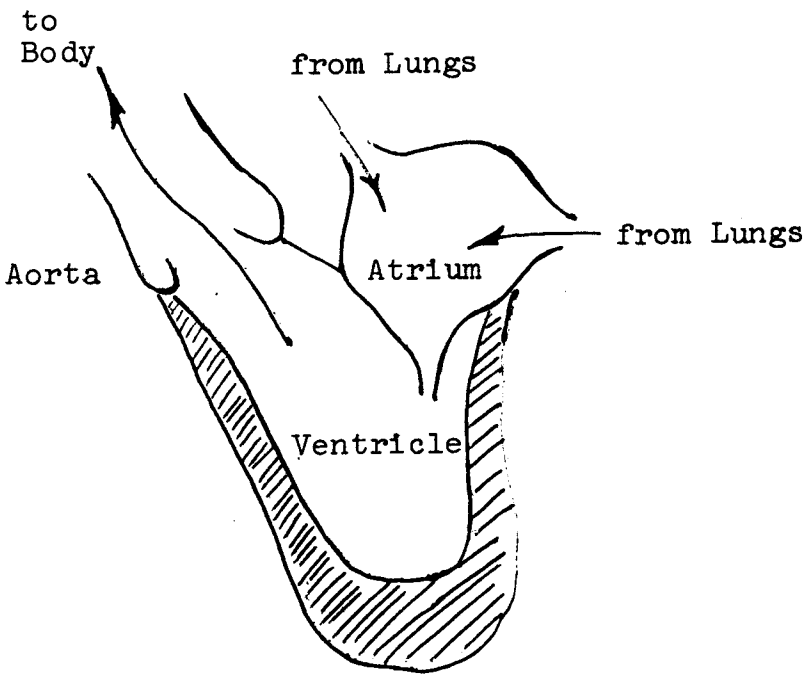
I. Introduction

The Cardiac Cycle

Each side of the heart receives blood at low pressure and pumps this blood out at high pressure. The left side receives oxygenated blood from the lungs and sends this blood out through the aorta to the tissues of the body. From these tissues it returns to the right side of the heart with a large part of the oxygen removed and replaced by carbon dioxide. The right side of the heart pumps this blood to the lungs, where it is oxygenated to complete the circulation. The pressure generated by the right side is only about 1/6 that generated by the left, but the quantities of blood pumped by the two sides of the heart are necessarily equal (on the time average) since the output of one side becomes the input to the other.

In the healthy mammalian heart (after birth) the chambers of the left side of the heart are completely separated from those of the right, and there is no mixture of oxygenated and deoxygenated blood in the heart. Despite this separation, the two sides are part of a single anatomical organ, and the heart beat is coordinated by a single clump of cells, the pacemaker region.

A schematic diagram of the left side of the heart looks like this:



The alternate contraction (systole) and relaxation (diastole) of the ventricles drive the cardiac cycle. Each ventricle has an inflow and an outflow valve, and in each of these phases one of the valves is open and the other is closed. The ventricle is connected through the open valve to either the atrium (in diastole) or the aorta (in systole), and the pressure difference across the open valve is nearly zero. Thus the left ventricle switches back and forth between states of near equilibrium with the low pressure left atrium and the high pressure aorta, and, by transfering blood from the one chamber to the other, maintains the pressure difference between them. This pressure difference drives blood through the tissues.

Some Mathematical Problems of Cardiac Physiology

These problems are mathematical in the sense that experiments alone could not lead to their complete resolution.

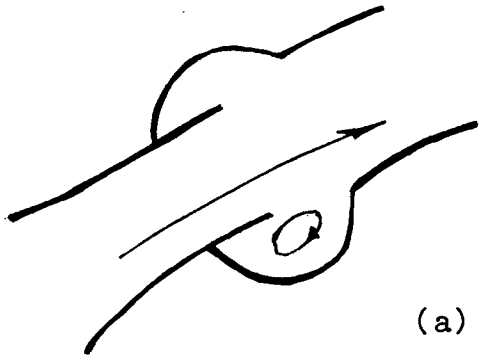
(1) The performance of heart valves. Is forward flow without dissipation compatible with closure without backflow? We shall show that vortex formation (a dissipative, irreversible process) during forward flow is a necessary feature of efficient value closure. In fact, with a vortex in the right place, it is theoretically possible to move the valve leaflet to its closed position without any backflow at all. During forward flow the valve forms one border of the vortex. At the cessation of forward flow, the vortex expands, incorporates the valve, and sweeps it toward closure. This is shown for the aortic valve (next page):

(2) Heart murmurs. It is believed that heart murmurs are related to turbulence. Why is flow in the normal heart not turbulent even though some of the criteria for turbulence are more than exceeded? Under what (pathological) conditions can turbulence be expected in the heart.

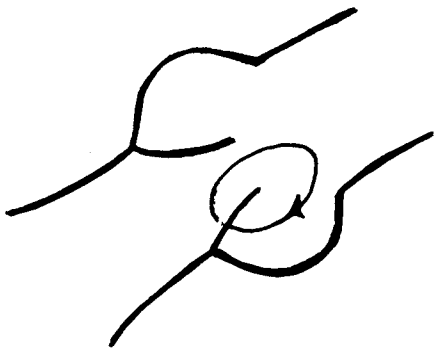
(3) Embryology. To what extent is the heart shaped by fluid forces during development?

(4) Control of the heart. How is the equality of output between the two sides of the heart maintained, and how does the cardiac output respond to the varying demands of exercise.

Aortic sinus streamlines:



(a) during forward flow,



(b) during valve closure,

(c) motion of the vortex core during valve closure.

A central aspect of this problem is to formulate equations of motion for heart muscle, since the relation between force, length, and velocity of shortening determines how much blood the heart pumps against any given load.

(5) Heart rate and rhythm. These are controlled by the electrical properties of cell membranes in the heart. In isolated heart cells, the membrane potential oscillates spontaneously because of a time-dependent, non-linear interaction between membrane potential and the permeability to various ions. During each cycle of membrane potential the cell contracts once. But the isolated cells oscillate at different frequencies, while in the healthy heart the oscillations are coupled and the changes in membrane potential spread as a wave over the heart muscle from the pacemaker region.

Mathematical Description of a Heart Beat

Each heart beat begins with electrical activity at the cell membrane. Ion pumps in the membrane establish certain concentration differences between the inside and the outside of the cell. Changes in membrane permeability to different ions then lead to electrical activity. The basic equations are

$$C \frac{dV}{dt} = \sum_i I_i$$

$$V_i = V + \frac{RT}{nF} \ln r_i$$

$$I_i = g_i V_i$$

where

C = membrane capacitance.

V = voltage across the membrane.

I_i = current carried by the i^{th} ionic species.

V_i = electrochemical potential for the i^{th} ionic species.

R = gas constant.

F = magnitude of charge on the mole of electrons.

n_i = valence of the i^{th} species of ion.

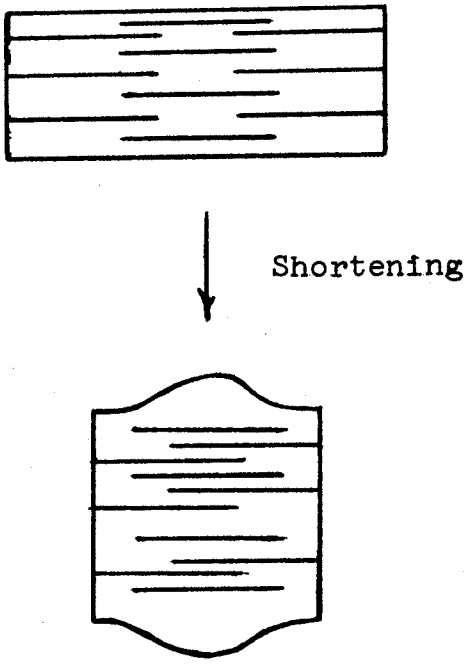
r_i = ratio of concentration for the i^{th} ion across the membrane.

g_i = conductance of the membrane channels specific for the i^{th} ion.

The conductances g_i have important dynamic properties which determine the dynamics of the heart beat. They are voltage controlled in the sense that they approach as $t \to \infty$ a value which is a function of voltage. But the approach to equilibrium has its own kinetics which may lead to spontaneous oscillations as in the pacemaker region or to single discharges following stimulation as in the rest of the heart.

A particularly important ionic current is the current of Ca^{++}, since this ion regulates the process of force generation in the heart muscle. The dynamics of this process is described as follows.

The muscle sarcomere looks like this:



Force is transmitted at the cross-bridges (not shown) which connect the two types of filaments shown. The cross-bridges are continually forming and breaking. Net force is generated because the cross-bridges are formed under strain. When shortening occurs, net work is accomplished because the cross-bridges break under less strain than when they were formed. The energy for this process comes from high energy compounds whose breakdown is chemically coupled to cross-bridge formation.

The equation of motion for the cross-bridge distribution $n(x,t)$ is

$$\frac{\partial n}{\partial t} + v \frac{\partial n}{\partial x} = f(x,t)(N_o - N) - g(x)n(x)$$

where

$f(x,t)$ = rate of formation of cross-bridges with strain x

$g(x)$ = rate of breakdown of cross-bridges with strain x

N_o = number of cross-bridges capable of forming links (This depends on the length of the muscle cell).

$N = \int n(x,t)dx$

v = velocity of sliding

and

$n(x,t)dx$ = # of cross-bridges with strain in the interval $(x, x+dx)$.

Given $n(x,t)$ the tension is given by

$$T = \int n(x,t)h(x)dx$$

where

$h(x)$ = force transmitted by a cross-bridge with strain x.

The time-dependence of the rate of attachment $f(x,t)$ comes from the time-variation of Ca^{++} ion concentration in the cell. Thus the electrochemical processes outlined above modulate the process of force generation.

The end result of this process is a tension T in each muscle fiber where T depends on the time-course of Ca^{++} concentration and also on the history of the velocity of shortenting during the contraction. The muscle fibers are embedded in incompressible fluid and there is a definite fiber orientation $\underline{\tau}$ at each point in space. Under these conditions we can express the force (per unit volume) applied by the heart muscle to the fluid in the following way

$$\underline{F}(\underline{x}) = \sigma \frac{d}{ds}(\underline{\tau}T)$$

where σ = fibers per unit area and s measures length along the fiber thorugh the point $\underline{x}$.

The equation of motion of the points of the muscle fibers can be written

$$\frac{d\underline{x}}{dt} = \underline{u}(\underline{x})$$

where $\underline{u}$ is the velocity field for both the heart muscle and the fluid. Finally the equations of motion for the fluid are the Navier-Stokes equations.

$$\rho\left(\frac{\partial \underline{u}}{\partial t} + \underline{u}\cdot\nabla\underline{u}\right) = -\nabla p + \eta\nabla^2\underline{u} + \underline{F}(\underline{x})$$

$$\nabla\cdot\underline{u} = 0$$

where

$\underline{u}$ = fluid velocity

p = pressure

ρ = density

η = viscosity

It is worth noting that, although $\underline{F}(\underline{x})$ is zero in the interior of the fluid, its effects are still felt in the interior through the pressure field.

This is because

$$\nabla^2 p = \nabla\cdot\underline{F} + \nabla\cdot(-\rho\underline{u}\cdot\nabla\underline{u} + \eta\nabla^2\underline{u}) \quad .$$

Thus the divergence of $\underline{F}$ is a source for the pressure in the same sense as electric charge is a source for the electrostatic potential.