A combined experience and model based design methodology of a fuzzy control system for mean arterial pressure and cardiac output

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Abstract: The control of physiological variables presents specific challenges, mainly due to the highly nonlinear, complex behavior of biological systems. Cardiovascular system stands as a clear example, with critical situations when control is desirable, but troublesome in the same time. This paper presents a fuzzy control system for two cardiovascular variables, blood pressure and cardiac output, through automatically infusion of two commonly used drugs, Sodium Nitroprusside and Dopamine, respectively. Simulations are possible, making use of a combined cardiovascular-pharmacological model, describing the effects of drugs' infusion rates on controlled variables. The fuzzy controllers used are PI type, designed by experience, and further tuned based on the nominal values of parameters of the cardiovascular-pharmacological model. The main goal is achieving the normal values of cardiovascular variables within a reasonable time period.

1. INTRODUCTION

Some medical emergency situations and procedures require simultaneous observation and control of several hemodynamic and respiratory variables, for efficient treatment. In congestive heart failure, as an example, cardiac output (CO) and mean arterial pressure (MAP) require simultaneous control through intravenously injected drugs, in order to return and remain to safe reference values. These two, possibly along with other variables that should be kept under observation, require an experienced physician or it can benefit from an automatic control system.

Designing control systems for hemodynamic variables has been treated in many research projects and papers. Over the years, a few difficulties had to be intensively analyzed and overcome. First, reliable models of the human cardiovascular system (CVS) had to be developed, considering the large number of uncertainties and the widely varying parameters. With that in mind, robust control strategies had to be verified in numerous simulations, with completely different values for cardiovascular parameters, going even to the extreme cases. Finally, yet very important, some ethical and legal issues were considered when verifying proposed control strategies and prototypes in practical situations, on humans or animals.

The first step made was to automate the drug infusion using an open-loop control approach. Programmable pumps are readily available, but the programming however, has to be carried out by a physician, and requires human intervention in response to changes in the patient's condition. This is the usual operating manner in most hospitals. In other words, no automatic feed-back mechanism is present. The next step was to design a closed loop control system. An initial necessary condition is the existence of a controllable pump through which drug infusion rate can be adjusted in real-time.

Several approaches and control algorithms have been investigated to control MAP by means of vasodilator drugs, among which Sodium Nitroprusside (SNP) is the most attractive solution. Some authors treated the SISO problem of controlling MAP as Ruiz and Borches (1990), Behbehain and Russel (1991), Ying and Sheppard (1994), Huang et al (2000), Gao and Er (2003), Osama and Wahdan (2004). Others, as Voss and Katona (1987), Gopinath et al (1994), Held and Roy (1995), Nie and Linkens (1995), Palerm (2003), proposed an extended two-loop control system for simultaneous control of MAP and CO, using SNP and dopamine (DOP). Rao et al. (1999), presented solutions for both single-input-single-outpu (SISO) and multi-input-multi-output (MIMO) problems, using a model predictive control strategy. Some authors presented multi-loop control systems including the pulmonary mean arterial pressure, as Rao et al. (1997), Huang and Roy (1998), or the central venous pressure and the system vascular resistance, Bauernschmitt et al. (2003). However, the benefits of multiple-loop systems are yet to be analysed from the medical viewpoint.

The development of a reliable controller is difficult due to the complex, multi-variable, nonlinear behaviour of physiological systems (Kappel and Batzel (2003), Casas and Timmons (2006)). For CVS, an example of nonlinearity comes from measurements of MAP, which indicates that the response to SNP infusion rate is nonlinear for large changes in pressure. Other relevant difficulty is the secondary effects of DOP and SNP on MAP and CO, respectively, which are non-negligible interactions between the two control loops. Nevertheless, significant patient to patient dynamic uncertainties and the presence of time variations in a given patient's response to drug dosages are also important difficulties to overcome.

Because of these complex issues, attention has been given to robust or adaptive control strategies, trying to benefit their

advantages for dealing with uncertainness. Authors like Yu et al. (1992), Ozcelik et al. (1999), Palerm (2003), used the model reference adaptive control strategy for simultaneous control of MAP and CO. Also, the fuzzy control solution was verified in Held and Roy (1995), Huang and Roy (1998), Ying and Sheppard (1994), Ying (2000), Held and Roy (2000), Bauernschmitt et al. (2003), Kumar et al. (2009). Furthermore, Nie and Linkens (1995), use an intelligent self-learning algorithm to build the fuzzy controllers of a two-loop control system and Srinivasa et al. (2001), Gao and Er (2003) presented hybrid fuzzy neural approaches.

Fuzzy control appears to be a reasonable solution as between its advantages there is the ability to handle systems with largely varying or unknown parameters. Although there are two decades of research in applying fuzzy control for hemodynamic variables, there are still some issues to be investigated as practical implementations are considered extremely critical. The fuzzy control solution and its design strategies are worth investigated, considering both the performances and the design efforts. This paper combines the experience-based design with a simple yet efficient method to tune scaling gains that includes details about the process.

2. MODELING THE COMBINED CARDIOVACULAR–PHARMACOLOGICAL DYNAMICS

Over the years, a variety of mathematical models of the CVS have been developed, which can be grouped by at least two criteria: 1) by the analysis of short time changes of hemodynamic variables, there are i) pulsatile and ii) non-pulsatile models, and 2) by the scope area of included variables, there are i) comprehensive models and ii) restricted models.

Along with mentioning major research efforts, Kappel and Batzel (2003) describe this classification, referring examples,. Also, they present an extended respiratory-cardiovascular model, initially proposed by Timischl (1998), with clear explanations on CV physiology and hemodynamic variables, which makes it a good reference for understanding CV physiology. A more recent survey on CV modelling and a simpler model are presented by Casas and Timmons (2006), which extend his research by considering the problem of external control through drug infusion.

In order to use a CV model in a control application, the pharmacological (Ph) effect of infused drugs needs to be analyzed. Several research works can be mentioned as extremely useful and applicative. Nie and Linkens (1995), extend the CV model previously proposed by Moeller et al. (1993), including the pharmaco-dynamics principles introduced by Serna et al (1983). The result is a very applicative model for external control of mean arterial pressure and cardiac output. However, it lacks on details about the ranges in which model's parameters can vary, knowing that this ranges are usually large from patient to patient.

This drawback is avoided by Yu et al. (1990). They present a 2-input-2-output first order system with delays, having 12 parameters, with the typical values and wide ranges of possible variation. The conceptual diagram of this model is depicted in Fig. 1, where the baroreflex auto-control mechanism

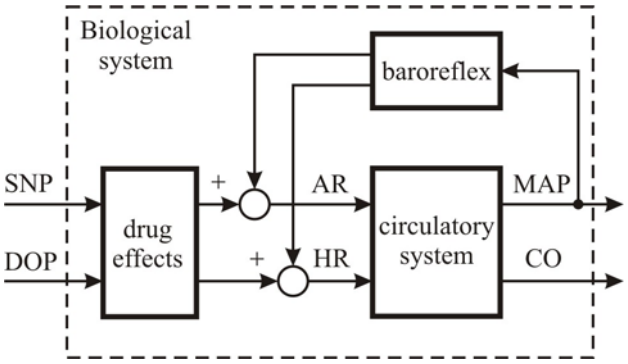

Fig. 1. Conceptual diagram of the combined cardiovascular pharmacological system.

is highlighted, as it is the fastest natural control loop for mean arterial pressure. Fig. 1 also highlights the direct action of SNP and DOP on the arterial resistance (AR) and on the heart rate (HR), respectively, which further determine the arterial pressure and the cardiac output, through direct and secondary effects. (For details on the physiology of the autonomous control of the CVS please refer to Palerm (2003), Kappel and Batzel (2003), as more technical presentations, or web resources for a generic presentation.) According to the classification previously mentioned, this is a comprehensive, non-pulsatile model. Its applicability for a control problem is sustained by the research work of Yu et al (1992), Gopinath et al (1994), Ozcelik et al. (1999), and Palerm (2003), which used this model in their work.

Derived from Yu et al, the combined CV+Ph model can be described as

$$\begin{bmatrix} \Delta MAP \\ \Delta CO \end{bmatrix} = \begin{bmatrix} \dfrac{K_{11}e^{-\tau_{11}s}}{sT_{11}+1} & \dfrac{K_{12}e^{-\tau_{12}s}}{sT_{12}+1} \\ \dfrac{K_{21}e^{-\tau_{21}s}}{sT_{21}+1} & \dfrac{K_{22}e^{-\tau_{22}s}}{sT_{22}+1} \end{bmatrix} \begin{bmatrix} I_{SNP} \\ I_{DOP} \end{bmatrix} \quad (1)$$

The inputs vector contains the infusion rates of SNP and DOP, given in μg/kg/min, and the outputs are the changes in MAP and CO, given in mmHg, respectively ml/kg/min.

The changes in physiological variables considered here are only those caused by the infusion of the above mentioned drugs and no effect of other nature is included.

The set points for these changes are calculated from the initial patient's conditions, MAP_0 and CO_0, as

$$\Delta MAP_{ref} = MAP_{ref} - MAP_0,\ \Delta CO_{ref} = CO_{ref} - CO_0 \quad (2)$$

with $MAP_{ref} = 100$ mmHg, $CO_{ref} = 6$ ml/kg/min being the clinically normal set points of MAP and CO. The parameters in (1) represent: i) K_{ij} - patient's sensitivity to infused drugs, ii) T_{ij} - time constants of the dynamic response to drugs and iii) τ_{ij} - time delays between starting the infusion and the first reacts of CVS (Palerm, 2003). The typical values and ranges are presented in Table 1.

Table 1. Nominal values and ranges of the parameters in Yu's CVS model.

Parameter	Range	Typical	Units
K_{11}	[-1; -50]	-15	ml/μg
K_{12}	[0; 9]	3	ml/μg
K_{21}	[-15; 25]	12	mmHg.kg.min/μg
K_{22}	[1; 12]	5	mmHg.kg.min/μg
T_{11}	[30; 60]	40	s
T_{12}	[30; 60]	40	s
T_{21}	[70; 600]	150	s
T_{22}	[70; 600]	300	s
τ_{11}	[15; 60]	50	s
τ_{12}	[15; 60]	60	s
τ_{21}	[15; 60]	50	s
τ_{22}	[15; 60]	60	s

3. MAP AND CO FUZZY PI CONTROLLERS DESIGN

As presented in all today's literature, fuzzy logic control (FLC) is a reliable solution for robust control. It is especially advantageous for problems difficult to represent by models, due to unavailable, incomplete, uncertain or inconstant data. There are at least two often mentioned situations for which fuzzy control suits better than the classical PID: i) ill-defined processes with unknown or largely varying parameters and ii) irrelevant or useless high performances for dynamic and/or steady-state response. A control application for physiological variables seems to fit in both cases. First, the parameters of the biological process are usually largely varying from patient to patient and often inconstant even for the same patient. Second, although high performances appear compulsory, the process' complexity entails compromises within safe clinical conditions. Even more, medical interpretations of recorded values for physiological variables are often rough. Hence, small steady-state errors and overshoot are accepted.

Although a large number of algorithms have been proposed, it is still hard to say there are some general, all accepted methods for designing fuzzy controllers and for finding their optimal rules. Anyway, by experience and interviewing skilled operators, some suggestions can set bounds to an initial approach that will result in obtaining a controller having just few details about the process. Such method should be able to build at least a rough controller, which can be subsequently improved to satisfy higher performances, if required.

3.1. The experience-based part of the methodology

Fuzzy controller design has at least four steps: i) choose system structure and controller type; ii) set ranges and fuzzy sets for each variable; iii) set the control rules; iv) set the scaling gains for measured crisp variables (Jantzen, 2007). The last step received the highest priority, due to the scaling gains' strong influence on the control performances and stability. Hence, the method presented here will consider engineer's and physician's experience only for the first three steps.

In this application, PI controllers are proposed for both MAP and CO control loops, with the structure depicted in Fig. 2. The fuzzy inference system of each controller has two inputs, the error and its derivative, and one output, the command action derivative representing the necessary change in infusion rate. Each variable is scaled to a standard [-1;+1] range, by its corresponding scaling gain. Standard triangular fuzzy sets (also called *attributes*) are defined uniformly distributed over the universe of discourse (see Table 2). The form and distribution of these fuzzy sets are justified by engineer's experience in FIS design. The control rules are obtained after interviewing a physician, by describing the fuzzy sets as attributes and the control actions as linguistically expressed rules, and so engineer's experience was completed by physician approval. The rule base is also presented in Table 2.

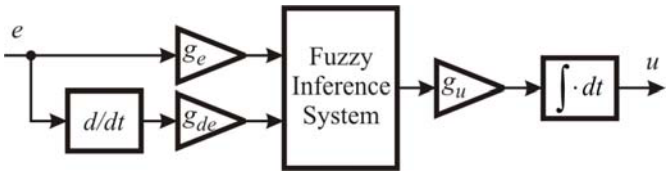

Fig. 2. The fuzzy PI controller.

3.2. The model-based part of the methodology

Techniques to tune the scaling gains of the fuzzy controllers have received the highest priority in literature due to their strong influence on the performance and stability of the control system. The simplest experience-based method is to set these scaling gains so that the maximum accepted value for a variable would correspond to the limit of its universe of discourse over which fuzzy sets are defined. For many applications, this could lead to satisfactory results, but there is no analytical study to prove its reliability. When some partial or complete model of the process is available , it is possible to adapt the Ziegler-Nichols classical PID tuning method to determine optimal scaling gains for a fuzzy PI controller.

Table 2. The rule base.

		Derivative error $\in[-1;+1]$		
		Neg = trimf(-1, -1, 0)	Zero = trimf(-1, 0, 1)	Big = trimf(0, 1, 1)
Error $\in[-1;+1]$	NegBig = trimf(-1, -1, -0.5)	-1	-1	-0.5
	NegSmall = trimf(-1, -0.5, 0)	-0.5	-0.5	0
	Zero = trimf(-0.5, 0, 0.5)	0	0	0
	PosSmall = trimf(0, 0.5, 1)	0	0.5	0.5
	PosBig = trimf(0.5, 1, 1)	0.5	1	1

Usually, biological process has large time constants T_p and time-delays τ for any input-output path, as described in (1). Hence, it appears reasonable to consider the Ziegler-Nichols tuning method for classical PI controller as a starting point in setting the scaling gains.

Let us consider the PI controller's differential equation

$$T_i \frac{du(t)}{dt} = K_r e(t) + T_i \frac{de(t)}{dt} \tag{3}$$

with K_r being the controller's gain factor and T_i the integral time constant. According to Ziegler-Nichols method, the optimal values for these two parameters are:

$$K_r = 0.9 \frac{1}{K_p} \frac{T_p}{\tau},\ T_i = 3.3 T_p \tag{4}$$

At the same time, consider the fuzzy inference described as:

$$(g_{du} du) = (g_e e) \wedge (g_{de} de) \tag{5}$$

with g_e the scaling gain for error, g_{de} the scaling gain for error derivative, and g_{du} the scaling gain for command action derivative (see Fig. 2). The coefficients in (5) correspond to those in (3), as they play the same role on the input and output variables:

$$g_e \leftrightarrow k_r,\ g_{de} \leftrightarrow T_i,\ g_{du} \leftrightarrow T_i. \tag{6}$$

Hence, the optimal scaling gains can be calculated with:

$$g_e = 0.9 \frac{1}{K_p} \frac{T_p}{\tau},\ g_{de} = 3.3 T_p,\ g_{du} = 3.3 T_p, \tag{7}$$

With (7) introduced in (5), a simplification is possible, reducing the factor $3.3T_p$, and (7) become

$$g_e = \frac{0.9}{3.3} \frac{1}{K_p \tau},\ g_{de} = 1,\ g_{du} = 1 \tag{8}$$

The time delays of the pharmacological dynamics, represented by τ_{ij} in (1) and described in Table 1, are relatively close enough. The main reason is that the delays represents the time from injecting the drug until it reaches the *effector site* in a useful concentration in order to have some effect over the system (Casas and Timmons 2006).

So far, it is reasonable the presumption that the distribution of both infused drugs in the circulatory system and their normalised concentrations are almost identical. Since exact values for these delays are difficult to record, it is acceptable the simplification of keeping a single relevant time delay τ_0. Choosing this value relies on experience and application particularities. Here, the biggest delay value in Table 1 is chosen: $\tau_0 = 60\,s$. With this assumption, scaling gains will only depend on process steady-state response, defined by gain factors in the model.

With the solution proposed in (8) and considering the above mentioned simplification, the scaling gains for the two control loops in our study are:

$$g_{e,\Delta MAP} = \frac{0.9}{3.3} \frac{1}{K_{11}\tau_0},\ g_{ce,\Delta MAP} = 1,\ g_{du,SNP} = 1 \tag{9a}$$

$$g_{e,\Delta CO} = \frac{0.9}{3.3} \frac{1}{K_{22}\tau_0},\ g_{ce,\Delta CO} = 1,\ g_{du,DOP} = 1 \tag{9b}$$

As a final remark, it is easy to notice that the controllers are designed separately for each control loop. The mutual influences between the control loops (described by the parameters having 12 and 21 indexes in (1) and in Table 1), are not included in this design procedure. Anyway these influences are expected to be managed by the obtained control system.

4. SIMULATION RESULTS

A two-loop control system with fuzzy controllers for simultaneous control of changes in MAP and CO produced by drugs infusion was tested in simulations under Matlab-Simulink environment. The system's schematic is depicted in Fig. 3. The SNP and DOP pumps are non-linear elements which limits the infusion rates calculated by the controllers to the safe or usual dosages (Table 4).

Table 4. The infused used drugs.

Drug	Infusion rates	Effects
Dopamine DOP	5 – 10 μg/kg/min	Increases MAP Increases CO
Sodium Nitroprusside SNP	0.3 – 4 μg/kg/min	Decreases MAP Increases CO

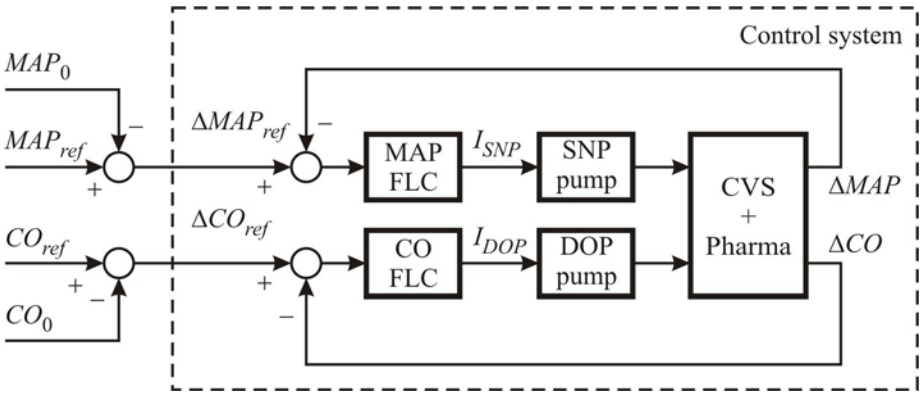

Fig. 3. The block diagram of the two-loop control system.

Table 3. Simulation results: the dynamic performances of the simulated scenarios.

	Stationary error		Overshoot		Settling time	
	ΔMAP	ΔCO	ΔMAP	ΔCO	ΔMAP	ΔCO
[1a]	0	0	~ 0,5%	~ 1%	~ 4 minutes	~ 6 minutes
[1b]	0	~ 1,5%	0	~ 1,5%	~ 6 minutes	~ 7 minutes
[1c]	0	< 1%	~ 1,5%	~ 1%	~ 3 minutes	~ 5 minutes
[2a]	0	0	0	0	~ 5 minutes	~ 8 minutes
[2b]	0	0	0	0	~ 7 minutes	~ 9 minutes
[2c]	0	~ 1,5%	0	0	~ 4 minutes	~ 7 minutes
[3a]	~ 10%	> 10%	0	0	~ 3 minutes	~ 6 minutes
[3b]	~ 1%	> 10%	0	0	~ 6 minutes	~ 9 minutes
[3c]	0	> 10%	~3%	0	~ 4 minutes	~ 6 minutes

To verify control performances and robustness, 9 simulation scenarios were analysed, combining 3 clinical situations:

1. moderate hypertension with moderate heart failure:

$MAP_0 = 120$ mmHg, $CO_0 = 5$ l/kg/min ;

2. acute hypertension with moderate heart failure:

$MAP_0 = 150$ mmHg, $CO_0 = 5$ l/kg/min ;

3. moderate hypertension with acute heart failure:

$MAP_0 = 120$ mmHg, $CO_0 = 3$ l/kg/min ;

with 3 types of reaction to infused drugs, defined by different values of model's parameters (see the ranges in Table 1):

a. patients with normal response – the nominal values;

b. patients with slower and less intense response - time constants 25% bigger and gains 25% smaller than nominal.

c. patients with faster and more intense response - time constants 25% smaller and gains are 25% bigger than nominal.

From the 9 scenarios proposed, the combination marked as [1a] stands as a standard case of a patient with congestive heart failure, having normal sensitivity to infused drugs. This is the scenario with which the control system is designed.

Simulations results are synthetically presented in Table 3. For the standard case [1a], MAP lowers from 120 mmHg to the set point in 4 minutes, with less than 1% overshoot, which for this case is negligible. A slower response is recorded for CO, yet after 6 minutes its value is close to the safe set point. No steady-state error is recorded. For [1c], the better patient's response to medication reduces the infused quantities by a significant amount and the injection time is reduced with about 1 min. In case [1b], a slower response medication due to smaller sensitivity determines a longer settling time, with about 2 minutes. Going to extreme insensitivity, the infusion rates could become too large and dangerous. Hence, the limitations of infusion rates to maximum allowed values (see Table 4) will result in a even longer settling time.

For the acute heart failure situation ([3a], [3b], [3c]), a larger stationary error is recorded. From the control engineering viewpoint, this value seems to be unacceptable, but, from the physician's experience, it is not surprising. It is expected to obtain a positive stationary error as cardiac output can be a little larger than the typical value, in patient's benefit.

5. CONCLUSIONS

The fuzzy control strategy has proven itself reliable in cardiovascular variables control and many research papers motivate this approach and verifies it reliability. The CV specific characteristics present the conditions and reasons for fuzzy control. As fuzzy control design has insufficient analytic methods, experienced based design is still a wide spread solution. The availability of CV models allows completing the experience based design with a way to calculate optimal scaling gains for fuzzy controllers. This approach is motivated by the important effects of these factors on the performances and stability of the fuzzy control system. The presented methodology is easy to implement, time effective and has satisfactory results.

This paper presents a fuzzy control solution for mean arterial pressure and cardiac output, but also extends the simulations by introducing several different clinical scenarios. Since process' conditions are highly varying from case to case, multiple simulations for different values of cardiovascular parameters should be considered by all researchers.

The control performances obtained for the acute hypertension and acute heart failure sustain the conclusions and the viability of the fuzzy logic based solution presented.

So far, the designed fuzzy control system is based on medical personal experience and does not include neural networks or self-learning based methodologies. The proposed controllers are simple and intuitive, and simulations have proven their reliability and robustness.

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