

# VASCULAR RESISTANCE ESTIMATION IN RENAL HEMODYNAMICS USING A TIME-VARYING WINDKESSEL MODEL

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## ABSTRACT

In studies of the dynamics of renal vascular response to blood pressure variations, measurements of pressure and flow rate are typically utilized to characterize a dynamic response with pressure as input and flow as output. However, the primary regulatory effect is the adjustment of vascular resistance, so that a record of a resistance time series would better serve as the regulated output. Toward this goal, a technique is developed for estimating the parameters of a three-element, time-varying Windkessel model of the renal vasculature that enables resistance estimation. The method is described, analyzed, and applied to renal pressure/flow data from rats.

## 1. INTRODUCTION

Variations in renal blood pressure elicit a dynamic response in the renal vasculature in order to regulate kidney function, to prevent transmission of blood pressure to the microvasculature, or both. Characterizing this autoregulatory response is important in studies of the progression of kidney disease [1]. Experiments to study the autoregulatory response in rats have been conducted using measurements of blood pressure (BP) and renal blood flow (RBF), with the dynamic relationship between pressure as the input and blood flow rate as the output used for such characterization [2, 3]. However, the primary dynamic response is in renal vascular resistance (RVR) changes, rather than in flow rate changes, so that study of the pressure/resistance dynamics would be more revealing of the characteristics of the autoregulation.

Several researchers have used simple techniques to estimate the RVR from measured BP and RBF [4, 5, 6]. The

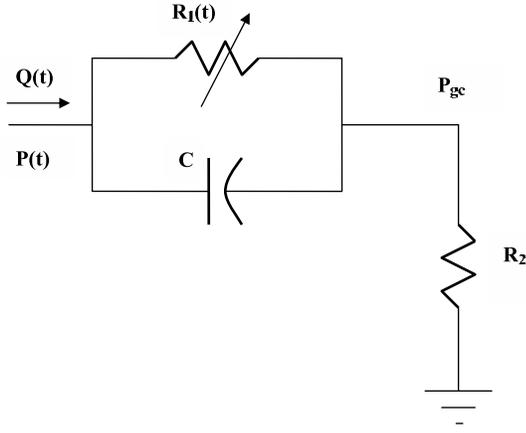
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general concept behind these estimators is to use the ratio of smoothed BP and RBF recordings as the resistance estimate. We propose in this paper to improve the quality of resistance estimates by accounting for the effects of vascular compliance. To achieve this goal we identify the parameters of a three-element, time-varying Windkessel model for the renal vasculature, depicted in Fig. 1, using measurements of the pressure and flow rate. We utilize the model in the analysis of measured pressure and flow signals from conscious rats, as described in [2], and show that the model that is obtained provides a more accurate estimate of flow than does the simple estimate of resistance via ratios of smoothed pressures and flows.

## 2. TIME-VARYING WINDKESSEL MODEL

The three-element time-varying Windkessel model shown in Fig. 1 reflects different physiological quantities inside the kidney. Roughly speaking,  $R_1(t)$  reflects an aggregate “preglomerular resistance,”  $R_2$  in the model reflects the resistance of an aggregate “postglomerular resistance,” and  $C$  simulates the vascular compliance. The vascular resistance is measured in units of millimeters mercury per milliliters per second ( $\text{mmHg} \cdot \text{s} \cdot \text{mL}^{-1}$ ), and the vascular compliance is measured in units of milliliters per millimeters mercury ( $\text{mL} \cdot \text{mmHg}^{-1}$ ).  $P(t)$  is the blood pressure at the renal artery and has the units of millimeters mercury (mmHg).  $Q(t)$  is the blood flow in the renal artery and has the units of milliliters per second ( $\text{mL} \cdot \text{s}^{-1}$ ). Autoregulation is known to be effected primarily through changes in afferent arteriolar diameter. The afferent arterioles form part of the preglomerular resistance; hence,  $R_1(t)$  is considered to vary in time.  $R_2$  remains constant in the model, as the postglomerular resistance does not vary with autoregulation. Fluctuations in  $R_2$  from other causes are assumed to be minimal in the time frames that are studied in this paper.



**Fig. 1.** Three-element time-varying Windkessel model of the kidney.

### 3. PARAMETERS ESTIMATION OF THE MODEL

The identification of the model's parameters is approached using a least squares technique based on an iterative minimization of the one-step-ahead flow prediction error. The model of Fig. 1 can be described by the state-space description

$$\begin{aligned} \frac{dP_c(t)}{dt} &= -a(t)P_c(t) + bP(t) \\ Q(t) &= -\frac{1}{R_2}P_c(t) + \frac{1}{R_2}P(t) \end{aligned}$$

where

$$a(t) = \frac{1}{C} \left( \frac{1}{R_1(t)} + \frac{1}{R_2} \right); \quad b = \frac{1}{R_2 C}.$$

These equations are discretized and the exponential terms that arise from the discretization process are then approximated by their first order polynomial expansion as described in [7]. The accuracy of this approximation depends on the exponent value  $a[k]T$ , where  $T$  is the sample time. As the exponent gets smaller, the first order polynomial approximation will be more accurate. The result is the equation

$$Q[k+1] = (1 - a[k]T)Q[k] + \frac{P[k+1]}{R_2} - \frac{1 - a[k]T + bT}{R_2}P[k] \quad (1)$$

that enables a one-step-ahead prediction of the flow via

$$\hat{Q}[k+1] = (1 - \hat{a}[k]T)Q[k] + \frac{P[k+1]}{\hat{R}_2} - \frac{1 - \hat{a}[k]T + \hat{b}T}{\hat{R}_2}P[k]. \quad (2)$$

Note that the coefficients of the prediction equation depend in a nonlinear way on the physical parameters  $C$ ,  $R_2$  and

$R_1[k]$ . To estimate these parameters, we minimize

$$J = \sum_{k=0}^{N-1} |e[k+1]|^2 = \sum_{k=0}^{N-1} |Q[k+1] - \hat{Q}[k+1]|^2. \quad (3)$$

First, an initial value for the total resistance is estimated as the ratio of smoothed BP and RBF recordings as described in [4, 5, 6]. This represents  $R_1[k] + R_2$ . Then an initial value for  $R_2$  is subtracted from the total resistance (usually 40% of the average total resistance). The result of the subtraction will be used as an initial value for  $R_1[k]$ . With these initial values,  $C$  is chosen to minimize  $J$  in (3). Then with the estimated  $C$  and the initial value of  $R_1[k]$ ,  $R_2$  is updated such that  $J$  in (3) is minimized. Now with  $C$  and  $R_2$  at these estimated values,  $R_1[k]$  is estimated as described in section 3.3. The function  $R_1[k]$  is then smoothed to reflect the bandlimited nature of the underlying resistance changes using knowledge of the maximal rate of vascular diameter change. This process is iterated until convergence of the  $R_1[k]$ ,  $R_2$ , and  $C$  estimates is observed. Though convergence is not guaranteed, the algorithm was observed to converge if proper initial conditions for the parameters are used.

#### 3.1. Estimating $C$

To determine  $\hat{C}$  for a given  $R_1[k]$  and  $R_2$ , we minimize  $J$  in (3). Defining

$$\begin{aligned} \alpha_1[k] &= Q[k+1] - Q[k] - \frac{P[k+1]}{R_2} + \frac{P[k]}{R_2}, \\ \beta_1[k] &= \frac{T}{R_1[k]R_2}P[k] - T \left( \frac{1}{R_1[k]} + \frac{1}{R_2} \right)Q[k], \end{aligned}$$

$\hat{C}$  can be expressed explicitly as

$$\hat{C} = \frac{\sum_{k=0}^{N-2} \beta_1^2[k]}{\sum_{k=0}^{N-2} \alpha_1[k]\beta_1[k]}. \quad (4)$$

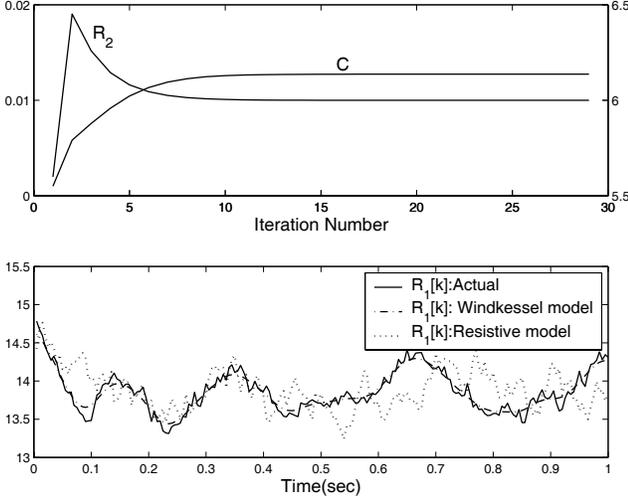
#### 3.2. Estimating $R_2$

$J$  in (3) is minimized by choice of  $\hat{R}_2$  for a given  $R_1[k]$  and  $C$ . With

$$\begin{aligned} \alpha_2[k] &= Q[k+1] + \left( \frac{T}{CR_1[k]} - 1 \right)Q[k], \\ \beta_2[k] &= P[k+1] + \left( \frac{T}{CR_1[k]} - 1 \right)P[k] - \frac{T}{C}Q[k], \end{aligned}$$

the minimizing  $\hat{R}_2$  can be expressed explicitly as

$$\hat{R}_2 = \frac{\sum_{k=0}^{N-2} \beta_2^2[k]}{\sum_{k=0}^{N-2} \alpha_2[k]\beta_2[k]}. \quad (5)$$



**Fig. 2.** Iterations of  $C$  and  $R_2$  (top plot) and sample of  $R_1[k]$  for both Windkessel and Resistive models.

### 3.3. Estimating $R_1[k]$

In the third step we determine  $\hat{R}_1[k]$  for a given  $R_2$  and  $C$ . We minimize  $|e[k+1]|^2 = |Q[k+1] - \hat{Q}[k+1]|^2$  for each  $k$ . Defining

$$\alpha_3[k] = Q[k+1] + \left(\frac{T}{CR_2} - 1\right)Q[k] - \frac{P[k+1]}{R_2} + \frac{P[k]}{R_2},$$

$$\beta_3[k] = \frac{T}{CR_2}P[k] - \frac{T}{C}Q[k],$$

the minimizing value of  $\hat{R}_1[k]$  can be expressed explicitly as

$$\hat{R}_1[k] = \frac{\beta_3[k]}{\alpha_3[k]}, \quad k = 0, 1, \dots, N-2. \quad (6)$$

Finally, the sequence  $\hat{R}_1[k]$  is smoothed using a simple moving average smoother. To reduce the effect of noise, the estimator for  $\hat{R}_1[k]$  (6) is slightly modified. We will consider the estimated resistance at each time point as being the actual resistance for some period of time that extends before and after that point. Then for the same  $\alpha_3[k]$  and  $\beta_3[k]$ , the estimated  $R_1[k]$  will be

$$\hat{R}_1[n] = \frac{\sum_{k=n-w}^{n+w} \beta_3^2[k]}{\sum_{k=n-w}^{n+w} \alpha_3[k] \beta_3[k]}, \quad (7)$$

for  $n = w, w+1, \dots, N-w$ .  $2w+1$  is the window length. Simulation results showed that using the modified estimator for  $R_1[k]$  (7) tends to improve the performance of the estimator in the noisy environment and tends to enhance the convergence.

**Table 1.** NMSE of the estimated resistance and flow.

		Windkessel model (dB)	Resistive model (dB)
SNR 80dB	NMSE-R	-42.25	-32.37
	NMSE-Q	-61.19	-17.54
SNR 30dB	NMSE-R	-34.63	-31.96
	NMSE-Q	-27.67	-17.35
SNR 10dB	NMSE-R	-22.68	-21.93
	NMSE-Q	-10.35	-9.91

## 4. RESULTS

The performance of the time-varying Windkessel model and the algorithm proposed to calculate the circuit parameters are evaluated using both simulation results and renal pressure/flow data from rats.

### 4.1. Simulation Results

The performance of the proposed model was tested using fictional pressure and flow data that were generated by the model. Pressure was generated by low pass filtering a white Gaussian random sequence of mean 100mmHg using a simple moving average filter. We set  $C = 0.012$ ,  $R_2 = 6$ , let  $R_1[k]$  be a low pass filtered sequence of a uniform random process in the range [6, 10], and generate  $Q[k]$  via (1). These values are similar to those observed in actual renal data. To test the performance of the proposed algorithm in the noisy environment, a zero mean white Gaussian noise was added to the flow at three different signal to noise ratios (SNR). Table 1 shows the average normalized mean square error (NMSE) of the estimated resistance and flow over an ensemble of 50 trials. Our proposed model out performs the resistive model both for resistance as well as flow. Figure 2 shows iterations of estimated  $C$  and  $R_2$  for one case and a representative one second segment of the final  $R_1[k]$ .

### 4.2. Renal Application

The circuit parameters of the proposed model are estimated for five data sets of BP/RBF recordings of 30 minutes in duration collected from normal Sprague Dawley rats as described in [2]. The data is initially sampled at 200 Hz, then resampled to 20 Hz before being used to estimate the parameters of the model. The estimated parameters are shown in Table 2. The last column is the mean value of the estimated time-varying  $R_1[k]$  sequence. On average, the mean value of the preglomerular resistance is about 51% of the total mean resistance. A plot of the estimated preglomerular resistance for the first data set is shown in Fig. 3.

**Table 2.** Estimated parameters for five renal data sets from normal Sprague Dawley rats.

Data Set	$\hat{C}$	$\hat{R}_2$	average $\hat{R}_1 [k]$
1	0.0096	8.63	9.20
2	0.0128	6.54	5.12
3	0.0127	7.76	11.93
4	0.0154	6.72	6.58
5	0.0096	7.75	11.52

**Table 3.** NMSE of the predicted flow for the time-varying Windkessel model and the resistive model.

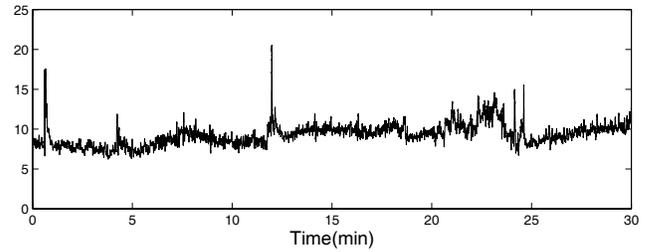
Data Set	NMSE: Windkessel model	NMSE: resistive model
1	-28.53 dB	-13.92 dB
2	-22.71 dB	-14.48 dB
3	-21.24 dB	-10.55 dB
4	-18.39 dB	-14.44 dB
5	-26.70 dB	-11.82 dB

The prediction error of the time-varying Windkessel model is compared with the prediction error of the time-varying resistive model. Both pressure and flow were smoothed using a zero phase moving average filter with a sliding window of one second length, similar to the method applied in [4, 5, 6]. The Normalized Mean Square Error (NMSE) of the estimated flow for both models is presented in Table 3. The flow prediction error of the time-varying Windkessel model is 4 – 15 dB less than that for the time-varying resistive model. This indicates that the presence of the compliance has a significant value in fitting the data.

## 5. CONCLUSION

In this study, we have addressed resistance estimation in renal hemodynamics. A 3-element time varying Windkessel model was proposed with parameters reflecting in some sense some actual physiological parameters in the kidney. The time varying resistance in the proposed model is estimated from pressure/flow data while taking into account the presence of the compliance. Including the compliance improves the resistance estimation in comparison to currently employed methods based on a pure time-varying resistance.

Results showed that the flow prediction error of the proposed three-element time-varying Windkessel model is 4 – 15 dB less than that for the time-varying resistive model. This improvement was due to a better fitting of the flow at



**Fig. 3.** Estimated preglomerular resistance for first data set.

the heart beat frequency. This suggests that the compliance of the vessels' walls should not be underestimated, and it should be accounted for in any model that tries to understand the pressure/flow dynamics at frequencies that include the heart beats.

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