1
The Heart and Circulation

This chapter begins a discussion of mathematics in physiology. The discussion begins with the heart and blood circulation in the body. We first outline the structure of the circulation, and then we derive models of blood flow and pressure and mechanisms for controlling them.

1.1 Plan of the Circulation

The function of the heart is to pump blood. The blood carries oxygen (O_2) from the lungs to the various tissues of the body, and it carries carbon dioxide (CO_2) from these tissues back to the lungs.

Since the circulation forms a closed loop, its description can begin anywhere. We begin on the left side of the heart (see Figure 1.1). The *left heart* receives blood that is rich in O_2 and pumps this blood into the systemic arteries. These form a tree of progressively smaller vessels that supply fully oxygenated (and hence bright red!) blood to all of the organs and tissues of the body. From the smallest of the *systemic arteries* blood flows into the systemic capillaries, which are roughly the diameter of a single red blood cell. It is in the capillaries that the actual exchange of O_2 and CO_2 takes place. The blood that leaves the systemic capillaries carries less O_2 and more CO_2 than the blood that entered. (The loss of O_2 causes a change in the color, so that the blood is now more bluish than before.)

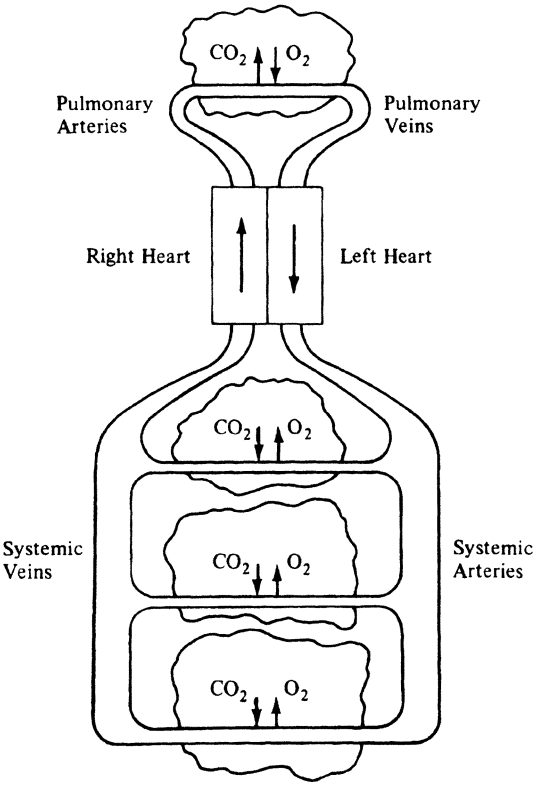

Figure 1.1. Plan of the circulation. Blood flows away from the heart in arteries and back towards the heart in veins. The pulmonary circulation begins on the right side of the heart and ends on the left side, whereas the systemic circulation begins on the left side and ends on the right side. In the pulmonary circulation, oxygen (O_2) is picked up by the blood, and carbon dioxide (CO_2) is removed, as blood flows through the lungs. In the systemic circulation, the reverse happens (O_2 is removed and CO_2 is picked up) as blood flows through the various tissues of the body.

Leaving the systemic capillaries, the blood enters the *systemic veins,* through which it flows in vessels of progressively increasing size toward the right side of the heart.

The *right heart* pumps blood into the *pulmonary arteries,* which form a tree that distributes the blood to the tissues of the lung. The smallest branches of this tree give rise to the *pulmonary capillaries,* where CO_2 leaves the blood stream and O_2 enters from the air space of the lungs. Leaving the pulmonary capillaries, the oxygenated blood is collected in the *pulmonary veins,* through which it flows back to the left heart. This

completes the circulation. The average time required for a red blood cell to complete the circuit that we have described is about 1 minute.

The reader has probably noticed an important symmetry in the plan of the circulation: The blood that leaves the left heart flows through the arteries, capillaries, and veins of the *systemic circulation* before returning to the right heart. Similarly, the blood that leaves the right heart flows through the arteries, capillaries, and veins of the *pulmonary circulation* before returning to the left heart. Of course, these partial "circulations" are not really closed loops, since there is no blood flow directly from one side of the heart to the other (except in the fetal circulation and in certain forms of congenital heart disease).

Because of this symmetry between the systemic and pulmonary circulations, we can expect that the equations of the systemic circulation will have the same form as the equations of the pulmonary circulation. Similarly, the equations of the right and left heart will be the same in form, and the relation of the right heart to the systemic circulation will be the same as the relation of the left heart to the pulmonary circulation. These symmetries in the *form* of the equations are not matched by corresponding symmetries in the *magnitude*, however. That is, the parameters appearing in the equations of the pulmonary circulation have values that are different from the corresponding parameters of the systemic circulation. Because of these differences, the systemic blood volume is about 10 times the pulmonary blood volume, and the systemic arterial pressure is about 6 times the pulmonary arterial pressure (see Table 1.1). One of the themes of this chapter is to study the consequences of this quantitative disparity between the two circulations.

1.2 Volume, Flow, and Pressure

The purpose of this section is to introduce the three physical variables that are needed in a quantitative description of the circulation, to explain the system of units used by physiologists, and to give typical values that occur in the different parts of the circulation.

Since blood is nearly incompressible, the volume of the blood serves as a convenient measure of the amount of blood in any part of the circulation. Volume will be measured in *liters* (1 liter = 1000 cm^3) and designated by the symbol V. The total blood volume (V_0) is about 5 liters, partitioned roughly as shown in Table 1.1.

The definition of the *flow* that we use in this book is the volume of blood per unit time passing a point in the circulation. Thus, flow is measured in liters/minute. We designate flow by the symbol Q. The most important flow in the circulation is the *cardiac output*, which is defined as the volume of blood pumped per unit time by either side of the heart. (This definition

Table 1.1. Normal Resting Pressures and Volumes of the Systemic and Pulmonary Arteries and Veins

	P(mmHg)	V(liters)
sa	100	1.0
sv	2	3.5
pa	15	0.1
pv	5	0.4

(s=systemic, p=pulmonary, a=artery, v=vein)

assumes that the two sides of the heart produce identical outputs. At this point, the reader should be wondering why this is so. The mystery will be cleared up later.) The cardiac output may be calculated as the product of the stroke volume (volume of blood pumped per beat) and the heart rate (number of beats per unit time). Typical values are

$$\begin{aligned} \text{stroke volume} &= 70 \text{ cm}^3/\text{beat} = 0.070 \text{ liters/beat}; \\ \text{heart rate} &= 80 \text{ beats/minute}; \\ \text{cardiac output} &= 5.6 \text{ liters/minute}. \end{aligned}$$

The usual definition of *pressure* (P) is force per unit area, and pressure is expressed in terms of the height of a column of mercury that can be supported by the pressure in question. (Note that this height is independent of the cross-sectional area of the column: If the area is doubled the weight of the column is doubled, but so is the force produced by a given pressure.) Thus, the conventional units of pressure in physiology are mmHg (millimeters of mercury).

When considering pressures, it is important to remember that only pressure *differences* produce observable effects. Thus, any reference pressure can be called zero, and other pressures can be reported as differences from the reference pressure. A particularly convenient reference pressure in physiology is the pressure of the atmosphere, since this is the pressure outside of most of the blood vessels of the circulation. Pressure differences with respect to the atmosphere can be measured directly by the simple device of leaving the far end of the (U-shaped) mercury column open to the atmosphere. Throughout this chapter the symbol P will stand for pressure measured with respect to the atmosphere. As we shall see, this definition of pressure has greater relevance for the circulation than the absolute pressure.

1.3 Resistance and Compliance Vessels

Consider the blood vessel shown in Figure 1.2. The volume of the vessel is V, its inflow is Q_1 at pressure P_1, and its outflow is Q_2 at pressure P_2. The external pressure is zero (atmospheric). Suppose that the vessel is in a

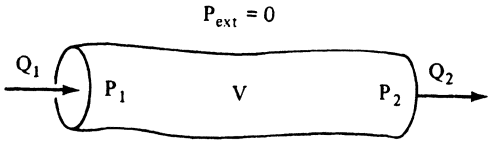

Figure 1.2. A typical blood vessel. V = volume of the vessel, P_1 = upstream pressure, P_2 = downstream pressure, P_{ext} = external pressure (pressure outside the vessel, which is here chosen as our reference pressure, hence $P_{\text{ext}} = 0$), Q_1 = inflow (volume per unit time), Q_2 = outflow.

steady state, which means that none of these quantities are changing with time. Then we must have $Q_1 = Q_2$ (why?), so we shall drop the subscript and just use the symbol Q to designate either the inflow or the outflow.

How are Q, P_1, P_2, and V related? This is a complicated question, since it involves two separate properties of the blood vessel: its *resistance* to blood flow and its *compliance* in response to distending pressure. We can isolate these properties by considering special cases.

First, suppose that the vessel is rigid, so that the volume is known and constant. Then we need only a relationship between Q, P_1, and P_2. Since only pressure differences matter, it is a safe assumption that Q is determined by $P_1 - P_2$. The simplest relationship of this sort is

$$Q = \frac{P_1 - P_2}{R}, \tag{1.3.1}$$

where R is a constant called the *resistance* of the vessel. If a vessel satisfies (1.3.1), we call it a *resistance vessel.* Next suppose that the vessel is elastic but that it has no resistance to blood flow, so that the pressures at the two ends of the vessel are equal for all Q. Because the vessel is elastic, there is some relation between the distending pressure $P = P_1 = P_2$ and the volume V. The simplest relation of this kind is

$$V = CP, \tag{1.3.2}$$

where C is a constant called the compliance of the vessel.

Alternatively, if we want to take into account the nonzero residual volume of the vessel at zero pressure, we could use the relationship

$$V = V_{\text{d}} + CP, \tag{1.3.3}$$

where C is still called the compliance and where V_{d} is the ("dead") volume at $P = 0$. A vessel satisfying (1.3.2) or (1.3.3) is called a *compliance vessel.*

Clearly, the concepts of resistance vessels and compliance vessels are idealizations. First, a real vessel must exhibit both resistance and compliance properties simultaneously. Second, we have assumed linear relationships that may be too simple to describe real blood vessels.

The reply to these objections is as follows. First, the circulation does seem to produce a clear separation between the resistance and compliance

functions of its different vessels. Thus, the large arteries and veins are primarily compliance vessels in the sense that only small pressure differences are needed to drive the cardiac output through these vessels, while their changes in volume are highly significant. The main site of resistance is in the tissues themselves (primarily at the level of the smallest arteries, the *arterioles*), where volume changes are less important but where large pressure drops are observed.

Second, the approximation of a linear relation between flow and pressure differences (1.3.1) is a good approximation when we allow for changes in resistance. This may appear to be a circular argument, since we can always make (1.3.1) true by introducing the definition $R = (P_1 - P_2)/Q$. In fact, tissues exhibit reasonably constant values of R under conditions where the diameters of their blood vessels remain constant. When R changes, a physiological explanation must be sought. This explanation usually involves a stimulus that leads to contraction or relaxation of the smooth muscles in the walls of the arterioles. Such a stimulus may be generated by the nervous system, by circulating hormones (or other substances circulating in the blood), or by the action of locally produced products of metabolism. Some of these effects will be studied in Section 1.9, on autoregulation.

Finally, there is no such justification for the linear compliance relations that we have assumed. It is an excellent approximation to say that the volume of a blood vessel is determined by the internal pressure, but the relationship between volume and pressure becomes progressively less compliant as it is distended. The linear model is introduced for simplicity.

1.4 The Heart as a Pair of Pumps

A pump is a device that can accept fluid at low pressure (P_1) and transfer it to a region where the pressure is high ($P_2 > P_1$). Thus, the pump performs work on the fluid; the rate at which work is performed by the pump is the product of the volume rate of flow Q and the pressure difference $P_2 - P_1$. To characterize the pump we need to say how Q depends on P_1 and P_2.

Consider, for example, the left side of the heart (Figure 1.3). The left ventricle is equipped with an inflow (mitral) valve and an outflow (aortic) valve. When the ventricle is relaxed (diastole) the inflow valve is open and the outflow valve is closed. During this period of time, the left ventricle receives blood from the left atrium at a pressure that is essentially that of the pulmonary veins. Thus, for the left ventricle, $P_1 = P_{sv} = 5$ mmHg. When the ventricle contracts (systole), the inflow valve closes and the outflow valve opens. Then the left ventricle actively pumps blood into the systemic arterial tree. Thus, for the left ventricle, $P_2 = P_{sa} = 100$ mmHg

What determines the output of the left ventricle under these conditions? To answer this question we follow an approach introduced by Sagawa and

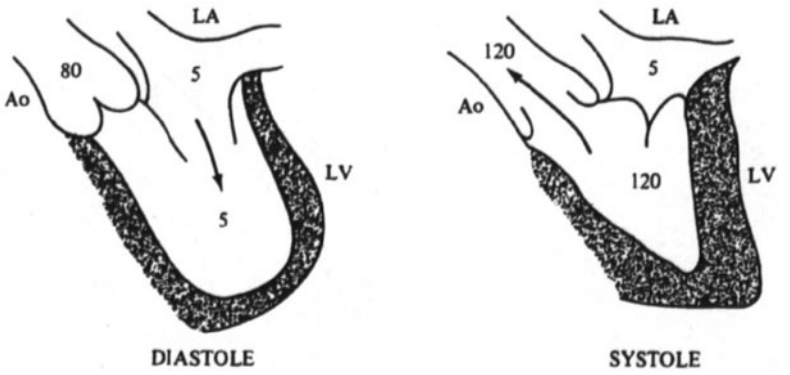

Figure 1.3. Cross section of the left side of the heart with the left ventricle in DIASTOLE (relaxed) and SYSTOLE (contracted). LA = left atrium, LV = left ventricle, Ao = Aorta. The numbers in the chambers are pressures in millimeters of mercury (mmHg). Note that the inflow (mitral) valve is open in diastole and closed in systole, whereas the outflow (aortic) valve is closed in diastole and open in systole. Pressures are approximately equal across an open valve, but can be very unequal, with the downstream pressure higher, across a closed valve. The valves ensure the unidirectional flow of blood from left atrium to left ventricle to aorta.

his collaborators: We regard the ventricle as a compliance vessel whose compliance changes with time. Thus, the ventricle is described by

$$V(t) = V_{\mathrm{d}} + C(t)P(t), \tag{1.4.1}$$

where $C(t)$ is a given function with the qualitative character shown in Figure 1.4. The important point is that $C(t)$ takes on a small value C_{systole} when the ventricle is contracting, and a much larger value C_{diastole} when the ventricle is relaxed. For simplicity, we have taken V_{d} to be independent of time.

Using (1.4.1), we can construct a pressure–volume diagram of the cardiac cycle (Figure 1.5). For a detailed explanation of this type of diagram, see the paper by Sagawa et al., cited in Section 1.14. For our purposes, it is sufficient to note that the maximum volume achieved by the ventricle (at end-diastole) is given by

$$V_{\mathrm{ED}} = V_{\mathrm{d}} + C_{\mathrm{diastole}}P_{\mathrm{v}}, \tag{1.4.2}$$

while the minimum volume (achieved at end-systole) is given by

$$V_{\mathrm{ES}} = V_{\mathrm{d}} + C_{\mathrm{systole}}P_{\mathrm{a}}, \tag{1.4.3}$$

where P_{a} is the pressure in the arteries supplied by the ventricle and P_{v} is the pressure in the veins that fill it. Thus, the stroke volume is given by

$$V_{\mathrm{stroke}} = V_{\mathrm{ED}} - V_{\mathrm{ES}} = C_{\mathrm{diastole}}P_{\mathrm{v}} - C_{\mathrm{systole}}P_{\mathrm{a}}. \tag{1.4.4}$$

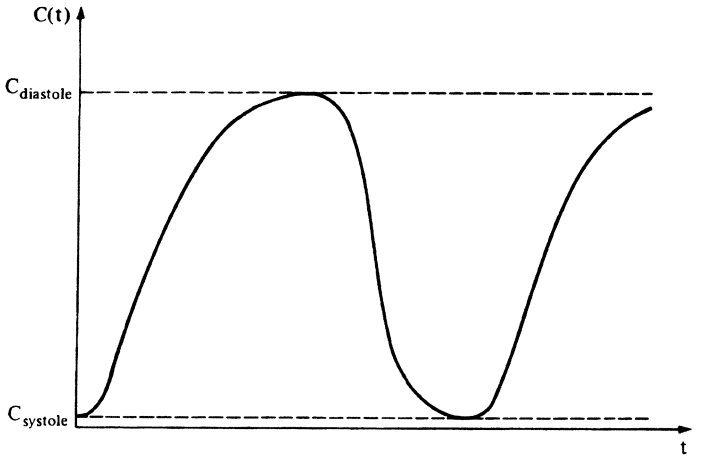

Figure 1.4. Compliance of either ventricle as a function of time. During diastole, the compliance rises from a low value C_{systole} to a high value C_{diastole} as the ventricle relaxes. During systole, it does the reverse as the ventricle contracts.

A particularly simple special case is when $C_{\text{systole}} = 0$, so that the systolic line is vertical in Figure 1.5. This gives a stroke volume

$$V_{\text{stroke}} = C_{\text{diastole}} P_{\text{v}}, \tag{1.4.5}$$

which is the model of the ventricle that we shall use. Finally, if F (frequency) is the heart rate (beats per minute), we get cardiac output

$$Q = FV_{\text{stroke}} = FC_{\text{diastole}} P_{\text{v}}. \tag{1.4.6}$$

For the present, F is taken to be constant, although we shall consider changes in heart rate later in the chapter. We define

$$K = FC_{\text{diastole}}, \tag{1.4.7}$$

so that $Q = KP_{\text{v}}$. We call K the *pump coefficient* of the ventricle. Although F is the same for the two sides of the heart (which are driven by the same pacemaker), the constant C_{diastole} is greater in the thin-walled right ventricle than in the thick-walled left ventricle, so K is greater on the right than on the left. Also, the two sides of the heart are connected to different venous systems. Thus, we have the following expressions for the right and

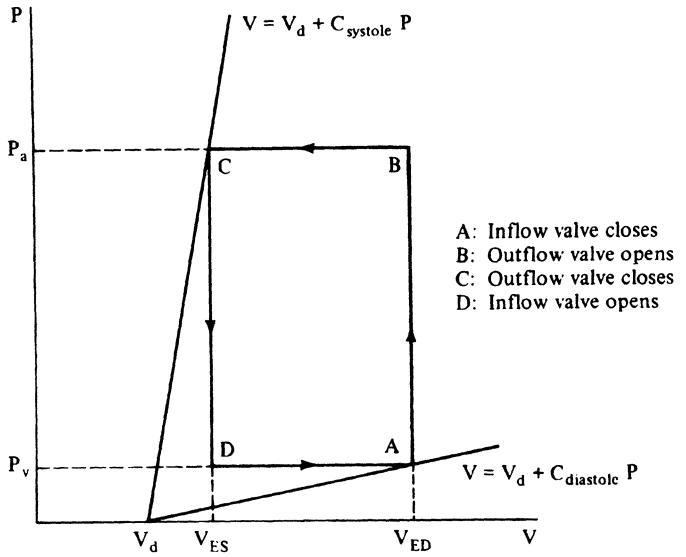

Figure 1.5. Pressure–volume diagram for either ventricle. Landmarks on the volume axis (V) are V_d = "dead volume," i.e., the volume at zero transmural pressure, V_{ES} = end-systolic volume, V_{ED} = end-diastolic volume. Landmarks on the pressure (P) axis are the venous (inflow) pressure P_v, and the arterial (outflow) pressure P_a. Since the venous pressure is essentially the same as the atrial pressure, it may be considered the inflow pressure for the ventricle. Slanting lines radiating from V_d describe the pressure–volume relationships of the ventricle at the end of diastole and at the end of systole; these lines are labeled with their equations. At other times, the pressure–volume relationship is indicated by a similar slanting line (not shown) that lies between the two lines shown. Rectangular loop ABCDA shows the path followed by the ventricle during the cardiac cycle. On the vertical branches (AB and CD), both valves are closed, so the volume of the ventricle is constant. On each of the horizontal branches, one valve is open: the arterial (outflow) valve along BC and the atrioventricular (inflow) valve along DA. The pressure difference across the open valve is here idealized as zero, and the arterial and venous pressures are idealized as constants. The names of the four phases of the cardiac cycle are AB = isovolumetric contraction, BC = ejection, CD = isovolumetric relaxation, DA = filling.

left cardiac outputs:

$$Q_{\mathrm{R}} = K_{\mathrm{R}} P_{\mathrm{sv}} \tag{1.4.8}$$

$$Q_{\mathrm{L}} = K_{\mathrm{L}} P_{\mathrm{pv}}. \tag{1.4.9}$$

Throughout this section we have tacitly assumed that the pressure outside the heart is zero (atmospheric). If not, then the distending pressures during diastole are not simply P_{sv} and P_{pv} but $P_{\mathrm{sv}} - P_{\mathrm{thorax}}$ and $P_{\mathrm{pv}} - P_{\mathrm{thorax}}$, where P_{thorax} is the pressure in the chest. In fact, P_{thorax} is slightly negative (with respect to the atmosphere), and this contributes to increased cardiac output by increasing the end-diastolic volume V_{ED}. This effect was first noticed because it disappears when the chest is opened during surgery. In the model developed below, we assume for simplicity that $P_{\mathrm{thorax}} = 0$ so that we can use (1.4.8) and (1.4.9) without modification. Then, effects of $P_{\mathrm{thorax}} < 0$ are considered briefly in Exercises 1.8 through 1.9.

1.5 Mathematical Model of the Uncontrolled Circulation

In this section we put together the ideas that have been developed above to construct a mathematical model of the circulation. In the form that we first present it, the model lacks the control mechanisms that regulate the circulation and make it serve the needs of the body. In subsequent sections we will use this model in several ways:

1. to study the *self*-regulating properties of the circulation, independent of external control mechanisms;

2. to explain the need for external control mechanisms;

3. to serve as a foundation on which we can construct a simple model of the control of circulation.

Our model is defined by the following equations (see Figure 1.6): First, we have the equations of the right and left hearts:

$$Q_{\mathrm{R}} = K_{\mathrm{R}} P_{\mathrm{sv}}, \tag{1.5.1}$$

$$Q_{\mathrm{L}} = K_{\mathrm{L}} P_{\mathrm{pv}}. \tag{1.5.2}$$

Second, we make the assumption that the systemic and pulmonary arteries and veins are compliance vessels. For simplicity, we use (1.3.2) instead of