Experience-Based Design and Simulations of a Fuzzy Control System for Cardiovascular Variables

Cristian BOLDIŞOR, Vasile COMNAC, Iulian ŢOPA
Automatics Department, Transilvania University of Braşov, Romania
cristian.boldisor@unitbv.ro

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 and troublesome in the same time. This paper presents a fuzzy control strategy for two cardiovascular variables, blood pressure and cardiac output, by automatic infusion of two commonly used drugs, sodium nitroprusside and dopamine, respectively. The fuzzy controllers proposed here are PI type, designed by experience, with rules established by interviewing a physician. Simulations are possible, making use of a mathematical model describing the effects of drugs infusion rates on controlled variables. The main goal is achieving the normal and safe values within a reasonable time period. Furthermore, cost reduction by minimized drug consumption and shortened period of clinical treatment is part of the main issues which motivate automation.**

Index Terms — **Cardiovascular system, Drug delivery systems, Fuzzy control, Fuzzy systems, Physiological variables control**

I. INTRODUCTION

Some clinical emergency situations require simultaneous observation and control of a large number of hemodynamic and respiratory variables, for adequate medical and clinical procedures. 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 to safe reference values. These two, possibly along with other variables that should be kept under observation, require an experienced person or imply the use of an automatic control system. An initial necessary condition for designing a closed loop control system is a programmable or controllable pump which controls the current infusion rate of the injection.

The design of automated systems to control 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 by numerous simulations, with completely different values for cardiovascular (CV) parameters, going even to the extreme cases. Finally, yet very important, some ethical and legal issues were involved when verifying control strategies and prototypes in real-time practical situations.

A first step 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 to respond to changes in the patient's condition. This is the usual operating manner in most hospitals. In other words, no automatic feedback mechanism is present. The next stage was the design of the first closed loop system. Several approaches have been investigated to control MAP by means of vasoconstrictor and vasodilator drugs. Some approaches consider a single-input single-output (SISO), problem as in [1], by controlling the mean arterial pressure (MAP) with Sodium Nitroprusside (SNP). Others, as in [2], proposed an extended approach to the simultaneous control system of CO and MAP using dopamine (DPM) and Sodium Nitroprusside.

The development of a reliable automated controller is difficult due to the complex, multi-variable, nonlinear behavior of physiological systems [3-6]. An example of nonlinearity comes from measurements of MAP, which indicate that the SNP dose response is nonlinear for large changes in pressure. Because of these complexities as well as the significant patient to patient dynamic uncertainties and the presence of time variations in a given patient's response to drug dosages, attention has been given to the use of fuzzy logic based controllers [7-8, 12-14]. As often mentioned in today's literature, the advantages of this type of controller are its robustness and ability to handle systems with varying and unknown dead times.

In [9], an adaptive drug delivery system was developed for use in controlling critical care patients suffering from cardiac failure. The approach taken assumed that adaptive control algorithms combined with expert system techniques are necessary to maintain stable patient status within narrow physiological bounds in the presence of large plant uncertainty. To this end, a hybrid controller was presented whose structure was adjusted by an expert system that attempts to match the best control scheme in accordance with the dynamic structure of the plant.

TABLE I. TALBE I. COMMONLY USED DRUGS AND THEIR EFFECTS ON CARDIOVASCULAR VARIABLES.

Drug	Usual 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

In [7], a complex study of neural fuzzy and self-learning based strategies is presented, with application to a two-loops control system for simultaneous CO and MAP control. Their work is based on the models proposed by Moeller [10] and Serna [2], joined in a compact model with narrow parameters' ranges. More recently [8], a PD fuzzy control algorithm has been analyzed for multiple hemodynamic variables control.

A different usage of fuzzy logic is proposed in [11], where a state-predictive control system is used in combination with a fuzzy risk control algorithm, for prevent dangerous.

Finally, the work of Palerm [15] can be noted, although the design solution is not the fuzzy controller, but based on the direct model reference adaptive control strategy. His work could be a useful reference for cardiovascular physiology description in a control application context.

II. MODELING THE COMBINED CARDIOVACULAR– PHARMACOLOGICAL DYNAMICS

Over the years, a variety of mathematical models of the cardiovascular system (CVS) have been developed, [4],[15], which can be grouped by several criteria:

- by the analysis of short time changes of hemodynamic variables: i) pulsatile models and ii) non-pulsatile models;
- by the scope area of included variables: i) comprehensive models and ii) restricted models.

The pulsatile models include effects of the heart cycle on blood flow, including an oscillatory feature to some variables. Changes that take place during a heart beat are included. However, although interesting for detailed studies, clinical situations rarely implies using any of these fast changes, hence non-pulsatile models received more attention. Moreover, since biological processes are slow from the control engineering viewpoint, as long-time effects are studied, control applications use mostly non-pulsatile models.

Comprehensive models describe several sub-systems or phenomena into an integrated, more general approach, enough for certain class of applications. In contrast, restricted models limit the scope of study to a single significant feature. A number of comprehensive models of the CVS have been developed, which involve either pulsatile or non-pulsatile description of blood flow. Generally, comprehensive models incorporate one or more mechanisms of cardiovascular control, and prove suitable for a control engineering specific analysis of the CVS.

Proposed CV models had to be completed with the pharmacological (Ph) effects of infused drugs. A model used to describe the effect of inotropic and vasoactive drugs on the physiological system was initially developed by Yu et al. [16], and has been used (in various forms) in a number of simulation studies for the control of MAP and CO using DPM and SNP. The initial model consists of three parts: (i) circulatory system (the effect of specific body parameters on the MAP and CO), (ii) drug effect relationships (the influence of the infused drugs on the specific body parameters) and (iii) the effect of the arterial baroreceptors in blood pressure regulation. A conceptual diagram is shown in Figure 1.
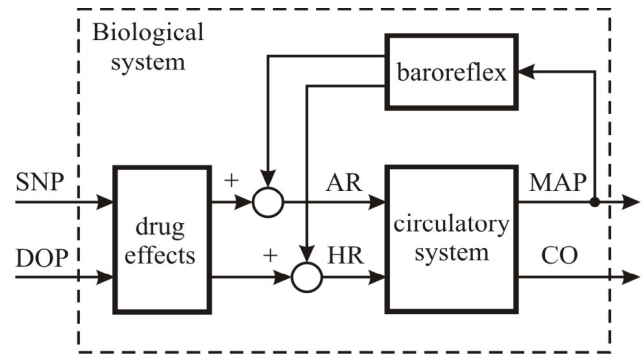

Figure 1. Conceptual diagram of the combined cardiovascular pharmacological system.

For more details on the model, see Yu et al. [16-18], Gopinath et al. [19-20], Huang and Roy [22] and Palerm [15]. Also, for a brief description of the baroreflex effect in the CV dynamics please see [6],[21].

The comprehensive, non-pulsatile CVS-Ph model derived from Yu ([16]) is a 2-input-2-output first order system with delays, as described by

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

or

$$\begin{bmatrix} \Delta MAP \\ \Delta CO \end{bmatrix} = \begin{bmatrix} G_{11}(s) & G_{12}(s) \\ G_{21}(s) & G_{22}(s) \end{bmatrix} \begin{bmatrix} I_{SNP} \\ I_{DOP} \end{bmatrix} \quad (1b)$$

with $G_{ij}(s) = K_{ij}e^{-\tau_{ij}}/(sT_{ij}+1)$. The inputs are 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 above mentioned drugs and no effect of other nature is included in the model. The set points for these changes are calculated from the initial patient conditions, MAP_0 and CO_0, and normal set points of MAP and CO, MAP_{ref} and CO_{ref}, as:

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

The parameters in (1a) are (from [15]): i) patient's sensitivity to infused drugs, K_{ij}, ii) time constants of the dynamic response to drugs, T_{ij}, and iii) time delays between drugs infusion moment and the first reacts of cardiovascular system, τ_{ij}. The typical values and ranges are presented in Table II.

Some modeling efforts limit only to steady-state response [23], defined by the matrix of the process' gain factors, which for the presented model is:

$$\begin{bmatrix} \Delta MAP_{st} \\ \Delta CO_{st} \end{bmatrix} = \begin{bmatrix} K_{11} & K_{12} \\ K_{21} & K_{22} \end{bmatrix} \begin{bmatrix} I_{NPS} \\ I_{DOP} \end{bmatrix} \quad (3)$$

With few reasonable assumptions, this information might be sufficient for a fuzzy controller design.

TABLE II.   NOMINAL VALUES AND RANGES OF MODEL'S PARAMETERS

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]

III.   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 systems. 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 logic 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 fit in both cases. First, the parameters of the biological process are usually largely varying from patient to patient and often inconstant for even the same patient. Second, although high performances appear to be compulsory, the process' complexity and nonlinearity entail compromises, but within safe clinical conditions.

Although a large number of algorithms have been proposed so far, it is still hard to say there are some general, all accepted methods for designing fuzzy controllers and for finding their optimal parameters. Anyway, by experience and interviewing skilled operators, some suggestions can set bounds to an initial approach that will result in obtaining a controller with just few details about the process. Such methodology should be able to build at least a rough controller, which can be subsequently improved to satisfy higher performances (if required). When based on experience, fuzzy controller design has at least four steps: i) choose system structure and controller type (P, PI, PD, PID); ii) set ranges and fuzzy sets for each variable; iii) set the control rules; iv) set the scaling gains for measured crisp variables. Techniques to tune the scaling gains have received the highest priority in literature due to their strong influence on the performance and stability.

Similar fuzzy PI controllers are proposed here for both MAP control loop and CO control loop. The structure of the fuzzy PI controller is depicted in Figure 2.

The fuzzy inference system (FIS) has two inputs, the error and its derivative, and one output, the command action derivative. Each input and output variable is scaled to standard $[-1; +1]$ range, in order to ease rule-base design. For each variable, standard triangular fuzzy sets are defined uniformly distributed over the universe of discourse, as presented in Table III. The rule base is presented in Table IV.
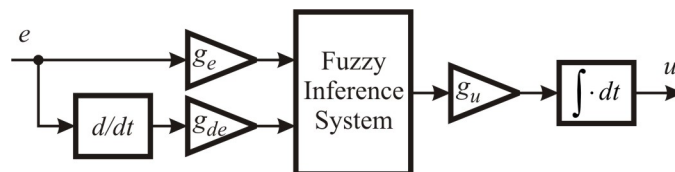

Figure 2. The fuzzy PI controller.

TABLE II. THE FUZZY SETS.

Error: $[-1; +1]$	
NegBig	trimf(-1, -1, -0.5)
NegSmall	trimf(-1, -0.5, 0)
Zero	trimf(-0.5, 0, 0.5)
PosSmall	trimf(0, 0.5, 1)
PosBig	trimf(0.5, 1, 1)
Derivative error: $[-1; +1]$	
Neg	trimf(-1, -1, 0)
Zero	trimf(-1, 0, 1)
Big	trimf(0, 1, 1)
Control output: $[-1; +1]$	
NegBig	-1
NegSmall	-0.5
Zero	0
PosSmall	0.5
PosBig	1
trimf – triangular membership function	

TABLE III. THE RULE BASE.

		Derivative error		
		Neg	Zero	Big
Error	NegBig	-1	-1	-0.5
	NegSmall	-0.5	-0.5	0
	Zero	0	0	0
	PosSmall	0	0.5	0.5
	PosBig	0.5	1	1

Adequate gains for the fuzzy PI controller are determined starting with the differential equation of the classical PI controller

$$K_r e(t) + T_i \frac{de(t)}{dt} = T_i \frac{du(t)}{dt} \qquad (4)$$

with K_r being the controller's gain factor and T_i the integral time constant. Based on (4), the gains can be highlighted as in

$$g_e e(t) + g_{de} \frac{de(t)}{dt} = g_u \frac{du(t)}{dt} \qquad (5)$$

with g_e the scaling gain for error, g_{de} the scaling gain for error derivative, and g_u the scaling gain for command action derivative.

Usually, biological process has large time constants T_p and time-delays τ for any input-output relation, as described in (1). Hence, it appears reasonable to consider the Ziegler-Nichols method for determining classical PI controller's parameters as a starting point in setting the scaling gains. The following formulas are initially proposed

$$g_e = K_r = 0.9 \frac{1}{K_p} \frac{T_p}{\tau}, \quad g_{ce} = g_u = T_i = 3.3 T_p \qquad (6)$$

With (7) introduced in (6),

$$0.9 \frac{T_p}{K_p \tau} e(t) + 3.3 T_p \frac{de(t)}{dt} = 3.3 T_p \frac{du(t)}{dt}$$

a simplification is possible, reducing the time constant T_p, and (7) become

$$g_e = \frac{0.9}{3.3} \frac{1}{K_p \tau}, \quad g_{ce} = g_u = 1 \qquad (7)$$

Studying the time delays of the pharmacological dynamics, represented by τ_{ij} in (1) and described in Table I, it is easy to observe that these values are relatively close enough. As fuzzy controller design itself remains a "fuzzy procedure", due to the fact that there are insufficient analytic design techniques, it is acceptable the simplification of keeping a single relevant time delay τ_0 in the process for both control loops. It means that it is possible to use the same time delay value in (8) for both control loops in our study, and so to generalize even more. With this assumption, scaling gains will only depend on process steady-state response, defined by gain factors within the model, as those described in (3), (4). Choosing this value relies on experience and application particularities. Here, we will consider the biggest time delay value in Table II.

The major reason for this simplification is that, in general, steady-state behavior is easy to describe analytically and so the gain factors in the process is available more often. Anyway, improvements are welcome when a more detailed model of the process is available and practical experiments are possible.

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

$$g_{e,\Delta MAP} = \frac{0.9}{3.3} \frac{1}{K_{11}\tau_0}, \quad g_{ce,\Delta MAP} = 1, \quad g_{u,SNP} = 1 \qquad (8a)$$

$$g_{e,\Delta CO} = \frac{0.9}{3.3} \frac{1}{K_{22}\tau_0}, \quad g_{ce,\Delta CO} = 1, \quad g_{u,DOP} = 1 \qquad (8b)$$

As a final remark, it is easy to notice in (9a,b) that the controllers are designed separately for each control loop. The mutual influences between the control loops, expressed in (1b) by $G_{12}(s)$ and $G_{21}(s)$, are not included in design procedure.
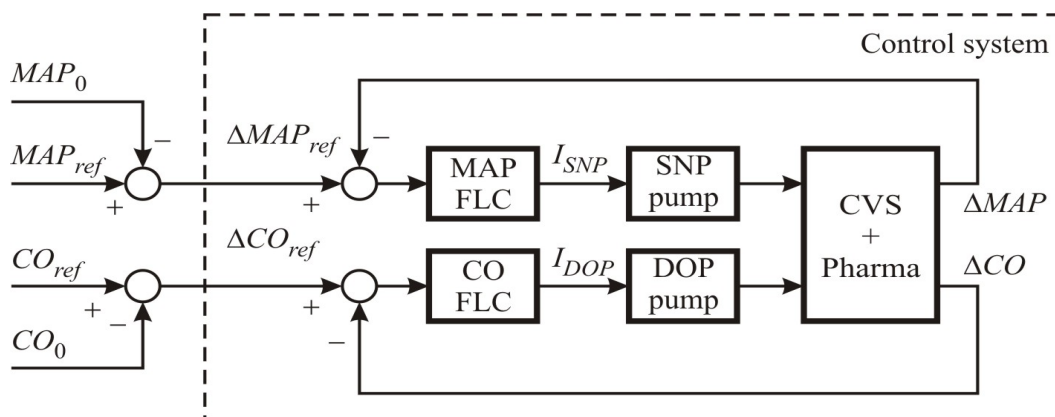

Figure 3. The block diagram of the control system.

- SIMULATION RESULTS FOR DIFFERENT SCENARIOS

A feedback control system with two fuzzy controllers for simultaneous control of changes in MAP and CO produced by drugs' infusion rates, as defined in (1), was tested in simulations, under Matlab/Simulink environment. The system's schematic is depicted in Figure 3.
Three scenarios were proposed for simulations and simulation results are presented in Figures 4 – 6:

- Case 1 – MAP lowers from 120 [mmHg] to set point in about 8 minutes, with less than 1% overshoot, which for this case is negligible. A slower response is recorded for CO, yet after 10 minutes its value is close enough to the safe set point.

- Case 2 – The better patient's response to medication reduces the infused quantities by a significant amount and the medication time is reduced with about 1 min (notice a shorter time for MAP, par example).

- Case 3 – A slower response medication due to smaller sensitivity causes insignificant longer settling time (about 8 minutes), but and requires bigger quantities of infused drugs. Going to extreme insensitivity, the infusion rates could become too large and dangerous. Hence, the limitations of infusion rates to maximum allowed values will result in a longer medication time (longer settling time).

TABLE III. SIMULATED SCENARIOS.

Case 1: hypertensive patient, with typical values of sensitivity to infused drugs	$MAP_0 = 120$ [mmHg] $CO_0 = 4.7$ [l/kg/min]	$\Delta MAP_{ref} = -20$ $\Delta CO_{ref} = +1$
	typical values of parameters in table I	
Case 2: hypertensive patient, with faster response to infused drugs	$MAP_0 = 120$ [mmHg] $CO_0 = 4.7$ [l/kg/min]	$\Delta MAP_{ref} = -20$ $\Delta CO_{ref} = +1$
	20% smaller values for time constants and time delays than the typical values in table I	
Case 3: hypertensive patient, with slower and smaller response to infused drugs	$MAP_0 = 120$ [mmHg] $CO_0 = 4.7$ [l/kg/min]	$\Delta MAP_{ref} = -20$ $\Delta CO_{ref} = +1$
	20% bigger values for time constants and time delays and 20% smaller values for patient sensitivities than the typical values in table I	

IV. CONCLUSIONS

The fuzzy control strategy proves itself reliable in physiological variables control. The main conditions and reasons for fuzzy control are met in this type of applications. Many research papers motivate this approach and verifies it reliability.

As fuzzy control design has insufficient analytic methods, experienced based design is still a wide spread solution. The procedure is easy and time effective, with satisfactory results.

The analysis of control systems for cardiac critical states is possible due to the intense modeling efforts in the last three decades. The complex, highly nonlinear cardiovascular system was intensively treated and trustful models are available for numerical simulations.

The designed fuzzy control system is based on medical personal experience and does not include (so far) neural networks or self-learning based methodologies. The proposed controllers are simple and intuitive. Several simulations have proven their satisfactory behavior.

V. FURTHER RESEARCH

For further research, the extension of Yu's model proposed by Huang and Roy (see [22]) is worth investigated, in order to develop a multiple loop fuzzy control system.

On the other hand, including more complex self-learning design method and fuzzy neural algorithms would increase the controller's adaptability and intelligent feature, in order to overcome the necessity of previously knowing patient's reactions to infused drugs.
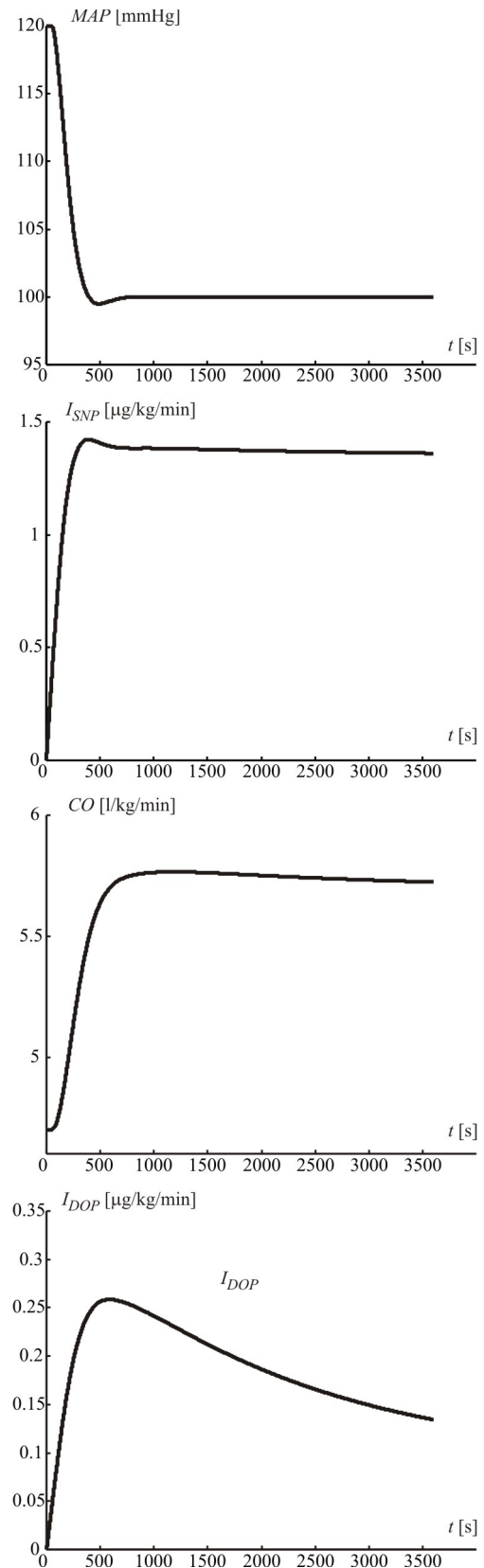

Figure 4. Simulation results for case 1: hypertensive patient, with typical values of sensitivity to infused drugs.
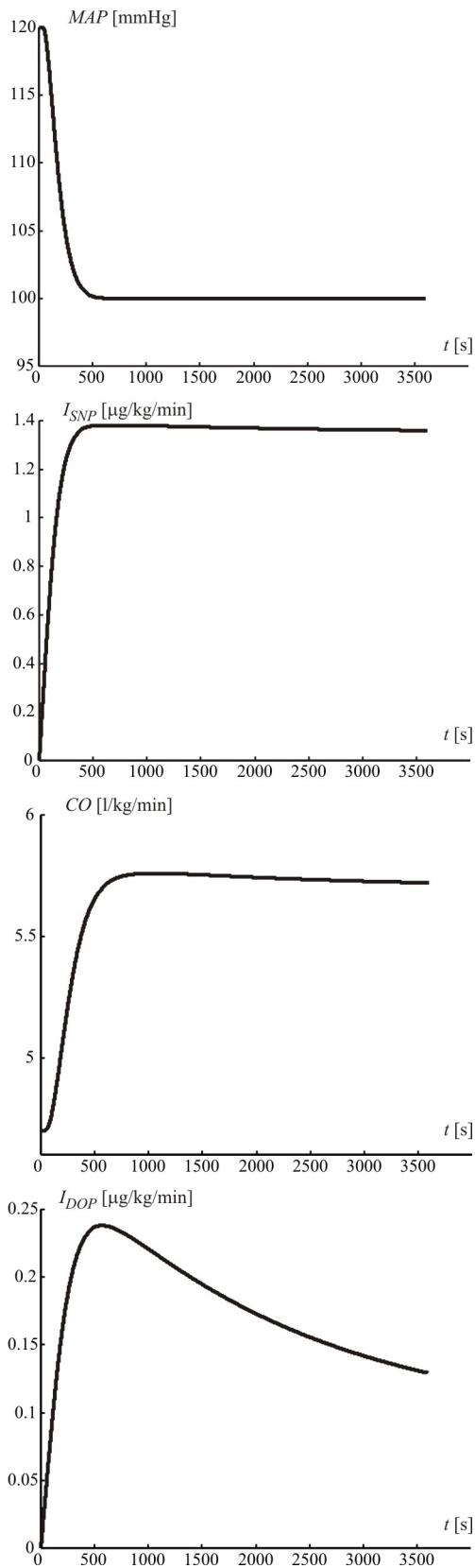
Figure 5. Simulation results for case 2: hypertensive patient, with faster response to infused drugs
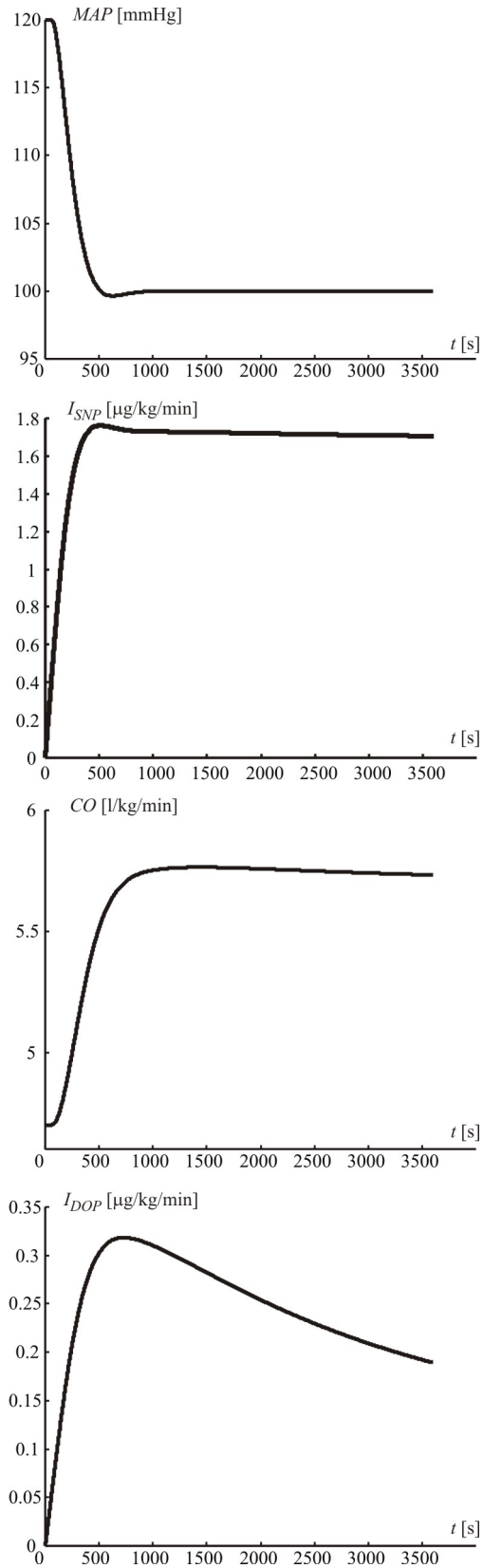

Figure 6. Simulation results for case 3: hypertensive patient, with slower and smaller response to infused drugs.

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