Original Article

Fuzzy Logic Controller for Hemodialysis Machine Based on Human Body Model

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ABSTRACT

Fuzzy controllers are being used in various control schemes. The aim of this study is to adjust the hemodialysis machine parameters by utilizing a fuzzy logic controller (FLC) so that patient's hemodynamic condition remains stable during hemodialysis treatment. For this purpose, a comprehensive mathematical model of the arterial pressure response during hemodialysis, including hemodynamic, osmotic, and regulatory phenomena has been used. The multi-input multi-output (MIMO) fuzzy logic controller receives three parameters from the model (heart rate, arterial blood pressure, and relative blood volume) as input. According to the changes in the controller input values and its rule base, the outputs change so that the patient's hemodynamic condition remains stable. The results of the simulations illustrate that applying the controller can improve the stability of a patient's hemodynamic condition during hemodialysis treatment and it also decreases the treatment time. Furthermore, by using fuzzy logic, there is no need to have prior knowledge about the system under control and the FLC is compatible with different patients.

Key words: *Biofeedback, fuzzy logic controller, hemodialysis control, human body model, simulation*

INTRODUCTION

Hemodialysis is a common therapy for patients with end-stage renal disease (ESRD). Toxic wastes and excess water absorbed between dialysis treatments have to be removed from the patients' organism. This process is controlled by a hemodialysis machine, which withdraws the patient's blood from a fistula and pumps it through an artificial kidney, the dialyzer.[1]

Acute hypotension is a common complication of chronic hemodialysis with the incidence still reported to be around 20–30% of treatments.[2] It can lead to serious vascular complications such as cerebral infarction and cardiac and mesenteric ischemia. It may contribute to chronic overhydration due to an inability to reach dry weight and may lead to under-dialysis. Prevention of dialysis hypotension, therefore, is an important challenge to the dialysis staff.[3] However, the morbidity associated with hypovolemia is not limited to hypotension.[4] has demonstrated that cramping and lightheadedness occurred in 28% of all treatment sessions, and in all cases those symptoms were preceded by a pronounced reduction in blood volume (BV).[5] The initiating factor in the pathogenesis of dialysis hypotension is a decrease in blood volume, which results from the imbalance between the ultrafiltration rate and the plasma refilling rate.[3]

A variety of therapeutic maneuvers have been suggested for the prevention and treatment of intradialytic hypotension. In the mid 1980s, a widespread switch from acetate to bicarbonate dialysis eliminated the vasodilating acetate hypotensive effects. Subsequently, higher dialysate sodium concentrations and/or use of ramped sodium modeling gained widespread currency.[6] One of the most promising approaches for avoiding these events was the application of profile dialysis, executed by a sequence of short intervals, with dynamically adjusted process parameters (e.g., composition of the dialysate).[7]

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The capability for a dialysis machine to use a measurement of the patient's status to automatically tune the dialysis session online is commonly addressed by physicians and bioengineers working in the hemodialysis field as 'biofeedback'.[8] Medical devices for monitoring and biofeedback control of the physiological parameters of a dialysis patient were introduced in the early 1990s. They have a wide range of applications, aimed at increasing the safety and ensuring the efficiency of the treatment, with an improved restoration of physiological conditions, leading to an overall reduction in morbidity and mortality.[9]

The aim of this work was designing a fuzzy logic controller for hemodialysis machine so that patient's hemodynamic condition remains stable during the treatment. The controller's effect on the statues of different groups of patients was investigated using a previously developed mathematical model of the arterial pressure response during hemodialysis in.[10] In order to evaluate the controller performance, two hemodialysis sessions, with and without fuzzy controller, for each patient were simulated, and hemodynamic statues of each patient was compared in these two cases. Results of simulations show the controller efficiency in stabilizing patient's hemodynamic statues. The remainder of this paper is organized as follows: The model is described in section 2.1. In section 2.2 the method used for FLC design is explained. We provide results of simulations in section 3. Discussion and indications for future work are given in Section 4. All quantitative equations of the mathematical model [Tables 1-4] and the abbreviations are given in the appendix [Table 5].

MATERIALS AND METHODS

Model Description

In a previous study,[10] a comprehensive mathematical model of the arterial pressure response during hemodialysis, including hemodynamic, osmotic, and regulatory phenomena has been developed. Here this model has been used in order to investigate the human cardiovascular response to hemodialysis treatment. The simulation results in[10] point out that this model is able to reproduce a variety of different conditions, including no hypotension, moderate hypotension, and severe hypotension with ultimate vasodepressor syncope, by adjusting a few parameters, with clear physiological meanings. As a perfect description of the model is available in[10], only the main aspects are summarized in this study. All quantitative equations are included in the appendix.

A schematic description of the main physiological factors incorporated in the model and their relationship is given in Figure 1.

This model includes three sections: 'Cardiovascular system', 'dynamic of water and ions exchange between different compartments of the body', and 'the short-term feedback regulatory system'. The model of the 'cardiovascular system' includes four vascular compartments (the systemic arteries, systemic veins, pulmonary arteries, and pulmonary veins) and two cardiac compartments (the right and left atrium), as shown in Figure 2.[10,11] Quantitative equations for pressure and volume changes of different parts in this system are given in Table 1 (Appendix).

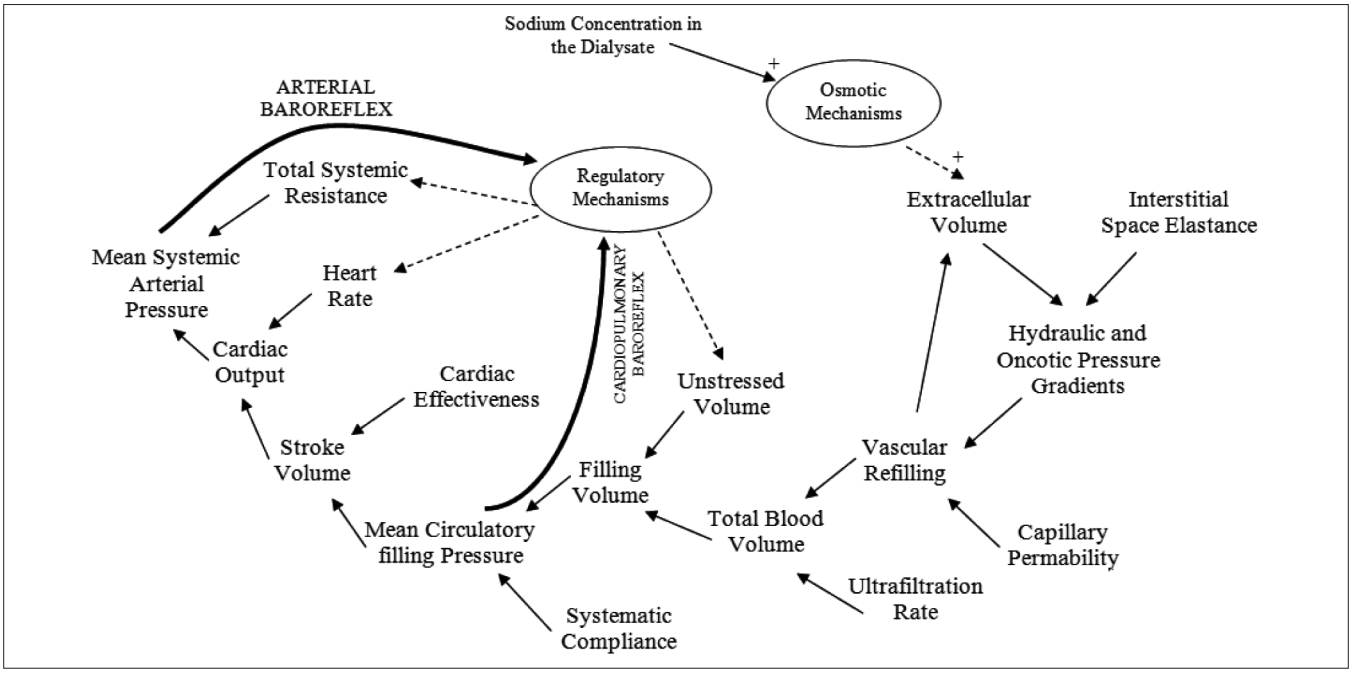

Figure 1: A schematic description of the main physiological factors incorporated in the model and their relationships[11]

Table 1: Equations for pressure and volume values of different parts of the cardiovascular system

Parameter	Pressure/Volume equation
Systemic arterial pressure (P_{sv})	$\frac{dp_{sa}}{dt} = \frac{1}{C_{sa}} \times \left(q_l - \frac{P_{sa} - P_{ac}}{R_{sl}} \right)$
Systemic venous pressure (P_{sv})	$P_{sv} = \frac{1}{C_{sv}} (V - V_u - C_{sa}P_{sa} - C_{pa}P_{pa} - C_{pv}P_{pv} - C_{ra}P_{ra} - C_{la}P_{la}$
Right atrium pressure (P_{ra})	$\frac{dp_{ra}}{dt} = \frac{1}{C_{ra}} \bullet \left(\frac{P_{sv} - P_{ra}}{R_{sv}} - q_r \right)$
Left atrium pressure (P_{la})	$\frac{dp_{la}}{dt} = \frac{1}{C_{la}} \bullet \left(\frac{P_{pv} - P_{la}}{R_{pv}} - q_l \right)$
Pulmonary artery pressure (V)	$\frac{dp_{pa}}{dt} = \frac{1}{C_{pa}} \bullet \left(q_r - \frac{P_{pa} - P_{pv}}{R_{pa}} \right)$
Pulmonary vein pressure (P_{pv})	$\frac{dp_{pv}}{dt} = \frac{1}{C_{pa}} \bullet \left(\frac{P_{pa} - P_{pv}}{R_{pa}} - \frac{P_{pv} - P_{la}}{R_{pv}} \right)$
Arterial capillary pressure (P_{ac})	$P_{ac} = \frac{G_v \bullet q_a + \frac{q_v}{R_{s2}}}{G_a \bullet G_v - \frac{1}{R_{s2}^2}}$
Venous capillary pressure (P_{vc})	$P_{vc} = \frac{G_a \bullet q_v + \frac{q_a}{R_{s2}}}{G_a \bullet G_v - \frac{1}{R_{s2}^2}}$
Blood volume (V)	$\frac{dv}{dt} = -F_a + R_v - Q_f + Q_{inf}$
Plasma volume (P_{pl})	$V_{pl} = V - V_{rc}$
Hematocrit (HCT)	$HCT = \frac{V_{rc}}{V} = 1 - \frac{V_{pl}}{V}$
Left ventricle	$q_l = S_l \bullet f$ $S_l = k_l \bullet (Pla - Pla0) / a_l$
Right ventricle	$q_r = S_r \bullet f$ $S_r = k_r \bullet (Pra - Pra0) / a_r$

$$F_a = L_a(P_{ac} - P_{is} - \pi_{pl} - \pi_{is}); R_v = L_v(\pi_{pl} - \pi_{is} - P_{vc} - P_{is}); G_a = \frac{1}{R_{s1}} + \frac{1}{R_{s2}} + L_a; G_v = \frac{1}{R_{s2}} + \frac{1}{R_{s3}} + L_v; q_a = \frac{P_{sa}}{R_{s1}} + L_a(P_{is} + \pi_{pl} - \pi_{is}); q_v = \frac{P_{sv}}{R_{s3}} + L_v(P_{is} + \pi_{pl} - \pi_{is})$$

$$\pi_{pl} = 2.1 \bullet C_{p,pl} + 0.16 \bullet C^2_{p,pl} + 0.009 \bullet C^3_{p,pl}; \pi_{is} = 2.8 C_{p.is} + 0.18 \bullet C^2_{p,is} + 0.012 \bullet C^3_{p.is}; P_{is} = E_{is}(V_{is} - V_{isn}) + P_{isn}; V_u = V_{usa} + V_{usv} + V_{upa} + V_{upv} + V_{ura} + V_{ula}$$

Main abbreviations and symbols are explained in the Table 5

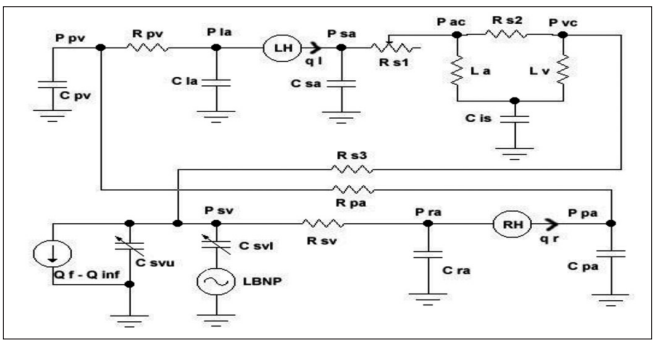

Figure 2: The model of cardiovascular system.[10]

For modeling the dynamic of water exchange between body compartments, three parts are assumed for the body, which reproduce 'intracellular fluid', 'interstitial fluid', and 'plasma'. Exchange of water between the intracellular and interstitial areas is caused by differential osmotic pressure, which is affected by the amount of sodium, urea, and potassium removed during the session.[10,11] Water transfer between the interstitial area and plasma depends on the differential hydraulic pressure and oncotic pressure in the capillary regions. An important factor in determining the hydraulic pressure is the elastance of the interstitial space (Eis), defined as the change in interstitial fluid pressure

per unit change in the interstitial fluid volume.[10,11] The mathematical relationships for water transfer are given in Table 2 (Appendix). As the concentration of major ions in plasma and the interstitial region is almost the same, only two compartments are assumed in the model of ion and urea exchange: Intracellular and extracellular (sum of plasma and interstitial area).[10,11] In this part of the model, urea and two major ions, sodium (Na) and potassium (K), are included. The ion exchange rate between the intracellular and extracellular regions depends on their concentrations. In particular, the Na concentration in dialysate (CNa,d) has an essential role in establishing Na concentration in the extracellular fluid (CNa,c), and thus, it affects on osmotic fluid exchange between the intracellular and extracellular compartments. Equations of Na, K, and urea mass changes with time are given in Table 3 (Appendix).[10,11]

The self-regulating autonomous nervous system is the main element for adjusting blood pressure and maintaining stability in the patient status. This is achieved by modification of the systemic arterial resistance, systemic venous unstressed volume, and heart period. The control mechanisms are triggered by information coming from both the arterial and cardiopulmonary baroreceptors. Moreover, the model hypothesizes that decreasing left arterial pressure below a given threshold causes a paradoxical withdrawal of the sympathetic drive and consequent vasodepressor syncope.[10] Relationships for this part of the model are given in Table 4 (Appendix).

Table 2: Mathematical relationships for water transfer

Process	Volume change equation
Fluid transfer from the intracellular to the interstitial area	$-\frac{dV_{ic}}{dt} = K_f(C_{is} - C_{ic})$, $C_{ic} = \frac{M_{K,ic} + M_{Na,ic} + M_{u,ic} + M_{eq,ic}}{V_{ic}}$ $C_{is} = C_{ex} = \frac{M_{K,ex} + M_{Na,ex} + M_{u,ex} + M_{eq,is}}{V_{pl} + V_{is}}$
Fluid transfer from the interstitial area to the plasma	$\frac{dV_{is}}{dt} = K_f \bullet (C_{is} - C_{ic}) + F_a - R_v$

Fuzzy Logic Controller Design

Fuzzy logic is a problem-solving control system methodology that provides a simple way to arrive at a definite conclusion based on vague, ambiguous, imprecise, noisy or missing input information.[12] A fuzzy logic controller is based on fuzzy logic and constitutes a way of converting a linguistic control strategy into an automatic one, by generating a rule base that controls the behavior of the system. The advantage of using this linguistic description is that it is very easy to modify the system. Moreover, no prior knowledge about the system under control is initially used to formulate the rules and a fuzzy model is constructed from the data.[13] A basic FLC can be decomposed into four basic components: The fuzzification unit, knowledge base (rule base and data base), decision-making unit (inference mechanism), and defuzzification unit.[13]

In this study, we employed a three-input, three-output fuzzy logic controller. A significant problem in designing a good fuzzy controller was selection of relevant and informative inputs and outputs for it. In this case the input parameters should be capable of reflecting the hemodynamic status of the patient and should be measurable by using preferably noninvasive biosensors. The output parameters should be adjustable in a real hemodialysis machine. By considering these properties 'systolic arterial blood pressure', 'heart rate,' and 'blood volume changes' were selected as the input parameters, and the 'ultrafiltration rate (UFR)', 'Na/K concentrations

Table 3: Equations of Na^+, K^+, and urea mass changes with time

Process	Mass changes equation
Na^+, K^+, and urea mass changes in the intracellular compartment	$\frac{dM_{s,ic}}{dt} = -K_s \bullet (C_{s,ic} - B_s C_{s,ex})$
Na^+, K^+, and urea mass changes in the extracellular compartment	$\frac{dM_{s,ex}}{dt} = K_s \bullet (C_{s,ic} - B_s C_{s,ex}) - J_s + Q_{inf} \bullet C_{s,inf}$ $J_s = \left\lfloor D_s \bullet (1 - Q_f / Q_{e,s}) + Q_f \right\rfloor \bullet C_{s,ex} - D_s \bullet (1 - Q_f / Q_{e,s}) \bullet C_{s,d}$ $Q_{e,s} = Q_B \bullet \left\lfloor F_p \bullet (1 - CHT) + F_r \bullet \gamma_s \bullet R_{ds} \right\rfloor$
Na^+, K^+, and urea concentration in intracellular compartment ($C_{s,ic}$)	$C_{s,ic} = \frac{M_{s,ic}}{V_{ic}}$
Na^+, K^+, and urea concentration in extracellular compartment ($C_{s,ex}$)	$C_{s,ex} = \frac{M_{s,ex}}{V_{is} + V_{pl}}$

$V_{ex} = V_{pl} + V_{is}; C_{s,ex} = C_{s,is} \cong C_{s,pl}; C_{s,pl} = \frac{F_p}{\alpha_s} \bullet C_{s,is}$

Main abbreviations and symbols are explained in the Table 5

Table 4: Relationships for the ANS model

Process	Mathematical relationships
Control of systemic arterial resistance	$\frac{dR_{sl}}{dt} = \frac{1}{\tau_R}(\sigma_R - R_{sl})$
	$\sigma_R = \frac{R_{slmax} + R_{slmin} \cdot \exp(X_R / K_R)}{1 + \exp(X_R / K_R)}$
	$R_{slmin} = \delta_{Rn} - \Delta\sigma_R / 2$
	$R_{slmax} = R_{slmin} + \Delta\sigma_R \cdot (1 - \delta(t)) \cdot \varepsilon(t)$
	$X_R = G_{aR} \cdot (P_{sa} - P_{san}) + G_{cR} \cdot (P_{ra} - P_{ran})$
	$\left.\frac{d\sigma_R}{dp_{sa}}\right\|_{x_R=0} = G_{aR}$
	$\left.\frac{d\sigma_R}{dp_{ra}}\right\|_{x_R=0} = G_{cR}$
	$\frac{dT}{dt} = \frac{1}{\tau_T}(\sigma_T - T)$
Heart rate control	$\sigma_T = \frac{T_{min} + T_{max} \cdot \exp(X_T / K_T)}{1 + \exp(X_T / K_T)}$
	$K_T = \frac{\Delta\sigma_T}{4}$
	$X_T = G_{aT} \cdot (P_{sa} - P_{san}) + G_{cT} \cdot (P_{ra} - P_{ran})$
	$T_{max} = \sigma_{Tn} + \Delta\sigma_T / 2$
	$T_{min} = T_{max} - \Delta\sigma_T (1 - \delta(t))$
	$\frac{dV_{usv}}{dt} = \frac{1}{\tau_v}(\sigma_v - V_{usv})$
Venous volume control	$\sigma_v = \frac{V_{usv,min} + V_{usv,max} \cdot \exp(X_V / K_V)}{1 + \exp(X_V / K_V)}$
	$K_V = \frac{\Delta\sigma_v}{4}$
	$X_v = G_{av} \cdot (P_{sa} - P_{san}) + G_{cv} \cdot (P_{ra} - P_{ran})$
	$V_{usv\,max} = \sigma_{vn} + \Delta\sigma_v / 2$
	$V_{usv\,min} = V_{usv\,max} - \Delta\sigma_v (1 - \delta(t))$
	$\delta(t): \begin{cases} \frac{d\delta(t)}{dt} = 0, P_{la} \geq P_{lat} \\ \frac{d\delta(t)}{dt} = [G_\delta \cdot (P_{lat} - P_{la}) - \delta(t)] / \tau_\delta \end{cases}$

Main abbreviations and symbols are explained in the Table 5

Table 5: Main abbreviations and symbols

Parameter	Explanation
K_s, B_s	Mass transfer coefficients between the intracellular and extracellular compartments for solute s.
C_{ex}	Concentration of all osmotic effective particles in the extracellular region
C_{ic}	Concentration of all osmotic effective particles in the intercellular region
C_{is}	Concentration of all osmotic effective particles in the interstitial region
C_{la}	Compliance of the left atrium
C_{pa}	Compliance of the pulmonary artery
$C_{p,is}$, $C_{p,pl}$	Protein concentrations in the interstitial region and plasma
C_{pv}	Compliance of the pulmonary vein
C_{ra}	Compliance of the right atrium
C_{sa}	Compliance of the systemic artery
$C_{s,d}$	Concentration of solute s in dialysate (s=K^+, Na^+, Urea)
$C_{s,ex}$	"s" concentration in the extracellular fluid (s=K^+, Na^+, Urea)
$C_{s,ic}$	"s" concentration in the interstitial fluid (s=K^+, Na^+, Urea)
C_{sv}	Compliance of systemic venous
D_s	Clearance for solute s (s=K^+, Na^+, Urea)
$\delta(t)$	Sympathoinhibitory signal
σ_{in}, $\Delta\sigma_i$	Basal value and amplitude of the sigmoidal static characteristic for the ith mechanism
E_{is}	Interstitial region elastance
$\varepsilon(t)$	Acetate buffer effect on the cardiovascular system
F_a	Rate of fluid from the plasma to the interstitial region
F_p, F_γ	Plasma and Red blood cell water fraction
G_{ai}, G_{ci}	Central gains of the arterial and cardiopulmonary controls for the ith mechanism
G_δ, τ_δ	Gain and time constants of the sympathoinhibitory mechanism
γ_s	Fraction of red blood cell water that participates in the transfer through the dialyzer
HCT	Hematocrit
J_s	Ions exchange flux in dialyzer
K_f	Water exchange coefficients between the intracellular and extracellular compartments for solute s.
K_R, K_L	Curve fitting parameters
K_l, K_r	Slop of the stroke volume versus the atrial pressure relationship for the left and right heart
L_a	Permeability coefficient of the arterial capillaries
L_v	Permeability coefficient of the venular capillaries
$M_{eq,ex}$, $M_{eq,ic}$	Volume of all osmotic effective particles in the extracellular and intracellular regions, other than K^+, Na^+, and urea
$M_{eq,is}$	Volume of all osmotic effective particles in the interstitial region other than K^+, Na^+, and urea
$M_{s,ex}$	Volume of "s" in the extracellular fluid (s=K^+, Na^+, Urea)
$M_{s,ic}$	Volume of "s" in the intercellular fluid (s=K^+, Na^+, Urea)
P_{ac}	Arterial capillary pressure
P_{is}	Hydraulic pressure of the interstitial fluid
P_{la}	Left atrium pressure

(*continued*)

in dialysate,' and 'blood flow rate in the dialyzer' were considered as the output signals.[14]

There are noninvasive relative blood volume (RBV) monitoring devices that permit real-time and repetitive RBV assessments during the entire hemodialysis session.[3] Noninvasive continuous measurement of blood pressure is desirable for monitoring patients during surgical operation or in Intensive Care Units and home health care. In,[15] a method of combining the pulse arrival time and intermittent calibration measurement are presented, to estimate systolic blood pressure continuously. The heart rate can be obtained from an echocardiography (ECG) signal, using signal processing techniques, and an ECG signal can be measured continuously and noninvasively. In,[16] an analysis method

Table 5: (*Continued*)

Parameter	Explanation
P_{lat}	Threshold value of the left aterial pressure for activation of the sympathoinhibitory mechanism
P_{pa}	Pulmonary artery pressure
P_{pv}	Pulmonary vein pressure
P_{ra}	Right atrium pressure
P_{ran}	Right atrium pressure (nominal)
P_{sa}	Systemic arterial pressure
P_{san}	Systemic arterial pressure (nominal)
P_{sv}	Systemic vein pressure
P_{pv}	Venous capillary pressure
π_{is}	Osmotic pressure in the interstitial fluid
π_{pl}	Osmotic pressure in the plasma
q_l	Left heart output
q_r	Right heart output
Q_B	Blood flow through the dialyzer
$Q_{e,s}$	Effective flow rate for "s" (s=K^+, Na^+, Urea)
Q_f, Q_{inf}	Ultrafiltration rate (in dialyzer) and infusion rate of the replacement fluid
$Q_{s,inf}$	Infused flow rate for "s" (s=K^+, Na^+, Urea)
R_{Ds}	Donnan coefficient for "s" (s=K^+, Na^+, Urea)
R_{pa}	Hydraulic resistance of pulmonary artery compartment
R_{pv}	Hydraulic resistance of pulmonary vein compartment
R_{sl}	Hydraulic resistance of systemic artery (from heart to capillary bed)
R_{s2}	Hydraulic resistance of capillary bed
R_{s3}	Hydraulic resistance from capillary bed to heart
R_{slmin}	Minimum of R_{sl}
R_{slmax}	Maximum of R_{sl}
R_{sa}	Hydraulic resistance of systemic artery compartment
R_{sv}	Hydraulic resistance of systemic vein compartment
R_v	Rate of fluid from interstitial region to plasma
T	Heart beat period
τ_R	Time constant for ANS control loop of systemic arterial resistance
τ_T	Time constant for ANS control loop of heart rate
τ_v	Time constant for ANS control loop of venous volume
V	Blood volume
V_{ic}	Intracellular fluid volume
V_{is}	Interstitial fluid volume
V_{isn}, V_{icn}	Interstitial and intracellular fluid volume (basal)
V_{pl}	Plasma volume
V_{rc}	Red blood cell volume
V_u	Total unstressed volume
V_{uj}	Unstressed volume of the j^{th} compartment

is presented for extracting the heart rate from an arterial blood pressure signal in the dialysis machine and its results show that with this method the heart rate can be extracted without using additional instruments like an ECG or pulse oximeter. Selected output variables are easily controllable in a real hemodialysis system.

We define some membership functions (MFs) for each of the input and output variables according to their variation limits. For reducing the effect of noise in the signals, triangular or Gaussian membership functions can be used, because they are less sensitive to small changes in input parameters than singleton membership function. Triangular MF is more sensitive to changes in its input value than the Gaussian MF; so in this case triangular MFs were used. In the defuzzification stage, we employed the center of gravity defuzzifier, because we needed smooth and continuous changes in the output parameters.

With increasing the number of MFs for a variable, the precision and sensitivity to changes in its value increases; but on the other hand it increases the number of rules and complexities; so only when high precision and sensitivity to a signal is required, more MFs are considered for it.

Membership functions for input parameters

For each of input and output signal, an individual permissible variation limit is defined. For blood pressure, the acceptable variation is ± 20% change relative to the patient's initial blood pressure.[17] This means that we consider the initial blood pressure for each patient as his/her normal pressure.

As arterial pressure is the most informative feedback signal from the body model, its permissible range is divided into 40 parts and one membership function (MF) is defined for each part [Figure 3]. Therefore, we have more rules for blood pressure in the inference engine, and this increases the sensitivity and precision of the controller to its changes.

The second input variable of the controller is the heart rate. The average heart rate for a normal person in the usual condition is 72 beats/minute.[18] During hemodialysis treatment, the patient's heart rate may change due to different factors like ultrafiltration. The range of these changes can be wide. Here changes from 45 to 120 beats/minute are considered as permissible. Membership functions for this parameter are defined in such a way that increasing (decreasing) of heart rate from the specified maximum (minimum) permissible limits can be specified in the fuzzy controller. As it is shown in Figure 3, this definition states that when the heart rate starts to decrease from about 60 beats/minute, it is specified gradually by the first membership function, and heart rate under 55 beats/minute is specified rapidly by the second membership function. For the upper limit of heart rate, two membership functions with a similar method are considered. The start of heart rate increasing from 105 beats/minute is specified gradually and more than 115 beats/minute is specified rapidly by the first and second membership functions, respectively.

The third input parameter is the relative blood volume or RBV instead of the absolute value of BV, because blood volume is different between patients and by using RBV instead of absolute BV, the controller can be used for different patients. The value of blood volume at the start of the dialysis session is considered to be 100% volume.

The permissible variation range for this variable is 85 to 100% of initial value and three MFs are defined for it. Critical BV changes are from 85 to 90%; so in this range we define two MFs as having their centers in 88 and 86% and having a coverage radius of 2%. The last MF is a Z-shaped slopped membership function, which shows the blood volume variations in the 87 to 84% range, much stronger than the first Z-shaped membership function. Membership functions for all three input variables are shown in Figure 3.

Membership functions for output parameters

One of the output parameters of the controller is the ultrafiltration rate or UFR. As ultrafiltration causes a direct decrease in the patient's blood volume, its rate is the most important factor in determining the patient's status during hemodialysis. A variation range for this variable can be very wide, based on the patient's condition. Therefore, we define its changes from 100 ml/hour to 3050 ml/hour as tolerable.[4] As it is shown in Figure 4, this limit is covered with 23 MFs. For increasing the sensitivity and precision of the controller in low UFR, the distance between the centers of MFs is gradually decreased with decreasing the UFR.

For the second output parameter, the sodium concentration, the acceptable variation range is defined as being from 0.135 mmol/ml to 0.157 mmol/ml.[17] For each 0.001 variation in the sodium concentration, a membership function is defined.

For the last output parameter, the blood flow rate in the dialyzer, we define changes from 300 ml/minute to 450 ml/minute as permissible.[4] These limits are selected based on theoretical and clinical data. 22 MFs are defined for the blood flow rate in the range of its variation. Membership functions for all output variables are given in Figure 4.

The fuzzy rule base

In order to generate a fuzzy controller rule base, we used a general principle. When the patient's hemodynamic condition is stable (input parameters of the controller have their normal values), the UFR and blood flow rate in the dialyzer are adjusted to their maximum values, and sodium concentration is adjusted to its minimum value. Falling blood pressure or RBV or rising heart rate show that the patient status is going to be unstable . Therefore, by observing each of these changes, the UFR and blood flow rate should be lowered and sodium concentration in the dialysate should be increased. The amplitude of the output changes depends on the input parameters' deviation from their normal values. In general the fuzzy rule base is generated in such a way that with regard to the values of the input parameters, changes in output signals guarantee the patient's hemodynamic stability. Some examples of the rules are included in Table 6.

Changes of each output parameter relative to the input parameter values are shown in Figure 5.

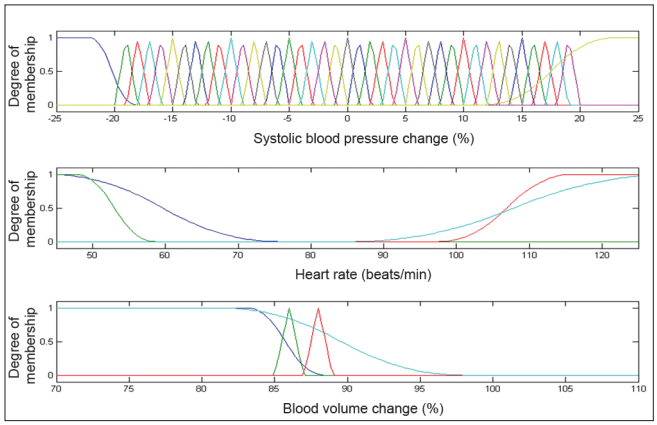

Figure 3: Membership functions for input variables of fuzzy controller

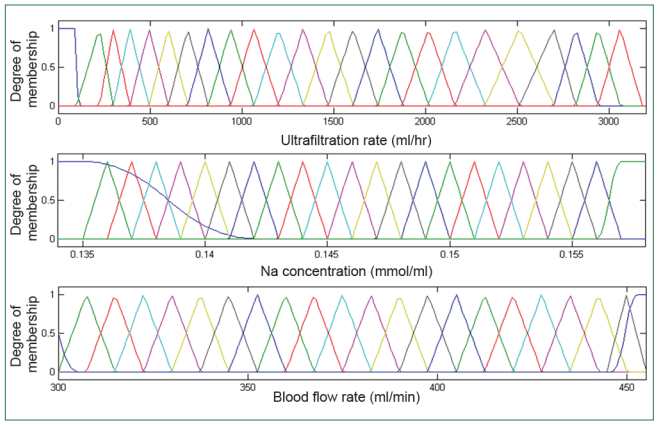

Figure 4: Membership functions for output variables of fuzzy controller

Table 6: Some examples of the fuzzy rules

If	Psa is 80	or	RBV is 85	then	Qf is 260	and	Na conc. is 155	and	Qb is 130
If	Psa is 81	or	RBV is 85	then	Qf is 330	and	Na conc. is 154	and	Qb is 130
If	Psa is 82	or	RBV is 86	then	Qf is 400	and	Na conc. is 153	and	Qb is 150
If	Psa is 90			then	Qf is 890	and	Na conc. is 147	and	Qb is 270
If	Psa is 94			then	Qf is 1160	and	Na conc. is 143	and	Qb is 315
If	Psa is 117	or	RBV is 86	then	Qf is 470	and	Na conc. is 152	and	Qb is 170
If	Psa is 120	or	RBV is 85	then	Qf is 260	and	Na conc. is 155	and	Qb is 130
If	RBV is 84			then	Qf is 100	and	Na conc. is 155	and	Qb is 130
If	HR is 45			then	Qf is 100	and	Na conc. is 157	and	Qb is 70
If	HR is 116			then	Qf is 150	and	Na conc. is 157	and	Qb is 70

The inference engine

Two main types of fuzzy modeling schemes are the Takagi–Sugeno model and the fuzzy relational model. The Takagi–Sugeno scheme is a data-driven approach where membership functions and rules are developed using a training data set. The final output is a weighted average of a set of crisp values. The Mamdani scheme is a type of fuzzy relational model, where each rule is represented by an IF-THEN relationship. It is also called a linguistic model, because both the antecedent and the consequent are fuzzy propositions. The output from a Mamdani model is a fuzzy membership function based on the rules created. Based on the fuzzy logic principles, the if-then fuzzy rules are combined by the inference engine. Mamdani is one of the most applicable inference engines. Here, the Mamdani inference engine has been used, because its implementation is easy and our intention is to keep the fuzzy rules independent of each other.

Software

Modeling of the human body and all simulations were carried out by Matlab/Simulink. The fuzzy controller was created using the Fuzzy Logic Toolbox of Matlab.

RESULTS

In this section the simulation results for two groups of patients, with and without the controller, are given. In the simulations, two conditions should be fulfilled for determining the simulation stop time. When both of these conditions are satisfied, the simulation of the hemodialysis treatment is stopped:

1. Excess water in a patient's body (specified at the beginning of simulation) is exerted from the body, via ultrafiltration
2. Extracellular urea is decreased to an acceptable level

In general, the efficiency of hemodialysis in end-stage renal disease is determined by calculating the adequacy. The adequacy of dialysis and its measurement have been debated over the past 20 years by authorities concerned about how much of this life-sustaining treatment is appropriate for patients with ESRD.[19] The blood urea concentration has been used as a surrogate marker for toxin elimination in hemodialyzed patients, and several indices based on it have been proposed in recent years for monitoring the treatment adequacy. The most widely used are the logarithmic Kt/V equation and the Urea Reduction Ratio (URR). The National Kidney Foundation Guidelines (DOQI) and the European Renal Association (ERA) have set standards for adequacy of hemodialysis treatment. They recommend minimum single pool doses of 1.2 (Kt/Vsp DOQI), and 1.4 (Kt/Vsp ERA) and a standard urea removal ratio (URR) of 65%.

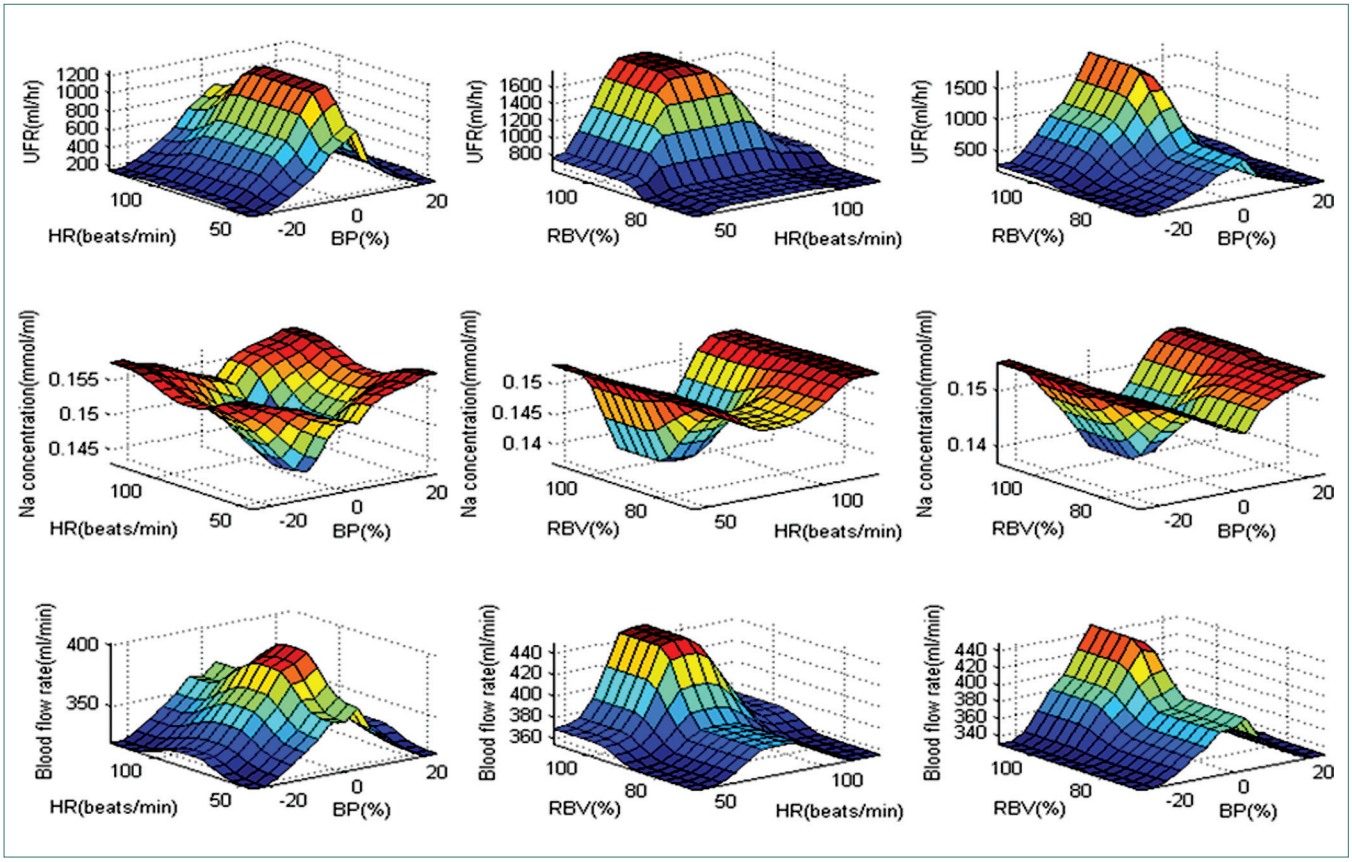

Figure 5: Changes of output signals relative to the input parameter values. (RBV: Relative blood volume, BP: Blood pressure, HR: Heart rate, UFR: Ultrafiltration rate)

The following equation is used to calculate URR:[20]

$$URR_x = 100(1 - U_x / U_0) \quad (1)$$

Where U_0 indicates extracellular urea at the beginning of session.[20]

The value of URR_X is compared during the simulation with the threshold value (65%) to decide if the dialysis is adequate or not. During the simulations we have the value of extracellular urea at each moment. In the real world, online urea monitoring (Ol-UM) has been proposed to provide the clinician with automated real-time bedside tools assessing dialysis efficacy and the protein nutritional status of dialysis patients. Ol-UM systems can be integrated into a dialysis monitor.[21]

Simulation Results

In order to analyze the FLC performance, two different groups of patients were simulated. All patient model parameters in the original study[10] were scaled to a hypothetical 70 kg body weight. The patients were simulated by changing a few parameters in the model with respect to their basal values. It is assumed that the model at the beginning of the treatment is in a steady state condition. For each group, a hemodialysis session was simulated in two cases — with a fuzzy controller and without a fuzzy controller. In cases without a controller, UFR, the Na concentration and blood flow in dialyzer were set to fixed values (1000 ml/hour, 0.142 mmol/ml, and 300 ml/minute, respectively). In all simulations, four liters of fluid had to be removed from the patient's body via ultrafiltration.

The first group of patients had an impaired autonomic nervous system (ANS). In these patients the arterial resistance control system was impaired. In order to model this group, all the parameters were set to their normal values, with the exception of a reduction in the amplitude of the systemic resistance static characteristic ($\Delta\sigma R = 0.3$ mmHg.s/ml). This change was necessary to simulate the rapid exhaustion of the sympathetic control on peripheral arterioles. The gains of the arterial and cardiopulmonary mechanisms on unstressed volume were reinforced (Gav=42 mmHg-1 and Gcv=1250 mmHg-1) to avoid an excessive fall in cardiac output.[10] The basal values of these parameters were $\Delta\sigma R = 1.4$ mmHg.s/ml, Gav=10.8 mmHg-1, and Gcv=417 mmHg-1.[10] In this patient ANS was unable to adjust the systemic resistance, hence, a decrease in the arterial blood pressure value was more than that in a normal patient. Simulation results for this group are given in Figures 6-8. Simulation results with fuzzy controller show that the patient status was much more stable during the controlled hemodialysis session [Figure 7]. In both cases, at the end of the hemodialysis session, four liters of liquid was removed from the body and extracellular urea decreased to the acceptable level [Figure 6]. Changes in the controller

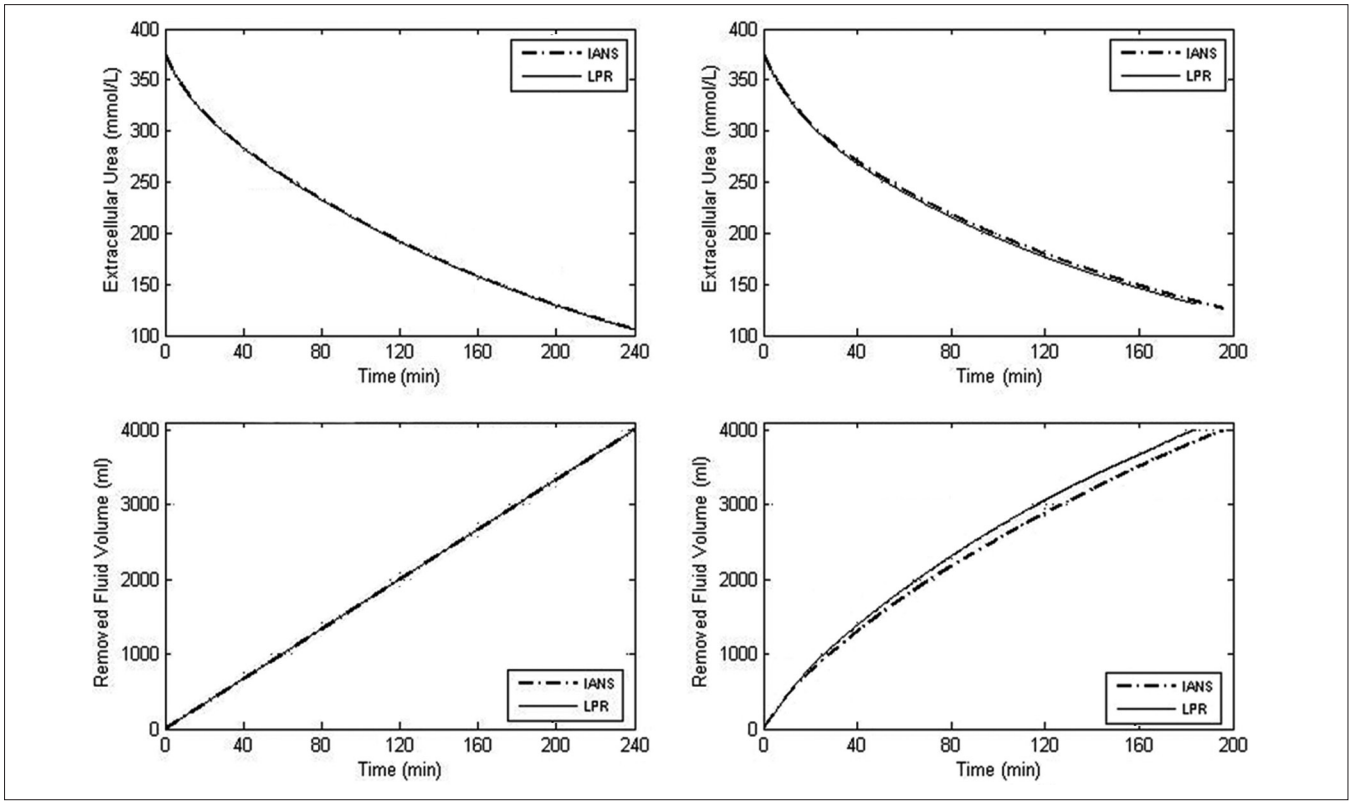

Figure 6: Simulation results for patients with impaired ANS (IANS) and with low plasma refilling rate (LPR) — removed fluid volume from body and extracellular urea (Left: Without controller, Right: With controller)

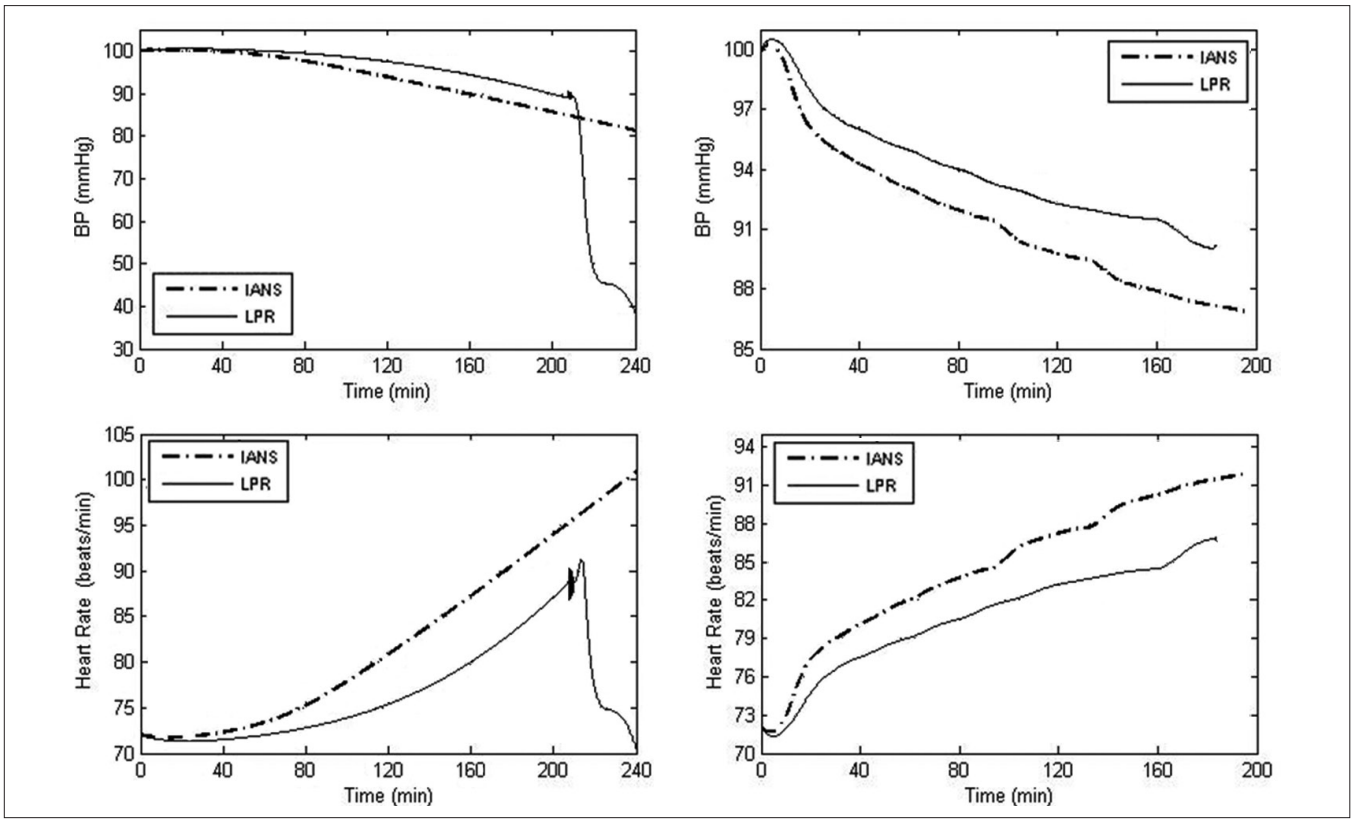

Figure 7: Simulation results for a patient with impaired ANS (IANS) and with low plasma refilling rate (LPR) — blood pressure (BP) and heart rate changes during treatment (Left: Without controller, Right: With controller)

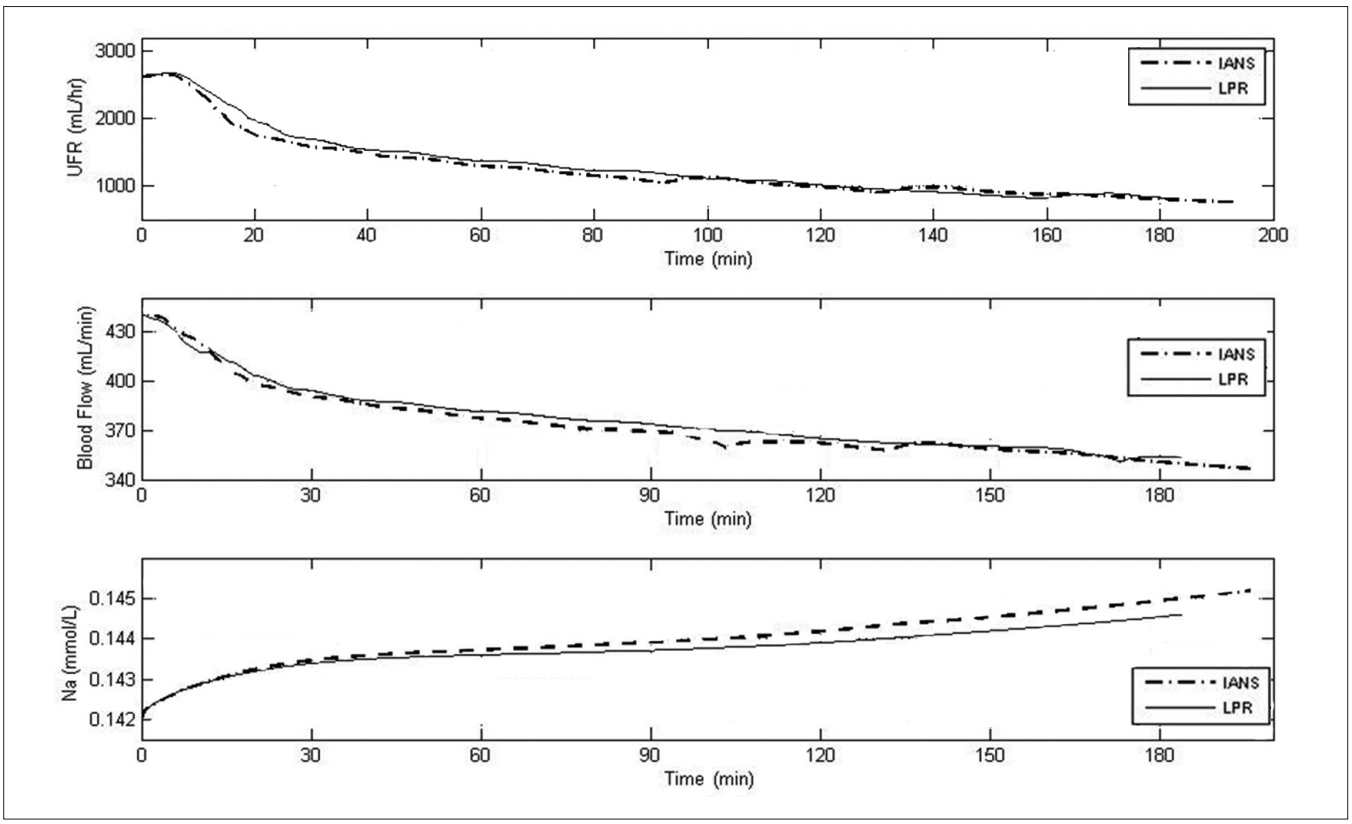

Figure 8: Simulation results for a patient with impaired ANS (IANS) and with low plasma refilling rate (LPR) — changes in controller outputs with time. UFR: Ultrafiltration rate. (These parameters are adjusted to fixed values in a controller-less session)

output parameters in this case are shown in Figure 8. In this case dialysis time in the controlled session was less than that in the one without the controller.

The second group of patients exhibited normal arterial and cardiopulmonary baroreflexes, but had a low plasma refilling rate. For modeling these patients, the permeability coefficient of the arterial and venous capillary walls (La, Lv) was decreased from 0.01 and 0.062 ml/mmHg/second to 0.003 and 0.02 ml/mmHg/second, respectively, and the elastance of the interstitial section (Eis) was increased from 2.45 mmHg/L to 3.2 mmHg/L. These changes worked against vascular refilling from the interstitial space.[10] In this situation, plasma volume reduction was faster and so venous pressure was decreased. This reduction produced a strong response from the cardiopulmonary receptor mechanism that kept the arterial pressure constant during the first two hours of hemodialysis. After two hours this mechanism was not sufficient to keep the arterial pressure constant and it started to decrease and the arterial baroreflex was also put into action. Finally, after three hours the controller mechanisms such as arterial resistance and venous unstressed volume, reached their saturation level; therefore, the decrease in plasma volume received only scarce compensation from the control mechanism action, and the arterial pressure began to decrease rapidly.[10]

Simulation results for this patient are also given in Figures 6-8. Results obtained from a controlled hemodialysis session for this patient show that the fuzzy controller is able to maintain patient hemodynamic stability and any unacceptable changes in patient parameters like blood pressure and heart rate is not observed [Figure 7]. In addition, the dialysis time is decreased, relative to the controller-less treatment.

As it can be seen, in both cases, the controller improves the patient status during dialysis and reduces treatment time, while dialysis remains efficient.

All the simulations were repeated using Gaussian MFs instead of triangular MFs. The results were almost the same; it could be because there was no sudden and fast change in signals, and also because, in all cases, the width of triangular MFs were considered small.

DISCUSSION

Online monitoring devices and biofeedback systems have evolved from toys for research use to tools for routine clinical application, particularly in patients with clinical complications.[21] At present, some biofeedback systems are commercially available. One of these systems is based on the concept of blood volume tracking (BVT): Based on target values for weight change and treatment duration. The BVT system guides the actual RBV along a pre-set individual RBV trajectory by continuously adjusting the UFR and dialysate conductivity (DC). In,[3] it is shown that better hemodynamic stability and the reduction of symptoms with BVT are not paralleled by better RBV preservation, in comparison to standard hemodialysis (HD).

A second system adapts the UFR in response to RBV changes, in order to stay on the safe side of a pre-set individual RBV limit, below which the patient is expected to be at risk for dialysis hypotension, on the basis of earlier observations. To date, only one study is available that demonstrates better intradialytic hemodynamic stability with this system.[3]

Another biofeedback control system for intra-HD blood volume (BV) changes modeling, based on an adaptive controller incorporated in an HD machine (Integra, Hospal Italy), has been developed to prevent destabilizing hypovolemia. The hemocontrol biofeedback system (HBS) monitors BV contraction during HD, with an optical device and modulates the BV contraction rates by adjusting the ultrafiltration rate (UFR) and the refilling rate by adjusting dialysate conductivity in order to obtain the desired pre-determined BV trajectories.[5] Results obtained in[5] show that HBS treatment is effective in lowering hypovolemia-associated morbidity, compared to the treatment equipped with a constant UFR and DC.

In[6] a biofeedback system was developed that avoids sudden excessive falls in BV by way of appropriate online adjustments to the weight loss rate (WLR) and DC.

Such devices include sensors for the measurement of temperature, optical parameters, sound speed in blood, electrical characteristics of the human body, and other parameters. Essential for the development of these devices is a detailed understanding of the pathophysiological background of a therapeutical problem. There is still a large potential to introduce new devices for further therapy improvement and automation.[9]

In[12] an automatic system (ABPS, automatic blood pressure stabilization) for BP control by fluid removal feedback regulation is implemented on a dialysis machine (Dialog Advanced, Braun). An FL control runs in the system, using instantaneous BP as the input variable governing the UFR according to the BP trend. The system requires the input of two data: Critical BP and the highest UFR applicable. They conclude that FL may be suited to interpreting and controlling the trend of BP. The medical knowledge of the patient and the consequent updating of input parameters depending on the patient's clinical conditions seem to be the main factors for obtaining optimal results.[12]

In this study we designed a closed-loop biofeedback system for hemodialysis control, by applying a fuzzy

logic controller. In order to study the performance of the controller and the human cardiovascular response to hemodialysis treatment, a model of a human body was used. Using the model and simulation tests, the values of different controller parameters could be changed without limitation and their effect on the patient model could be investigated, to assure fuzzy logic controller success. In addition, this eliminated the need to do the primary tests on real patients.

Three signals from the patient body model were used as controller inputs and three hemodialysis parameters were used as its outputs. The change in the patient's blood volume, relative to its initial value, was used as the first input signal. Online monitoring of circulatory blood volume reduction is rapidly gaining clinical acceptance as a valuable tool for monitoring hypovolemic stress in subjects prone to acute hypotension.[2] The reason to use multiple inputs rather than one input is a poor predictive value of RBV reductions, for the occurrence of dialysis hypotension, in most studies. Hemodynamic stability is determined not only by the course of blood volume, but also by the response of the compensatory mechanisms to hypovolemia, such as, decrease in venous capacity, increase in vascular resistance, and increase in cardiac contractility and rate.[3] In other words the interplay of UF and vascular refilling, reflected in the relative BV reduction curve, is only a part of the complex puzzle of the model predicting intra-HD hypotension, which must necessarily include other clinical variables related to additional compensatory mechanisms to gain clinical reliability.[21]

The second input parameter is the patient blood pressure change relative to its normal value. Due to complex BP regulation under dynamic dialysis conditions, the BP itself appears to be the most consistent input parameter for a device addressed to preventing dialysis hypotension.[12]

An indicator for the possible occurrence of hypotension is a change in heart rate (HR).[22] HR and HR variability provide important information about a patient's cardiovascular state. By interpreting these values, hypotensive episodes could be detected and prevented before they actually occurred.[16] Thus, patient heart rate was used as the third input signal.

One of the output signals is the Na concentration in dialysate. Many studies have demonstrated the importance of dialysate sodium content in the control of plasma refilling and blood volume changes.[6] In,[22] it has been shown that dialysate sodium and ultrafiltration profiling significantly reduce hemodialysis-related symptoms. UFR as the second output signal has a direct effect on patient's blood volume and his/her hemodynamic status.

Using FL has a lot of advantages. FL mimics how a person would make decisions and it may control the nonlinear systems that would be difficult or impossible to model mathematically. It incorporates a simple, rule-based 'if X and Y then Z' approach to solving a control problem rather than attempting to model a system mathematically.[12] It is known that incorporating artificial intelligence into control systems allows these systems to be more flexible, to adapt various operating conditions and disturbances, and to include human expertise and thinking into their decision-making process. Fuzzy logic-based control is a powerful expert system technique to effectively control and describe real, complex, and vague processes with time-varying properties. In a rule-based controller the control strategy is stored in a natural language; so it is easy to use expert knowledge in implementing the FLC rule base. It is also simple to modify, add or delete a rule in future according to new information. A rule-based controller is easy to understand and to maintain for a non-specialist end-user. The controller is independent of the patient status and can be used for various patients, because there are no patient-specific parameters that need to be determined in an identification/optimization process.

According to our simulation results, FLC can reduce treatment time relative to a controller-less session, in addition to stabilizing the patient status. Shortening of dialysis time may be beneficial to many patients. It may also reduce the treatment costs and more patients can be treated with a hemodialysis machine. As the treatment time is reduced, the patient will be under stress for a lesser time.

The important point is that in all cases dialysis efficiency is guaranteed. It means that shortening the dialysis time will not reduce dialysis efficiency.

Due to the high demand and increasing rate of patients with kidney failure, as well as, for the most needed medical centers and hospitals in Iran, for the last twelve years a group of medical engineer scientists cooperating with the Iranian Research Organization for Science and Technology (IROST) have succeeded in designing and making three improved versions of the dialysis machine for the first time in Iran and Middle East. This group of experts has spent nearly four years (2000–2004) in the research and development of the new model IROST 2001 D.[23] Our future study is to incorporate the fuzzy logic controller in a real hemodialysis system.

APPENDIX

All quantitative equations, main abbreviations, and symbols are explained in the tables.

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REFERENCES

1. U. Moissl, P. Wabel, and R. Isermann. Model-based control of hemodialysis. *Proceedings of American Control Conference*, vol. 5, pp. 3809-10, 2001.
2. A. Ciandrini, S. Cavalcanti, S. Severi, L. Garred, and G. Avanzolini. Effects of dialysis technique on acute hypotension: A model-based study. Cardiovasc Eng: An Int J 4, pp.163-71, 2004.
3. J. J. Dasselaar, R. M. Huisman, P. E. de Jong, and C.F. Franssen. Measurement of relative blood volume changes during haemodialysis: Merits and limitations. Nephrol Dial Transplant 20, pp. 2043-9, 2005.
4. J. T. Daugirdas, P. G. Blake, and T. S. Ing. Hanbook of dialysis. Philadelphia: Lippincott Williams and Wilkins; 2001.
5. C. Basile, R. Giordano, L. Vernaglione, A. Montanaro, P. De Maio, F. De Padova, *et al*. Efficacy and safety of haemodialysis treatment with the Hemocontrol biofeedback system: A prospective medium-term study. Nephrol Dial Transplant 16, pp. 328-34, 2001.
6. A. Santoro, E. Mancini, C. Basile, L. Amoroso, S. Di Giulio, M. Usberti, *et al*. Blood volume controlled hemodialysis in hypotension-prone patients: A randomized, multicenter controlled trial. Kidney Int 62, pp. 1034-45, 2002.
7. H. Scharfetter, and H. Hutten. *Individual adjustment of a multicompartment model for the simulation of exchange processes during hemodialysis*, *Proceedings of the 15th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, pp. 521-22, 1993.
8. F. Paolini, and A. Bosetto. Biofeedback systems architecture. Adv Ren Replace Ther 6, pp. 255-64, 1999.
9. M. Kraemer. Physiological monitoring and control in hemodialysis: State of the art and outlook. Expert Rev Med Devices 3, pp. 617-34, 2006.
10. M. Ursino, and M. Innocenti. Modeling arterial hypotension during Hemodialysis. Artif Organs 21, pp. 873-90,1997.
11. M. Ursino, and M. Innocenti. Mathematical investigation of some physiological factors involved in hemodialysis hypotension. Artif Organs 21, pp. 891-902, 1997.
12. E. Mancini, E. Mambelli, M. Irpinia, D. Gabrielli, C. Cascone, F. Conte, *et al*. Prevention of dialysis hypotension episodes using fuzzy logic control system. Nephrol Dial Transplant 22, pp. 1420-7, 2007.
13. D. Karaboga, A. Bagis, and T. Haktanir. Controlling spillway gates of dams by using fuzzy logic controller with optimum rule number. Appl Soft Comput 8, pp. 232-8, 2008.
14. C. Ronco, P.M. Ghezzi, and GL. Greca. The role of technology in hemodialysis. J Nephrol 12(suppl 2), pp. S68-S81, 1999.
15. W. Chen, T. Koboyashi, S. Ichikawa, Y. Takeuchi, and T. Togawa. Continuous estimation of systolic blood pressure using the pulse arrival time and intermittent calibration. Med Biol Eng Comput 38, pp. 569-74, 2000.
16. U. Moissl, P. Wabel, S. Leonhardt, R. Isermann, and M. Krämer. Continuous observation and analysis of heart rate during hemodialysis treatment. *European Medical & Biological Engineering Conference (EMBEC '99)*.J Int Fed Med Biomed Eng 37(Suppl 2), pp. 558-9, 1999.
17. J. F. Maher. *Replacement of renal function by dialysis*. The Netherlands: Kluwer Academic Publishers;1992.
18. Al. Mark, and G. Mancia. *Cardiopulmonary baroreflexes in human*. In: Jt Shepherd, FM Abboud, editors. Handbook of physiology, vol. 3, Sec.2, Circulation. Bethesda, MD: American physiological society; pp. 795-813, 1983.
19. M. Ray, and U. Qidwai. Artificial intelligence approach to determining minimum dose of haemodialysis. *Proceedings of the International Joint Conference on Neural Networks,*vol. 1, pp. 137- 142, 2003.
20. E. A. Fernández, R. Valtuille, J. M. Presedo, and P. Willshaw. Comparison of different methods for hemodialysis evaluation by means of ROC curves: From artificial intelligence to current methods. Clin Nephrol 64, pp. 205-13, 2005.
21. F. Locatelli, U. Buoncristiani, B. Canaud, H. Kohler, T. Petitclerc, and P. Zucchelli. Haemodialysis with on-line monitoring equipment: Tools or toys?. Nephrol Dial Transplant 20, pp. 22-33, 2005.
22. M. J. Oliver, L. J. Edwards, and D. N. Churchill. Impact of sodium and ultrafiltration profiling on hemodialysis-related symptoms. J Am Soc Nephrol 12, pp. 151-6, 2001.
23. M. Eghbal, V. R. Nafisi, and M. Firouzmand. *IROST 2001D hemodialysis machine- Technical report*, Biomedical Engineering Group, Iranian Research Organization for Science and Technology, 2003.

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