J. Biomed. Eng. Res : 449-454, 2007

Electrohydraulic Pump-Driven Closed-Loop Blood Pressure Regulatory System

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(Received March 27, 2007. Accepted May 31, 2007)

Abstract

An electrohydraulic (EH) pump-driven closed-loop blood pressure regulatory system was developed based on flow-mediated vascular occlusion using the vascular occlusive cuff technique. It is very useful for investigating blood pressure-dependant physiological variability, in particular, that could identify the principal mediators of renal autoregulation, such as tubuloglomerular feedback (TGF) and myogenic (MYO), during blood pressure regulation. To address this issue, renal perfusion pressure (RPP) should be well regulated under various experimental conditions. In this paper, we designed a new EH pump-driven RPP regulatory system capable of implementing precise and rapid RPP regulation. A closed-loop servo-controlwas developed with an optimal proportional plus integral (PI) compensation using the dynamic feedback RPP signal from animals. An in vivo performance was evaluated in terms of flow-mediated RPP occlusion, maintenance, and release responses. Step change to 80 mmHg reference from normal RPP revealed steady state error of ± 3 % during the RPP regulatory period after PI action. We obtained rapid RPP release time of approximately 300 ms. It is concluded that the proposed EH RPP regulatory system could be utilized in *in* vivo performance to study various pressure-flow relationships in diverse fields of physiology, and in particular, in renal autoregulation mechanisms.

Key words: renal perfusion pressure (RPP), proportional plus integral (PI) compensation, electrohydraulic pump, tubuloglomerular feedback (TGF), myogenic (MYO)

I. INTRODUCTION

A sophisticated feedback-controlled system for renal perfusion pressure (RPP) regulation has been recognized significantly to discover the profound impact of blood pressure on renal blood flow (RBF) and to identify the principal mediators of renal autoregulation mechanisms (Mattson D.L., et al, 1993, A. W. Cowley Jr., 1997, Armin Just, et al, 1998, W. A. Cupples, et al, 1996, Hengliang Wang, et al, 2005). Since RBF is auto-regulated by the rapid myogenic (MYO) response due to RPP step change, the servo-controlled RPP regulation system is required to evaluate the individual contribution of these mediators to RBF autoregulationfollowed by the slow tubuloglomerular feedback (TGF) mechanism (T. Wronski, et al, 2003, Hengliang Wang, et al, 2005). To help explore these underlying RBF autoregulation mechanisms, which are still unclear, several feedback servo- control devices have so far been constructed to maintain the RPP in a desired pressure range using a pneumatic servo- control system (Benn Nafz, et al, 1992), bidirectional DC motor syringe pump system (Hester, R. L., et al, 1983), and unidirectional occlusive mechanical system (Morff, R J., et al, 1978). There are, however, some limitations residing in all these pumps such as longer control latencies, less accurate pressure control, less steady-state stabilization, and an overly bulky system due to hardware-oriented implementation.

Therefore, in this paper, we present a development of the EH pump-driven closed-loop blood pressure regulatory system based on a simple EH configuration. In the present study, an EHconfiguration is newly introduced not only to overcome all limitations mentioned above and but also to implement a sophisticated EH servo-control system for RPP regulation. Also, we developed a user-friendly monitor program to be useful in diverse applications of physiology inopen-loop and closed-loop configurations using the LabVIEW 8.0 program (National Instruments, Austin, TX, USA). An *in vivo* performance evaluation of the proposed system was conducted with an extensive set of animal experiments. We tested whether a predetermined pressure would be well maintained by PI control action under various physiological conditions.

This research was supported by Hallym University Research Fund.
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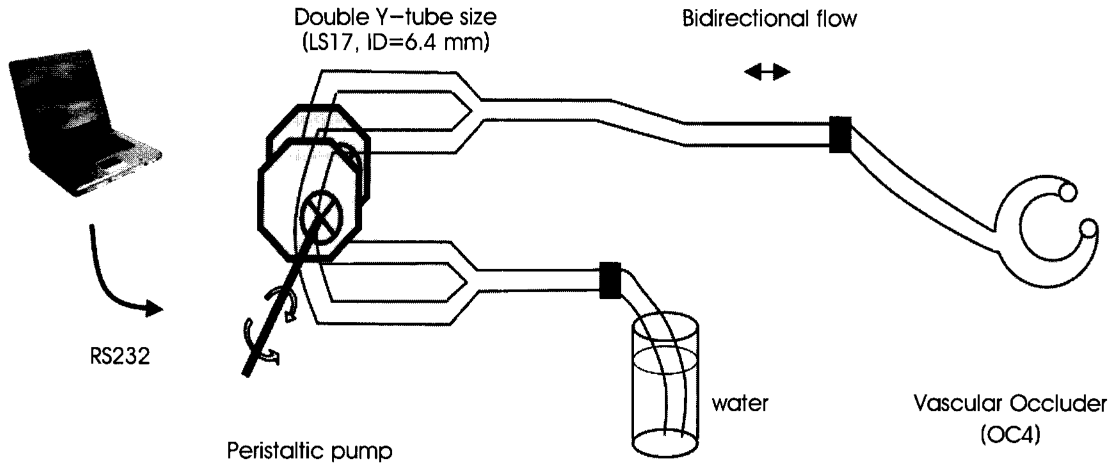

Fig. 1. Optimized electrohydraulic (EH) configuration.

II. METHODS

A. Electrohydraulic (EH) Pump Configuration

The EH pump configuration has been optimized to meet a precise and fast regulation of RPP, in particular, by means of the flow-mediated vascular occlusion/release. It consists of an EH peristaltic pump (LS brushless computer-programmable drive, Cole-Parmer Instrument Co., Vernon Hills, IL, USA) with a double pump head, each having four rollers (L/S® Easy-Load II pump head 77201-60, Cole-Parmer Instrument Co., Vernon Hills, USA), and it is directly coupled to a drive shaft in the range of 10 to 600 motor rpm with double Y- pump tubing (L/S® 17, ID=6.4 mm, Cole-Parmer Instrument Co., Vernon Hills, USA) for generating fluid hydraulic pressure, and finally a software monitor program activating the pump drive. Figure 1 shows the optimized EH configuration. The pump operation is activated by a monitor program developed using the LabVIEW 8.0 program, based on a RS-232C serial communication protocol. In order to realize the RPP regulation, a mechanical vascular occluder (OC4, IN VIVO METRIC Co., Healdsburg, CA, USA) was used with the cuff's width, thickness, and lumen diameter (5 mm, 2 mm, and 4 mm, respectively). Double Y-pump tubing is directly connected to the actuating tubing of the vascular occluder on the end. The peristaltic pump controls the hydraulic pressure inside the tubing by injecting fluid to the vascular occluder. Occlusion of blood vessels is created by the flow-mediated occluder's cuff inflation until a predetermined pressure approaches. The vascular occluder's cuff must be inflated to create at least more than 50 mmHg systolic pressure for complete occlusion. Precision pump tubing with silicone material was determined to be able to handle the continuous fluid hydraulic pressure, which is over the minimum 250 mmHg inside the tubing.

Proper occluder size and tubing inner diameter are key factors for improving the occlusion/release time (ORT) because flow generation per revolution is different even with the same motor rpm of the peristaltic pump. The ORT decreases as the occluder's dimension increases, and the ORT increases as its dimension decreases. The occluder's dimension was selected for arteriessmaller than 2.5 mm in diameter in our laboratory rats. Therefore, for implementation of ORT as rapid as possible, the larger diameter pump tubing size may be preferable, but an oversized one can make it difficult to achieve fine adjustments of flow due to high flow generation per revolution. In this study, the 6.4 mm inner diameter pump tubing sizewas determined to obtain reasonably fine flow adjustments in the EH configuration with a continuously varying RPP feedbacksignal. The double head, connected to the inlets/outlets of each channel with a Y-connector, plays an important role in improving the system's performance because smooth occlusion of the vascular cuff is generated by continuous low pulsation flow in every roller's revolution.

Preparation of animals for in vivo performance evaluation An intensive set of experiments was performed on10 male Sprague-Dawley rats, weighing between 200 and 300 grams, in accordance with the guidelines and practices established by the care and use of research animals in State University of New York Hospital at Stony Brook. Rats were anesthetized with 1 mg/kg Inaction (Sigmal) and body temperature was maintained at around 20-25 oC by placing the animals on an operating table with a heating fan. The trachea was cannulated, and a stream of 100 % oxygen was guided through the tracheal tube throughout the experiment. A hydraulic vascular occluder cuff was applied around the surgically exposed blood vessel in the supra-renal aorta. Figure 2 shows our whole animal experiment setup including the EH pump. In some papers, a simple adjustable clamp was placed around the aorta proximal to the origin of the renal arteries and an in vivo performance evaluated (Volker Vallon, et al, 2001).

The occlusion, maintenance, and release responses were obtained by PI action while changing the RPP in a stepwise manner from approximately 120-140 mmHg of a baseline pressure level to the predetermined level of 80 mmHg. Theassessment was repeated several times to confirm the reproducibility of an in vivoperformance based on these three responses with overshoots. After 1- to 10- min maintenance, the RPP was recovered to the baseline level within 300 ms by quickly discharging the fluid volume that had filled into the occlusion cuff. From the data of the whole period including RPP occlusion, maintenance, and release responses, we studied to identify transient renal autoregulation mechanisms using advanced time-frequency spectral techniques (Hengliang Wang, et al, 2005). Proportional plus Integral (PI) Controller Design

The PI control was implemented to maintain the dynamic RPP at a predetermined pressure in the EH pump drive. The schematic diagram of the EH pump servo-control used in the experiments is shown in Figure 3. Flow is deliberately mediated by the PI control into the occluder's cuff throughthe actuating pump tubing for pressurization. To determine optimal PI parameters, the PI controller was analyzed in the continuous time domain. The corresponding transfer function is given as Equation (1), where E(s) and U(s) denote the input error signal, which means the tracking error between a reference RPP and a feedback RPP, and the controller's output providing the excitation of the animal model, respectively. A symbol 's' is the Laplace variable, andK_P and K_I are the two parameters of

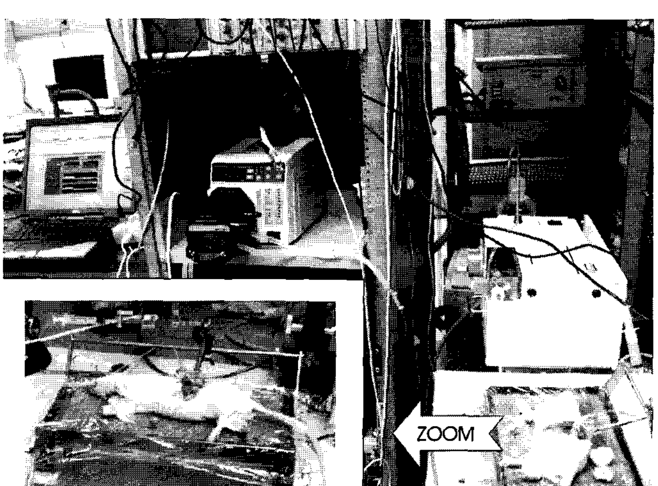

Fig. 2. The completeanimal experiment setup including a real EH pump.

the PI controllers associated with the proportional(P) and integral (I) part. Equation (1) was modified to equation (2) for a discrete transformation.

$$\frac{U(s)}{E(s)} = K_P + \frac{K_I}{s} \tag{1}$$

$$\begin{aligned} U(s) &= K_P \cdot \left(1 + \frac{K_I}{K_P} \cdot \frac{1}{s}\right) \cdot E(s) = \\ &K_P \cdot w_{PI} \cdot \left(\frac{s / w_{PI} + 1}{s}\right) \cdot E(s) \end{aligned} \tag{2}$$

where $w_{PI} = \frac{K_I}{K_P}$ (expressed in rad/s).

The integration of the Laplace transform, 1/s, is based on a discrete summation with the zero order hold approachand expressed in the z-domain like Equation (3).

$$\sum(z) = \frac{T_{sample}}{Z-1} E(z) \tag{3}$$

where T_{sample} is the sample time corresponding to controller frequency.

The transfer function in the discrete domain is obtained from equations (2) and (3) to generate a difference equation as the following:

$$\begin{aligned} U(z) &= K_p \cdot \left(1 + w_{PI} \cdot \frac{T_{sample}}{z-1}\right) \cdot E(z) = \\ &\frac{K_P z + K_P \cdot (w_{PI} \cdot T_{sample} - 1)}{z-1} E(z) \end{aligned} \tag{4}$$

Equation (4) was programmed after converting it to the following difference equation:

$$\begin{aligned} U_{k+1} &= K_P \cdot E_{k+1} + K_P \cdot (w_{PI} \cdot T_{sample} - 1) \cdot \\ &E_k + U_k \end{aligned} \tag{5}$$

$T_{sample}$was decided in advance due to fixed serial communication speed with 4800 bps provided by the peristaltic pump. The PI controller was tuned in the discrete domain. Tuning of the PI controller was elaborated using Ziegler-Nichols criteria to reduce oscillatory effects and generate an appropriate pump speed. The most well known tuning methods are those that are stated by Ziegler and Nichols. These methods do not need any mathematical calculation to find PI parameters. Its methodis based on

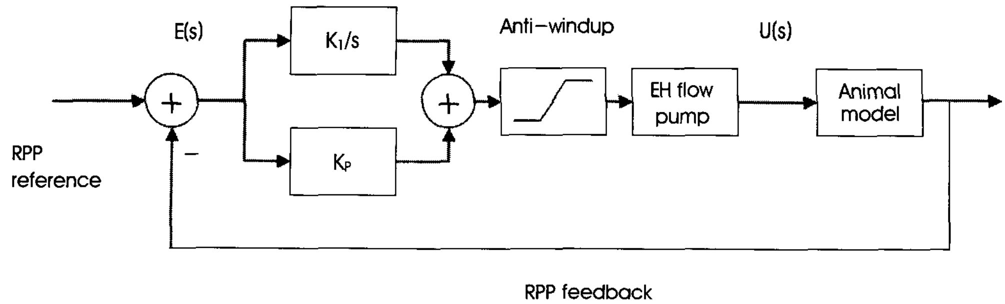

Fig. 3. Schematic diagram of the EH servo-control.

system gain, which is redounded until the system makes oscillation, and then PI parameters can be found from system response graphic. It is an experimental open-loop tuning method and is only applicable to open-loop stable systems. Taken together with an intensive set of animal experiments, we designed the PI controller with the following parameters: $K_P = 1000, K_I = 2, w_{PI} = 0.002$ rad/s, and $T_{sample} = 50ms$

It is well known that there are non-linear input-output characteristics in the EH pump system of a biological environment: non-linear gain, saturation, and dead-band (U. Pinsopon, et al, 1999). Hence, if the integrator output is not limited, the total of the integrated (summed) error (Equation (6)) will continue to build, leading to instability. To avoid this, an anti-windup algorithm with ± 200 motor rpm limits on the integral accumulation was added in the forward loop of the EH system (Figure 3). In practice, in order to speed up this occlusion time, derivative action (D gain) must be applied to thecontrol action proportional to the rate of change of the feedback error, but since it could cause possible instability due to noise susceptibility in the error signal, a designated PI controller was developed. Instead, the proportional gain was determined to require a higher value to improve the occlusion time.

The RPP feedback signal from experiment ratswas acquired using a DAISYLAB device (DT9800 series, Data Translation Inc., Marlboro, MA, USA) as a data acquisition board on a PC running windows 2000/XP. The sampling time of the feedback RPP signal is 5 ms, which has a faster sampling rate in animals than the dynamic RPP. The sampled data are used in the PI computation algorithm to produce a motor rpm controlling an optimal pump speed at every T_{sample}. During the PI action, if the RPP falls below a predetermined level, the PI algorithm quickly deflates the cuff by discharging fluid to increase the RPP. The occluder's cuff begins to be inflated by injecting fluid into it at the moment when theRPP rises above a predetermined pressure. After finishing the PI action, the accumulated fluid in that cuff is quickly released to return to a baseline pressure.

$$\approx \sum K_I e(t) dt \qquad (6)$$

III. RESULTS

The PI controller combined with a dynamic feedback RPP signal wasimplemented and tested on an in vivo performance evaluation in terms of initially occlusive oscillation, maintenance, and release responses of the RPP as indicated in Figure 4(c). Figure 4 shows the data recording segments of thein vivo performance for approximately 4 hours under various animal conditions. The in vivo performance was greatly affected by the PI control parameters and serial communication speed in the initial state of the RPP control. In particular, maintenance response was most affected by the ADC sampling rate. It showed an unacceptable steady-state error of over 10 % when the ADC sample rate was set to 30 ms as in Figure 4(a). It was significantly improved by applying ADC sample rates of 20 ms and 10 ms to the PI control algorithm in Figures 4(b) and 4(c), respectively, but the occlusive oscillation at the beginning of the PI action was not significantly improved. The occlusion response ranged from 5 sec to 10 sec following the PI action startup. Fast release time of the occluded blood vessel following the PI termination was achieved in approximately 300 ms. A serial data transmission requires a minimum of 50 ms for completion. During this transmission, no rpm output signal is generated even if a real change in RPPin animals occurs. Since it is very difficult to obtain accurate PI compensation due to this limitation, rpm during serial communication was fixed with the previous value. As a result, sometimes slightly occlusive and maintenance oscillation reflected the results of the PI action due to the delay in serial data transmission in Figure 4(d). However, the delay in the feedback circuit connected to the ADC channel didn't affect the performance.The pump speed was varied between 10 and 30 percent of the maximum speed of 600 rpm.

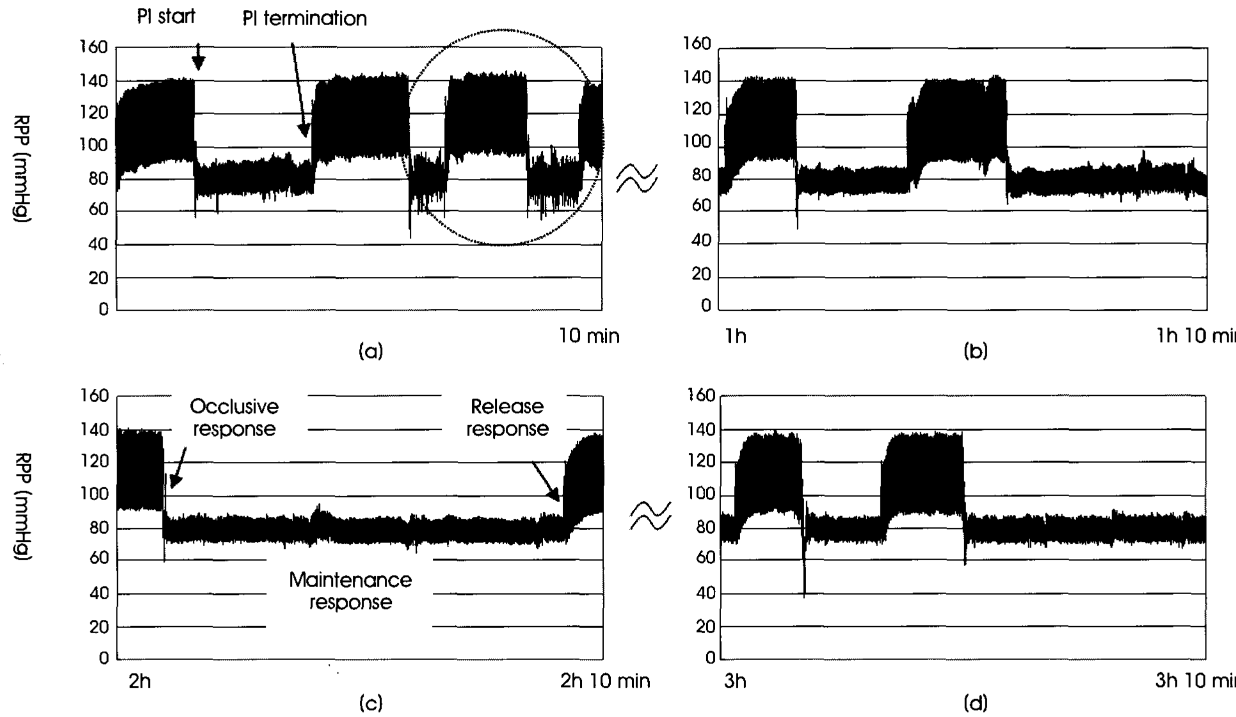

Fig. 4. Recorded segments of the in vivo performance evaluation conducted via animal experiments using the proposed EH pump-driven closed-loop RPP regulatory system results of the ADC sample rate with 30 ms (a) and 20 ms (b), responses improved by the ADC sample rate of 10 ms(c), and slight oscillation due to the delay in serial data transmission(d).

An extensive set of experiments was conducted on the laboratory set-up for approximately 4hours to test the reliability of the real-time EH pump control system. Most results were obtained with a steady-state error of approximately 3 % during the whole period, but only a few experimental results showed oscillations with more than 3 % error for short specific periods as shown in Figures 4(c) and (d).

IV. CONCLUSIONS

Renal perfusion pressure was servo-controlled by using a vascular occluder cuff connected to the proposed EH pump drive. The optimized EH configuration for blood pressure regulation by means of occlusion cuff techniques could provide stable operation under a PI control condition. Using the LabVIEW program, we could design a user-friendly interface displaying the interest parameters, graphics, and waveforms in real time. In addition, the RPP data and the motor rpm were displayed on the front panel in real time and could be saved for off-line post-processing.

Control was based on the PI controller that was elaborated using Ziegler-Nichols criteria. The PI compensation was designed with sufficient stability margin and has been verified with animal experiments. The tuned PI controller showed slightovershoots, but most of the closed-loop responses including occlusion, maintenance,and release were acceptable for the duration of the whole experiment,when approximately 120 mmHg in a baseline in RPP was decreased stepwise toan 80 mmHg by the PI action. All responses were very rapid with an occlusion response of 5 to 10 sec and with release response of below 300 ms. In particular, in all animals in which RPP was servo-controlled by the PI controller, similar performances were observed in all three responses. Therefore, the newly-developed EH pump-driven closed-loop blood pressure regulatory system demonstrated both good in vivo performance and simple implementation.

However, the rapid changes in pump speed calculated in the PI compensation algorithm couldn't generate real changes in flow due to the limitation of the serial communication speed. In such circumstances, only a few tests showed that part of the whole experimental durations to have more oscillatory effects in the beginning of the PI action and during maintenance.It demonstrates that renal hemodynamics regarding changes in RPP is probably involved in complex physiological control systems (Persson P.B, et al, 1993).

In conclusion, the results indicate that PI controlin conjunction with the EH pump during renal autoregulation studies or any blood pressure-dependent studies could be, in practice, applied even in non-linear experimental models. In the future, we would conduct a lot of animal experiments to see if our proposed system is applicable under a wide range of animal conditions.

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