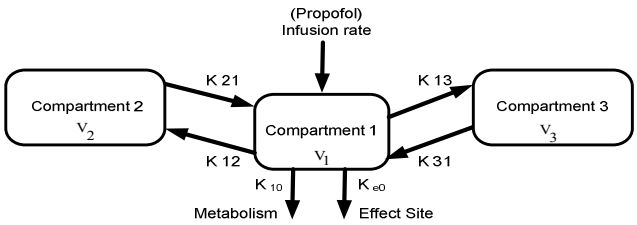

Fig. 1 The pharmacokinetic model

The PK can be expressed as a time course of the concentration of any given drug within the plasma and other tissues of the human body. Throughout the absorption phase following an intravenous bolus administration, the anaesthetic (propofol) mixes quickly within the central blood pool, resulting in a plasma peak concentration [8]. There is a delay elapses between the actual injection of the anaesthetic (propofol) and its mixing within the blood pool. Systemic circulation then distributes the anaesthetic to a variety of tissues within the body [6]. The time course of the concentration for most drugs, within the blood plasma after the intravenous administration and uptake can be fitted to resemble a decaying function, with two distinct modes corresponding to the distribution and elimination phase respectively. This behavior can be expressed mathematically as:

$$\boldsymbol{C_p(t) = Xe^{-At} + Ye^{-Bt}} \qquad \left(\frac{\boldsymbol{\mu g}}{\boldsymbol{ml}}\right) \qquad (\mathbf{2})$$

where $\mathrm{C_p(t)}$ is the drug plasma concentration expressed in microgram per milliliter (propofol), A is the rate constant of the distribution phase, B is the rate constant of the elimination phase.

In many cases, a tri-exponential model will capture the kinetic of the drug much better [6].

$$C_p(t) = Xe^{-At} + Ye^{-Bt} + Ze^{-Ct} \quad \left(\frac{\mu g}{ml}\right) \qquad (3)$$

where Z and C to describe the fast dynamics corresponding to the distribution phase.

A main advantage of exponential models is that they can be simply derived using graphical means. The identification can be carried out directly by using either bolus data or analysing the decaying blood plasma characteristic, or by using infusion data and analysing how the plasma concentration increases over time [6].

In terms of control and system engineering, the exponential model in (3) can be directly expressed as:

$$PK(s) = \frac{C_p(s)}{u(s)} = \frac{X}{s+A} + \frac{Y}{s+B} + \frac{Z}{s+C} \qquad (4)$$

The total amount of the anaesthetic delivered into compartment one ($\mathrm{C_1}$) is eliminated according to the rate constant $\mathrm{k_{10}}$. The anaesthetic is distributed in the other two compartments ($\mathrm{C_2}$, $\mathrm{C_3}$) at a rate of $\mathrm{k_{12}}$ and $\mathrm{k_{13}}$. The concentration of $\mathrm{C_1}$ decreases quickly while the concentrations $\mathrm{C_2}$, $\mathrm{C_3}$ increase. Once the concentrations in the compartment one and any of the peripheral compartments ($\mathrm{C_2}$, $\mathrm{C_3}$) attain and reach equilibrium, the distributive process setback and the anaesthetic stored in the peripheral compartment returns back to the central compartment at the rate of $\mathrm{k_{21}}$ or $\mathrm{k_{31}}$. Because the blood of the compartment one acts as a transporter for the anaesthetic, that is mean there is no direct exchange between the two peripheral compartments. In other words, only the anaesthetic presents in the compartment one can be eliminated [7].

The mathematical expressions in a state space representation can be obtained by writing the mass balance equations in (5):

$$\begin{bmatrix} \dot{\mathrm{C}_1}(\mathrm{t}) \\ \dot{\mathrm{C}_2}(\mathrm{t}) \\ \dot{\mathrm{C}_3}(\mathrm{t}) \end{bmatrix} = \begin{bmatrix} -\mathrm{k_{10}} - \mathrm{k_{12}} - \mathrm{k_{13}} & \mathrm{k_{21}} & \mathrm{k_{31}} \\ \mathrm{k_{12}} & -\mathrm{k_{21}} & 0 \\ \mathrm{k_{13}} & 0 & -\mathrm{k_{31}} \end{bmatrix} \begin{bmatrix} \mathrm{C_1(t)} \\ \mathrm{C_2(t)} \\ \mathrm{C_3(t)} \end{bmatrix} + \begin{bmatrix} \frac{1}{\mathrm{V_1}} \\ 0 \\ 0 \end{bmatrix} \mathrm{u\ (t)}$$

$$\mathrm{C_p(t)} = \begin{bmatrix} 1 & 0 & 0 \end{bmatrix} \begin{bmatrix} \mathrm{C_1(t)} \\ \mathrm{C_2(t)} \\ \mathrm{C_3(t)} \end{bmatrix} \qquad (5)$$

where $\mathrm{V_1}$ is the volume of compartment one. Also, by definition, the plasma blood concentration equals the drug concentration of the compartment one, i.e., $\mathrm{C_p(t)} = \mathrm{C_1(t)}$.

In order to simplify the PK(s) model as a SISO transfer function using both the exponential and compartmental parameters as in (6) [9]:

$$PK(s) = \frac{C_p(s)}{u(s)} = \frac{1}{V_1} \frac{(s+k_{21})(s+k_{31})}{(s+A)(s+B)(s+C)} \qquad (6)$$

B. Pharmacodynamics

Pharmacodynamics (PD) is the study of the effects of drugs and the relationship between drug concentration and effect. The function of the PD model is to mathematically express the observed effect of a drug as a low-pass filter is used to relate the propofol plasma concentration as shown in Fig. 2 [6]:

$$PD(s) = \frac{E(s)}{C_p(s} \qquad (7)$$

where PD(s) is the pharmacodynamic model and E(s) is the drug effect.

The effect-site concentration is related to DoA as (Hill equation) [10].

$$E(t) = E_0 - E_{max} \cdot \frac{{C_e}^{\gamma}(t)}{{C_e}^{\gamma}(t) + EC_{50}^{\gamma}} \qquad (8)$$

The mathematical express of the effect site drug concentration $C_e(s)$ as a function of the plasma concentration $C_p(s)$ as in equation (9):

$$C_e(s) = \frac{k_{e0}}{s + k_{e0}} C_p(s) \tag{9}$$

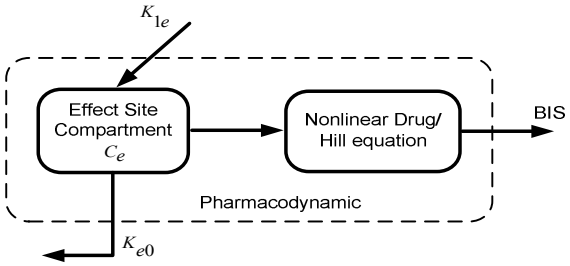

Fig. 2 The pharmacodynamic model

III. DEADBEAT CONTROL FOR DOA

Fig. 3 shows the basic structure of the robust deadbeat control system, and Table I is the deadbeat controller coefficients and response times. This technique is initially works only for lower-order plants [11]. If a higher–order plant systems considered, then there is a need for higher gain, therefore this design with a proper and accurate high gain result in systems that are intensive to plant parameters variation and uncertainties of up to 50% [5]. Changes in patient's PK and PD parameters (k_{10}, k_{12}, k_{13},…….. EC_{50}, γ and k_{e0}) form 10% to 20%, 30%, 40% up to 50% the robust deadbeat controller is still able to tolerate these parameter changing.

The deadbeat controller design and derivation method utilizes the following procedures. Firstly using a PID controller as $G_c(s)$, and then adding a cascade gain K before the PID controller. Add a state variable feedback gain K_a, that will make the system over specified by at least one variable. Determine the number of poles for $G_cG(s)$, where n_p equals the number of poles in $G_cG(s)$.Refer to Fig. 3 the feedback H(s) it depends on the number of poles in $G_cG(s)$,and the following steps are involved with this method:

1) $\boldsymbol{H(s) = 1}$ *for* $\boldsymbol{n_p = 2}$.
2) $\boldsymbol{H(s) = 1 + K_b s}$ *for* $\boldsymbol{n_p = 3}$ *or 4.*
3) $\boldsymbol{H(s) = 1 + K_b s + K_c s^2}$ *for* $\boldsymbol{n_p = 5}$.

And then select gains, using the coefficients from Table 1, to achieve the deadbeat response with the following requirements:

4) *Set* $\boldsymbol{K = 1}$.
5) *Set* $\boldsymbol{\omega_n = \frac{T_s'}{(80\%\ of\ the\ desired\ settling\ time)}}$
6) *The characteristic equation of the closed loop transfer equation will equal to:*

$$\boldsymbol{s^{n_p} + \alpha\omega_n s^{n_p-1} + \beta\omega_n^2 s^{n_p-2} + \cdots + \omega_n^{p_n}}$$

7) *The root of H(s) must be real and negative.*
8) *The smallest root of H(s) will set the desired settling time by the relationship: [4/ (smallest root)] and equal approximately to the desired settling time.*

Then increase K until the response becomes deadbeat and the settling time is approximately equal to the desired value.

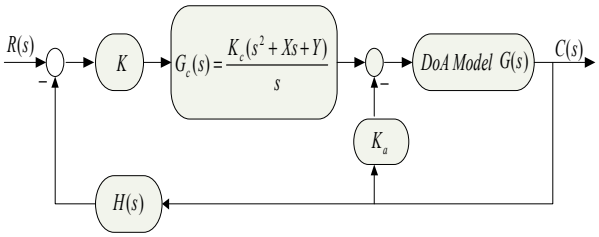

Fig. 3 Robust deadbeat control structure

TABLE I
DEADBEAT COEFFICIENTS AND RESPONSE TIMES

Order (n_p)	α	β	γ	δ	Tr_{90}'	T_s'
2nd	1.82				3.47	4.82
3rd	1.90	2.20			3.48	4.04
4th	2.20	3.50	2.80		4.16	4.81
5th	2.70	4.90	5.40	3.40	4.48	5.43

The design procedure of a PID-based robust deadbeat control, taking fourth-order $F_1(s)$ and fifth-order $F_2(s)$ systems as examples

$$F_1(s) = \frac{\omega_n^4}{s^4 + \alpha\omega_n s^3 + \beta\omega_n^2 s^2 + \gamma\omega_n^3 s + \omega_n^4} \tag{10}$$

and

$$F_2(s) = \frac{\omega_n^5}{s^5 + \alpha\omega_n s^4 + \beta\omega_n^2 s^3 + \gamma\omega_n^3 s^2 + \delta\omega_n^4 s + \omega_n^5} \tag{11}$$

For equations (10) and (11), the coefficients α, β, γ and δ are selected from Table 1. Taking the fourth-order system first as an example and then using the same procedure with fifth-order system with a desired settling time 0.95 s, from Table 1 the normalized settling time can be found as:

$$T_s = \frac{4.81}{\omega_n}$$

Therefore ω_n can be found as:

$$T_s = \frac{4.81}{0.95} = 5.0632$$

The characteristic equation of the closed-loop transfer function of the forth-order systems is:

$$s^4 + \alpha\omega_n s^3 + \beta\omega_n^2 s^2 + \gamma\omega_n^3 s + \omega_n^4$$

From Table I, α, β and γ can be found as:

$$\alpha = 2.20;\ \beta = 3.50;\ \gamma = 2.80$$

The transfer function of the forth-order systems is:

$$F_1(s) = \frac{657.183399}{s^4 + 11.139s^3 + 89.72448s^2 + 363.4314s + 657.183399} \quad (12)$$

To apply the deadbeat technique to DoA model, first comparing the characteristic equation in equation (12), with the characteristic equations different patients.

A. DoA Controller Design

The block diagram of the DoA designed system is depicted in Fig. 4.

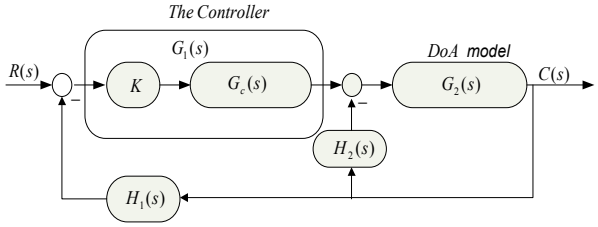

Fig. 4 Robust deadbeat control structure for DoA

$$G_1(s) = KG_c(s) = \frac{K[K_c(s^2 + Xs + Y)]}{s}$$

$$G_2(s) = \frac{0.040382(s + 0.025992)(s + 0.0018266)}{(s + 0.37891)(s + 0.005896)(s + 0.0012622)}$$

$$H_1(s) = (1 + K_b s)$$

$$H_2(s) = K_a$$

The closed-loop control function for DoA model can now be written as:

$$\frac{C(s)}{R(s)} = \frac{G_1(s)G_2(s)}{1 + G_2(s)H_2(s) + G_1(s)G_2(s)H_1(s)}$$

Then, using the technique initially proposed by Dorf et al. in 1994 [5], to determine these parameters. The characteristic equation of the above transfer faction is equal to the characteristic equation of the deadbeat transfer function. By using the characteristic equation of the deadbeat transfer function to obtain the characteristic equation of the closed-loop transfer function of DoA as:

$$s^4 + \alpha\omega_n s^3 + \beta\omega_n^2 s^2 + \gamma\omega_n^3 s + \omega_n^4$$

$$\alpha = 2.20;\ \beta = 3.50;\ \gamma = 2.80$$

$$\omega_n = \frac{T_s'}{80\%\ of\ the\ desired\ settling\ time\ T_s}$$

The desired settling time for DoA is 6 minutes, then ω_n can be found as:

$$\omega_n = \frac{T_s'}{T_s \times 80\%} = \frac{4.81}{6 \times 60 \times 80\%} = 0.0167$$

Therefore the characteristic equation now can be written as:

$$s^4 + 0.03674s^3 + 9.76115 \times 10^{-4}s^2 + 1.304 \times 10^{-5}s + 7.7779 \times 10^{-8}$$

Let K equal to 1, and then by comparing the characteristic equation to find the variables as:

$$K_c = 1 \times 10^{-4}\ ;\ K_b = 1 \times 10^{-7}$$

$$X = 363 \times 10^4\ ;\ Y = 342.78 \times 10^4;\ K_a = -8.212$$

Increase K until the response becomes deadbeat and settling time becomes approximately to the desired value.

IV. SIMULATION AND RESULTS

The proposed control schemes were implemented and evaluated using Simulink and Matlab control toolbox to thoroughly investigate the system performance.
Fig. 5 shows the diagram of implementation of the deadbeat DoA control system.

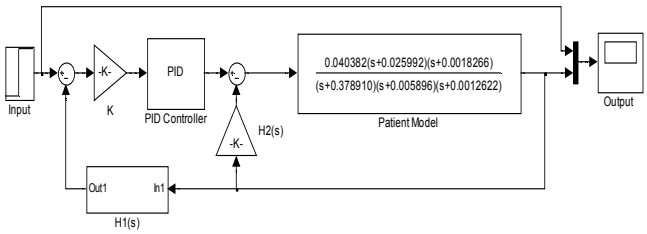

Fig. 5 Implementation of a robust deadbeat control structure for DoA

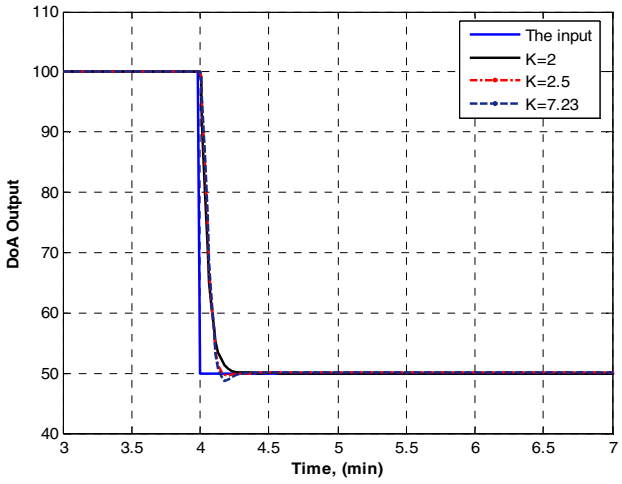

Fig. 6 DoA robust deadbeat control response for different values of K

Fig. 6 shows the responses of DoA system in different situations, in other words the value of K are changing from 1 until the system reach better response, for example K equal 2,

2.5 and 7.23. It is clear that all the responses settle and reach the desired positions with the time frames. While, there are overshoot but the system responses still meet with all the requirements and specifications.

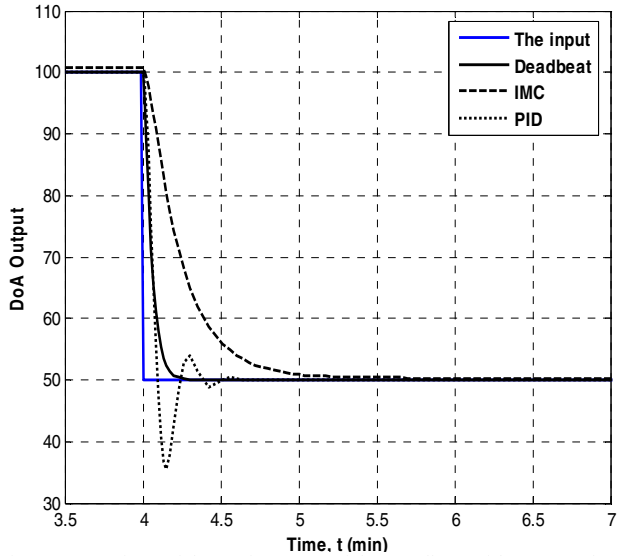

Fig. 7 Comparison of the performance of the Deadbeat with, IMC and PID controllers

Fig. 7 shows the response of a traditional PID control for DoA. The parameters of PID controller for DoA are K_p =1000, K_i= 10 and K_d=32.

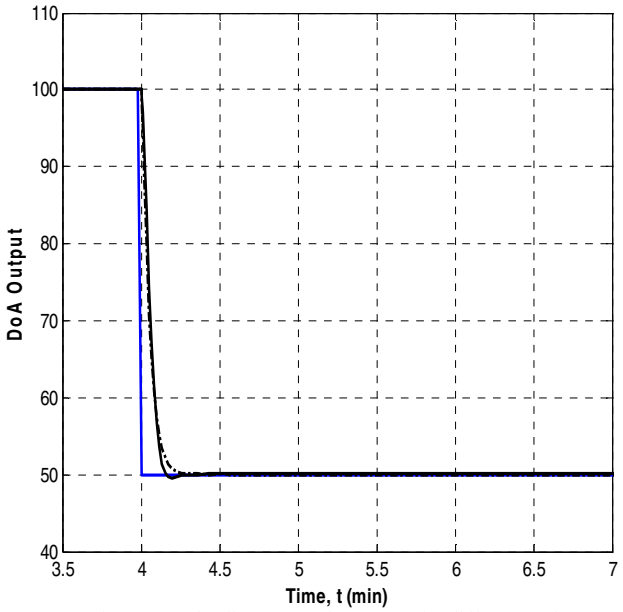

Fig. 8 DoA deadbeat control response for different patients

Fig. 8 shows the response of the deadbeat control for DoA. Comparing Figs. 7 and 8, it is also clear that the robust control performance is much better that the IMC, where the settling time is approximately 8 minutes for IMC and about 4.3 minutes for the robust deadbeat control.

V. CONCLUSIONS

This study investigates a robust deadbeat control technique in DoA control. This technique was originally designed to suppress system parameters uncertainties. We applied this technique to accommodate the inter-patient differences for DoA control

The proposed method is implemented and evaluated in simulation using realistic data. The results are compared with the results obtained using two other methods. The comparisons show that the proposed robust deadbeat control scheme performs better both in overshoot/undershoot and settling time. The system settling time has been reduced to 1.5 minutes and the over and undershoot also has been shorted about 15%.

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