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## Chemistry and Mechanics Underly Models of Heart Physiology

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This article gives a brief discussion of cardiac physiology, with emphasis on aspects where mathematics is likely to be useful.

If embryonic heart cells are grown in tissue culture, they beat spontaneously, their rate being controlled by the non-linear oscillations of the electrical potential difference across their cell membranes. When two cells make contact, the faster cell drives the slower, and the members of the pair beat synchronously.

In the heart, the faster cells are gathered together in the region of the sinoatrial node, or pacemaker. The signal to contract is carried to the rest of the heart through specialized muscle fibers which are functionally analogous to nerves. The equations governing the propagation of this electrical signal are very similar to the Hodgkin-Huxley equations for the nerve impulses; they are non-linear diffusion equations with traveling wave solutions.

The signal travels rapidly through the atria, is delayed at the atrioventricular node, and then travels rapidly again to all parts of the ventricular muscle. If part of the conduction system becomes dis-

eased, abnormal rhythms of the heart may develop. For example, the signal may be blocked at the level of the atrioventricular node, in which case the atria and the ventricles will beat independently, the ventricles being driven by a pacemaker which, free from the influence of the sinoatrial node, arises somewhere in the conduction system below the block. Such a pacemaker will drive the ventricles at a lower rate. More complicated rhythms arise when partial block exists.

### The Cardiac Waveform

The waveform of the cardiac impulse, the electrical signal which triggers contraction, differs from that of the nerve impulse in one important respect. The cardiac impulse has a prolonged "plateau" phase, during which a current carried by  $Ca^{++}$  ions flows into the muscle cell from the extracellular space. This  $Ca^{++}$ , together with  $Ca^{++}$  released from intracellular storage sites, is believed to turn on the contractile machinery of the muscle cell. The kinetics of the uptake and release of the  $Ca^{++}$  from these internal and external sites are believed to be responsible for the

relation between the strength of a heartbeat and the duration of the preceding several beats.

Within limits, ventricular muscle becomes stronger when it is driven at a higher heart rate. This effect, which is important during exercise, is believed to be mediated by an increased flux of  $Ca^{++}$  ion per beat. When the heart rate is suddenly changed, the subsequent beats go through an interesting transient on their way to the new equilibrium strength of contraction. This transient can be used to study the  $Ca^{++}$  kinetics.

### The Contractile Machinery

The contractile machinery itself consists of molecular filaments which slide past each other to effect the contraction of the muscle cell. The filaments are of two types: thick (myosin) and thin (actin). The thick filaments have projections, called cross bridges, which can attach to the thin filaments, pull a little way, and then let go. A chemical reaction is believed to force the cross bridges into a strained conformation immediately after attachment to the thin fila-

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## Heart

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ment, so that they can perform the necessary work of movement by relaxing against the thin filament.

The chemical energy for putting the cross bridge in its strained conformation comes ultimately from the oxidation of sugar by the cell but more directly from the splitting of a high energy phosphate bond.

At any instant, one has a population of cross bridges, the members of the population being characterized by their strain. The mechanical behavior of the muscle is determined by the dynamics of this population under the three processes: attachment, detachment, and sliding. These are analogous to birth, death, and aging in age-dependent population models.

The muscle fibers of the heart wall are not randomly oriented. On the contrary, at each point there is a characteristic fiber direction which changes smoothly as one moves through the heart wall. This fact places an important restriction on the form of the muscle stress tensor. Under certain simplifying assumptions one can show that the fibers ought to be geodesics along the surfaces of constant pressure. (A simpler example of this occurs in the arteries where the surfaces of constant pressure are cylindrical and the fibers are helical.)

### Valve Configurations

Considerations from differential geometry also plays a role in the analysis of the heart valves. The valves themselves are thin, flexible leaflets which move easily in the flow of blood. It is a consequence of the conditions of mechanical equilibrium that when two valve leaflets meet along a curve, the oscillating plane to this curve must be tangent to both leaflets. Hence

the leaflets form cusps along the line of closure (and are often called "cusps" for this reason). One can also show that special supports are needed along the line of closure, and indeed there is a fibrous ridge on the arterial valves and a network of cords supporting the atrioventricular valves in the appropriate places.

The tension developed in the muscle fibers of the ventricular walls acts to push blood out of the ventricles. When the muscle relaxes, the ventricles can fill. Each ventricle has two openings, to a low pressure atrium and a high pressure artery, and the valves guarding these openings ensure that the inflow is always from the atrium while the outflow is always to the artery.

An intricate fluid dynamic mechanism (first described by Leonardo da Vinci) ensures that the valves are already nearly closed at the moment of flow reversal. This mechanism involves vortices which form during the period of forward flow and which sweep the valve leaflets toward closure while the flow is still in the forward direction.

The mathematical description of this process involves the Navier-Stokes equations for a viscous incompressible fluid coupled to an immersed elastic boundary which moves at the local fluid velocity and exerts forces locally on the fluid. This system of equations can be generalized to include the muscular properties of the heart wall, and their numerical solution yields a computer test chamber for studying the performance of artificial heart valves.

### Heart Murmurs

The fluid dynamics of heart valves is fundamental to the understanding of heart sounds and murmurs. The normal heart sounds

arise at the closure of the valves and are caused by the vibration of the elastic heart tissue loaded with the mass of the incompressible blood. Heart murmurs are associated with turbulence that results when a valve opens narrowly or fails to close completely, forming a jet.

The absence of turbulence in the normal heart is remarkable when the low viscosity, high flow rate, and large dimensions of the heart are considered. It may be that the flow is stabilized by its pulsatile character, but this question remains open.

Within a single heartbeat, electrical, biochemical mechanical, and fluid dynamic phenomena interact to produce a coordinated effort which pumps blood around the circulation. The mathematical description of these phenomena has just begun. Already, it is clear that partial differential equations drawn from the fields of non-linear wave propagation, age-dependent population models, differential geometry, and fluid dynamics will play an important role in improving our understanding of heart physiology.

Although many of the problems that arise have a classical aspect, they also have special difficulties associated with the peculiarities of the heart problem. For example, the modeling of cardiac arrhythmias requires the solution of a non-linear wave propagation problem in an inhomogeneous medium. Similarly, in the cross bridge population equation, the factor that corresponds to the rate of aging is neither constant nor given in advance. In the same way, the fluid dynamic equations involve moving immersed boundaries whose motions are not known in advance. Moreover all of these problems are coupled to each other.

Confronting the heart, then, the mathematician is faced at the same time with a very difficult challenge and a very great opportunity.

(Editor's note: Dr. Peskin is Assistant Professor of Mathematics in the Courant Institute. He received his Ph.D. in physiology from the Albert Einstein College of Medicine of Yeshiva University. Most of his research is directed toward computational methods in cardiac fluid dynamics. Those who would like more information about this area may wish to read his Courant Institute Lecture Notes, *Mathematical Aspects of Heart Physiology*.)