HEMODYNAMICS IN HUMANS: PHYSIOLOGY AND MATHEMATICAL MODELS

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Contents

Summary

This paper provides an overview of areas of modeling related to hemodynamics. Hemodynamics involves important aspects of the cardiovascular system related to characteristics of blood, blood pressure, blood flow, tissue perfusion, and physical quantities governing fluid flow through the arteries, veins, and capillaries of the vascular tree. This article is written as a companion to the Circulatory System article in this encyclopedia. The article begins with a discussion of basic hemodynamic principles and fundamental mathematical expressions. Several models related to hemodynamic topics are discussed in detail and extensive references are given for other representative models in these and other key areas with a focus on models related to clinical issues. Models of the cardiovascular system as a whole and its control mechanisms will be discussed in the Circulatory System article.

Given space limitations, we will focus primarily on lumped compartment models in this discussion although areas where distributive models can be applied will also be examined.

1. Introduction

Hemodynamics focuses on those aspects of the cardiovascular system related to characteristics of blood, blood pressure, blood flow, tissue perfusion, and physical quantities governing fluid flow through the arteries, veins, and capillaries of the vascular tree.

This article is written as a companion to the *Circulatory System* article in this encyclopedia. Obviously hemodynamics and the circulatory system are highly interrelated topics so that the partition of topics for the two articles is a question of emphasis. In this article we focus on those important components that form the basis for cardiovascular function while reserving topics related to system structure and behavior for the circulatory system article. Hence, this article discusses the physical and physiological components that are involved in the transport of blood around the body issues, while topics such as blood pressure control and mechanisms such as the baroreflex will be primarily discussed in the circulatory system article.

Models of the overall cardiovascular system and control system will be discussed in the *Circulatory System* article while example component submodels will be discussed in this article. We will choose examples primarily from lumped compartment models in this discussion although areas where distributive models can be applied will also be examined as well. This choice is based on space limitations related to the fact that distributive models generally are represented by partial differential equations and involve both greater complexity and numerical challenges.

2. Cardiovascular System and Hemodynamics

In this section we review the key concepts, principles, and physiological facts necessary for modeling in hemodynamics.

2.1. Principal Elements of Hemodynamics of the Human Cardiovascular System: Structure and Function

2.1. 1. Pressures

Blood pressure provides the force that drives blood through the vasculature. This pressure is produced during a heart beat which generates a pulse pressure wave. This pressure wave is transmitted throughout the vasculature. A number of key pressures characterize flow at various levels of the vascular tree. Some important pressures are:

- Pulse pressure which is the difference between the systolic P_{sys} and diastolic P_{dias} blood pressures reflecting the action of the pumping heart (see Section 2.1.7). Typical values are 120 mmHg for systolic and 80 mmHg for diastolic pressure.
- Mean arterial pressure $\overline{P_{\text{as}}}$ which is a weighted average of diastolic and systolic pressures (weighted because blood is longer in the diastolic phase) represents a pressure at the level of the main arteries: $\overline{P_{\text{as}}} = P_{\text{dias}} + (P_{\text{sys}} - P_{\text{dias}})/3$.

- Mean capillary pressure which is the mean pressure at the level of the capillaries. Capillary pressure represents the force driving blood perfusion of the various tissues. A typical value for arterial capillary pressure is 35 mmHg while a typical venous capillary pressure is 15 mmHg. Capillary pressure is one of the four Starling forces governing exchange between interstitial fluid and blood.
- Central venous pressure (CVP) which is the pressure at the entrance to the right atrium with a typical value from 0 to 7 mmHg.
- Mean circulatory pressure (MCP) which is the pressure at which the entire circulatory system pressures are in equilibrium and hence blood flow would cease (around 7 mmHg).

Note that CVP must be lower than MCP because as CVP increases the positive difference between CVP and capillary pressure decreases. This lowers venous return of blood to the right atrium.
See the text book on the cardiovascular system by J.R. Levick (2003) and the text on hemodynamics by N. Westerhof et al. (2005) for further discussion on physiological aspects of the vascular tree, flows, and pressures. And the article by K. Muralidhar (2002) for listing of pressure ranges and approaches to measurements.

2.1. 2. Physical Flow Quantities

A vascular element such as an artery or vein has characteristics very much like a tube. Blood flow F through such a vascular tube depends on the pressure difference P between the input and output ends of the vascular tube and on the resistance R to the flow inherent in the vascular tube.

The input and output sources are typically adjacent physiological compartments. Given adjacent compartments A and B, laminar flow between the compartments is quantified via Ohm's law:

$$F = \frac{1}{R}(P_A - P_B). \qquad (1)$$

Flow is laminar if it is smooth with parallel adjacent flow trajectories which may vary in velocity but do not mix. Laminar flow is found in the major arteries and veins, while bolus flow (one blood cell at a time) is found in the capillaries, and turbulent flow is found in the ventricles. Non-laminar flow, vortices, and turbulence can develop at vascular branches, at partial blockages, at surgical bypasses, and at stenosi. These perturbations generate stresses on the vascular wall and may initiate or further the formation of unwanted deposits at the sites of these disturbances.

Flow is pulsatile, since the heart pumps in cycles of filling and ejection (Section 2.1.7). A topic of interest related to pulsatile flow involves the reflection back to the ventricle of pulse pressure waves. These waves are reflected from vascular branch points such as where the aorta branches into smaller arteries, for example. Both the speed, and timing of such waves have been studied for potential clinical meaning. For an example of the physical modeling of this phenomenon see the work of F. Pythoud and colleagues in 1994, while for mathematical analysis see the model of D. S. Berger and colleagues of

1994, and for potential clinical interpretations see the research of W. W Nichols presented in 2005.

The resistance to flow in a vascular element is determined by vascular cross-sectional radius and other factors described in the *Hagen-Poiseuille* equation. This equation, assuming a slow viscous incompressible flow F through a fixed circular cross-sectional tube of length L and radius r, takes the form

$$\Delta P = \frac{8\mu LF}{\pi r^4},$$

where $\Delta P = P_A - P_B$ is the pressure drop between compartments A and B. Dividing this expression by F gives us an expression for R via Eq. (1). Hence R is given as

$$R = \frac{8\mu L}{\pi r^4},$$

which reflects the fact that R varies inversely with the fourth power of the radius and is directly proportional to the length of the tube.

2.1. 3. Compliance and Capacitance: Physical Vascular Volume Quantities

Considered again as a tube that directs flow, a vascular tube contains a volume of fluid that fills the tube but does not distend the walls of the tube. We refer to this as the *unstressed volume* V_{u} of the vascular element. The introduction of extra volume generates a pressure that necessarily distends the tube to accommodate the extra volume. This volume is referred to as *stressed volume* V_{s}. The ease of distension of a vascular wall by a pressure is referred to by the term *compliance* c. The relation between the stressing pressure P and the volume introduced by the wall stretch is given by

$$V_{\mathrm{s}} = cP. \qquad (2)$$

The above equation reflects a linear volume-pressure relation for the vascular element assuming that c is constant which is reasonable in vasculature elements (and compartments) where pressure variations cause minor variations in the distension of the element. Significant distension can change the wall stretch characteristics and hence compliance can change with distension. The systemic arterial vasculature is under high pressure but is comparatively stiff (the aorta does stretch with the heart beat pulse) so c is almost constant while the venous compartment is under less pressure but very distensible and hence c may vary as distension develops over an operating pressure range.

Hence, in certain cases and over certain pressure intervals, it is too much of a simplification to assume that compliance is constant. See for example the study by M.R. Risk and colleagues (2003) for an examination of variable compliance in the venous

system. Given that c varies in a generally non-linear fashion as distension increases, a more detailed modeling of the pressure-volume relation may become important to capture the true functioning of a system.

Assuming a constant compliance, we express the total volume V of a vascular element by including stressed and unstressed volume so that:

$$V = cP + V_{\mathrm{u}}, \tag{3}$$

The entire volume in a vascular element is referred to as the capacitance of that element.

2.1. 4. Schematic Diagrams

In many ways (such as in the above formulas) blood fluid flow and electrical flow behave similarly.
Thus, in the early years of modeling, electrical symbols and indeed electrical circuits were used to describe and model cardiovascular and hemodynamic behavior. Table 1 illustrates the parallels between the two flows. Based on these parallels, electrical and electronic circuit symbols have been used to describe cardiovascular structures. The symbols given in Figure 1 are used to illustrate some of the elements in the table. To see how such symbols are employed, consider the Windkessel model configuration given in Figure 2. Although appearing as an electrical circuit, this figure represents a lumped model of the vascular system connected to a heart. This model will appear in a modeling example in Section 4.2.1.

Electrical	Physiological
Voltage E	Fluid pressure P
Current I	Fluid flow F
Resistance R	Vascular resistance R
Capacitance C	Compliance C
Inductance L	Fluid mass or inertia forces L
Diode	One way valve

Table 1. Electrical-Physiological comparisons

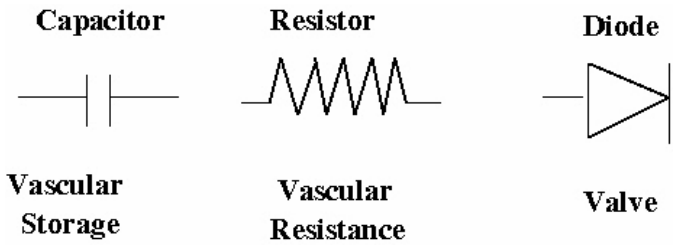

Figure 1. Electrical symbols used for physiological quantities

2.1. 5. Combining Vascular Elements

We also need to note the following rules for combining electrical resistances R and capacitances C following Kirchhoff's Laws in the electrical flow setting.

- If R_1 and R_2 are connected in series then the total resistance R is given by

$$R = R_1 + R_2 \tag{4}$$

so that a resistances in series will contribute to the total resistance additively.

- If R_1 and R_2 are connected in parallel we have

$$R = (\frac{1}{R_1} + \frac{1}{R_2})^{-1} \tag{5}$$

so that a parallel arrangement reduces the overall resistance by adding extra pathways for flow.

- If capacitances are connected in series we have

$$C = \left(\frac{1}{C_1} + \frac{1}{C_2} \right)^{-1} \tag{6}$$

so that when capacitances are connected in series the total effective storage is lower than the individual capacitances.

- If capacitances are connected in parallel we have

$$C = C_1 + C_2 \tag{7}$$

so that a resistances in series will contribute to the total additively.

These rules carry over to analogously to rules for physiology as reflected in Table 1.

Finally, we note

$$V = \int F dt \tag{8}$$

reflecting the fact that fluid volume V is the integral of fluid flow F .

2.1.6. Windkessel Model

The Windkessel model, first introduced by Otto Frank in 1899, has been used as an excellent but simple approximation of the load placed on the heart for studies of heart

function. Windkessel models include lumped parameter models of the vasculature. The two-element version includes a resistor and capacitor to simulate vascular resistance and vascular compliance.

The three-element version includes an extra resistance reflecting resistance of a ventricular valve while the four-element version includes an element for inductance representing inertia of blood flow. See Shim et al. (1994) for an example of how the application of a three-element Windkessel model can be used to estimate arterial parameters. See the interesting study by N. Stergiopulos and colleagues given in 1999 for an examination of the potential advantages of a four-element Windkessel model over simpler versions.

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The schematic model given in Figure 2 contains a three-element Windkessel model in the systemic circuit loop. This arrangement will be applied to a pulsatile heart model described in Section 4.2.1. In this diagram following the symbolism given above, Q represents cardiac output and consequent blood flows, with Q_s the systemic blood flow and Q_c the blood stored in the compliant arteries. Q_{in} denotes the flow into the ventricle, Q_v the flow out. R again represents resistance to flow, with R_0 representing the aortic resistance (impedance), R_s the total systemic resistance. The mitral (left) and the aortic (right) valves in the diagram are represented as diodes with p_r as the fixed preload, p_v and p_a as ventricular and arterial pressures respectively.

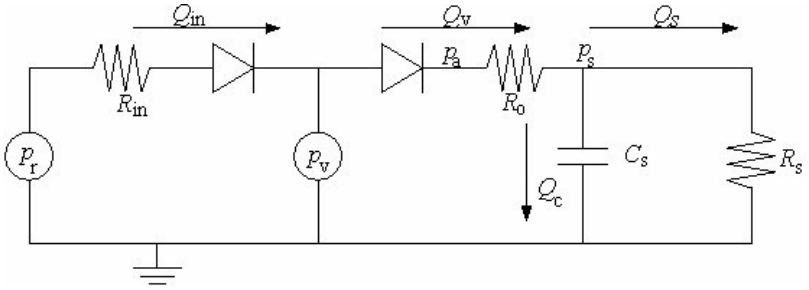

Figure 2. Windkessel model applied to the Ottesen pulsatile heart. Q denotes blood flows from cardiac output, R resistance, p pressure, and C compliances. Details are discussed in the text.

2.1.7. The Heart

The heart is essentially two pumps connected in series. Each pump consists of an atrium connected by a one-way valve to a ventricle. The atrium contributes to the process of filling the ventricle. The right atrium and right ventricle combination (we will refer to these as the right heart) pumps blood through the pulmonary circuit while the left atrium and left ventricle combination (left heart) pumps blood to the systemic circuit as depicted in Figure 3.

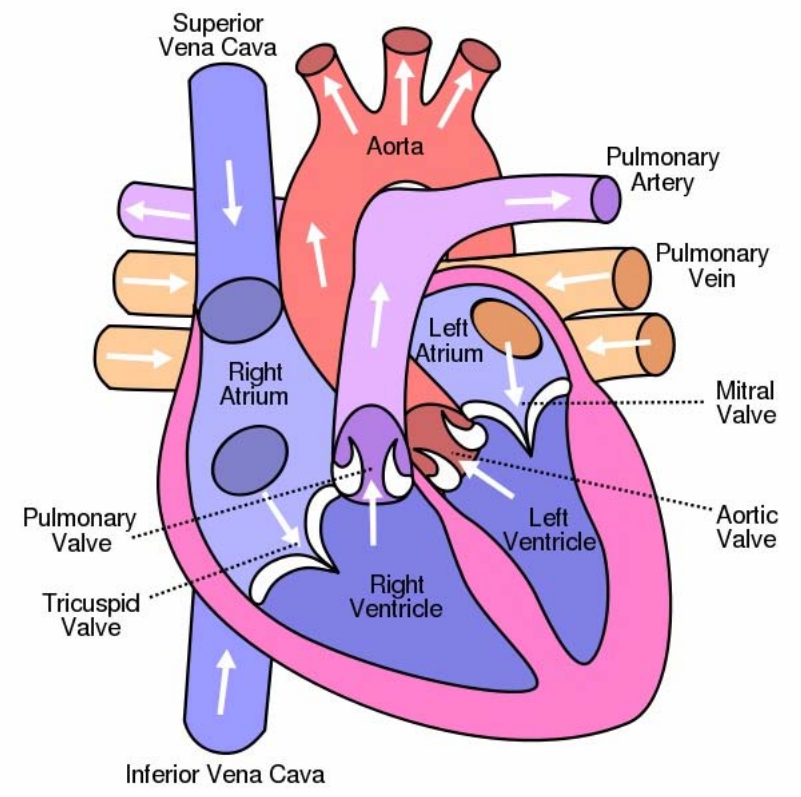

Figure 3. The four chambers of human heart

The filling phase is referred to as the diastolic phase while the pumping phase is referred to as the systolic phase of the cardiac cycle.

As mentioned above the left heart and right heart essentially act as two pumps in series, the smooth functioning of which during perturbations is in general a difficult pump arrangement to engineer. The Frank-Starling mechanism describes the effect that increased distention of the heart due to increased filling of the ventricle during diastole produces an increased energy of contraction during the following systole. This relation is essentially linear in normal operating regimes. It is this mechanism that allows for adjustments to momentary differences in the outputs of the left and right hearts creating the smooth functioning of these two pumps in series. For further details on the heart pumping characteristics, see the important study by A. Noordergraaf and J. Melbin published in 1982.

The cardiac output Q represented in liters per minute generated by a ventricle is given by

$$Q = HV_{\text{str}} \tag{9}$$

where H denotes the heart rate and V_{str} *the stroke volume* which is the volume of blood ejected by one beat of the ventricle.

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Biographical Sketches

Jerry J. Batzel received his PhD from North Carolina State University in 1998 with area of research applied mathematics.
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