Adaptive Control of Depth of Anesthesia using a Fractional Order Gradient Based Adaptation Mechanism

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ABSTRACT:
In this paper, a model reference adaptive controller (MRAC) with an RST control structure is employed to control the depth of the anesthesia. The polynomial coefficients of the RST controller are adjusted according to a fractional order normalized gradient based adaptation mechanism. The propofol infusion rate and the Bispectral Index (BIS) are considered as the system input and output, respectively. The propofol distribution in the patient model is described with a Pharmacokinetic-Pharmacodynamic (PK-PD) model. The PK-PD model parameters depend on physical specifications of the patient including age, weight, and gender. The proposed MRAC is employed to reach the desired BIS in the presence of disturbance and the measurement noise for different patients. Simulation results have demonstrated the effectiveness of the proposed method.

KEYWORDS: Model Reference Adaptive Controller; Fractional-Order Adaptation Mechanism; Gradient Based Adaptation Mechanism; Depth of Anesthesia.

1. INTRODUCTION

Control of depth of anesthesia to improve the quality and accuracy of the anesthesia process is inevitable [1]. The most popular indicator for measurement of the depth of the anesthesia is the Bispectral index (BIS) [2]. To determine the infusion rate of the drug dose during the anesthesia process, the effect of the propofol infusion on the patient body should be described with a mathematical model. The drug distribution and the drug effect on the human body could be described with Pharmacokinetic (PK) and pharmacodynamic models (PD), respectively [3].

Different control strategies have been proposed to regulate the BIS during anesthesia [4]. In [5], an optimal PID controller has been employed to control the depth of anesthesia in which its parameters are calculated using genetic algorithms [5]. Nonlinear controllers like sliding mode controllers have been utilized in this area [6]. In [7], the sliding mode and backstepping controllers have been compared for hypnosis regulation. Robust controllers like H_∞ controller have been employed to reach the desired BIS during anesthesia [8]. A multi-model mixed H_2 / H_∞ robust control scheme has been proposed for control of depth of hypnosis [9]. In [10], an event-based control strategy has been applied to the closed-loop control of the depth of anesthesia. The model predictive controller has been utilized for the induction and maintenance of intravenous anaesthesia [11]. Robust multi-parametric model predictive control has been employed for hypnosis control during anesthesia [12], [13].

Since the PK-PD model parameters could vary with patient specifications, the adaptive controllers have been employed to control the depth of the anesthesia in the literature. In [14], a Lyapunov-based adaptive controller ensuring positive infusion rate has been provided. Moreover, a neuroadaptive output feedback controller for automated anesthesia with noisy EEG measurements has presented [15]. In [16], an adaptive method to model the patient response to propofol under general anesthesia has been proposed in which the compartmental model parameters are continuously estimated. In [17], the L_1 adaptive controller for anesthesia delivery to patients in surgical settings has been developed.

Employing fractional order operators for modelling and control increases the modelling and design flexibility [18]. In [19], propofol diffusion in anesthesia has been described with a fractional order pharmacokinetic model. In [20], a fractional order robust controller has been proposed to compensate for the patients inherent drug–response variability during the anesthesia. In [21], a Lyapunov based fractional order

model reference adaptive control for anesthesia using a fractional order PK-PD model has been developed.

Employing fractional order derivative in the adaptation mechanism of adaptive controllers improves the performance of the controller. Utilizing the fractional order derivative instead of the ordinary derivative in the adaptation mechanism of the gradient-based MRAC could improve the transient response of the closed loop system [22]. Moreover, the noise rejection capability of the adaptive controllers could be improved with the fractional order operators [23]. The gradient and the Lyapunov based fractional order adaption mechanisms have been employed for velocity control of a Permanent Magnet Synchronous Motor (PMSM) [24].

In this paper, a fractional order MRAC (FOMRAC) with RST control structure and a fractional order normalized gradient adaptation mechanism is proposed for control of depth of anesthesia. Numerical simulations for different patients in the presence of the external disturbance and the measurement noise are presented to show the robustness of the proposed method.

This paper is arranged as follows. Section II gives a brief review on the PK-PD model. The MRAC strategy with the fractional order normalized gradient adjustment rule is introduced in Section III. The application of the proposed method to control the depth of the anesthesia is illustrated in Section IV. The simulation results on different patients are given in Section V. Section VI concludes the paper.

2. THE PK-PD MODEL

The PK-PD model is a two-compartment model describing the propofol infusion rate on the patient body. The propofol infusion rate impact on the intravascular blood is modeled with the Pharmacokinetic (PK) model.

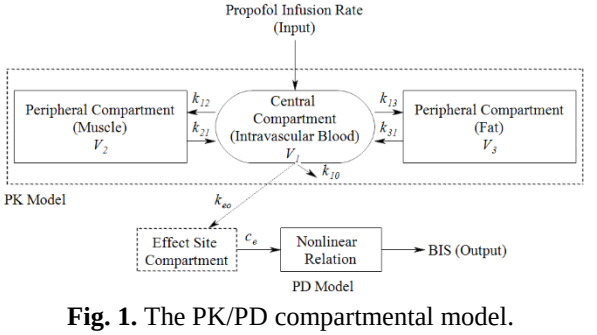

Fig. 1. The PK/PD compartmental model.

The relation between drug concentration in the effect side component and the BIS is described with the Pharmacodynamics (PD) model. Fig. 1 shows the PK/PD model [25]. The state space equations for the PK model could be written as [25]

$$\dot{\underline{x}} = \begin{bmatrix} -(k_{10}+k_{12}+k_{13}) & k_{21} & k_{31} \\ k_{12} & -k_{21} & 0 \\ k_{13} & 0 & -k_{31} \end{bmatrix} \underline{x} + \begin{bmatrix} \frac{1}{V_1} \\ 0 \\ 0 \end{bmatrix} u \qquad (1)$$

Where $\underline{x} = \begin{bmatrix} x_1 & x_2 & x_3 \end{bmatrix}^T$ is the state vector and u is the propofol infusion rate in (mg/min) into the central compartment, x_1 is the drug concentration in the central compartment (mg/L), x_2 and x_3 are the drug concentrations in the peripheral compartments. k_{10} is the elimination rate of the drug through metabolism (min^{-1}). v_i is the volume of the $i-th$ compartment (Liter). $k_{ji}, j \neq i, i, j = 1,2,3$ are the drug transfer rate constants from $i-th$ compartments to $j-th$ component (min^{-1}). The PK model parameters could be calculated in terms of the patient weight (in kilogram), height (in centimeter), lean body mass (lbm), gender (male or female), and age (in years) as follows [25].

$$k_{10} = \frac{C_{l1}}{V_1}, k_{12} = \frac{C_{l2}}{V_1}, k_{13} = \frac{C_{l3}}{V_1}, k_{21} = \frac{C_{l2}}{V_2}, \\ , k_{31} = \frac{C_{l3}}{V_3}, k_{e0} = 0.456 \qquad (2)$$

Where

$$V_1 = 4.27, V_2 = 18.9 - 0.391(age - 53), V_3 = 238. \qquad (3)$$

$$C_{l1} = 1.89 + 0.0456(weight - 77) - \\ 0.0681(\text{lbm} - 59) + 0.0264(height - 177), . \qquad (4)$$

$$C_{l2} = 1.29 - 0.024(age - 53), C_{l3} = 0.836$$

$$lbm(male) = 1.1 weight - 128 weight^2 / height, \\ lbm(\ female) = 1.07 weight - 148 weight^2 / height \qquad (5)$$

The concentration of drug in the effect site compartment ($C_e(t)$) could be obtained in terms of its concentration in the central compartment through the following differential equation [25].

$$\dot{C}_e(t) = k_{e0}(x_1(t) - C_e(t)) \qquad (6)$$

Where k_{e0} is the drug elimination rate from the effect site compartment. The relation between BIS and $C_e(t)$ could be described with the following static nonlinear equation [25]

$$BIS(t) = BIS_0\left(1 - \frac{C_e^{\gamma}(t)}{EC_{50}^{\gamma} + C_e^{\gamma}(t)}\right) \qquad (7)$$

Where BIS_0 is the index value in an awake state, without drug. The typical value of BIS_0 is 100. EC_{50} is the drug concentration at half maximal effect and γ is the degree of nonlinearity of the function. The desired value for BIS for surgery goals could be considered in the range [40, 60]. However, its typical value is 50.
According to (1), the transfer function of the system with input u and output x_1 (called $G(s)$) is obtained as

$$G(s) = \frac{\gamma_0(s^2 + b_1 s + b_0)}{s^3 + a_2 s^2 + a_1 s + a_0} \tag{8}$$

Where

$$\begin{aligned} &a_2 = k_{10} + k_{12} + k_{13} + k_{21} + k_{31}, a_1 = k_{10}k_{31} + k_{12}k_{31} \\ &+k_{10}k_{21} + k_{13}k_{21} + k_{31}k_{21}, a_0 = k_{10}k_{21}k_{31}, \\ &b_1 = k_{21} + k_{31}, b_0 = k_{31}k_{21}, \gamma_0 = \frac{1}{V_1} \end{aligned} \quad . \tag{9}$$

3. THE FRACTIONAL ORDER GRADIENT BASED MRAC

Consider an RST control structure shown in Fig. 2. In this structure, the polynomials $R(s)$, $S(s)$ and $T(s)$ are selected such that the output of the closed loop system (y) tracks the output of a reference model (y_m) or equivalently the tracking error $e = y - y_m$ will be equal to zero. The transfer functions of the plant and the reference model are denoted by $G(s) = \frac{B(s)}{A(s)}$ and $G_m(s) = \frac{B_m(s)}{A_m(s)}$, respectively. Moreover, consider that $B = B^+B^-$ where B^+ and B^- are the minimum phase and non-minimum phase parts of B, respectively. Consider that B^+ is a monic polynomial. In the remaining part of the paper, the plant is considered as a minimum phase system or $B^- = \gamma_0$ where γ_0 is a positive number.

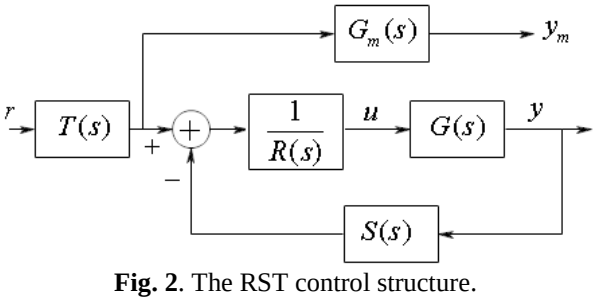

Fig. 2. The RST control structure.

According to Fig.2, the signals y and y_m are calculated as

$$y(t) = \frac{B(p)T(p)}{A(p)R(p) + B(p)S(p)} r(t) . \tag{10}$$

$$y_m(t) = \frac{A_0(p)B^+(p)B_m(p)}{A_0(p)B^+(p)A_m(p)} r(t) \tag{11}$$

Where p is the derivative operator and $A_0(p)$ is the observer polynomial [26]. According to (10) and (11), the perfect model following will be obtained if

$$\frac{B(p)T(p)}{A(p)R(p) + B(p)S(p)} = \frac{B_m(p)A_0(p)B^+(p)}{A_m(p)A_0(p)B^+(p)} . \tag{12}$$

If the plant parameters are considered as fixed known parameters, the controller polynomials could be obtained from relation (12). However, due to the external disturbances and model uncertainties, the plant parameters are unknown parameters that may change slowly with time. Thus, perfect model following and relation (12) could not be effective in real applications. In this case, the controller polynomials parameters should change according to an appropriate adaptation mechanism to reach the model following. Accordingly, the tracking error will tend to zero. Or

$$\lim_{t\to\infty} e(t) = 0 . \tag{13}$$

According to the normalized gradient adaptation mechanism, the controller parameters (denoted by θ) should be adjusted as [26]

$$\frac{d\theta}{dt} = \frac{-\gamma'\varphi e}{\beta + \varphi^T\varphi} \tag{14}$$

Where $\varphi = \frac{\partial e}{\partial \theta}$,the regression is vector and $\gamma' > 0$ is the adaptation gain.

Replacing the ordinary derivative with the fractional order derivative in the left side of (14) could increase the performance of the controller. The fractional order derivative of a function $f(t)$ (${}_0D_t^\alpha f(t)$) in accordance with the Caputo definition is given by [18]

$${}_0D_t^\alpha f(t) = \frac{1}{\Gamma(n-\alpha)} \int_0^t \frac{f^n(\tau)}{(t-\tau)^{1+\alpha-n}} d\tau \tag{15}$$

Where α ($n-1 \le \alpha < n, n \in N$) is the fractional order and $\Gamma(.)$ is the Gamma function.

Incorporating the fractional order derivative in (14) gives the following fractional order normalized gradient adaptation mechanism [22]

$${}_0D_t^\alpha \theta = \frac{-\gamma'\varphi e}{\beta + \varphi^T\varphi}, \qquad \alpha > 0 \tag{16}$$

Where α is the fractional order belongs to (0,1] and β is a positive small number.

Now, consider that the polynomials $R(p)$, $S(p)$ and $T(p)$ are selected as

$$\begin{aligned} R(p) &= p^{n_r} + r_{n_r-1}p^{n_r-1} + \ldots + r_i p^i + \ldots + r_0 \\ S(p) &= s_{n_s}p^{n_s} + s_{n_s-1}p^{n_s-1} + \ldots + s_j p^j + \ldots + s_0 \\ T(p) &= t_{n_t}p^{n_t} + t_{n_t-1}p^{n_t-1} + \ldots + t_k p^k + \ldots + t_0, \\ i &= 0,\ldots,n_r-1, \quad j = 0,\ldots,n_s, \quad k = 0,\ldots,n_t \end{aligned} \tag{17}$$

Where n_r, n_s and n_t are the degree of the polynomials $R(p)$, $S(p)$ and $T(p)$, respectively.

Now, the estimated parameters vector θ is defined as

$$\theta = [r_{n_r-1},\ldots,r_0,s_{n_s},\ldots,s_0,t_{n_t},\ldots,t_0]^T. \tag{18}$$

According to (17), we have

$$\begin{aligned} &\frac{\partial e}{\partial r_i} = \frac{\partial y}{\partial R}\frac{\partial R}{\partial r_i} = p^i \frac{\partial y}{\partial R}, \quad \frac{\partial e}{\partial s_j} = \frac{\partial y}{\partial S}\frac{\partial S}{\partial s_j} = p^j \frac{\partial y}{\partial S} \\ &\frac{\partial e}{\partial t_k} = \frac{\partial y}{\partial T}\frac{\partial T}{\partial t_k} = p^k \frac{\partial y}{\partial T} \end{aligned}. \tag{19}$$

According to (10), (11) and (19) and perfect model following relation given in (12), we have

$$\frac{\partial e}{\partial r_i} = -\frac{\gamma_0 p^i}{A_0 A_m}u, \ \frac{\partial e}{\partial s_j} = -\frac{\gamma_0 p^j}{A_0 A_m}y, \frac{\partial e}{\partial t_k} = \frac{\gamma_0 p^k}{A_0 A_m}r. \tag{20}$$

Now, from (20) and (14), the regressor vector φ and the adaptation mechanism ${}_0D_t^\alpha\theta$ could be written as

$$\varphi = \frac{-1}{A_0 A_m}[p^{n_r-1}u,\ldots,u,p^{n_s}y,\ldots,y,-p^{n_t}r,\ldots,-r]^T. \tag{21}$$

$${}_0D_t^\alpha\theta = \frac{-\gamma\varphi e}{\beta+\varphi^T\varphi} \tag{22}$$

Where $\gamma = \gamma'\gamma_0 > 0$. The control signal $u(t)$ could be calculated as

$$u(t) = \frac{T(p)}{R(p)}r(t) - \frac{S(p)}{R(p)}y(t). \tag{23}$$

4. BIS CONTROL USING THE FRACTIONAL ORDER GRADIENT BASED MRAC

To apply the proposed method for control of depth of anesthesia, the system with the transfer function (8) should be utilized. But, x_1 could not be directly measured. Thus, x_1 should be calculated in terms of the BIS. To attain this goal, C_e should be firstly calculated from the BIS in accordance with (8). Or

$$C_e(t) = EC_{50}\left(\frac{BIS_0}{BIS(t)} - 1\right)^{\frac{1}{\gamma}}. \tag{24}$$

Now, x_1 could be obtained in terms of C_e as

$$x_1(t) = \frac{p + k_{e0}}{k_{e0}(\tau p + 1)}C_e(t) \tag{25}$$

Where τ is an arbitrary small positive time constant. In (25), the term $\tau p + 1$ is considered to make the transfer function between C_e and x_1 proper. The control structure for BIS control using the fractional order gradient based MRAC (FOGMRAC) is shown in Fig. 3.

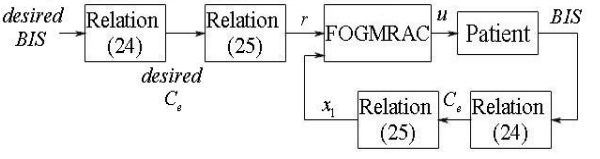

Fig. 3. The FOGMRAC structure for BIS control.

For plant (8), the reference model and the controller polynomials are selected as

$$G_m(s) = \frac{\omega_n^2}{s^2 + 2\xi\omega_n s + \omega_n^2}, \tag{26}$$

$$\begin{aligned} &R(s) = s^2 + r_1 s + r_0, S(s) = s_2 s^2 + s_1 s + s_0 \\ &,T(s) = t_1 s + t_0, A_0(s) = s + a_0 \end{aligned}, \tag{27}$$

Where ζ and ω_n are the damping ratio and natural frequency, respectively. Moreover, a_0 is a positive arbitrary number.

The regressor vector φ and the estimated parameters vector θ are considered as

$$\varphi = \frac{-1}{A_0 A_m}\left[pu, u, p^2 y, py, y, -pr, -r\right]^T, \tag{28}$$

$$\theta = \left[r_1, r_0, s_2, s_1, s_0, t_1, t_0\right]^T \tag{29}$$

5. SIMULATION RESULTS

To verify the performance of the proposed method, four different patients that their physical specifications are presented in Table 1 are selected [27].

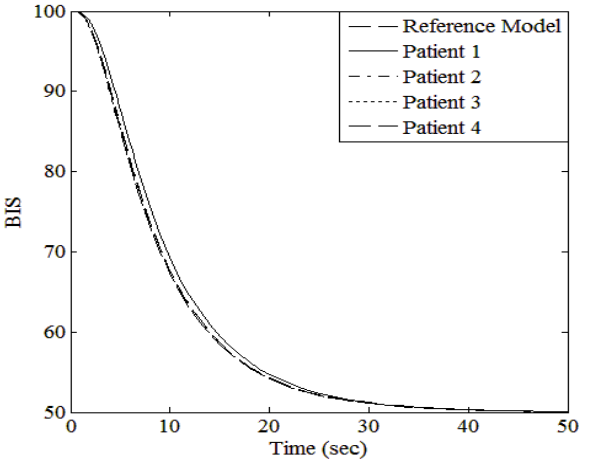

Fig. 4. The closed loop responses of BIS.

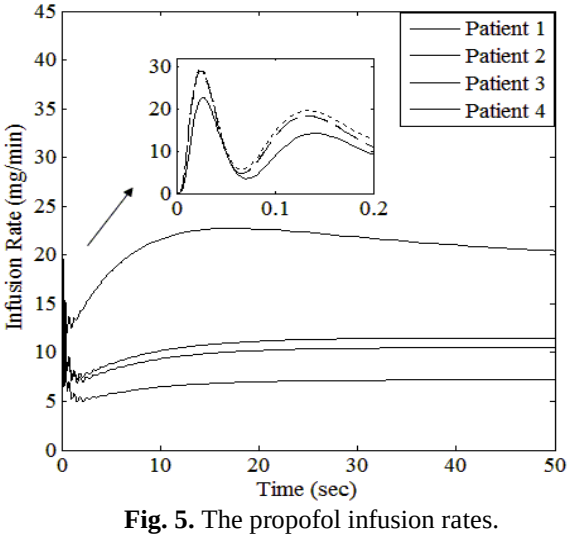

Fig. 5. The propofol infusion rates.

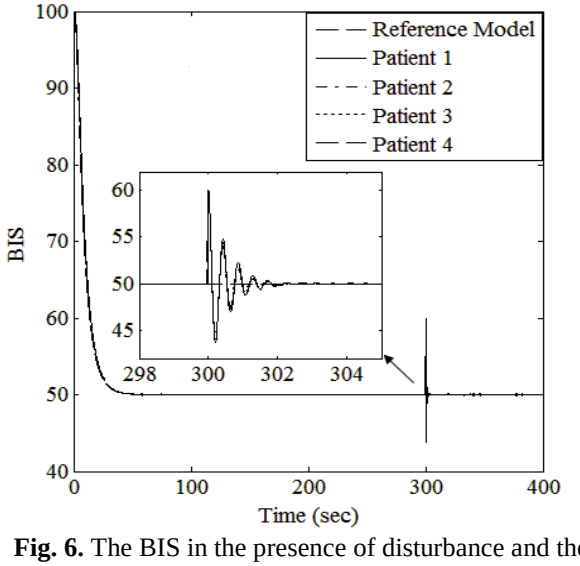

Fig. 6. The BIS in the presence of disturbance and the measurement noise.

Table 1. The physical specification of patients.

Patient number	Gender	Age	Height	Weight	γ	EC_{50}
1	M	28	164	60	2.46	4.93
2	M	42	179	78	1.85	4.82
3	F	50	163	83	2.18	6.44
4	F	40	163	54	2.24	6.33

The desired BIS is considered as 50. The controller parameters are considered as $\omega_n = 0.5, \xi = 2, a_0 = 0.6$, $\tau = 0.01$, $\alpha = 0.8, \gamma = 1000, \beta = 0.01$. The closed loop responses of BIS and the propofol infusion rates for different patients are shown in Fig. 4 and Fig. 5, respectively. As could be seen from Fig.4, the close loop system could track the desired BIS for different patients with approximately similar transient response. Fig. 5 shows that the propofol infusion rates are admissible. For evaluating the controller performance in the presence of disturbance, a constant disturbance with an amplitude of 10 in $t = 300$ seconds is applied. Moreover, a zero-mean Gaussian noise with a variance of 10 is applied. The results in the presence of the measurement noise and the external disturbance are presented in Fig. 6. Fig. 6 shows that the effect of the measurement noise and the disturbance is eliminated.

6. CONCLUSIONS

In this paper, the fractional order normalized gradient based MRAC is applied to control the BIS during the anesthesia. An RST control structure is employed in which the control polynomials are adjusted according to a fractional order adaptation mechanism. Although the stability of the normalized gradient based MRAC could not be proved generally, this adaptation mechanism is simple and could be employed for transfer functions with relative degree one. The simulation results performed on different patients demonstrate the performance of the proposed controller. The simulation results show that the proposed control structure is not sensitive to the measurement noise and the external disturbance.

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