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Performance Comparison of Anesthesia Using Conventional PI And Fuzzy Logic Based Controller

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Abstract

One of the most important aspects during any surgical intervention is that the anesthetist involved in the procedure must ensure that after the surgical stimulus, the transition between the fully anesthetized state and the awake state is very smooth. This can only be achieved when the amount of anesthetic and analgesic drug to be used in combination is accurate, so as to avoid a situation of overdosing or under dosing. This ideal combination gives rise to a situation known as Depth of Anesthesia (DoA). Anesthetists consider the human body to be divided into a number of compartments. This assumption has given rise to the concept of compartmental models, which are most commonly used in practice. Compartmental models are actually a combination of various homogenous interconnected subsystems known as compartments which ensure that transfer of materials like drugs and other fluids are carried out according to the laws associated with transfer, accumulation, and elimination between the compartments. These models form the backbone of biological and physiological sciences as they play a key role in understanding these processes. In this paper, a nonlinear three compartment model, which is known as the PK-PD patient model is used. A rule based fuzzy PI controller in Matlab is then designed for this compartmental model to close this loop. The proposed framework guarantees stability of the closed-loop system associated with the plant. In addition, the controller ensures that the physical system states remain unaltered in the state space form. The efficiency of the system is then tested for the optimum quantity of the anesthetic drug propofol and an analgesic remifentanil to be administered, so as to maintain a desired constant level of depth of anesthesia.

Index Terms— Compartmental model, Closed loop system, Depth of Anesthesia (DoA), Fuzzy Controller, PK-PD Patient Model.

1. INTRODUCTION

Anesthesia can be described as a temporary reversible phase from unconsciousness to consciousness during any surgical stimulus ensuring lack of memory of any of the pain or trauma undergone during the surgical procedure [1]. General process of anesthesia can be divided into the phases of induction, maintenance, emergence, and recovery [2]. The depth of anesthesia (DoA) represents the level of consciousness [3], which is to be controlled during the process of anesthesia spanning over a number of control targets such as steady error, settling time, and overshoot. The process of anesthesia needs to be controlled and closely monitored so as to avoid a situation of overdosing or under dosing of the anesthetic drug. In general, control strategies can be categorized into two classes: open-loop control and closed-loop control. In open-loop control, anesthetists manually adjust the drug dosage based on his/her knowledge and experience, so as to maintain the DoA. In closed-loop control, the drug dosage is automatically adjusted according to some predefined and fixed indices of DoA, which ensures that the infusion of the anesthetic drugs is continuously controlled and responsive based on the ever changing requirements of the patient. Closed-loop control also incorporates in itself inter patient variability that arises due to difference in response to the same drug by different individuals[4]. Despite of its advantages, the stability of closed-loop control needs to be ensured as it is an automated process without any supervision [5].

1.1 The propofol – Remifentanil combination

Earlier a large dose of an anesthetic agent (propofol) was used to achieve anesthesia. But nowadays, small anesthetic drug quantities are used in combination with an opioid (remifentanil) to achieve balanced state of anesthesia, while the side effects are reduced. A combination of intravenous agents like propofol and remifentanil in boluses results in strong effects that last for short duration of time. But these types of interactions give rise to significant interactions. Out of the various types of interactions possible like additive, antagonistic etc., the most favored interaction is the synergistic type, which signifies greater resulting effect than just superposition [5].

For proper representation of the control system involved in anesthesia, a three compartment Pharmacokinetic (PK) and Pharmacodynamics (PD) model is used. Main difficulties involved in such a modeling procedure are the determination of PD model parameters. It is customary that the parameters of PK and PD models be determined beforehand. For the PK model, parameters are estimated depending on sex, age, and weight of patients. But on the other hand, for the PD model, it is not possible to estimate the parameters for certain patient. As such in this context, the controller which controls the DoA, needs to be robust [6]. In this paper a closed loop control system using a fuzzy controller has been designed for anesthesia control. Closed-loop systems are designed to automatically achieve and maintain the desired output condition by comparing it with the actual condition. It does this by generating an error signal which is the difference between the output and the reference input. In other words, a “closed-loop system” is a fully automatic control system in which its control action being dependent on the output in some way. Once the infusion of the anesthetic drug has been controlled using the closed loop control theory, the bispectral

(BIS) index [7] is an extensively accepted index to measure the DoA It is a dimensionless parameter measured in a scale from 0 to 100, where a value of 100 signifies awake state, 80 to 100 shows sedated state, 60 to 80 signifies a moderate hypnotic level and 40 to 60 indicates deep hypnotic level [8]. The process of closed-loop control of anesthesia is tested on the basis of: stability-which is the basic control objective of any controller; robustness-which accounts for the uncertainty of PD model parameters, and adaptiveness-which ensures that the controller is adaptive to different patients. Commonly used controllers include PID controllers, model-based controllers, and knowledge-based controllers [10]. The model-based controller is a reflection of the patient's current pharmacological behavior. For this reason, the patient model needs to be updated continuously. In this paper the Fuzzy logic Controller (FLC), which is used in the closed loop structure is based on Fuzzy Logic Theory proposed by L. A. Zadeh in 1965. Fuzzy logic is the logic which is used in fuzzy controllers and it stands out amongst all other controllers as it mimics human thinking and natural language much better than any other traditional logical systems. As such during the past several years, fuzzy control has emerged as one of the most active area for research in the applications of fuzzy set theory. It provides an artificial but appropriate platform of capturing the uncertain nature of the real world [11].

2. DEPTH OF ANESTHESIA (DOA) MODEL

A model can be best understood as a concept of reality, which accounts for those properties of a system or a process that are inherent to the function of the model [12]. Models are used in anesthesia to identify the various physiological, pharmacological and physical processes that take place during general anesthesia. The distributions of anesthetic medications in the body are dependent on transport and metabolic processes [13]. Diverse models have been proposed for modeling the drug effect, such as experimental models, compartmental models and physiological models. Out of all the modeling options available, the standard modeling paradigm that has been commonly used to describe the relationship between anesthetic input and patient output is that of compartmental models [14]. Compartmental models are formulated based on the minimum number of compartments that effectively fit the observed data. Physiologically based models are more near to the actual representation of drug kinetics. In this paper a three compartment PK model and a corresponding PD model has been used[15]. The PK model is dependent on the input-output data sequences. An input drug is administered and the time course is measured by taking blood samples. The infusion time of the bolus is neglected and therefore the response is an approximation of an impulse response. The plasma compartments are used as central compartment (compartment 1) [16]. The purpose of the effect-site concentration is only to account for the time lag between drug concentration and drug effect [8]. Since remifentanil does not contribute significantly to the effect site, as such Ce is assumed to be given and as such the modeling is then done only for propofol.

The DoA model is divided into three main parts (Fig. 1). The PK model describes how the hypnotic drug (propofol) administered with an infusion rate r spreads through the blood and tissue resulting in a plasma concentration Cp. The second part, the

effect compartment, models the transport of a certain plasma concentration Cp to the brain resulting in a concentration effect Ce. Finally the third part, the interaction model, describes the actual effect the drug has on the body measured by BIS.

2.1 Pharmacokinetic (PK) model

Pharmacokinetics is the affect of the body on the administered drug, which ranges from the administration of the drug to its absorption, metabolism and its excretion from the body. As such pharmacokinetics can be expressed as the relation between blood plasma concentration Cp(t) to the administered dose I(t). The main purpose of the PK model is to predict the blood plasma concentration of the drug. This is done on the basis of the study of the absorption, distribution and the metabolism and finally the elimination of the drug from the body. The PK model relates the blood plasma concentration Cp(s) to the drug infusion I(s).

$$\mathrm{PK(S)} = \frac{\mathrm{Cp(s)}}{\mathrm{I(s)}} \tag{1}$$

When the drug is administered in the body, then the blood plasma level increases. This process is known as absorption and involves a time delay[9]. This time delay process can be expressed as :

$$\mathrm{Cp(t)} = \mathrm{Xe^{-At}} + \mathrm{Ye^{-Bt}} + \mathrm{Ze^{-Ct}} \tag{2}$$

Where Cp(t) is measured in microgram/milliliter, A is the rate constant of the distribution phase is the rate constant of the distribution phase, and C is an additional constant that is associated with the dynamics distribution phase and can be used if required.

$$\mathrm{PK(s)} = \frac{\mathrm{Cp(s)}}{\mathrm{I(s)}} = \frac{\mathrm{X}}{\mathrm{s+A}} + \frac{\mathrm{Y}}{\mathrm{s+B}} + \frac{\mathrm{Z}}{\mathrm{s+C}} \tag{3}$$

Both infusion and elimination of the anesthetic drug takes place from the central compartment as the carrier of the drug is blood plasma (Fig. 2). Infusion is denoted by I and the elimination takes place according to the rate constant k_{10}. After infusion, the drug is distributed to Compartment 2 and Compartment 3 according to the rate constants k_{12} and k_{13}. As such the concentrations of both the compartments increases until any one of them have the same concentration as the central compartment. When this condition is achieved, the process of distribution stops. The mathematical expression pertaining to the above arrangement can be represented as:

$$\begin{bmatrix} \dot{c_1} \\ \dot{c_2} \\ \dot{c_3} \end{bmatrix} = \begin{bmatrix} -k_{10} - k_{12} - k_{13} & k_{21} & k_{31} \\ k_{12} & -k_{21} & 0 \\ k_{13} & 0 & -k_{31} \end{bmatrix} \begin{bmatrix} c_1(t) \\ c_2(t) \\ c_3(t) \end{bmatrix} + \begin{bmatrix} \frac{1}{v_1} \\ 0 \\ 0 \end{bmatrix} \mathrm{I(t)} \tag{4}$$

If the plasma concentration of the central compartment becomes equal to the concentration of compartment 1, then

$Cp(t) = C_1(t)$

In simplified form:

$$PK(S) = \frac{Cp(s)}{I(s)} = \frac{(s+k_{21})(s+k_{31})}{v_1(s+A)(s+B)} \quad (5)$$

2. 2 Pharmacodynamic (PD) model

Pharmacodynamics can be described as the effect of the drug on the body which involves both the biological and physiological aspects. When two drugs with different schemes of action but inherent similar therapeutic effects are used in combination, it results in a cumulative effect.

PD model represents the observed effect of the drug to the drug plasma concentration.

$$PD(s) = \frac{O(s)}{Cp(s)} \quad (6)$$

The above relation (6) can be observed in the effect site. The effect site is in turn related to the DoA (Depth of Anesthesia) by the Hill Equation:

$$E(t) = E_0 - E_{max}\left[\frac{Ce^{\gamma}(t)}{ce^{\gamma}(t) + Ec50^{\gamma}}\right] \quad (7)$$

Where E_0 denotes the awake state and is allotted a value of 100, E_{max} denotes patient sensitivity to the drug, Ce is the concentration of the effect site, and γ represents steepness of the curve:

$$c_e(s) = \frac{1}{\frac{1}{k_{e0}}s+1} c_p(s) \quad (8)$$

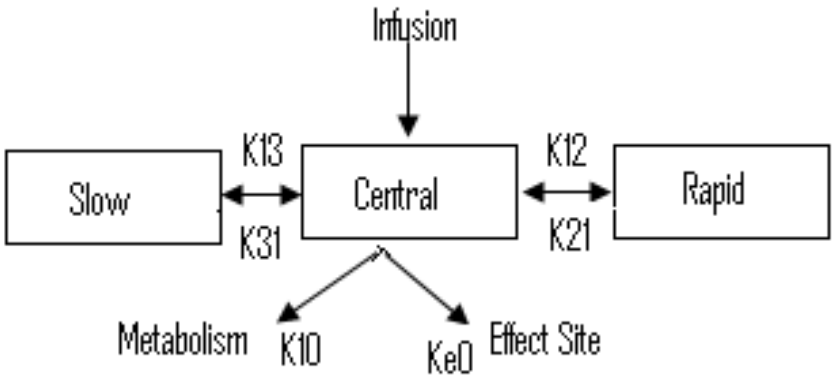


Fig. 1: The Compartmental Model of DoA

3. CLOSED-LOOP CONTROL OF ANESTHESIA

In closed-loop controlled anesthesia, feedback from a measure of the clinical effect is used to continuously adjust drug infusion rates. Anesthetic drugs are delivered at a variable rate that is personalized to the individual patient. The aim is to provide greater hemodynamic and respiratory stability, more stable depth of anesthesia, the ability to predict recovery and to administer a lower total dose of drug. Computer controlled, or automatic, drug delivery is the process of administering a therapeutic regime to a patient with computer assistance for calculation of optimal dose and delivery schedules. Computer control can improve drug therapy by reducing drug usage and costs, by permitting health care staff to work more efficiently and to provide better standard of care, by allowing the safe use of drugs that are difficult to administer, and by compensation for human failings with computer strengths, such as unlimited attention span and patience, and capacity for quick, accurate and redundant calculation. Our goal is to develop an automatic control system for anesthesia and to demonstrate its efficacy, safety and benefits in an operating room.

4. PI CONTROLLER

A PI Controller should be able to account for the difference between the current plant output and the desired value. If this difference is found to be large, then the system has to undergo a lot of control action and vice-versa.

So P*(desired-current) where P is the constant proportional gain set by the system architecture. The P should be so chosen so that the set point is reached as soon as possible. This is achieved because an appropriate value of P ensures that overshoot, undershoot and oscillation are minimized.

But a controller incorporating only P factor will settle to a value that is far from the desired value. This problem is compounded when each individual error tends to remain below the threshold value by the proportional term. The factor which drives the plant towards the set point is known as the integral term. The integral term is the sum over time and in case of anesthesia control it is the sum of all past errors involved in the plant errors.

$I=\Sigma$ (desired value-current value)

Even though the value of I is small, but a persistent error will result in the sum error to become a large value and as such the integral value will become the cause for a change in the drive signal.

5. MULTIVARIABLE FUZZY LOGIC CONTROLLER

In 1965, Prof. L. A. Zadeh, the founder of fuzzy logic laid the foundations of fuzzy set theory [17], as a tool to deal with the imprecision of any practical systems. The decision making process involved in the practical world takes place in an environment in which the constraints and the consequences involved in any process or activity are not known beforehand[18], [19]. This "imprecision" or fuzziness forms the core of fuzzy logic applications. Fuzzy sets were thus proposed as a generalization and

extension of the conventional set theory. As a result, fuzzy logic remains as a popular choice amongst all conventional controllers to be used in any closed loop process[20]. Fuzzy logic control (FLC) theory accounts for the vagueness and uncertainty of any physical process. FLC allows accommodating all non-precise or ill-defined components of a system or a process. It can be so designed so as to roughly emulate the human decision making process where conclusions are drawn from expert knowledge and experience. Since FLC is nonlinear and adaptive in nature, so it ensures a robust performance under any condition involving parameter variation. Any controller using a fuzzy logic technique actually reflects the understanding of human being of the system's behavior and is based on qualitative control rules which are involved in the system. These rules are in practice simple linguistic rules based only on IF…. THEN statements. The key features of any FLC are as follows:

a) Fuzzy controllers have the ability to cover wider range of operating conditions and can also operate in environments having noise and disturbance of different natures; as such they are considered to be more robust than PID controllers
b) Fuzzy controllers are cheaper to develop as compared to other controllers used for the same purpose.
c) Since fuzzy controllers are rule based; they are easy to understand and modify based on the ever changing requirements of the imprecise working environment.
d) FLC provides systematic efficient frame work for incorporating linguistic fuzzy information which can later be deciphered by human experts.
e) As it is a rule based operation, any reasonable number of inputs can be processed and numerous outputs can be generated.
f) Fuzzy controllers are non-linear in nature and as such can be used in dynamic situations where there is a constant need to change the parameters involved in the system.
g) A fuzzy controller can be designed so as to roughly mimic the human deductive process i. e., the process whereby one successively infers conclusions from their knowledge.

The functional architecture of the fuzzy system is composed of four basic elements; a fuzzy knowledge base, an inference mechanism, a fuzzification interface and a defuzzification interface. The basic block diagram of fuzzy controller is given in Fig. 2, where a fuzzy controller is embedded in a closed loop control system. The plant outputs are denoted by $y(t)$, its inputs are denoted by u(t), and the reference input to the fuzzy controller is denoted by $r(t)$.

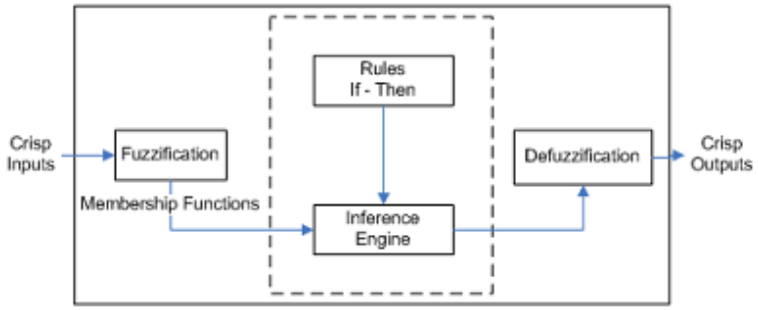


Fig. 2: Block diagram of fuzzy logic controller

A) **The fuzzification interface**

It involves the following functions:

1) measures the values of input variables,
2) Performs a scale mapping that transfers the range of values of input variables into corresponding universes of discourse,
3) Performs the function of fuzzification that converts input data into suitable linguistic values which may be viewed as labels of fuzzy sets. The number of fuzzy sets defined in the input discourse and their specific membership functions define the fuzzification interface design. There are many types of different membership functions and their choice for a specific problem is not unique. The initial form of the membership functions can be obtained by using expert considerations or by clustering the input data.

B) **The rule base**

Comprises of the knowledge of the application domain and the attendant control goals. It consists of a "data base" and a "linguistic (fuzzy) control rule base:"

1) The data base provides necessary definitions, which are used to define linguistic control rules and fuzzy data manipulation in an FLC.
2) The rule base characterizes the control goals and control policy of the domain experts by means of a set of linguistic control rules.

C) **The decision making logic**

Known as the kernel of an FLC; it has the capability of simulating human decision making based on fuzzy concepts and of inferring fuzzy control actions employing fuzzy implication and the rules of inference in fuzzy logic.

D) **The defuzzification interface**

Performs the following functions:

1) A scale mapping, which maps the range of values of output variables into the corresponding universes of discourse,
2) Defuzzification, which gives a non-fuzzy entity from an inferred fuzzy control action.

The defuzzification method used in this paper is the centroid method.
This method selects the output value corresponding to the centroid (center of gravity) of the output membership function as the crisp value for an output. The defuzzification interface takes into account the conclusions reached by the fuzzy inference mechanism and provides a crisp value as an output. Overall, the fuzzy control design methodology, which primarily involves designing of the specifications of the rule base, provides a heuristic technique to construct non-linear controllers, and this seems to be one of its main advantages.
The three variables of FLC: the error, change in error and the change in control signal i. e. change in duty ratio have seven membership functions (MF) each. A triangle shaped membership function has been used for fuzzy logic controller design. The fuzzy variables are expressed by linguistic variables such as PL for positive large, PM for positive medium, PS for positive small, Z for zero, NS for negative small, NM for negative medium, and NL for negative large. The linguistic dimensions for the MF‟s are the same for the three variables. The basic fuzzy partition of membership functions for three variables is shown in Fig. 4. The membership functions for both inputs and outputs of the controller are defined on the common interval [-1, 1].

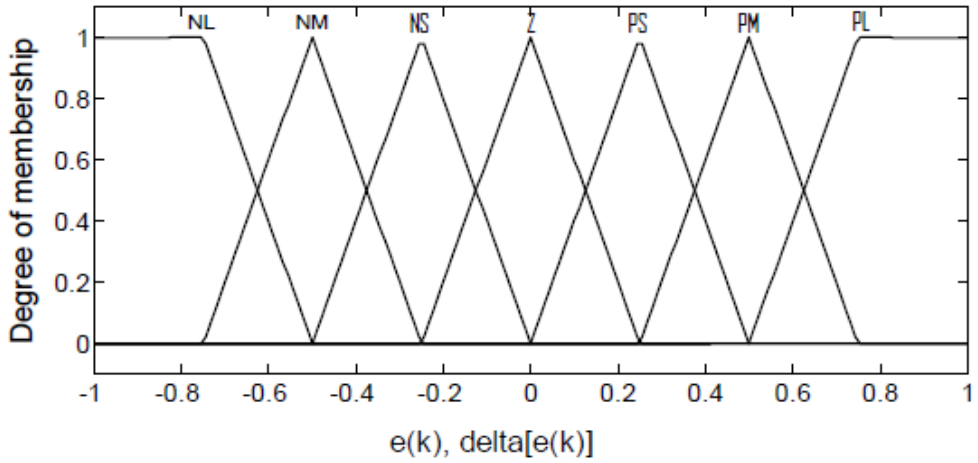


Fig. 3: Membership function for e(k), Δe(k) and Δu(k)

The rules set are generated based on the knowledge and requirement of the system. The inference method used is Min-Max method which is basic and simple. The output membership function of each rule is given by the MIN operator, whereas the combined fuzzy output is given by the Max operator. The centroid defuzzification method generates the crisp output value from the centre of gravity of the output membership function. The membership functions of error " $e(k)$ ", change in error " Δe(k) " and change in output"$\Delta u(k)$ " are shown in Fig. 3.
Basically, defuzzification is a mapping from a space of fuzzy control actions defined over an output universe of discourse into a space of non-fuzzy (crisp) control actions.

It is employed because a crisp control action is required as an output. A defuzzification strategy is aimed at producing a non-fuzzy control action that represents the best possible distribution of an inferred fuzzy control action. In this paper the mean of maximum and the center of area (COA) or center of gravity method is used. This method obtains the center of area ($\bar{x}$) occupied by the Fuzzy set.

5. 1 Fuzzy Controller Developed For Anesthesia

In clinical practice anesthesiologist have to process and initiate control action pertaining to a large number of hemodynamic and respiratory variables along with clinical signs to ensure an adequate level of hypnosis and analgesia. In order to get a more methodical and accurate system of anesthesia in place, a closed loop is generated [21]. A major concern in the development of such a closed loop system is that, the majority of the used drugs operate not only straight forward to the desired effect but also have varying effects on different patients. For example the hypnotic drug propofol affects not only on hypnosis level but also increases the analgesia level[22]. The design of such drug infusion controllers has often been based upon simplified linear models.

The automated management of hemodynamic variables in patients with critical conditions, in the operating room, using the optimum amount of anesthesia is the goal of this research paper. Earlier automated drug infusion was done using an open loop control approach, which had to be carried out by a physician, and required human intervention to respond to changes in the patient's condition [23]. Because of these complexities as well as the significant patient to patient dynamic uncertainties and the presence of time variations in a given patient's response to drug dosages, a more comprehensive and an adaptive controller like a Fuzzy rule based Controller has been considered [24].

Since fuzzy controller design remains a fuzzy process due to the fact that analytic design technique has still not been much explored as compared to well developed linear control systems. As explained earlier the standard procedure includes of the three main parts Fuzzification, Fuzzy logic rule base, and Defuzzification., the actual validation procedure requires a more comprehensive nonlinear model which has been used in this paper, so as to imitate the real time system.

The controller used considers the following fuzzy terms-

NB: negative big
NM: negative medium
NS: negative small
NO: negative zero
Z : zero
PO: positive zero
PS: positive small
PM: positive medium
PB: positive big

When a fuzzy controller runs, a numerical error e(k) and a numerical rate of change of error $\Delta e(k)$ are first fuzzified and respective values are assigned to membership

functions following in the universe of discourse. Then the rate of change of controller output is calculated from the membership values of error and rate of change of error by applying the rule base table I.

A minimum combined effect concentration of propofol and remifentanil is desired during the entire duration of the surgical procedure to ensure unconsciousness. The minimum values lies close to 2225ng/ml for propofol and 3. 0ng/ml for remifentanil. The multivariable fuzzy logic controller is dependent on the linguistic rules that in turn interact with the rule bases for change in concentration of remifentanil and a fuzzy PI controller for change in concentration of propofol. The inputs are error and change of error while the output is change in the concentration of propofol. The controllers rule base is given in Table 1.

TABLE 1. Rule Base for fuzzy PI Controller for Propofol infusion

Error	Change in Error				
	NB	NS	ZE	PS	PB
NB	NB	NB	NB	NS	ZE
NS	NB	NS	NS	ZE	PS
ZE	NB	NS	ZE	PS	PB
PS	NS	ZE	PS	PS	PB
PB	ZE	PS	PB	PB	PB

5. 2 Fuzzy Rule-base for remifentanil

The remifentanil rule base are fragmented as rule-base1 and rule-base2, which shows the desired changes in the remifentanil infusion rates so as to compensate the change in error component. In Rule-base 1, the stimulus is graded on a scale of 0 to 1, where values below 0. 25 are considered to be negligible as these values have very little effect on the vital parameters of the patient.

The remifentanil rule-base predicts the increment in the remifentanil infusion rate when the DoA is low in the presence of stimulus. This required change in the remifentanil infusion rate is normalized in the range of [0, 1]. the maximum changes were observed in the value of 0. 02μg/kg/min.

TABLE2. Rule–Base1 for changes in infusion rate of Remifentanil.

Stimulus	Change in error			
	Negative	Zero	Positive Small	Positive Big
Low	Small	Small	Medium	Big
Medium	Small	Medium	Medium	Big
High	Medium	Big	Big	Big

The remifentanil rule-base 2 evoked in case the DoA is very deep but is accompanied by stimulus, thus increasing the infusion of the remifentanil concentration becomes an

absolute necessity. As in the case of rule-base 1, the stimulus level and the change in error are used to determine the change in the infusion of remifentanil. In rule-base 2, remifentanil is increased due to its analgesic properties, and since the DoA is deep so even the slightest changes are very prominent as compared to rule-base 1.

TABLE3. Rule–Base2 for changes in infusion rate of Remifentanil.

Stimulus	Change in error			
	Negative Big	Negative Small	Zero	Positive
Low	Small	Small	Small	Small
Medium	Small	Small	Medium	Medium
High	Small	Medium	Medium	Big

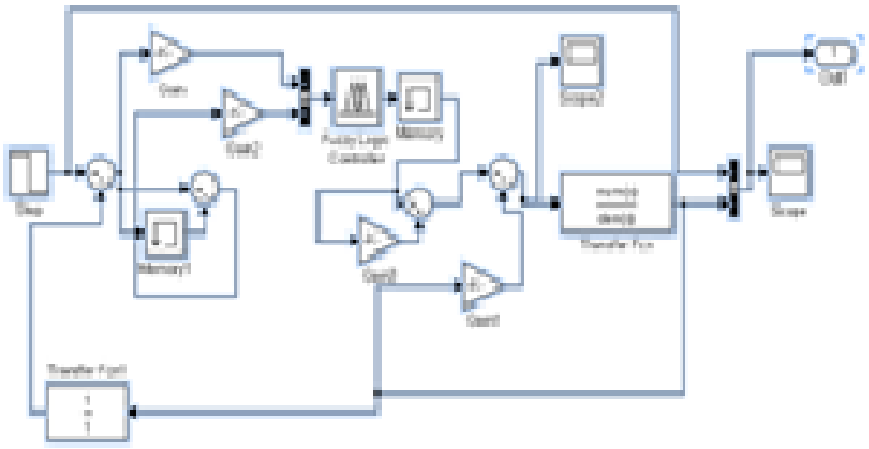


Fig. 4:Block diagram of control system for DoA in Simulink.

The obtained fuzzy model was placed in the controller architecture as presented in Fig. 5. The fuzzy controller was able to provide good control performance [25], [26], [27]. It shows the effect of the prediction horizon on the performance of the controller under noise-free conditions. If the result which is obtained is not accurate then the number of iterations can be increased. The patient model incorporating the fuzzy controller is shown in Fig. 4.

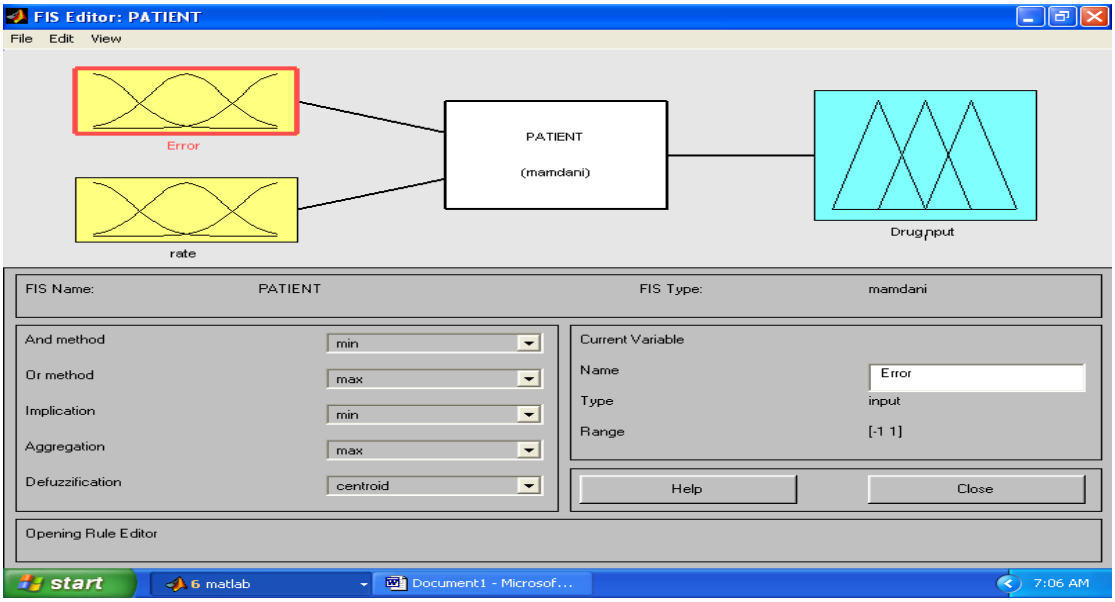
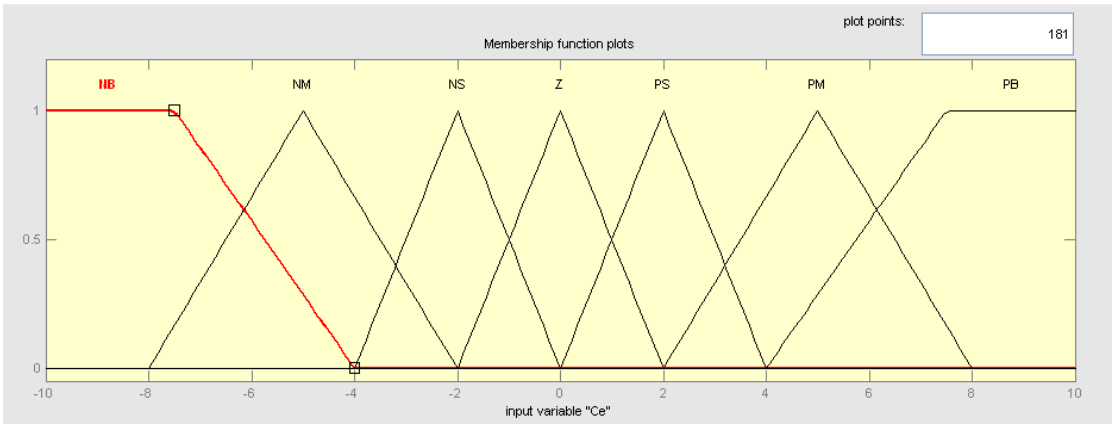
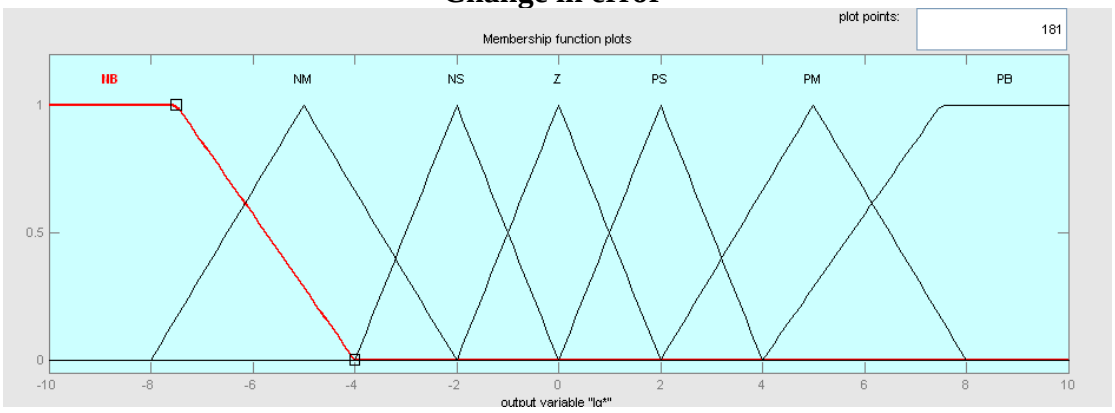


Fig. 5: FIS Editor for patient model incorporating Fuzzy Controller



Change in error



Output variable

Fig. 6: Membership Function for patient model incorporating Fuzzy Controller.

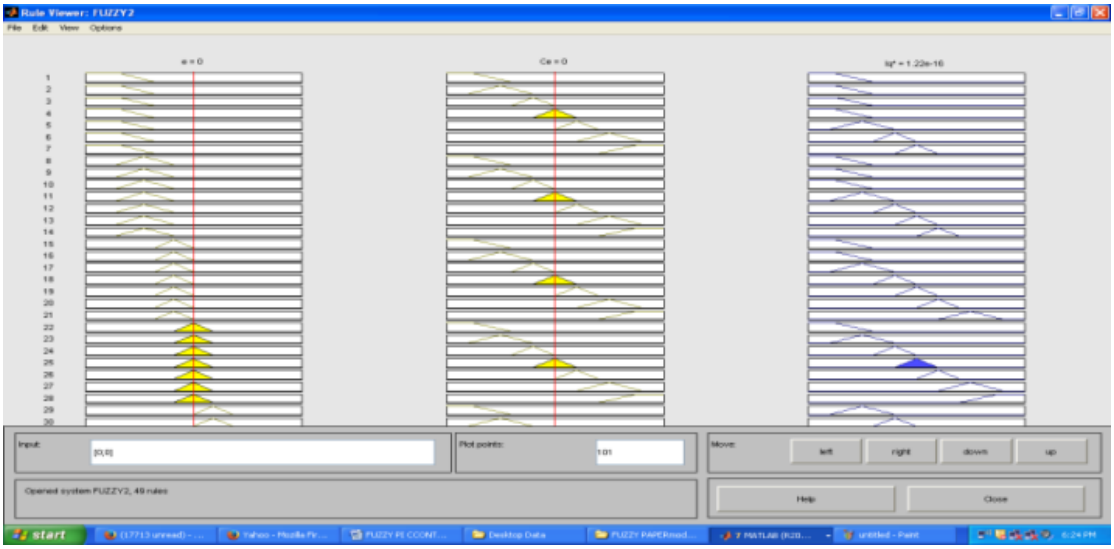


Fig. 7 :Rule Viewer for patient model incorporating Fuzzy Controller.

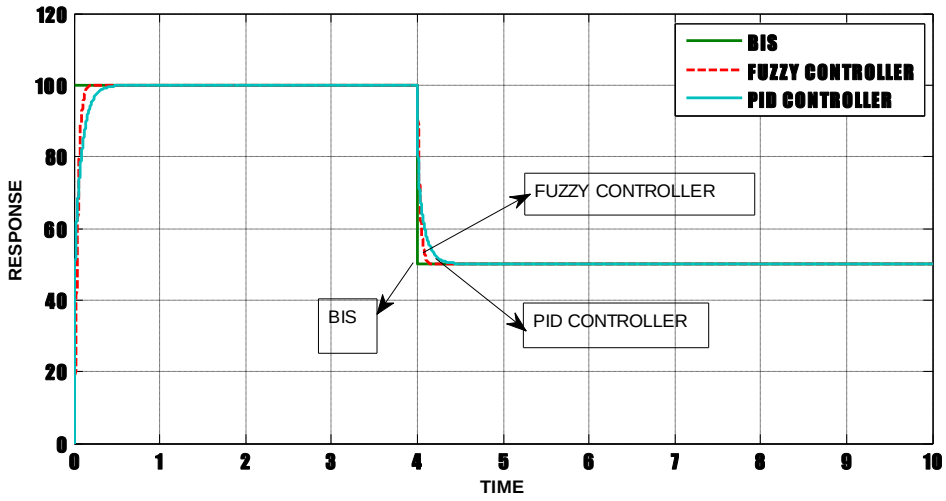


Fig. 8: Controller Response for patients in terms of BIS reading.

The above figure shows that the BIS is affected more by variations in PD parameters than the PK parameters. The PK parameters are categorized into three levels of minimum, average and maximum. Any change in volumes of the three compartments hardly affects the performance of the controller[28] [29]. In the PD parameters, higher values of EC_{50} gives an indication that further induction of drug is required to maintain the same DoA level whereas a smaller value of EC_{50} indicates sluggish response. Whereas in the PD parameters, lower values of EC_{50} indicates the need of a smaller amount drug to get the same DoA level, and higher indicates that the response obtained will be very rapid[13] [30].

6. INTERACTION AND RESPONSE SURFACE

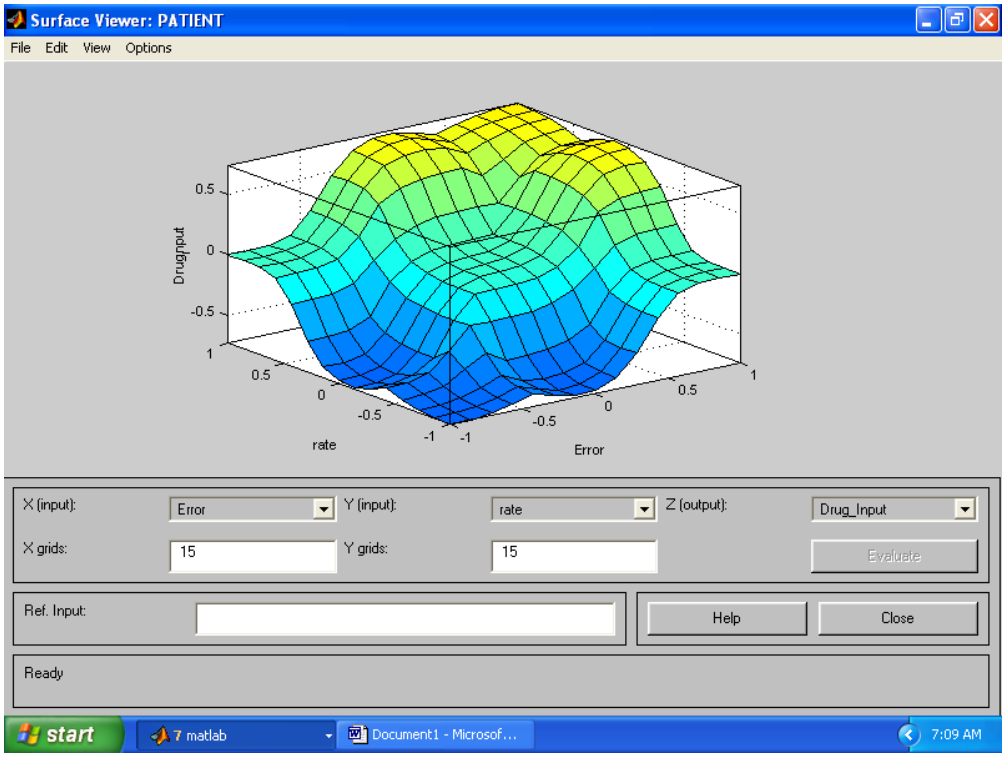


Fig. 9:Response surface of drugs used to control the process

Propofol and remifentanil are mostly given at a constant rate so that a constant plasma level is maintained with one of the drugs adjusted up as needed for additional analgesia/sedation or drop in anesthetic effect if less respiratory depression is important. The nonlinear shape of the response surface results in marked differences clearly pointing that

(1) Increasing propofol has little effect but adding remifentanil however has a marked-synergistic-effect.

(2) Increasing remifentanil increases regularly with only some potentiating by the addition of propofol. The response surface plot indicates that it is safer to titrate the propofol dose with a constant remifentanil background if more or less sedation is needed, but if less respiratory depression is required, then remifentanil would required to be reduced. The plot shows

(1) The synergistic interaction between propofol and Remifentanil on the 50% probability to “wake-up” after anesthesia.

(2) Whether consciousness has been regained or not, ventilation improves best by reducing the remifentanil concentration.

(3) Without the addition of propofol, remifentanil concentrations up to 2 ng/ml cause only limited respiratory depression and may be applied for postoperative pain relief. Furthermore, especially for rapidly acting drugs, such as

remifentanil and propofol, the degree of non steady-state respiratory depression may be dependent on the rate of drug infusion. When combined, the respiratory effects were strikingly synergistic with clinically important respiratory depression at already low doses.

7. CONTROLLER PERFORMANCE

The model used in this paper continuously updates the amount of anesthesia used in the system. Each iteration ensures that the hemodynamic variables are continuously updated. Thus the controller intervenes before the stipulated time for the circulatory model lapses. But a high rate of intervention is desirable in case the pharmacological effects of the infused drugs are present in the loop. Alternatively, a low rate of intervention can only be permitted if any further deterioration in the hemodynamic states of the patient is not observed. The fuzzy controller used in the above arrangement takes stock of the physical parameters involved and thus initiates necessary action and adjusts the dose of the infusion drugs. At the end of every controller intervention, a new set of infusion rates is generated by the controller which forms the basis of the appropriate dosages of each drugs to be infused in the circulatory model.

8. RESULTS AND DISCUSSIONS

A multivariable fuzzy logic controller has been designed for the simultaneous administration of propofol and remifentanil, which is based on the experience and knowledge of the anesthetist and in turn translated to linguistic rules. The controller is tested on the parameters of introducing set point changes and disturbances in the form of noises in the system. The controller responded equally well under all conditions by adjusting the amount of both propofol and remifentanil as a response to DoA changes. A stable DoA can be ensured as the controller reacts to the changes in the DoA in a smooth way. The property of fast onset of remifentanil as compared to propofol allows the controller to initiate slight changes in the infusion of remifentanil as and when required. The perfect synergistic interaction between the combination of propofol and remifentanil assisted further to maintain the desired level of DoA by infusing small amount of propofol, thus guaranteeing a speedy recovery. The right combination of an hypnotic and an analgesic drug also assists the working of the controller. The above system can compliment an anesthetist by reducing his/her workload, utilizing the combination of the minimum amount of the combination of the two drugs

9. CONCLUSION

The proposed fuzzy controller used in this paper comprises of 49 rules. The mathematical model selected for this study is the PK-PD compartmental model where the PD parameters are uncertain and vary from patient to patient. The interaction between the anesthetic and the analgesic drug is synergistic in nature which can be

seen from the nature of the surface plot obtained by Matlab. The controller used in this case is found to be adaptive and robust and ensures a good set point value. The adaptiveness and ability to mimic human understanding and ensure constant and appropriate infusion rates of anesthetic drugs by the fuzzy controller proves that its performance is better that traditional PID controller and is much more reliable One of the key features of fuzzy control design is that since it has insufficient analytic methods, experienced based design is thus preferred, leaving scope to calculate optimal scaling gains for fuzzy controllers. This approach leads to better effect on the factors pertaining to performances and stability of the fuzzy control system[28]. The fuzzy controller used can also be extended to several different clinical scenarios. Since process conditions vary highly from case to case, multiple simulations should be considered. The proposed controllers are simple and intuitive, and simulations have proven their reliability and robustness.

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