Fuzzy Logic to Model the Effect of Surgical Stimulus on the Patient Vital Signs

Catarina S. Nunes*, Mahdi Mahfouf, Derek A. Linkens and John E. Peacock

Abstract-- The study of the effects of surgical stimulus on the patient vital signs is of great importance when considering the control of the anaesthetic drugs during general anaesthesia. In this article, a stimulus model is developed in order to establish the effects of the surgical stimulus on the patient cardiovascular parameters, according to the level of analgesia. This stimulus model is constructed into a Mamdani type of fuzzy model, using the anaesthetist knowledge described by fuzzy IF-THEN rules. First, the stimulus perceived by the patient is modelled, in order to reflect the analgesic action of the drug remifentanil. Finally, the change on the value of systolic arterial pressure (SAP) and heart rate (HR) is modelled so as to reflect the effect of the perceived stimulus. The stimulus model is incorporated into an existing patient model, and tested against data collected in the operating theatre. The results showed a timed-delay for SAP and HR in response to stimulus. This proved to be an adequate model, incorporating the effect of surgical stimulus reflected in SAP and HR.

Index Terms-- fuzzy logic, Mamdani models, biological modelling, anaesthesia.

I. INTRODUCTION

Anaesthesia can be defined as the lack of response and recall to noxious stimuli. This complex branch of the medical area is divided into three components: muscle relaxation, unconsciousness (depth of anaesthesia) and analgesia. Anaesthesia involves the use of three drugs, a muscle relaxant, an anaesthetic (hypnotic) and an analgesic. However, the muscle relaxant will not be considered in this research, since it has no influence on the degree of hypnosis, which is the main concern in the operating theatre. The analgesic drug is of more importance since it affects the pharmacodynamics of the anaesthetic drug and there is no clear indicator of the degree of pain. The analgesic and anaesthetic drugs are interconnected, since they interact with each other so as to achieve an adequate level of depth of anaesthesia (DOA) and analgesia [1].

Overall, general anaesthesia consists of both loss of consciousness through the action of anaesthetic drugs, and the inhibition of noxious stimuli reaching the brain through the acting of the analgesics. The anaesthetic and analgesic drugs may have different types of interactions, increasing or decreasing the effects of each drug, potentiating the different side effects or even introducing new side effects [2], [3]. The anaesthetist needs to be aware of the interactions between drugs for the safety of patients. When considering drug interactions, several aspects need to be considered, such as the properties of the two drugs, the presence of surgical stimulus and the level of DOA.

The intravenous anaesthetic drug propofol is used in combination with different opioids. In this article, only one and new analgesic is considered: remifentanil.

Surgical stimulus increases the value of systolic arterial pressure (SAP) and heart rate (HR) [4], [5]. Therefore, the value of the cardiovascular parameters is the result of the effect of the two drugs and of the surgical stimulus present. Propofol provides unconsciousness, while remifentanil provides pain relief. Remifentanil action can be viewed as a reduction on the patient's perception of surgical stimulus.

In this article a model was developed in order to establish the effect of surgical stimulus on the cardiovascular parameters, considering the level of analgesia. Such a model can be incorporated into patient models that model the cardiovascular parameters based on the drugs used. In addition, this model provides an insight into the mechanism of general anaesthesia and could be used to develop a practical guideline for the optimal drug dosing during anaesthesia.

The rest of this paper is organized into four sections. In Section 2, the structure of the stimulus fuzzy model is presented. The patient model used in the simulations is outlined in Section 3. The results of the developed model are presented in Section 4. Finally, in Section 5 the conclusions regarding the application of the stimulus fuzzy model.

II. STIMULUS MODEL STRUCTURE

The effect of the surgical stimulus on SAP and HR is modelled considering the level of analgesia, the level of depression of the parameters and the intensity of the stimulus. The action of the analgesic can be viewed as a reduction on the patient's perception of pain, i.e. surgical stimulus. In fact, remifentanil effect concentration

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determines the quality of analgesia and therefore the level of stimulus perceived by the patient. The objective is to model the surgical stimulus effect on the cardiovascular parameters, considering the analgesic component of anaesthesia (i.e. the remifentanil effect or brain concentration).

Figure 1 presents a diagram illustrating the overall stimulus model scheme. Note that only the maintenance phase of anaesthesia is considered, since it is the main concern in the operating theatre. The maintenance phase was considered to be from 1500 seconds (assuming that the patient is stable, already in the operating room, and incision is about to start) until the infusion of propofol stops and recovery begins.

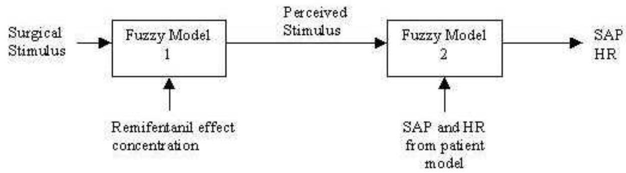

Figure 1: Block diagram of the stimulus model.

In Figure 1, the Fuzzy Model 1 describes the analgesic component of remifentanil in reducing the level of stimulus perceived by the patient (i.e. the perceived stimulus). Fuzzy Model 2 comprises two fuzzy models describing the effect of the perceived stimulus on SAP and HR, respectively.

The remifentanil effect concentration was obtained using a 3-compartmental pharmacokinetic model with mean population parameters from [6], and an effect compartment describing the delay between the plasma and the effect concentration [7].

First, the perceived stimulus model will be presented (Fuzzy Model 1 in Figure 1). Secondly, the fuzzy model for the changes in SAP will be presented, followed by the fuzzy model for HR, using the perceived stimulus. Overall, the stimulus model comprises three Mamdani type fuzzy models based on the anaesthetist knowledge and presented in IF-THEN rules.

A. *Perceived Stimulus*

The surgical stimulus intensity was described as Zero, Low, Medium and High, considering the following events as labelled by the anaesthetist:

Incision - high intensity stimulus
Retractors - high intensity stimulus
Cutting – medium intensity stimulus
Diathermy – low to medium intensity stimulus
Suture – low intensity stimulus.

The remifentanil effect concentration was established as being between 0-10 ng/ml throughout the procedure. However, in the maintenance phase this is more restrict. The remifentanil effect concentration was labelled by the anaesthetist as Zero, Low, Medium, High and VeryHigh.

The surgical stimulus and the remifentanil effect concentration are the inputs to the fuzzy model. The output is the perceived stimulus, obtained using the rule-base in Table 1. The perceived stimulus is labelled Zero, VeryLow, Low, Medium and High.

Evenly distributed triangular membership functions were used for the input and output variables. The output surface of the perceived stimulus fuzzy model is presented in Figure 2. The center of gravity defuzzifier was used as the defuzzification method.

Table 1: Perceived stimulus fuzzy rule-base. Surgical stimulus $\in [0,1]$, remifentanil effect concentration $\in [0,10$ ng/ml$]$ and perceived stimulus $\in [0,1]$.

Surgical Stimulus	**Remifentanil effect concentration (ng/ml)**				
	Zero	**Low**	**Medium**	**High**	**VeryHigh**
Zero	Zero	Zero	Zero	Zero	Zero
Low	Low	VeryLow	Zero	Zero	Zero
Medium	Medium	Low	VeryLow	Zero	Zero
High	High	Medium	Low	VeryLow	Zero

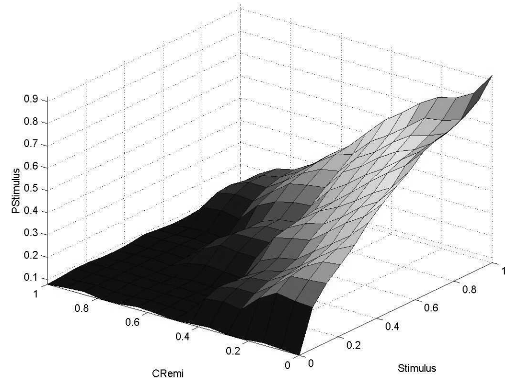

Figure 2: Perceived stimulus fuzzy model output surface. *CRemi* is the remifentanil effect concentration and *PStimulus* is the perceived stimulus.

The membership function of VeryLow for the perceived stimulus is necessary so as to describe the effect of a low surgical stimulus in the presence of a low remifentanil effect concentration. In other words, a low remifentanil concentration does not suppress completely a low stimulus.

The model output surface reflects the smooth decrease in the perceived stimulus as the remifentanil concentration increases.

B. *Systolic Arterial Pressure*

Figure 3 presents the block diagram for the fuzzy model describing the effect of the perceived stimulus on SAP. The inputs to the model are: *PrevSAP*, the value of SAP from a patient model; and *PerStimulus*, the perceived stimulus level obtained from the perceived stimulus fuzzy model described in the previous section (Fuzzy Model 1 in Figure 1).

After considering the effect of the perceived stimulus the value of SAP is described using the rule-base in Table 2, constructed with the cooperation of the anaesthetist. The perceived stimulus was labelled as Zero, Low, Medium and High, using evenly distributed triangular membership functions.

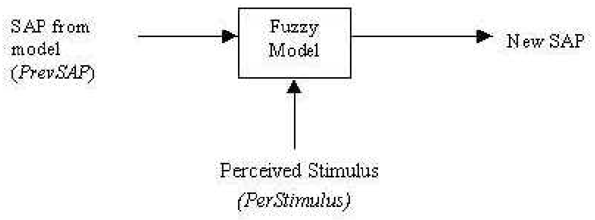

Figure 3: Block diagram of the fuzzy model describing the effect of surgical stimulus on SAP.

Table 2: Rule-base for the new value of the SAP after the stimulus.

Perceived Stimulus	**Previous value of SAP**		
	Low	**Medium**	**High**
Zero	Low	Medium	High
Low	Low	Medium	High
Medium	Medium	High	VeryHigh
High	High	VeryHigh	VeryHigh

The different SAP classes are described as follows:

- **Situation A:** baseline SAP>130 mmHg
  Low: SAP<70% of baseline;
  Medium: SAP between 70-80% of baseline;
  High: SAP>80% of baseline.
- **Situation B:** baseline SAP between 120-130 mmHg
  Low: SAP<75% of baseline;
  Medium: SAP between 75-85% of baseline;
  High: SAP>85% of baseline.
- **Situation B:** baseline SAP<120 mmHg
  Low: SAP<90 mmHg;
  Medium: SAP between 90-120 mmHg;
  High: SAP>120 mmHg.

This class division was establish by the anaesthetist and also used by [8].

The membership functions for the previous value of SAP are presented in Figure 4, taking into account Situations A and B. These two situations were modelled together considering a normalized range between [0,1], and using different scaling factors.

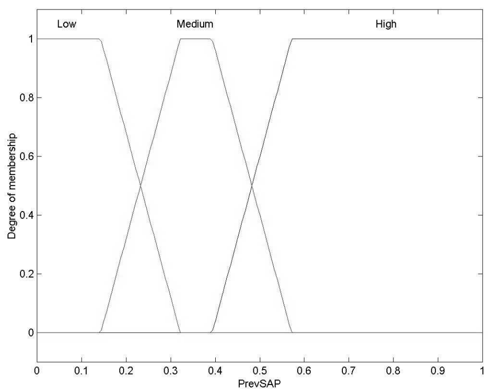

Figure 4: Input membership functions describing the previous value of SAP (*PrevSAP)*, considering situations A and B. The range is normalized between [0,1].

After considering the perceived stimulus effect, the new value of SAP (i.e. the output of the fuzzy system) is labelled Low, Medium, High and VeryHigh according to the membership functions in Figure 5, for situations A and B. The SAP output surface is presented in Figure 6. The center of gravity defuzzifier was used as the defuzzification technique.

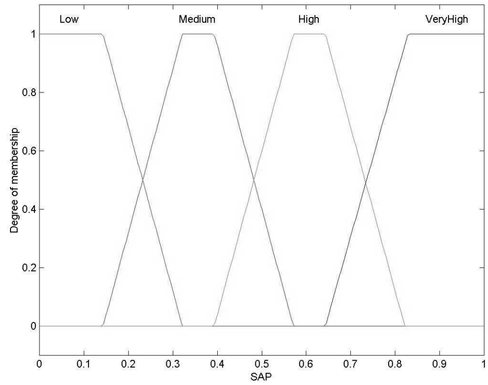

Figure 5: Output membership functions describing the new value of SAP, considering situations A and B. The range is normalized between [0,1].

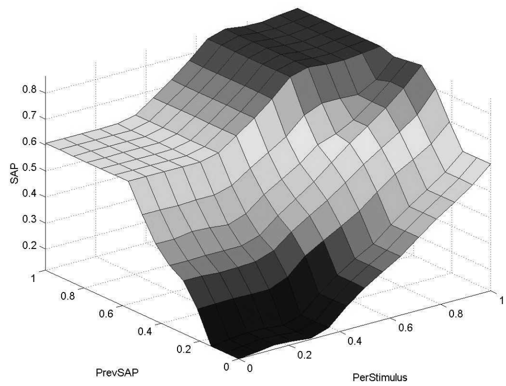

Figure 6: Output surface for SAP fuzzy model, situations A and B. *PerStimulus* is the perceived stimulus and *PrevSAP* is the previous value of SAP.

Situation C is treated separately, since it is not expressed in terms of a percentage from the baseline. The membership functions for the previous value of SAP and the membership functions for output value of SAP are shown in Figures 7 and 8, respectively. Note that, the input and output ranges are not normalized, i.e. they are represented in mmHg. The output surface for SAP is presented in Figure 9, considering situation C. The output surface is different from the one obtained for situations A and B (Figure 6), but reflects the same change trend.

C. Heart Rate

The effect of the perceived stimulus on HR is described as a change in its value. Figure 10 shows the block diagram describing the change in HR as a result of the perceived stimulus. This change in HR is labelled as Zero, Little and

Large according to the anaesthetist opinion. A little change represents a change of 5% of the previous value, and a large change could be as big as 10%. Therefore, the value of HR after the stimulus model will be increased by a certain percentage.

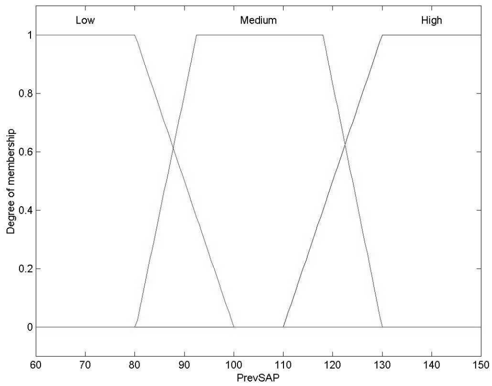

Figure 7: Input membership functions for the previous value of SAP (*PrevSAP*), considering situation C.

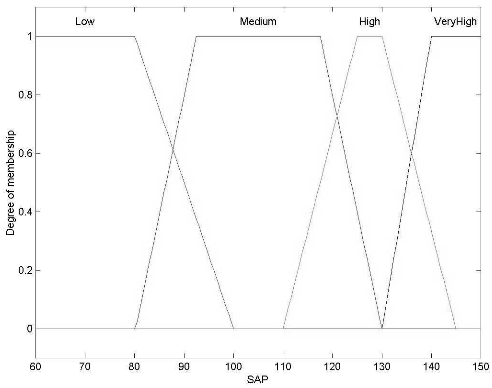

Figure 8: Output membership functions for the new value of SAP, considering situation C.

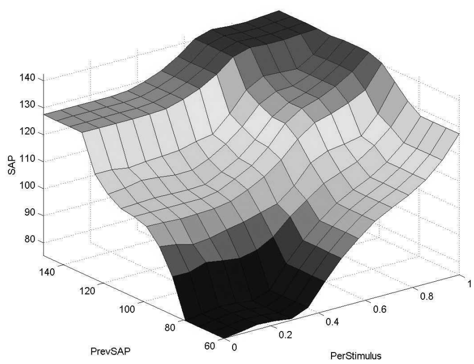

Figure 9: Output surface for the SAP fuzzy model, considering situation C. *PerStimulus* is the perceived stimulus and *PrevSAP* is the previous value of SAP.

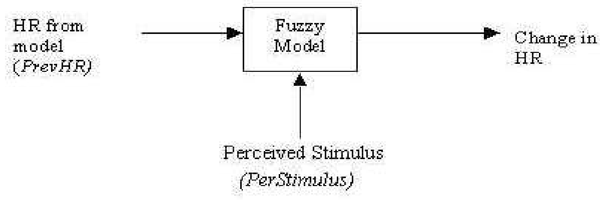

Figure 10: Block diagram for the fuzzy model describing the effect of surgical stimulus on HR.

The change in HR is modelled using the rule-base in Table 3. The perceived stimulus membership functions are the same as the ones used for SAP.

Table 3: Rule-base for the change in HR after the stimulus.

Perceived Stimulus	**Previous value of HR**		
	Low	**Medium**	**High**
Zero	Zero	Zero	Zero
Low	Zero	Zero	Little
Medium	Zero	Little	Large
High	Little	Little	Large

The HR class values were classified by the anaesthetist as follows:

Low: HR<70% of baseline;
Medium: HR between 70-90% of baseline;
High: HR>90% of baseline.

The membership functions of the previous value of HR are presented in Figure 11 according to the above description. The HR has lower normal values when using remifentanil than with other opioids, due to its depressive effect. This was taken into consideration when establishing the HR ranges.

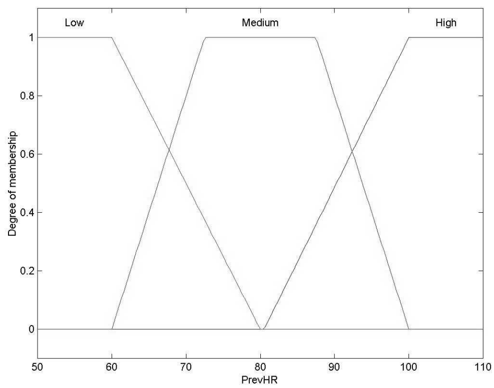

Figure 11: Input membership functions describing the previous value of HR (*PrevHR*). The HR range represents 50-110% of baseline.

Figure 12 shows the output membership functions for the change in HR. The change in HR is presented as a percentage of the previous value. The output surface for the change in HR fuzzy model is presented in Figure 13. The center of gravity defuzzifier was used as the defuzzification method.

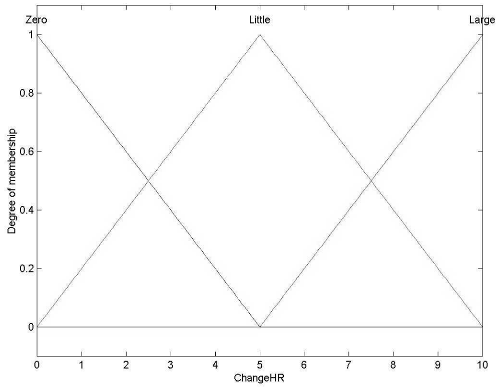

Figure 12: Output membership functions for the change in HR (effect of stimulus). The range of 0-10 represents 0-10% change.

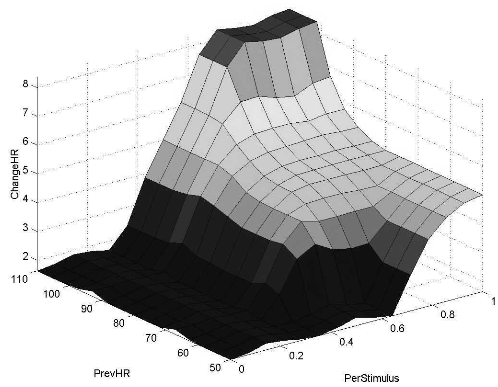

Figure 13: Output surface for the change in HR fuzzy model. *PerStimulus* is the perceived stimulus and *PrevHR* is the previous value of HR.

III. SIMULATION MODEL

In previous work [9], a patient model was developed in order to incorporate the effects of drug interactions on the cardiovascular parameters, and on the auditory evoked potentials. The objective was to model the pharmacodynamic properties of the two drugs and the interactions between them, during the maintenance phase of anaesthesia. Data collected in the operating theatre was used to develop this patient model.

Overall, the patient model includes the pharmacokinetic compartmental models of both drugs, and a pharmacodynamic model constituted by the effect compartment and by a structure of fuzzy models describing the relationship between the effect concentrations and the different effects. Takagi-Sugeno-Kang fuzzy models, trained using an Adaptive Network-Based Fuzzy Inference System, were used to model the relationship between the effect concentrations of both drugs (including the drug interactions) and HR, SAP and features of the auditory evoked potentials [9].

The objective is to link the fuzzy stimulus model with the patient model [9], in order to incorporate the effect of surgical stimulus on SAP and HR. Since, the final value of the cardiovascular parameters is not only the result of the drugs used but also of the surgical stimulus present.

IV. RESULTS AND DISCUSSION

The stimulus fuzzy model was applied to the results of the simulation with the patient model [10], with the infusion profile of a patient (Pat1) recorded in the operating theatre. Figure 14 shows the SAP value before and after the stimulus model, solid versus dashed line respectively. Note how the presence of stimulus is affecting the value of SAP, introducing changes and peaks to the smooth output of the patient model.

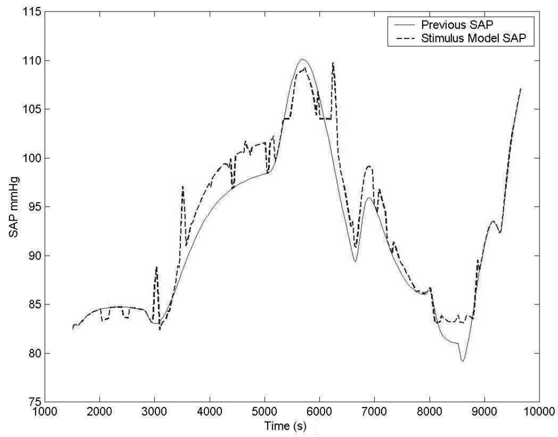

Figure 14: SAP from patient model in [10] without stimulus (solid line) versus SAP after the stimulus model (dashed line). The infusion profile of patient Pat1 was used for the simulation.

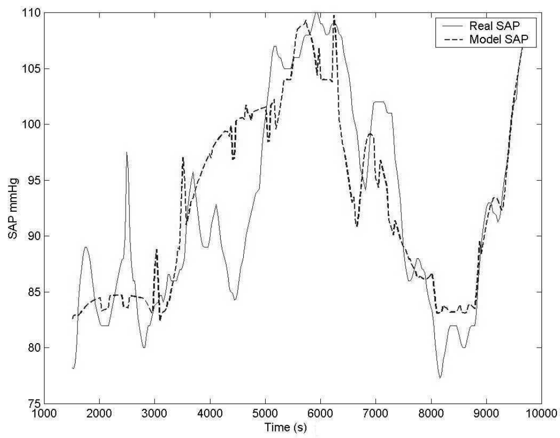

Figure 15: SAP from patient Pat1 (solid line) versus SAP from patient model including the stimulus model (dashed line).

Figure 15 shows the observed SAP from patient Pat1 (solid line) versus the value of SAP after the stimulus model. The results of the model including the stimulus effect have a reasonable approximation to the observed value of SAP. This was expected, since the stimulus level affects the cardiovascular responses. However, there is a small delay between the model results and the observed SAP. This happens because in reality it takes 2-5 minutes for the stimulus effect to be reflected in the SAP value; meaning that the influence of the stimulus is not instantaneous. This time-delay has not been included in the SAP model. Therefore, the stimulus model responds immediately to the stimulus, altering the SAP value.

The same simulation was performed with HR. Figure 16 shows the HR value before the stimulus model (solid line) versus the HR after considering the change resulting from the stimulus model (dashed line). The HR value was increased throughout due to the stimulus effect. The peaks resulting from the stimulus are quantitatively less than the ones on SAP, which demonstrates that HR is a more stable variable.

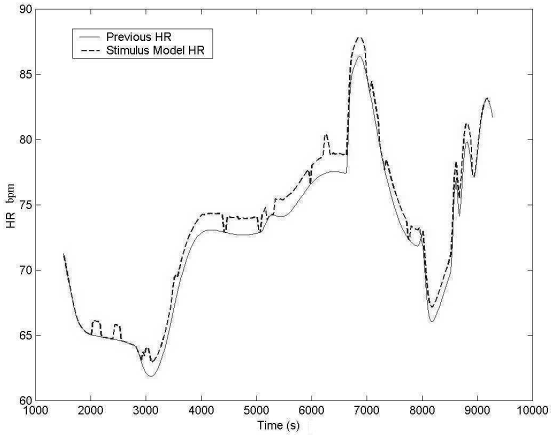

Figure 16: HR from patient model in [10] without stimulus (solid line) versus HR after the stimulus model (dashed line). The infusion profile of patient Pat1 was used for the simulation.

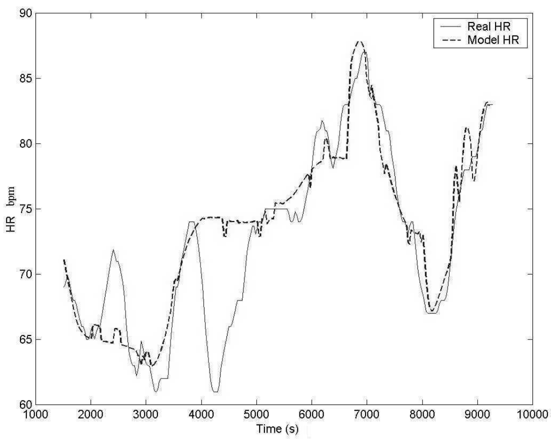

Figure 17: HR from patient Pat1 (solid line) versus HR from patient model including the stimulus model (dashed line).

Figure 17 shows the HR observed from patient Pat1 (solid line) versus the HR from the patient model after the inclusion of the stimulus effect. The model approximation has improved, considering the result before the stimulus model. This reflects the appropriateness of the stimulus model. In addition, the HR model seems to be averaging-out disturbances in the HR signal. When considering the time period of 4000 to 6000 seconds, the HR model is reflecting the HR trend but smoothing out the sharp "valley" in the data.

The existing time-delay for HR is different from the one for SAP. It appears that the HR reacts faster than SAP to the stimulus.

V. CONCLUSIONS

The development of a model that includes the analgesic action of remifentanil is a new area of research since there is no clear indicator of pain. The objective was to detect the action of remifentanil when comparing the model results with data collected in the operating theatre. The main action of an analgesic is to inhibit noxious stimulus from reaching the brain, and therefore alter the level of DOA (i.e. causing arousal). Therefore, it is important to include the effect of surgical stimulus on a patient model, and consider it in the development of a control system from drug infusions in anaesthesia.

The inclusion of the stimulus model in the simulation, improved the results of the patient model. The fuzzy stimulus model is able to capture changes due to the effect of stimulus, which are reflected in the observed data but not in the results of the patient model.

The output surfaces reflect the effect of increasing concentrations of remifentanil on the perception of stimulus. Note that, HR is a more stable variable, presenting oscillations with smaller amplitude than the ones in SAP. In addition, the level of depression of the cardiovascular parameters has influence in the stimulus effect. If SAP or HR are at a Low level, the effect of a stimulus is less than if the parameters were at a High level. This result demonstrates that the adequate level of DOA depends on the type of operation, i.e. intensity of surgical stimulus.

In conclusion, it was found that: 1. the DOA level has some influence on the stimulus effect; 2. the cardiovascular variables include a time-delay in response to stimulus; 3. the stimulus effect is proportional to its intensity.

The existing time-constant is different for SAP and HR, and to our knowledge there are no studies defining its value. It was not considered adequate to estimate the time-delay based on the existing data. However, this will be included in future research.

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