Brief Reviews

A Commentary on Muscle Mechanics

By Bernard C. Abbott and Donald G. Gordon

Numerous studies of cardiac muscle mechanics have produced contradictory conclusions. The present paper discusses a few salient points about cardiac muscle mechanics, but it is not a critical review of the literature such as that recently published by Jewell and Blinks (1). An analysis of ventricular contraction is also presented; we hope that it will stimulate fresh thought about the relationship between isolated muscle experiments and the functioning of the intact heart.

Isolated muscle experiments on papillary muscles have, in many cases, been made in an overly optimistic manner. The literature of only a few years ago suggests that cardiac muscle mechanics is a highly quantitative science operating on universally accepted, well-defined principles. More recently, however, the tenuous state of our knowledge has been recognized by many investigators: classical theories are being attacked and entirely new viewpoints are being advanced. This situation makes the study of cardiac muscle mechanics academically challenging but causes no little consternation for cardiologists and others who desire practical parameters of cardiac performance based on fundamental physiology.

The application of the concepts of skeletal muscle mechanics to isolated cardiac papillary muscle demonstrated by Abbott and Mommaerts (2) stimulated a large body of work which tended to emphasize the common principles of the two fields (1). In these efforts, however, the important differences between cardiac and skeletal muscle were not always appreciated (3, 4). These studies were made assuming an analogy between cardiac muscle contractions and contractions of frog skeletal muscle with its parallel fibers that run the length of the muscle. This analogy is poor because the papillary muscle consists of typical cardiac cells that run only a few hundred microns. The general fiber pattern shows a spiral organization along the muscle axis (5) with tension transmission between cells made through limited specialized desmosomal areas of cell contact. These contact areas may be partly responsible for the surprisingly large series elastic component that extends internally up to 10% at the small tensions developed by cardiac muscle (6). Not all of the reasons for this large compliance are clear, but, perhaps, the limited areas for tension transmission cause the cells to experience shape deformations during isometric contractions. If this possibility is true, then the stress pattern across the cell, the sarcomere pattern, and the filament overlap are nonuniform.

The basic analogue mechanical model on which most of the thinking has been based is essentially very simple, far too simple to be extrapolated to cardiac muscle. The mechanical and thermal studies of two decades on frog sartorius muscle culminated in the description by Hill (1938) of a working model. Skeletal muscle operates in the body over a range of lengths at which no resting tension exists. The only significant tensions are those developed by activation, although small steady and larger transient tensions can occur. As a result of measurements at a series of constant loads, Hill described the contractile machine as one in which speed of movement is defined uniquely by the load lifted according to the familiar force-velocity equation. To explain the time course of isometric contractions and constant-speed releases, Hill suggested that this contractile (protein-based) machine operates through an undamped series element. This element was not defined anatomically but was an inevitable result of the analysis, since all material displays a stress-strain relationship, and the forces developed by the contractile system must be transmitted by the long polymer chains of the myosin and actin molecules. Only far more recently have the active bridges between actin and
myosin been described and the series elasticity attributed at least in part to these bridges. Thus, the model for striated muscle has moved from a purely analogue representation to one that is anatomically oriented.

For cardiac muscle, there is no simple reference length such as that defined by the physical limits of movement in skeletal muscle. Resting tension in papillary muscle appears well down the rising arm of the developed tension curve. The usefulness of this phenomenon is usually discussed in relation to the Starling phenomenon in the intact heart, but this resting tension demands a different model from the Hill two-component model and causes much of the current complexity in the literature on cardiac muscle.

The appearance of resting tension on the rising arm of the tension-length curve has recently been discussed by Abbott (7) in an effort to suggest that this phenomenon is due to the large series elastic compliance rather than to a fundamental difference of mechanism from the contractile machine of skeletal muscle. In skeletal muscle, resting tension becomes significant only at lengths long enough for the number of cross-bridges to begin to decrease as thick and thin filaments are pulled apart. In such a muscle, the series elastic element is very stiff and, even in tetanic contraction, amounts to less than 2% of length (8) or about 0.04 μm/sarcomere. By contrast, the 10% series elastic shortening of papillary muscle implies that, even in an isometric beat with much lower tension, an effective internal shortening of about 0.2 μm/sarcomere occurs. In other words, at an actual measured initial length corresponding to a 2-μm sarcomere, the tension developed at the peak of contraction corresponds in filament overlap to a length of only 1.8 μm, a length at which the tension is significantly decreased. A simple graph shows that such internal shortening will inevitably transform a skeletal muscle type of tension-length curve into one in which the peak isometric tension occurs at lengths at which resting tension is considerable. If this transformation occurs, then the papillary tension-length curve holds less mystery.

Another source of confusion is our present understanding of the time course of the active state as demonstrated by the widely divergent views held by two groups of distinguished investigators. Since heart muscle cannot ordinarily sustain a tetanus, the measurement of active state, which was originally defined for tetanized skeletal muscle, must be attacked indirectly. Brady (9) has devised an elegant system in which the series elastic characteristic is first determined. From the profile of the isometric tension, the internal shortening is then predictable. The muscle is stretched during a length-controlled contraction by precisely the amount which should clamp the contractile component at a constant length. Brady's group found that the resultant active state measured as the tension recorded from the clamped system rises slowly and follows somewhat the form of the isometric tension curve. This rise seems very reasonable when one notes that, in an afterloaded isotonic contraction, the speed of shortening only reaches its full value well into the beat (1, 10).

The limitations of this method must be recognized. It assumes the existence of nonviscous elastic elements; it is complicated by the contribution of resting tension, and it implicitly assumes a homogeneity of the muscle so that within each cell the stress is uniformly distributed. Even in skeletal muscle, the determination of the active state by applied stretch can be disputed because, with the quick-stretch technique, the "correct" result is obtained only if the stretch velocity lies within an acceptable range (Abbott, unpublished observation). Furthermore, when activated skeletal muscle is forcibly lengthened, tension rises well above the isometric value (11, 12). Activated cross-bridges, which break readily to produce shortening with concomitant breakdown of adenosine triphosphate (ATP), resist strongly when they are extended, and the breakdown of ATP is hindered. Such extension of activated skeletal muscle (so-called negative work) is a normal physiological function; for every limb movement which involves the active shortening of a muscle, the inverse movement demands the extension of exactly that same muscle activated to resist and control the extension. Thus, stretch of activated skeletal muscle constitutes 50% of normal movements undertaken. Such forced extensions are never imposed on active heart muscle in vivo. Also, when a papillary muscle is stretched, no large plateau of tension occurs as it does in skeletal muscle. The absence of augmented tension in the extension of papillary muscle suggests that the cross-bridges in these muscles are able to develop force isometrically but are unable to resist extension with increased force or that imposed stretch emphasizes the internal heterogeneity so that only a limited number of fibers bear the tension. The experiments of Brady's group are specifically designed not to extend the contractile element, but nevertheless the study of active state by applied stretch becomes suspect.

Another approach to the active state has been
developed by Brutsaert et al. (13). Using a light lever with tension applied through a magnetic torque device at the fulcrum, Brutsaert et al. can program the loads presented to an isolated cardiac muscle. By electronically controlling the electric current to the torque device, any load function of force versus time can be produced. The results are displayed as velocity of shortening versus muscle length. From studies on cat papillary muscle, Brutsaert et al. (14, 15) deduced that the active state rises quickly to a peak value and stays there for a significant part of the rising tension phase. In particular, they traced these velocity versus length functions over a range of lengths using steady coil currents to set the resting tensions. From a given starting length, they unloaded the papillary muscle as it shortened so that the resisting torque at each length corresponded to the resting tension at that length. Starting from a given length, a plateau of velocity was reached early in the contraction and remained constant for most of the unloaded shortening. The same results were obtained after different early transients, if the load was quickly changed to zero just after the muscle began to shorten. In either case, Brutsaert et al. found that for different resting lengths the plateau velocity is the same. If active state is measured as the unloaded velocity of shortening, these results suggest a quick rise of active state.

Brutsaert et al. (13) also found uniqueness in the velocity versus length function obtained for various afterloads. With their lever they imposed isotonic afterloads, i.e., contraction was isometric until tension reached the afterload value. The resultant velocity-length curves started from the same initial length, but, with heavier loads, the velocity-length relationship obviously changed. During the progress of any single contraction, the applied load could readily be changed as a step function of the coil current. When the load was changed, the velocity versus length function immediately shifted to precisely the curve for the new load. Over most of the curve it was possible to switch back and forth between the curves accurately by just changing the load. Brutsaert et al. used these results as further support for an active state that develops rapidly to a full value.

These opposing viewpoints are clearly the result of the interpretation of sophisticated experiments. In both cases, the papillary muscles were subjected to unphysiological maneuvers to uncover the basic contractile mechanisms postulated. The question arises as to whether these maneuvers change the active state itself. That is, does the act of measurement change the quantity being measured? The answer is far from obvious.

Sophisticated experiments such as those just discussed attract increasing attention because of difficulties in choosing between the classical muscle models illustrated in Figure 1. These logical constructs were proposed to account for a series of phenomena including (1) the time course of isometric tension rise, (2) the virtually instantaneous drop in muscle tension when a quick release of length is made and the rise in tension when a quick stretch is imposed, and (3) the behavior of series elasticity which is measured with quick release from developed isometric tensions to various isotonic loads. For cardiac muscle, the stiffness (dP/dL, where P is tension or load and L is length) is a linear function of developed tension, but the relationship is not unique, and a different, but parallel, line is obtained for each higher resting tension.

The resting contractile element has been considered to be freely extensible in each model. Using the two-component model, parallel elasticity was neglected in early experiments with cardiac muscle, and the unloaded velocity of the contractile element (Vmax) was advanced as a measure of inotropic state independent of preload and afterload. This neglect of parallel elasticity created many quantitative and conceptual problems such as how and in what manner the freely extensible contractile element bore the resting tension. Parallel elasticity was then introduced in the Voigt and Maxwell models. (Fung [16] has correctly pointed out that these titles, which were taken by analogy from the classical theory of elasticity, are not strictly correct). In spite of considerable experimentation and discussion, the selection between models is still not clear (9, 16, 17). Parmley et al. (17) found that no one muscle model is adequate to

![Figure 1](http://circres.ahajournals.org/)

**FIGURE 1**

account for all of the experimental data but noted that the Voigt model gave more constant values for Vmax at low preloads and the Maxwell model gave more constant values at higher preloads. For the variation in stiffness with preload (6), the Voigt model offers the best solution. Fung (16) points out that Brady described muscles that fell into three categories: Maxwell, Voigt, and neither. It is, indeed, probable that a compromise solution exists, and we suggest that the assumption of a freely extensible resting contractile element be reconsidered.

In the case of skeletal muscle, A. V. Hill (18) has shown that for small extensions beyond the reference length (L0) the resting tension is derived from a source whose thermoelastic properties are entropic in origin, changing over at about 1.25 L0 to a stiffer elasticity that is thermoelastically similar to normal elasticity. D.K. Hill (19) has demonstrated that the tensions in this lower range are active and probably produced by the cross-bridges. In fact, it seems that the muscle is freely extensible up to that length at which the number of potential bridges begins to decrease. Stretch beyond that length is opposed and resting tension appears, perhaps, due to forces between the sliding filaments. Only at considerably longer lengths and tensions do the more rigid supporting elements intervene.

If this finding is true for skeletal muscle, it may well be true for cardiac muscle and would then suggest a model in which, at moderate preloads, the internal filament tension would predict a Voigt model, with the apparent elasticity as an element of and drawn in parallel to the contractile element. At higher loads, the entrance of a stiffer support element in parallel would transform the system to a Maxwell model.

The present difficulties in analyzing the single muscle twitch are compounded by the generally neglected area of intrinsic cardiac control. Studied mainly in the intact heart as "homeometric autoregulation" (20), these phenomena have also been demonstrated in isolated muscle. Thus, for example, if isolated muscle contracting isometrically is released to an isotonic load, a change in activation occurs that affects not the immediate beat but also several succeeding beats before a new steady state is reached (21). Most studies do not consider such transients. Instead, interventions are studied as single imposed events spaced either methodically or randomly. More consideration needs to be given to the implications of these transients and to other temporal accommodations in heart muscle.

Efforts to relate the muscle fiber unit to the whole organ followed the isolated cardiac muscle work of Sonnenblick in 1962 (22). The main goals were to demonstrate that an inverse relationship between force and velocity exists for the intact heart and to show that contractility can be characterized by the mathematically extrapolated unloaded velocity of shortening of the contractile element (Vmax) of the muscle wall fiber. In practice, this approach required the measurement of the isovolumic pressure (P) and calculation of the velocity of the contractile element (VCE) as:

\[ V_{CE} = \frac{dP/dt}{kP + c/R} \]

where \( t = \) time, \( k \) and \( c \) = stiffness constants determined from isolated animal muscle preparations, and \( R = \) Laplace relation factor given by \( \sigma = RP \), where \( \sigma = \) wall stress. \( R \) was not used in most earlier papers, but most analyses showed that both \( c \) and \( c/R \) were negligible compared with \( kP \); they were, therefore, set equal to zero in equation (1). VCE was then plotted against \( P \) and extrapolated to zero yielding Vmax. This quantity was calculated from measurements in dogs using balloon occlusion of the ascending aorta (23) and in man using the physiological isovolumic phase of the cardiac contraction. The hope was that beat-to-beat quantification of contractility would be possible and that subtle cardiac dysfunction independent of preload and afterload would be detectable.

A review of the literature of the late 1960's yields many papers that apply the above scheme to human subjects with normal and diseased hearts. The prevailing opinion at that time was that muscle mechanics provided a unified theory of cardiac action and that the work of muscle physiologists experimenting with isolated muscle strips could be directly related to clinical problems.

About the same time, however, investigations were begun into the behavior of cardiac muscle strips at high preloads nearer to the peak of the tension-length relationship. Vmax was found to be preload dependent using the simple two-component model of A. V. Hill; this finding gave impetus to the use of the more complex models discussed previously. Subsequently, experiments in both isolated and intact dog hearts have emphasized the importance of the model chosen in the calculation of Vmax (24). These findings make it all the more important for the present controversies regarding the elastic properties of heart muscle to be resolved; otherwise, the absence of a unified theory will continue to cause much confusion.
DIFFICULTIES also exist with regard to pragmatic application. On the positive side, Burns et al. (25) have shown, in isolated perfused dog hearts, the apparent equivalence of isovolumic and isobaric Vmax calculated from the Maxwell model. This work tends to support earlier assumptions about the value of the series elastic constant in the intact heart, because the isovolumic calculation used this quantity and the isobaric one did not. Force-velocity relationships obtained with this preparation look very similar to those of isolated muscle.

In addition, other studies (24-28) have demonstrated a relative constancy of Vmax with changes in preload over limited ranges. Although controversy still exists in the proper choice of muscle model, it is possible that Vmax is useful to follow acute changes in the same subject. The comparison of different subjects, or even of the same subject in long-term follow-up studies is more difficult because (1) the value of the elastic constants may vary from heart to heart or change in the same heart with time especially with myocardial disease, (2) the short duration of isovolumic systole and the uncertainty as to the shape of the force-velocity curve makes rational extrapolation to Vmax difficult, and (3) normal values for Vmax vary from laboratory to laboratory, depending on the extrapolation method and the experimental techniques (29).

In separating patients with normal and abnormal hearts, Vmax has not shown a clear superiority to other more empirical indexes such as peak (dP/dt)/P and mean velocity of circumferential fiber shortening normalized to end-diastolic volume (30). Considerable scatter and overlap is often found between such groups. Krayenbuehl et al. (28) have recently employed a handgrip maneuver during cardiac catheterization to decrease this overlap problem. The theoretical controversies discussed previously in this paper demand more experimentation in both isolated muscle and intact heart as well as greater clinicopathological correlation from clinical studies.

In view of these difficulties, we feel that it would be fruitful to extend the correspondence between isolated muscle experiments and intact heart investigations so that the meeting point of the two fields will not focus so completely on the issue of the validity of Vmax as a measure of the inotropic state. The intense preoccupation with this interesting question has diverted attention from the biophysics of the ejection phase and the possible implications of hemodynamics for muscle mechanics. After all, it is not the left ventricular pressure per se that determines directly the ejection of blood from the ventricle into the aorta but rather the small differential pressure between the ventricle and the aorta. The aortic valve opens when the ventricular pressure rises to equal that of the aorta. Then, for ejection to occur, the resistance to change in motion of the blood, which involves the mass of the blood and the outflow tract geometry, must be overcome by a driving gradient along the axis from the left ventricle to the aorta. It has been shown (31, 32) that ventricular pressure exceeds aortic pressure for only the first third to half of the ejection period and that a negative pressure gradient exists throughout the remainder of the period with the blood continuing its forward motion due to momentum (32). This remarkable hammerlike quality of ventricular ejection led Rushmer (33) to urge an analysis in terms of impulse. Archie (34) has recently provided theoretical justification to these experimental findings using the equations of hydrodynamics.

From considerations such as those just described, it can be seen that the kinematic quantities of ejection such as instantaneous and peak flow, acceleration of flow, and time to peak flow are fundamentally important, because they directly reflect the physical phenomenon taking place. Recently, Noble et al. (35-37) have conducted an extensive series of experiments on the outflow characteristics of the intact heart using open-chest anesthetized dogs, closed-chest conscious dogs (with and without denervated hearts), and isolated cat hearts. Nutter et al. (38) have also studied open-chest anesthetized dogs. Electromagnetic flowmeters were placed around the aortic root, and excellent time resolution was achieved.

The attempt to use these methods to find new indexes of contractility have met with only limited success (39, 40), but as these studies are refined we may expect very accurate characterization of the kinematics of the intact heart. This knowledge must then be related to isolated heart muscle kinematics. For each instant in time, the instantaneous blood flow and the acceleration of flow are correlated with the instantaneous velocity and the acceleration of each myocardial wall fiber. Studies of these and related quantities in isolated muscle are highly desirable, because insight into the coupling between muscle action and blood flow would be gained. This coupling should be studied from many points of view and not simply as a search for a contractility index. For such experiments to have maximum usefulness, however, the isolated muscle preparation must be subjected to the same type of
resistance to changes in motion that are experienced by a muscle fiber in the wall of the intact heart.

As an illustration of how the dynamic loads of the intact heart might be simulated in isolated muscle, a simplified ventricular model can be considered. We have made calculations using an idealized ventricle shaped like an ellipsoid of revolution and contracting in such a way that the major diameter remains constant and the minor diameter shortens. Given these boundary conditions, $\Delta P$, the pressure drop $P$ between the center of the ellipse and the aortic outflow tract, is given by:

$$\Delta P = \frac{A}{b} Q^2 + \frac{B}{b} \dot{Q},$$  \hspace{1cm} (2)$$

where $A$ and $B = \text{constants}$ that depend only on the fixed major diameter and the ellipsoidal geometry, $b = \text{minor semiaxis}$ that shortens with time, $Q = \text{instantaneous flow rate}$ in the root of the aorta, and $\dot{Q} = \frac{dQ}{dt}$, the acceleration of flow.

$\Delta P$ is the pressure drop at each instant in time and reflects the driving gradient necessary to overcome the inertia of the system which includes (1) the mass of the blood, (2) the geometrical constriction of the outflow tract as one moves downstream (Bernoulli effect), and (3) the added effect of the moving walls.

By considering the geometrical relationships between wall stress and pressure, the kinematic relationship for an average circumferential wall fiber in the equator of the ellipse is

$$\Delta F = C a_{CF} + D v_{CF}^2,$$  \hspace{1cm} (3)$$

where $\Delta F$ = force excess over the force necessary to match aortic pressure, $a_{CF}$ = acceleration of the equatorial circumferential wall fiber, $v_{CF}$ = velocity of the circumferential fiber, and $C$ and $D$ = geometrical parameters related to the size and shape of the ventricle. These latter two parameters vary slowly with time compared with $a_{CF}$ and $v_{CF}$; thus, without a great loss of accuracy, $C$ and $D$ can be taken as constants. With this assumption and for this mathematical model, Eq. 3 defines the dynamics of the myocardial wall fiber. $\Delta F$ can be thought of as the force excess over the classical afterload. This overshoot of force is necessary to overcome the inertia of the system. Thus, Eq. 3 can be used to construct a mechanical analogue to circumferential myocardial wall fiber dynamics using an isolated muscle lever system. The muscle would be presented with a load consisting of the sum of the classical afterload $F_A$ and $\Delta F$ so that the force $F_M$ generated by the muscle at each instant in time would be:

$$F_M = F_A + \Delta F,$$

or, using Eq. 3,

$$F_M = F_A + C a_{CF} + D v_{CF}^2.$$  \hspace{1cm} (4)$$

The three load terms in Eq. 4 could be simulated by a lever system with an equivalent mass equal to $C$ and a nonlinear viscosity for the $D v_{CF}^2$ term. Instantaneous electronic feedback through a magnetic countertorque is one good method for effecting this simulation. The load $F_A$ could then be further programmed to simulate the auxotonic loading which is at least partly due to the filling of the elastic reservoir formed by the aorta and its large branches. More complex (and more realistic) modes of contraction will result in more complex relationships than Eq. 4, but the same principles could still be applied, perhaps, with the aid of computers.

Once in situ myocardial fiber dynamics are simulated in isolated muscle, the effects of fiber length and inotropic alterations on the velocity, acceleration, and impulse of a muscle can be studied in a systematic manner. Such a program would greatly encourage communication between muscle physiologists and students of the intact heart.

\section*{References}

5. Rødbærd S: Tissue capsules and lymph capillaries elicited by intraparenchymal plastic (abstr). Anat Rec 166:410, 1970

Circulation Research, Vol. 36, January 1975
COMMENTARY ON MUSCLE MECHANICS


Circulation Research, Vol. 36, January 1975
A commentary on muscle mechanics.
B C Abbott and D G Gordon

Circ Res. 1975;36:1-7
doi: 10.1161/01.RES.36.1.1

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/36/1/1.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/