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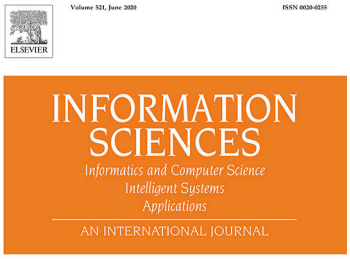

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Application of Fuzzy Learning in IoT-Enabled Remote Healthcare Monitoring and Control of Anesthetic Depth during Surgery☆

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Abstract

Smart remote patient monitoring and early disease diagnosis systems have made huge progresses after the introduction of Internet of Things (IoT) and Artificial Intelligence (AI) concepts. This paper proposes an AI-enabled IoT system to monitor and adjust the depth of anesthesia via network channels. More precisely, fuzzy learning systems are employed to develop a control system for the depth of anesthesia in surgeries. This scheme is composed of variable structure control and adaptive type-II fuzzy systems. Therefore, the controller is adaptive and robust to any perturbations and disturbances that may happen during a patient's surgery. The adaptive type-II fuzzy system is designed as an intelligent online estimator to approximate patient model uncertainties. This estimation helps in boosting the performance of the variable structure control system. An artificial neuron is also designed to reduce chattering for the proposed control system. The designed control system can efficiently adjust the anesthesia drug infusion rate and regulate the Bispectral index. The networked structure of the proposed system makes remote tuning of drug infusion possible. Performance

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of the designed controller is evaluated on several patient models. Simulation results confirm the validity and effectiveness of the proposed remote drug delivery system.

Keywords: Remote Healthcare, Artificial Intelligence, Internet of Things, Anesthesia, Networked Control System, Fuzzy Learning System.

1. Introduction

Integration of Artificial Intelligence (AI) and Internet of Things (IoT) can create several digital health devices including wearable, implantable, mobile, and remote healthcare systems which contribute to recording and monitoring of the vital signs and symptoms of people. It is a foundation to paradigms which make the implementation of biomedical, telemedicine and smart healthcare systems possible. Since adding intelligent learning algorithms to medical things can accelerate the decision-making process, it is expected that these algorithms e.g. the fuzzy learning ones, to be commonly employed in both theoretical and practical aspects of future AI-enabled healthcare IoT. Applying learning algorithms in medical areas including monitoring, control, prevention, and treatment can make handling difficulties resulting from the lack of information, imprecise information, and seemingly contradictory evidences (due to e.g. limited understanding of biological mechanisms, imprecise test measurements, highly subjective and imprecise medical history, or inconsistency of different sources) possible.

In this paper, we aim to address the concepts of AI and IoT not only for sensing, but also for actuation. We tend to do automatic control and monitoring of the depth of patient's anesthesia during surgery by fuzzy learning. Fuzzy learning systems can provide powerful analysis capabilities and enhance the performance of adjusting anesthesia depth during surgery in comparison to traditional methods.

Anesthesia is one of the important parts of most surgeries. It is defined as the lack of response or reaction to stimuli during surgery, which includes three

main parts: unconsciousness, lack of pain (analgesia), and muscle relaxation. The purpose of the anesthesia monitoring and automatic control system is to determine the exact amount of medicine required to be injected to achieve an appropriate depth of anesthesia. Excessive injection of anesthetic drugs interferes with patient's recovery after surgery, and insufficient injection of these drugs causes patient to regain consciousness at the middle of surgery, which can have very dangerous consequences. The solution to this issue is to use the least amount of medicine that can achieve the desired depth of anesthesia for patient during surgery. Such a drug delivery control system should be robust to surgical circumstances and uncertainties of various kinds so as to provide the optimal performance. Automatic smart drug delivery systems not only can lead to a decrease in the number of operation tasks, but also can maintain patients' safety.

An intelligent anesthesia control system requires some essential parts, including sensing or measurement subsystems and intelligent controllers. To automatically control anesthesia, first, the depth of anesthesia should be determined in the current state and then, the amount of anesthetic drug should be determined based on the difference between the current and the desired depth of anesthesia. In this process, patient's condition should be taken into account. Unfortunately, the depth of anesthesia cannot not be easily measured. Anesthesiologists regularly uses clinical symptoms to determine the depth of patient's anesthesia. These symptoms and indicators include blood pressure, sweating, tears, body movements, etc. However, nowadays, a number of signal processing techniques are used to quantify EEG signals and derive a surrogate measurement of patient's hypnosis [1]. Bispectral index (BIS) is a prevalent indicator in monitoring the depth of anesthesia, which is a number between 0 and 100. Very low values correspond to deep hypnotic states and very high values represent the fully awake state. This index is normally between 40 to 60 in general anesthesia [2]. BIS decreases by the reduction of anesthesia depth. Propofol is a short-acting medication that leads to a decrease in the level of consciousness and is widely used in the starting and maintenance steps of general anesthesia during surgery.

It is a hypnotic drug with no negative side-effects [3]. In fact, some of its positive points, like great solubility, short onset time, and quick recovery, have made it very popular. BIS monitoring (as a measurement subsystem) and propofol injection (as a drug delivery subsystem) are the main components of a closed loop anesthesia control system.

On the other hand, a networked control systems (NCS) consists of computational and physical processes which work interconnectedly through communication networks. NCS instances are available in different domains, e.g., networked-gantry systems [4], medical devices [5, 6], autonomous vehicles [7, 8], and smart grids. Since the components of networked control systems and cyber-physical systems communicate through computer networks, their physical subsystems are prone to the threats and attacks which come through the cyber space. Some studies tried to develop methods to detect and compensate such attacks [9, 10, 11, 12].

In this study, an NCS is designed to monitor and intelligently control the anesthesia depth of a patient. The BIS index is used to monitor the performance of the control system. Control efforts are made through injection of propofol. The main control (sub)system is designed using the variable structure control concept as well as the adaptive type-II fuzzy concept. The control objective is to maintain the depth of anesthesia and to adjust the amount of propofol injection during operation. The control commands are sent through a computer network. The proposed scheme is depicted in Fig. 1. In practice, patient plays the role of the plant in the loop. However, in our endeavors to design an adaptive robust controller, we will use a mathematical model as the plant which describes the relationship between anesthetic drug delivery as the system input and patient variables as the output. This is a Pharmacokinetics and Pharmacodynamics (PK-PD) model and contains a variety of covariates. In particular, the performance of the system is investigated while the patient is prone to uncertainties during surgery.

The rest of this paper is organized as follows. In Section 2, a brief review of related papers is presented. In Section 3, the PK-PD model is described. In

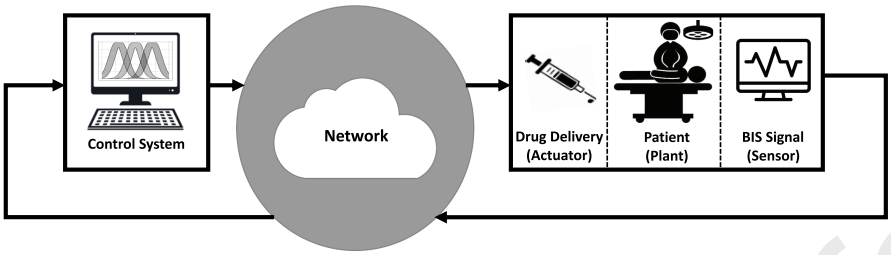

Figure 1: Mapping of remote drug delivery to a networked control system.

Section 4, the proposed control system is designed. Simulations are presented in Section 5. The paper is finally concluded in Section 6.

2. Related Work

In this section, we briefly review the related work on automatical control of anesthesia depth.

There are two approaches to control the depth of anesthesia; open-loop and closed-loop. In the open-loop injection system, the target point is set by the anesthesiologist and the control system remains at the reference level. But the control systems are not robust to some uncertainties during surgery. In fact, this type of control aims to optimize the prescribed dose of the injectable drug. Pumps of the target control infusion system work using an algorithm based on the pharmacological data. If there is a change in the level of anesthesia during surgery due to e.g. bleeding in the patient's body, the controller is unable to adjust the system to reach the desired target point. This is one of the major drawbacks of this system [13, 14].

Regarding the closed-loop approach, traditional PID systems are commonly used for control purposes. The main features of PID controllers are the rapid transient response and the ability to reduce the steady state error of the system. In [15], a closed-loop anesthesia control has been designed in which a multi-part model of the patient's body and its linearization model have been used. A PID controller is employed to keep patient in hypothetical anesthesia. It is indicated that the reference anesthesia level is achievable. However, if some data are lost

during the model operation, results become inaccurate. In [16], the open-loop control method is adjusted with the variation of patients' attributes including age, weight and height. The differences vary from patient to patient, and each patient responds differently to drug injection. A closed-loop control system can compensate the undesirable effect of these variabilities as well as the dynamics in the same patient including changes in blood pressure and the depth of anesthesia due to blood loss during surgery, wound condition, et cetera. In [17], a closed-loop control system is employed to decrease the workload of the anesthesiologist. Experimental results obtained from 47 different patient models were valid. A similar study was performed on children aged 6 to 16 to monitor and measure the depth of anesthesia using nerve sensors. In [18], to control propofol and remifentanil, a multi-input model is employed. Remifentanil metabolism is more rapid than propofol. A robust adaptive PID controller is applied to adjust the level of anesthesia around the reference level. Such a controller, which works based on patients' parameters, performs better in the face of external disturbances, like surgical stimuli. The paper confirms this via a set of clinical trials on 44 patients.

PID controller is easy to implement, but setting it up is difficult. In addition, there are a number of limitations with PID control systems which lead to a rise in instability of the resultant closed-loop systems. Classic nonlinear robust control has widely been used for high-order nonlinear systems in the presence of environmental uncertainties [19, 20]. The Sliding Mode Control (SMC) method is one of the most effective ones in this family of control systems. It is less sensitive to noise and highly robust to uncertainties [21, 22]. In [23], the SMC controller is designed by using a PK-PD model that describes patient's different behaviors and responses to propofol injection. Initially, high-order SMC was used for insulin injection and glucose monitoring in Type 1 diabetic patients. This technique has since been used to inject propofol under general anesthesia. The main advantage of SMC is its less sensitivity to patient's parameters. Moreover, it is highly robust in comparison to other control systems, such as model predictive control (MPC), in the presence of surgical stimuli like bleeding.

Adaptive control strategies have overcome the limitations of the PID controllers. In [24], nonlinear adaptive control is used to control the level of BIS. The model-based predictive control algorithm is an optimal one and is also used to manage propofol injection. This algorithm has several features including BIS tracking, noise cancellation and the ability to change perturbations. In [25], a robust predictive control algorithm is developed in which the system has one input (propofol) and one output (BIS). A group of 12 patients were studied and the controller was designed using predictive principles to ensure that interpatient variabilities were properly managed. Due to the nonlinear model of patient's body, parameters of the control system are adapted with interpatient variations.

Fuzzy control system does not require a model of the process and can be used for nonlinear and complex models with uncertainties. The most important drawback is the need for an expert to define the rules, which is not always possible, and sometimes some conditions remain hidden even to experts. Scientists of the University of Sheffield have done substantial work in the field of anesthesia control. They have used fuzzy controllers, and in most cases, those controllers has been studied in clinical trials and have yielded good results [26, 27, 28]. In [29], the BIS signal is used for the assessment of patients' hypnotic state. A fuzzy controller is designed to achieve the target BIS and reject disturbances. In [30], monitoring of EEG variations during anesthesia is carried out by analysis of detrended fluctuations and artificial neural networks. In [31], a deep neural network is employed for detection of anesthesia states, which is based on heart rate variability-derived features.

In this paper, we focus on monitoring and networked control of anesthesia depth during surgeries using adaptive robust control systems.

3. Pharmacokinetics & Pharmacodynamics Model

In this section, a pharmacokinetics-pharmacodynamics (PK-PD) model is presented to explain physiological effects of drugs. Pharmacokinetics (PK) stud-

ies the change of drug in body after its distribution, while pharmacodynamics (PD) investigates drug effects on patient's parameters.

Pharmacokinetics models drug concentration progression in patient's body over the time. Several factors contribute to the drug concentration progression including absorption, distribution, metabolism, and elimination from the body. Specifically, pharmacokinetics model of anesthetic drugs includes intravascular blood, muscle, and fat compartments. It is assumed that the drug concentration is uniform in each compartment because of the perfect and instantaneous mixing assumption. Pharmacodynamics model is applied to depict the drug concentration effect on patient's parameters. The diagram of the PK-PD model is illustrated in Fig. 2. The PK-PD mathematical model, which is validated by anesthesiologists using real patients' data, is as follows [32]:

$$\begin{aligned}
\dot{x}_1(t) &= -\left(\lambda_{10} + \lambda_{12} + \lambda_{13}\right) x_1(t) + \lambda_{21} x_2(t) \\
&\quad + K_{31} x_3(t) + u(t)/V_1 \\
\dot{x}_2(t) &= \lambda_{12} x_1(t) - \lambda_{21} x_2(t) \\
\dot{x}_3(t) &= \lambda_{13} x_1(t) - \lambda_{31} x_3(t) \\
\dot{x}_e(t) &= \lambda_{1e} x_1(t) - \lambda_{e0} x_e(t)
\end{aligned} \tag{1}$$

where x_1, x_2, and x_3 are the drug concentration in intravascular blood, muscle, and fat compartments, respectively. x_e is the drug concentration at the effect site. Moreover, $u(t)$ $[mg/min]$ denotes the rate of anaesthetic drug infusion into the intravascular blood compartment. Parameters λ_{ij} for $i \neq j$ represent the frequency of the drug transfer from i to j compartments. In clinical practice, for propofol, it is observed that the drug transfer frequency from the intravascular blood compartment to the effect site is equal to the drug elimination frequency from the effect site, $\lambda_{e0} = \lambda_{1e} = 0.456$ $[min^{-1}]$ [33, 34]. Other parameters are dependent on patient's parameters such as gender (M/F), weight (W), age (A), height (H), and the lean body mass (LBM), which can obtained as follows:

$$\lambda_{10} = C_{l1}/V_1 \ [min^{-1}]$$
$$\lambda_{12} = C_{l2}/V_1 \ [min^{-1}]$$
$$\lambda_{13} = C_{l3}/V_1 \ [min^{-1}]$$
$$\lambda_{31} = C_{l3}/V_3 \ [min^{-1}] \quad (2)$$

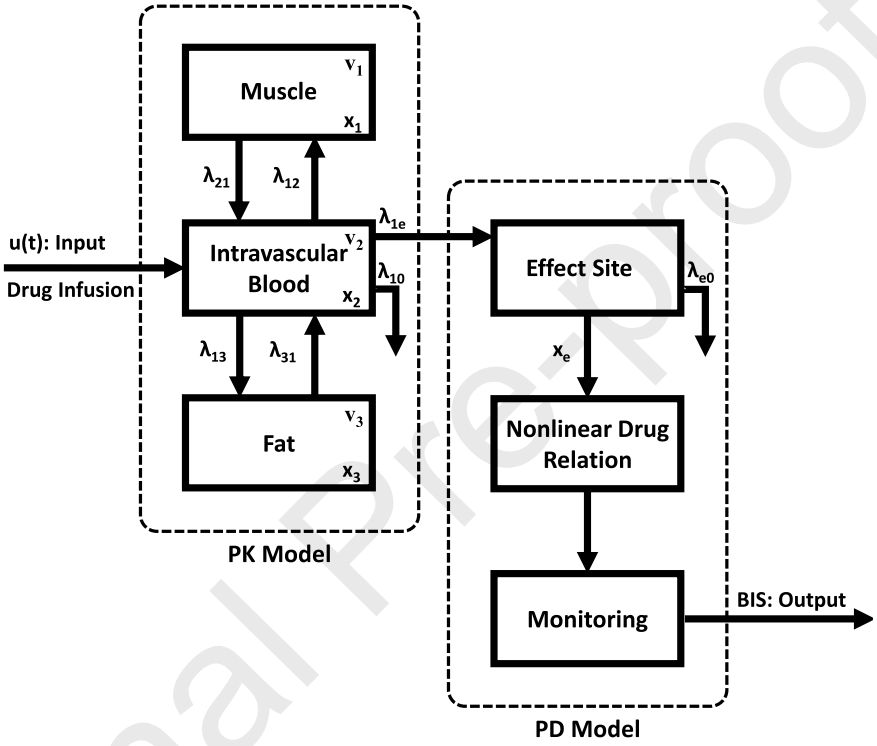

Figure 2: Scheme of the PK-PD Model.

where

$$
\begin{aligned}
V_1 &= 4.27\ [l] \\
V_2 &= 18.9 - .391\,(A-53)\ \ [l] \\
V_3 &= 2.38\ [l] \\
LBM_M &= 1.1\ W - 128\ W^2/H^2 \\
LBM_F &= 1.07\ W - 148\ W^2/H^2 \\
C_{l1} &= 1.89 + 0.456\,(W-77) - 0.0681\,(LBM-59) \\
&\quad + 0.264\,(H-177)\ \ [l/min] \\
C_{l2} &= 1.29 - 0.024\,(A-53)\ \ [l/min] \\
C_{l3} &= 0.836\ [l/min]
\end{aligned}
\tag{3}
$$

As mentioned, the PD model explains patient's parameter changes after anesthetic drug injection. The effect of the drug concentration x_e on physiological parameters is presented by the BIS index as follows [2, 32]:

$$
BIS = E_0 - E_{max}\frac{x_e(t)^\gamma}{x_e(t)^\gamma + EC_{50}^\gamma} \tag{4}
$$

where E0 is the baseline parameter related to the awake state with no drug injection, and is typically equal to 100. E_{max} represents the maximum effect of the drug. Moreover, as mentioned before, $x_e(t)$ is the drug concentration at the effect site, which is derived from the pharmacokinetics model. γ is the Hill coefficient obtained from the dose response Hill curve. EC_{50}, the patient's sensitivity to drug, is the drug concentration at 50 % of the maximum effect and can be read from the dose response curve.

In the next section, we employ fuzzy systems and nonlinear controllers to design $u(t)$ and then, apply it to the plant as the control input sent through network.

4. Adaptive Type-II Fuzzy Variable Structure Control System

In this section, the proposed control system is designed using a combination of variable structure control system and type-II fuzzy system, which is so called Adaptive Type-II Fuzzy Variable Structure Control system. Then, the stability of the proposed control system is proven. The scheme of the proposed control system is depicted in Fig. 3. In this scheme, the main controller is a variable structure control system which is a classic nonlinear control system. It works based on switching surfaces calculated by using errors and the system functions. Since the PK-PD model which presents the patient's parameters consists of functions with uncertainties, type-II fuzzy systems are employed to approximate the system functions. These approximations assist the classic controller in making the control signal. Moreover, there is an artificial neuron applied in order to reduce chattering of the control signal. A modulator tunes the working regions of the controller and the artificial neuron to achieve better control performance. More details will be presented in the following subsections.

To design the control system, first, let us generalize the PK-PD model presented in Eq. (1) and Eq. (4) as a nonlinear system written as follows:

$$\begin{aligned} \dot{x}_i(t) &= f_i(\underline{x}(t)) + g_i(\underline{x}(t))u(t) \\ y(t) &= h(\underline{x}(t)) \end{aligned} \tag{5}$$

where $i = \{1, 2, 3, 4\}$ and $\underline{x} = [x_1, x_2, x_3, x_e]^T$ is the variable state vector. $f_i(.)$ and $g_i(.)$ are nonlinear functions which can be obtained via Eq. (1). $u(t)$ is the control input which is the propofol infusion and $y(t)$ is the BIS index which can be obtained by Eq. (4). The dynamic system presented in Eq. (5) can be rewritten as follows:

$$\begin{aligned} \dot{X}(t) &= F(X(t)) + G(X(t))u(t) \\ y(t) &= h(X(t)) \end{aligned} \tag{6}$$

where $F(X) = [f_1(\underline{x}), f_2(\underline{x}), f_3(\underline{x}), f_4(\underline{x})]^T$, $G(X) = [g_1(\underline{x}), g_2(\underline{x}), g_3(\underline{x}), g_4(\underline{x})]^T$,

and $X = \underline{x}$. Matrix $G(X)$ is positive definite, then, according to Assumption 1 presented in [35], there exists a positive scalar δ_0 such that $G(X) \geq \delta_0 I_{4\times 4}$ where I_4 is an identity matrix. As mentioned before, the control objective is to regulate the BIS signal on the standard value defined for surgery which is equal to 50, i.e. $R = 50$. Thus, the control error is obtained as follows:

$$e(t) = 50 - y(t) \tag{7}$$

The control error is applied as an input for the proposed control system shown in Fig. 3. The main control system is a variable structure one, and it is combined with a type-II fuzzy system. Since the nonlinear functions highly depend on patient's parameters, this study assumes that the mentioned functions are unknown to the control system because of their uncertainties. Hence, the type-II fuzzy is employed to approximate the functions of the PK-PD model which models the physiological drug effects on patient's body and patient's parameters after drug distribution. These functions are presented by *F(X(t))* and *G(X(t))* in Eq. (6), whose approximations will be constructed by $\hat{f}_i(.)$ and $\hat{g}_i(.)$.

Moreover, a saturation function and modulator are added in the control scheme to reduce the chattering of the variable structure controller. In the next subsections, all components of Fig. 3 will be explained.

4.1. Variable Structure Control

Variable Structure (VS) control is a robust nonlinear control technique which includes two steps. First, a proper switching surface should be chosen such that moving on the switching manifold remains stable. Next, a control effort is designed such that the switching surface converges to zero, while the system works under uncertainty and disturbance conditions [36]. The switching surface is defined as follows:

$$S(t) = \left(\frac{d}{dt} + \delta\right)^{n-1} e(t) \tag{8}$$

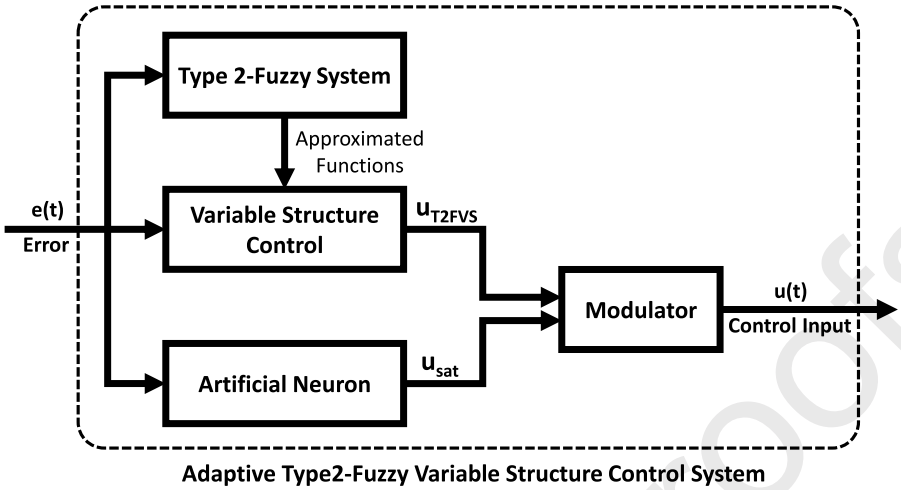

Figure 3: Scheme of the adaptive type-II fuzzy variable structure control system.

where δ is a real positive constant parameter which can adjust the convergence rate of the switching surface. It is assumed that the system is an n-order one. The derivative of the switching surface written in Eq. (8) is obtained as follows:

$$\dot{S}(t) = P(e(t)) - F(X(t)) - G(X(t))u(t) \tag{9}$$

where $F(.)$ and $G(.)$ are nonlinear functions described before, $u(t)$ is the control input, $e(t)$ is defined in Eq. (7), and $P(.)$ is presented as follows:

$$P(t) = \binom{n-1}{1}\delta e^{n-1}(t) + \binom{n-1}{2}\delta^2 e^{n-2}(t) + \\ ... + \binom{n-1}{n-2}\delta^{n-2}\ddot{e}(t) + \binom{n-1}{n-1}\delta^{n-1}\dot{e}(t) \tag{10}$$

To design an appropriate VS control law, the derivative of the switching surface has been taken into consideration as follows:

$$\dot{S}(t) = -k_v \ sgn(S) - k_o S \tag{11}$$

where k_v and k_o are positive constant parameters and sgn is the sign function. The VS control input is obtained as follows:

$$u_{vs}(t) = G^{-1}(X(t))[k_v\ sgn(S) + k_o S + P(t) - F(X(t))] \tag{12}$$

Moreover, it is essential that $G(X(t)) \neq 0$. According to the Lyapunov stability theorem, the error trajectory converges to the switching surface $S(t) = 0$ by applying the control input presented in Eq. (12). As mentioned before, $F(X)$ and $G(X)$ are unknown functions estimated by the type-II fuzzy system. Hence, the control law can be rewritten as follows:

$$\begin{aligned} u_{FVS}(t) = \hat{G}^{-1}(X(t), \zeta_g)[k_v\ sgn(S) + k_o S \\ + P(t) - \hat{F}(X(t), \zeta_f)] \end{aligned} \tag{13}$$

where ζ_f and ζ_g are adjustable parameters. Since $\hat{G}^{-1}(X(t))$ might be non invertible, it is replaced as follows:

$$\hat{G}^{-1}(X, \zeta_g) = \hat{G}^T(X, \zeta_g)[\alpha I + \hat{G}(X, \zeta_g)\hat{G}^T(X, \zeta_g)]^{-1} \tag{14}$$

where α is a small positive constant value and I is an identity matrix. Thus, Eq. (13) can be written as follows:

$$\begin{aligned} u_{FVS}(t) = (\hat{G}^T(X, \zeta_g)[\alpha I + \hat{G}(X, \zeta_g)\hat{G}^T(X, \zeta_g)]^{-1}) \\ [k_v\ sgn(S) + k_o S + P(t) - \hat{F}(X, \zeta_f)] \end{aligned} \tag{15}$$

Therefore, the type-II fuzzy system is designed to approximate the mentioned functions.

4.2. Type-II Fuzzy System

Interval type-II fuzzy systems have been widely used for modeling and control purposes because of their ability to handle model uncertainty in comparison to conventional fuzzy systems [37, 38]. The scheme of type-II fuzzy systems is

similar to conventional fuzzy systems, but in the fuzzy sets, there exist interval type-II fuzzy sets in the rule base. It is essential to reduce the type of fuzzy sets to conventional fuzzy systems before the defuzzification step. Components of the interval type-II fuzzy system are as follows:

- *Fuzzifier.* In this step, input values have been mapped into type-II fuzzy system (T2FS) using membership functions which are Gaussian or trapezoidal in order to represent intervals.
- *Rule Base.* Mamdani and Takagi-Sugeno-Kang (TSK) fuzzy interface systems (FIS) can be used for *if-then* rules.
- *Type-Reduction.* Type of fuzzy sets should be reduced to type-II fuzzy.
- *Defuzzifier.* Outputs of the fuzzy system is obtained after this step.

A fuzzy rule can be presented as follows:

Rule ^{q} : IF X_1 is $\tilde{B}_1^q$ & $\cdots$ & X_n is $\tilde{B}_n^q$ THEN Y is $\tilde{w}^q$.

where $B_1^q, B_2^q, \cdots, B_n^q$ are fuzzy sets, $X = [X_1, \cdots, X_n]^T$ is the input to T2FS and Y is the T2FS output. In this study, the output of T2FS is obtained by using singleton fuzzifier, product inference, and center-average defuzzifier. The T2FS output is as follows:

$$Y(X_{in}) = w^T(X_{in})\zeta \tag{16}$$

where X_{in} is the T2FS input which is composed of the control error $e(t)$ and its derivative $\dot{e}(t)$ in this study, i.e. $X_{in} = [e(t) \;\; \dot{e}(t)]^T$. Moreover, $\zeta = [\zeta^l \;\; \zeta^u]^T$ is a vector of adjustable parameters. w is the normalized form of the antecedent part in fuzzy rules which is as follows:

$$w_k(X_{in}) = \frac{\mu_k(X_{in})}{\sum_{j=1}^{N} \mu_j(X_{in})} \tag{17}$$

where μ is the membership function, N is the number of fuzzy rules, and $k = 1, 2, ..., N$.

4.3. Adaptive Type-II Fuzzy Variable Structure Control System

The type-II fuzzy system is designed as an intelligent estimator to approximate $F(X)$ and $G(X)$. The approximations ($\hat{F}$ and $\hat{G}$) are usually given as:

$$\begin{aligned}\hat{f}_i &= w_{fi}^T(M\zeta_{f_i}^u + (1-M)\zeta_{f_i}^l)\\ \hat{g}_i &= w_{gi}^T(M\zeta_{g_i}^u + (1-M)\zeta_{g_i}^l)\end{aligned} \tag{18}$$

where $i = 1, 2, 3, 4$ and w_{f_i} and w_{g_i} are the normalized antecedent terms in fuzzy rules. M is a parameter between zero to one, which represents the upper bound or lower bound effect on type-II fuzzy systems. ζ_{f_i} and ζ_{g_i} are adjustable parameters which should converge to their optimums defined as below:

$$\begin{aligned}\zeta_{f_i}^* &= arg\ min\ _{\zeta_{f\,i}}(sup|f_i(X) - \hat{f}_i(X, \zeta_{f_i})|)\\ \zeta_{g_i}^* &= arg\ min\ _{\zeta_{g\,i}}(sup|g_i(\underline{x}) - \hat{g}_i(X, \zeta_{g_i})|)\end{aligned} \tag{19}$$

Therefore, the approximation errors are as follows:

$$\begin{aligned}\varepsilon_f(X) &= F(X) - \hat{F}(X, \zeta_f^*)\\ \varepsilon_g(X) &= G(X) - \hat{G}(X, \zeta_g^*)\end{aligned} \tag{20}$$

It is assumed that ε_f and ε_g are bounded, i.e. $|\varepsilon_f(\underline{x})| < \gamma_f$ and $|\varepsilon_g(\underline{x})| < \gamma_g$, where γ_f and γ_g are positive constant parameters. The approximation functions, $\hat{f}_i$ and $\hat{g}_i$ that were presented in Eq. (20), are adapted using the adjustable variables which are updated as follows:

$$\begin{aligned}\dot{\zeta}_{f_i}^u &= -\eta_f w_{f_i} S(t)\\ \dot{\zeta}_{f_i}^l &= -\eta_f w_{f_i} S(t)\\ \dot{\zeta}_{g_i}^u &= -\eta_g w_{g_i}\ S(t)\ u_{FSV}(t)\\ \dot{\zeta}_{g_i}^l &= -\eta_g w_{g_i}\ S(t)\ u_{FSV}(t)\end{aligned} \tag{21}$$

where η_f and η_g are the adaptation rate parameters which should be positive and constant. Here, S is the switching surface, u_{FSV} is presented in Eq. (15), w_f and w_g are the normalized antecedent parts of type-II fuzzy systems. Adaptive type-II fuzzy VS control is designed as follows:

$$u_{T2FSV} = u_{FSV} + u_c \tag{22}$$

where u_{FSV} is presented in Eq. (15) and u_c is as follows:

$$u_c = sgn(s)(\gamma_f + \gamma_g|u_{FSV}| + |u_\alpha|)/\delta_o \tag{23}$$

γ_f, γ_g, and δ_o are positive constant parameters, and u_α is defined as:

$$\begin{aligned} u_\alpha = (\alpha[\alpha I + \hat{G}(X,\zeta_g)\hat{G}^T(X,\zeta_g)]^{-1}) \\ [k_v\ sgn(S) + k_o S + P(t) - \hat{F}(X,\zeta_f)] \end{aligned} \tag{24}$$

in which α is a constant parameter and I is the identity matrix. k_v and k_o are parameters of the defined switching surface.

Proof. According to the Lyapunov stability theorem, stability proof of the proposed control system can be written similar to what was presented in [35]. Therefore, the type-II fuzzy variable structure control designed in Eq. (22) and the adaptation laws of online intelligent approximations presented in Eq. (21) will stabilize the PK-PD model in presence of uncertainties. Control error trajectory will converge to zero accordingly. Moreover, based on the proof, adjustable parameters of the online estimator will converge to their optimum values.

4.4. AI-enabled Chattering Reduction

In the variable structure control system, the control signal switches from one value to another at a very high speed, which is not possible in practice because of the delays and physical limitations of actuators. These constraints lead to output fluctuations as a result of stimulating high frequency dynamics of the controlled system and cause instability. Using the boundary layer or

replacing the discontinuous terms of the control law (originating from the sign function) with a smooth function around the switching surface is a way to reduce chattering and gain better performance.

In this case, in the adaptive type-II fuzzy variable structure control designed before, there exists a sign function which leads to undesirable chattering. Therefore, we apply a hyperbolic tangent function inside an artificial neuron to limit the control input bounds [39]:

$$u_{sat} = \alpha_h \left(\frac{1 - (1 - \beta_h \exp(net))}{1 + (1 - \beta_h \exp(net))} \right) \tag{25}$$

where net is the function input which is defined in this study as $net(t) = e(t) + \dot{e}(t)$. The parameters α_h and β_h can be adjusted in a way that the best performance is achieved. α_h and β_h are adapted using an online learning algorithm. The adaptation law will be presented in Eq.(29).

4.5. Modulator

As observed in Fig. (3), there is a modulator to tune the working regions of the main controller as well as the artificial neuron. It works using a function defined as follows:

$$M(u_{T2FVS}, u_{sat}) = \begin{cases} u_{T2FVS}, & if\ |S(e)| > \phi + \xi \\ \sigma(e) u_{T2FVS} & \\ \qquad + (1 - \sigma(e)) u_{T2FVS}, & \\ \qquad\qquad if\ \phi < |S(e)| \leqslant \phi + \xi & \\ u_{sat}, & if\ |S(e)| \leqslant \phi \end{cases} \tag{26}$$

where S is the switching surface, $\phi > 0$ is the boundary layer thickness, and ξ is a small positive value to form an intermediate region. The value of σ is obtained as follows [39]:

$$\sigma(e) = \frac{1}{\xi}(|S(e)| - \phi) \tag{27}$$

Table 1: Biometric Parameters of Patients[40]

Patient No	Age	Height[cm]	Weight[kg]	Gender	$E_{C_{50}}$	E_0	E_{max}	γ
1	40	163	54	F	6.33	98.80	94.10	2.24
2	37	187	75	M	8.02	92.00	104.00	2.10
3	37	167	58	F	13.70	83.10	151.00	1.65
4	42	172	58	F	4.95	96.20	90.80	1.84

Adaptive parameters used in the hyperbolic tangent function and modulator are written as $\rho = [\alpha_h, \beta_h, \phi]^T$. Parameters can be adapted using an online learning algorithm which minimizes the cost function defined below:

$$E = \frac{1}{2}e^2(t) \tag{28}$$

where $e(t)$ is defined in Eq. (7). Therefore, adaptation law can be calculated using the tuning algorithm presented in [39] as follows:

$$\dot{\rho} = -\eta e(t)\frac{\partial u_{sat}}{\partial \rho} sgn(\frac{\partial y}{\partial u_{T2FSV}}) \tag{29}$$

Here, η is the learning rate and y is the patient's BIS value. Other parameters have been defined before.

5. Results & Discussions

In this section, the designed networked control system is evaluated to control depth of anesthesia. First, features of the communication network are described. Second, a description of the patients' parameters is given. Then, the proposed adaptive type-II fuzzy variable structure control plus the AI-enabled chattering reduction mechanism depicted in Fig.(3) are applied on the infusion rate of propofol to adjust the BIS value. To validate the robustness of the controller, disturbance has been added to the system during the hypothetical surgery. Moreover, the performance of the proposed controller is compared with the adaptive type-II fuzzy variable structure control system.

Communication Network. The control commands are applied to the system

through a communication network which works ideally, without packet loss or delay. The network rate and frame/message size are set to 240Kbps and 80bits, respectively. Hence, the average rates of sending control signals and reading samples from the output sensor are both 3000/s.

Patient Model. Characteristics of patients are presented in Table 1 [40]. For each patient, the biometric parameters given in Table 1 are substituted into Eq. (2) and Eq. (3). The PK-PD model presented in Eq. (1) can be obtained accordingly. Moreover, the BIS index is calculated using Eq. (4). Notice that $u(t)$ is the propofol infusion dose which will be defined by the control system. The control input commands are applied to the system through the communication network. The target BIS is 50.

Simulations. Simulations have been carried out on four patients by ap-

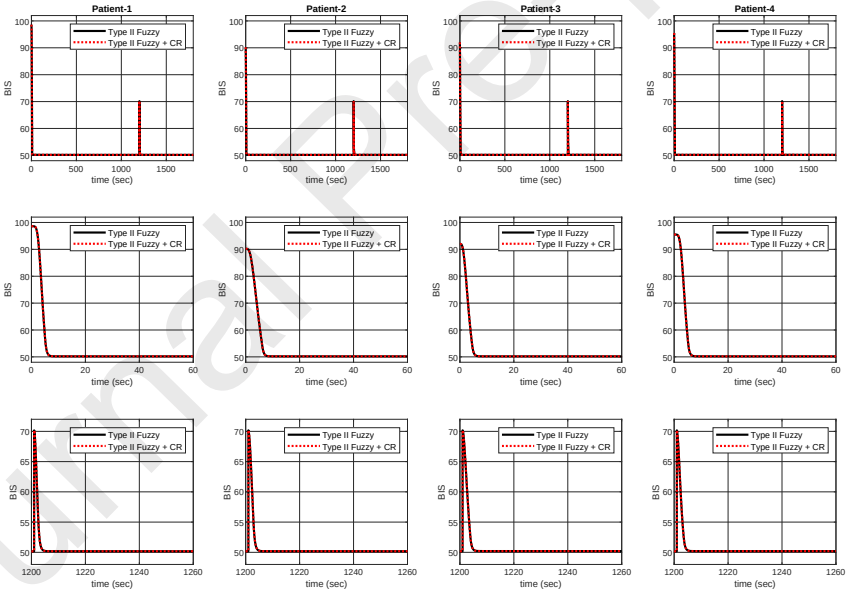

Figure 4: BIS trajectories of four patients when applying 1)the adaptive type-II fuzzy variable structure control system, and 2)the adaptive type II fuzzy variable structure control system plus AI-enabled chattering reduction. The first row shows the signal variations during the monitoring time. In the second row, the focus is on the transition time after propofol injection while the third row demonstrates the BIS variations after a disturbance occurs at $t = 1200s$

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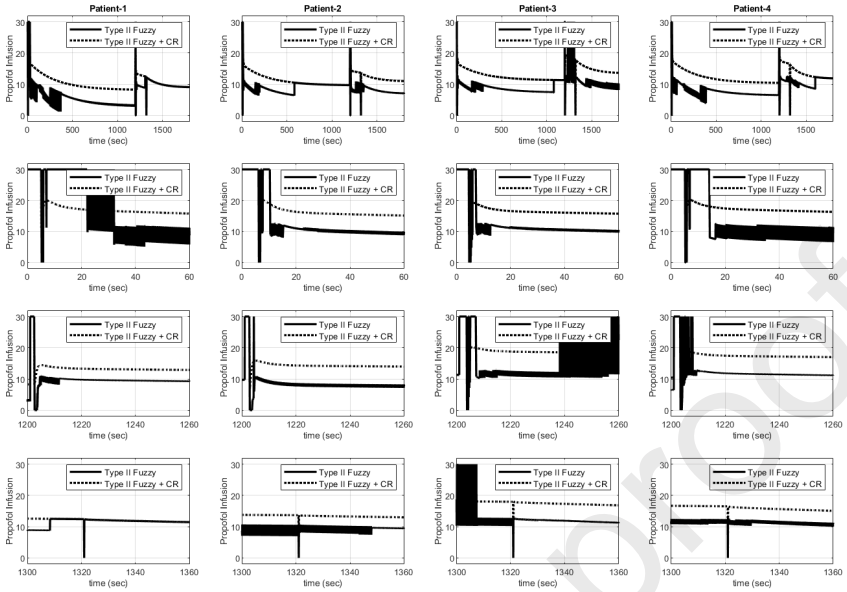

Figure 5: The propofol infusion dose obtained by using 1) the adaptive type-II fuzzy variable structure control system and 2) the adaptive type II fuzzy variable structure control system plus AI-enabled chattering reduction for four patients. The first row shows the signal variations during the monitoring time. In the second row, the focus is on the transition time after propofol injection. The third row demonstrates the propofol dose after a disturbance occurs at $t = 1200s$. The last row depicts the signal after removing the disturbance at $t = 1320s$.

plying the control input provided by the control systems, which have been 1) adaptive type-II fuzzy variable structure control system plus AI-enabled chattering reduction, 2) adaptive type-II fuzzy variable structure system, 3) variable structure control system plus AI-enabled chattering reduction.

First, the performance of the proposed method is compared with that of the adaptive type-II fuzzy variable structure control system (i.e. comparison between the control methods 1 and 2). It is important to investigate the effectiveness of the AI-enabled chattering reduction part. This is because the signal of infusion dose should be smooth enough for propofol to be injected to patient.

Then, a comparison between the classic robust control and the proposed method will be done to highlight the advantages of the new one (Comparison between the control methods 2 and 3). In the implementation of the variable structure control, a saturation function is used instead of the sign function writ-

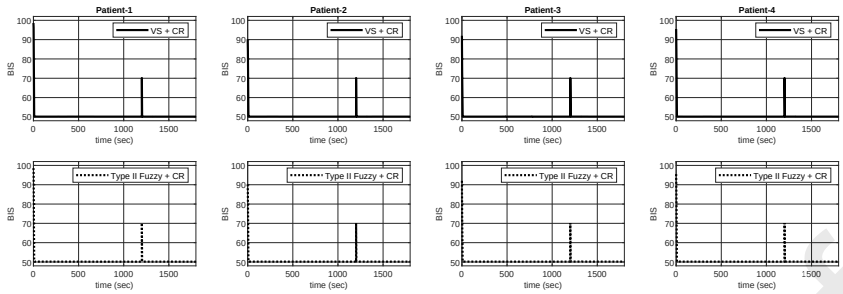

Figure 6: The BIS trajectories for four patients when applying 1) the variable structure control plus AI-enabled chattering reduction, 2) the adaptive type-II fuzzy variable structure control system plus AI-enabled chattering reduction. The first row shows the signal variations during the monitoring time when a robust control is applied. In the second row, the BIS signal is presented when the proposed method is applied. To investigate the performance and robustness of both control methods, a simulated disturbance is added at $t = 1200s$.

ten in the equations to reduce the chattering of the input signals. Moreover, the designed artificial neuron helps the controller to further reduce the chattering.

To simulate realistic conditions during a surgery, a disturbance is added at $t = 1200s$. The control parameters are as follows: $\delta = 2$, $k_v = 20$, k_o=50, $\delta_o = 0.5$, $\alpha = 0.1$, $\zeta = 1$, $\gamma_f = \gamma_g = 10^{-5}$, , $\eta_f = \eta_g = 10^{-9}$. Notice that $\rho = [\alpha_h, \beta_h, \phi]^T$, ζ_f and ζ_g are adaptively adjusted during the process. Simulations were done in SIMULINK of MATLAB software on a computer whose processor was Core i7-7600U CPU @2.80GHz.

In Fig. 4, the BIS trajectories are shown for each patient by applying the control methods 1 and 2. The control inputs (propofol infusion doses) corresponding to the depicted BIS trajectories are illustrated in Fig. 5. In Fig. 4, the first row shows the signal variations over the monitored period. In the second row, the focus is on the transition time after propofol injection while the third row demonstrates BIS variations after the disturbance occurred at $t = 1200s$. Fig. 5 depicts the propofol infusion signal. Obviously, the signal of the proposed method is smoother than that of the other method.

Fig. 6 illustrates the BIS trajectories for four patients when the proposed method and the variable structure control method are employed. The propofol infusion doses shown in Fig. 7 are applied by the proposed method and the

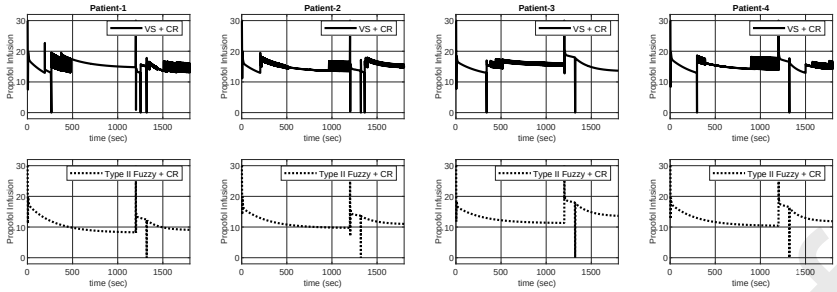

Figure 7: Propofol infusion dose obtained by using 1) the variable structure control plus AI-enabled chattering reduction, 2) the adaptive type II fuzzy variable structure control system plus AI-enabled chattering reduction for four patients. The first row shows the signal variations during the monitoring time when the variable structure control is applied. In the second row, the proposed control method is used. A disturbance has occurred at $t = 1200s$.

variable structure control. As mentioned before, since the sign function generates more fluctuations, we employ a saturation function to create a soft signal. Obviously, the proposed method has outperformed its competitor.

Regarding Fig. 4 and Fig. 6, the BIS obtained by the proposed control method is adjusted to its target even though the patient is in presence of disturbances. The control error converges to zero. According to Fig. 5 and Fig. 7, it is obvious that the control input produced by the adaptive type-II fuzzy system plus AI-enabled chattering reduction is softer than the ones made by the two other control methods.

Simulation results indicate the capability of the proposed control scheme to regulate patients' BIS indices during surgery. The proposed control scheme outperforms the conventional control systems in terms of robustness and output smoothness.

6. Conclusion

In this paper, in the context of artificial intelligence of medical things, we proposed a remote drug delivery system to control the depth of anesthesia during surgery. The control system is designed using nonlinear robust control and adaptive type-II fuzzy systems. A computer network relays the messages ex-

changed between the designed control system and the drug infusion pump. The proposed networked drug delivery system is evaluated on PK-PD patient models. The contribution of the proposed method can be summarized as follows: (1) Providing AI-enabled IoT systems in healthcare monitoring and control, (2) Remote tuning of drug infusion through network channels, (3) Designing an adaptive intelligent control system using a classic robust control system, fuzzy systems, and an artificial neuron, (4) Employing the type-II fuzzy system to provide an intelligent estimator for patient model uncertainties. Our results confirm adaptivity and robustness of the proposed strategy, especially when the models are exposed to the uncertainties and disturbances that may happen in an operation room.

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