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# Adaptive fuzzy predictive controller for anesthesia delivery

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ABSTRACT

The problem of automating the infusion of anesthesia using fuzzy predictive control techniques is afforded. The control objective is to keep the hypnosis level of the patient in a proper and safe value. To provide accurate predictions, an adaptive model based on fuzzy logic and genetic algorithms is included. Thus, the drug infusion is adapted to the real needs of the patient and, consequently, the performance compared to other approaches is improved. The controller was evaluated both in simulation and in the operating room with patients undergoing surgery. Results obtained attest for the efficiency of the proposed method.



## 1. Introduction

To achieve adequate anesthesia and compensate the effect of surgical manipulation while maintaining the patient vital functions, anesthesiologists regularly adjust the configuration of different drug infusion devices and the parameters of the breathing system. There are three main variables in the process: hypnosis (degree of unconsciousness), analgesia (degree of suffered pain) and muscular relaxation (see Fig. 1). These variables are controlled by manipulating the drug infusion rates (propofol for hypnosis, remifentanil for analgesia and rocuronium for muscle relaxation). In standard practice the drug administration is done based on certain objectives and from the information collected from the monitors.

The results presented in this paper refer to the problem of automatic control of the hypnotic level during surgery while the patient is under general anesthesia. The objective is to apply the correct dose of propofol to keep the patient in a safe hypnotic state and to minimize adverse effects. In this study, no automatic control for analgesia and muscle relaxation is considered. Instead, a standard clinical protocol to regulate these variables is used in parallel to the automatic control of hypnosis.

The application of control techniques to automate the infusion of anesthesia has gained interest in the last decade. Initially most of the proposals were based in PID controller (Absalom & Kenny, 2003; Méndez, Torres, Reboso, & Reboso, 2009a; Reboso, Méndez, Reboso, & León, 2012). Other approaches have introduced alternative methodologies like in Heyse et al. (2008) where a Bayesian-based closed-loop control is presented. In this case, the controlled variable is not a direct measure of the hypnotic variable, but the concentration of drug. Results offer similar performance than manual control. In Ionescu et al. (2008) a predictive controller based on a linearized model is presented. The algorithm was applied successfully in a set of 12 patient models. In Moore, Pyeatt, and Doufas (2009) a proposal based on fuzzy logic was simulated with a clinically acceptable performance. In Liu et al. (2012) a controller based on the EEG entropy monitoring was tested in a population of 30 patients. The study demonstrated that the control of hypnosis and analgesia guided using entropy is clinically feasible and more precise than skilled manual. The benefits of these methods are clear: increase in patient safety, cost reduction, reduction of anesthesiologist's workload, etc.

The existing proposals guarantee at least the same performance that obtained with a manual infusion (although in many cases the performance is even higher). However, one important issue that the automation systems must cope with is the patient variability. There are variations in the response from one patient to another and also for the same patient his response is different in different surgery stages. One way of accommodating these variations is through the design of controllers with robust (van Heusden et al., 2014). A different approach, considered in this paper, is the design of an adaptive controller that takes into account the actual patient state to compute the infusion dose.

The contribution of this paper is the proposal of an advanced technique to control the hypnosis level that can adapt to patient characteristics. To achieve this, a fuzzy model predictive controller

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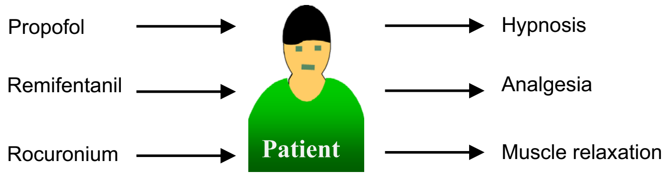


**Fig. 1.** Input–ouput diagram of the anesthetic process in a patient.

with adaptive capabilities was designed. The main problem in predictive controller is to have an accurate model for the process under control (Camacho and Bordons, 2007). In most anesthesia control applications the model considered to describe the patient are compartmental models (Absalom, Mani, De Smet, & Struys, 2009; Hahn, Dumont, & Ansermino, 2012). Although these models provide an approximation to the patient dynamics, the accuracy of its predictions greatly depends on its model parameters. In this work an alternative based on fuzzy models to represent the patient's dynamics is used. Genetic algorithms are used to adjust the fuzzy sets during surgery. The use of fuzzy models offers several advantages over compartmental (Sproule, Naranjo, and Türksen, 2002). First, a fuzzy inference system has the universal approximator property (it is possible to approximate any continuous function into a compact domain with a certain level of accuracy). On the other hand, the use of fuzzy logic provides a formal methodology to model the process using human's heuristic knowledge (Sugeno and Yasukawa, 1993). This allows for the clinicians to validate the resulting model or even contribute to fine tune it.

The paper begins with the problem statement and describing the experimental setup of the control system. Then the modelling of the process is described. In this section fuzzy and genetic algorithms are used to build the model. Section 3 describes the predictive controller. Section 5 presents both results in simulation and in a real application. The paper ends summarizing the contributions of the work in Section 6.

## 2. Control objective and experimental setup

As commented, this work focuses on the hypnosis control problem. As the hypnosis (level of unconsciousness) cannot be directly measured, an indirect measure derived from the EEG that correlates with hypnosis is used: the Bispectral Index (BIStm) (Sigl & Chamoun, 1994; Bennett, Voss, Barnard, & Sleigh, 2009). BIS is a dimensionless index that varies between 100 (awake) and 0 (no electrical activity in brain). General anesthesia corresponds to a BIS signal between 40 and 60.

The control problem can be formulated as calculating the correct dose with time to maintain the patient in an adequate hypnotic state. The controller must be capable to reject the disturbances that appear during surgery (blood loss, surgical stimulus, etc.). In terms of the BIS signal the objective is to maintain the state in the BIS reference proposed. In general, a value of 50 is considered appropriate for standard surgical procedures (Dumont & Ansermino, 2013).

To measure the BIS signal a BIS Vista™ monitor (Aspect Medical System, Newton, USA) using four ZipPrep® electrodes (Aspect Medical System, Newton, USA) is used. BIS monitor provides the feedback signal via a RS232 port connection to a laptop. The laptop hosts the software that implements the control algorithm. This software manipulates the infusion rate of hypnotic (propofol) applied to the patient. The infusion pump is a Graseby 3500® infusion pump (Graseby Medical Ltd, Watford, UK) with propofol 1% and is connected via RS232 port to the PC. Fig. 2 shows a patient in the operating room with all the devices involved in the closed loop control.

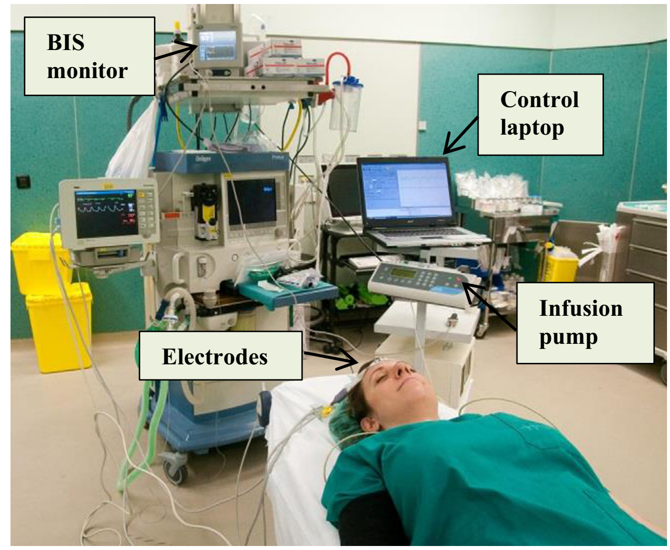


**Fig. 2.** General view of an operating room with a patient connected to the control system elements.

The controller includes an alarm module to prevent failures in the system. This module alerts to errors in transmission or connection between different devices, poor quality of the BIS signal, artifacts, etc. The program continuously monitors the BIS quality index, the electromyogram and the suppression rate. According to the values of these signals, the controller can activate alarms to alert the anesthesiologist. Additional safety measures include a mechanism to stop the infusion below a given BIS value (30) and to apply a bolus dose when the BIS signal is excessively high to prevent eventual awareness.

Concerning clinical protocol, a standard monitoring routine was used, including pulse oximetry, ECG and non-invasive blood pressure. A venous catheter with an antireflux valve was placed in one arm. The protocol for remifentanil administration consisted of an infusion of 0.25 mcg/kg/min started just before induction and adjusted according to the requirements of analgesia. The clinicians were instructed to maintain this rate as long as the hemodynamic situation of the patient allowed it. Thus preventing unexpected painful stimuli or an inadequate level of analgesia could affect the stability of BIS. Doses could be changed in steps of 0.05 mcg/kg/min. If bradycardia is observed, a treatment with atropine 0.01 mg/kg is applied. In case, bradycardia persists remifentanil infusion rate is decreased. Hypotension was treated with an increase in the infusion of saline solution and ephedrine 10 mg iv. If no response is observed, the next step is to reduce remifentanil infusion rate. The criteria to increase the remifentanil infusion rate were tachycardia, hypertension and movement or any other indirect sign of inadequate anesthesia. The patients received for induction a propofol bolus of 2 mg/kg and rocuronium bromide (0.6 mg/kg) for muscle relaxation. Once the patients lost consciousness and BIS value was around 50, they were intubated and mechanical ventilation was maintained using air with an oxygen percentage of 40%.

## 3. Genetic fuzzy modelling of the anesthetic process

The aim of this section is to develop a model of the patient so that the evolution of the BIS variable can be predicted. These predictions are provided to a predictive controller to compute the optimal infusion rate to be applied to the patient. The complexity of the anesthetic process is high so that the synthesis of a