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Arterial pressure control with isoflurane using fuzzy logic

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Summary

Arterial pressure is still one of the most important measures in estimating the required dose of inhaled anaesthetics. It is measured easily and reacts rapidly which makes it suitable as a variable for feedback control of depth of anaesthesia. Fuzzy logic, a novel approach to feedback control, was used to control arterial pressure in 10 patients during intra-abdominal surgery by automatic adjustment of the concentration of isoflurane in fresh gas. During anaesthesia, fuzzy control periods of 45-min duration were alternated randomly with human control periods of equal duration. During the skin incision period (−3 to +12 min) 48.2% of all fuzzy control pressure values were within ±10% of the desired mean arterial pressure compared with 40.4% of the human control values ($P < 0.05$). The corresponding values for the remainder of the operation were 78.3% and 83.2%, respectively. Thus fuzzy outperformed human control at skin incision, but was slightly inferior during the rest of the operation. We conclude that fuzzy logic is a promising new technique for control of isoflurane delivery during routine anaesthesia. (*Br. J. Anaesth.* 1995; **74**: 66–72)

Key words

Anaesthetics volatile, isoflurane. Computers. Model, computer simulation.

Computers are used extensively in the operating room, both for monitoring and, to a lesser extent, for control of anaesthetic drug delivery. Depth of anaesthesia is difficult to control because it cannot be measured easily. Since the pioneering work of Bickford [1] EEG signals have been used repeatedly as a variable to measure depth of anaesthesia. A major drawback of all EEG signal processing methods is the high susceptibility to artefacts and also the agent-specific influence of the anaesthetics being used. Anaesthetists are more accustomed to using cardiovascular variables such as arterial pressure and heart rate when estimating depth of anaesthesia [2], as these are easier to measure. Automatic control using arterial pressure as a measure of depth of anaesthesia was achieved by Fukui, Smith and Fleming [3], Robb and colleagues [4, 5] and Monk and colleagues [6] and by Suppan [7] using heart rate. Arterial pressure was controlled automatically using sodium nitroprusside by Smith and colleagues [8, 9], Meline and co-workers [10] and others. Today, feedback controlled pumps are commercially available [11]. Previous experiments in our laboratory with control systems using proportional integral-derivative (PID) or rule-based algorithms have shown disappointing results as the controllers (after a period of satisfactory performance) suddenly failed when new situations (new extremes of age, surgical stimulation, etc.) occurred. Existing conventional algorithms such as PID controllers [12], adaptive controllers [13] and state estimation controllers which update initial values using least-squares online estimation [14], need computer modelling of the system to be controlled.

Uptake and haemodynamic effects of inhaled anaesthetics in the human body show properties of a non-linear time-varying system and are thus difficult to model [15]. Interestingly, even one of the most extensive reviews published recently on the use of computers for controlling the delivery of anaesthesia [16] does not mention a class of promising modern feedback control algorithms, the fuzzy control algorithms, which are now increasingly used for various applications in industry, ranging from the car to manufacturing industries. Fuzzy algorithms are suitable for control of black box systems which cannot be modelled easily, such as the human body or the anaesthesia system (which, although basically very simple, is also difficult to model). An introduction to the principles of fuzzy logic control is given in the appendix. It was the aim of this study to quantitatively compare the performance of a fuzzy control system with the usual human control in patients undergoing intra-abdominal surgery. The observation period was divided into skin incision (where the human controller should in theory have the advantage of foreseeing the disturbing event) and the remainder of the operation.

Patients and methods

CLINICAL INVESTIGATION

The study was approved by the Ethics Committee of the Medical Faculty of the University of Bern. Written informed consent was obtained from 10 patients, five males and five females, ASA I–II, age

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39.7 (range 25–44) yr, weight 69.9 (49–89) kg, height 173 (168–184) cm, who were undergoing elective abdominal surgery in the supine position. Exclusion criteria included age greater than 55 or less than 20 yr, a history of coronary heart disease, hypo- or hypertension, drug or alcohol abuse, opioid medication or an expected or measured blood loss of more than 500 ml. The patients received an infusion of Ringer's solution 2 ml kg^{-1} h^{-1} before the peritoneum was opened and 10 ml kg^{-1} h^{-1} subsequently via a cannula in a peripheral vein. Anaesthesia was induced with thiopentone 4–5 mg kg^{-1} and the trachea was intubated after providing neuromuscular block with vecuronium 0.1 mg kg^{-1} i.v. A semi-closed circle system (Sulla with an 8 ISO circle system, Drägerwerke AG, Lübeck, Germany) was used with a fresh gas flow of oxygen 3 litre min^{-1}. The following variables were monitored: ECG, body temperature (rectal), fresh gash concentration using a main-stream infrared analyser (Irina, Drägerwerke AG, Lübeck, Germany), end-tidal carbon dioxide and isoflurane concentrations sampled at the Y-piece using a side-stream infrared analyser (Capnomac, Datex, Helsinki, Finland). Arterial pressure was measured via a 20-gauge cannula inserted into a radial artery and attached via a Y-piece to two Utah DPT200 transducers. One of the transducers was used for monitoring arterial pressure, the other for the feedback system. The damping and resonance properties of the arterial pressure monitoring system in use had been determined previously with the method described by Gardner [17]. The damping coefficient of the complete system was 0.25 and the natural frequency 21 Hz, thereby lying within the ideal range as defined by Gardner.

During the first period which started 3 min before skin incision patients were allocated randomly to either human or fuzzy control. After 45 min the control mode was switched to the alternative mode. A mean arterial pressure of 80 mm Hg was used as the desired set-point. In order to avoid awareness a lower pressure was allowed if the end-tidal concentration decreased to less than 0.4 vol%, for example while waiting for the surgeons. Human control was alternated between either one of two qualified anaesthesia nurses or one of two consultant anaesthetists. The anaesthetist in charge of the control also had to perform the other activities of routine anaesthesia such as adjusting the rate of infusion, keeping the anaesthesia record, administering drugs, etc. If heart rate increased to greater than 120 beats min^{-1} for more than 5 min during human or fuzzy control periods, esmolol 100 μg kg^{-1} min^{-1} was given i.v. until heart rate was less than 120 beats min^{-1}.

Table 1 Scoring system used to clinically evaluate depth of anaesthesia

Variable	Condition	Score
Systolic arterial pressure (mm Hg)	< set-point + 15	0
	< set-point + 30	1
	> set-point + 30	2
Heart rate (beat min^{-1})	< 85	0
	< 110	1
	> 110	2
Sweating	Nil	0
	Skin moist to touch	1
	Visible beads of sweat	2
Tears	No excess of tears in open eye	0
	Excess of tears in open eye	1
	Tear overflow from closed eye	2
Pupils	Miotic	0
	Intermediate	1
	Dilated	2

In order to evaluate depth of anaesthesia clinically, a modification of the scoring system described by Evans and Davies [18] using systolic pressure, heart rate, sweat, tears and also pupil size (as we did not use opioids) was used every 5 min, as shown in table 1.

FEEDBACK CONTROL ENGINEERING

Data for optimizing the controller and for performing purely inhalation anaesthesia had been obtained in previous studies where isoflurane was used as the sole agent in patients of the same age and physical condition, and undergoing similar surgical procedures [19–21].

The principles of the feedback control system have been reported previously [22]. In short, the relationship between fresh gas concentrations of isoflurane and the resulting arterial pressure was

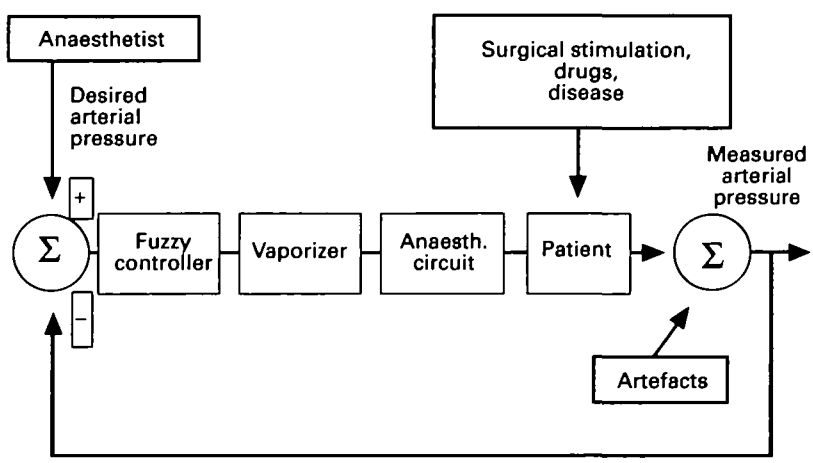

Figure 1 Block diagram of the control loop.

modelled as the sum of two first-order terms (fig. 1). The variables used in the design of the controller process had been identified previously offline in a recursive way from arterial pressure data collected after step changes in the fresh gas concentration of isoflurane.

DATA PROCESSING

The signals of end-tidal and inspired isoflurane concentration, and the desired ("set-point") and measured mean arterial pressure were digitized at 0.1 Hz using an A/D conversion card (Burr Brown Corporation, Tucson, AZ, USA). Artefacts caused by electrocautery, calibration, etc., were eliminated using a median filter applied on the last 20 values measured. For the statistical data processing, the unfiltered values were stored on the hard disk of an IBM compatible personal computer. For safety reasons all data were recorded simultaneously on paper (Philips PM 8252A recorder, Philips, Eindhoven, The Netherlands). After the experiment the digitally recorded data were plotted and inspected visually; excessive values caused by artefacts were adjusted manually to the previously measured values. Data were then split into a file covering the time from 3 min before until 12 min after skin incision and a subsequent file containing all other data in order to analyse the effect of skin incision separately. The results of the clinical scores were tested for normality and then the human periods were compared with the fuzzy periods using t tests both for the skin incision period and for the remainder of the operation. For the arterial pressure values, data were processed as follows: data of all patients of one group (e.g. skin incision period, fuzzy control) were pooled into one file. The relative error values of the mean arterial pressure values were calculated as the difference of the measured minus the desired pressure value divided by the desired pressure value. The mean and median of all of these values were compared using a t test or a Mann–Whitney test, respectively. The test for normality was performed using a Pearson chi-square test of normality. We used the L_1-norm to define the difference between the desired and actual arterial pressure according to the following equation:

$$L_1 = \frac{\Delta t}{T} \sum_{i=1}^{n} |\mathrm{MAP}_{\mathrm{measured}}(i) - \mathrm{MAP}_{\mathrm{desired}}(i)|$$

where Δt = sampling time (10 s), T = total time of observation of one period (normally 2700 s) and n = total number of measurements in the observation period (normally 270).

The values of the L_1-norm of the human control periods were compared with the fuzzy control periods using a Mann–Whitney test. To compare the capability of avoiding excessive pressure changes, the percentage of values within the range $\pm 10\%$ of the desired arterial pressure was computed. The resulting percentage values for human and fuzzy control were compared using a chi-square test. For all statistical testing the RS/1 statistical package (Bolt Beranek and Newman Inc, Cambridge, MA, USA) was used. $P < 0.05$ was considered significant.

Results

No patient complained of awareness when questioned after operation. During human control, two patients needed a single dose of ephedrine because of low arterial pressure. This was not caused by the

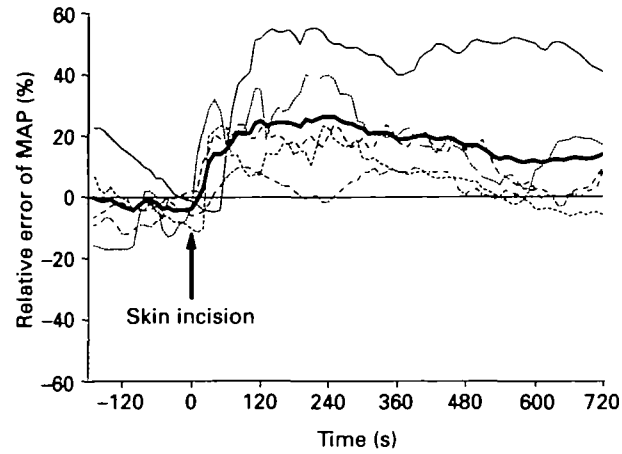

Figure 2 Relative error of mean arterial pressure (MAP) *vs* time during skin incision period (3 min before, 12 min after) using fuzzy control. ——— = Mean of all five curves.

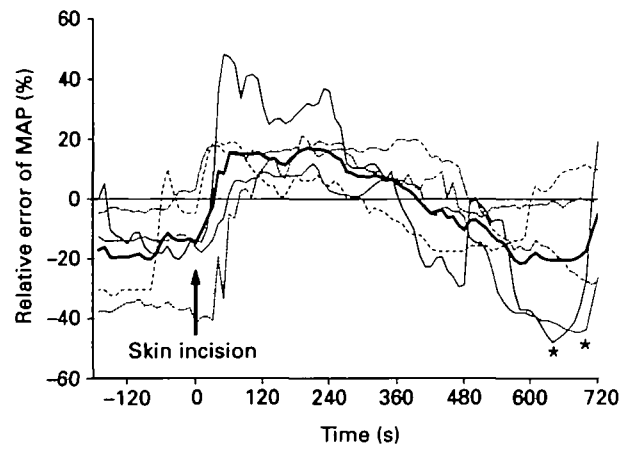

Figure 3 Relative error of mean blood pressure (MAP) *vs* time during skin incision period (3 min before, 12 min after) using human control. * Single dose of ephedrine 10 mg i.v. ——— = Mean of all five curves.

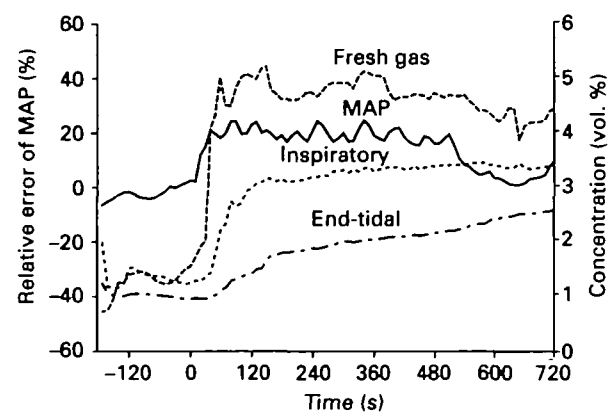

Figure 4 Fresh gas, inspiratory and end-tidal isoflurane concentrations, and relative error of mean arterial pressure (MAP) of one patient during the skin incision period using fuzzy control.

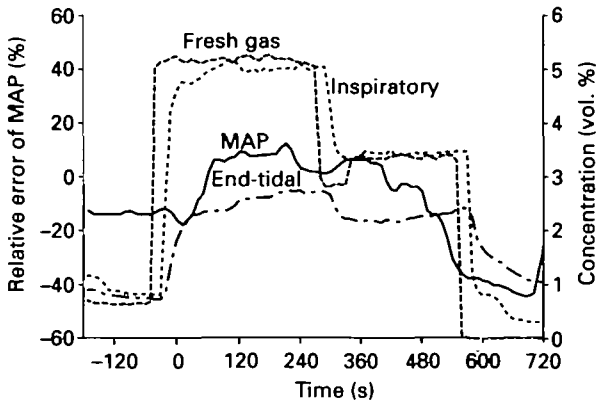

Figure 5 Fresh gas, inspiratory and end-tidal isoflurane concentrations, and relative error of mean arterial pressure (MAP) of one patient during the skin incision period using human control. Typically, the inspired fresh gas isoflurane concentration is increased before skin incision, before arterial pressure increases.

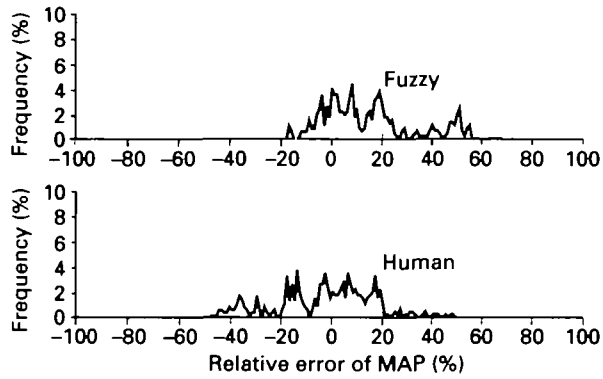

Figure 6 Frequency distribution of the relative errors of mean arterial pressure (MAP) during the skin incision period. Top = fuzzy control, bottom = human control.

abnormal physiological condition of the patient but by a delayed reaction of the anaesthetist. During the fuzzy control period one patient was given esmolol for 15 min because heart rate exceeded 120 beat min^{-1}.

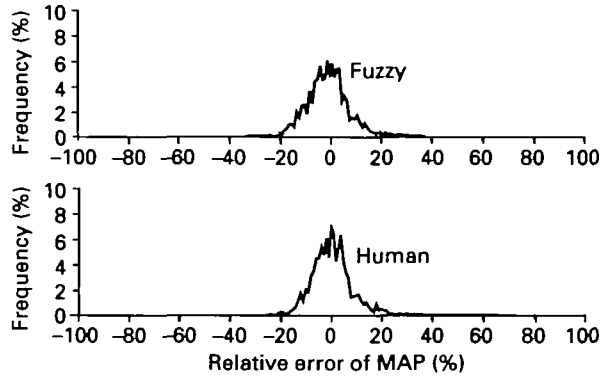

Figure 7 Frequency distribution of the relative error of mean arterial pressure (MAP) during the non-skin incision periods. Top = fuzzy control, bottom = human control.

During the whole study we tried to keep the set-point at 80 mm Hg; however, in four patients the set-point had to be adjusted initially to 75, 70, 70 and 65 mm Hg as during the period before skin incision the end-tidal isoflurane concentration would have had to be decreased to values less than 0.4% which might have caused awareness. When processing the digitally recorded data, 19 of 1868 values in seven episodes were recognized as artefacts and adjusted to the previously measured values. In four episodes 110 of 1080 values were adjusted manually to the values recorded on paper by the recorder; these values were caused by an initialization problem of the A/D conversion card. The mean arterial pressure changes during the skin incision periods are shown for fuzzy control in figure 2 and for human control in figure 3. The two control modes showed entirely different characteristics: in anticipation of the increase in arterial pressure at skin incision the human controller tended to decrease arterial pressure values before incision. Thereby, however, the hypertension caused by skin incision cannot completely be prevented. The human controller tended to keep isoflurane concentrations at a high value for too long a time,

Table 2 Comparison of various variables for the human and fuzzy control periods during skin incision and subsequent periods. *P = 0.01, **P = 0.001, ***P = 0.0001 compared with fuzzy control period

	Skin incision		Non-skin incision		
	Fuzzy	Human	Fuzzy	Human	Statistic
Measurements					
No. of episodes	5	5	11	11	
Total time	1 h 15 min	1 h 15 min	7 h 21 min 50 s	8 h 11 min 20 s	
No. of measurements	450	450	2651	2948	
Clinical scores					
Median	3	2.0	2	1***	
Range	0–5	0–5	0–5	0–6	
Arterial pressure values					
Relative error (mean (%))	14.0	3.8***	−1.0	0.1***	*t* test
SD of mean of all patients (%)	18.0	19.3	8.5	7.7	
Median (%)	9.3	2 0***	−0.9	−0.2**	Mann–Whitney
Distribution	Not normal	Not normal	Not normal	Not normal	Pearson chi-square test of normality
L_1-norm (mm Hg)	13.1	12.0	5.0	4.5	Mann–Whitney
% Values within ±10% (%)	48.2	40.4*	78.3	83.2**	Chi-square

resulting in a hypotensive period which, in two cases, had to be controlled with ephedrine. Fuzzy control resulted in a hypertensive period immediately after incision and a subsequent gradual approach to normotensive values.

Between the fresh gas, inspiratory and end-tidal concentrations, a gradient persisted, as shown in an example of the fuzzy control period and the human control period in figures 4 and 5. Fresh gas and inspiratory isoflurane concentrations differed considerably; as with all other patients an inspiratory to end-tidal concentration gradient also existed.

The frequency distribution of the relative errors are plotted in figure 6 (skin incision period) and figure 7 (non-skin incision period). During the skin incision period human control tended to result in low arterial pressure values whereas during fuzzy control arterial pressure values were higher.

Quantitative values of the relative error are shown in table 2. Both parametric and non-parametric tests revealed significant differences for the relative error of mean arterial pressure between fuzzy control and human control for all periods. A significant difference between fuzzy control and human control can be shown by the ability to avoid large errors (deviations of more than 10%). The clinical scores showed a significantly higher score for the fuzzy compared with the human control during the non-skin incision phase. Thus fuzzy control was superior to human control during the skin incision period whereas human control was slightly superior during the remainder of the operation. The L_1-norm, a measure of the absolute error, did not result in significant differences in each group.

Discussion

We are aware of the fact that using arterial pressure as a measure of depth of anaesthesia may be questioned. However, clinically, arterial pressure is still the major variable for judging depth of anaesthesia and it allows quantification of the quality of control. Additional variables such as inspired or expired anaesthetic gas concentration or the processed EEG signal may be incorporated in a future feedback control system while other commonly used variables such as sweating, movement and pupil size may be difficult to include. Information based on direct observation of a forthcoming event such as skin incision has to be transmitted to the controller by the anaesthetist.

The rationale of using a purely inhalation anaesthetic technique in this study was to make the groups more comparable by avoiding the use of other drugs and to use the large amount of quantitative data obtained previously with this type of anaesthesia in several extensive investigations [19–21]. The controller had been tuned using data from these studies and the anaesthetist had become acquainted with the technique. However, during a purely inhalation technique when opioids or nitrous oxide were not used, there were more frequent and extensive changes in arterial pressure than when opioids were used [23–26]. Thus the controller had to cope with far larger pressure changes than during balanced anaesthesia. We speculate that during balanced anaesthesia the controller would perform well, even if patients differed considerably in age, weight and general health. Tachycardia was not affected by the controller and we interpreted this as a direct effect of isoflurane and not as inadequate anaesthesia [27]. Consequently esmolol was used in one patient.

The anaesthetic technique chosen for this study caused other problems: during long periods without stimulation (before skin incision) arterial pressure decreased and isoflurane would have had to be decreased to concentrations where awareness may have occurred. Therefore a minimum concentration of 0.4 vol% was chosen. This concentration corresponds to our previously measured MAC_{awake} value [20] but is lower than the concentration recommended by McCrirrick, Evans and Thomas [28] needed to prevent awareness. It corresponds to the concentration at which Newton and colleagues [29] found loss of response, loss of recall and recognition and, in 62% of subjects, loss of eyelash reflex.

Although the anaesthetists were familiar with the technique used in this study, their behaviour was not the same as that of anaesthetists working under normal circumstances. They regarded the fuzzy controller as a competitor and tried to out-perform it. Also, the effect of decreasing vigilance over prolonged periods could not be simulated in this experiment. Anaesthetists in training would probably not have performed as well as (experienced) anaesthetists in this study. Furthermore, the algorithms used in this fuzzy controller have not yet been obtained in a large population of patients. However, for this selection of patients we considered the number of patients sufficient to account for the biological variability. In this study, fresh gas flows were set at a constant rate of 3 litre min^{-1}. A future controller should use higher flows during episodes where a rapid reaction is required and reduce flows during stable conditions, thus minimizing gas consumption.

Safety is an important requirement for a control system and only limited conclusions may be drawn from this study. Interestingly, the only two critical situations occurred during the human control phase, where the anaesthetists over-reacted to the hypertension caused by skin incision. During the fuzzy control phase no critical situation occurred.

There are many limitations to this system: signal artefacts may be caused by a clotted arterial cannula, faulty calibration, a baseline shift of the sensors or electrocautery. Most of these artefacts can be detected using filtering algorithms, as was the case in this study. The potentially fatal effects of measurement artefacts can, at least in part, be avoided, as in this study by application of two independent measurement systems, one for feedback control and one for patient monitoring. Even when measured correctly, arterial pressure may erroneously feign an incorrect level of depth of anaesthesia for reasons other than artefacts: hypotension may be caused not only by an overdose of isoflurane but also by blood loss, or concomitant use of analgesic or sedative drugs, whereas hypertension may be caused not only

by insufficient isoflurane but also by other problems, for example phaeochromocytoma. In all of these cases the controller would change the inspired isoflurane concentration in the same direction as an anaesthetist. Future arterial pressure control algorithms should be able to operate with intermittent non-invasive pressure measurements. Software design errors may lead to disastrous results. Even extensive testing cannot circumvent this problem. Apart from using software quality assurance techniques and extensive testing, independent alarm systems have to warn early against an erroneous control. A supervisor system has to control the execution of the program and reassure that the entire system switches to a safe basic condition should one part break down. System identification is usually very difficult for a control system. Whereas a human controller can easily assess the type of patient and the stage of the operation (e.g. skin incision), such data are usually not available to an automatic system unless they have been entered previously into the system. At the beginning of the operation, body weight and age of the patient could be entered; before skin incision a button could be pressed, which would temporarily reduce the arterial pressure set-point. Both the anaesthesia system and the human body remain a "black box", the reaction of which can only be predicted to some extent. In such a situation fuzzy logic algorithms appear favourable as a well defined model is not required and rules similar to those used in daily practice can be applied. We conclude from this study that fuzzy logic appears to be a novel approach to overtake control in an ill-defined system, such as the human being.

Appendix

INTRODUCTION TO FUZZY LOGIC CONTROL

Fuzzy logic

In many areas of daily life we work with what are "crisp objects". By "crisp" we imply something is of a yes-or-no type rather than a more-or-less type. We are therefore used to looking at "sets" as crisp objects. In set theory an element can either belong to a set or not, for instance, we look at a set of male individuals and say "John is a boy". But if we go further and attempt to define a set of male individuals as tall or short we then have to define the terms "tall" and "short". The drawing of distinct borders is obviously somewhat arbitrary. If we decide that a person of 170 cm or more is tall and the rest are short, we do not consider the borderline cases such as Peter, who is 169.9 cm and must therefore be classified as "short", whereas John, who at 170 cm is only 1 mm taller, is classified as "tall". This method leaves no room for doubt, although we may "know" that Peter and John are of the same size. Obviously the use of arbitrary rigid limits for classifying a set of elements in subsets may be counter-productive. This type of logic associated with crisp sets is termed crisp or binary logic, implying that the true value of a statement such as "John is tall" can only be either 0 or 1.

In order to avoid this dilemma fuzzy logic is introduced, that is the boundaries of a set are fuzzy instead of crisp. This makes it possible to classify an element as being "to a certain degree" a member of a set. Obviously, it would not be reasonable to apply this approach to the first-mentioned "set of male individuals". But as soon as we talk about the "tall or short male individuals" its convenience becomes immediately apparent. We can now introduce membership function values between 0 and 1 [30]. It will also be noted that fuzzy sets and continuous membership functions are closer to human thinking. There are different ways of defining basic set operations in fuzzy logic [31]; in the limit case, however, all of these definitions match standard definitions of classical binary logic.

It has to be stressed that fuzzy logic and probability theory are conceptually very different. Probability theory deals with questions such as: "there are 30 white balls and 70 black balls in a bag. I draw a ball without looking. Is this ball black? Answer: with a 70% probability it is." Fuzzy logic, on the other hand, deals with questions such as: "I have a grey ball in my hand. Is this ball black? Answer: we assign the value 0 for absolute white and 1 for absolute black. Now the statement "the ball is black" has a truth value of, say 0.2. In other words, the ball is light grey." Fuzziness, therefore, does not imply randomness [32].

Table 3 List of input and output values used for the controller. Both for the input and output, integral values were used to account for the cumulated error in the past. The following fuzzy variables were used: nb = negative big, nm = negative medium, zel = zero large, ns = negative small, ze = zero, ps = positive small, pm = positive medium, pb = positive big, pvb = positive very big. The error is defined as (set value − measured value)/set value. Thus if measured arterial pressure is less than the desired value, a positive relative error results

Input		Output	
Error MAP	Integral of error MAP	Isoflurane	Integral of *Fi* isoflurane
nb		pvb	pb
nm		pb	pb
zel		pm	
ns	ns		pb
ns		pb	ps
ze		pm	ze
ps		ps	ns
ps	ps		nb
pm		ps	nb
nb		ze	nb

KNOWLEDGE-BASED CONTROL

The classical controller calculates the input signal of the plant to be controlled based on the difference between a reference signal and the actual output of the plant. For example, a so-called PID controller considers the error, its integral and its range of change in computing the input signal for the "plant" according to a mathematical formula.

It is, however, also possible to design a controller which uses a knowledge base to perform the controller function. For instance, it is possible to control the speed of a car so that it is constant with the following set of rules:

IF (speed is very low) THEN (accelerate sharply)
IF (speed is low) THEN (accelerate slightly)
IF (speed is high) THEN (decelerate)
IF (speed is very high) THEN (brake)
IF (speed is low AND road is uphill) THEN (accelerate sharply)

Of course, the values for "very low", "low", "high", "sharply", "slightly", etc., have to be defined crisply. It is important to note that, in this example, the input of the plant (car) which is the position of the acceleration and brake pedals can only have four distinct values depending on the crisp definition of sharply and slightly.

FUZZY CONTROL

A fuzzy controller is basically a knowledge-based controller based on "if–then" rules where the variables have fuzzy instead of crisp values. A fuzzy controller consists of: a *fuzzification module* which does a linguistic classification of variables; a *fuzzy knowledge-base* which is similar to a regular knowledge-base as in the car example above containing rules of the type "IF (error is slightly negative) THEN (fresh gas concentration is small). An example of the if–then rules applied to the controller described in this study is given in table 3; an *inference engine* which uses the fuzzy rules in the knowledge-base to produce a fuzzy control output based on

control inputs; and a *defuzzification module* which determines a crisp control value from a fuzzy control value.

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