Analysis of signal propagation in an elastic-tube flow model

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ABSTRACT

We combine linear and nonlinear signal analysis techniques to investigate the transmission of pressure signals along a one-dimensional model of fluid flow in an elastic tube. We derive a simple, generally applicable measure for the robustness of a simulated vessel against in vivo pressure fluctuations, based on quantifying the degree of synchronization between proximal and distal pressure pulses. The practical use of this measure will be in its application to simulated pulses generated in response to a stochastic forcing term mimicking biological variations of root pressure in arterial blood flow.

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1. Introduction

We present an analysis of how pressure forcing effects signal propagation along a modeled collapsible elastic tube. The pressure signals are generated using a one-dimensional flow model based on the inviscid, one-dimensional (area-averaged) form of the mass and momentum conservation equations, and a state equation between the vessel cross-sectional area and pressure [2, 12]. While previous studies have assumed fixed, periodic functions for the excitation pressure pulse as the proximal boundary condition, here we consider stochastic forcing pulses applicable to in vivo arterial flow dynamics. Using spectral analysis methods based on synchronization theory, we introduce a novel index for measuring the robustness of the model against fluctuations in the forcing signal, based on a general scheme for deriving low-dimensional measures of (biological) performance from higher-dimensional systems of equations.

2. Methods

2.1. Flow modeling: generation of pressure signals

The one-dimensional model equations for flow in an elastic tube can be written in conservative form [2], viz.,

\[
\frac{\partial \mathbf{U}}{\partial t} + \frac{\partial \mathbf{F}}{\partial z} = \mathbf{Q},
\]

where the vectors \( \mathbf{U} \), \( \mathbf{F} \) and \( \mathbf{Q} \) are defined below:

\[
\mathbf{U} = \begin{bmatrix} S \\ V \end{bmatrix}, \quad \mathbf{F} = \begin{bmatrix} SV \\ \frac{1}{2} V^2 \end{bmatrix}, \quad \mathbf{Q} = \begin{bmatrix} -\psi \\ \frac{1}{\rho} \frac{\partial p}{\partial z} \end{bmatrix}.
\]

Here, \( V(z, t) \) is the instantaneous, area-averaged flow velocity, \( p(z, t) \) is the local vessel pressure, \( \psi \) is the rate of volumetric outflow per unit length, and the effect of wall friction is parameterized by the force term \( f \) (force per unit mass of fluid in the axial \( z \)-direction). Assuming no branching or seepage in the elastic tube, it is sufficient to set \( \psi = 0 \). Fluid density is \( \rho \), and the cross-sectional area of the vessel \( S \), which is a function of the vessel pressure \( p \) and axial coordinate \( z \), is calculated as [2]:

\[
S(p, z) = S_0(p_0) e^{-\beta z/(p-p_0)/\rho c(p, z)c(p_0, z)},
\]

(2)

\( S_0(p_0) \) is the cross-sectional area at the left (inflow) boundary. In our model we used \( S_0(p_0) = 7.07 \text{ cm}^2 \) and \( \beta = 0.25 \) as a rough approximation for the human pulmonary artery. At this preliminary stage of our research, the emphasis is on the analysis technique for signal propagation in an elastic tube model of short length with no bifurcations; more comprehensive and accurate modeling of pulse propagation in the human pulmonary artery is ongoing.

In Eq. (2), \( S(p, z) \) depends on \( c \), the wave speed in the fluid which varies linearly with tube length, \( z \), written as:

\[
c(p, z) = (97 + 2.03p)(1 + 0.02z).
\]

(3)

Anliker et al. [2] derived (2) and (3) for the dog aorta from a general form of the Moens–Korteweg equation. Here, we set equation constants within ranges applicable to human blood.
We assume the flow is laminar and unsteady, so that the friction term $f$ can be written using Poiseuille's formula for circular pipes:

$$f_{\text{laminar}} = -8\pi\frac{\mu V}{\rho S}. \quad (4)$$

We consider an elastic tube of reference length, $L = 25$ cm and use fluid properties relevant to human blood such as density, $\rho = 1.06$ g/cm$^3$; viscosity, $\mu = 0.049$ poise; and reference pressure, $p_0 = 80$ mm Hg which represents the approximate maximum pressure in the system.

The proximal boundary condition for pressure $p_L(t)$ is time-varying while the distal boundary condition was fixed at 15 mm Hg. The distal boundary condition requires that the diameter at this end is very small. This requirement is roughly satisfied here, as the outlet diameter is approximately 0.076 cm at full distension, much smaller than the maximum inlet diameter of 3.14 cm. In hyperbolic equations such as (1), it is sufficient to impose a constant pressure outflow condition as in [12].

We numerically integrate the resulting system of hyperbolic equations (1), using the two-step explicit [10] finite-difference method [4]. This method is dissipative, and consists of a forward-difference predictor step and a backward-difference corrector step; it has been widely used in aerodynamics applications. In our computations, a very small amount of numerical dissipation in the form of a small numerical dissipation was maintained with a time step $\Delta t = 0.25$ cm, numerical stability of this system of hyperbolic equations was maintained with a time step $\Delta t = 0.0002$ s. Calculations with half the mesh size demonstrated that the solution is largely mesh independent. Initial conditions have very little effect on the solution once statistical steady state is reached; consequently it was sufficient to assume that pressure, velocity and area were exponentially decreasing functions of distance, based on inflow–outflow boundary conditions [12].

2.2. Stochastic boundary conditions and the synchronization index

We investigated how variations in the proximal boundary condition $p_L(t)$ affect the pressure signal $p(z,t)$ along the vessel. A rate of $B$ beats/min (bpm) generates a forcing pulse with frequency $f_B = B/60$ Hz. The primary outputs of the model were to be the pressure time series $p(z,t)$ sampled at several points along the tube. We chose $z = 0.041$, $0.2L$, $0.4L$, $0.6L$, $0.8L$ and $0.96L$, focusing on the downstream pressure $p_D(z,t)$ and respiration $D(t)$, where $0 \leq D(t) \leq 0.2$ cm.

Initially, we considered periodic proximal boundary conditions $p_L(t)$. Assuming a basic pressure pulse profile $p_L^{(1)}(t)$ defined on the interval $[0, 1]$ with $p_L^{(0)}(t) = p_L^{(0)}(0)$, $p_L(t)$ was defined for a given forcing frequency $f_B$ by $p_L(t) = p_L^{(0)}(p_L, t)$. Next, to assess how the model responds to the aperiodic forcing signals frequently observed in vivo, caused by higher order effects such as the movement of the vessel with each heart beat and respiration [9,5], simulations were carried out with a stochastic forcing pressure pulse $p_L(t)$. This was constructed by taking the frequency of the kth successive forcing cycles $f_B$ to be a normally distributed random variable with mean and standard deviation equal to 85/60 Hz and 10/60 Hz, respectively, corresponding to a rate distributed normally around a typical value of 85 bpm. Formally, the stochastic simulations were obtained by integrating the model equations with proximal boundary conditions $p_L(t)$ given by,

$$p_L(t) = p_L^{(0)} \left( \sum_{n=1}^{k-1} \frac{1}{f_B} \right) : \sum_{n=1}^{k-1} \frac{1}{f_B} \leq \frac{k-1}{f_B}, \quad (5)$$

for $k \geq 1$.

The manner in which the pressure signal was modified by the tube was quantified by the degree to which the distal pressure signal was synchronized with the proximal forcing pulse. Given a general time series $x(t)$, a simple measure of the instantaneous phase $-\pi < \phi(x(t)) \leq \pi$ can be computed from the analytic signal $x(t)+\text{sign}(x(t))|x(t)|^{1/2}$, where $x(t)$ is the Hilbert transform of $x(t)$. In signal processing, the Hilbert transform provides a robust way of calculating the instantaneous phase of a nonstationary signal [3]. Consequently, in recent years, it has become a popular tool for determining whether aperiodic, or even chaotic, time series are synchronized [11,8]. In particular, two signals $x(t)$ and $y(t)$ are defined as synchronized at a given time $t$ if

$$|\phi(x(t)) - \phi(y(t))| < \epsilon, \quad (6)$$

where $\epsilon$ is small compared to $2\pi$ [11]. A simple measure $S_I$ of how well $x(t)$ and $y(t)$ are synchronized over a time interval $(t_1, t_2)$ can then be obtained by dividing the length of time that (6) holds within $(t_1, t_2)$ by the interval length $t_2 - t_1$, with values of 1 and 0 denoting complete synchronization and desynchronization, respectively. It follows that setting $x(t) = p_L(t)$ and $y(t) = p(z,t)$ in (6) yields a measure of how well the pressure signal at point $z$ along the tube is synchronized to the forcing pulse.

3. Results

For periodic proximal boundary conditions, over a broad range of forcing frequencies, the model asymptotically converged to a closed curve, or limit cycle, in the phase space; that is the downstream time series were periodic pulses with the same frequency (and hence period) as that of the forcing cycle [6]. This frequency-locking is plotted over the interval $2/3 \leq f_B \leq 8/3$ (Fig. 1A), corresponding to the bpm range $40 \leq B \leq 160$ (Fig. 1B) shows the synchrony between the upstream and downstream pressure time series for a particular frequency value near the middle of this range). The model is thus robust to periodic forcing signals over a biological range of frequencies, in the sense that the input and output signals are synchronized; this corresponds to a physiological system for which the arterial root pressure pulse is being effectively propagated along the vessel.

For stochastic forcing pulses, generated as described above, the pressure pulse is modified by the dynamics of the elastic tube model in a nontrivial manner; high frequency components appear in the power spectrum of $p_L(t)$ that are not simple harmonics of the forcing signal, reducing the fidelity of pressure pulse transmission along the tube (Fig. 2A and B).

Application of the synchronization index $S_I$ quantified the conversion of the stochastic pressure pulse $p_L(t)$ into the downstream pressure signal $p_D(t)$ by the elastic tube (Fig. 3A and B). $S_I$ was computed over each of the intervals that define $p_L(t)$ through equation (5), yielding a measure $S_I(f_B)$ of how well the downstream pulse synchronizes to the components of the forcing pulse with frequency $f_B$. The dependence of $S_I$ on forcing cycle frequency $f_B$, obtained by pooling the $S_I(f_B)$ values computed for a simulation with $k \geq 1$, reveals that overall, $S_I$ decreases with $f_B$, as a result of the high frequency oscillations in $p_D(t)$ elicited by short forcing periods (Fig. 4A). This synchronization–frequency distribution $S_I(f_B)$ leads to a simple measure for the robustness $R$ of the flow dynamics at a point $z$ along the tube with respect to the forcing pressure signal. Following the general scheme proposed by [7], $R$ has the form

$$R = \frac{1}{f_2 - f_1} \int_{f_1}^{f_2} |\theta(f)|S_I(f)|df| \quad (7)$$

where $\theta(f)$ is the frequency probability distribution, $(f_1, f_2)$ is the physiological frequency range and $S_I(f)$ is the synchronization–frequency distribution computed for the pres-
Robustness of the model to a periodic forcing pressure pulse $p_L(t)$. Panel (A) shows how the frequency $f_{p_D}$ of the downstream pressure signal $p_D(t)=p(D,t)$ varies with the frequency $f_{p_L}$ of the forcing pulse; it can be seen that $f_{p_D}$ is locked to $f_{p_L}$ across the physiological range. This locking is illustrated for the forcing frequency 1.42 Hz (corresponding to 85 beats/min) in (B), which shows a portion of both the forcing pulse and the downstream time series.

Frequency response of the model to a stochastic forcing pressure pulse $p_L(t)$. (A) and (B) plot the energy spectral density $|F(f)|^2$ for $p_L(t)$ and the downstream pressure signal $p_D(t)$ respectively, calculated from the Fourier transforms $F(f)$ of the signals. The dotted lines indicate multiples of the mean forcing frequency.

Measurement of the synchronization of the pressure signal $p(z,t)$ with the stochastic forcing pulse $p_L(t)$. The signals are considered synchronized when $|\phi(p(z,t)) - \phi(p_L(t))| < \varepsilon$ (here, $\phi(\cdot)$ denotes the instantaneous phase of its argument, computed using the Hilbert transform: see text for further details). For a forcing cycle with frequency $f_{p_L}$, this yields a synchronization–frequency measure $S(f_{p_L})$, defined as the fraction of the cycle for which the signals are synchronized. The application of these measures to a representative portion of the downstream pressure signal $p_L(t)=p(D,t)$ is plotted. Panel (A) shows the variation of the signals and (B) the corresponding variation in phase difference $\phi(p_L(t)) - \phi(p_L(t))$. Dotted lines denote the synchronization threshold $\varepsilon = \pi/4$ in this case and gray lines delineate individual forcing cycles. From left to right, the cycles shown yield the $S(f_{p_L})$ values 0.58, 0.83, 1.00 and 0.77.
be a threshold process, with reduced robustness only observed in the distal region of the elastic tube.

4. Discussion

We have presented a new method for analyzing the propagation of pressure signals along collapsible elastic vessels, based on a more general scheme for assessing the robustness of a simulated biological system to environmental perturbations. Robustness is one of the most fundamental properties of biological systems and in recent years there has been increasing interest in using robustness indices to assess biological performance, including transitions to disease states such as cancer [7,1]. Within this framework, our method leads to a simple, scalar measure of the fidelity of pressure transmission. Analysis of simulated waveforms generated by stochastic forcing pulses revealed a complex, threshold-dependent variation in robustness along the vessel. This finding shows that our robustness index provides a simple, low-dimensional measure of system performance that could, in principle, be used to compare model simulations against experimental data. We are currently extending this work to quantitative modeling of blood flow in human arteries. As part of this programme, we are exploring the use of vessel robustness as an index of hemodynamic pathology, complementing approaches based on direct waveform analysis, such as the average velocity and pressure profiles that have been employed for this purpose previously [9].

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Conflict of interest statement

There is no conflict of interest between any of the authors and any organization, person or any other entity regarding the referenced manuscript and the related research work.

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