Microvascular Research 100 (2015) 40–47

Contents lists available at ScienceDirect

Microvascular Research

journal homepage: www.elsevier.com/locate/ymvre

An effective model of blood flow in capillary beds

Sebastian Acosta *, Daniel J. Penny, Craig G. Rusin

Department of Pediatrics — Cardiology, Baylor College of Medicine, Houston TX, USA
Department of Pediatric Medicine — Cardiology, Texas Children's Hospital, Houston TX, USA

ARTICLE INFO

Article history:
Accepted 24 April 2015
Available online 30 April 2015

Keywords:
Microcirculation
Compliance
Resistance
Hypertension
Critical closing pressure
Perfusion
Lumped-parameter models
Nonlinear Windkessel
Computational hemodynamics

ABSTRACT

In this article we derive applicable expressions for the macroscopic compliance and resistance of microvascular networks. This work yields a lumped-parameter model to describe the hemodynamics of capillary beds. Our derivation takes into account the multiscale nature of capillary networks, the influence of blood volume and pressure on the effective resistance and compliance, as well as, the nonlinear interdependence between these two properties. As a result, we obtain a simple and useful model to study hypotensive and hypertensive phenomena. We include two implementations of our theory: (i) pulmonary hypertension where the flow resistance is predicted as a function of pulmonary vascular tone. We derive from first-principles the inverse proportional relation between resistance and compliance of the pulmonary tree, which explains why the RC factor remains nearly constant across a population with increasing severity of pulmonary hypertension. (ii) The critical closing pressure in pulmonary hypotension where the flow rate dramatically decreases due to the partial collapse of the capillary bed. In both cases, the results from our proposed model compare accurately with experimental data.

Introduction

For a model of the circulatory system to be useful, it must incorporate accurate estimates of the elastic compliance and flow resistance of vascular components. These two properties govern hemodynamic characteristics such as the propagation of pressures waves in the arterial tree, the pressure drop across capillary beds, and the distribution of the cardiac output to the organs. Lumped-parameter or Windkessel models are often used to describe the dynamics of these systems, by simplifying the governing equations of hemodynamics, in local regions or the entire circulatory system, into a set of linear differential equations (Westerhof et al., 2009; Shi et al., 2011). These models may have one or several compartments. In turn, each compartment is described by a combination of resistance R, compliance C and inertance I, leading to differential equations of the form

$$I\frac{dQ}{dt} + RQ = P_{\text{in}} - P_{\text{out}} \qquad \text{and} \qquad C\frac{dP}{dt} = Q_{\text{in}} - Q_{\text{out}}, \tag{1}$$

for the pressure P and flow rate Q. In such models, it is common to approximate the resistance, compliance and inertance parameters of the vascular elements as separate constants. While linear Windkessel models have provided a framework for understanding many circulatory phenomena, they are inherently limited to the *fixed* conditions defined by their parameters.

In reality vascular compliance and resistance are dynamic properties whose values depend on each other. Moreover, the hemodynamic properties of a given capillary bed also depend on the conditions of other major capillary beds in the circulatory system. Such global interaction may follow from redistribution of blood volume due to vasoconstriction, from variations of cardiac output (natural or induced), from surgical changes in circulatory anatomy, etc. We claim that most of the currently employed lumped-parameter models of the circulatory system do not take into account such unavoidable interactions and may fail to realistically simulate the circulatory system under pathological or abnormal conditions.

In this article, we propose a novel derivation of the effective resistance and compliance of capillary beds. This derivation is carried out from the basic principles of mechanics which take into account the influence of blood volume/pressure on the resistance and compliance, as well as, the nonlinear interdependence between these two properties. As a result, we obtain a single effective model for studying hypo- and hyper-tensive phenomena in regimes where the assumption of constant values for resistance and compliance is no longer appropriate. By *effective* we mean results that depend only on *macroscopic* quantities such as pressure, volume, viscosity, etc. The goal is to lump microscopic properties into correction factors while respecting the underlying physical laws governing these systems and avoiding large errors that could arise from the naive manipulation of the multiscale nature of capillary beds.

* Corresponding author at: Department of Pediatrics — Cardiology, Baylor College of Medicine, Houston TX, USA.
E-mail addresses: sacosta@bcm.edu (S. Acosta), djpenny@texaschildrens.org (D.J. Penny), crusin@bcm.edu (C.G. Rusin).

http://dx.doi.org/10.1016/j.mvr.2015.04.009
0026-2862/

Several different approaches have been considered for modeling the microscopic architecture of capillary networks including fractal scaling laws (Krenz et al., 1992; West et al., 1997; Kamiya and Takahashi, 2007; Huo and Kassab, 2012) and vascular imaging segmentation (Molthen et al., 2004; Burrowes et al., 2005; Cassot et al., 2006; Reichold et al., 2009; Smith et al., 2015). See also the reviews (Clough et al., 2006; Tawhai et al., 2011; Tawhai and Bates, 2011). Although a high level of fidelity may be achieved by accounting for detailed microstructure, it is at the expense of incorporating a large number of adjustable morphometric parameters which are often difficult to measure. In contrast, our objective is to build a macroscopic model with the least possible number of parameters while still providing a robust and accurate solution.

We demonstrate that this novel model can describe both hypertensive and hypotensive scenarios, and validate the model against clinical measurements. In the case of pulmonary hypertension due to progressive stiffening of pulmonary vessels (Wang and Chesler, 2011, 2013), a reduction in pulmonary compliance eventually induces an increment of vascular resistance. This inverse proportional relationship between resistance and compliance is an example of the interdependence of these two properties. Our model predicts the resistance as a function of vascular stiffness. In turn, we explain from first-principles why the RC-time of the pulmonary tree is nearly constant across a population with increasing severity of pulmonary hypertension. This relationship has been observed experimentally (Reuben, 1971; Lankhaar et al., 2006, 2008; Saouti et al., 2010a), leading to other striking consequences such as the proportionality between diastolic, systolic and mean pulmonary arterial pressure (Saouti et al., 2010a; Kind et al., 2011) and the proportionality between the oscillatory and total power delivered by the right ventricle (Saouti et al., 2010a,b). In the case of hypotension, it is believed that critical closing pressure plays an important role in the cessation of blood flow (Lopez-Muniz et al., 1968; Czosnyka et al., 1999; Thees et al., 2002; Panerai, 2003; Varsos et al., 2013) resulting in ischemia. Hence, it is imperative to account for this phenomenon in a hemodynamic model. Experimental data indicates that capillary beds experience a gradual collapse as the transmural pressure diminishes. This is a multiscale effect in which the mechanical action of a large number of small vessels conspires to produce the macroscopic behavior of the entire bed. We propose an effective model to quantify the partial collapse of a capillary bed and explain from first-principles the pressure-flow curves observed from empirical data (Badeer and Hicks, 1992; Permutt et al., 1962; Graham et al., 1982). We acknowledge that our model is validated against experimental data for the pulmonary microcirculation only. However, qualitatively similar behavior has been observed for flow cessation in the liver (Mitzner, 1974; Brienza et al., 1995), and in skeletal muscle of humans (Nielsen, 1983) and Hamsters (Vollmar et al., 1999). It remains to perform quantitative comparisons between our model and experimental data for these and other organs.

This paper is structured as follows: Stochastic model of a capillary bed Section contains a derivation of an effective stress–strain law for the entire capillary bed. This derivation is carried out from the basic stress–strain relation for compliant vessels taking into account their ability to collapse when the transmural pressure is sufficiently small. The effective stress–strain law is then employed in Effective compliance and resistance Section to obtain the overall compliance and resistance of the capillary bed. In Pulmonary hypertension Section, we use our model to replicate the experimentally observed inverse proportional relationship between resistance and compliance in pulmonary hypertension. Critical closing pressure Section contains concrete examples of the effect of vascular collapse on the pressure-flow curves of lungs. In both Sections Pulmonary hypertension and Critical closing pressure, we compare our theoretical results with experimental data found in the literature. Discussion Section concludes with a short discussion of the limitations of our model and its importance to physiological and clinical applications.

Stochastic model of a capillary bed

In this section we set forth a model of a capillary bed as a stochastic collection of connected vessels having physical properties characterized by certain random distributions. The network is assumed to conserve blood mass and to dissipate fluid momentum due to viscous friction which is a dominant factor in microcirculation. The capillary bed is parametrized along the inlet-to-outlet direction by the variable $x \in [0, L]$ where L represents the circulatory length of the capillary bed. The geometric dimensions of the vessels within the bed vary dramatically along this longitudinal x-direction. We take into account this transition from arterioles to capillaries to venules by considering vessels with changing cross-sectional area. This cross-sectional area is allowed to vary many orders of magnitude, that is, from $(mm)^2$ to $(\mu m)^2$ and back to $(mm)^2$. For each value of x, we consider a cross-sectional plane which intersects a number $N(x)$ of vessels. This varying number also attains multiple scales ranging from ~10 at the arterial entrance, to ~10^8 in the capillary region, back to ~10 at the venous outlet of the bed. For each point x, the elastic and geometric characteristics of the vessels on the cross-sectional plane are modeled statistically with an abstract random variable $\omega \in \Omega(x)$. Here $\Omega(x)$ denotes a probability space representing the variety of paths that a blood cell may take when traveling across the capillary bed.

To obtain sufficiently accurate results, we must correctly account for transitions to and from disparate scales which is one of major challenges in modeling the multiscale nature of microcirculation (Secomb and Pries, 2011; Lee and Smith, 2012; Popel and Johnson, 2005). However, in order to obtain simple expressions, we also tolerate uncertainty within one order of magnitude which we calibrate with certain correction factors. We start from the basic relationship between pressure and radius of a single vessel including its ability to collapse. Then, in the next section, we will appropriately scale up our model to obtain effective or average properties. For a generic vessel, we assume the following idealized stress–strain law,

$$\frac{r-r_o}{r_o} = \begin{cases} \gamma(P-P_o) & \text{if } P-P_o > P_{cr} \\ -1 & \text{if } P-P_o < P_{cr} \end{cases} \tag{2}$$

where P and P_o represent the pressure inside and outside the vessel, respectively. The wall compliance coefficient γ is of the form,

$$\gamma = \frac{(1-\sigma^2)}{E}\frac{r_o}{h_o}. \tag{3}$$

Here h_o is wall-thickness and r_o is the unperturbed radius of the vessel. We assume that the ratio r_o/h_o remains bounded across the network, with changes no greater than one order of magnitude. Empirical measurements show that $r_o/h_o \approx 10$ on the arterial side, and $r_o/h_o \approx 60$ on the venous side. We also assume small variations in the Young's modulus E and the Poisson's ratio σ. Notice that Eq. (2) models the ability of the blood vessel to collapse when the transmural pressure $P - P_o$ is sufficiently small. The critical value of this transmural pressure is denoted by P_{cr} which we assume to be a random variable.

The vessel stress–strain law Eq. (2) is valid under nearly isobaric conditions. Hence, for now we assume that both P and P_o are nearly constant. Moreover, in order to simplify the calculations, we assume that r_o, P_{cr} and γ are *statistically independent* on each probability space $\Omega(x)$. Let $H(s)$ denote the Heaviside function, that is, $H(s) = 1$ if $s > 0$ and $H(s) = 0$ otherwise. Then the stress–strain law (Eq. (2)) leads to

$$\begin{aligned} r^2 - r_o^2 &= r_o^2(1 + r/r_o)(\gamma P_{tr} H(P_{tr} - P_{cr}) - H(P_{cr} - P_{tr})) \\ &= r_o^2(\gamma P_{tr} H(P_{tr} - P_{cr}) - H(P_{cr} - P_{tr}))(2 + \gamma P_{tr} H(P_{tr} - P_{cr}) - H(P_{cr} - P_{tr})), \end{aligned} \tag{4}$$

where $P_{tr} = P - P_o$ is the transmural pressure. After taking the expectation value (average over the random variable $\omega \in \Omega$), we obtain terms