Design of control systems for regulation of mean arterial blood pressure of hypertension patients

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Design of Control Systems for Regulation of Mean Arterial Blood Pressure of Hypertension Patients

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SCHOOL OF ELECTRICAL & ELECTRONIC ENGINEERING

NANYANG TECHNOLOGICAL UNIVERSITY

2006

Design of Control Systems for Regulation of Mean Arterial Blood Pressure of Hypertension Patients

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School of Electrical & Electronic Engineering

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in fulfillment of the requirement for the degree of
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Summary

It is known that postoperative hypertension is common in cardiac patients and untreated hypertension patients may result in complications. This thesis mainly presents a fuzzy logic multiple-model adaptive control system for postoperative blood pressure management. Multiple-model adaptive control (MMAC) algorithm is used to identify the patient model, and it is a feasible system identification method even in the presence of large noise. A fuzzy control (FC) method is used to design a controller bank. Each fuzzy controller in the controller bank is in fact a nonlinear proportional-integral (PI) controller, whose proportional gain and integral gain are updated by using the error and its change of the plant, resulting in improved control performance compared to the regular PI controller, especially when handling a wide range of parameter changes and nonlinearities in the plant. For a demonstration, a nonlinear pulsatile-flow patient model is used for simulation, and the results show that the proposed multi-model control system can effectively handle the changes in patient's dynamics and provide satisfactory performance in blood pressure control of hypertension patients.

This thesis also presents a self-tuning controller. A new algorithm updating variations in time delay and sensitivity of the system is proposed. The controller can also be used to control sodium nitroprusside (SNP) delivery, and its performance is discussed.

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Acronyms

AP	Arterial pressure
CICU	Cardiac surgical intensive care units
FC	Fuzzy control
MAP	Mean arterial pressure
MMAC	Multiple-model adaptive control
PI	Proportional-integral
RLS	Recursive least squares
SNP	Sodium nitroprusside

Chapter 1

Introduction

1.1 Motivation

After completion of open-heart surgery, patients are usually sent to cardiac surgical intensive care units (CICU) for recovery. While in the CICU, some patients develop high mean arterial pressure (MAP). Such hypertension should be treated timely to prevent severe complication. To decrease the chances of complication, it is necessary to reduce the elevated blood pressure. Continuous infusion of vasodilator drugs, such as sodium nitroprusside (SNP), would quickly lower the blood pressure in most patients. However, it is known that a wide range of patient drug sensitivities to SNP occurs and critical patient care often requires the infusion of blood, fluid, or drugs to regulate cardiovascular system variables. Therefore, manual control by clinical personnel could be very tedious, time consuming and inconsistent. Automation of these therapies by application of feedback control techniques can be effective.

1.2 Objectives

The main objective of this study is to develop and improve the automatic control system in

order to effectively and accurately adjust the patient's arterial blood pressure. Conventional control methods cannot satisfy the requirements, because the mean arterial pressure system has some unique characteristic such as the wide range of patient sensitivities to the drugs. To resolve the problem of time delay, nonlinear time-varying system, adaptive fuzzy logic control algorithms are investigated.

1.3 Major Contributions of the Thesis

1) Utilization of the Strongpoint of Two Control Algorithms

To improve the quality of patient care, automatic closed-loop control systems for SNP delivery have been developed. A proportional-integral (PI) controller-based multiple-model adaptive control (MMAC) system was built in [1], and was improved by Martin [2-4] [11]. MMAC is a feasible system identification method even in the presence of large noises. However, our simulations have shown that PI controller cannot work well because the system is nonlinear. A fuzzy control system was presented in [6] [17] for regulation of hypertensive blood pressure, and a general fuzzy control method is proposed in [18-20]. These fuzzy controllers can overcome the shortcomings that the PI controller has inherently. However, no identification of the plant model is considered, and the wide range of patient drug sensitivities to SNP is not considered. In this thesis, we present a multiple-model adaptive control (MMAC) algorithm to

identify the patient model, and use a fuzzy control algorithm to design a controller bank. It is shown that the proposed control method can provide satisfactory control performance and can handle changes in patient's dynamics.

2) Generalized Fuzzy Control Algorithms

The details about the fuzzy controller are described in [6] [17], where the expert-system-shell-based fuzzy controller is converted to nonfuzzy control algorithms, and a total of ten different nonfuzzy control algorithms for 20 different input combinations were obtained. We compare the nonfuzzy control algorithms, and generalize them into one algorithm.

3) Improvement of the Convergence Algorithm of Weighting Factors

The convergence algorithm of weighting factors in [1-4] is improved, so that the computation precision of the weighting factors can be enhanced.

4) Physiological Systems Modeling

The thesis presents a nonlinear pulsatile-flow patient model, and it is an extension based on the result presented in [11-14]. It is a complex patient model compared to the Slate's model [7], and is used as a patient plant in our computer simulation.

5) Improvement of Slate's Model

Improvement is made to Slate's model according to the nonlinear pulsatile-flow patient model mentioned above. Furthermore, we find out the relationship between the modified Slate's model and the nonlinear pulsatile-flow patient model through many simulations. A particular nonlinear pulsatile-flow patient model corresponds to a modified Slate's model with larger gain when the bolus input becomes smaller, and corresponds to a modified Slate's model with smaller gain when the bolus input becomes larger.

6) Contribution on Self-tuning Controller Design

In the self-tuning controller design, a new algorithm updating variations in time delay and sensitivity of the system is proposed, which is useful when the approximated model of the

system has the first-order-plus-time-delay transfer function, $F(s) = \frac{Ke^{-T_i s}}{1 + \tau s}$.

1.4 Organization of the Thesis

The thesis is divided into 7 Chapters.

Chapter 2 introduces some biological background on physiological and pharmacological concepts. A patient model developed by Slate [7] is described for subsequent discussion.

Literature survey about efforts on blood pressure regulation is also provided.

Chapter 3 describes the fuzzy controller-based multiple-model adaptive control system for

blood pressure control.

In Chapter 4, computer simulation results are presented to evaluate the response of the system designed in Chapter 3 over a representative plant parameter envelope. Comparisons with previous control systems are also made.

Chapter 5 describes a nonlinear pulsatile-flow patient model, which is used for further computer simulation. Comparison with Slate's model is made, and improvement is made to Slate's model.

In Chapter 6, a self-tuning controller is introduced. A new algorithm updating variations in time delay and sensitivity of the system is proposed.

Chapter 7 gives the conclusion of the thesis. Some recommendations for future work are also discussed in this chapter.

Chapter 2

Problem Formulation

2.1 Physiological and Pharmacological Background

2.1.1 Blood Circulation and Heart

Figure 2.1: Blood circulation and heart

The left figure in Figure 2.1 shows blood circulation. There are really two separate circulatory circuits, the pulmonary circuit and the systemic circuit, with the heart as the common link. In the pulmonary circuit, blood leaves the heart through the pulmonary arteries,

goes to the lungs, and returns to the heart through the pulmonary veins. In the lungs, the blood gives up carbon dioxide and takes on oxygen. In the systemic circuit, blood leaves the heart through the aorta, goes to all the organs of the body through the systemic arteries, and then returns to the heart through the systemic veins.

The right figure in Figure 2.1 shows the cross section of heart. There are four chambers in the heart – two atria and two ventricles. The atria receive blood from the veins. When they contract, they pump blood into the ventricles. Between the atria and the ventricles are valves, that allow blood to flow only in one direction. Valves are also present between the ventricles and the vessels leading from it.

2.1.2 Arterial Blood Pressure Measurement

Arterial pressure is usually measured noninvasively, since this technique is accurate, painless, and convenient to use. The measurement is made with a sphygmomanometer, illustrated in use in Figure 2.2. A pressure cuff is wrapped around the upper arm. The cuff pressure is increased until the pressure on the brachial artery exceeds the systolic arterial pressure, P_s . This stops blood flow in the artery. A stethoscope is then placed on the skin above the brachial artery. No sounds are heard. As the cuff pressure is released, the pressure on the artery falls below P_s , allowing blood to flow through a constriction in the artery. The turbulence of the blood flow makes a pulsing noise known as Korotkoff's sounds. The pressure at which these sounds begin is noted as P_s . The cuff pressure is further released,

and Korotkoff's sounds continue until the brachial artery opens completely and the turbulence stops. The silence returns when the cuff is at the diastolic pressure, P_d .

Figure 2.2: Typical indirect blood pressure measurement

The mean arterial pressure is found by taking the time average of pressure waveform:

$$Mean = \frac{1}{T} \int_0^T P(t) dt. \quad (2.1)$$

Because diastole usually lasts longer than systole, the mean pressure is not simply the value halfway between systolic and diastolic pressures. Instead, the MAP is roughly equal to the diastolic pressure plus one third of the pulse pressure. This can be shown in equation form as:

$$Mean = P_d + \frac{P_s - P_d}{3}, \quad (2.2)$$

where P_d is the diastolic pressure in mmHg. P_s is the systolic pressure in mmHg.

In some cases, it is necessary to measure the blood pressure invasively. This may be done by inserting a sterile, saline-filled catheter into the blood stream. The pressure at the tip of the catheter is then transmitted through the catheter fluid to an external pressure transducer. The physician may choose to enter the catheter into the carotid, femoral, or brachial arteries, as illustrated in Figure 2.3.

Figure 2.3: A pressure monitor connected to a catheter inserted into blood vessel

Our drug delivery control system needs continuous arterial blood pressure, therefore, we adopt invasive blood pressure measurement method. The catheter is entered into the brachial artery, as illustrated in Figure 2.4.

Figure 2.4: The blood pressure measurement method used in our thesis

2.1.3 Sodium Nitroprusside

Sodium nitroprusside is the drug most commonly administered to control transient hypertension because it decreases systemic vascular resistance and has a rapid onset and short duration of action [16]. The action of SNP was simplified to three vascular elements. It would cause a decrease of the systemic resistance (depending upon the concentration of SNP in the small arteries compartment), and increase in the unstressed volume of the veins (depending on the concentration of the drug in the venous compartment), and would reduce the critical closing pressure of the pulmonary vessels [15]. In hospitals, the infusion pump in Figure 2.5 is used to delivery SNP, and the administration set from the pump is connected to a venous puncture. Nurses can set the infusion rate then the pump can work. However, nurses should set the infusion rate from time to time.

Figure 2.5: SNP infusion pump

2.2 Patient Model Developed by Slate

2.2.1 Model and Parameter

A dynamic model of patient mean arterial pressure response to SNP infusion rate developed by Slate [7] will be introduced. It is obtained using animals' as well as actual patients' data together with physiological knowledge about SNP effect. The model has been used as patient model in many papers, such as [1] [5] [6] [8] [10] [15] [17] [26-29]. The model is given by

$$MAP = MAP_0 + \Delta MAP + MAP_n, \quad (2.3)$$

where MAP is the measured mean arterial pressure, MAP_0 is the initial blood pressure, ΔMAP is the change in blood pressure due to infusion of SNP, MAP_n is noise. MAP_0 is usually 115-140 mmHg[1]. The variance of MAP_n is typically 4 (for normal noise levels) or 16-36 (for high noise levels). In the thesis, the unit for blood pressure is mmHg.

Note that the initial blood pressure MAP_0 is usually considered as a constant in many papers.

However, in fact the value of MAP_0 may change with time [9]. For example, after the

patient is cured, his MAP_0 greatly declines and the infusion of SNP can be terminated. Therefore, we consider here that MAP_0 is a parameter in (2.3) and it will change with time.

The transfer function describing the relationship between the change in the blood pressure ΔMAP and the drug infusion rate is given by

$$\frac{\Delta MAP(s)}{SNP(s)} = \frac{K e^{-T_i s} (1 + \alpha e^{-T_c s})}{1 + \tau s}, \quad (2.4)$$

where $\Delta MAP(s)$ is the change in blood pressure due to infusion of SNP, $SNP(s)$ is the SNP infusion rate, K represents the sensitivity of patients to SNP, T_i is the initial delay which results from the transport delay from the injection site and the gradual relaxing of the vascular muscle in response to SNP, α is the recirculation constant, T_c is the recirculation time delay, τ is the lag time constant resulting from the uptake, distribution, and biotransformation of the drug. Note that steady-state gain of dose response is $K(1 + \alpha)$. A range of values for the parameters in the model for different patients is given in Table 2.1. In the thesis, the unit of SNP infusion rate is ml/hr and the concentration of SNP is 200mg/l.

2.2.2 Clinical Constraints

Two clinical constraints are required. The first of them is a maximum allowable infusion rate (a function of patient weight and drug concentration). The reason for this constraint is that SNP is metabolized by the body into cyanide, and hence, too much SNP can be toxic to the patient. The other constraint is that incremental increases in the infusion rate should be limited in magnitude (i.e., no impulses). This is to prevent rapid decreases in pressure which

can cause diminished blood flows or circulatory collapse. Therefore, the following physical and physiological constraints have to be introduced for this system:

The patient's acceptable range of the SNP infusion rate is:

$$0 \leq SNP(k) \leq U_M, \quad (2.5)$$

where k is the sampling time, U_M is the maximum infusion rate. The following equation in [1] is used to compute U_M ,

$$U_M = 60 \times W_p \times i_m \times C_s^{-1}, \quad (2.6)$$

where

W_p = patient weight (the unit is kg),

i_m = maximum recommended dose (the value is $10\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$),

C_s = drug concentration (the unit is $\mu\text{g}/\text{ml}$).

Table 2.1: The range of values for transfer function parameters

Parameter	Unit	Minimum	Maximum	Normal
K	$\text{mmHg}(\text{ml/hr})^{-1}$	-0.25	-9.00	-1.00
T_i	sec	20	60	40
α	-	0	0.4	0.4
T_c	sec	30	75	45
τ	sec	30	60	40

For example, if $W_p = 70\text{kg}$, then

$$U_M = \frac{(60\text{min/hr}) \times 70\text{kg} \times (10\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1})}{200\mu\text{g/ml}} = 210\text{ml/hr}.$$

The patient's acceptable range of the SNP infusion rate change per 10s sampling interval is:

$$-40\text{ml/hr} \leq \text{SNP}(k) - \text{SNP}(k-1) \leq 7\text{ml/hr}. \quad (2.7)$$

2.3 Review of Control Strategy for SNP Delivery

Classical PID control method is widely used in industry. However, classical PID control method is infeasible for the SNP delivery system because a wide range of patient drug sensitivities to SNP occurs and the system is nonlinear.

From 1978 to today, many researchers used classical adaptive control [8] [9] [16] [21-25], adaptive predictive control [5] [26-28] or adaptive neural network control [29-30] method to control blood pressure. These control methods can handle changes in the system dynamics and the wide range of patient drug sensitivities to SNP, but it is difficult to identify the plant when large noise is present.

A proportional-integral (PI) controller-based multiple-model adaptive control (MMAC) system was built in [1], and was improved by Martin [2-4] [11]. MMAC is a feasible system identification method even in the presence of large noises. However, our simulations have shown that PI controller cannot work well because the system is nonlinear.

A fuzzy control system was presented in [6] [17] for regulation of hypertensive blood pressure, and a general fuzzy control method is proposed in [18-20]. These fuzzy controllers can overcome the shortcomings that the PI controller has inherently. However, no identification of the plant model is considered, and the wide range of patient drug sensitivities to SNP is not considered.

2.4 Summary of the Chapter

This chapter briefly introduces some biological background on physiological and pharmacological concepts, including blood circulation, heart structure, heart basic function, blood pressure measurement, SNP pharmacology, etc. A patient model developed by Slate [7] is described for subsequent discussion, and two clinical constraints on SNP delivery are discussed. Literature survey about efforts on blood pressure regulation is also provided.

Chapter 3

Control System Design

3.1 Overview

The MMAC procedure shown in Figure 3.1 is based upon the assumption that the plant can be represented by one of a finite number of models and that for each such model a controller can be *a priori* designed. All of these controllers together then constitute a controller bank. An adaptive mechanism is then needed for deciding which controller should be dominant for a given plant. One procedure for solving this problem is to form a weighted sum of all the controller outputs, where the weighting factors are determined by the relative residuals between the plant response and the model responses.

In Figure 3.1, since the plant gain is negative, the system error is expressed as

$$e(k) = MAP(k) - MAP_c(k), \quad (3.1)$$

where k is the sampling time and $MAP_c(k)$ is the commanded or set-point pressure level.

Figure 3.1: MMAC system structure

The rate change of error is defined by

$$r(k) = [MAP(k) - MAP(k-1)]/T, \quad (3.2)$$

where T is the sampling interval (with $T = 10$ sec).

For patient safety, two nonlinear units are built into the system. The nonlinear unit limiting

SNP infusion rate change is given as

$$f_1(x) = \begin{cases} -40 & \text{for } x < -40 \\ x & \text{for } -40 \leq x \leq 7 \\ 7 & \text{for } x > 7 \end{cases} \quad (3.3)$$

The nonlinear unit limiting SNP infusion rate is given as

$$f_2(x) = \begin{cases} 0 & \text{for } x < 0 \\ x & \text{for } 0 \leq x \leq U_m \\ U_m & \text{for } x > U_m \end{cases} \quad (3.4)$$

where U_M is the maximum infusion rate.

An automated SNP infusion system for blood pressure control should have some performance requirements. These include, after a step change in set point, a 20 percent settling time of less than 15 minutes, a maximum overshoot of less than 10 mmHg, and a steady-state error within ± 5 mmHg [2]. These requirements are used to design the control system. The model bank is described in Section 3.2; the controller bank is given in Section 3.3; and finally, the actual control computation is described in Section 3.4.

3.2 Model Bank Design

The number of models is determined by the performance requirements in Section 3.1. When the fuzzy controllers, which will be described in Section 3.3, are used, eight models are sufficient to meet the requirements. If the number of models is less than 8, the performance of the control system will be deteriorated. On the other hand, if the number of models is larger than 8, the performance won't be better because large noise is usually present.

The model bank in Figure 3.1 consists of 8 models with constant parameters characterizing the individual plant subspace. These models are modified Slate's model, which is described in Section 5.7. These models are given by

$$\frac{\Delta MAP_j(s)}{SNP(s)} = \frac{K_j e^{-20s} (1 + 0.2e^{-50s})}{(1 + 40s)(1 + 45s)}, \quad j = 1, \dots, 8, \quad (3.5)$$

$$MAP_j = MAP_{0\text{INIT}} + \Delta MAP_j, \quad j = 1, \dots, 8, \quad (3.6)$$

where $\Delta MAP_j(s)$ is the blood pressure change of the j^{th} model due to infusion of SNP, $SNP(s)$ is the input of these 8 models, MAP_j is the output of the j^{th} model, $MAP_{0\text{INIT}}$ is the estimated initial value of patient's MAP_0 . $MAP_{0\text{INIT}}$ is calculated in the first 30 seconds, as the average of $MAP(0)$, $MAP(1)$, and $MAP(2)$.

Note that in (3.5), as the recirculation time delay T_c has trivial effect on the control system because the value of α is small, it is frozen in the model bank ($T_c = 50$).

T_{id} and τ are lag time constants, and they can affect the dynamic behavior of the system. In general, smaller T_{id} and τ result in smaller settling time. However, the variable range of T_{id} and τ is not significant and the influence of the variation can be covered by the sensitivity K . Therefore, T_{id} and τ can also be frozen. In the model bank, $T_{cj} = 50$, $T_{idj} = 25$, and $\tau_j = 45$ for $j = 1, \dots, 8$ are selected.

It is noted that while K reflects patient response sensitivity, the effective steady state gain due to the recirculation effect is $K(1 + \alpha)$. That is, the recirculation enhances the effect of infusion [10]. However, the effect of α can be compensated by different K_j for $j = 1, \dots, 8$ and therefore, α can also be frozen with $\alpha_j = 0.2$ for $j = 1, \dots, 8$.

It is known that the transport delay T_{ik} significantly affects undershoot. Controlling a high-infusion-delay patient with a low-infusion-delay model will cause large undershoot. For a blood pressure control system, as large undershoot is not allowed, the maximum transport

delay $T_{ikj} = 20$ for $j = 1, \dots, 8$ should be chosen. Although controlling a low-infusion-delay patient with a high-infusion-delay model causes long settling time, it can be partly compensated by different K_j (for $j = 1, \dots, 8$).

The patient sensitivity K has the greatest effect on controller performance. If the plant has high gain and is being controlled by a low-gain model, large overshoots will occur; if the plant has low gain and is being controlled by a high-gain model, long settling time will occur. Table 3.1 shows the eight models and the range of plants they cover. In the table, columns 2 and 3 are the gains of the eight models and the range of plants they cover, $K_{j\text{MIN}}$ and $K_{j\text{MAX}}$ are the minimum and maximum plant gains that K_j covers. The plant gain partition factor is about 1.56, i.e., $K_{j\text{MAX}} / K_{j\text{MIN}} \approx 1.56$. Notice that $\sqrt{1.56} \approx 1.25$, therefore $K_{j\text{MAX}} / K_j \approx K_j / K_{j\text{MIN}} \approx 1.25$.

Table 3.1: The eight models in the model bank and the range of plants they cover

Model Number	Model Gain (mmHg/(ml/hr))	Plant Gain (mmHg/(ml/hr))
1	-0.3125 (K_1)	from -0.25 ($K_{1\text{MIN}}$) to -0.39 ($K_{1\text{MAX}}$)
2	-0.4875 (K_2)	from -0.39 ($K_{2\text{MIN}}$) to -0.61 ($K_{2\text{MAX}}$)
3	-0.7625 (K_3)	from -0.61 ($K_{3\text{MIN}}$) to -0.95 ($K_{3\text{MAX}}$)
4	-1.1875 (K_4)	from -0.95 ($K_{4\text{MIN}}$) to -1.48 ($K_{4\text{MAX}}$)
5	-1.8500 (K_5)	from -1.48 ($K_{5\text{MIN}}$) to -2.30 ($K_{5\text{MAX}}$)
6	-2.8750 (K_6)	from -2.30 ($K_{6\text{MIN}}$) to -3.60 ($K_{6\text{MAX}}$)
7	-4.5000 (K_7)	from -3.60 ($K_{7\text{MIN}}$) to -5.60 ($K_{7\text{MAX}}$)
8	-7.2000 (K_8)	from -5.60 ($K_{8\text{MIN}}$) to -9.00 ($K_{8\text{MAX}}$)

3.3 Controller Bank Design

3.3.1 Method

The details about the fuzzy controller are described in [6] [17], and we only illustrate the fuzzy control rules used.

- Rule 1: if MAP is above than setpoint and is increasing, then SNP infusion rate is increased.
- Rule 2: if MAP is above than setpoint and is decreasing, then SNP infusion rate should not be varied.
- Rule 3: if MAP is below than setpoint and is increasing, then SNP infusion rate should not be varied.
- Rule 4: if MAP is below than setpoint and is decreasing, then SNP infusion rate should be decreased.

These rules, though very simple, represent the knowledge and experience of human operators like medical doctors and other clinical personnel.

The expert-system-shell-based fuzzy controller is converted to nonfuzzy control algorithms in [6] [17], and a total of ten different nonfuzzy control algorithms for 20 different input combinations are obtained. We compare the nonfuzzy control algorithms, and generalize them into one algorithm as follows

$$\Delta SNP(k) = -GI \cdot T \cdot L \cdot \frac{f(GE \cdot e(k)) + f(GR \cdot r(k))}{3L - \max[f(GE \cdot e(k)), f(GR \cdot r(k))]}, \quad (3.7)$$

where $\Delta SNP(k)$ is the incremental SNP infusion rate, $e(k)$ is error, $r(k)$ is rate change of error, GI is the scalar for incremental SNP infusion rate, T is the sampling interval, GE is the scalar for error, GR is the scalar for rate change of error, L is a turning point of the fuzzy sets in the fuzzy controller and $f(x) = \text{sign}(x) \cdot \min(L, |x|)$. Table 3.2 shows the units of the parameters in (3.7).

Table 3.2: The units of the parameters in (3.7)

Parameter	Unit	Parameter	Unit
$\Delta SNP(k)$	ml/hr	$e(k)$	mmHg
GI	(ml/hr)/sec	GE	(mmHg) ⁻¹
T	sec	$r(k)$	mmHg
L	-	GR	(mmHg) ⁻¹

As illustrated in Figure 3.2, the fuzzy controller is in fact a nonlinear PI controller, whose proportional gain and integral gain are adjusted continuously according to error and rate change of error. The gains become larger when process output is far from desired set-point, resulting in better dynamic and stable control performance than the regular PI controller, especially when a nonlinear process is involved.

Note that the generalized control algorithm given in (3.7) makes the design of the controller bank much easier. There are eight controllers in the controller bank and all of the parameters

except GI are same in the eight controllers, and they are chosen as $L=16$, $GE=0.25$, $GR=15$. Table 3.3 shows GI values of the eight controllers. In the table, column 2 is GI values of the eight controllers, columns 3 and 4 are the gains of the eight models and the range of plants they cover, $K_{j\text{MIN}}$ and $K_{j\text{MAX}}$ are the minimum and maximum plant gains that K_j covers. Notice that, $K_j \cdot GI_j \approx 0.0460$ for $j=1, \dots, 8$.

$$\Delta SNP(k) = \frac{-GI \cdot T \cdot L}{3L - \max[f(GE \cdot e(k)), f(GR \cdot r(k))]} \cdot f(GE \cdot e(k)) + \frac{-GI \cdot T \cdot L}{3L - \max[f(GE \cdot e(k)), f(GR \cdot r(k))]} \cdot f(GR \cdot r(k))$$

Integral gain

Proportional gain

Figure 3.2: The fuzzy controller is in fact a nonlinear PI controller

Table 3.3: GI values of the eight controllers

Model Number	GI	Model Gain (mmHg/(ml/hr))	Plant Gain (mmHg/(ml/hr))
1	-0.1843 (GI_1)	-0.3125 (K_1)	from -0.25 ($K_{1\text{MIN}}$) to -0.39 ($K_{1\text{MAX}}$)
2	-0.1183 (GI_2)	-0.4875 (K_2)	from -0.39 ($K_{2\text{MIN}}$) to -0.61 ($K_{2\text{MAX}}$)
3	-0.0755 (GI_3)	-0.7625 (K_3)	from -0.61 ($K_{3\text{MIN}}$) to -0.95 ($K_{3\text{MAX}}$)
4	-0.0485 (GI_4)	-1.1875 (K_4)	from -0.95 ($K_{4\text{MIN}}$) to -1.48 ($K_{4\text{MAX}}$)
5	-0.0311 (GI_5)	-1.8500 (K_5)	from -1.48 ($K_{5\text{MIN}}$) to -2.30 ($K_{5\text{MAX}}$)
6	-0.0200 (GI_6)	-2.8750 (K_6)	from -2.30 ($K_{6\text{MIN}}$) to -3.60 ($K_{6\text{MAX}}$)
7	-0.0128 (GI_7)	-4.5000 (K_7)	from -3.60 ($K_{7\text{MIN}}$) to -5.60 ($K_{7\text{MAX}}$)
8	-0.0080 (GI_8)	-7.2000 (K_8)	from -5.60 ($K_{8\text{MIN}}$) to -9.00 ($K_{8\text{MAX}}$)

3.3.2 Simulation

Figure 3.3 shows the structure of a simple system with a single controller (instead of controller bank) and without model bank. The parameter GI of the fuzzy controller is selected as $GI = GI_6 = -0.0160$. The parameters of the patient model are chosen as $MAP_0 = 140$, $K = K_6 = -2.8750$, $T_{ik} = 20$, $T_{id} = 25$, $\tau = 45$, $T_c = 50$ and $\alpha = 0.2$. The pressure set-point is chosen as $MAP_c = 100$. The patient weight is $W_p = 70\text{kg}$, so the maximum infusion rate is $U_M = 210\text{ml/hr}$. Figure 3.4 shows the simulation result. Since the range of plants that Model 6 covers is from -2.30 to -3.60 , it is necessary for us to take into account the conditions when the plant gain is at the boundary of Model 6. Figure 3.5 shows the simulation results when the plant gain is -2.3000 , -2.8750 and -3.6000 respectively. The results satisfy the performance requirements in Section 3.1.

Figure 3.3: A simple system with a single controller and without model bank

Figure 3.4: Use of Controller 6 for Model 6

Figure 3.5: Use of Controller 6 for the plants that Model 6 covers

Notice that, $K_{j\text{MAX}} / K_{j\text{MIN}} \approx 1.56$, $K_{j\text{MAX}} / K_j \approx K_j / K_{j\text{MIN}} \approx 1.25$, $K_j \cdot GI_j \approx 0.0460$

(for $j=1,\dots,8$), so, if we use the j^{th} controller to control plants that the j^{th} model covers, then we can also get the similar simulation results as Figure 3.5. Therefore, if the plant identification is correct, the controller bank can provide satisfactory control performance.

3.4 Identification Algorithm

3.4.1 Weighting Factors

To achieve desirable system performance and guarantee patient safety, the identification algorithm should converge quickly to the desired values and should react to time-varying plant characteristics, as well as ensure a reasonable rate of blood pressure change. Thus, the control output is computed as a weighted sum of controller bank signals, i.e.,

$$\Delta SNP(k) = \sum_{j=1}^8 [W_j(k) \times \Delta SNP_j(k)], \quad (3.8)$$

where $W_j(k)$ is the weighting factor of the j^{th} controller, $\Delta SNP_j(k)$ is the output of the j^{th} controller.

3.4.2 Values of the Weighting Factors in the First 3 Minutes

In the first 30 seconds, $MAP_{0\text{INIT}}$ is calculated and during this period, the SNP infusion rate should be set to zero. Therefore, in the first 30 seconds,

$$W_j(k) = 0 \quad (j = 1, \dots, 8).$$

A further discussion on the convergence of W_j will be given later. Since the control variable $SNP(k)$ will be in error before the convergence of W_j , large overshoots could occur for plants with high gain. Therefore, from time $t=0.5 \text{ min}$ to 3 min , the infusion rate is based on the assumption that the most matched model is Model 8, i.e.,

$$W_j(k) = \begin{cases} 0 & \text{for } j = 1, \dots, 7 \\ 1 & \text{for } j = 8 \end{cases}.$$

3.4.3 Convergence Algorithm of Weighting Factors

The convergence algorithm is run from $t=30 \text{ sec}$, and the weighting factors then begin to converge. But their values will not be used until $t=3 \text{ min}$, because the values may not converge from time $t=0.5 \text{ min}$ to 3 min . The algorithm for computing the weighting factors is given by

1) Recursive update

$$W'_j(k) = \frac{\exp[-R_j^2(k)/2V^2] \overline{W}_j(k-1)}{\sum_{i=1}^8 \exp[-R_i^2(k)/2V^2] \overline{W}_i(k-1)}, \quad j = 1, \dots, 8, \quad (3.9)$$

2) Bounding from zero

$$\overline{W}_j(k) = \begin{cases} \delta & \text{for } W'_j(k) \leq \delta \\ W'_j(k) & \text{for } W'_j(k) > \delta \end{cases}, \quad j = 1, \dots, 8, \quad (3.10)$$

3) Normalization

$$W_j(k) = \frac{[W'_j(k)]^2}{\sum_{i=1}^8 [W'_i(k)]^2}, \quad j = 1, \dots, 8, \quad (3.11)$$

where $R_j^2(k)$ is the relative residual which will be given in (3.12), V is a parameter

controlling the convergence rate of $W_j'(k)$ with $R_j^2(k)$. Equation (3.10) is used to prevent

$\sum_{i=1}^8 \exp[-R_i^2(k)/2V^2]W_i'(k-1)$, the denominator on the right in (3.9), from being zero. In the

algorithm, the initial weighting factors $\overline{W}_j(0)$ ($j=1, \dots, 8$) must be determined *a priori*.

They are chosen as $\overline{W}_j(0)=1/8$ for $j=1, \dots, 8$.

The relative residual $R_j^2(k)$ is defined as the normalized squared error between plant and model, i.e.,

$$R_j^2(k) = \left[\frac{MAP_j(k) - MAP(k)}{MAP_{0\text{INIT}} - MAP_c} \right]^2, \quad j=1, \dots, 8, \quad (3.12)$$

where $MAP_j(k)$ is the output of the j^{th} model. In the first 30 seconds, $MAP_{0\text{INIT}}$ is calculated, and the SNP infusion rate should be set to zero in the meantime. Therefore, the relative residual $R_j^2(k)$ for $j=1, \dots, 8$ is set to zero in the first 30 seconds.

Compare [1] with [5], and we found out that

$$V^2 = \frac{\sigma_n^2}{(MAP_0 - MAP_c)^2}, \quad (3.13)$$

where σ_n^2 is the variance of noise associated with MAP. For rapid convergence of $W_j(k)$, a smaller value of V is desired. However, if we choose a small value of V when high noise level is present, the system will be unstable, and therefore, $V=0.1$ is chosen in the thesis.

3.5 Summary of the Chapter

In this chapter, a fuzzy controller-based MMAC algorithm is proposed to control

postoperative hypertension. MMAC algorithm is used to identify the patient model, and fuzzy control algorithm is used to design the controller bank, i.e., the strong points of the two control algorithm are utilized in our control method. We also generalize the fuzzy control algorithm in [6] [17], and improve the convergence algorithm of weighting factors in [1-4].

Chapter 4

Simulation Study

4.1 Introduction

Computer simulations are carried out to evaluate the control system designed in Chapter 3 over a representative plant parameter envelope. The patient's weight is $W_p = 70\text{kg}$, so the maximum infusion rate is $U_M = 210\text{ml/hr}$. In this chapter, modified Slate's model is used to represent a patient. Many computer simulations, which are listed as follows, have been done to test our control system.

- Without Time-varying parameters and without Noise

Different K

Different MAP_c

Different MAP_0

Different T_{ik}

Different T_{id} and τ

Different α

Different T_c

- With Time-varying parameters but without Noise

Time-varying K

Time-varying MAP_c

Time-varying MAP_0

Time-varying T_{ik} , T_{id} , τ and T_c

Time-varying α

- With Time-varying parameters and Noise

The results of simulations indicate that the fuzzy controller-based MMAC algorithm can automatically control blood pressure over a fairly wide plant parameter envelope, even in the presence of large background noise. Comparisons with previous control systems are also made in the chapter.

4.2 A Patient without Time-varying and without Noise

4.2.1 Different Plant Gains

The plant gain K is -0.25 (lowest sensitivity), -1.00 (normal sensitivity), and -9.00 (highest sensitivity), respectively. Other parameters of the patient model are chosen as $MAP_0 = 140$, $T_{ik} = 20$, $T_{id} = 40$, $\tau = 45$, $T_c = 50$, $\alpha = 0.2$. The pressure set-point is chosen as $MAP_c = 100$. Figure 4.1 shows the simulation results. The results satisfy the performance

requirements in Section 3.1.

Figure 4.1: Different plant gains

4.2.2 Different Pressure Set-points

The pressure set-point is often different between patients because it depends on the physiological state of the patient. Even for a particular patient, his pressure set-point sometimes may be adjusted due to his time-varying physiological state. Therefore, it is necessary for us to evaluate the system responses to different pressure set-points.

The pressure set-point MAP_c is chosen as 130 and 70 respectively. The plant gain K is -0.25 (lowest sensitivity), -1.00 (normal sensitivity), and -9.00 (highest sensitivity), respectively. Other parameters of the patient model are chosen as $MAP_0 = 140$, $T_{ik} = 20$, $T_{id} = 40$, $\tau = 45$, $T_c = 50$, $\alpha = 0.2$. Figure 4.2-4.3 show the simulation results.

Figure 4.2: Simulation results when $MAP_c = 130$ Figure 4.3: Simulation results when $MAP_c = 70$

For the patient with plant gain $K = -0.25$ (lowest sensitivity), the pressure set-point 70

cannot be reached, as shown in Figure 4.3, because SNP infusion rate has reached the upper limitation boundary (210ml/hr), as shown in Figure 4.4.

Figure 4.4: SNP infusion rate when $K = -0.25$ and $MAP_c = 70$

4.2.3 Different T_{ik}

T_{ik} is 10 and 20, respectively. Other parameters of the patient model are chosen as $MAP_0 = 140$, $K = -0.25$, $\tau = 45$, $T_{id} = 40$, $T_c = 50$, $\alpha = 0.2$. The pressure set-point is chosen as $MAP_c = 100$. Figure 4.5 shows the simulation result.

Figure 4.5: Different T_{ik}

4.2.4 Different T_{id} and τ

T_{id} is 10 and 40, respectively. Other parameters of the patient model are chosen as $MAP_0 = 140$, $K = -1$, $\tau = 45$, $T_{ik} = 20$, $T_c = 50$, $\alpha = 0.2$. The pressure set-point is chosen as $MAP_c = 100$. Figure 4.6 shows the simulation result.

τ is 30 and 60, respectively. Other parameters of the patient model are chosen as $MAP_0 = 140$, $K = -1$, $T_{ik} = 20$, $T_{id} = 40$, $T_c = 50$, $\alpha = 0.2$. The pressure set-point is chosen as $MAP_c = 100$. Figure 4.7 shows the simulation result.

Figure 4.6: Different T_{id} Figure 4.7: Different τ

Some parameters of the patient model are chosen as $MAP_0 = 140$, $K = -1$, $\tau = 45$,

$T_{ik} = 20$, $T_c = 50$, $\alpha = 0.2$, other parameters (T_{id} and τ) are shown in Figure 4.8. The pressure set-point is chosen as $MAP_c = 100$. Figure 4.8 shows the simulation result.

Figure 4.8: Different T_{id} and τ

4.2.5 Different MAP_0

MAP_0 is chosen as 150 and 115 respectively. The plant gain K is -0.25 (lowest sensitivity) and -9.00 (highest sensitivity), respectively. Other parameters of the patient model are chosen as $T_{ik} = 20$, $T_{id} = 40$, $\tau = 45$, $T_c = 50$, $\alpha = 0.2$. The pressure set-point is chosen as 90.

Figure 4.9 shows the simulation result.

Figure 4.9: Different MAP_0

4.2.6 Different α

α is chosen as 0 and 0.4 respectively. Other parameters of the patient model are chosen as $MAP_0 = 140$, $K = -1$, $T_{ik} = 20$, $T_{id} = 40$, $\tau = 45$, $T_c = 50$. The pressure set-point is chosen as 100. Figure 4.10 shows the simulation result. It is noted that while K reflects patient response sensitivity, the effective steady-state state gain is $K(1+\alpha)$ [10]. Figure 4.11 and Figure 4.12 shows the convergence of the weighting factors. The numerals appearing in them represent the model with the highest weight during that time interval. Weighting factors' values in the first 3 minutes are determined according to Section 3.4.2.

Figure 4.10: Different α Figure 4.11: Convergence process of the weighting factors when $\alpha = 0$

Figure 4.12: Convergence process of the weighting factors when $\alpha = 0.4$

In the model bank, α_j (for $j=1,L,8$) is frozen as 0.2 and the effect of α can be compensated by different K_j (for $j=1,L,8$). Here is a good example. The model with the highest weight during steady state is Model 3 when $\alpha = 0$, as shown in Figure 4.11, and Model 4 when $\alpha = 0.4$, as shown in Figure 4.12.

4.2.7 Different T_c

T_c is chosen as 30 and 75 respectively. Other parameters of the patient model are chosen as $MAP_0 = 140$, $K = -1$, $T_{ik} = 20$, $T_{id} = 40$, $\alpha = 0.2$, $\tau = 45$. The pressure set-point is chosen as 100. Figure 4.13 shows the simulation result.

Figure 4.13: Different T_c

4.3 A Patient with Time-varying Parameters but without Noise

4.3.1 Time-varying Plant Gain

Now let us consider the system response to a time-varying plant gain. The parameters of the patient model are chosen as $MAP_0 = 140$, $T_{ik} = 20$, $T_{id} = 40$, $\tau = 45$, $T_c = 50$, $\alpha = 0.2$.

The pressure set-point is chosen as $MAP_c = 100$. For Line A in Figure 4.14, the plant gain is -1 initially, then decreased by 20% at the 5 min mark (during the transient state), increased by 20% at the 30 min mark (during the steady state). For Line B in Figure 4.14, the plant gain is -1 initially, then increased by 20% at the 5 min mark (during the transient state), decreased by 20% at the 30 min mark (during the steady state).

Figure 4.14: Time-varying plant gain

4.3.2 Time-varying Pressure Set-point

Now let us consider the system response to a time-varying pressure set-point. The parameters of the patient model are chosen as $MAP_0 = 140$, $K = -1$, $T_{ik} = 20$, $T_{id} = 40$, $\tau = 45$, $T_c = 50$, $\alpha = 0.2$. For Line A in Figure 4.15, the pressure set-point is 100 initially, then increased to 120 at the 4 min mark (during the transient state), decreased to 100 at the 30 min mark (during the steady state). For Line B in Figure 4.15, the pressure set-point is 100 initially, then decreased to 80 at the 4 min mark (during the transient state), increased to 100 at the 30 min mark (during the steady state).

Figure 4.15: Time-varying pressure set-point

4.3.3 Time-varying MAP_0

Note that the initial blood pressure MAP_0 is usually considered as a constant in many papers. However, in fact the value of MAP_0 may change with time [9]. Now let us consider the system response to a time-varying MAP_0 . The plant gain K is -0.25 (lowest sensitivity), -1.00 (normal sensitivity), and -9.00 (highest sensitivity), respectively. Other parameters of the patient model are chosen as $T_{ik} = 20$, $T_{id} = 40$, $\tau = 45$, $T_c = 50$, $\alpha = 0.2$, and the pressure set-point is 100. In Figure 4.16, MAP_0 is 140 initially, then increased to 150 at the 4 min mark (during the transient state), decreased to 140 at the 30 min mark (during the steady state). In Figure 4.17, MAP_0 is 140 initially, then decreased to 130 at the 4 min mark (during the transient state), increased to 140 at the 30 min mark (during the steady state).

Figure 4.16: Time-varying MAP_0 Figure 4.17: Time-varying MAP_0

4.3.4 Time-varying T_{ik} , T_{id} , τ and T_c

In clinical applications, it is unlikely that T_i ($T_i = T_{ik} + T_{id}$) would change by more than 20% [8]. Sudden changes in T_i , although not likely to occur in clinical applications, can provide an exacting challenge to the controller stability [10]. T_{ik} , T_{id} , τ and T_c depend strongly on the cardiac index, high cardiac indices result in faster transport and recirculation times [10]. Therefore, T_{ik} , T_{id} , τ and T_c usually simultaneously increase, or simultaneously decrease. Now let us consider the system response to time-varying T_{ik} , T_{id} , τ and T_c . The plant gain K is -0.25 (lowest sensitivity), -1.00 (normal sensitivity), and -9.00 (highest sensitivity), respectively, and $MAP_0 = 140$, $\alpha = 0.2$, $MAP_c = 100$. Initially, T_{ik} , T_{id} , τ and T_c are 10, 10, 30, 30, respectively. Then, they are increased to 20, 40, 60, 75, respectively at the 5 min mark (during the transient state), and decreased to 10, 10, 30, 30, respectively at the 30 min mark (during the steady state). Figure 4.18 shows the simulation results. Note that, during the steady state, the change in T_{ik} , T_{id} , τ or T_c has no impact on the system, because the patient's output, MAP , does not change in the meantime.

4.3.5 Time-varying α

Now let us consider the system response to time-varying α . The plant gain K is -0.25 (lowest sensitivity), -1.00 (normal sensitivity), and -9.00 (highest sensitivity), respectively. $MAP_0 = 140$, $T_{ik} = 20$, $T_{id} = 40$, $\tau = 45$, $T_c = 50$, $MAP_c = 100$. In Figure 4.19, α is 0.1 initially, then increased to 0.3 at the 4 min mark (during the transient state), decreased to 0.1

at the 30 min mark (during the steady state). In Figure 4.20, α is 0.3 initially, then decreased to 0.1 at the 4 min mark, increased to 0.3 at the 30 min mark.

Figure 4.18: Time-varying T_{ik} , T_{id} , τ and T_c

Figure 4.19: Time-varying α

Figure 4.20: Time-varying α

4.4 A Patient with Time-varying Parameters and Noise

The pressure set-point is initially chosen as $MAP_c = 100$. The parameters of the patient model are initially chosen as $MAP_0 = 140$, $K = -2.875$, $T_{ik} = 10$, $T_{id} = 25$, $\tau = 30$, $T_c = 30$, $\alpha = 0.2$. Then, T_{ik} , T_{id} , T_c and τ are changed to 20, 40, 75 and 60 respectively at the 4 min mark, K is increased to -4.5 at the 20 min mark, MAP_c is decreased to 80 at the 35 min mark, α is changed to 0.1 at the 50 min mark, MAP_0 is increased to 150 at the 60 min mark. White Gaussian noise (mean 0, variance 9) is included. Figure 4.21 shows the simulation result. Figure 4.22 shows the convergence of the weights. In the first 30 seconds, all the weights equal zero, so that SNP infusion rate equals zero. From 0.5 min to 3 min, the main weight is W_8 . From 3 min to 20 min, the main weight converges to W_6 because the patient's gain is covered by Model 6. From 20 min to 60 min, the main weight converges to

W_7 because the patient's gain changes to -4.5 , which is covered by Model 7. From 60 min to 70 min, the main weight converges to W_6 because MAP_0 changes. Figure 4.23 shows SNP infusion rate.

Figure 4.21: Mean arterial pressure of a patient with time-varying parameters and noise

Figure 4.22: The convergence of the weights

Figure 4.23: SNP infusion rate

It is necessary to explain why MAP_0 change may cause main weight change. In model bank, MAP_{0INIT} is the estimated initial value of patient's MAP_0 , and is calculated in the first 30 seconds, as the average of $MAP(0)$, $MAP(1)$, and $MAP(2)$. After the first 30 seconds, MAP_{0INIT} remains unchanged. At the 60 min mark, MAP_0 is increased to 150. Although the patient's gain is still -4.5 (covered by Model 7), our control system finds that the output of Model 6 mostly resembles the patient's output because the increase in MAP_0 causes the patient looks being more insensitive to SNP. Therefore, the main weight converges to W_6 . Together with the simulation results in Figure 4.16-4.17, we conclude that MAP_0 change can be compensated by selecting different main weight.

4.5 Comparison with a PI Controller-based MMAC System

A PI controller-based MMAC system for blood pressure control was first built in [1]. The system was improved by Martin [2-4], but PI controllers were still used in the controller bank. Our simulation has shown that PI controller cannot work well because the system is nonlinear.

Figure 4.24 shows the structure of a simple system with a single controller (instead of controller bank) and without model bank. The parameters of the patient model are chosen as $MAP_0 = 140$, $T_{ik} = 20$, $T_{id} = 25$, $\tau = 45$, $T_c = 50$, $\alpha = 0.2$. The plant gain K ranges from -2.30 to -3.60, i.e. the patient model is covered by Model 6 in Table 3.1. The pressure set-point is chosen as $MAP_c = 100$. No noise is introduced. The controller used to control the system is a fuzzy controller (the 6th controller in Table 3.3) and a PI controller (the 6th controller in controller bank of a PI controller-based MMAC system), respectively. Figure 4.25 shows the simulation results when the plant gain is -2.3 and -3.6 respectively. The PI controller in Figure 4.25 has proportional gain $K_p = 0.048$, and integral gain $K_i = 0.001$. Note that we get the parameter values of the PI controller ($K_p = 0.048$, $K_i = 0.001$) through many simulations under the condition of Figure 4.25.

Figure 4.24: A simple system with a single controller and without model bank

Figure 4.25: Use of Controller 6 for the plants that Model 6 covers, $MAP_0 = 140$ and $MAP_c = 100$

Then, let us change the pressure set-point to compare the performances of the fuzzy controller and the PI controller. In Figure 4.26, the pressure set-point is 70, note that the settling time is much longer when PI controller is used. In Figure 4.27, the pressure set-point is 130, and undershoot is too large when PI controller is used. Through many simulations, it is found out that the shape of the system response curves strongly depends on the difference between MAP_0 and MAP_c . For example, in Figure 4.27, if MAP_0 and MAP_c change to 110 and 100 respectively, the shape of the system response curves will only have a little change because the difference between MAP_0 and MAP_c has not changed and figure 4.28 shows the simulation result.

Figure 4.26: Use of Controller 6 for the plants that Model 6 covers, $MAP_0 = 140$ and

$$MAP_c = 70$$

Figure 4.27: Use of Controller 6 for the plants that Model 6 covers, $MAP_0 = 140$ and

$$MAP_c = 130$$

Figure 4.28: Use of Controller 6 for the plants that Model 6 covers, $MAP_0 = 110$ and

$$MAP_c = 100$$

We cannot design a suitable PI controller for the wide range of the difference between MAP_0 and MAP_c because the nonlinear unit limiting SNP infusion rate change exists. Therefore, in the controller bank of a PI controller-based MMAC system, the sixth controller cannot be suitably designed. Some of the other controllers in the PI controller bank have the same problem. On the contrary, the performance of the fuzzy controllers is satisfactory.

4.6 Comparison with a Previous Fuzzy Control System

A fuzzy control system for blood pressure control was built in [6] [17]. However, no identification of the plant model is considered, i.e., a single fuzzy controller is used to control all patients regardless of the wide range of patient drug sensitivities to SNP. Of course, the

controller performance is not good.

Some parameters of the patient model are chosen as $MAP_0 = 140$, $T_{ik} = 20$, $T_{id} = 25$, $\tau = 45$, $T_c = 50$, and other parameters are shown in Figure 4.29 or Figure 4.30. The pressure set-point is $MAP_c = 100$. Figure 4.29 shows the simulation results when the control system in [6] [17] is used. Figure 4.30 shows the simulation results when our control system is used. It is noted that while K reflects patient response sensitivity, the effective steady state gain is $K(1+\alpha)$ [10]. Therefore, the effective steady state gain reaches its minimum value when $K = -0.25$ and $\alpha = 0$, maximum value when $K = -9.00$ and $\alpha = 0.4$. In Figure 5.6, the settling time is too long when $K = -0.25$ and $\alpha = 0$; the system can work well when $K = -1.00$ and $\alpha = 0.2$; the system is unstable when $K = -9.00$ and $\alpha = 0.4$. On the contrary, the performance of our fuzzy controller-based MMAC system in Figure 4.30 is satisfactory.

Figure 4.29: Simulation results when a previous fuzzy control system is used

Figure 4.30: Simulation results when our control system is used

4.7 Summary of the Chapter

In this chapter, computer simulations are carried out to evaluate the control system designed in Chapter 3 over a representative plant parameter envelope, and modified Slate's model is used to represent a patient. The results of simulations indicate that the fuzzy controller-based MMAC algorithm can automatically control blood pressure over a fairly wide plant parameter envelope, even in the presence of large background noise. Comparisons with previous control systems are also made in the chapter. In next chapter, a nonlinear pulsatile-flow patient model, a complex patient model, will be introduced for further computer simulations.

Chapter 5

A Nonlinear Pulsatile-Flow Patient Model

5.1 Introduction

In the chapter, a nonlinear pulsatile-flow patient model will be introduced, and it is an extension based on the result presented in [11-14]. It is a complex patient model compared to the Slate's model [7], and is used as a patient plant in our further computer simulation.

There are both disadvantages and advantages in the use of a model of this type instead of dog experiments. The major disadvantage is that no model will ever perfectly represent a human. However, a dog is not a perfect model of a human either. The major advantage of using a model for the testing of a controller is that a much wider range of patients can be simulated by a model than can be accomplished in experiments on a few different dogs. In the cardiovascular model used for these simulations, it is possible to change, independently or in any combination, the resistances of the arteries and veins, their compliances, the strength of the heart's contraction, heart rate and many other parameters. The effect of different values of the infusion delay, sensitivity to SNP, amount of recirculation, and speed of action of SNP, can all be studied. Simulations on models are also much quicker than dog experiments

allowing for many more simulations to be performed in a given time. Furthermore, model simulations are much less expensive than dog experiments.

As shown in Figure 5.1, the patient model includes three sections as follows:

- SNP pharmacokinetic model,
- SNP pharmacodynamic model,
- Cardiovascular model.

Figure 5.1: A nonlinear pulsatile-flow patient model

For the SNP pharmacokinetic model, the input is SNP infusion rate, the outputs are the concentration of SNP in the arteries and the concentration of SNP in the veins, which are used as the inputs of the following model. For SNP pharmacodynamic model, the outputs are arterial resistance change and venous unstressed volume change, which are used as the inputs of the following model. Finally, for cardiovascular model, the output is arterial pressure, which is used to compute MAP.

The cardiovascular model is described in Section 5.2, the SNP pharmacokinetic model is given in Section 5.3, and the SNP pharmacodynamic model is introduced in Section 5.4. The

three models constitute a nonlinear pulsatile-flow patient model, a much more complex patient model than Slate's model [7]. Computer simulations are made to compare the two models, and improvement is made to Slate's model. Finally, the nonlinear pulsatile-flow patient model is used to test our control system developed in Chapter 3.

5.2 Cardiovascular Modeling

Figure 5.2 shows the electrical equivalent diagram of the cardiovascular model. For example, in the left ventricle, capacitor C_{LV} represents the varying compliance of left ventricle, voltage P_{LV} represents the pressure in left ventricle, resistance R_{LV} represents the resistance between the left atrium and the left ventricle, inductance L_{LV} represents the blood inertance in left ventricle. Mitral valve is between the left atrium and the left ventricle, and aortic valve is between the left ventricle and the aorta. These valves are used to allow blood to flow only in one direction. When left ventricle contracts, it pumps blood into the aorta. Blood goes through arterial pool, venous pool, right atrium, right ventricle, pulmonary circuit, and then goes back to left atrium. With changes in the parameters, a quite number of hypertensive patient's dynamics can be represented.

The electric current F represents blood flow, the quantity of charge Q denotes compartment volume, and the volume of any compartment at a given time is given by

$$Q(t) = \int_0^t [F_{in}(\tau) - F_{out}(\tau)] d\tau + Q(0), \quad (5.1)$$

where $F_{in}(\tau)$ is the flow into the compartment, $F_{out}(\tau)$ is the flow out of the compartment.

Figure 5.2: Electrical equivalent diagram of a nonlinear pulsatile-flow cardiovascular model

The voltage P represents blood pressure, capacitor C represents compartment compliance, and the blood pressure of any compartment at a given time is given by

$$P(t) = \frac{Q(t) - Q_U(t)}{C(t)}, \quad (5.2)$$

where $Q(t)$ is the volume of the compartment, $Q_u(t)$ is the unstressed volume of the compartment.

Blood flow computation has three cases, which are shown in Figure 5.3.

Figure 5.3: Three cases in blood flow computation

In Case One, there is only a resistance between P_1 and P_2 . $F(t)$ is given by

$$F(t) = \frac{P_1(t) - P_2(t)}{R}, \quad (5.3)$$

where $F(t)$ is the blood flow, $P_1(t)$ is the compartment's pressure, $P_2(t)$ is the pressure of the next compartment, R is the resistance. In Case Two, an inductance is added to the circuit. The following equation can be integrated to compute $F(t)$,

$$P_1(t) - P_2(t) = R \cdot F(t) + L \cdot \frac{dF(t)}{dt}, \quad (5.4)$$

where L represents the inductance of blood flow. In Case Three, a valve is added. The

following equations can be solved by computer.

$$\begin{aligned} P_1(t) - P_2(t) &= R \cdot F(t) + L \cdot \frac{dF(t)}{dt}, \\ P_2(t) &= \begin{cases} P_2(t) & \text{if } P_2(t) \leq P_3(t) \\ P_3(t) & \text{if } P_2(t) > P_3(t) \end{cases} \end{aligned} \quad (5.5)$$

The left ventricle is modeled with a varying capacitance, which is given by

$$C_{LV}(t) = \frac{1}{SLV(t)}, \quad (5.6)$$

where $SLV(t)$ is the muscle stiffness of left ventricle.

Figure 5.4 shows the waveform of $SLV(t)$ for a heart period of 0.8 sec. SLS is the maximum value of $SLV(t)$ and SLD is the minimum value. Note that, the waveform has a somewhat slower rise and a faster fall. Right ventricle modeling is similar to left ventricle

Figure 5.4: SLV waveform

modeling. Figure 5.5 shows the pressure waveforms in systemic circuit, which are similar to real human blood pressure waveforms. We don't plot $P_{A1}(t)$ curve because it is very close to $P_{A2}(t)$ curve.

Figure 5.5: Pressure waveforms in systemic circuit

5.3 SNP Pharmacokinetic Modeling

Consider a compartment with average blood flow F (ml/s), and let us assume that the flow is uniform across the diameter of the compartment and that any pulsatility in F is small and may be neglected. The input concentration $\gamma_0(t)$ and output concentration $\gamma_1(t)$ are given by

$$\begin{aligned}\gamma_0(t) &= f_0(t) / F, \\ \gamma_1(t) &= f_1(t) / F,\end{aligned}\tag{5.7}$$

where $f_0(t)$ is the input solute flow, $f_1(t)$ is the output solute flow.

The quantity of solute $q_1(t)$ in the compartment, by mass balance, is

$$q_1(t) = \int_0^t (f_0(t) - f_1(t)) dt + q_1(0), \quad (5.8)$$

where $q_1(0)$ is the initial quantity. Assume that the solute gets perfect mixing immediately in the compartment, then

$$\gamma_1(t) = q_1(t) / V_1(t), \quad (5.9)$$

where $V_1(t)$ is the volume of the compartment. Using (5.7) and (5.9) in (5.8), we get

$$\gamma_1(t) = \frac{F}{V_1(t)} \int_0^t (\gamma_0(t) - \gamma_1(t)) dt + \gamma_1(0). \quad (5.10)$$

If we take delay into account, then we get

$$\gamma_1'(t) = \gamma_1(t - T_d), \quad (5.11)$$

where $\gamma_1'(t)$ is the output concentration of the compartment when we take delay into account, T_d is the delay.

A single compartment is modeled by (5.10) and (5.11). Figure 5.6 shows a complete mass transport model of the cardiovascular system using ten compartments, and includes an input solute flow, $f(t)$, to the venous compartment. It has been postulated that SNP elimination occurs in the interstitial space [13]. The elimination of SNP is modeled by multiplying $\gamma_9(t)$ by λ ($0.3 \leq \lambda \leq 0.6$). Figure 5.7 and Figure 5.8 show the simulation results of a bolus injection of 0.1 mg SNP when λ equals 0.4 and 0.6 respectively. Note that, the concentration curves decline slower when λ equals 0.6.

Figure 5.6: SNP pharmacokinetic model

Figure 5.7: Simulation results of SNP pharmacokinetic model when $\lambda = 0.4$

Figure 5.8: Simulation results of SNP pharmacokinetic model when $\lambda = 0.6$

5.4 SNP Pharmacodynamic Model

The pharmacodynamics of SNP have been modeled with logarithmic functions to compute the change in arterial resistance ΔR_A and change in venous unstressed volume ΔQ_{UV} ,

$$\Delta R_A = A_1 \cdot \log_{10} \left(1 + \beta_1 [SNP]_A \right), \quad (5.12)$$

$$\Delta Q_{UV} = A_2 \cdot \log_{10} \left(1 + \beta_2 [SNP]_V \right), \quad (5.13)$$

where $[SNP]_A$ and $[SNP]_V$ are the steady-state concentration of SNP in the arteries and veins respectively, A_1 and A_2 are constants, β_1 and β_2 are sensitivity parameters to account for interpatient variability. Table 5.1 shows the units of the parameters in (5.12) and (5.13). The constants A_1 and A_2 have values of -1250 and 695 respectively. The range of values for β_1 and β_2 are listed in Table 5.2.

Table 5.1: The units of the parameters in (5.12) and (5.13)

Parameter	Unit	Parameter	Unit
ΔR_A	$10^{-9} \Omega$	ΔQ_{UV}	ml
A_1	$10^{-9} \Omega$	A_2	ml
β_1	ml/mcg	β_2	ml/mcg
$[SNP]_A$	mcg/ml	$[SNP]_V$	mcg/ml

Table 5.2: The range of values for the sensitivity in SNP pharmacodynamic model

	Min	Max	Normal
β_1	16.9	550	75
β_2	22.1	730	100

The blood pressure response lags behind the SNP concentration curves because of the gradual relaxing of the vascular muscle in response to SNP. Therefore, after (5.12) and (5.13) determine the magnitude of the changes in arterial resistance and venous unstressed volume, these values are passed through a first-order lag $\frac{1}{1+T_d}$ ($10 \leq T_d \leq 40$).

5.5 Patient Modeling

We combine the cardiovascular model, the SNP pharmacokinetic model and SNP

pharmacodynamic model, which are mentioned above, to develop a much more complex patient model than [7]. Figure 5.9 shows the patient model. The input of the patient model is solute flow $f(t)$, the output of the patient model is $P_{A2}(t)$ which is used to compute MAP. The outputs of SNP pharmacokinetic model, $\gamma_7(t)$ and $\gamma_0(t)$, are used as the inputs of SNP pharmacodynamic model. The inputs of the cardiovascular model are given by

$$\Delta R_{A1}(t) = \frac{\Delta R_{A1}(0)}{\Delta R_{A1}(0) + \Delta R_{A2}(0) + \Delta R_{A3}(0)} \cdot \Delta R_A(t),$$

$$\Delta R_{A2}(t) = \frac{\Delta R_{A2}(0)}{\Delta R_{A1}(0) + \Delta R_{A2}(0) + \Delta R_{A3}(0)} \cdot \Delta R_A(t),$$

$$\Delta R_{A3}(t) = \frac{\Delta R_{A3}(0)}{\Delta R_{A1}(0) + \Delta R_{A2}(0) + \Delta R_{A3}(0)} \cdot \Delta R_A(t),$$

$$\Delta Q_{UV1}(t) = \frac{\Delta Q_{UV1}(0)}{\Delta Q_{UV1}(0) + \Delta Q_{UV2}(0)} \cdot \Delta Q_{UV}(t),$$

$$\Delta Q_{UV2}(t) = \frac{\Delta Q_{UV2}(0)}{\Delta Q_{UV1}(0) + \Delta Q_{UV2}(0)} \cdot \Delta Q_{UV}(t),$$

where $\Delta R_A(t)$ and $\Delta Q_{UV}(t)$ are the outputs of the SNP pharmacodynamic model, $\Delta R_{A1}(0)$, $\Delta R_{A2}(0)$, $\Delta R_{A3}(0)$, $\Delta Q_{UV1}(0)$ and $\Delta Q_{UV2}(0)$ are the initial values of $\Delta R_{A1}(t)$, $\Delta R_{A2}(t)$, $\Delta R_{A3}(t)$, $\Delta Q_{UV1}(t)$ and $\Delta Q_{UV2}(t)$, respectively.

5.6 Comparison with Slate's Model

In Section 2.2, a patient model developed by Slate is introduced. Table 5.3 shows the parameters' comparison between Slate's model and the nonlinear pulsatile-flow patient model.

Figure 5.10 shows the simulation results of a bolus injection of 0.1 mg SNP. The parameters of Slate's model are chosen as $MAP_0 = 143.9$, $K = -1.2$, $\alpha = 0.2$, $T_i = 53.5$, $T_c = 50$, $\tau = 45$. There are too many parameters in the nonlinear pulsatile-flow patient model, so it is inconvenient to list all of them. Therefore, we only show several most important parameters, and they are chosen as $\beta_1 = 75$ ml/mcg, $\beta_2 = 100$ ml/mcg, $\lambda = 0.4$, $T_d = 40$ sec. No noise is introduced.

Figure 5.9: Nonlinear pulsatile-flow patient model

Table 5.3: Comparison between Slate's model and the nonlinear pulsatile-flow patient model

	Slate's model:	Nonlinear pulsatile-flow patient model:
Initial Blood Pressure	MAP_0	Determined by the parameters in cardiovascular model
The Sensitivity of Patients to SNP	K	β_1 and β_2 in SNP pharmacodynamic model
Recirculation Effect	α	λ in SNP pharmacokinetic model
Initial Delay	T_i	The transport delay from the injection site is determined by the parameters in SNP pharmacokinetic model. The gradual relaxing of the vascular muscle in response to SNP is determined by T_d in SNP pharmacodynamic model.
Recirculation Time Delay	T_c	Determined by the parameters in SNP pharmacokinetic model
Lag Time Constant	τ	Determined by the parameters in cardiovascular model and SNP pharmacokinetic model.

Figure 5.10: Comparison between Slate's model and the nonlinear pulsatile-flow patient model

Figure 5.11 shows the dog experiment result in [13]. A mongrel dog (weight 28 kg) was used for this study. Although a dog is not a perfect model of a human, the shape of their SNP response curves is similar. Compare Figure 5.10 with Figure 5.11, we can conclude that the nonlinear pulsatile-flow patient model is much better than Slate's model, and that improvements need to be made to Slate's model.

5.7 Improvement Made to Slate's Model

In Slate's model, the parameter T_i , initial delay, is constituted by two parts, T_{ik} and T_{id} , as show in (5.14). The first part, T_{ik} , is the transport delay from the injection site. The second part, T_{id} , results from the gradual relaxing of the vascular muscle in response to SNP, and approximately equals T_d , the lag time constant in SNP pharmacodynamic model.

Figure 5.11: Strip chart recording from dog experiment showing a bolus injection of 0.1 mg SNP.

$$T_i = T_{ik} + T_{id} \quad (20 \leq T_i \leq 60, 10 \leq T_{ik} \leq 20, 10 \leq T_{id} \leq 40), \quad (5.14)$$

Therefore, we model the initial delay in Slate's model as a delay and a first-order lag in series.

The transfer function for this model is

$$\begin{aligned} MAP &= MAP_0 + \Delta MAP + MAP_n, \\ \frac{\Delta MAP(s)}{SNP(s)} &= \frac{Ke^{-T_{ik}s}(1 + \alpha e^{-T_c s})}{(1 + T_{id}s)(1 + \tau s)}. \end{aligned} \quad (5.15)$$

Figure 5.12 shows the simulation results of a bolus injection of 0.1 mg SNP. The parameters of the modified Slate's model are chosen as $MAP_0 = 143.9$, $K = -1.2$, $\alpha = 0.2$, $T_{ik} = 13.5$, $T_{id} = 40$, $T_c = 50$, $\tau = 45$. The values of the parameters in the nonlinear pulsatile-flow patient model remain unchanged compared with Figure 5.10. The two blood pressure curves are quite similar.

Figure 5.12: Comparison between modified Slate's model and the nonlinear pulsatile-flow patient model

Next, the relationship between the modified Slate's model and the nonlinear pulsatile-flow

patient model will be illustrated. Figure 5.13 shows the simulation results of a bolus injection of 0.05 mg SNP. All parameters of both models remain unchanged. In this case, the two blood pressure curves are not similar. Then, the parameter K in the modified Slate's model is increased to -1.43 . Figure 5.14 shows the simulation results. Note that, the two blood pressure curves are similar. Through many simulations, It is found out that, a particular nonlinear pulsatile-flow patient model corresponds to a modified Slate's model with larger gain when the bolus input becomes smaller, and corresponds to a modified Slate's model with smaller gain when the bolus input becomes larger.

Figure 5.13: Simulation results when the bolus injection of SNP is decreased

Figure 5.14: Simulation results when the bolus injection of SNP is decreased

In the model bank, eight modified Slate's models instead of eight nonlinear pulsatile-flow patient models are used because of the following reasons.

- If nonlinear pulsatile-flow patient models are used in the controller bank, it is very difficult to tune the parameters of the models so that the initial outputs of the models equal MAP_{0INIT} .
- The modified Slate's model with the parameter range in Table 2.1 can approximately cover every particular nonlinear pulsatile-flow patient model.
- As a real-time control system, the computation speed should be considered. If modified Slate's models are used, computation needs to be carried out only every ten seconds. However, if nonlinear pulsatile-flow patient models are used, computation needs to be carried out at least every 0.1 seconds. Furthermore, the

nonlinear pulsatile-flow patient models are much more complex than modified Slate's models. Therefore, even for some up to date computers, it is very difficult to run a controller bank with eight nonlinear pulsatile-flow patient models in real time.

5.8 Simulation Study

In Chapter 4 and Chapter 5, modified Slate's model is used as the patient plant. Here, the nonlinear pulsatile-flow patient model is used for further computer simulations.

5.8.1 A Patient with Time-varying Parameters and Noise

The pressure set-point is initially chosen as $MAP_c = 100$. The parameters of the patient model are initially chosen as $\beta_1 = 90$, $\beta_2 = 120$, $\lambda = 0.4$ and $T_d = 40$. Then, T_d is changed to 25 at the 4 min mark, β_1 and β_2 are increased to 135 and 180 respectively at the 20 min mark, MAP_c is decreased to 80 at the 35 min mark, λ is changed to 0.6 at the 50 min mark. White Gaussian noise with mean 0 and variance 9 is included. Figure 5.15 shows the simulation result. Figure 5.16 shows the arterial pressure (AP), which is corrupted by noise, between 220 sec to 230 sec. Figure 5.17 shows the convergence of the weights. In the first 30 seconds, all the weights equal zero, so that SNP infusion rate is also zero. From $t = 0.5$ min to 3 min, the main weight is W_8 . From $t = 3$ min to 20 min, the main weight converges to W_4 because the patient's gain is covered by Model 4. From $t = 20$ min to 35 min, the main

weight converges to W_5 as the patient's gain is increased. From $t = 35$ min to 50 min, the main weight converges to W_4 because MAP_c changes. Note that, when the nonlinear pulsatile-flow patient model is used as the patient plant, MAP_c change may lead to the main weight change. The reason is that a particular nonlinear pulsatile-flow patient model does not correspond to a particular modified Slate's model because it depends on the input. From $t = 50$ min to 70 min, the main weight converges to W_5 because λ changes. Note that, λ is the recirculation constant, therefore λ effects the effective steady state gain. Figure 5.18 shows SNP infusion rate. From this simulation, we can see that the proposed control system can effectively update the dynamic changes.

Figure 5.15: Mean arterial pressure

Figure 5.16: Arterial pressure between 220 sec to 230 sec

Figure 5.17: The convergence of the weights

Figure 5.18: SNP infusion rate

5.8.2 Comparison with a PI Controller-based MMAC System

The pressure set-point is chosen as $MAP_c = 105$. The parameters of the patient model are $\beta_1 = 445$, $\beta_2 = 592$, $\lambda = 0.4$ and $T_d = 40$. No noise is introduced. Figure 5.19 shows the simulation result. The fuzzy controller is the 8th controller in Table 3.3. The PI controller is the 8th controller in a controller bank of a PI controller-based MMAC system, and it has proportional gain $K_p = 0.048 \times 1.56^4$, and integral gain $K_i = 0.001 \times 1.56^4$. Then, the pressure set-point is changed to compare the performances of the fuzzy controller and the PI controller. In Figure 5.20, the pressure set-point is 75, and note that the settling time is longer when PI controller is used. In Figure 5.21, the pressure set-point is 135, and note that undershoot is too large when PI controller is used.

Figure 5.19: Comparison with a PI controller-based MMAC system, $MAP_c = 105$

Figure 5.20: Comparison with a PI controller-based MMAC system, $MAP_c = 75$

Figure 5.21: Comparison with a PI controller-based MMAC system, $MAP_c = 135$

5.8.3 Comparison with a Previous Fuzzy Control System

$T_d = 40$, and other parameters of the patient model are shown in Figure 5.22 or Figure 5.23. The pressure set-point is chosen as $MAP_c = 100$. Figure 5.22 shows the simulation results when the fuzzy control system in [6] [17] is used, and Figure 5.23 shows the simulation results when our control system is used. In Figure 5.22, the settling time is too long when $\beta_1 = 16.9$, $\beta_2 = 22.1$ and $\lambda = 0.3$; the system can work well when $\beta_1 = 75$, $\beta_2 = 100$ and $\lambda = 0.4$; when $\beta_1 = 550$, $\beta_2 = 730$ and $\lambda = 0.6$, although the system is stable eventually, the large oscillation during the transient state is unsatisfactory. On the contrary, the performance of our fuzzy controller-based MMAC system in Figure 5.23 is satisfactory.

Figure 5.22: System simulation results of a previous fuzzy control system

Figure 5.23: System simulation results of our control system

5.9 Summary of the Chapter

This chapter presents a nonlinear pulsatile-flow patient model, which consists of a SNP pharmacokinetic model, a SNP pharmacodynamic model and a cardiovascular model. The model is a complex patient model compared to the Slate's model [7], and it is developed for computer simulation. The simulation results show that the fuzzy controller-based MMAC system can effectively control blood pressure over a fairly wide plant parameter envelope, even in the presence of large background noise.

Improvement is made to Slate's model according to the nonlinear pulsatile-flow patient model mentioned above. Furthermore, the relationship between the modified Slate's model and the nonlinear pulsatile-flow patient model is discovered through many simulations. A particular nonlinear pulsatile-flow patient model corresponds to a modified Slate's model with larger gain when the bolus input becomes smaller, and corresponds to a modified Slate's model with smaller gain when the bolus input becomes larger.

Chapter 6

A Self-tuning Controller Design

6.1 Introduction

In the chapter, we will introduce a self-tuning controller. A new algorithm updating variations in time delay and sensitivity of the system is proposed, which is eligible when the approximate model of the system has the first-order-plus-time-delay transfer function

$$F(s) = \frac{Ke^{-T_i s}}{1 + \tau s}. \quad (6.1)$$

Note that, many actual systems can be approximately represented by the model in (6.1).

The controller is used in SNP delivery control, but it has some shortcomings because of some particular characteristics in SNP delivery control, which will be illustrated in Section 6.3.

Therefore, we develop the fuzzy controller-based MMAC system instead, which is described in Chapter 1-5.

6.2 Self-tuning Controller Design

6.2.1 Method

The following discrete-time PI controller is used to control the system which is given by (6.1),

$$PI = K_p \left(1 + \frac{T}{T_{\text{INT}}(1 - q^{-1})} \right), \quad (6.2)$$

where K_p is the gain of the controller, T_{INT} is the integral time, T is the sampling interval and q^{-1} denotes a unit delay operator.

Ziegler-Nichols tuning method is used in this design. Hence,

$$K_p = \phi_1 \frac{\tau}{KT_i}, \quad (6.3)$$

$$T_{\text{INT}} = \phi_2 T_i, \quad (6.4)$$

where ϕ_1 and ϕ_2 are constants, while K , τ and T_i are the sensitivity, time constant and time delay of the system, which is given by (6.1).

Discretizing the continuous-time model given in (6.1) with the sampling time of 15 sec yields the following discrete-time model

$$f(t) = \frac{q^{-d}(b'_0 + b'_1 q^{-1})}{1 - a q^{-1}}, \quad (6.5)$$

where $a = e^{-\frac{T}{\tau}}$, d is the time delays obtained from sampling the continuous-time model. b'_0 and b'_1 are given by

$$b'_0 = K(1 - e^{-\frac{mT}{\tau}}), \quad (6.6)$$

$$b'_1 = K(e^{-\frac{mT}{\tau}} - e^{-\frac{T}{\tau}}), \quad (6.7)$$

where m ($0 < m \leq 1$) is given by

$$m = 1 - \frac{\text{the remainder of } T_i / T}{T}. \quad (6.8)$$

To handle variations of the system parameters, especially time delay, the following model will be used in the design and estimation

$$f(t) = \frac{q^{-2}(b_0 + b_1q^{-1} + b_2q^{-2} + b_3q^{-3})}{1 - aq^{-1}}. \quad (6.9)$$

If compared with (6.5), a numerator with two extra parameters is used in (6.6). This is to cover the variation of time delay (reaction time) and a recursive least squares (RLS) algorithm for estimation is associated.

By imposing

$$q^{-d_1} K \left[(1 - e^{-\frac{mT}{\tau}}) + (e^{-\frac{mT}{\tau}} - e^{-\frac{T}{\tau}})q^{-1} \right] = q^{-2}(b_0 + b_1q^{-1} + b_2q^{-2} + b_3q^{-3}), \quad (6.10)$$

we have the following results describing the evolution of the parameters b_i (for $i = 0, 1, 2, 3$), due to the changes in time delay T_i . Figure 6.1 shows the evolution of b_i with respect to T_i , where $T = 15s$, $\tau = 40s$ are chosen.

$$\text{a) } b_0 = K \left(1 - e^{-\frac{mT}{\tau}} \right), \quad b_1 = K \left(e^{-\frac{mT}{\tau}} - e^{-\frac{T}{\tau}} \right) \text{ and } b_2 = b_3 = 0, \text{ for } T \leq T_i < 2T,$$

$$\text{b) } b_1 = K \left(1 - e^{-\frac{mT}{\tau}} \right), \quad b_2 = K \left(e^{-\frac{mT}{\tau}} - e^{-\frac{T}{\tau}} \right) \text{ and } b_0 = b_3 = 0, \text{ for } 2T \leq T_i < 3T,$$

$$c) \quad b_2 = K \left(1 - e^{-\frac{mT}{\tau}} \right), \quad b_3 = K \left(e^{-\frac{mT}{\tau}} - e^{-\frac{T}{\tau}} \right) \text{ and } b_0 = b_1 = 0, \text{ for } 3T \leq T_i < 4T.$$

Figure 6.1: Evolution of b_i with respect to T_i

Through the examination above, we propose here an algorithm used to directly estimate time delay from the system parameters. That is

$$\hat{T}_i = \left(1 + \frac{b_1 + 2b_2 + 3b_3}{b_0 + b_1 + b_2 + b_3} \right) T, \quad (6.11)$$

where $\hat{T}_i$ represents an estimate of T_i . In the next, we will verify its validity.

Suppose that the value of time delay is $T_i \in (T, 2T]$, then it has, $b_0 = K \left(1 - e^{-\frac{mT}{\tau}} \right)$,

$b_1 = K \left(e^{-\frac{mT}{\tau}} - e^{-\frac{T}{\tau}} \right)$, and $b_2 = b_3 = 0$. Hence,

$$\hat{T}_i = T + \frac{e^{-\frac{mT}{\tau}} - e^{-\frac{T}{\tau}}}{1 - e^{-\frac{T}{\tau}}} T \approx T + \frac{1 - m\frac{T}{\tau} - 1 + \frac{T}{\tau}}{\frac{T}{\tau}} T = (2 - m)T = T_i. \quad (6.12)$$

If $T_i \in (2T, 3T]$, it has $b_1 = K\left(1 - e^{-\frac{mT}{\tau}}\right)$, $b_2 = K\left(e^{-\frac{mT}{\tau}} - e^{-\frac{T}{\tau}}\right)$, and $b_0 = b_3 = 0$.

Hence,

$$\hat{T}_i = T + \frac{\left(1 - e^{-\frac{mT}{\tau}}\right) + 2\left(e^{-\frac{mT}{\tau}} - e^{-\frac{T}{\tau}}\right)}{1 - e^{-\frac{T}{\tau}}} T \approx 2T + \frac{m\frac{T}{\tau} + 2\left(-m\frac{T}{\tau} + \frac{T}{\tau}\right)}{\frac{T}{\tau}} T = (3 - m)T = T_i. \quad (6.13)$$

Similarly, it can also be verified that, for $T_i \in (3T, 4T]$, it leads to

$$\hat{T}_i \approx (4 - m)T = T_i. \quad (6.14)$$

This has completed the verification.

To evaluate accuracy of the algorithm presented in (6.11), an error equation is defined as follows

$$\Delta T_i = \left| \frac{T_i - \hat{T}_i}{T} \right|. \quad (6.15)$$

Using (6.11) to (6.14), we can easily have

$$\Delta T_i = \left| \frac{1 - e^{-\frac{mT}{\tau}} - m(1 - e^{-\frac{T}{\tau}})}{(1 - e^{-\frac{T}{\tau}})} \right|, \quad 0 < m \leq 1. \quad (6.16)$$

Note that it depends on m and the ratio of T/τ . Furthermore, when $m \rightarrow 0$, $\Delta T_i \rightarrow 0$;

when $m = 1$, $\Delta T_i = 0$. When the sampling time T equals 15 sec and the time constant

τ varies from 30s to 60s, we can calculate the error ΔT_i for $15/60 \leq T/\tau \leq 15/30$.

Figure 6.2 shows ΔT_i when both m and T/τ vary. It is found that

$\max(\Delta T_i) \leq 0.046$ and the maximum ΔT_i for any T/τ occurs at $m \approx 0.5$.

Figure 6.2: The error ΔT_i with respect to m and T/τ

Figure 6.3 represents an example of this estimation when increasing T_i , where

$T = 15s$, $\tau = 40s$ are chosen. This result shows that an accurate estimate of time delay

can be achieved using the proposed algorithm.

The sensitivity K , and time constant τ , used in the PI controller tuning are computed by

$$\hat{K} = \frac{b_0 + b_1 + b_2 + b_3}{1 - a}, \quad (6.17)$$

$$\hat{\tau} = -\frac{T}{\ln |a|}, \quad (6.18)$$

which are obtained directly from the system models (6.5) and (6.9).

Figure 6.3: Variation of time-delay and its estimate

Many systems have such an approximate model like (6.1). Consider a system, whose transfer function is given by

$$F(s) = \frac{Ke^{-T_i s}(1 + \alpha e^{-T_c s})}{1 + \tau s}, \quad (6.19)$$

where α ($0 \leq \alpha \leq 0.4$) is a small number. Our self-tuning controller is also eligible for the system, only ϕ_1 in (6.3) and ϕ_2 in (6.4) may need to be tuned to partly compensate the effect of α . Next, let us consider a system, whose transfer function is given by

$$F(s) = \frac{Ke^{-T_i s}(1 + \alpha e^{-T_c s})}{(1 + \tau_1 s)(1 + \tau_2 s)}, \quad (6.20)$$

where α ($0 \leq \alpha \leq 0.4$) is a small number. The system can be simplified as

$$F(s) = \frac{Ke^{-T_i s}(1 + \alpha e^{-T_c s})}{1 + (\tau_1 + \tau_2)s}, \quad (6.21)$$

therefore, our self-tuning controller is also eligible for the system.

6.2.2 Simulation

The parameters of the controller are chosen as $T = 15$ sec, $\phi_1 = 0.25$, and $\phi_2 = 1$. In the first 2.5 minutes, an initial estimation of the system parameters using a recursive least squares (RLS) algorithm is carried out and on-line tuning of the PI controller based on the proposed formulas is achieved. Persistent excitation signal, $2\sin(66.7t)$, is used. Figure 6.4-6.6 show

the simulation results when the system model is given by $OUT(s) = 150 - \frac{e^{-40s}}{1 + 50s} IN(s)$,

where $OUT(s)$ is the system output, $IN(s)$ is the system input. The set-point is 100, and no noise is included. The performance of the controller is satisfactory. Figure 6.7-6.9 show the simulation results when the system model is given by

$OUT(s) = 150 - \frac{e^{-40s}(1 + 0.2e^{-30s})}{1 + 50s} IN(s)$. The set-point is 100, and no noise is included.

6.3 Use of the Controller for SNP Delivery Control

Slate's model has the same transfer function as (6.19), and modified Slate's model has the same transfer function as (6.20). However, some particular characteristics in SNP delivery control should be considered. Firstly, in Section 5.1, we have mentioned the shortcoming of PI controller due to the nonlinear unit limiting SNP infusion rate change. Our self-tuning

controller is also a PI controller and has the same problem. Secondly, many parameters of the plant need to be identified by RLS algorithm, hence it is very difficult to identify the plant when large noise is present.

Figure 6.4: System output

Figure 6.5: System input

Figure 6.6: Parameter estimation

Figure 6.7: System output

Figure 6.8: System output

Figure 6.9: Parameter estimation

6.4 Summary of the Chapter

In this chapter, a self-tuning controller is designed, and a new algorithm updating variations in time delay and sensitivity of the system is proposed, which is useful when the approximated model of the system has the first-order-plus-time-delay transfer function,

$F(s) = \frac{Ke^{-T_i s}}{1 + \tau s}$. Both Slate's model and modified Slate's model can be simplified as the

first-order-plus-time-delay transfer function, however, the controller has some shortcomings in SNP delivery control due to some particular characteristics in SNP delivery control.

Chapter 7

Conclusion and Recommendations

7.1 Conclusion

The needs for more accurate adjust the patient's mean arterial pressure and to set the clinical personnel free from the tedious manually adjusting task become more and more necessary. Many control schemes for handling blood pressure control of postoperative patients have been presented over the past decades. However, it is noted that few of them is applicable to clinical practice. The main reasons behind this should be due to a wide range of patient drug sensitivities to SNP and strong uncertainties associated in the estimated model and unpredictable noises in the measurement.

In this thesis, a fuzzy controller-based MMAC algorithm is proposed to control postoperative hypertension. MMAC algorithm is used to identify the patient model, and fuzzy control algorithm is used to design a controller bank, i.e., the strong points of the two control algorithm are utilized in our control method. We also generalize the fuzzy control algorithm in [6] [17], and improve the convergence algorithm of weighting factors in [1-4].

The thesis presents a nonlinear pulsatile-flow patient model, which is an extension based on the result presented in [11-14]. The model is a complex patient model compared to the Slate's model [7], and it is developed for computer simulation. The simulation results show that the fuzzy controller-based MMAC system can effectively control blood pressure over a fairly wide plant parameter envelope, even in the presence of large background noise.

Improvement is made to Slate's model according to the nonlinear pulsatile-flow patient model mentioned above. Furthermore, the relationship between the modified Slate's model and the nonlinear pulsatile-flow patient model is discovered through many simulations. A particular nonlinear pulsatile-flow patient model corresponds to a modified Slate's model with larger gain when the bolus input becomes smaller, and corresponds to a modified Slate's model with smaller gain when the bolus input becomes larger.

In order to prepare for further animal or human experiments, the fuzzy controller-based MMAC algorithm has been implemented using Visual Basic so that the corresponding hardware (for example, the pump for SNP delivery) can be driven, as shown in Figure 7.1.

A self-tuning controller is designed, and a new algorithm updating variations in time delay and sensitivity of the system is proposed, which is useful when the approximated model of the system has the first-order-plus-time-delay transfer function, $F(s) = \frac{Ke^{-T_i s}}{1 + \tau s}$. Both Slate's model and modified Slate's model can be simplified as the first-order-plus-time-delay transfer function, however, the controller has some shortcomings in SNP delivery control due to some

particular characteristics in SNP delivery control.

Figure 7.1: Overview of blood pressure control system

7.2 Recommendations for Future Research

1) Many incidents occur that could greatly disturb the performance of any blood-pressure controller. Among these disturbances are:

- drawing blood and/or flushing of the arterial pressure line;
- injection of vasoactive drugs;
- painful stimuli registering in the patient due to low anesthesia;

- accidental disconnection of the infusion line, with later connection without regard to the state of the controller;
- blockage of the arterial pressure line.

Therefore, the control system needs a SUPERVISOR that reacts to disturbances, and that modifies the controller response appropriately. The SUPERVISOR should have at least three levels:

- The first sets infusion-rate limits, which has been implemented.
 - The second is concerned with detection of unphysiological changes in MAP.
 - The third is designed to respond to potentially dangerous physiological changes in MAP.
- 2) Refinements are necessary to enhance the performance of the fuzzy SNP delivery control system. Some “intelligent” digital filters should be developed to identify and process different MAP waveforms that generated from different clinical activities, such as bathing the patient and suctioning the airway.
- 3) The scope of this research study will be enlarged to consummate the algorithm of the controller. Other control algorithms would be investigated. A number of data of mean blood pressure and infusion rate for different sensitivities should be obtained to enrich our database.

- 4) In the clinical setting, it is often desirable to simultaneously regulate multiple variables by infusing more than one drug. The interaction between them should be studied. For example, in congestive heart failure subjects, MAP and cardiac output should be simultaneously regulated by adjusting the infusion rates of SNP and dopamine, and dopamine also has effect on MAP.
- 5) Although the algorithms mentioned in this work have been implemented with Matlab for simulation, we expect in the following research, real tests based on animal or human experiments could be done.

Author's Publications

1. H. Zheng, K. Y. Zhu, S. M. Krishnan, and Y. S. Tan, "Multiple-Model Adaptive Control by Means of a Fuzzy Controller-based Control System," Proceedings of 1st International Bioengineering Conference, pp.282-285, Singapore, September 8-10, 2004.
2. H. Zheng, and K. Y. Zhu, "A Fuzzy Controller-based Multiple-Model Adaptive Control System for Blood Pressure Control," Proceedings of 8th International Conference on Control, Automation, Robotics and Vision, pp.1353-1358, Kunming, China, December 6-9, 2004.
3. H. Zheng, K. Y. Zhu, and D. G. Zhang, "Design of An Adaptive Drug Delivery Control System," Proceedings of 5th International Conference on Control and Automation, pp.846-851, Budapest, Hungary, June 27-29, 2005.
4. H. Zheng, K. Y. Zhu, "Automated Postoperative Blood Pressure Control," Proceedings of 24th Chinese Control Conference (International), pp.1591-1595, Guangzhou, China, July 15-18, 2005.
5. H. Zheng, K. Y. Zhu, "Automated Postoperative Blood Pressure Control," Journal of Control Theory and Applications, vol.3, pp.207-212, 2005.
6. H. Zheng, K. Y. Zhu, "Automated Postoperative Blood Pressure Control Using Gain Scheduled Controller," submitted to International Journal of Adaptive Control and Signal

Processing.

7. K. Y. Zhu, H. Zheng, and J. Lavanya, "Adaptive PI Regulation of Blood Pressure of Hypertension Patients", Proceedings of 27th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, Shanghai, China, September 1-4, 2005.
8. K. H. Ew, C. L. Wee, D. G. Zhang, K. Y. Zhu and H. Zheng, "Effects of Functional Electrical Stimulation relating to Leg Movement," Proceedings of 27th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, Shanghai, China, September 1-4, 2005.

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