Estimation of changes in instantaneous aortic blood flow by the analysis of arterial blood pressure

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AORTIC BLOOD FLOW (ABF), defined as the instantaneous flow rate of blood across the aortic valve, is one of the most fundamental cardiovascular signals. The beat-to-beat integral of the ABF waveform yields stroke volume (SV), and the time average of ABF over many beats yields cardiac output (CO). Individual ABF waveforms reflect the detailed time dependence of ventricular contractions; however, ABF data are not clinically available. The availability of ABF data would be particularly valuable for evaluating the contractile function of the left ventricle during normal and abnormal beats and for optimizing pacing parameters during biventricular pacing. The most accurate currently available method for the continuous measurement of ABF, SV, and CO is the surgical placement of an ultrasonic flow probe (Transonic Systems, Ithaca, NY) around the aortic root. The drawback of the flow probe is that it requires a highly invasive open-chest surgical procedure (11). Noninvasive methods include Doppler echocardiography, which requires a skilled technician to hold the probe at the correct angle on the patient’s body. Thus, long-term, continuous measurement is not feasible with this method.

We introduce a novel algorithm to continuously estimate beat-to-beat ABF waveforms by analysis of the arterial blood pressure (ABP) signal. The algorithm can continuously estimate ABF on a beat-to-beat basis less obtrusively than the aforementioned methods, because ABP is readily accessible by minimally invasive or noninvasive means. This algorithm models the arterial tree as a system with ABF input and ABP output. The algorithm involves an autoregressive with exogenous input (ARX) model. The key feature of the algorithm is that ARX coefficients are estimated by applying the algorithm to a diastolic ABP waveform and forcing the estimated ABF to be zero during this period. Then the algorithm incorporating the estimated coefficients is applied to the single ABP signal to estimate ABF on a beat-to-beat basis.

METHODS

Algorithm

Over a short time interval, the cardiovascular system can be described as a time-invariant system with an input of ABF \([F(n)]\) and output of ABP \([P(n)]\), as illustrated in Fig. 1.

An ARX model can be used to relate the ABP values \([P(n)]\) to the ABF values \([F(n)]\)

\[
P(n) = \sum_{j=1}^{L} a(j)P(n-j) + \alpha F(n) + e(n)
\]  

where \(a(j)\) represents the autoregressive (AR) weighting coefficients, \(L\) is the length coefficient, \(\alpha\) is the weighting coefficient for the exogenous input \(F(n)\), and \(e(n)\) is noise. The ARX model can be rewritten as

\[
\alpha F(n) = P(n) - \sum_{j=1}^{L} a(j)P(n-j) + e(n)
\]  

During diastole, ABF (system input) is approximately zero

\[
P(n) = \sum_{j=1}^{L} a(j)P(n-j) + e(n)
\]  

Therefore, the weighting coefficients \(a(j)\) are AR coefficients, which can be obtained by solving the matrix equation (using MATLAB, Mathworks, Natick, MA) that involves data from multiple beats during diastole. These coefficients are then applied to the single ABP waveform to estimate ABF on a beat-to-beat basis.

Arai T, Lee K, Marini RP, Cohen RJ. Estimation of changes in instantaneous aortic blood flow by the analysis of arterial blood pressure. J Appl Physiol 112: 1832–1838, 2012. First published March 22, 2012; doi:10.1152/japplphysiol.01565.2011.—The purpose of this study was to introduce and validate a new algorithm to estimate instantaneous aortic blood flow (ABF) by mathematical analysis of arterial blood pressure (ABP) waveforms. The algorithm is based on an autoregressive with exogenous input (ARX) model. We applied this algorithm to diastolic ABF waveforms to estimate the autoregressive model coefficients by requiring the estimated diastolic flow to be zero. The algorithm incorporating the coefficients was then applied to the entire ABP signal to estimate ABF. The algorithm was applied to six Yorkshire swine data sets over a wide range of physiological conditions for validation. Quantitative measures of waveform shape (standard deviation, skewness, and kurtosis), as well as stroke volume and cardiac output from the estimated ABF, were computed. Values of these measures were compared with those obtained from ABF waveforms recorded using a Transonic aortic flow probe placed around the aortic root. The estimation errors were compared with those obtained using a windkessel model. The ARX model algorithm achieved significantly lower errors in the waveform measures, stroke volume, and cardiac output than those obtained using the windkessel model (\(P < 0.05\)).
MAP/CO = TPR \quad (6)

where TPR is total peripheral resistance. TPR can be related to the arterial compliance (Ca) and the characteristic time constant of the system (τ)

\[ τ = Ca \times TPR \quad (7) \]

where τ can be obtained by analyzing the exponential decay curve of the impulse response of the system h(n) (Fig. 2B)

\[ h(n) = \sum_{j=1}^{L} a(j)h[n-j] + aδ(n) \quad (8) \]

Equations 5–7 can be combined to compute α

\[ α = \frac{[1 - \sum_{j=1}^{L} a(j)]}{Ca} \quad (9) \]

Therefore, using Eqs. 1 and 9, instantaneous ABF can be expressed as

\[ F(n) = \frac{Ca}{τ - \sum_{j=1}^{L} a(j)} \left[ P(n) - \sum_{j=1}^{L} a(j)P(n-j) \right] \quad (10) \]

The AR coefficient length L was chosen to minimize Σa(j) and updated on a beat-to-beat basis.

The integral of F(n) was calculated on a beat-to-beat basis to obtain proportional SV estimates (the proportionality constant is the unmeasured Ca), and the time average of F(n) over 6 min was calculated to obtain a proportional estimate of CO. Thus the algorithm presented here provides a comprehensive set of cardiovascular indexes (ABF, SV, CO, and τ) based on an analysis of ABP waveforms.

**Implementation**

**Onset and peak of systole.** For each beat, the onset and peak of systole were identified in the following manner. 1) A normalized Gaussian distribution (width = 4σ) was prepared. For the first iteration, the width was arbitrarily set to 75 samples. 2) The Gaussian distribution (Fig. 3A) was convoluted with the 10-s ABP signal. 3)
The local maxima of the convolution waveform were identified. Once the systolic peaks were identified, the local minima prior to the peaks were regarded as end diastole. For the following 10-s ABP signals, the width of the Gaussian distribution was updated by

\[ 4\sigma = RR\text{interval} \]

**Onset of diastole.** The onset of diastole and length of diastole in each beat were obtained from analysis of the measured ABF waveform; in each beat, the first local minimum after the systolic peak was regarded as the onset of diastole. The ABF diastolic interval in each beat was mapped onto the ABP waveforms (Fig. 4). However, the onset of diastole is not always available clinically. Regarding estimation of diastolic onset, Weissler et al. (14) showed that the systolic duration of the present beat is an exponential function of the preceding RR interval. With use of pilot Yorkshire swine data sets, the following equation was adopted to estimate systolic duration, which was used to identify the onset of diastole

\[ Sys_i = 436 \left[ 1 - \exp(-0.0057RRI_{meas}) \right] \]

where Sys is the systolic duration (samples) and RR is the RR interval (samples). Equation 11, while empirical, is quite robust. It provided good results in our studies over a very wide range of physiological conditions, including a wide range of heart rates and administration of vasoactive drugs. It is possible that disease states may alter the value of numerical parameters of Eq. 11. Results using the true onset of diastole and the estimated onset of diastole using Eq. 11 are reported.

**Conditioning of data.** To increase the robustness of the AR coefficient estimation, the original ABP data were horizontally and vertically scaled, so that systolic ABP, diastolic ABP, and RR interval of all the beats in the 17-beat moving window were the same as those of the middle (9th) beat in the window. Note that this data conditioning was conducted solely for the purpose of the AR coefficient estimation. Once the AR coefficients were obtained, the algorithm was applied to the original ABP waveform in the middle (9th beat) of the 17-beat window. The moving window was shifted on a beat-to-beat basis.

**Experimental Protocol**

To validate the algorithm, previously reported (11) data from six Yorkshire swine (30–34 kg body wt) recorded under a protocol approved by the MIT Committee on Animal Care were processed and analyzed offline. ABF was recorded using an ultrasonic flow probe (model T206 with A-series probes, Transonic Systems) placed around the aortic root. A micromanometer-tipped catheter (SPC 350, Millar Instruments, Houston, TX) was fed retrograde to the thoracic aorta from the femoral artery for central ABP (CAP) measurement. Radial ABP (RAP) and femoral ABP (FAP) were measured using an external pressure transducer (model TSD104A, Biopac Systems, Santa Barbara, CA). ABF and ABPs were recorded using an analog-to-digital conversion system (model MP150WSW, Biopac Systems) at a sampling rate of 250 Hz and 16-bit resolution (see Ref. 11 for more details of the data acquisition). A wide range of physiological conditions was obtained by administration of vasoactive drugs, including phenylephrine, nitroglycerin, dobutamine, and esmolol. Table 1 provides a summary of the cardiovascular indexes of the swine data sets.

**Data Analysis**

All the signal processing and analyses were conducted using MATLAB R2009a. The standard deviation (SD), skewness, and kurtosis of estimated systolic ABF waveforms were compared with those of the measured waveforms. The SD, skewness, and kurtosis are given by

\[ \sigma = \sqrt{E[(F_S - \mu)^2]} \]  
\[ \text{skewness} = E[(F_S - \mu)^3/\sigma^3] \]  
\[ \text{kurtosis} = E[(F_S - \mu)^4/\sigma^4] \]

where FS is the ABF (measured or estimated) of a single beat; \( \mu \) and \( \sigma \) are the mean and SD of FS, respectively; and \( E[.] \) represents the expected value. The SD, skewness, and kurtosis of the measured and estimated ABF were calculated on a beat-to-beat basis. For comparison, the SD, skewness, and kurtosis of the ABF estimated using the standard windkessel model were also computed. The proportional ABF using the windkessel model was estimated as follows

\[ F/C_a = dP/dt + P/\tau \]

where \( \tau \) was estimated from an exponential decay fitted to the measured diastolic ABP waveforms and \( dP/dt \) is rate of change in pressure.

### Table 1. Cardiovascular indexes of the swine data sets

<table>
<thead>
<tr>
<th>Animal No.</th>
<th>Length, min</th>
<th>CO, l/min</th>
<th>SV, ml</th>
<th>MAP, mmHg</th>
<th>Femoral</th>
<th>Radial</th>
<th>HR, beats/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>113</td>
<td>3.6 ± 1.0</td>
<td>28.4 ± 5.8</td>
<td>63 ± 19</td>
<td>61 ± 19</td>
<td>129 ± 29</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>97</td>
<td>3.2 ± 0.6</td>
<td>25.0 ± 5.0</td>
<td>83 ± 21</td>
<td>73 ± 20</td>
<td>135 ± 38</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>88</td>
<td>4.0 ± 0.7</td>
<td>31.7 ± 7.1</td>
<td>83 ± 16</td>
<td>87 ± 15</td>
<td>133 ± 32</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>106</td>
<td>3.2 ± 0.6</td>
<td>25.2 ± 4.3</td>
<td>89 ± 19</td>
<td>79 ± 18</td>
<td>129 ± 34</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>90</td>
<td>3.3 ± 0.5</td>
<td>26.7 ± 6.4</td>
<td>80 ± 21</td>
<td>85 ± 19</td>
<td>130 ± 32</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>68</td>
<td>3.4 ± 1.2</td>
<td>28.5 ± 8.1</td>
<td>72 ± 19</td>
<td>75 ± 20</td>
<td>130 ± 26</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>94</td>
<td>3.5 ± 0.8</td>
<td>27.5 ± 6.7</td>
<td>79 ± 21</td>
<td>76 ± 21</td>
<td>131 ± 32</td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SE. CO, cardiac output; SV, stroke volume; MAP, mean arterial pressure; HR, heart rate.

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The errors in SD, skewness, and kurtosis were defined as the difference between the values obtained from the estimated ABF and the values obtained from the measured ABF. The errors obtained using the algorithm and the windkessel model were compared by the Mann-Whitney U-test.

For comparison of the estimated and measured SV and CO, the proportionality constant $C_a$ in each animal was calculated by

$$C_a = \frac{\text{mean}(\text{CO}_\text{Meas})}{\text{mean}(\text{CO}_\text{Est})}$$  \hspace{1cm} (14)$$

where $\text{CO}_\text{Meas}$ and $\text{CO}_\text{Est}$ are the measured and estimated CO, respectively. Although $C_a$ declines with age (10), $C_a$ is nearly constant on the time scale of months over a wide pressure range (2, 6); thus, $C_a$ was assumed to be constant (equal to the mean estimated CO divided by the mean estimated CO) throughout the experimental period in each animal, and the SV and CO estimates were scaled by the constant in each animal to compare estimated with measured values. The root normalized mean square error (RNMSE) was used as the error measure for SV and CO

$$\text{RNMSE} = 100 \sqrt{\frac{1}{N} \sum_{i=1}^{N} \left[ \frac{(\text{Meas} - \text{Est})}{\text{Meas}} \right]^2}$$  \hspace{1cm} (15)$$

where Meas and Est are the measured and estimated values, respectively, $N$ is the number of data points, and $N_f$ is the number of free parameters (i.e., $C_a$ for each animal).

In the present study, the onsets of diastole were determined from the measured ABF. These onsets have to be estimated when only ABP is known. To test the sensitivity of the algorithm to errors in diastolic onset, the time stamp of the onset of diastole was offset from its actual location by $\pm 10\%$ of the diastolic interval, and the RNMSEs in SV and CO estimation were calculated.

RESULTS

Over 60,000 beats were processed and analyzed for ABF and SV, and >110 six-minute windows were processed and analyzed for CO. Figure 5 shows the examples of the ABF waveforms estimated from ABP waveforms with the true onset of diastoles given. The ABF estimated by the ARX model followed the trend of the measured ABF (Fig. 5, A–C) and presented similar morphology, while the windkessel ABF presented distorted waveforms (Fig. 5, D–F, shown in gray). For the ABF waveforms, offsets in the SD (Fig. 6, A–C), skewness (Fig. 6, D–F), and kurtosis (Fig. 6, G–I) errors estimated by the ARX model were smaller than the results of the windkessel model, except for the femoral and radial kurtosis errors. The ARX model achieved RNMSEs of 12.7 and 15.3% in CO and SV, respectively, derived from CAP, 15.2 and 19.6% in CO and SV, respectively, derived from FAP, and 15.8 and 21.8% in CO and SV, respectively, derived from RAP (Fig. 7). The errors were lower than those from the windkessel model, which achieved RNMSEs of 17.0 and 23.7% in CO and SV, respectively (CAP), 16.6 and 18.8% in CO and SV, respectively (FAP), and 44.8 and 33.7% in CO and SV, respectively (RAP).

With the estimated onset of diastole (Eq. 11), the algorithm achieved RNMSEs of 13.7 and 20.0% in CO and SV, respectively, derived from CAP, 15.2 and 22.9% in CO and SV, respectively, derived from FAP, and 16.7 and 25.9% in CO and SV, respectively, derived from RAP. SD, skewness, and kurtosis errors were smaller than errors from the windkessel model.

A sensitivity analysis regarding the onset of diastole was conducted. With the diastolic intervals increased by 10%, estimation errors increased by 0.5 and 3.9% in CO and SV, respectively, 4.0 and 6.1% in CO and SV, respectively, and 3.7 and 2.3% in CO and SV, respectively, derived from CAP, FAP, and RAP, respectively. With diastolic intervals decreased by 10%, the errors increased by 3.4 and 10.5% in CO and SV, respectively, derived from CAP, FAP, and RAP, respectively. With the diastolic intervals increased by 10%, the errors increased by 3.4 and 10.5% in CO and SV, respectively, derived from CAP, FAP, and RAP, respectively. For the $\pm 10\%$ cases, the SD, skewness, kurtosis errors were hardly changed compared with the values reported in Fig. 6.

DISCUSSION

We have introduced a novel algorithm to continuously estimate ABF, SV, and CO from the analysis of central and peripheral ABP waveforms. As opposed to the existing pulse contour methods that also analyze ABP to calculate CO and SV (1, 3–5, 7, 9, 11–13), the present method reconstructs more fundamental information, i.e., instantaneous ABF across the

![Fig. 5. Measured and computed ABF waveforms for central ABP (CAP), femoral ABP (FAP), and RAP by the algorithm applied to data from swine 5. Nitroglycerin was administered. A, B, and C: waveforms using CAP, FAP, and RAP, respectively. D, E, and F: close-ups of A, B, and C, respectively.](http://jap.physiology.org/)
The algorithm utilizes the notion that the flow input to the arterial system is zero during diastole. In the ABF estimation routine, 17 diastolic ABP waveforms were used in the left-hand side of Eq. 4 to obtain the AR coefficients (Fig. 2A). The AR coefficients and the derived weighting coefficient $\alpha$ were integrated into the ARX model (Fig. 1) and applied to the entire ABP waveform of the middle beat to obtain the ABF waveform. The AR coefficients were also used to obtain the impulse response (Fig. 2B) and characteristic time constant $\tau$ (Eq. 8) to properly scale the estimated ABF (Eq. 10). In Fig. 2B, the impulse response reveals a rapid initial decay, which may be associated with aortic impedance, in addition to a slower decay corresponding to $\tau$. These descriptors are comprehensively incorporated in the ARX model.

The data were conditioned to synthesize the systolic and diastolic ABP within the moving window. Without conditioning, instability in the impulse response and noisiness in the estimated ABF waveforms were observed. We found that the cause of the estimated impulse response instability was beat-to-beat variations in ABP. The instability could be removed by rescaling the amplitude and duration of the ABP waveform of each beat in the window prior to estimation of the AR coefficients. The derived AR coefficients were applied to the original ABP waveform of the middle beat to obtain ABF.

The 17-beat moving window size was empirically chosen. If the window is too short, one cannot excite enough modes to identify the system. On the other hand, if the window is too long, time invariance of the pertinent cardiovascular system cannot be assumed (e.g., baroreflex feedback changes of TPR and $\tau$).

To determine the AR length coefficient $L$, we minimized $\sum a_j$, because the resulting sets of AR coefficients were most likely to result in a stable impulse response $h(n)$. In cases where there were multiple local minima of $\sum a_j$ in the search space, the minimum with the shortest AR length coefficient $L$ was adopted.

The algorithm achieved RNMSEs of 12.7–15.8% and 15.3–21.8% in CO and SV, respectively, with the true onset of diastole given and RNMSEs of 13.7–16.7% and 20.0–25.9% in CO and SV, respectively, with the estimated onset of diastole using Eq. 11. For both cases, the ABF estimated by the algorithm provided SD, skewness, and kurtosis values that matched those of the measured ABF waveforms.

The sensitivity analysis regarding the onset of diastole indicates that the error in estimating SV and CO was greater when the diastolic interval was shortened than when it was lengthened. This may be due to the more rapid diastolic decay in early diastole and the adverse effects of loss of this information in estimating the AR coefficients on the accuracy of the method.

The classical windkessel model assumes an exponential decay during diastole and, thus, represents a first-order AR model. The windkessel model results in an early systolic peak [also indicated by the leftward shift of the skewness error histogram (Fig. 6, D–F)] in the estimated ABF waveforms. The present algorithm,
on the other hand, obtains higher-order AR coefficients (Fig. 2A) from diastolic ABP waveforms. The advantage of the new algorithm is that it may take into account the possible distortion involved in the diastolic ABP waveform that results from its propagation through the arterial tree. Therefore, when applied to the systolic ABP, the filter created by the algorithm may compensate for the distortion and more accurately reconstruct the systolic ABF waveform (Fig. 5, shown in black). The distortion varies from artery to artery, as well as from subject to subject. The algorithm is able to measure and correct for such distortion. The present algorithm is easy to implement in existing medical systems that continuously monitor ABP. The ABF waveform, CO, and SV estimated by the analysis of ABP waveforms may enable multimodal evaluation of the cardiovascular system in clinical and ambulatory settings.

**Conclusion**

We have introduced a novel algorithm that estimates ABF waveforms by the analysis of ABP waveforms. The algorithm uses diastolic ABP waveforms in a 17-beat moving window to obtain AR coefficients, as well as the characteristic time constant. The AR coefficients are used in the ARX model to estimate ABF waveforms. Integrals and time averages were taken to calculate beat-to-beat SV and CO values. The algorithm was applied to six Yorkshire swine data sets encompassing a wide physiological range, and it achieved low RNMSEs in CO (12.7–15.8%) and SV (15.3–21.8%) estimation when the true onset of diastole was given. With the estimated onset of diastole, it achieved low RNMSEs in CO (13.7–16.7%) and SV (20.0–25.9%) estimation. The estimated

Fig. 7. Agreement of measured and estimated stroke volume (SV) and cardiac output (CO) derived from CAP, FAP, and RAP in the 6 Yorkshire swine data sets. Gray and black lines represent measured and estimated values, respectively. A, B, and C: CO estimates from CAP, FAP, and RAP, respectively. D, E, and F: SV estimates from CAP, FAP, and RAP, respectively.
ABF waveforms accurately track features of the measured ABF waveforms.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

T.A. and R.J.C. are responsible for conception and design of the research; T.A. analyzed the data; T.A. and R.J.C. interpreted the results of the experiments; T.A. prepared the figures; T.A., K.L., and R.J.C. edited and revised the manuscript; T.A. and R.J.C. approved the final version of the manuscript; R.P.M. performed the experiments.

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