

# Pulse wave parameters based on wave derivatives gained via impedance separation

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## Abstract

Quantification of pulse waves in the human cardiovascular system traditionally focused on pressure measurements, but flow curves might contain additional information. In a transmission model of the arterial system, the aortic pressure and flow can be described as the sum of forward and backward travelling waves. For the separation of the measured pressure and flow, both signals are needed, and it can be performed in the frequency (impedance separation) or time domain. The aim of this study is to show that parameters assigned to wave intensity analysis which are based on the first derivative of the signals and therefore usually gained in a time domain separation, can also be achieved via impedance separation.

In a study population of 148 patients, pressure and flow curves were measured non-invasively using tonometric and ultrasound techniques. Wave intensity is the product of the changes in pressure and flow and can be calculated for forward and backward travelling waves. To quantify wave intensity, areas under the intensity curves assigned to compression waves can be calculated.

The areas under the forward and backward compression waves are derived in two ways: The classical wave intensity method performs wave separation in the time domain. The impedance separation method operates in the frequency domain, the resulting waves are differentiated afterwards to gain the wave intensity. Correlations between the two methods for the area under the forward travelling compression wave of  $R=0.99$  and for the area under the backward travelling compression wave of  $R=0.96$  are obtained.

This comparison of the two methods shows that the impedance method as well as the wave intensity method can be used for wave separation with comparable results, even for parameters based on the differentiation of the signals, which are up to now solely gained via time domain separation.

# 1 Introduction

Quantification of pulse waves in the human cardiovascular system traditionally focused on pressure measurements. Until the end of the last century, the main interest has been on diastolic and systolic blood pressure, and these values still play a major role in prognostics today. Within the last decade emphasis has been laid on the determination of arterial stiffness and its clinical surrogates using dynamical systems, and the concepts of pulse wave analysis (PWA) and pulse wave velocity (PWV) have come into play, which is also visible in the ESH–ESC (European Society of Hypertension – European Society of Cardiology) guidelines for the management of arterial hypertension [5].

In PWA the augmentation of the aortal blood pressure due to reflections in the arterial system is expressed by the augmentation index (AIx) or the augmentation pressure (AP), which are utilized in the time domain by analyzing aortal pressure signals. One of the drawbacks of these parameters is their dependence on the timing of the reflected pressure waves. Further useful information to overcome these problems might be found in the corresponding flow signals. In a transmission model of the arterial system, the aortic pressure and flow can be described as the sum of forward and backward travelling waves. For the separation of the measured pressure and flow, both signals are needed, and it can be performed in the frequency (impedance separation) or time domain. The separation in the frequency domain is also called wave separation analysis (WSA) and has been introduced by Nico Westerhof and co-workers already in 1972 [22]. The time domain approach for wave separation has been introduced by Kim Parker and co-workers in 1990 and is known as wave intensity analysis (WIA) [11].

Wave intensity analysis is not just providing a model for wave separation, but – as the name is indicating – furthermore introduces wave intensity as another parameter. Net wave intensity is the product of the changes in pressure and flow, which is the flux of energy per unit area carried by the wavefronts of the forward and backward travelling waves [10]. To quantify wave intensity, areas under the intensity curves assigned to compression waves can be calculated. The ratio of the areas under the compression waves of the backward and forward going waves is called wave reflection index (WRI). Recently it has been shown in a substudy of ASCOT (Anglo-Scandinavian Cardiac Outcome Trial) that this wave reflection index predicts cardiovascular events in hypertensive individuals independent of blood pressure and other risk factors [6]. Additionally it has been reported that there was a significant difference in WRI in groups of hypertensive patients treated with unequal medications [7, 8].

The frequency and time domain methods for wave separation have been compared in previous studies and a good agreement was shown [2, 3, 17]. But up to now wave intensity was only calculated within the time domain framework, where it is originated. The aim of this study is to show that parameters assigned to wave intensity analysis which are based on the first derivative of the signals can also be achieved via impedance separation.

## 2 Methods

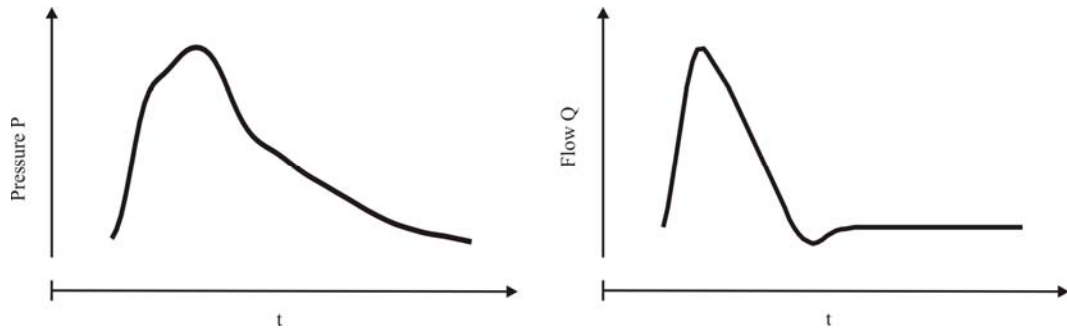
### 2.1 Data assessment

The measurements were carried out at the department of cardiology in the Paracelsus Medical University teaching hospital of Wels-Grieskirchen in Wels, Austria. They were authorized by the local ethics committee and patients gave informed consent. Overall 148 patients were included in the study, 120 experimentees were male, 28 female. The mean age was 60 years with a standard deviation of 12 years. The mean peripheral systolic blood pressure was 131 mmHg with a standard deviation of 17 mmHg, the mean peripheral diastolic blood pressure was 81 mmHg with a standard deviation of 9 mmHg. More information on the basic clinical data can be found in Tab. 1.

Patients	148
Men/Women	120/28
Age (years)	60 (12)
Weight (kg)	85 (15)
Height (cm)	173 (9)
Heart rate (1/min)	64 (10)
SBP peripheral (mmHg)	131 (17)
DBP peripheral (mmHg)	81 (9)
SBP central (mmHg)	121 (16)
DBP central (mmHg)	82 (10)

**Tab. 1:** Basic clinical data, given as: mean value (standard deviation)

Pressure and velocity signals were gained using two devices in parallel. Velocity waveforms were measured by Doppler Echocardiography over several heartbeats. Thereafter the waveform for one heartbeat was manually digitalized, trying to follow the sonogram as close as possible. Aortic pressure waves were taken from a SphygmoCor device (AtCor Medical Pty. Ltd., West Ryde, Australia), which synthesizes an aortic pressure wave from a peripheral measured pressure signal. An exemplary central pressure curve and the corresponding flow curve can be seen in Fig. 1.



**Fig. 1:** left: aortic pressure curve; right: aortic flow curve

## 2.2 Impedance wave separation analysis (WSA)

The ratio of pressure (P) and flow (Q) in the frequency domain is called impedance (Z).

$$\frac{P}{Q} = Z \quad (1)$$

Depending on the specific situation, different impedances can be defined [9]. If no reflections are present, the characteristic impedance ( $Z_c$ ) can be obtained. However the absence of reflections is not true for physiological conditions in the arterial tree. Therefore it is only possible to calculate the so-called input impedance ( $Z_i$ ).

Following the wave theory, the measurable pressure ( $P_m$ ) in the aorta is the sum of forward ( $P_f$ ) and backward ( $P_b$ ) going waves [22].

$$P_m = P_f + P_b \quad (2)$$

The same is valid for the corresponding flow waves:

$$Q_m = Q_f + Q_b \quad (3)$$

Subsequently the relationship between pressure and flow can be described as

$$P_f = Z_c \cdot Q_f \quad (4)$$

$$P_b = -Z_c \cdot Q_b \quad (5)$$

So far it is only possible to measure the sum of the forward and backward going waves. To obtain the forward and backward going parts separately in explicit formulas, Eq. (2) – (5) have to be transformed:

$$P_f = \frac{P_m + Z_c \cdot Q_m}{2}, \quad P_b = \frac{P_m - Z_c \cdot Q_m}{2} \quad (6)$$

$$Q_f = \frac{Q_m + \frac{P_m}{Z_c}}{2}, \quad Q_b = \frac{Q_m - \frac{P_m}{Z_c}}{2} \quad (7)$$

To perform the separation, obviously three variables are needed: The pressure and flow in the aorta and furthermore the characteristic impedance which represents the impact of the arterial wall.  $Z_c$  is estimated in the frequency domain using the input impedance, which is the ratio of the present pressure and flow. The frequencies in the range of 4 to 10 Hz are taken into account, which is a commonly used span [12, 4, 16, 21, 14]. For higher frequencies there could be inaccuracy due to noise [9]. To minimize the influence of outliers, all input impedances which are greater than a factor of 3 of the median of the considered impedances are not taken into account [3, 15].

### 2.3 Wave intensity analysis separation (WIA)

The second technique for wave separation is strongly related to the idea of wave intensity [10], even though it is not necessary to calculate the wave intensity for pulse wave decomposition.

WIA has its origin in the development of gas dynamics in the middle of the last century, when new phenomena, particularly shock waves, were detected and had to be explained.

The waves are represented as successive wavefronts which describe the change in properties during a sampling period  $\Delta t$ , exemplarily the corresponding formula for pressure can be seen in Eq. (8). All computations take place in the time domain. These are the main conceptual differences to impedance analysis, where the waves are represented as a sum of sinusoidal waves and the analysis is realized in the frequency domain.

$$dP = P(t + \Delta t) - P(t) \quad (8)$$

Starting point are the Euler equations in one dimension [1]. They involve three state variables, the cross-sectional area of the artery ( $A$ ), the velocity averaged over the cross-section ( $U$ ), and the pressure averaged over the cross-section ( $P$ ). After specifying the relationship between  $A$  and  $P$  with a tube law equation, the mass and momentum conservation equations can be written in the following form:

$$P_t + UP_x + \frac{A}{A_P} U_x = -\frac{UA_x}{A_P} \quad (9)$$

$$U_t + \frac{1}{\rho} P_x + UU_x = 0 \quad (10)$$

In Eq. (9) and (10) the subscript notation is used for partial derivatives, and  $\rho$  stands for the blood density.

The dynamical system can be solved using the method of characteristics introduced by Riemann [13], which leads to the water hammer equations (cf. Eq. (13)). If it is assumed just as in WSA that the forward and backward waves are additive when they

intersect, the formula for the changes in forward and backward pressure waves finally can be written as:

$$dP_f = \frac{dP_m + \rho \cdot c \cdot dU_m}{2}, \quad dP_b = \frac{dP_m - \rho \cdot c \cdot dU_m}{2} \quad (11)$$

$$dU_f = \frac{dU_m + \frac{dP_m}{\rho \cdot c}}{2}, \quad dU_b = \frac{dU_m - \frac{dP_m}{\rho \cdot c}}{2} \quad (12)$$

Following the notation introduced above,  $dP_m$  are differences in the measured pressure over a certain small time interval and  $dU_m$  are differences in velocity. The wave speed is denoted by the parameter  $c$ .

The wave speed can be determined using the PU-loop method. It is assumed that during the first period of the systole there are only forward going waves present in the artery. Therefore  $P_m = P_f$  and the water hammer equation can be written as:

$$dP_m = \rho \cdot c \cdot dU_m \quad (13)$$

The ratio of  $dP_m$  and  $dU_m$  should be almost the same for the first time steps due to the lack of backward going waves and therefore a value for  $c$  can be calculated.

### 2.3 Wave intensity

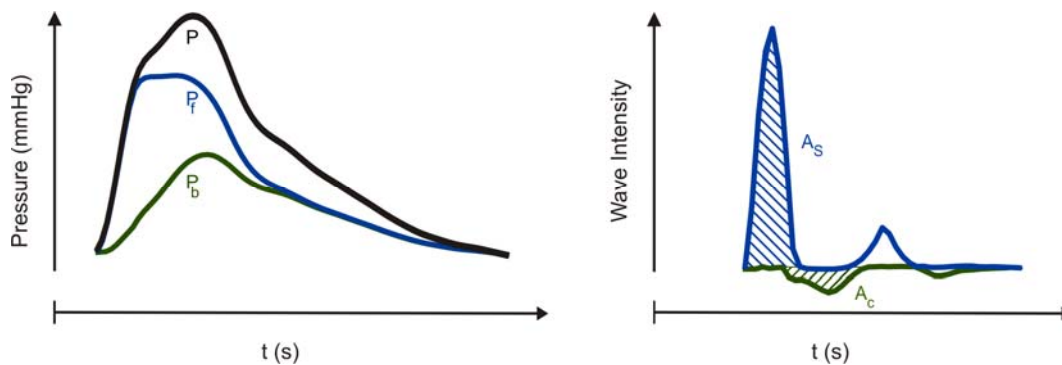
Wave intensity ( $dI$ ) was introduced by Parker and co-workers together with the separation in the time domain [11]. It is defined as the product of  $dP$  and  $dU$ . Analogous it can be calculated for changes in pressure and flow for the forward and backward travelling waves [10]:

$$dI_f = dP_f \cdot dU_f \quad (14)$$

$$dI_b = dP_b \cdot dU_b \quad (15)$$

The most prominent wave that can be seen in the forward wave intensity is a forward travelling compression wave (S). In the backward wave intensity mainly a backward travelling compression wave (c) can be detected. To quantify such a compression wave the area under the curve during the duration of the wave is calculated. These areas are denoted as  $A_S$  and  $A_c$ , see Fig. 2 for illustration.

After calculations in the frequency domain, the results of WSA are pressure and flow curves separated in forward and backward travelling directions. Before wave intensity can be obtained, the differences in each time step for these four curves (Eq. (6) and Eq. (7)) have to be computed as in Eq. (8). Then the formulas of Eq. (14) and Eq. (15) are applied again to get wave intensity, and the same algorithm as for WIA is used to measure the area under the intensity curves.



**Fig 2:** left: Wave separation of pressure curve ( $P$ ) into forward ( $P_f$ ) and backward ( $P_b$ ) travelling waves; right: Wave intensity and areas under the forward ( $A_S$ ) and backward ( $A_c$ ) travelling compression waves.

### 3 Results

Since the areas under the forward and backward wave intensity curves are the major parameters gained from wave intensity analysis in previous studies [6, 7, 8], this comparison of the two methods concentrated on these parameters as well. For the area under the forward compression wave ( $A_S$ ) a correlation of 0.99 could be obtained between the wave intensity from classical WIA method and the wave intensity calculated after impedance separation. For the area under the backward compression wave ( $A_c$ ) a correlation of 0.96 is reached. The mean difference for  $A_S$  is 0.07 mmHg cm with a standard deviation of 0.15 mmHg cm. For  $A_c$  the mean difference is 0.08 mmHg cm with a standard deviation of 0.19 mmHg cm.

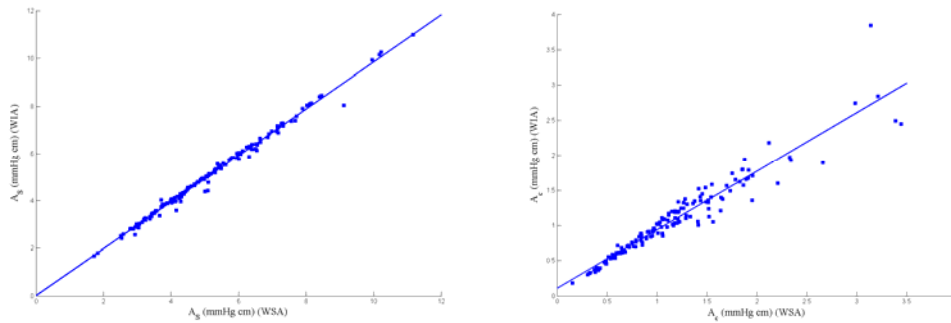
### 4 Discussion

The analysis of the areas under the compression waves shows only slight differences. For both parameters the mean area over all measurements is higher for the values gained via impedance wave separation. Thus, when  $A_c$  and  $A_S$  are compared in a relative manner, as it is done for the wave reflection index, the mean difference between the two methods will not be that relevant.

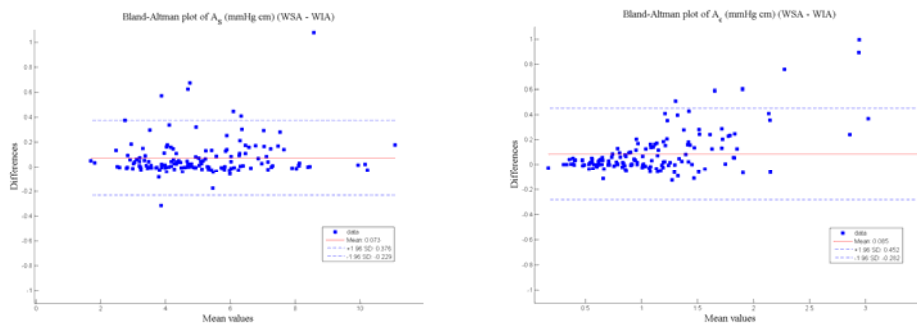
A very good correlation between the two methods is obtained for both parameters. It can be seen in the scatter plot in Fig. 3 that the deviation for  $A_c$  is slightly more for higher values of this parameter. This trend cannot be seen for  $A_S$ .

This different behaviour of the two parameters can also be detected in a Bland-Altman analysis, which is done in Fig. 4. For  $A_S$  no specific trends in the plot can be found, whereas a widening of the cluster of points for higher values is visible in the graph for  $A_c$ .

Furthermore it can be seen that for most measurements with a large area the impedance method gives higher values for  $A_c$ .



**Fig 3:** Scatter plots for the area under the wave intensity curve of the forward ( $A_S$ , left) and backward ( $A_c$ , right) compression waves



**Fig 4:** Bland Altman plots for the area under the wave intensity curve of the forward ( $A_S$ , left) and backward ( $A_c$ , right) compression waves

#### 4.1 Limitations

The digitalization of the measured velocity profiles is carried out manually, therefore a certain amount of subjectivity in this process cannot be excluded. Since acquisition and processing of flow curves is rather cumbersome, in the last years concepts to generate artificial flow curves for wave separation were introduced [21, 4, 19], and have been applied in studies to characterize cardiovascular risk [18, 20]. These different kinds of modelled flows were not tested in this study, and the comparability of wave intensity between WSA and WIA might depend on the specific choice of the method for flow generation.



Both methods, WSA and WIA, are applied in one specified way. But both can be altered without changing the procedure per se, which might lead to other results. For WSA it is mainly the range of the frequencies taken into account for the estimation of the characteristic impedance that could be modified. For WIA there exist other ways to estimate the pulse wave velocity, particularly a so-called sum of squares method.

## 4.2 Conclusion

This comparison of two methods for pulse wave separation shows that the impedance method and the wave intensity method provide parameters for the quantification of wave intensity with comparable results. This implies that both approaches can be used for wave separation and the determination of parameters based on such a separation into forward and backward travelling arterial waves.

## 5 References

- [1] L. Euler. Principia pro motu sanguinis per arterias determinando. *Opera Posthuma*, 2:814–823, 1844.
- [2] B. Hametner, J. Kropf, C. Mayer, T. Weber, B Eber, and S. Wassertheurer. Pulse wave separation: a comparison of methods. In *Proceedings of the 7th EUROSIM Congress on Modelling and Simulation*, pages 932–938, 2010.
- [3] A.D. Hughes and K.H. Parker. Forward and backward waves in the arterial system: impedance or wave intensity analysis? *Medical and Biological Engineering and Computing*, 47(2):207–210, 2009.
- [4] J.G. Kips, E.R. Rietzschel, M.L. De Buyzere, B.E. Westerhof, T.C. Gillebert, L.M. Van Bortel, and P. Segers. Evaluation of Noninvasive Methods to Assess Wave Reflection and Pulse Transit Time From the Pressure Waveform Alone. *Hypertension*, 53(2):142–149, 2009.
- [5] G. Mancia, G. De Backer, A. Dominiczak, R. Cifkova, R. Fagard, G. Germano, G. Grassi, A.M. Heagerty, S.E. Kjeldsen, S. Laurent, et al. 2007 Guidelines for the management of arterial hypertension - The task force for the management of arterial hypertension of the European society of hypertension (ESH) and of the European society of cardiology (ESC). *European Heart Journal*, 28:1462–1536, 2007.
- [6] C. Manisty, J. Mayet, R.J. Tapp, K.H. Parker, P. Sever, N.H. Poulter, S.A.M.G. Thom, and A.D. Hughes. Wave Reflection Predicts Cardiovascular Events in Hypertensive Individuals Independent of Blood Pressure and Other Cardiovascular Risk Factors: An ASCOT (Anglo-Scandinavian Cardiac Outcome Trial) Substudy. *Journal of the American College of Cardiology*, 56(1):24–30, 2010.
- [7] C. Manisty, J. Mayet, R.J. Tapp, P.S. Sever, N. Poulter, et al. Atorvastatin Treatment Is Associated With Less Augmentation of the Carotid Pressure Waveform in Hypertension: A Substudy of the Anglo-Scandinavian Cardiac Outcome Trial (ASCOT). *Hypertension*, 54(5):1009–1013, 2009.
- [8] C. Manisty, A. Zambanini, K.H. Parker, J.E. Davies, D.P. Francis, J. Mayet, S.A. McG Thom, A.D. Hughes, et al. Differences in the magnitude of wave reflection account for differential effects of amlodipine-versus atenolol-based regimens on central blood

- pressure: an Anglo-Scandinavian Cardiac Outcome Trial substudy. *Hypertension*, 54(4):724–730, 2009.
- [9] W.W. Nichols and M.F. O'Rourke. *McDonald's Blood Flow in Arteries*. Arnold, London, 4th edition, 1998.
- [10] K.H. Parker. An introduction to wave intensity analysis. *Medical and Biological Engineering and Computing*, 47(2):175–188, 2009.
- [11] K.H. Parker and C.J.H. Jones. Forward and Backward Running Waves in the Arteries: Analysis Using the Method of Characteristics. *Journal of Biomechanical Engineering*, 112(3):322–326, 1990.
- [12] A. Qasem and A. Avolio. Determination of Aortic Pulse Wave Velocity From Waveform Decomposition of the Central Aortic Pressure Pulse. *Hypertension*, 51(2):188–195, 2008.
- [13] B. Riemann. Über die Fortpflanzung ebener Luftwellen von endlicher Schwingungsweite. *Abhandlungen der Königlichen Gesellschaft der Wissenschaften zu Göttingen*, 8:43–65, 1860.
- [14] P. Segers, E.R. Rietzschel, M.L. De Buyzere, D. De Bacquer, L.M. Van Bortel, G. De Backer, T.C. Gillebert, and P.R. Verdonck. Assessment of pressure wave reflection: getting the timing right! *Physiological Measurement*, 28(9):1045–1056, 2007.
- [15] P. Segers, E.R. Rietzschel, M.L. De Buyzere, S.J. Vermeersch, D. De Bacquer, L.M. Van Borte, G. De Backer, T.C. Gillebert, and P.R. Verdonck. Noninvasive (Input) Impedance, Pulse Wave Velocity, and Wave Reflection in Healthy Middle-Aged Men and Women. *Hypertension*, 49(6):1248–1255, 2007.
- [16] A. Swillens and P. Segers. Assessment of arterial pressure wave reflection: methodological considerations. *Artery Research*, 2(4):122–131, 2008.
- [17] J.P.H.M. van den Wijngaard, M. Siebes, and B.E. Westerhof. Comparison of arterial waves derived by classical wave separation and wave intensity analysis in a model of aortic coarctation. *Medical and Biological Engineering and Computing*, 47(2):211–220, 2009.
- [18] K.L. Wang, H.M. Cheng, S.H. Sung, S.Y. Chuang, C.H. Li, H.A. Spurgeon, C.T. Ting, S.S. Najjar, E.G. Lakatta, F.C.P. Yin, et al. Wave Reflection and Arterial Stiffness in the Prediction of 15-Year All-Cause and Cardiovascular Mortalities: A Community-Based Study. *Hypertension*, 55(3):799–805, 2010.
- [19] S. Wassertheurer, B. Hametner, J. Kropf, C. Mayer, B. Eber, and T. Weber. Novel non-invasive method to assess wave reflection from the pressure waveform alone. *Artery Research*, 4(4):145, 2010.
- [20] T. Weber, M. Ammer, C. Biber, M. Windpessl, S. Wassertheurer, B. Hametner, C. Mayer, J. Kropf, M. Rammer, E. Lassnig, and B. Eber. Arterial wave reflection and arterial stiffness independently predict cardiovascular events. *Journal of Hypertension*, 28:e597, 2010.
- [21] B.E. Westerhof, I. Guelen, N. Westerhof, J.M. Karemaker, and A. Avolio. Quantification of wave reflection in the human aorta from pressure alone: A proof of principle. *Hypertension*, 48(4):595–601, 2006.
- [22] N. Westerhof, P. Sipkema, G.C. van den Bos, and G. Elzinga. Forward and backward waves in the arterial system. *Cardiovascular Research*, 6:648–656, 1972.