

## Novel wave intensity analysis of arterial pulse wave propagation accounting for peripheral reflections (supplementary material)

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### 1. EFFECT OF VESSEL COMPLIANCE AND PERIPHERAL RESISTANCE ON TRANSIT TIME AND APPARENT REFLECTION COEFFICIENT IN THE PRESENCE OF A SINGLE PERIPHERAL REFLECTION SITE

We will use the single-vessel aortic model coupled to a matched RCR Windkessel outflow model (Fig. 3b) to show that, in the presence of a single peripheral reflection site, the new forward ( $d\hat{I}_f$ ) and backward ( $d\hat{I}_b$ ) wave intensity profiles allow us to estimate theoretical changes in transit time (TT) due to varying vessel compliance and peripheral resistance (Section 1.1). We also provide numerical results on the effect of varying vessel compliance and peripheral resistance on the apparent reflection coefficient ( $R_f^{app}$ ) (Section 1.2).

#### 1.1. Transit Time

Calculation of the TT using Eq. (16) in the midpoint of the aortic model with several values of the Young's modulus of the arterial wall ( $E$ ), from 0.2 MPa to 0.8 MPa, shows a decrease in TT with increasing  $E$  (Fig. 1c, supp. mat.) and, hence, decreasing vessel compliance. According to Eq. (5), the theoretical pulse wave velocity (PWV) decreases by 28% with half the original  $E = 0.4$  MPa and increases by 41% with double the original  $E$ ; that is, pulse wavefronts travel at a greater speed in stiffer vessels. Given that the distance to the peripheral reflection site is constant in our aortic model, the corresponding changes in theoretical TT are +39% and -29%. The changes in TT given by Eq. (16) are 38% and -25% using foot values of  $d\hat{I}_f$  and  $d\hat{I}_b$ , 19% and -16% using peak values, and 6% and -9% using area-average values. These results support the use of foot values, rather than peak or area-average values, when calculating the TT to a dominant reflection site using our modified WIA.

Furthermore, the TT given by Eq. (16) in the midpoint of the aortic model decreases with increasing peripheral resistance ( $R_T$ ) (Fig. 1f, supp. mat.), since the increase in pressure associated with the increase in  $R_T$  yields greater luminal area ( $A$ ) and, hence, greater PWV, according to Eq. (5). Changes in the theoretical TT with  $R_T$  are also better captured by TT estimates given by Eq. (16) using foot values than peak or area-average values.

The results in this section show the ability of our new WIA to estimate the transit time to a dominant peripheral reflection site, using foot values of wave intensity  $d\hat{I}_{f,b}$  to calculate the times of the incident and reflected waves.

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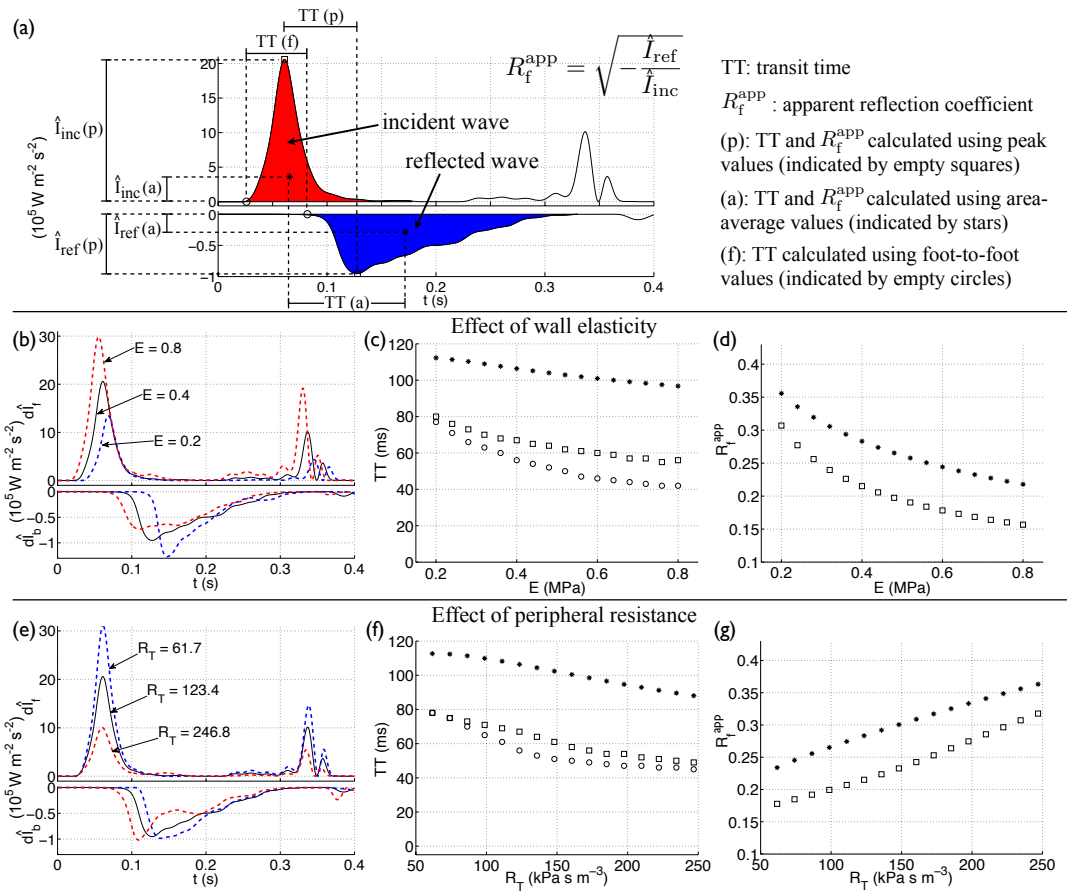


Figure 1. (a) Illustration of the calculation of the transit time (TT) between the incident and reflected waves and apparent reflection coefficient ( $R_f^{\text{app}}$ ) using the new wave intensity profiles  $d\hat{I}_{f,b}$ . (b,e) Forward ( $d\hat{I}_f$ ) and backward ( $d\hat{I}_b$ ) components of modified wave intensity with time in the midpoint of the single-vessel aortic model coupled to a matched RCR Windkessel outflow model (Fig. 3b). They were calculated using the original model (black solid lines), with  $c$  at diastolic pressure, and changing the (b) wall elastic modulus ( $E$  in MPa) or (e) peripheral resistance ( $R_T$  in  $\text{kPa s m}^{-3}$ ) as indicated by the labels (red and blue dashed lines). In the original model we have  $E = 0.4$  MPa and  $R_T = 123.4$   $\text{kPa s m}^{-3}$ . Note the different scaling of  $d\hat{I}_f$  and  $d\hat{I}_b$ . Effect of (c,d)  $E$  and (f,g)  $R_T$  on TT and  $R_f^{\text{app}}$  calculated using foot (circles), peak (squares) or area-average (stars) values, as illustrated in (a).

## 1.2. Apparent Reflection Coefficient

The estimate of  $R_f^{\text{app}}$  given by Eq. (16) in the midpoint of our aortic model decreases with increasing  $E$  (Fig. 1d, supp. mat.), since the amplitude of the incident wave raises and the amplitude of the reflected wave drops with increasing  $E$  (Fig. 1b, supp. mat.). Changes in  $R_T$  affect the amplitude of the incident wave, but produce little changes in the amplitude of the reflected wave (Fig. 1e, suppl. mat.). The incident amplitude decreases with increasing  $R_T$ , since the increase in  $A$  with  $R_T$  yields smaller flow velocities ( $U$ ) and, hence, smaller wavefronts  $dU$  contributing to  $d\hat{I}_f$ . As a result, the  $R_f^{\text{app}}$  increases with increasing  $R_T$  (Fig. 1g, suppl. mat.).

## 2. NOMENCLATURE AND ABBREVIATIONS

Table I. Nomenclature, abbreviations and SI units. Units commonly used in the clinic that differ from SI units are shown after a semicolon.

1-D		one-dimensional
$A$	( $\text{m}^2$ ; $\text{cm}^2$ or $\text{mm}^2$ )	area of the luminal cross section of the vessel
$A_0$	( $\text{m}^2$ )	luminal cross-sectional area at zero blood pressure
$a$	( $\text{m}^2$ )	linear perturbation for the luminal cross-sectional area
CCA		common carotid artery
CO	( $\text{m}^3 \text{ s}^{-1}$ ; $\text{ml s}^{-1}$ , $\text{l min}^{-1}$ )	cardiac output generated by the left ventricle
C-R	(m)	rabbit crown-to-rump length
$C$	( $\text{m}^3 \text{ Pa}^{-1}$ )	compliance of the peripheral RCR Windkessel model
$C_{0D}$	( $\text{m}^3 \text{ Pa}^{-1}$ )	compliance of an arterial segment
$C_{1D}$	( $\text{m}^2 \text{ Pa}^{-1}$ )	compliance per unit length of arterial segment
$C_T$	( $\text{m}^3 \text{ Pa}^{-1}$ ; $\text{ml mmHg}^{-1}$ )	total systemic compliance
$C_c, C_p$	( $\text{m}^3 \text{ Pa}^{-1}$ )	total conduit or peripheral compliance, respectively
$C_f, C_b$		forward or backward characteristic path, respectively
$c$	( $\text{m s}^{-1}$ )	pulse wave velocity
$c_0$	( $\text{m s}^{-1}$ )	pulse wave velocity at zero blood pressure
$c_{AU}$	( $\text{m s}^{-1}$ )	pulse wave velocity calculated using the $\ln AU$ -loop method
$c_{PA}$	( $\text{m s}^{-1}$ )	pulse wave velocity calculated from simultaneous pressure and area measurements
$c_{PU}$	( $\text{m s}^{-1}$ )	pulse wave velocity calculated using the $PU$ -loop method
$\hat{c}_{PU}$	( $\text{m s}^{-1}$ )	pulse wave velocity calculated using the modified $\hat{P}U$ -loop method
$c_{ff}$	( $\text{m s}^{-1}$ )	pulse wave velocity calculated using the 'foot-to-foot' method
DG		discontinuous Galerkin
$dA$	( $\text{m}^2$ )	change in luminal area across a wavefront
$dA_f, dA_b$	( $\text{m}^2$ )	change in luminal area across a forward or backward wavefront, respectively
$dI$	( $\text{W m}^{-2}$ )	traditional wave intensity
$d\hat{I}$	( $\text{W m}^{-2}$ )	new wave intensity cleared of contributions of waves reflected in previous cardiac cycles
$dI_f, dI_b$	( $\text{W m}^{-2}$ )	traditional wave intensity of a forward or backward wavefront, respectively
$d\hat{I}_f, d\hat{I}_b$	( $\text{W m}^{-2}$ )	new wave intensity of a forward or backward wavefront, respectively, cleared of contributions of waves reflected in previous cardiac cycles
$dI_{inc}, dI_{ref}$	( $\text{W m}^{-2}$ )	wave intensity of an incident or reflected wavefront, respectively
$dI_s$	( $\text{W m}^{-2}$ )	wave intensity during early systolic ejection
$dI_w$	( $\text{W m}^{-2}$ )	wave intensity in diastole given by the Windkessel pressure and flow
$dP$	(Pa)	change in blood pressure across a wavefront
$d\hat{P}$	(Pa)	change in blood pressure across a wavefront cleared of contributions of waves reflected in previous cardiac cycles
$dP_f, dP_b$	(Pa)	traditional change in blood pressure across a forward or backward wavefront, respectively
$d\hat{P}_f, d\hat{P}_b$	(Pa)	change in blood pressure across a forward or backward wavefront, respectively, cleared of contributions of waves reflected in previous cardiac cycles
$dP_{inc}, dP_{ref}$	(Pa)	change in blood pressure in the incident or across the reflected wavefront, respectively
$dP_s$	(Pa)	change in blood pressure across a wavefront during early systolic ejection
$dp_w$	(Pa)	change in $p_w$ across a wavefront during diastole
$dq_w$	( $\text{m}^3 \text{ s}^{-1}$ )	change in $q_w$ across a wavefront during diastole
$dU$	( $\text{m s}^{-1}$ )	change in blood flow velocity across a wavefront

Table II. Continuation of nomenclature, abbreviations and units.

$dU_f, dU_b$	(m s <sup>-1</sup> )	traditional change in blood flow velocity across a forward or backward wavefront, respectively
$d\hat{U}_f, d\hat{U}_b$	(m s <sup>-1</sup> )	change in blood flow velocity across a forward or backward wavefront, respectively, cleared of contributions of waves reflected in previous cardiac cycles
$dU_{inc}, dU_{ref}$	(m s <sup>-1</sup> )	change in blood flow velocity in the incident or across the reflected wavefront, respectively
$dU_s$	(m s <sup>-1</sup> )	change in blood flow velocity across a wavefront during early systolic ejection
$dW_f, dW_b$	(m s <sup>-1</sup> )	change in forward or backward characteristic variable, respectively
$dt$	(s)	time between two adjacent sampling points of $P$ or $U$
ECG		electrocardiogram
$E$	(Pa)	Young's modulus of the arterial wall
$f$	(N m <sup>-1</sup> )	frictional force per unit length of vessel
HR	(s <sup>-1</sup> ; beats min <sup>-1</sup> )	heart rate
$h$	(m; mm)	wall thickness of the artery
$I_{inc}, I_{ref}$	(W m <sup>-2</sup> )	magnitude of the incident or reflected wave, respectively, of the wave intensity profile
$\hat{I}_{inc}, \hat{I}_{ref}$	(W m <sup>-2</sup> )	magnitude of the incident or reflected wave, respectively, of the wave intensity profile cleared of contributions of waves reflected in previous cardiac cycles
LV		left ventricle
$L_{1D}$	(kg m <sup>-5</sup> )	blood inertia per unit length of vessel
$l$	(m; cm)	length of an arterial segment
M1		normal young 55-artery model
M2		normal old 55-artery model
M3		hypertensive young 55-artery model
M4		hypertensive old 55-artery model
$M - 1$		total number of terminal arterial segments in a distributed 1-D model
$N$		total number of arterial segments in a distributed 1-D model
PP	(Pa; mmHg)	pulse pressure; that is, difference between the maximum, systolic, and minimum, diastolic, pressures
PWV	(m s <sup>-1</sup> )	pulse wave velocity
$P$	(Pa; mmHg)	blood pressure averaged over the luminal cross section
$\hat{P}$	(Pa)	blood pressure cleared of contributions of waves reflected in previous cardiac cycles
$P_0$	(Pa)	reference blood pressure for the calculation of forward and backward pressure components
$P_{con}, P_{per}$	(Pa)	conduit or peripheral component of blood pressure, respectively
$P_d$	(Pa; mmHg)	diastolic pressure
$P_e$	(Pa)	elastic component of blood pressure
$P_f, P_b$	(Pa; mmHg)	traditional forward or backward component of blood pressure, respectively
$\hat{P}_f, \hat{P}_b$	(Pa)	forward or backward component of blood pressure, respectively, cleared of contributions of waves reflected in previous cardiac cycles
$P_m$	(Pa; mmHg)	mean blood pressure
$P_{out}$	(Pa; mmHg)	blood pressure at which flow to the microcirculation ceases
$p_e$	(Pa)	linear perturbation for the elastic component of blood pressure
$p_w$	(Pa)	space-independent Windkessel blood pressure
$Q$	(m <sup>3</sup> s <sup>-1</sup> ; ml s <sup>-1</sup> , l min <sup>-1</sup> )	blood volume flow rate
$Q_{con}, Q_{per}$	(m <sup>3</sup> s <sup>-1</sup> )	conduit or peripheral component of the flow rate, respectively
$Q_{in}$	(m <sup>3</sup> s <sup>-1</sup> ; l min <sup>-1</sup> )	blood volume flow rate at the aortic root
$q$	(m <sup>3</sup> s <sup>-1</sup> )	linear perturbation for the blood volume flow rate
$q_{in}, q_{out}$	(m <sup>3</sup> s <sup>-1</sup> )	linear perturbation of the volume flow rate at the inlet or outlet, respectively, of an arterial segment
$q_w$	(m <sup>3</sup> s <sup>-1</sup> )	blood volume flow rate driven by $p_w - P_{out}$
$R_1, R_2$	(Pa s m <sup>-3</sup> )	inflow or outflow resistance, respectively, of the peripheral RCR Windkessel model

Table III. Continuation of nomenclature, abbreviations and units.

$R_{1D}$	(Pa s m <sup>-4</sup> )	resistance per unit length of vessel due to blood viscosity
$R_T$	(Pa s m <sup>-3</sup> ; mmHg s ml <sup>-3</sup> )	net peripheral resistance of the arterial network
$R_f$		reflection coefficient for a pulse wavefront at a local site of impedance mismatch
$R_f^{\text{app}}$		apparent reflection coefficient calculated from the incident and reflected waves of the wave intensity profile
$R_f^{p,d1,d2}$		reflection coefficient of a wavefront propagating respectively in the parent, first daughter or second daughter vessels joining in an arterial junction
$r$	(m; cm)	radius of the luminal cross section of the vessel
$r_d$	(m; cm)	luminal radius at diastolic pressure
SEM		standard error of the mean
SF	(s <sup>-1</sup> ; Hz, kHz)	sampling frequency
TT	(s; ms)	transit time between the incident and reflected waves of the wave intensity profile
$T_0$	(s)	reference time in the calculation of the space-independent Windkessel blood pressure $p_w$
$\mathcal{T}_{\text{inc}}, \mathcal{T}_{\text{ref}}$	(s)	time of arrival of the incident or reflected wave, respectively, in the wave intensity profile
$t$	(s)	time
$t_{\text{ini}}, t_{\text{end}}$	(s)	time at the start or end, respectively, of a wave in the wave intensity profile
$U$	(m s <sup>-1</sup> ; cm s <sup>-1</sup> )	axial blood flow velocity averaged over the luminal cross section
$U_0$	(m s <sup>-1</sup> )	reference average flow velocity for the calculation of forward and backward velocity components
$U_{\text{inc}}, U_{\text{ref}}$	(m s <sup>-1</sup> )	average flow velocity during the propagation of an incident or reflected wavefront, respectively
$U_f, U_b$	(m s <sup>-1</sup> ; cm s <sup>-1</sup> )	traditional forward or backward component of blood velocity, respectively
$\hat{U}_f, \hat{U}_b$	(m s <sup>-1</sup> ; cm s <sup>-1</sup> )	forward or backward component of blood velocity, respectively, cleared of contributions of waves reflected in previous cardiac cycles wave intensity analysis
WIA		
$W_f, W_b$	(m s <sup>-1</sup> )	nonlinear forward or backward characteristic variable, respectively
$w_f, w_b$	(m <sup>3</sup> s <sup>-1</sup> )	linear forward or backward characteristic variable, respectively
$x$	(m)	axial coordinate of an arterial segment $\Omega$
$\hat{x}(t)$		parametric function in the $(x, t)$ space
$Y_0$	(m <sup>3</sup> Pa <sup>-1</sup> s <sup>-1</sup> )	characteristic admittance of the vessel
$Z_0$	(Pa s m <sup>-3</sup> )	characteristic impedance of the vessel
$\beta$	(Pa m)	parameter related to the elastic tone of the vessel wall
$\Gamma$	(Pa s m)	parameter related to the viscosity of the vessel wall
$\Delta a$	(m <sup>2</sup> )	linear perturbation of luminal cross-sectional area propagating toward a junction
$\Delta p_e$	(Pa)	linear perturbation of elastic component of pressure propagating toward a junction
$\Delta q$	(m <sup>3</sup> s <sup>-1</sup> )	linear perturbation of flow rate propagating toward a junction
$\Delta u$	(m s <sup>-1</sup> )	linear perturbation of flow velocity propagating toward a junction
$\delta a$	(m <sup>2</sup> )	linear perturbation of luminal cross-sectional area propagating away from a junction
$\delta p_e$	(Pa)	linear perturbation of elastic component of pressure propagating away from a junction
$\delta q$	(m <sup>3</sup> s <sup>-1</sup> )	linear perturbation of flow rate propagating away from a junction
$\delta u$	(m s <sup>-1</sup> )	linear perturbation of flow velocity propagating away from a junction
$\mu$	(Pa s)	dynamic viscosity of blood
$\rho$	(kg m <sup>-3</sup> )	blood density
$\varphi$	(Pa s)	viscosity of the vessel wall
$\Omega$		1-D domain of an arterial segment