Fuzzy Control of Mean Arterial Pressure in Postsurgical Patients with Sodium Nitroprusside Infusion

Hao Ying, *Member, IEEE,* Michael McEachern, Donald W. Eddleman, *Member, IEEE,* Louis C. Sheppard, *Fellow, IEEE*

Abstract—**We developed a fuzzy control system to provide closed-loop control of mean arterial pressure (MAP) in postsurgical patients in a cardiac surgical intensive care unit setting by regulating sodium nitroprusside (SNP) infusion. The fuzzy controller, originally expert-system-based, was analytically converted to ten nonfuzzy control algorithms, which reduced execution time dramatically. The core of the control algorithms was a nonlinear proportional-integral (PI) controller whose proportional gain and integral gain adjusted continuously according to error and rate change of error of the process output. The gains became larger when process output was far from desired setpoint and smaller when process output was close to desired setpoint, resulting in more dynamic and stable control performance than the regular PI controller, especially when a linear process with time-delay or a nonlinear process was involved. The control algorithms, encoded in C programming language, were implemented to control MAP in patients. Preliminary clinical results showed that the average percentage of time in which MAP stayed between 90% and 110% of the MAP setpoint was 89.31%, with a standard deviation of 4.96%. These were calculated based on 12 patient trials, with total trial time of 95 and 13 min.**

I. Introduction

THE fast-acting vasodilator drug sodium nitroprusside (SNP) is used to treat patients who demonstrate elevated systematic arterial blood pressure after open-heart surgery. The rapid and powerful action of SNP imposes upon nursing personnel the task of frequent monitoring of mean arterial pressure (MAP) followed by adjustment of SNP infusion rate. Because nurses have many other duties, inappropriate or infrequent control actions on SNP adjustment may occur, which may lead to poor system performance.

To improve the quality of patient care, automatic closed-loop control SNP delivery systems have been developed. A nonlinear proportional-integral-derivative (PID) control system was first built and used clinically in the mid-1970's [9]. A similar control system was also implemented clinically later [2]. Various control algorithms including nonlinear adaptive control, multiple-model adaptive control and adaptive multivariable control were developed and tested [3], [5]–[8], [12], [13]. Clinical study indicated that automatic control was effective and superior to manual control [1], [2]. Furthermore, as the result of over six years of intensive collaborative effort between IVAC^{TM} Corporation and The Cleveland Clinic, IVAC Corporation began marketing its TITRATOR^{TM} SNP Closed Loop Module Model 10K in recent years.

The success of developing the above-mentioned drug delivery control systems, especially the adaptive control systems, heavily depended on mathematical models of patients. However, accurately identifying a mathematical model of patients is a very difficult task, due to the complexity of the human body. Modelling a process is not easy. Even if a process model is available, it may still be challenging to design an appropriate controller to achieve desired system performance. For a simple linear process without time-delay, designing a suitable linear controller is relatively easy. However, if a process involves time-delay, nonlinearity, or time-variance, a suitable controller may be difficult to design. For these kinds of processes, nonlinear controllers normally perform better than linear controllers do. But, designing nonlinear controllers is much more difficult because of the lack of general nonlinear control theory. To control complex systems involving time-delay, nonlinearity or time-variance, fuzzy controllers may be needed, because they can be constructed empirically without explicit mathematical models of the processes involved.

Following the invention of fuzzy set theory in 1965 [19], the first fuzzy controller was developed in 1974 [4]. Fuzzy controllers are linguistic if-then rule-based and can be designed using control operators' knowledge and experience about processes. A fuzzy controller can thus be regarded as an expert system employing fuzzy logic for its reasoning. Fuzzy controllers, being generally nonlinear, provide an alternative means to solve time-delay, nonlinear and time-variant control problems whether mathematical models of processes involved are available or not.

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H. Ying was with the Department of Biomedical Engineering, University of Alabama at Birmingham, Birmingham, AL 35294. He is now with the Department of Physiology and Biophysics, Biomedical Engineering Center, and Office of Academic Computing, University of Texas Medical Branch, Galveston, TX 77555.

M. McEachern and D. W. Eddleman are with Kemp-Carraway Heart Institute, Carraway Methodist Medical Center, Birmingham, AL 35234.

L. C. Sheppard was with the Department of Biomedical Engineering, University of Alabama at Birmingham, Birmingham, AL 35294. He is now with the University of Texas Medical Branch, Galveston, TX 77555.

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Biological systems such as the human body involve time-delay, nonlinearity and time-variance. Designing appropriate controllers for such systems based on existing nonfuzzy control theories is very challenging and time-consuming. The fact that human operators like medical doctors and other clinical personnel can control various physiological parameters of the human body successfully by using their knowledge and experience suggests the possibility of using fuzzy controllers in these situations.

Because fuzzy controllers are linguistic rule-based and have much in common with expert systems, experts' knowledge and experience can be incorporated into the fuzzy controllers. Merger of fuzzy controllers and expert systems will provide potent controllers that are capable of learning, adapting, and self-organizing. These types of controllers may be useable for complicated biological control problems that are solvable by human operators but unsolvable by existing nonfuzzy controllers.

We had previously developed a generalized expert-system-shell-based fuzzy controller [15], which we then utilized to control MAP by regulating SNP infusion, in both digital computer simulation and real-time in pigs [16], [17]. The encouraging results of this previous research of fuzzy control of MAP clearly indicated that success of fuzzy control MAP in patients was achievable. The results of fuzzy control of MAP in postsurgical patients clinically, which is the first use of a fuzzy controller in a clinical setting, is reported in this paper.

II. Methods and Materials

A. Reduction of Execution Time of the Expert-System-Shell-Based Fuzzy Controller by Analytically Converting It to a Group of Nonfuzzy Control Algorithms

The fuzzy controller that we used in computer simulation and real-time animal experiments was based on a general-purpose fuzzy logic production system shell (FLOPS) [15]. Although the fuzzy controller could take the advantage of the capabilities of the expert system shell and could change its structure flexibly by utilizing different rules and commands of the expert system shell, it was slow in execution time. To make real-time fuzzy control of MAP in patients possible, we analytically converted the expert-system-shell-based fuzzy controller into nonfuzzy control algorithms. The conversion was to reduce execution time considerably and reveal the structure of the fuzzy controller. The method of the conversion is briefly described and the result of the conversion is given in this section. Detailed information is available in a previous paper [18].

Designating MAP(nT) and MAP($nT - T$) as MAP at sampling time nT and $nT - T$ respectively (T is sampling period), the inputs of the fuzzy controller could be represented as

$$e(nT) = \text{MAP}(nT) - \text{setpoint} \tag{1}$$

$$r(nT) = [\text{MAP}(nT) - \text{MAP}(nT - T)]/T \tag{2}$$

where the setpoint was the desired MAP level. The expert-system-shell-based fuzzy controller was made up of following six components.

The first component scaled the inputs, $e(nT)$ and $r(nT)$, respectively by multiplying GE, the scalar for error of MAP, and GR, the scalar for rate change of error of MAP, to obtain scaled inputs, $\text{GE}\cdot e(nT)$ and $\text{GR}\cdot r(nT)$.

The second component comprised the fuzzification algorithms illustrated in Fig. 1 that fuzzified $\text{GE}\cdot e(nT)$ and $\text{GR}\cdot r(nT)$ to obtain fuzzy sets for the inputs. In our study, the same fuzzification algorithm was used to fuzzify both scaled inputs. This yielded a fuzzy set for $\text{GE}\cdot e(nT)(\text{GR}\cdot r(nT))$, $\tilde{e}(nT)(\tilde{r}(nT))$, which was associated with two memberships for two members of the fuzzy set respectively, $\mu_{e+}(\mu_{r+})$ for "positive" and $\mu_{e-}(\mu_{r-})$ for "negative."

The third component contained the four fuzzy control rules listed below that linguistically related the fuzzy sets for inputs to the fuzzy set for incremental SNP infusion rate, $\delta\tilde{\text{SNP}}(nT)$.

If $\tilde{e}(nT)$ is positive and $\tilde{r}(nT)$ is positive then $\delta\tilde{\text{SNP}}(nT)$ is negative; or (r1)

if $\tilde{e}(nT)$ is positive and $\tilde{r}(nT)$ is negative then $\delta\tilde{\text{SNP}}(nT)$ is zero; or (r2)

if $\tilde{e}(nT)$ is negative and $\tilde{r}(nT)$ is positive then $\delta\tilde{\text{SNP}}(nT)$ is zero; or (r3)

if $\tilde{e}(nT)$ is negative and $\tilde{r}(nT)$ is negative then $\delta\tilde{\text{SNP}}(nT)$ is positive. (r4)

The fuzzy set $\delta\tilde{\text{SNP}}(nT)$, shown in Fig. 2, had three members, namely "positive," "zero," and "negative."

The fourth component was Zadeh AND and OR fuzzy logic [19]

$$\text{AND}(\mu_1, \mu_2) = \min(\mu_1, \mu_2) \tag{3}$$

$$\text{OR}(\mu_1, \mu_2) = \max(\mu_1, \mu_2) \tag{4}$$

that defined the relation of the if-part with the then-part in the fuzzy control rules, r1 to r4. Here μ_1 and μ_2 are two memberships of fuzzy sets while min (max) is a fuzzy logic operator which yielded smaller (larger) membership between μ_1 and μ_2. Zadeh AND was used to evaluate the individual fuzzy control rules, and Zadeh OR was used to evaluate the implied OR between fuzzy control rules r2 and r3.

The fifth component defuzzified the fuzzy set $\delta\tilde{\text{SNP}}(nT)$ into a crisp incremental SNP infusion rate, $\delta\text{SNP}(nT)$, using the following defuzzification algorithm:

$$\delta\text{SNP}(nT) = \frac{(\mu_{\delta\text{SNP}+} + \mu_{\delta\text{SNP}-})L}{\mu_{\delta\text{SNP}+} + \mu_{\delta\text{SNP}0} + \mu_{\delta\text{SNP}-}} \tag{5}$$

where $\mu_{\delta\text{SNP}+}$, $\mu_{\delta\text{SNP}0}$ and $\mu_{\delta\text{SNP}-}$ were the memberships corresponding to the respective members of "positive," "zero," and "negative" of the fuzzy set $\delta\tilde{\text{SNP}}(nT)$. These memberships were generated by the four fuzzy con-

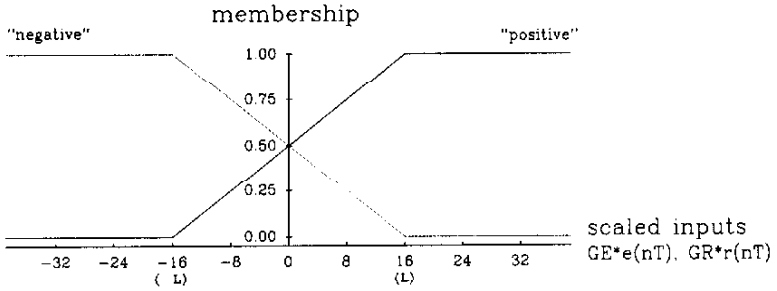

Fig. 1. Fuzzification algorithm for the inputs of the fuzzy controller, scaled error, GE · $e(nT)$, and scaled rate change of error, GR · $r(nT)$, of MAP. The fuzzy sets have two members, "positive" and "negative."

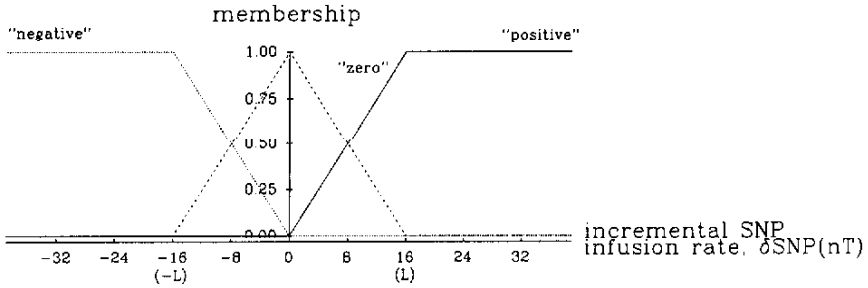

Fig. 2. Fuzzy set for the incremental SNP infusion rate, $\delta\text{SNP}^{\sim}(nT)$. The fuzzy set has three members, "positive," "zero," and "negative."

trol rules. L, defined both in Figs. 1 and 2, was a turning point of the fuzzy sets.

The last component scaled $\delta\text{SNP}(nT)$ by GI, the scalar for incremental SNP infusion rate, to obtain a scaled incremental SNP infusion rate, $\text{GI}\cdot\delta\text{SNP}(nT)$. $\text{GI}\cdot\delta\text{SNP}(nT)$ was then multiplied by sampling time T and was then added to $\text{SNP}(nT - T)$, the SNP infusion rate at sampling time $nT - T$, to get a new SNP infusion rate, $\text{SNP}(nT)$. That is

$$\text{SNP}(nT) = \text{SNP}(nT - T) + \text{GI} \cdot \delta\text{SNP}(nT) \cdot T. \quad (6)$$

To analytically convert the above-described expert-system-shell-based fuzzy controller to a group of nonfuzzy control algorithms, the phase plane of the scaled inputs, $\text{GE}\cdot e(nT)$ and $\text{GR}\cdot r(nT)$, were divided into 20 different regions, shown in Fig. 3. In the figure, IC stands for input combination and ICx means input combination No. x. To show how the conversion worked, let's take IC2 as an example. Suppose that the memberships obtained by using the fuzzification algorithm shown in Fig. 1 are μ_{e+} and μ_{e-} for the scaled error $\text{GE}\cdot e(nT)$, and μ_{r+} and μ_{r-} for the scaled rate change of error $\text{GR}\cdot r(nT)$. Here μ_{e+} and μ_{e-} are the respective memberships for the members "positive" and "negative" of the fuzzy set $e^{\sim}(nT)$ while μ_{r+} and μ_{r-} are the respective memberships for the members "positive" and "negative" for the fuzzy set $r^{\sim}(nT)$. Note that for scaled inputs in the IC2 region,

$$0 \le \text{GR}\cdot r(nT) \le \text{GE}\cdot e(nT) \le L. \quad (7)$$

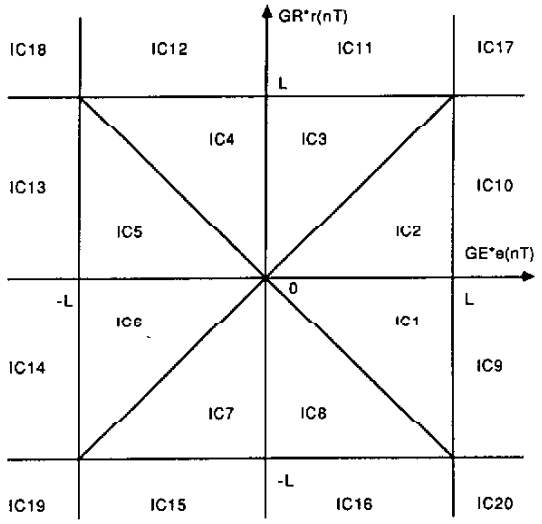

Fig. 3. Input combination (IC) of scaled error, $\text{GE}\cdot e(nT)$, and rate change of error, $\text{GR}\cdot r(nT)$, of MAP. $L = 16$, as shown in Fig. 1.

Therefore according to Fig. 1, $\mu_{e+} \ge \mu_{r+}$ and $\mu_{e-} \le \mu_{r-}$. The memberships for the fuzzy set $\delta\text{SNP}^{\sim}(nT)$ can be obtained by using Zadeh AND and OR fuzzy logic.

"positive" or $\delta\text{SNP}^{\sim}(nT)$ with membership μ_{e-}, (8)

"zero" of $\delta\text{SNP}^{\sim}(nT)$ with membership μ_{r-}, (9)

"negative" of $\delta\text{SNP}^{\sim}(nT)$ with membership μ_{r+}. (10)

Be aware that Figs. 1 and 2 can be expressed as

$$\mu_{e+} = [\mathrm{GE}\cdot e(nT) + L]/2L \tag{11}$$

$$\mu_{e-} = 1 - \mu_{e+} \tag{12}$$

$$\mu_{r+} - [\mathrm{GR}\cdot r(nT) + L]/2L \tag{13}$$

$$\mu_{r-} = 1 - \mu_{r+}. \tag{14}$$

Substitute the memberships in the expressions (8) through (10) into the defuzzification algorithm (5). We can then simplify the algorithm by utilizing (11)–(14) to get

$$\delta\mathrm{SNP}(nT) = -\frac{L\cdot\mathrm{GI}}{3L - \mathrm{GE}\cdot e(nT)} \cdot [\mathrm{GE}\cdot e(nT) + \mathrm{GR}\cdot r(nT)]. \tag{15}$$

Similarly, we can convert the expert-system-shell-based fuzzy controller to nonfuzzy control algorithms for other input combinations. A total of ten different nonfuzzy control algorithms for 20 different input combinations can be obtained: these are listed in Table I.

It should be noted that these nonfuzzy control algorithms are the analytical description of the expert-system-shell-based fuzzy controller. Therefore, they precisely represent the fuzzy controller. Usually, such precise representation is not possible because the structures of fuzzy controllers are so complicated that they can not be described analytically.

The resultant ten control algorithms discussed above were employed in the patient trials. The control algorithms were encoded in C programming language and the execution time for each input was only a fraction of a second. Not only was the execution time reduced dramatically but the time used to design the control system was also reduced. The analytical expressions shown in Table I enabled us to analyze the structure of the fuzzy controller as well as the role of the different components and parameters of the fuzzy controller.

B. Nonlinear Characteristic of the Fuzzy Controller

Among the ten control algorithms discussed above, the most important in affecting performance are two nonlinear control algorithms corresponding to the input combinations of scaled inputs IC1, IC2, IC5, and IC6 and IC3, IC4, IC7 and IC8 shown in Fig. 3.

If $\mathrm{GR}\cdot|r(nT)| \le \mathrm{GE}\cdot|e(nT)| \le L$,

$$\delta\mathrm{SNP}(nT) = -\frac{L\cdot\mathrm{GI}}{3L - \mathrm{GE}\cdot|e(nT)|} \cdot [\mathrm{GE}\cdot e(nT) + \mathrm{GR}\cdot r(nT)] \tag{16}$$

if $\mathrm{GE}\cdot|e(nT)| \le \mathrm{GR}\cdot|r(nT)| \le L$,

$$\delta\mathrm{SNP}(nT) = -\frac{L\cdot\mathrm{GI}}{3L - \mathrm{GR}\cdot|r(nT)|} \cdot [\mathrm{GE}\cdot e(nT) + \mathrm{GR}\cdot r(nT)]. \tag{17}$$

TABLE I
THE SCALED INCREMENTAL SNP INFUSION RATE OF THE FUZZY CONTROLLER, $\mathrm{GI}\cdot\delta\mathrm{SNP}(nT)$, FOR THE DIFFERENT SCALED INPUT COMBINATIONS (IC) ILLUSTRATED IN FIG. 3. GI IS THE SCALAR FOR $\delta\mathrm{SNP}(nT)$. GE AND GR ARE THE SCALARS FOR THE INPUTS, $e(nT)$ AND $r(nT)$, RESPECTIVELY. L, ILLUSTRATED IN FIGS. 1 AND 2, IS THE TURNING POINT OF THE FUZZY SETS, $\tilde{e}(nT)$ AND $\tilde{r}(nT)$

Input Combinations (IC) of the Scaled Inputs	Scaled Incremental SNP Infusion Rate, $\mathrm{GI}\cdot\delta\mathrm{SNP}(nT)$
IC1, IC2, IC5, and IC6	see equation (16)
IC3, IC4, IC7, and IC8	see equation (17)
IC9 and IC10	$-[\mathrm{GR}\cdot r(nT) + L]\cdot\mathrm{GI}/2$
IC11 and IC12	$-[\mathrm{GE}\cdot e(nT) + L]\cdot\mathrm{GI}/2$
IC13 and IC14	$-[\mathrm{GR}\cdot r(nT) - L]\cdot\mathrm{GI}/2$
IC15 and IC16	$-[\mathrm{GE}\cdot e(nT) - L]\cdot\mathrm{GI}/2$
IC17	$-L\cdot\mathrm{GI}$
IC18	0
IC19	$L\cdot\mathrm{GI}$
IC20	0

If the fuzzy controller is appropriately designed, MAP should stay in these input combination regions most of the time and gradually approach the origin of the phase plane of $\mathrm{GE}\cdot e(nT)$ and $\mathrm{GR}\cdot r(nT)$ ($e(nT) = 0$ and $r(nT) = 0$).

Comparing (16) and (17) to the proportional-integral (PI) control algorithm in the discrete-time form

$$\delta\mathrm{SNP}(nT) = -[K_i \cdot e(nT) + K_p \cdot r(nT)] \tag{18}$$

where K_p and K_i are the proportional gain and integral gain, the fuzzy controller can clearly be regarded as a nonfuzzy nonlinear PI controller, with a proportional gain

$$K_{\mathrm{pd}} = \frac{L\cdot\mathrm{GI}\cdot\mathrm{GR}}{3L - \mathrm{GE}\cdot|e(nT)|} \quad \text{or} \quad \frac{L\cdot\mathrm{GI}\cdot\mathrm{GR}}{3L - \mathrm{GR}\cdot|r(nT)|} \tag{19}$$

and an integral gain

$$K_{\mathrm{id}} = \frac{L\cdot\mathrm{GI}\cdot\mathrm{GE}}{3L - \mathrm{GE}\cdot|e(nT)|} \quad \text{or} \quad \frac{L\cdot\mathrm{GI}\cdot\mathrm{GE}}{3L - \mathrm{GR}\cdot|r(nT)|} \tag{20}$$

continuously changing with error, $e(nT)$, and rate change of error, $r(nT)$, of the system output. When MAP is in a steady state, that is, when $e(nT) = 0$ and $r(nT) = 0$, (16) and (17) become

$$\delta\mathrm{SNP}(nT) = -\frac{\mathrm{GI}}{3}[\mathrm{GE}\cdot e(nT) + \mathrm{GR}\cdot r(nT)] \tag{21}$$

which is a PI controller with $K_p = \mathrm{GI}\cdot\mathrm{GR}/3$ and $K_i = \mathrm{GI}\cdot\mathrm{GE}/3$. If MAP is not in a steady state, K_{pd} and K_{id} in (19) and (20) are always greater than the respective K_p and K_i of the corresponding PI controller. That is

$$\frac{K_{\mathrm{pd}}}{K_p} = \frac{K_{\mathrm{id}}}{K_i} = \frac{3L}{3L - \mathrm{GE}\cdot|e(nT)|} \ge 1, \quad \text{if } \mathrm{GR}\cdot|r(nT)| \le \mathrm{GE}\cdot|e(nT)| \le L \tag{22}$$

$$\frac{K_{\mathrm{pd}}}{K_p} = \frac{K_{\mathrm{id}}}{K_i} = \frac{3L}{3L - \mathrm{GR}\cdot|r(nT)|} \ge 1, \quad \text{if } \mathrm{GE}\cdot|e(nT)| \le \mathrm{GR}\cdot|r(nT)| \le L. \tag{23}$$

The larger $e(nT)$ and $r(nT)$ are, the greater the difference between K_{pd} and K_p(K_{id} and K_i). Nevertheless, the maximum difference is reached when $GE \cdot |e(nT)| = L$ and/or $GR \cdot |r(nT)| = L$. At these points, K_{pd} and K_{id} are $GI \cdot GR/2$ and $GI \cdot GE/2$, respectively, which are 50% larger than the integral gain and the proportional gain, namely $K_p = GI \cdot GR/3$ and $K_i = GI \cdot GE/3$, associated with a corresponding PI controller.

The nonlinearity of the fuzzy controller expressed in (16) and (17) can be also changed by using different values of GE, GR, and L. As one extreme, if the value of $L \rightarrow \infty$, then $K_{pd} \rightarrow K_p$ and $K_{id} \rightarrow K_i$, which means the fuzzy controller becomes the PI controller. On the other hand, the smaller the value of L, the more nonlinear the fuzzy controller is.

The controller may switch from one control algorithm to another in Table I, depending on the change of input combination from time to time. However, the switching is always continuous and smooth on the boundaries of two or more adjacent input combinations involved. For example, on the boundary between IC6, IC7, IC14, IC15, and IC19 on which $GE \cdot e(nT) = -L$ and $GR \cdot r(nT) = -L$, any control algorithm for the input combinations involved produces the same $\delta SNP(nT)$ as others do.

Two of the control algorithms shown in Table I impose restraints on maximum increment and decrement of SNP infusion rate for any sampling period. The maximum decrement, $L \cdot GI \cdot T$, is reached when the scaled inputs are in the IC19 region. The maximum increment, $-L \cdot GI \cdot T$, is earned when the scaled inputs are in region IC17. For the values of the parameters we chose, $L = 16$, $GI = -0.06$, and $T = 10$ s (the choice of these values will be discussed in the next section), the maximum increment was 9.6 mL/h and the maximum decrement was 9.6 mL/h. It should be noted that the restraints are characteristics of the fuzzy controller itself rather than safety mechanisms built in by the authors.

The understanding of the structure and the role of the parameters of the fuzzy controller made it more effective to design the fuzzy control SNP delivery system for patients by utilizing appropriate nonlinearity and the values of the adjustable parameters of the fuzzy controller.

C. Design of Fuzzy Control SNP Delivery System Based on Computer Simulation

The nonlinearity of the fuzzy controller discussed above was desirable because the controller was to deal with MAP, which was an unknown function involving time-delay, nonlinearity and time-variance of many physiological variables of the human body. However, the nonlinearity of the fuzzy controller had to be confined within an adequate range. This confinement was important in order to adapt to a wider range of the patient's dynamic parameters, and to restrict adverse effects possibly associated with the nonlinear fuzzy controller. Most importantly, properly limiting the range of the nonlinearity and thus avoiding some possible unstable states of the fuzzy control system improved safety of the patients who were extremely sensitive to SNP.

There are five adjustable parameters of the fuzzy controller, namely GE, GR, GI, L and T, which significantly affect the performance of the fuzzy controller. Based on our previous experience, a sampling period of ten seconds was used for the patient trials. To determine the effect of adjusting the other parameters, the mathematical model in Laplace transfer function describing the relationship between SNP infusion rate, SNP(s), and change in MAP in patients, $\delta MAP(s)$ [10], [11]

$$\frac{\delta MAP(s)}{SNP(s)} = \frac{Ke^{-30s}(1 + 0.4e^{-50s})}{1 + 40s} \tag{24}$$

was used in computer simulation. K represented the sensitivity of patients to SNP. K is -0.72 for the normal patients, -0.18 for the insensitive patients and -2.88 for the sensitive patients [10].

As stated in the last section, the nonlinearity of the fuzzy controller can be adjusted by changing the parameters of the controller, GE, GR, and L (GI does not affect nonlinearity). The equations (16) and (17) were utilized to guide tuning of the parameters. The larger GE and/or GR values are, the more nonlinear the fuzzy controller is when L is fixed. We chose the same GE and GR values as those used in the pig experiments [17] for initial patient trials, that is, $GE = 0.25$ and $GR = 8.0$. We increased L from 10, used in the previous study, to 16 to avoid possibly excessive overshoot of MAP for the sensitive patients. Fig. 4 illustrates the effect of the increase in L value on the performance of MAP when the sensitive patients ($K = -2.88$) were tested. The overshoot of MAP was lowered from 16.4% for $L = 10$ to 13.2% for $L = 16$.

After the determination of T, GE, GR, and L values, the value of the scalar for incremental SNP infusion rate, GI, was to be set. GI should be a negative number since the patient sensitivity, K, is negative. According to (16) and (17), GI changes the overall gain of the fuzzy controller. As indicated by (19) and (20), the larger the absolute value of GI, the greater the nonlinear proportional gain K_{pd} and integral gain K_{id} of the fuzzy controller. Too large an absolute value of GI may cause the SNP control system to become unstable. This is especially true when patients are extremely sensitive to SNP. The GI value used in the computer simulation and the pig experiments was -0.08. To attenuate possible large overshoot of MAP and improve the patients' safety, the GI value used in the patient trials was -0.06. The effect of $GI = -0.08$ and $GI = -0.06$ on the performance of MAP for both the sensitive patients ($K = -2.88$) and the normal patients ($K = -0.72$) is shown in Figs. 5 and 6, respectively. According to Figs. 5 and 6, the reduction of absolute value of GI resulted in the decrease of overshoot of MAP from 18.6% to 13.2% for the sensitive patients at the expense of prolonging the rise-time of MAP from 100 to 120 s for the normal patients. This necessary compromise improved the stability of the fuzzy control SNP delivery system for the sensitive patients while losing little dynamic

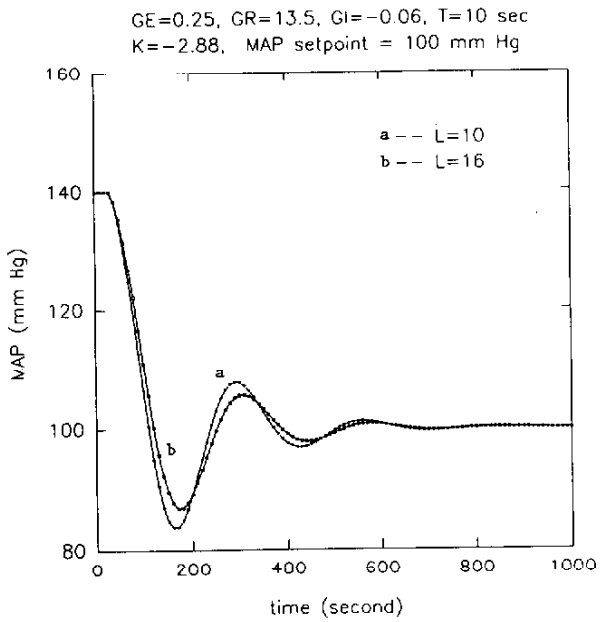

Fig. 4. The effect of increasing the value of L from 10 to 16 on the performance of the fuzzy controller regulating MAP in the sensitive patients ($K = -2.88$) based on computer simulation.

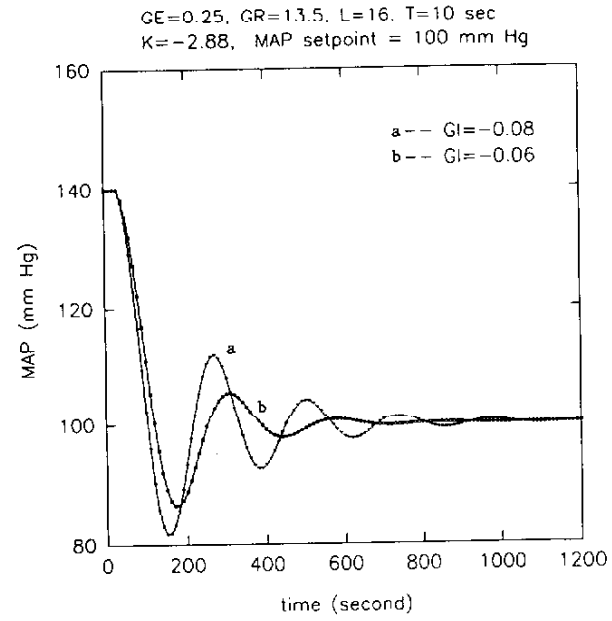

Fig. 5. The effect of decreasing the absolute value of GI from −0.08 to −0.06 on the performance of the fuzzy controller regulating MAP in the sensitive patients ($K = -2.88$) based on computer simulation.

control performance for the normal patients. Further tuning in a clinical setting was necessary to achieve better transient and steady-state response.

To improve patients' safety, we limited the maximum increment of SNP infusion rate to 7.0 mL/h for any sampling time, overriding 9.6 mL/h imposed automatically by the fuzzy controller itself. We also set the increment of SNP infusion rate to zero when MAP was more than 20 mm Hg below the MAP setpoint and when calculated

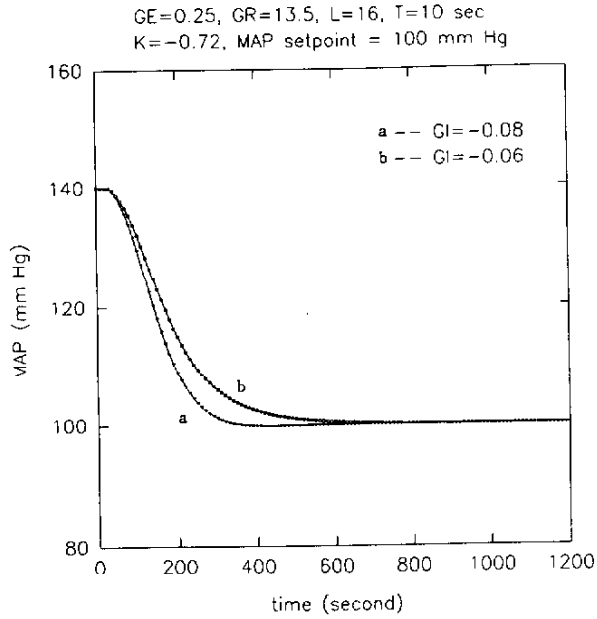

Fig. 6. The effect of decreasing the absolute value of GI from −0.08 to −0.06 on the performance of the fuzzy controller regulating MAP in the normal patients ($K = -0.72$) based on computer simulation.

SNP infusion rate was less than zero. These measures were similar to those used in [9].

D. Clinical Setting

The fuzzy controller designed above was used to maintain desired MAP in patients in the Cardiac Surgical Intensive Care Unit (CICU) of the Carraway Methodist Medical Center. Fig. 7 is a block diagram of the implemented fuzzy control SNP delivery system. A Hewlett-Packard 78534 Monitor/Terminal was used to collect, process, and display MAP, systolic pressure, diastolic pressure, left atrial pressure, right atrial pressure, heart rate, and the electrocardiogram. A Puritan-Bennett 7200a Microprocessor Ventilator was connected to the patients to maintain respiration. MAP values were fed from the Hewlett-Packard Monitor into an IBM PS/2 Model 70 computer, ran the fuzzy controller in the form of the nonlinear control algorithms encoded in C programming language. SNP infusion rate calculated by the fuzzy controller was sent to an Abott/Shaw LifeCare™ Pump Model 4. The pump infused SNP to patients.

Twelve postoperative patients who exhibited elevated MAP following coronary artery bypass grafting procedures took part in the study. Typically the trials began within 1–2 h after the patients arrived in CICU. The typical MAP setpoint, determined by the attending medical doctors or the nurses, was 80 mm Hg. The fuzzy control system was started by technical personnel when the attending nurses thought SNP was needed for a patient. The fuzzy control system was always initiated at a SNP infusion rate of zero. The technical personnel constantly monitored the operation of the control system. During the operation of the fuzzy control system, no special care was given to the patient by the nurses.

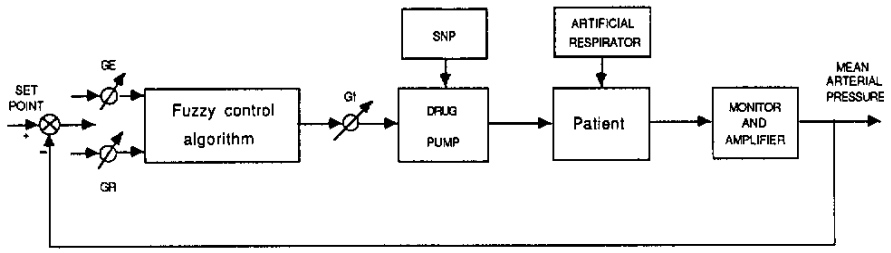

Fig. 7. Block diagram of the fuzzy control SNP delivery system.

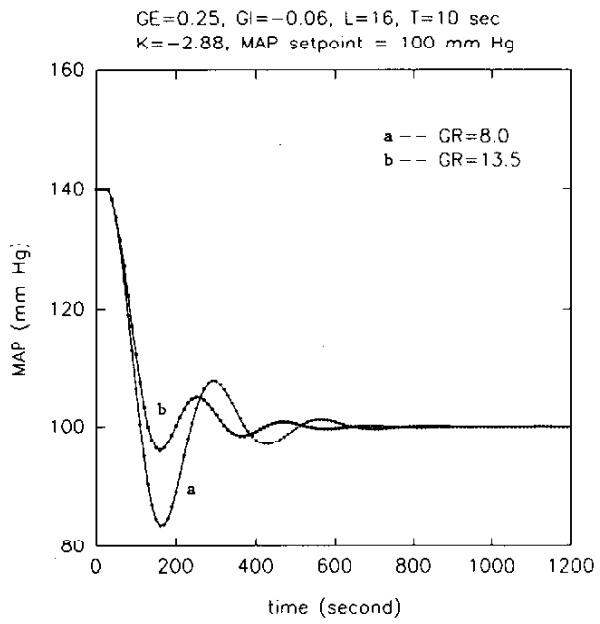

Fig. 8. Comparison of MAP in the sensitive patients ($K = -2.88$) before and after increasing the value of GR from 8.0 to 13.5 based on computer simulation.

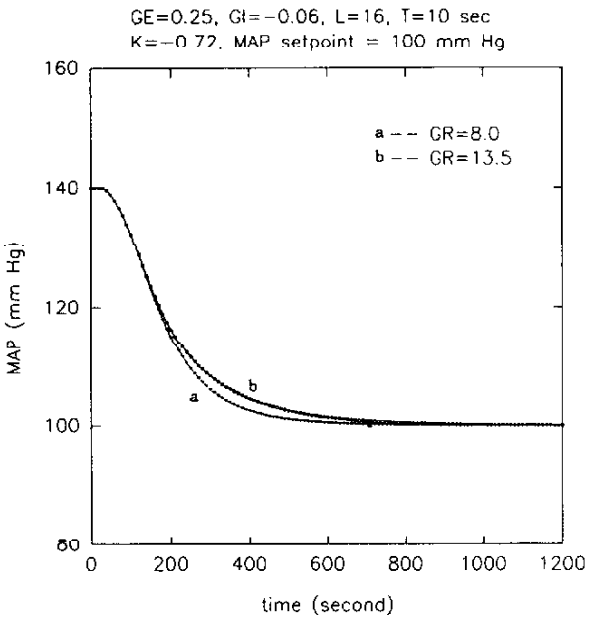

Fig. 9. Comparison of MAP in the normal patients ($K = -0.72$) before and after increasing the value of GR from 8.0 to 13.5 based on computer simulation.

III. Clinical Performance of the Fuzzy Control SNP Delivery System

In the first two patient trials, it was found that SNP infusion rate was not regulated satisfactorily to handle rapid and large changes of MAP. We analyzed the results and concluded that the fuzzy controller did not increase or decrease SNP infusion rate fast enough when MAP was changing dramatically. The problem occurred due to inadequate nonlinearity and lack of sensitivity of the fuzzy controller with respect to the rate change of error of MAP.

To achieve better results, the parameters of the fuzzy controller chosen before the clinical trials should be modified. The mathematical model of the patient described in (24) was utilized to further tune the parameters of the fuzzy controller, especially GR, which scaled the rate change of error of MAP. By varying the nonlinearity and sensitivity of the fuzzy controller with respect to rate change of error of MAP for patients with different sensitivities, a larger GR value 13.5 was found which resulted in better control performance. Figs. 8 and 9 demonstrate the simulated results of the fuzzy control SNP delivery system for the sensitive patients ($K = -2.88$) and the normal patients ($K = -0.72$), before and after GR was increased from 8.0 to 13.5. Obviously, the larger GR made the fuzzy control system considerably more robust. Consequently, the performance of the fuzzy controller was significantly improved and better clinical results were obtained for the remaining ten patients.

Fig. 10 shows a typical trend plot of both MAP and the corresponding SNP infusion rate obtained from a fuzzy controller controlled patient, after the larger GR was implemented. Fig. 11 illustrates how the nonlinear proportional gain K_{pd} and integral gain K_{id} of the fuzzy controller continuously changed with time to cope with the nonlinearities of the MAP response shown in Fig. 10, compared to the constant proportional gain K_p and integral gain K_i of the PI controller.

During the trials, all normal patient care duties were performed by the nurses. The duties included sampling patient blood, suctioning the patient to clear his/her airway, bathing the patient, changing bed linen, injecting drugs other than SNP, infusing blood, and so on. MAP in the patient frequently fluctuated considerably when the above-mentioned duties were being carried out. Sampling blood normally caused MAP to jump up to a high value (say, 150 mm Hg) or down to a low value (say, 20 mm

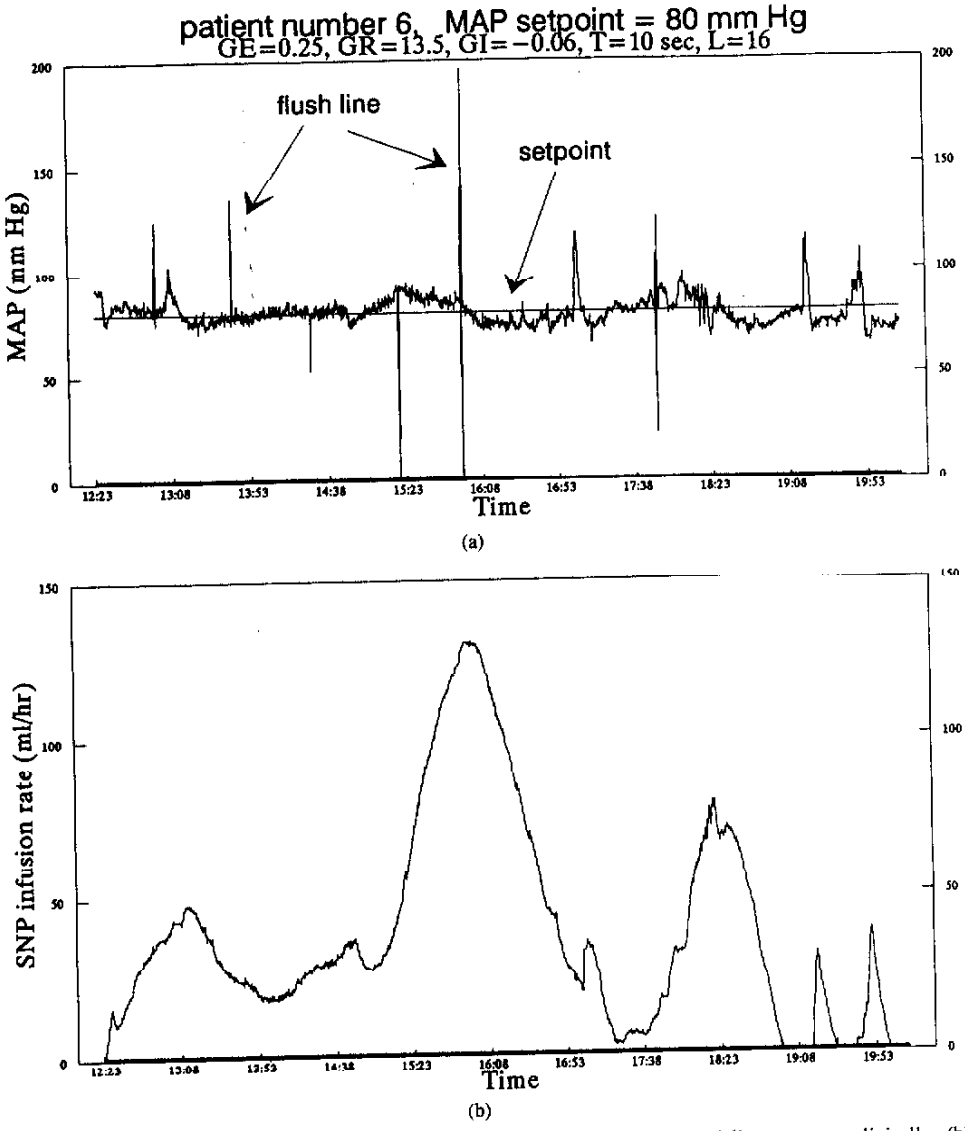

Fig. 10. (a) MAP response for a single patient obtained by using the fuzzy control SNP delivery system clinically. (b) The corresponding SNP infusion rate. The patient had blood sampled at 12:57, 13:42, 15:56, and 17:50. Suctioning the patient began at 13:04, 17:00, and 19:17. The patient was bathed between 15:36 to 15:50. Changing bed linen stated at 19:45 and lasted for several minutes. Injection of Valium took place at 13:09, 14:41, and 17:57. The drugs Pavulon and morphine were injected into the patient at 14:50 and 17:10, respectively.

Hg) within a very short period of time. This temporary fluctuation of MAP signal can be filtered by a digital filter. Such a digital filter, however, was not used in our trials, but is planned for use in future studies. In these trials, the fuzzy controller was manually put into a hold mode right before blood was sampled. The hold mode of the fuzzy controller ignored the MAP signal and sent the previous SNP infusion rate as the current rate to the infusion pump. Fuzzy control resumed upon completion of sampling. The fuzzy controller was always in operation when the patients were being injected with other drugs or infused with blood. The fuzzy controller was generally in operation when the patients were being suctioned, bathed, or having bed linens changed. Suctioning, bathing, and changing bed linen usually caused large fluctuation of MAP, especially when such activities were prolonged. The fuzzy controller was sometimes temporarily put into the hold mode if the fluctuation of MAP was too large. The fuzzy control resumed immediately after the duties were performed. The patient whose MAP is shown in Fig. 10 had blood sampled blood at 12:57, 13:42, 15:56, and 17:50. Suctioning the patient began at 13:04, 17:00 and 19:17. The patient was bathed between 15:36 and 15:50. Changing bed linen started at 19:45 and lasted for several minutes. Injection of Valium took place at 13:09, 14:41, and 17:57. The drugs Pavulon and morphine were injected into the patient at 14:50 and 17:10, respectively.

Besides the situations listed above, other factors also affected MAP. Substantial fluctuation of MAP took place as body temperature of the patients was changing or if the patients were in pain. Spontaneous fluctuation of MAP occurred as well. In addition to these, sensitivity of the

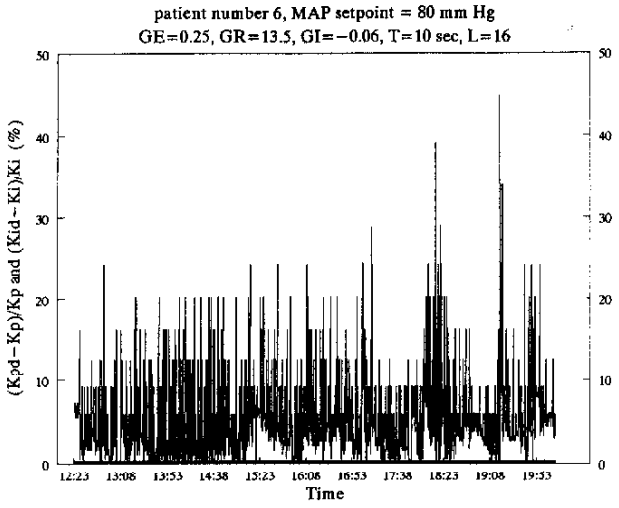

Fig. 11. Comparison of the nonlinear proportional gain K_{pd} of the fuzzy controller to the constant proportional gain K_p of the corresponding PI controller ($(K_{pd} - K_p)/K_p$) showed change of K_{pd} over time corresponding to the nonlinearities in MAP for this patient. Change of K_{id} over time is the same as that of K_{pd} since $(K_{id} - K_i)/K_i = (K_{pd} - K_p)/K_p$.

TABLE II
MEAN (μ) PERCENT OF TOTAL FUZZY-CONTROLLER-RUN TIME (AND STANDARD DEVIATION σ) FOR DIFFERENT MAP INTERVALS. THE CALCULATION IS BASED ON 12 PATIENT TRIALS. MAP_d IS THE DESIRED MAP SETPOINT

	$<0.8\ MAP_d$	$(0.8\text{–}0.9)\ MAP_d$	$(0.9\text{–}1.1)\ MAP_d$	$(1.1\text{–}1.2)\ MAP_d$	$>1.2\ MAP_d$
μ	1.00	3.92	89.31	3.85	1.92
σ	1.09	2.72	4.96	1.84	1.14

patients to SNP changed with time. The response delay to SNP varied among the patients. Nevertheless, as the result shown in Fig. 10 illustrates, the fuzzy control SNP delivery system regulated MAP satisfactorily even with the fluctuation of MAP caused by the various factors stated above. For this patient, the percentage of time in which MAP stayed within the band between 90% and 110% of the MAP setpoint was 86.5%. The trial lasted 7 h and 49 min.

The length of time that 12 patients were on the fuzzy control system ranged from 1 h 45 min to 18 h 7 min. The total fuzzy-controller-run time was 95 h 13 min. This includes the time for the patient trials undertaken both before and after the further tuning of the controller parameters. The times for which SNP infusion rate was zero and the patients' own system was regulating MAP were excluded. Time for which the fuzzy controller was put in the hold mode was also excluded. For the sampling period $T = 10$ s, 34 278 MAP samples were collected from the patients. The overall performance of the fuzzy control SNP delivery system in 12 patient trials is summarized in Table II. The table exhibits that MAP is tightly controlled around the desired MAP level.

IV. DISCUSSION

A wide variation of patient sensitivity to SNP was experienced during the clinical trials. Even through different patient sensitivity resulted in different MAP response, it was not estimated since the sensitivity was not needed by the fuzzy controller. The fuzzy controller could cope with different sensitivity by continuously adjusting its nonlinear proportional gain K_{pd} and integral gain K_{id}. To evaluate the ability of the fuzzy control system handling the patients with different sensitivity, computer simulation was conducted by again using the patient model given in (24). The simulated results illustrated in Fig. 12 indicate that the clinically fine-tuned fuzzy control SNP system could adapt to a wide range of patient sensitivity, from the sensitive patients ($K = -2.88$) to the insensitive patients ($K = -0.18$), a ratio of 16:1. This range of sensitivity covers that of most patients [10].

To enhance the performance of the fuzzy control SNP delivery system, refinements are necessary. Some "intelligent" digital filters should be developed to identify and process different MAP waveforms generated by different clinical activities such as suctioning the airway and

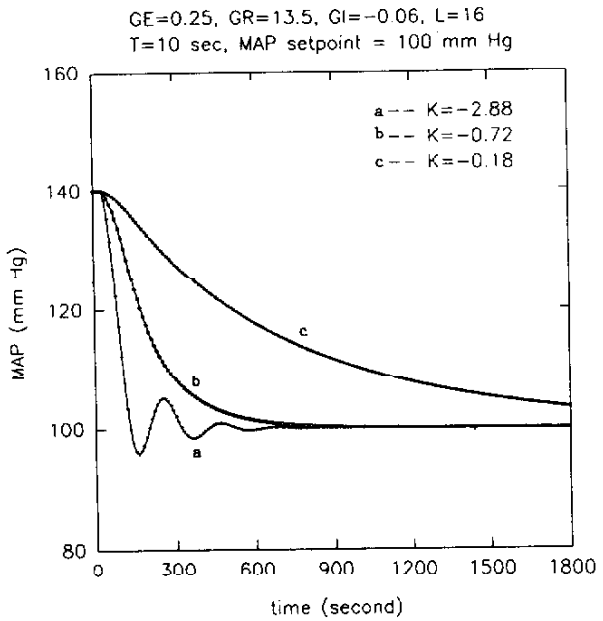

Fig. 12. Simulated MAP for the sensitive patients ($K = -2.88$), the normal patients ($K = -0.72$) and the insensitive patients ($K = -0.18$), using the clinically fine-tuned parameters of the fuzzy controller.

bathing the patient. It would be helpful to let the filters guide the action of the fuzzy controller and adjust the parameters of the fuzzy controller on-line. Additionally, the safety measures and the warning system need to be modified to further improve patient safety.

V. Conclusion

Results of the clinical trials on 12 patients revealed that the performance of the fuzzy control SNP delivery system was clinically acceptable. Based on the clinical results and the simulated results, we expect the fuzzy control SNP delivery system to perform reasonably well for most patients.

The preliminary successful implementation of the nonlinear control algorithms for controlling MAP in patients shows effectiveness in a case involving nonlinearity, time-delay, and time-variance. Therefore, the algorithms should be effective on other physiological variables involving these factors.

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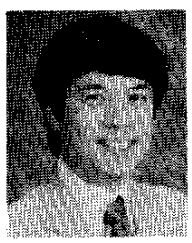
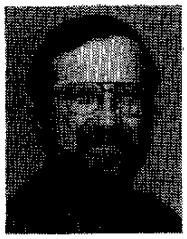


Hao Ying (S'88–M'91) was born in Shanghai, China, on Dec. 11, 1958. He received B.S. and M.S. degrees in electrical engineering from China Textile University, Shanghai, in 1982 and 1984, and the Ph.D. degree in biomedical engineering in 1990 from the University of Alabama at Birmingham. While studying for the Ph.D. degree, he worked as a Research Fellow in the Kemp-Carraway Heart Institute and as an Instructor in the Department of Mathematics at UAB.

He is presently an assistant professor in the Department of Physiology and Biophysics, University of Texas Medical Branch. His research interests include theory and application of fuzzy control, and application of expert systems and neural networks. The focus of his current research is on intelligent control in biomedical environments.



Michael McEachern received the B.A. degree in 1966 and the M.A. degree in 1968 from California State University, Sacramento with a speciality in archeology.

He has worked on various archeological projects in the US, Canada, and Mexico. He began working with the Department of Anthropology at the University of Alabama, Birmingham, in 1977 using computers to analyze archeological materials. He has been with Carraway Methodist Medical Center since 1981 developing software used in the clinical environment.

Donald W. Eddleman (M'87) was born in Key West, FL, on June 8, 1963. He received the B.S. degree in computer science from Southern College of Technology, GA in 1987.

Since 1987 he has been with Carraway Methodist Medical Center implementing a real-time object-oriented device-monitoring system for use in a cardiac surgery intensive care unit.

Mr. Eddleman is a member of the IEEE P1073 standards committee which is developing a family of standards to provide open systems communication in health care applications.

Louis C. Sheppard (SM'79–F'92) was born in Pine Bluff, AR, on May 28, 1933. He received the B.S. degree in chemical engineering from the University of Arkansas in 1957 and the Ph.D. degree in electrical engineering from the University of London, Imperial College of Science, Technology and Medicine, in 1976.

He is now Associate Vice President for Research and Director of the Biomedical Engineering Center at the University of Texas Medical Branch at Galveston (UTMB). He has faculty appointments as Professor of Physiology and Biophysics at UTMB, Professor of Biomedical Engineering at the University of Texas at Austin and Adjunct Professor of Electrical Engineering at the University of Houston. From 1966 until 1988 while a member of the faculty of the Department of Surgery at the University of Alabama at Birmingham (UAB) he was developing and implementing computer-based systems for intensive care that included automated blood and drug infusion for closed-loop, feedback control of cardiac and vascular pressures. From 1979 through 1988 he was the first Chairman of the Department of Biomedical Engineering at UAB. His experience in industry exceeded nine years, six years (1957–1963) in petrochemicals (Diamond Shamrock) and over three years (1963–1966) in medical computing (International Business Machines).

Dr. Sheppard is a Registered Professional Engineer in Texas and Alabama.