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Real-time expert-system-based fuzzy control of mean arterial pressure in pigs with sodium nitroprusside infusion

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Abstract

This paper deals with real-time fuzzy control of mean arterial pressure (MAP) in pigs by regulating the infusion rate of the vasodilator drug, sodium nitroprusside (SNP). The fuzzy controller was based on the parallel firing mode of a general-purpose Fuzzy LOgic Production System shell, FLOPS [2, 3, 16, 20]. One of the major advantages of this fuzzy control drug delivery system over other existing automatic drug delivery systems is that the fuzzy control system may be designed by using experts' knowledge and experience without any explicit mathematical models involved. Mean arterial pressure in pigs was controlled satisfactorily in real-time by the fuzzy control system. It comes to the conclusion that it may be feasible to employ this fuzzy controller in the management of mean arterial pressure of patients clinically. Also, various applications of the fuzzy controller may exist in industry and in biomedical engineering.

I. Introduction

After cardiac surgery, many patients exhibit acute arterial hypertension that may cause complications such as increased bleeding, disruption of vascular suture lines, rhythm disturbances, poor perfusion of cardiac muscle and possible cerebrovascular accident. Treatment with intravenous infusion of SNP has become a widespread practice. Since the drug is very fast acting and extremely potent, control systems have been developed to automatically administer the infusion of SNP for reducing and regulating mean arterial pressure. Some examples are nonlinear proportional-integral-derivative (PID) control, adaptive control, self-tuning control and optimal control. The control systems were successfully applied to patients in the hospital or to animals in the laboratory [1, 6–10, 14, 15, 17–19, 22, 23]. The results were superior to those obtained manually.

Modeling biological systems in humans and animals is complex and automation of control may be more difficult than for industrial processes. But, a fuzzy controller may be better suited for automatic control than other controllers because fuzzy controller design may be achievable without a mathematical model of the process [5, 11–13, 24, 27, 28].

Fuzzy controller is based on Zadeh's fuzzy set theory [26]. An example of fuzzy set 'old' is given in Fig. 1. The y coordinate is grade-of-membership and the x coordinate is universe of discourse. The curve is called grade-of-membership function measuring the extent to which a universe belongs to the fuzzy set. For any fuzzy set, the grade-of-membership runs from zero (does not belong) to one (belongs completely). Of course, different people may have different definition of 'old'. Therefore, the shape of the grade-of-membership function shown in Fig. 1 may be different from one person to another. Fuzzy set theory provides a very powerful

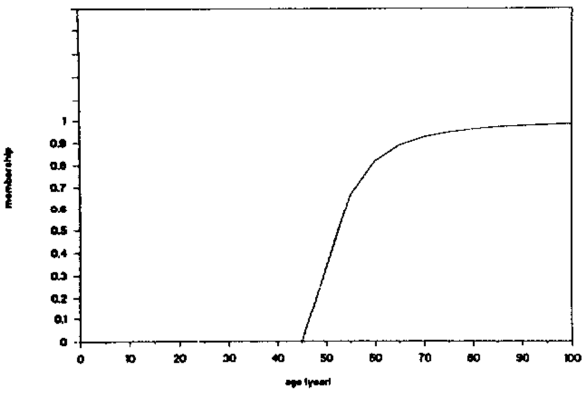

Fig. 1. An example of fuzzy set – 'old'.

tool to quantitize quality variables, such as 'old' in the example.

A fuzzy controller employs a group of control rules from experts which describes in words the relationship between inputs and outputs of the process. It first converts its crisp inputs into fuzzy sets and, then, obtains its fuzzy output by using fuzzy reasoning and the control rules. Finally, the fuzzy output is defuzzified to get the crisp output of the fuzzy controller and the crisp output is transmitted to the process to be controlled. Obviously, a fuzzy controller works like a process operator who can manipulate the outputs of the process very well by using his knowledge, operational experience and control strategy.

We reported our previous work on developing a new kind of fuzzy controller based on a fuzzy expert system shell FLOPS and applying the fuzzy controller to control mean arterial pressure by regulating the infusion rate of SNP based on digital computer simulation [25]. This paper describes our further effort on this project, i.e., real-time fuzzy control of mean arterial pressure in pigs by adjusting the infusion of SNP based on the fuzzy expert system shell, FLOPS. The fuzzy control drug delivery system is, in fact, an expert system since it is rule-based and is incorporated with an expert system shell. We built the fuzzy controller into the expert system shell because they had much in common. In our previous research, a DEC MicroVAX II computer was used to do computer simulation study. But, to achieve fuzzy control of MAP in pigs in real-time by using a popular and inexpensive computer like IBM personal computer, the FLOPS-based fuzzy controller had to be simplified so that execution time and amount of RAM required would be reduced to an acceptable range.

It is worth notice that the design of the fuzzy controller was entirely independent of any mathematical models. The parameters of the fuzzy controller can be tuned by using designer's experience with the controller and the process to be controlled as well as trial and error method. Of course, a mathematical model of the process is always helpful. Fuzzy controller is especially useful when a mathematical model of a process is not achievable, but it may also be useful even when a model is available because fuzzy control provides an alternative control method. Better control performance may be achieved due to the nonlinear nature of fuzzy controller.

II. Fuzzy control drug delivery system based on FLOPS

The structure of the fuzzy control drug delivery system is illustrated in Fig. 2. Mean arterial pressure in pigs was controlled by regulating the infusion rate of the drug SNP.

The hardware of the fuzzy control system includes:

1. a COMPAQ PORTABLE II portable personal computer (8 MHz clock speed and with a 80287 mathematical co-processor),
2. a DATA TRANSLATION DT2801 series 10-bit 16-channel data acquisition board,
3. a computer controlled digital drug infusion pump IMED 927 (resolution 1 ml),
4. a RS232C serial port,
5. an animal respirator Harvard 613, and
6. HP 78200 series monitors with amplifiers.

The computer and the drug infusion pump can communicate with each other through the RS232C serial port so that the computer can read and write the statuses of the pump and control the pump to transmit desired infusion rate of SNP to pigs. The signals from pigs were sent to the amplifiers of the

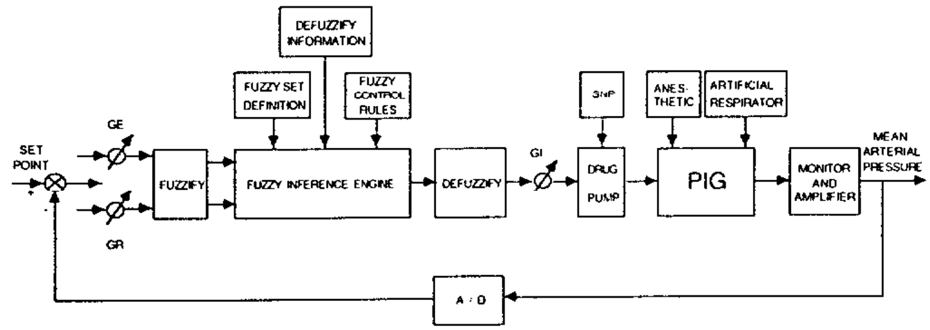

Fig. 2. Structure of the fuzzy control drug delivery system which was based on the fuzzy expert system shell, FLOPS.

monitors by the transducers. The multi-channel A/D converters on the DT2801 board sampled in real-time the amplified signals at a sampling period of 10 seconds. The variables sampled were systolic pressure, diastolic pressure, MAP, right atrial pressure, left atrial pressure and heart rate. Among these variables, MAP was sampled for control. A data file was used to real-time keep infusion rate of SNP and infused volume of SNP, in addition to above six variables, for off-line analysis purpose. The animal respirator was used to maintain respiration of pigs.

The fuzzy controller was based on the fuzzy expert system shell, FLOPS. FLOPS is a general-purpose fuzzy production system shell developed at the Kemp-Carraway Heart Institute in 1985. It is commercially available on the market. FLOPS runs on IBM PC/XT/AT compatible computers and the DEC MicroVAX II computer. FLOPS, which employs fuzzy logic concepts, is a non-procedural data-driven programming language suitable for reasoning under conditions of contradictions, uncertainties and ambiguities. The features of FLOPS include:

1. deductive and inductive reasoning,
2. fully automatic backtracking in sequential mode,
3. parallel firing mode,
4. rules to generate new rules, and
5. working with a powerful blackboard system.

The parallel firing mode of FLOPS was used to develop the fuzzy controller. The sequential firing mode of FLOPS could also be used but it would be slower. Since the parallel FLOPS implements inductive reasoning, all rules which are fireable by data will be fired simultaneously.

In addition to the fuzzy controller program written in FLOPS, several other programs written in C programming language were used to control timing, to control the multi-channel A/D board, to control the digital infusion pump and to keep the necessary information in a data file. The fuzzy controller program in FLOPS, running as the main program among the programs, could communicate with other programs in C, passing commands and data back and forth between the fuzzy controller program and these auxiliary C programs.

III. Method of designing the real-time FLOPS-based fuzzy controller

The fuzzy controller sequentially performed during every sampling period the following:

1. calculated scaled error and rate change of error (rate, for short) of mean arterial pressure,
2. fuzzified the crisp scaled error and rate of mean arterial pressure into corresponding fuzzy sets, 'error' and 'rate',
3. employed fuzzy reasoning on the fuzzy sets, 'error' and 'rate' of mean arterial pressure, by using the fuzzy control rules to get fuzzy output of the fuzzy controller, and
4. defuzzified the fuzzy output to get the crisp output of the fuzzy controller and transmitted the crisp output to the drug infusion pump.

At nT sampling time (n was a positive integer and T was the sampling period of the fuzzy controller), scaled error, e(nT), and scaled rate, r(nT), were calculated by

$$e(nT) = [MAP(nT) - \text{setpoint}] \times GE$$
$$r(nT) = [MAP(nT) - MAP(nT - T)] \times GR/T$$

where MAP(nT) and MAP(nT − T) were mean arterial pressures at nT and (n − 1)T sampling times, respectively. GE and GR were scalers for error and rate of mean arterial pressure, respectively. The scaled inputs, e(nT) and r(nT), were then fuzzified into corresponding fuzzy sets, 'error' e~(nT) and 'rate' r~(nT), according to the definitions of the fuzzy sets.

The number of member and the shape of membership functions of the fuzzy sets effect the performance of the fuzzy controller. The shape of the membership functions includes triangle, normal distribution and trapezoid, etc. Unfortunately, so far, there is no sound theory on how the number of member and the shape of membership functions of the fuzzy sets effect control performance and how to select them correctly to meet controller designer's performance specifications. Therefore, the definitions of the fuzzy sets must be decided by using controller designer's experience with fuzzy controller. In our computer simulation project on fuzzy control of mean arterial pressure, 11 members with shape of trapezoid for the fuzzy sets, 'error' and 'rate', were used. Generally speaking, if M members were employed for the fuzzy set 'error' and N members were used for the fuzzy set 'rate', then, MN fuzzy control rules need to be used to cover all possible inputs of the fuzzy controller. Obviously, the more members, the more fuzzy control rules. However, the more fuzzy control rules, the more execution time and computer RAM are required. In the simulation study, 11 members of the fuzzy sets, 'error' and 'rate', were employed and, therefore, 121 fuzzy control rules were needed. To save execution time and computer RAM in the real-time fuzzy control project, we used the definitions of 'error' and 'rate' shown in Fig. 3. The definitions of the fuzzy sets, 'error' and 'rate', were the same and were stored in the first of the three fuzzy databases. The interval [−L, L] was the range in which the fuzzy controller worked. Normally, L should be so chosen that the maximum of |e(nT)| (|r(nT)|) is less than or equal to L. We decided L = 10 in the real-time control study because L = 10 in simulation study worked properly. After fuzzification, the fuzzy set e~(nT) (r~(nT)) always had two grade-of-memberships that associated respectively with the members, 'positive' and 'negative'. The summation of these two memberships was always equal to 1.0. The following is the corresponding four fuzzy control rules used in real-time control:

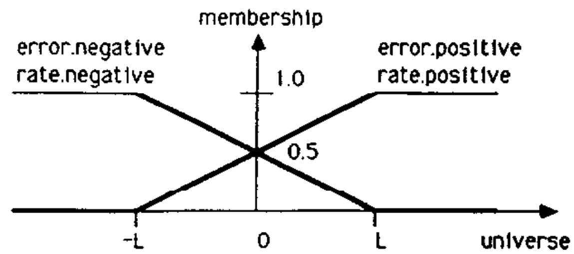

Fig. 3. Definitions of the fuzzy sets 'error' and 'rate change of error'.

if e~(nT) is positive and r~(nT) is positive
then i~(nT) is negative
if e~(nT) is positive and r~(nT) is negative
then i~(nT) is zero
if e~(nT) is negative and r~(nT) is positive
then i~(nT) is zero
if e~(nT) is negative and r~(nT) is negative
then i~(nT) is positive

where i~(nT) stood for the fuzzy set 'rate change of SNP infusion rate'. The fuzzy control rules were held in the third of the three fuzzy databases. Figure 4 illustrates the simulated performance comparison of fuzzy control of mean arterial pressure between the fuzzy controller with 121 fuzzy control rules and the fuzzy controller with four fuzzy control rules. Other parameters of the fuzzy controllers were the same. The difference between two performances was insignificant. However, execution time and computer RAM were reduced considerably.

To obtain the fuzzy set 'rate change of SNP infusion rate' i~(nT) from the fuzzy sets, e~(nT)

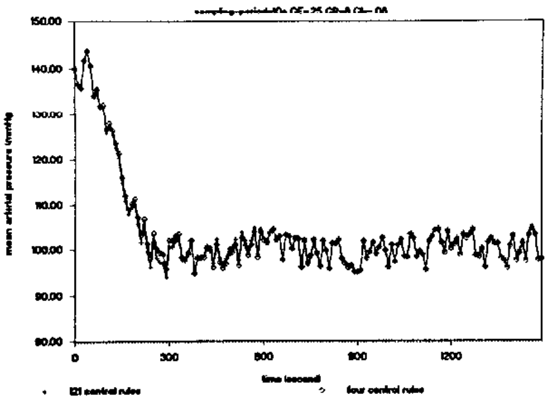

Fig. 4. Performance comparison between the fuzzy controller with 121 fuzzy control rules and that with four fuzzy control rules.

and r~(nT), the fuzzy reasoning shown below was used:

i~(nT) is 'positive' with grade-of-membership
Min(en, rn)
i~(nT) is 'zero' with grade-of-membership
Max (Min(ep, rn), Min(en, rp))
i~(nT) is 'negative' with grade-of-membership
Min(ep, rp),

where Min is Zadeh's fuzzy AND operator while Max is Zadeh's fuzzy OR operator, respectively. Ep and en (rp and rn) were the grade-of-memberships of e~(nT) (r~(nT)) for the members 'positive' and 'negative', respectively. The fuzzy controllers with different fuzzy control rules and fuzzy reasoning methods have different control performances [4, 21].

Following is an example to show how the fuzzy reasoning mentioned above worked and how the fuzzy set 'rate change of SNP infusion rate' i~(nT) was resulted from e~(nT) and r~(nT).

Suppose, after fuzzifying e(nT) and r~(nT), we have

e~(nT) is 'positive' with grade-of-membership
0.931
e~(nT) is 'negative' with grade-of-membership
0.069
r~(nT) is 'positive' with grade-of-membership
0.853
r~(nT) is 'negative' with grade-of-membership
0.147

In other words, mean arterial pressure is highly above the setpoint of mean arterial pressure (membership for 'positive' 'error' is 0.931) and mean arterial pressure has a strong tendency to run away from the setpoint further (membership for 'positive' 'rate' is 0.853).

By using above fuzzy reasoning, the fuzzy set 'rate change of SNP infusion rate' i~(nT) will be

i~(nT) is 'positive' with grade-of-membership
Min(0.069, 0.147) = 0.069
i~(nT) is 'zero' with grade-of-membership
Max (Min(0.931, 0.147), Min(0.069, 0.853)) =
Max(0.147, 0.069) = 0.147
i~(nT) is 'negative' with grade-of-membership
Min(0.931, 0.853) = 0.853

which means infusion rate of SNP should be reduced greatly (membership for 'negative' i~(nT) is 0.853).

The fuzzy set 'rate change of SNP infusion rate' should be defuzzified into a crisp value since the fuzzy set i~(nT) is not acceptable by the pump. The defuzzification algorithm used in the simulation study was

$$i(nT) = GI \times S \times T/W.$$

In the expression, GI was the output scaler of the fuzzy controller and T was the sampling period. A sampling period of 10 seconds is preferred based on our experience with automatic drug delivery control system which has been used clinically at the University of Alabama Hospital for 13 years. On the other hand, the sampling period 10 seconds was achievable because use of only four fuzzy control rules reduced execution time of the fuzzy controller to about nine seconds. S = grade-of-memberships of i~(nT) multiplying corresponding midpoints of i~(nT) (According to Fig. 2, the midpoints of i~(nT) in our research were L (+10) for 'positive', 0 for 'zero' and −L (−10) for 'negative'. The defuzzification information was stored in the second of the three fuzzy databases). W = the summation of all the grade-of-memberships of i~(nT). Since the defuzzification algorithm was effective in the simulation study, it was also used in the real-time control study.

If we still take above example, then,

$$i(nT) = \frac{GI \times (0.069 \times 10 + 0.147 \times 0 + 0.853 \times (-10)) \times 10}{0.069 + 0.147 + 0.853} = -73.34 \times GI.$$

That means the infusion rate of SNP will be reduced greatly which makes sense since mean arterial pressure is far above the setpoint and has strong tendency to run away from the setpoint further.

The scalers GE, GR and GI used in real-time control study were the same as those used in computer simulation study for average patients, i.e., $GE = 0.25$, $GR = 8$ and $GI = -0.08$. The effect of changing GE, GR and GU on control result was not studied in real-time experiments because it was studied in the simulation study.

The i(nT) was summed with the previous drug infusion rate (the drug infusion rate sent to pigs at sampling time $nT - T$) to produce new drug infusion rate. The new drug infusion rate was transmitted to the drug infusion pump to control mean arterial pressure in pigs.

The fuzzy controller program consisted of 22 FLOPS rules. When the program ran, it first generated an additional 16 FLOPS new rules automatically. Among these 16 FLOPS rules, 11 rules were generated by the FLOPS rules from the three fuzzy databases, with a total of 11 records. To achieve different performance for a process or to control different processes, controller designer may change the three fuzzy databases easily. No program change is required.

IV. Description of the pig experiment

Female pigs weighing from 15 to 20 Kg were used as the experimental subject. Food was held for 24 hours prior to the experiments. On the day of the experiment, the pig was anesthetized with a bolus of pentobarbitol sodium, 30 mg/Kg IP, and anesthesia maintained by continuous IV infusion of about 200 mg pentobarbitol sodium plus 0.6 mg pancuronium per hour into the right external jugular vein.

The pig was intubated and connected to a Harvard respirator with a respiration rate of 13, using a gas mixture of 60% N_2O-40% O_2. Arterial cannulation was performed through the right carotid artery to measure systolic pressure, diastolic pressure and mean arterial pressure. The right external jugular vein was used for right atrial pressure measurement, and the left external jugular vein for SNP infusion. A median sternotomy was done and pericardium incised to expose the heart of the pig. A cannula was placed in the left atrial appendage for pressure measurement. The heart rate was monitored through leads I or II of the ECG.

After cannulation of the pig, systolic pressure, diastolic pressure, MAP, right atrial pressure, left atrial pressure and heart rate were monitored for about five minutes to make sure that all the variables were stable. Then, the fuzzy control test began and the setpoint of MAP, the scalers GE, GR and GI and time period of the test were inputted into the fuzzy controller manually. On each pig, there were four or five trials. A typical trial lasted for 30 to 45 minutes. In some of the pigs with low MAP, Neosynephrine was infused at a rate of approximately 6 mg/hr to produce higher initial MAP.

MAP in pigs was controlled by infusing SNP. The SNP was mixed just prior to the pig experiments in D5W (Dextrose 5% in Water) 0.5 mg/ml. It was infused by an IMED 927 infusion pump through an IMED Accuset polyethylene administration set to avoid adsorption problems.

V. Discussion of control results

Figure 5 illustrates the typical real-time fuzzy control result of mean arterial pressure in pigs. For this trial, the high initial MAP was obtained by infusing Neosynephrine. Figure 6 is the infusion rate of SNP corresponding to mean arterial pressure shown in Fig. 5. The desired specifications for the drug deliv-

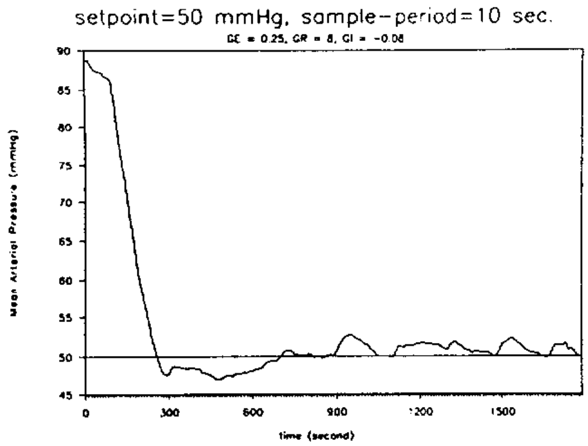

Fig. 5. A typical real-time fuzzy control result of mean arterial pressure in pigs.

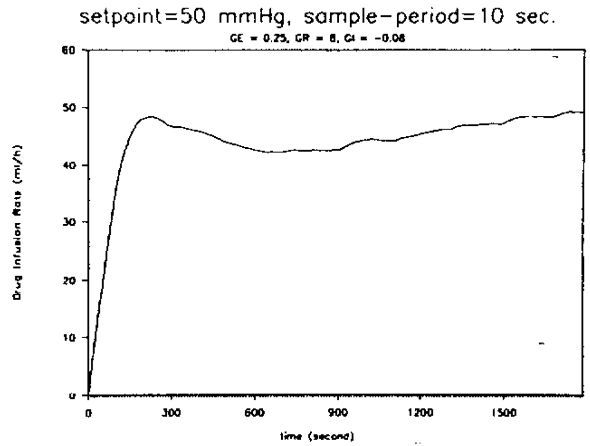

Fig. 6. Infusion rate of sodium nitroprusside corresponding to the fuzzy control result of mean arterial pressure shown in Fig. 5.

ery system are that MAP should be settled from one setpoint to another within 5 to 20 minutes with no more than 5 mm Hg overshoot and no permanent offset. Also, the control system should be able to maintain mean arterial pressure near the setpoint within a tolerance of ±5 mm Hg. The results shown met these specifications.

It is desirable to compare the performances of the fuzzy control drug delivery system with a non-fuzzy control drug delivery system. However, this kind of comparison is difficult because the biological systems in pigs are changing with time. Different results may be obtained even by the same controller with same set of parameters but running at different time. Therefore, the comparison was not pursued in this project and may be pursued in future project.

Summary

The experimental results of fuzzy control of mean arterial pressure in pigs revealed that the performance of the fuzzy control drug delivery system was satisfactory. It may be feasible to apply this fuzzy control system to control other variables in the biomedical engineering area as well as in other industry areas. The next reasonable and logical step is to test this fuzzy control drug delivery system on patients and eventually implement this control system at a hospital for clinical management of hypertension.

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