A Computer Study of the Left Ventricular Performance Based on Fiber Structure, Sarcomere Dynamics, and Transmural Electrical Propagation Velocity

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SUMMARY. A model of the left ventricle which combines a spheroidal geometry with a spatial fiber angle distribution is presented. The mechanics of each muscle fiber is described by its passive stress-strain relationship, active stress-strain relationship, and an activation function (half a sinusoid) which represents the time-dependent degree of activation of the fiber. A stress-strain rate relationship which characterizes the muscle fibers is used to calculate the mechanics of left ventricular contraction during ejection. Furthermore, a radial electrical signal propagation from the endocardium to the epicardium is used here as a first approximation to the actual depolarization sequence. The model is used to describe the process of contraction throughout the systole. The different calculated parameters and indices of left ventricular function are presented and discussed for different preloading, afterloading and contractility conditions. The maximum elastance is found to be an optimal macroscale parameter of contractility, as it is completely preload and afterload independent, and is a good reflection of the active microscale sarcomere stress-strain relationship. (Circ Res 55: 358-375, 1984)

NUMEROUS ventricular-mechanics models have been studied to elucidate the complex phenomena associated with the performance of the left ventricle (LV). These models can be divided, roughly, into those simulating diastole mechanics (Moskowitz, 1979; Weiss and Forrester, 1975; Glantz, 1975; Mirsky et al., 1974; Pierce, 1981; Feit, 1979; Janz et al., 1973, 1974), and others simulating systolic performance (Weber and Janicki, 1979; Deswysen, 1977). The models vary from simple thin or thick shell spheres, with homogeneous and isotropic properties of the myocardium (Mirsky et al., 1974), to complex structural models incorporating a spatial (angle) distribution of the fibers (Streeter et al., 1970) and nonisotropic nonlinear material properties (Van der Broeck and Van der Broeck, 1979). In most of the analytical models, the LV geometry is approximated either by a sphere, a spheroid, an ellipsoid, or a truncated ellipsoid. "Real," nonregular, geometrical features of the LV shape are tackled by numerical techniques, mainly by the finite element method (Pao et al., 1974; Yettram et al., 1982; Pao and Ritman, 1977; Ghista and Hamid, 1977).

The classical force-velocity relationship attributed to the muscle fibers have been introduced into models based on simple geometries, thus allowing a quantitative description of the ejection phase (Weber and Janicki, 1980). A model of the LV which yields the velocity of contraction of the muscle fibers, based on a specific elastance function, the force-length velocity relationship, and the well-known properties of cardiac muscle, was recently proposed by Beyar and Sideman (1984). Another approach, which includes the velocity of fiber shortening and simulates the LV ejection, is based on the electrical analogy of the LV to a pressure source with an internal resistance (Welkowitz, 1981; Min et al., 1976, 1978). The source pressure is derived from the elastance function and the instantaneous volume, while the internal resistance, which is derived experimentally, relates to the force-velocity relationship of the cardiac muscle. The extension of this approach to more complex structural models is rather promising and is followed here.

A simultaneous excitation of the whole myocardium is usually assumed, based on the fact that the electrical signal progresses almost instantaneously throughout the entire endocardium via a special conduction system (Berne and Levy, 1967; Dürer et al., 1970). However, the importance of defining a proper excitation wave is obvious, in view of the direct relationship between potential disturbances in the electrical conduction through the myocardium and the ventricular performance.

In this paper we formulate a mathematical model of the LV contraction based on a thick-walled spheroidal geometry. The model describes both the passive and active properties of the ventricle, incorporating the fiber angle distribution throughout the wall, the sarcomere mechanics in terms of the force-
velocity length relationship, and an activation function of the sarcomere. The latter is triggered by an electrical signal which propagates from the endocardium to the epicardium. It is assumed that a simultaneous excitation of the entire endocardial layer occurs via the Purkinje system, followed by a radial propagation of the electrical signal (Dürrer et al., 1970; Myerburg et al., 1972; Sano et al., 1959). The apex-to-base component of the electrical signal (Dürrer et al., 1970; Myerburg et al., 1972; Sano et al., 1959). The instantaneous endocardial semi-major and semi-minor axes are denoted a and b, respectively, and h is the wall thickness. Although the LV shape changes to elliptization during the contraction, the change in the semi-axes ratio k = a/b is relatively small and sometimes inconsistent (Rankin et al., 1976). Thus, k is taken as constant throughout the cycle.

The state of the LV at a zero transmural pressure is defined as the reference state. This state is characterized by zero passive stress in all the muscle layers in the myocardium. A brief discussion and justification for utilizing this reference state is presented by Feit (1979). The semi-axis b0 and the wall thickness h0 in the reference unstressed state are used to calculate the LV muscle volume

\[ V_m = \frac{4}{3} \pi [(b_0 + h_0)(kb_0 + h_0) - kb_0^3]. \]

1) Consider a muscle layer of thickness dg at a distance g from the endocardium in the reference state. Assuming that the LV shape is essentially constant (i.e., k = a/b = a0/b0) and that the volume of the muscle layer dg under consideration (assumed incompressible) is unchanged during the cycle, the thickness of the corresponding layer dy in the general state is given by

\[ dy = \frac{V_m}{4\pi} \left( \frac{1}{(b_0 + h_0)} - \frac{1}{(kb_0 + h_0)} \right) \]
TABLE 1
Assumptions Used in the LV Model

| (1) | The geometry is a thick-walled prolate spheroid with a time-independent endocardial shape during contraction: i.e., the axis ratio is constant. |
| (2) | The LV wall is incompressible. |
| (3) | The fiber angle across the myocardium varies linearly from $-60^\circ$ to $+60^\circ$, in the reference, unstressed, configuration. |
| (4) | The sarcomere length distribution is uniform at the reference configuration. |
| (5) | The electrical activation propagates radially from endocardium to epicardium. |
| (6) | The mechanical activation function is half a sinusoidal wave. |
| (7) | The stress-strain rate relationship for the muscle fiber is linear. |
| (8) | The active stress-sarcomere length relationship is linear. |
| (9) | The passive stress-sarcomere length relationship is exponential. |
| (10) | Transfiber stresses are not included. |

where $y$ denotes the distance of the muscle layer from the endocardium at any given state during the LV contraction cycle and is related to $g$ by

$$y = \int_0^g \frac{dy}{dg} \, dg$$

The value of $S(Y)$ is given by a surface area of a spheroid with a semi-minor axis $b + y$ and a semi-major axis $a + y$

$$S(Y) = 2\pi \left\{ (b + y)^2 + \frac{(a + y)^2 \cdot (b + y)}{\sqrt{(a + y)^2 - (b + y)^2}} \arcsin \sqrt{(a + y)^2 - (b + y)^2} \right\}$$

The extension ratio $\lambda$ of any linear segment in the muscle layer initially located at a distance $g$ from the endocardium, is given by

$$\lambda = \frac{y + b}{g + b_0}$$

The strain rate of the different muscle layers can now be derived from the geometrical parameters. First, the volume of a muscle layer of thickness $y$ is obtained from equation 1, by replacing $b_0$ and $h_0$ with $b$ and $y$. The time derivative of this equation, assuming that the volume remains constant ($dV_m/dt = 0$), yields:

$$\dot{\epsilon}_y = -\epsilon_b \left( \frac{4kb^2 + kby + 2b^2 + 2yb}{2kb^2 + 2ykb + b^2 + 4by + 3y^2} \right)$$

where

$$\dot{\epsilon}_y = \frac{dy}{dt} \quad \text{and} \quad \dot{\epsilon}_b = \frac{dB}{dt}.$$ 

Note that $\dot{\epsilon}_y$, the strain rate of the segment, $y$, and $\dot{\epsilon}_b$, the strain rate of the semi-minor axis of the LV cavity, are of opposite signs, and $b$ increases as $y$ decreases. $\epsilon_y$ can be calculated for a given strain $\epsilon_b$, according to Equation 6, knowing that $\epsilon_y/\epsilon_b = \dot{\epsilon}_y/\dot{\epsilon}_b$.

The circumferential strain rate at a distance $y$ from the endocardium, $\epsilon_{cd}$, is equal to the radial strain rate of the layer and is given by:

$$\epsilon_{cd} = \frac{b_0 + y}{b + y} \epsilon_y$$

$\epsilon_b$ is evaluated from the changes in the LV volume and $\epsilon_y$ is then evaluated by Equation 6. Rewriting Equation 7 as

$$\epsilon_{cd} = \frac{\epsilon_b (b + y \epsilon_y)}{b + y}$$

indicates that the circumferential strain rate $\epsilon_{cd}$ decreases.
as $y$ increases from the endocardium to the epicardium, since $c_0/c_0$ is always negative. Replacing $y$ by $h$ in Equation 8 gives the relationship between the wall thickness and the semi-minor axis. (For thin-walled shells ($b \gg h$), the value of $c_0/c_0$ in Equation 6 approaches $-2$.)

**Fiber Orientation, Stress, and Pressure Calculations**

Following the description in 1969, by Streeter et al., of the fibers' orientation along the equator, the fiber angle $\alpha$ at the reference state is postulated to vary from $+60^\circ$ at the endocardium to $-60^\circ$ at the epicardium, and is given, at any distance $g$, by:

$$\alpha = \frac{\pi}{3} \left( 1 - \frac{2y}{h} \right) \quad (9)$$

The wall thickness in the reference state is now divided into $n$ thin layers of equal thickness, $dg$. As the volume of the LV changes, the different muscle layers change their spatial location and thickness within the LV wall, according to the nonlinear transformation of $g$ to $y$ (Eq. 3). However, as neither a change in shape nor a twist is introduced in the model, the muscle fibers in the different layers are assumed to retain their original orientation throughout systole.

As higher strain rates are associated with higher strains, there is a greater increase in thickness in the endocardial layers during the LV contraction than in the epicardial layers. Note that the linear fiber distribution defined by Equation 9 for the reference state is distorted as the volume changes from the unstressed volume. However, the fiber angle distribution as a function of the layer number remains linear.

The pressure gradient in a thin muscle shell, of thickness $dy$, is given by Mirsky (1970):

$$\frac{dP(y, t)}{dy} = \left( \frac{\sigma_{ei}}{r_1} + \frac{\sigma_{em}}{r_2} \right) \quad (10)$$

where $r_1$ and $r_2$ are the principal curvature radii ($r_1 = b$ at the equator) of the cavity. $\sigma_{ei}$ and $\sigma_{em}$ are the stress components in the circumferential and meridional directions, respectively, of the stress $\sigma$, which is assumed to exist along the fiber, i.e., Equations 11 and 12 (see also Appendix A),

$$\sigma_{ei} = \sigma_i \cos^2 \alpha \quad (11)$$

$$\sigma_{em} = \sigma_i \sin^2 \alpha \quad (12)$$

A unidirectional stress was also stipulated by Van der Broek and Van der Broek (1979), thus neglecting the transfiber stress. Indeed, as discussed below, the effect of the latter in the overall LV performance is rather minor.

Combining Equations 10, 11, and 12 yields:

$$\frac{dP(y, t)}{dy} = \sigma_i \left( \frac{\cos^2 \alpha}{r_1} + \frac{\sin^2 \alpha}{r_2} \right) \quad (13)$$

For a prolate spheroid, the two endocardial principal radii at the equator are $r_1 = b$ and $r_2 = a^2/b = k^2b$ and:

$$\frac{dP(y, t)}{dy} \bigg|_{y=b} = \frac{\sigma_i}{b} \left( \frac{\cos^2 \alpha + \sin^2 \alpha}{k^2} \right) \quad (14)$$

or, for any value of $y$,

$$\frac{dP(y, t)}{dy} \bigg|_{y} = \frac{\sigma_i}{b + y} \left( \frac{\cos^2 \alpha + \sin^2 \alpha}{k^2} \right) \quad (15)$$

where

$$k_i = \frac{a + y}{b + y} \quad (16)$$

The pressure within the myocardium at any $y$ is calculated by integrating Equation 15:

$$P(y, t) = \int_b^y \frac{\sigma_i}{b + \gamma} \left( \frac{\cos^2 \alpha + \sin^2 \alpha}{k_i} \right) dy. \quad (17)$$

Note that the value of $\alpha$ in Equations 11–17 is defined by Equation 9, which is transformed by Equation 3 to a function of $y$.

**Fiber Kinetics and Propagation of the Electrical Activation Signal**

To interrelate the muscle's fiber stresses, strains, and strain rates for different fiber lengths, a normalized stress $\tilde{\sigma}$ is defined with respect to the fibers' density (i.e., number of fibers per unit cross-section). The approach adopted here is based on an assumption that the properties of a muscle strip relate to the total number of fibers of which it is composed, rather than to their density in a cross-section area, which changes during contraction. Thus, assuming that the fiber density in the reference state is uniform across the wall, and is arbitrarily taken as unit 1, gives

$$\tilde{\sigma} = \frac{\sigma}{1} = \sigma \quad (18)$$

i.e., the normalized stress is equal to the actual stress in the reference configuration (which is unstressed in the passive state but definitely stressed in the active state). When a muscle with a given fiber density contracts against a constant force, its cross-sectional area increases, the fiber density decreases, and the developed stress decreases. However, the normalized stress remains constant and reflects the actual force resisted by a constant number of fibers. When LV ejection occurs, the LV cavity volume decreases, the thickness of each layer changes from $dg$ to $dy$, and the normalized stress $\tilde{\sigma}$ is related to the stress $\sigma$ by:

$$\tilde{\sigma} = \sigma \cdot \frac{dA}{dA_0} \quad (19)$$

where $dA_0$ and $dA$ are the differential cross-sectional areas perpendicular to the corresponding stress directions for the reference and the deformed configurations, respectively (Fig. 2).

For the circumferential direction:

$$\frac{dA_0}{dA} = \frac{dA}{dA_0} \cdot \frac{dg}{dg} = \frac{a + g}{a + y} \frac{dy}{dy} \quad (20)$$

whereas, for the meridional stresses, the ratio is given by

$$\frac{dA_0}{dA} = \frac{dA}{dA_0} \cdot \frac{dg}{dy} = \frac{b + g}{b + y} \frac{dy}{dy} \quad (21)$$

Each fiber develops a time-dependent stress function which is approximated by half a sinusoidal function of the form:
FIGURE 2. The differential unit cross-section areas inside the myocardium wall used for normalization of circumferential and meridional stresses. The shaded areas are the unit areas of the thin layers at distances \( g \) and \( y \) from the endocardium.

\[
\dot{\sigma}_l = \begin{cases} 
\delta_{l,\text{max}} \cdot \sin \left[ \frac{\pi}{T} (t - \tau(y)) \right] + \sigma_{l,p}; & 0 < (t - \tau(y)) < T \\
\delta_{l,p}; & 0 > (t - \tau(y)) > T 
\end{cases}
\]  

(22)

where \( \sigma_{l,p} \) is the normalized stress of the passive fiber, \( \delta_{l,\text{max}} \) is the maximum normalized isometric active stress for a given sarcomere length, and \( \tau(y) \) is the time, in which the electrical activation front propagates from the endocardium to a distance \( y \). Obviously, \( \tau(y) \) is a function of the transversal electrical signal propagation velocity \( c \), and is simply given by:

\[
\tau(y) = \frac{y}{c}.
\]  

(23)

The choice of the sin function in Equation 22 is supported by the form of the isometric contraction of an isolated papillary muscle (Hurst and Logue, 1970; Berne et al., 1979). A skewed wave with a long relaxation tail is familiar in isometric contraction of papillary muscles. However, a sensitivity analysis (see below) shows that utilization of long-tailed activation functions here results in only minute differences in the systolic performance, compared with those seen with the sine wave.

The relationship between the maximum normalized isometric stress \( \delta_{l,\text{max}} \) and the sarcomere length shown in Figure 3, is given by Pollack and Krueger (1978), and has the following form:

\[
\delta_{l,\text{max}} = \begin{cases} 
\frac{(SL - SL_0)\delta_0}{0.55}; & 1.65 < SL < 2.2 \mu \\
\delta_0; & 2.2 < SL < 2.4 \mu \\
\delta_0 - \frac{(SL - 2.4)\delta_0}{0.55}; & SL > 2.4 \mu 
\end{cases}
\]  

(24)

where \( \delta_0 \) is the maximum normalized isometric stress at a sarcomere length \( SL \) between 2.2 and 2.4 \( \mu \) (which corresponds to the maximum stress), \( SL_0 \) is the minimum sarcomere length required for active stress development, and \( SL_{P0} \) is the sarcomere length at the passive unstrained state. The extension ratio (Eq. 5) is now defined as the ratio between the instantaneous and the passive unstrained sarcomere lengths, i.e.:

\[
\lambda = \frac{SL}{SL_{P0}}.
\]  

(25)

The laws governing passive fiber mechanics, as given by Braunwald et al. (1976) and Feit (1979), are:

\[
\frac{\sigma}{E} = \frac{A - X}{B} \quad (A > 1) \\
(26)

\[
\frac{\sigma}{D} = \begin{cases} 
eq (\lambda + 1) & \lambda > 1 \\
\lambda (1 - \lambda) & \lambda < 1
\end{cases}
\]  

where \( E, B, \) and \( D \) are empirical constants. Equation 26 is plotted as line 2 in Figure 3.

Stress-Strain Rate Relationships

The stress-strain rate relationship is an essential feature which allows for the calculation of the strain rate of the fibers at any moment during systole. This relationship, intrinsic to muscle fibers, is actually the physiological basis for the source impedance of the LV.

The simple stress-strain rate (or force-velocity) relationship for cardiac fibers in the fully activated state described by Ross et al. (1966) (represented by line 1 in Figure 4, which intersects the axes at the maximum stress and the maximum strain rate), is given by:

\[
\text{STRAIN RATE} (\varepsilon) = \text{NORMALIZED STRESS} (\dot{\sigma})
\]

FIGURE 4. The stress-strain rate relationship used by the model. Line (1) represents the maximum active state; (2) = partial active state, (3) = increased length for the maximum active state and (4) = increased contractility for the maximum active state.
Aortic valve is assumed negligible. The LV outflow, \( Q(t) \),
model (Noordegraaf, 1978). The pressure drop across the
in the unstressed state. The sensitivity of the model to the
constant sarcomere length of 1.9 \( \mu m \) exists across the wall
between 1.85 and 2 \( \mu m \) (Sonnenblick, 1967, 1973). Studies
with zero transmural pressure drop, hence a uniform
pressure across the wall) have been reported to range
length values in the reference unstressed state of the LV
experiments to human hearts seems justified. Sarcomere
similar mechanical properties, and extrapolation of animal
to believe that the sarcomere units in most mammals have
a small degree of imbrication (between the fiber and the
shell surface) is neglected here, as it represents a very
small value (Streeter et al., 1969)).

3. Calculate the ejection phase according to the stress-
strain rate relationship for the cardiac muscle (Eq. 27).
[Note that a strain rate of the endocardial fibers is sought
which equates the intraventricular pressure calculated by
Equation 17 to the afterload-dependent pressure (Eq. 29)].
The strain rates of the different layers are related to the
diastolic pressure across the wall, including the LV cavity pressure.
[The fibers are assumed to lie parallel to the ellipsoidal shells.
A small degree of imbrication (between the fiber and the
shell surface) is neglected here, as it represents a very
small value (Streeter et al., 1969)].

4. Repeat the steps used to calculate the LV pressure
distribution. A strain rate of the endocardium is sought
which corresponds to an intraventricular pressure which
equals the aortic pressure. [The search is carried out by
modifying the endocardial strain rate at each iteration by
0.01 circ/sec until \( P(0, t) \leq P_{ao}(t) \)].

5. Modify the aortic pressure at each step, using the
previous flow and pressure values combined with Equa-
tion 29.

6. Calculate the various indexes of the LV function.
These include the isovolumic pressure index \( (dP/dt)_{iso} \),
stroke volume, stroke work, ejection fraction, average \( \varepsilon_{a} \),
maximum \( \varepsilon_{a} \), and maximum flow.
Results

Sarcomere Length and Stress Distribution in Diastole

The utilization of the parameter values listed in Table 2 yields a LV muscle volume of 172 ml, an unstressed LV cavity volume of 53 ml, and an end-diastolic cavity volume of 101 ml (corresponding to a semi-minor axis of 2.3 cm and k = 2). The end-diastolic LV pressure is calculated by the model for these values (Eq. 17 for the passive state). The reference geometry parameters are associated with the assumed uniform sarcomere length of 1.9 μm throughout the wall.

Increasing the LV volume by increasing the values of the LV axes results in a decrease of the LV wall thickness and an extension of the fibers. Figure 6A shows the sarcomere length distribution across the wall at end diastole, assuming no changes in the shape of the LV. It is clearly shown that the subendocardial layers undergo larger extensions than the subepicardial layers. The combination of the local sarcomere stress and fiber angle yields the corresponding circumferential stress shown in Figure 6B. Larger extensions in the subepicardial layers are the cause for higher local circumferential stresses. However, because of the inclination angle of the fibers, the circumferential stress within the subendocardial and subepicardial layers is smaller than in the middle layers. As seen, the pressure distribution within the wall, which is identical with the radial stress distribution, increases from the epicardium to the endocardium. The pressure is zero at the epicardial layer and increases slowly in the outer wall, followed by rapid increase in the inner wall to an endocardial pressure which is equal to the cavity pressure.

Effect of Twisting on Sarcomere Length and Stress Distribution (at End Diastole)

Twisting, as well as changes in LV shape, are normal phenomena. As twisting occurs, at a given cavity volume, the LV wall pressure changes due to the changes in the stress distribution within the wall. The effects of twisting on the sarcomere length and stress distribution, for an end-diastolic volume of 102 ml, were calculated (see Appendix B) and are shown in Figure 6, C and D. The corresponding cavity pressure decreases from 5.8 mm Hg without twisting to a minimum of 4.2 mm Hg at a twist angle β = 34°. Note that β = 34° is the theoretical angle of twist which yields a minimum LV cavity pressure at the given LV volume and, hence, a maximum LV compliance. However, this angle is greatly modified in vivo by the circumferential shear stresses that exist between the fibers that inhibit the free slippage of the muscle fibers. Thus, consistently lower twist angles are reported in vivo during the cardiac cycle (Arts et al., 1979). Similar to earlier models (Van der Broek and Van der Broek, 1979; Feit, 1979), the complete systole is modeled here assuming that twisting has but a minor effect on the LV mechanics. It is noteworthy that the twisting of the LV allows for a more uniform sarcomere length distribution through the wall, preventing overextension of the endocardial layers. In other words, a LV of given material properties is more compliant when the ventricle is allowed to twist and reach its optimal (i.e., minimal pressure) state.

Stress Distribution in Systole

The high stresses which develop due to muscle activities in systole are associated with higher LV cavity and wall pressures. Two phenomena characterize the systole: (1) the individual fiber stress depends on the activation function, as well as on the velocity of the electrical signal propagating within the wall. Only part of the fibers are activated at the beginning or the end of systole, but all of the fibers are activated during the systole; (2) the stress-length relationship for the sarcomere results from the combination of the (linear) active and the (exponential) passive stresses.
### Table 2
Reported Values of the Parameters and the Corresponding Values Used in the Present Model

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Symbol</th>
<th>Reported values</th>
<th>Units</th>
<th>Reference</th>
<th>Value used</th>
<th>Units</th>
</tr>
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<tbody>
<tr>
<td>Passive stress strain (Eq 26)</td>
<td>$E$</td>
<td>6; 6.85</td>
<td>(g/cm²)</td>
<td>Glantz et al., 1975; Pao et al., 1980; Feit, 1979; Braunwald et al., 1976; Capello et al., 1981</td>
<td>6</td>
<td>(g/cm²)</td>
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<tr>
<td></td>
<td>$D$</td>
<td>14; 19.7; 6.3; 9.5; 10</td>
<td>(g/cm²)</td>
<td></td>
<td>10.5</td>
<td>(g/cm²)</td>
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<tr>
<td></td>
<td>$B$</td>
<td></td>
<td></td>
<td></td>
<td>10</td>
<td>(g/cm²)</td>
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<tr>
<td>Maximum active sarcomere stress</td>
<td>$\varepsilon_0$</td>
<td>1500</td>
<td>(g/cm²)</td>
<td>Pollack and Krueger, 1978</td>
<td>1500</td>
<td>(1140 mm Hg)</td>
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<td>Sarcomere length at:</td>
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<tr>
<td>Unstressed state</td>
<td>$SL_{Po}$</td>
<td>1.9; 1.8+2; 1.9+2</td>
<td>(µm)</td>
<td>Feit, 1979; Spotnitz et al., 1966; Krueger, et al., 1975; Grimm et al., 1970; Baan et al., 1979</td>
<td>1.9</td>
<td>(µm)</td>
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<td>Zero active stress</td>
<td>$SL_{0}$</td>
<td>1.65</td>
<td>(µm)</td>
<td>Pollack and Krueger, 1978</td>
<td>1.65</td>
<td>(µm)</td>
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<td>$SL_{m}$</td>
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<td>(µm)</td>
<td>Pollack and Krueger, 1978</td>
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<td>(µm)</td>
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<td>(sec⁻¹)</td>
<td>Pollack et al., 1970</td>
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<td>(sec⁻¹)</td>
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<td>Unstressed sarcomere length distribution</td>
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<td>Equal; 1.9</td>
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<td></td>
<td></td>
<td>Feit, 1979; Yoran et al., 1975</td>
<td>Equal; 1.9</td>
<td>(µm)</td>
</tr>
<tr>
<td>Not equal</td>
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<td></td>
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<tr>
<td>Fiber angle distribution</td>
<td>$\alpha(y)$</td>
<td>+60° $\rightarrow$ $-60°$</td>
<td></td>
<td>Streeter et al., 1969</td>
<td>$+60° \rightarrow -60°$</td>
<td>(linear)</td>
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<td>Muscle fiber activation function</td>
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<td>Hurst and Logue, 1970</td>
<td>Half a sinusoidal wave</td>
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<td>Electrical propagation velocity (radial)</td>
<td>$C$</td>
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<td>(cm/sec)</td>
<td>Berne and Levy, 1967</td>
<td>30</td>
<td>(cm/sec)</td>
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<td>Semiminor axis</td>
<td>$b_0$</td>
<td>1.9; 2.4 (man); 1.5 (dog)</td>
<td>(cm)</td>
<td>Gault et al., 1968; Braunwald et al., 1976; Glantz, 1975</td>
<td>1.85</td>
<td>(cm)</td>
</tr>
<tr>
<td>Semiaxes ratio</td>
<td>$k$</td>
<td>1.9; 2.4 (man); 1.5 (dog)</td>
<td>(cm)</td>
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<td>Wall thickness</td>
<td>$h_0$</td>
<td>1.4</td>
<td>(cm)</td>
<td>1975; Diamond et al., 1971</td>
<td>1.4</td>
<td>(cm)</td>
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<tr>
<td>Volume</td>
<td>$v$</td>
<td>28, 30 (dog)</td>
<td>(ml)</td>
<td></td>
<td>53</td>
<td>(ml)</td>
</tr>
<tr>
<td>End-diastolic geometry:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Semiminor axis</td>
<td>$b$</td>
<td>2.3</td>
<td>(cm)</td>
<td>Gault et al., 1968; Gaash et al., 1972</td>
<td>2.3</td>
<td>(cm)</td>
</tr>
<tr>
<td>Wall thickness</td>
<td>$h$</td>
<td>0.8</td>
<td>(cm)</td>
<td></td>
<td>1</td>
<td>(cm)</td>
</tr>
<tr>
<td>Volume</td>
<td>$v$</td>
<td>107</td>
<td>(ml)</td>
<td></td>
<td>102</td>
<td>(ml)</td>
</tr>
<tr>
<td>LV muscle volume</td>
<td>$V_m$</td>
<td>100–200</td>
<td>(ml)</td>
<td>Altman and Dittmer, 1971</td>
<td>172</td>
<td>(ml)</td>
</tr>
<tr>
<td>Arterial system</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capacitance</td>
<td>$C$</td>
<td>1</td>
<td>(ml/mm Hg)</td>
<td>Noordegraaf, 1978</td>
<td>1</td>
<td>(ml/mm Hg)</td>
</tr>
<tr>
<td>Resistance</td>
<td>$R$</td>
<td>2</td>
<td>(mm Hg·sec/ml)</td>
<td>Noordegraaf, 1978</td>
<td>2</td>
<td>(mm Hg/ml per sec)</td>
</tr>
</tbody>
</table>
The sarcomere length, stress, and pressure distributions within the wall (without twisting) are calculated here for four different situations: (1) the beginning of ejection (LV volume = 102 ml, pressure = 96.8 mm Hg); (2) maximum outflow (LV volume = 72.9 ml, pressure = 101.6 mm Hg); (3) maximum LV pressure (LV volume = 33.8 ml, pressure = 132.9 mm Hg); (4) end systole (LV volume = 31.3 ml, pressure = 129.1 mm Hg).

At the beginning of ejection, calculated to occur 60 msec after endocardial excitation, the maximum circumferential stresses are observed in the middle layers (curve is Fig. 7A). An almost linear increase in the intramural pressure, from the epicardium to the endocardium, occurs. The ejection velocity at this moment is practically zero, and the fiber stresses are not yet affected by the force-velocity relationship.

The stress and pressure distributions at peak ejection flow, calculated to occur 160 msec after endocardial excitation, are shown in Figure 7B. Here, the fiber stresses are modified by the strain rate according to Equation 27. The isovolumic stress distribution (assuming that the strain rate is zero at that particular volume) is shown in Figure 7B for comparison, and demonstrates the large effect of the ejection velocity on the intramural stresses and pressures in this case of maximum outflow.

Much lower flow rates are encountered at the maximum pressure point, calculated to occur 300 msec after endocardial excitation. The theoretic isovolumic stress and pressure distributions, shown in Figure 7C, are close to the calculated stresses, considering the effect of the strain rate. The circumferential stress in the endocardial layer is low, mainly due to the fact that the length of the sarcomere at the volume corresponding to the maximum pressure is rather small.

A similar picture is observed in end systole, Figure 7A calculated 380 msec after endocardial excitation. The endocardial circumferential stresses in this situation are lower than at the maximum pressure situation, due to the added shortening of the sarcomere, shown in Figure 7D, and the decrease in the activation function value at end systole.

The Passive Pressure-Volume Relationship

The exponential stress-strain relationship for the sarcomeres in the passive state (Eq. 26) yields the exponential pressure-volume relationship shown in Figure 8. The parameters for Equation 26 were adjusted to fit the normal pressure-volume relationship for man and are listed in Table 2. As the reported values listed in Table 2 for D, the stiffness of the cardiac muscle, vary between 6 and 19.7, the value of 11.5 used here seems like a logical average value. The quasi-static relationship used in this model neglects the viscoelastic effects which play a major role in diastole. The LV volume at the beginning of diastole is smaller than the unstressed volume, and negative cavity pressure is predicted by the model. However, in reality, the rapid inflow of blood in early diastole causes higher LV pressures than those predicted by the present model due to viscoelastic effects. Thus, although the passive pressure-volume relationship of the LV is shown in Figure 8D, the actual diastolic period is not simulated in the current model, as the diastolic viscoelastic properties are not included in the present model.

LV Ejection under Different Conditions

The calculated pressures within the LV, the ejection flow rates and the LV volumes, are presented
in Figures 8–10 as a function of time. The LV contraction process is compared under different preloading conditions (i.e., for different values of the end-diastolic LV semi-minor axis), different afterloading conditions (represented by the end-diastolic aortic pressures), and the contractility of the cardiac muscle (represented by the maximum sarcomere stress, $\sigma_{s,max}$).

The LV contraction cycles (excluding diastole) for different preloads are shown in Figure 8. Higher pressures are obtained for higher preloads (Fig. 8A). Higher flow rates in Figure 8B, which characterize increased preloads, are associated with larger volume changes in Figure 8C. The pressure volume plot (Fig. 8D) clearly demonstrates the classical loops for the four cycles under consideration. Note that the slope of the line connecting the end-systolic points in Figure 8D has been used by Suga et al. (1974, 1977) to characterize muscle contractility.

A summary of the corresponding indices of the four different cycles that are commonly used in practice is given in Table 3. The increase in the stroke work and stroke volume with the increase in preload characterizes the Frank Starling mechanism.
TABLE 3
Performance Parameters of the LV Calculated for Different Preloads

<table>
<thead>
<tr>
<th>No.</th>
<th>End-diastolic semi-minor axis (cm)</th>
<th>End-diastolic volume (ml)</th>
<th>End-diastolic pressure (mm Hg)</th>
<th>Stroke volume (ml)</th>
<th>Stroke work (erg x 10^3)</th>
<th>Ejection fraction (%)</th>
<th>Maximum flow (ml/sec)</th>
<th>Maximum dp/dt (mm Hg/sec)</th>
<th>Average c_e (sec^-1)</th>
<th>Maximum c_e (sec^-1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.9</td>
<td>57</td>
<td>0.4</td>
<td>36.2</td>
<td>0.45</td>
<td>63</td>
<td>234</td>
<td>1301</td>
<td>1.1</td>
<td>1.92</td>
</tr>
<tr>
<td>2</td>
<td>2.1</td>
<td>77.6</td>
<td>2.1</td>
<td>51.7</td>
<td>0.67</td>
<td>67</td>
<td>317</td>
<td>1679</td>
<td>1.17</td>
<td>2.1</td>
</tr>
<tr>
<td>3</td>
<td>2.3</td>
<td>101.9</td>
<td>5.8</td>
<td>70.6</td>
<td>1.02</td>
<td>69</td>
<td>411</td>
<td>1959</td>
<td>1.21</td>
<td>2.16</td>
</tr>
<tr>
<td>4</td>
<td>2.5</td>
<td>130.9</td>
<td>7.6</td>
<td>95.7</td>
<td>1.4</td>
<td>73</td>
<td>526</td>
<td>2023</td>
<td>1.35</td>
<td>2.22</td>
</tr>
</tbody>
</table>

The above results were obtained for aortic end-diastolic pressure of 80 mm Hg.

As seen in this table, only the ejection fraction is relatively independent of the preload, whereas the rest of the parameters are strongly preload dependent. The performance curves for different afterloads are shown in Figure 9. Higher pressures in Figure 9A are associated with lower flows (Fig. 9B), due to the classical inverse relationship between the fibers' strain rate and stress. Smaller volume changes (Fig. 9C) occur with increased arterial pressures. The slope of the line connecting the end-systolic pressure-volume curves shown in Figure 9D (again, a measure of muscle contractility) is identical with the one which was obtained for the differently preloaded cycles in Figure 8D, thus showing that the contractility index is independent of the preload and the afterload in the present model.

Table 4 lists the values of the various indices for the different afterloads. The stroke volume and ejection fraction are seen to be afterload dependent. However, an increase in the stroke work is observed with an increased afterload. The maximum dp/dt is seen to be afterload independent, consistent with experimental data (Braunwald et al., 1976; Parmley et al., 1973). However, the other indices (maximum flow rate, average c_e, maximum c_e) are quite sensitive to variations in the blood pressure.

Changes in contractility are simulated here by changes in the maximum sarcomere stress. As shown in Figure 4, these changes shift the stress-strain rate line, and give different values of c_e, max. As seen in Figure 10, increased contractility slightly increases the LV cavity pressure (Fig. 10A), increases the ejection flow rate (Fig. 10B), and increases LV volume changes (Fig. 10C). The end-systolic points of the pressure-volume loops move to the left (i.e., to lower volumes) as the contractility increases (Fig. 10D). Table 5 also shows that all the performance indices increase with increased contractility. The end-systolic pressure-volume relationship is clearly shown to be strongly dependent on the contractility.

As stated earlier, this index has a great advantage...
over other indices because it is independent of the preload and afterload, and can thus be considered a "pure" index of contractility.

Discussion

The model of the LV presented here describes the performance of the LV based on its shape, structure, and muscle fiber kinetics which are derived from the basic sarcomere physiology summarized in Table 2. The model incorporates a number of assumptions which are summarized for convenience in Table 1. The analysis of the dependence of the global LV performance on some of the major assumptions used here is highly instructive.

Sensitivity Analysis

Transfiber Stresses

The systolic performance of the LV model without transfiber stresses (σf) is compared here (see Appendix C), with one which includes the maximum effect of σf. Only minor differences are noted (Table 6) in the global LV performance. These results, which seem surprising at first glance, can be explained by the counteraction of the extension and compression stresses at different values of α. Thus, employing only σf along the fibers in the present model is consistent with Van der Broek and Van der Broek (1979), and does not introduce any significant error in the global performance of the model.

Elastance Function

It is known from experiments with isolated papillary muscles that the relaxation time is somewhat longer than the activation time, and the effect of a longer relaxation tail is compared here with the assumed sinusoidal activation function. As demonstrated in Table 6, introducing into the model a relaxation time that is twice as long as the sinusoidal one does not affect the systolic LV performance. As systole terminates close to the maximum point in the elastance function, the systole is practically independent of the relaxation time. Obviously, the initial phase of diastole does depend on the relaxation time, but this point is outside the scope of this study.

Stress-Strain Rate Relationship

The linear stress-strain rate relationships (Eq. 27) is compared with Hill’s hyperbolic relationship, which, in terms of stresses, is given by

$$(\bar{\sigma} + a)\varepsilon_f = b(\bar{\sigma}_{0,\text{max}} - \bar{\sigma})$$

where

$$\bar{\sigma} = \frac{b\sigma_{0,\text{max}} - a\varepsilon_f}{\varepsilon_f + b}.$$  

A choice of values consistent with known physiological data ($\sigma_{0,\text{max}} = 1140$ mm Hg, $a = 2480$ mm Hg, $b = 6$ sec$^{-1}$) shows (Table 6) that the difference between the effects of the hyperbolic and linear relationships on the global LV function is rather small, and the use of the linear relationship is well justified.

Sarcomere Length at Reference Configuration

The assumption that a relatively uniform distribution of the sarcomere length exists in the reference state (Feit, 1979; Krueger and Pollack, 1975; Pollack and Hunzman, 1974) is used here. Van der Broek and Van der Broek (1979) used a different distribution, based on the work of Yoran et al. (1973), which assumes that the sarcomere length distribution is uniform in the end diastole, rather than in the reference, stress-free configuration. Experimental evidence is obviously desired to determine the correct sarcomere length distribution function in humans. The dependence of the model performance on this parameter is demonstrated in Table 6. However, the selection of SL = $SL_{P_0} = 1.9 \mu m$ in the reference state in the present model is justified in view of the agreement of the calculated global performance indices of the LV with the ones known from the literature.

Zero Active Pressure Sarcomere Length

Increasing the value of the SL at zero active pressure ($SL_{a}$) affects the cardiac performance by decreasing the ejection fraction and (dP/dt)$_{\text{max}}$ (Table 6), while simultaneously increasing the elastance from a value of 4.1 to 5.5 mm Hg/ml. The latter can be explained by the increased slope of the active

<table>
<thead>
<tr>
<th>No.</th>
<th>End-diastolic aortic pressure (mm Hg)</th>
<th>Stroke volume (ml)</th>
<th>Stroke work (erg x 10$^8$)</th>
<th>Ejection fraction (%)</th>
<th>Maximum flow (ml/sec)</th>
<th>Maximum pressure (mm Hg/sec)</th>
<th>Average $\varepsilon_f$ (sec$^{-1}$)</th>
<th>Maximum $\varepsilon_f$ (sec$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>60</td>
<td>74.6</td>
<td>0.91</td>
<td>73</td>
<td>427</td>
<td>1953</td>
<td>1.32</td>
<td>2.37</td>
</tr>
<tr>
<td>2</td>
<td>80</td>
<td>70.6</td>
<td>1.02</td>
<td>69</td>
<td>412</td>
<td>1959</td>
<td>1.22</td>
<td>2.16</td>
</tr>
<tr>
<td>3</td>
<td>100</td>
<td>67.1</td>
<td>1.11</td>
<td>66</td>
<td>397</td>
<td>1959</td>
<td>1.18</td>
<td>1.98</td>
</tr>
<tr>
<td>4</td>
<td>120</td>
<td>64.1</td>
<td>1.21</td>
<td>63</td>
<td>380</td>
<td>1959</td>
<td>1.09</td>
<td>1.83</td>
</tr>
</tbody>
</table>

The above results were obtained for end-diastolic volume of 102 ml (corresponding to end-diastolic endocardial semi-minor axis of 2.3 cm).
stress-strain relationship for an individual sarcomere, which is associated with an increase in $S_L_0$ (see Fig. 3).

**Passive Stress-Sarcomere Length Relationship**

Introducing a linear passive stress-SL relationship, i.e., $\sigma_{fp} = \text{const} (\lambda - 1)$, instead of an exponential one (Eq. 26), has almost no effect on the end-diastolic volume-to-stroke work relationship (Table 7). Thus, the Frank Starling mechanism does not seem to be affected by the passive properties of the muscle. However, the passive pressure-volume relationship is greatly influenced by the passive properties of the muscle, thus affecting the relationship between the end-diastolic pressure and stroke work.

In view of the data, which prove the exponential relationship between the passive stress and SL, the use of a linear relationship is not justified here.

**Fiber Mechanics and LV Deformation**

The mechanical properties of a fiber, which are used to describe the muscle behavior, can be represented by the behavior of different lumped parameters, such as the contractile or elastic elements (Grood et al., 1979). Alternatively, as used here, the classical stress-length relationship is combined with the stress-velocity relationship to characterize the dynamics of the muscle fiber. This approach has the advantage of utilizing the preload-independent maximum velocity of shortening of the whole fiber (Pollack, 1970) to define the contractility, whereas Grood’s approach is preload dependent. Furthermore, treating the fiber as a whole enables the application of a time-dependent activation function to the fiber, and the stress function, at a constant length, is approximated by (half) a sin function. Clearly, this function can eventually be replaced by a more precise activation function for the human cardiac muscle.

The shape of the LV, and the fiber angle distribution, are assumed constant throughout the cycle. However, as demonstrated in Figure 6 for end diastolic systolic pressure: volume ratio

<table>
<thead>
<tr>
<th>No.</th>
<th>$\sigma_0$ (mm Hg)</th>
<th>Stroke volume (ml)</th>
<th>Stroke work (erg x 10$^7$)</th>
<th>Ejection fraction (%)</th>
<th>Maximum flow (ml/sec)</th>
<th>Maximum acceleration (mm Hg/sec)</th>
<th>Maximum $\frac{dP}{dt}$ (mm Hg/sec)</th>
<th>Average $\varepsilon_f$ (sec$^{-1}$)</th>
<th>Maximum $\varepsilon_f$ (sec$^{-1}$)</th>
<th>End-systolic pressure: volume ratio (mm Hg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>740</td>
<td>56.9</td>
<td>0.76</td>
<td>56</td>
<td>286</td>
<td>4580</td>
<td>1272</td>
<td>0.82</td>
<td>1.29</td>
<td>2.57</td>
</tr>
<tr>
<td>2</td>
<td>940</td>
<td>64.5</td>
<td>0.92</td>
<td>63</td>
<td>351</td>
<td>6409</td>
<td>1616</td>
<td>1.04</td>
<td>1.68</td>
<td>3.37</td>
</tr>
<tr>
<td>3</td>
<td>1140</td>
<td>70.6</td>
<td>1.02</td>
<td>69</td>
<td>411</td>
<td>7322</td>
<td>1959</td>
<td>1.21</td>
<td>2.16</td>
<td>4.12</td>
</tr>
<tr>
<td>4</td>
<td>1340</td>
<td>77.8</td>
<td>1.06</td>
<td>76</td>
<td>473</td>
<td>9147</td>
<td>2296</td>
<td>1.44</td>
<td>2.73</td>
<td>5.26</td>
</tr>
</tbody>
</table>

The above results are obtained for an end-diastolic aortic pressure of 80 mm Hg and end-diastolic volume of 102 ml.
TABLE 6
Sensitivity Analysis of Various Assumptions

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Ejection fraction (%)</th>
<th>(dP/dt) max (mm Hg/sec)</th>
<th>Stroke volume (ml)</th>
<th>Stroke work (erg)</th>
<th>Peak systolic pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic model</td>
<td>67</td>
<td>1672</td>
<td>68</td>
<td>1.00 x 10^7</td>
<td>134</td>
</tr>
<tr>
<td>Maximum transfiber stresses</td>
<td>70</td>
<td>1562</td>
<td>71</td>
<td>1.02 x 10^7</td>
<td>130</td>
</tr>
<tr>
<td>Doubled relaxation time in the elastance function</td>
<td>66</td>
<td>1672</td>
<td>67</td>
<td>1.02 x 10^7</td>
<td>134</td>
</tr>
<tr>
<td>Hyperbolic stress-strain rate, Eq. 30</td>
<td>63</td>
<td>1672</td>
<td>64</td>
<td>0.91 x 10^7</td>
<td>125</td>
</tr>
<tr>
<td>Increased SL at reference configuration (from 1.9 to 2.0 μm)</td>
<td>83</td>
<td>1860</td>
<td>84</td>
<td>1.28 x 10^7</td>
<td>138</td>
</tr>
<tr>
<td>Decreased SL at reference configuration (from 1.9 to 1.8 μm)</td>
<td>51</td>
<td>1342</td>
<td>52</td>
<td>0.76 x 10^7</td>
<td>120</td>
</tr>
<tr>
<td>Increased SLa active pressure, (from 1.65 to 1.7 μm)</td>
<td>57</td>
<td>1870</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\( E_{max} = 5.5 \text{ mm Hg/ml.} \)

tole, twisting of the LV affects the fiber length distribution and stress distribution. It seems that twisting the LV minimizes the changes in the SL distribution across the LV wall during the volumetric changes throughout the cycle, and thus keeps the mechanical work of the heart at a minimum. The twisting of the ventricle may be associated with circumferential shear stresses acting between muscle layers, and should thus be related to the shear elastic modulus of the muscle. Unfortunately, this information is still unknown, and the effect of shear stresses in the LV wall so far has been neglected.

Both the passive and active circumferential stresses are minimal at the endocardium and epicardium and are related to the specific pattern of fiber angle distribution. These results, both in systole and diastole, are consistent with other reports (Streeter et al., 1970; Feit, 1979). The pressure in the endocardial layer in systole is of the same order of magnitude as the coronary arterial pressure, and may even be higher. This explains the collapse of the endocardial vessels and zero perfusion during systole. However, the hydrostatic pressure in the epicardial layers is not as high, and these are therefore perfused during both the systole and the diastole (Feigl, 1983).

**Electrical Propagation Rate**

The effect of the electrical activation velocity on the stress distribution is of particular interest. Active stress development propagates from the endocardial layer toward the epicardium, following the electrical activation. This may result in squeezing the blood (venous as well as arterial) from the endocardial layers outward. Toward the end of the contraction, the relaxation of the fibers propagates in the same direction, i.e., outwards. The fact that the action potentials at the outer layers are shorter than at the inner layers (Berne and Levy, 1967) may be associated with a shorter mechanical activity time of the epicardial sarcomeres. Thus, one may speculate that the reversal of the stress relaxation propagation may occur as a normal pattern. This phenomenon, unexplored, to the best of our knowledge, may have a strong relationship to the uneven coronary perfusion and energy balance in the different muscle layers.

**Strain Rate Effects**

The calculated stress distribution during the ejection phase, studied with and without inclusion of the strain rate, shows (Fig. 7) that the difference between isovolumic and nonisovolumic stress distributions is high at peak velocities and low toward the end systole where the strain rate is low. Thus, the effects of the strain rate during systole cannot be neglected. However, the beginning and end of the systole are associated with minimal strain rates and can be approached (Chadwick, 1982) as being strain rate independent.
LV Performance Indices

The calculated performance of the LV in different preloads, afterloads, and contractility states indicates that: (1) The maximum elastance value is the best index of contractility, particularly since it can be conveniently measured. This conclusion is strongly supported by experimental and clinical studies (Suga and Sagawa, 1974; Suga et al., 1973, 1976, 1977; Schuler et al., 1981, 1982; Slutzky et al., 1980). (2) The ejection fraction is moderately dependent on the afterload and only slightly dependent on the preload. However, it can still be used as a good contractility index for relatively similar loads. (3) Other indices studied here (Tables 3–5) show a strong dependence on the loading conditions. Although these indices can still be used to quantify the heart status, strict attention should be given to the loading conditions.

The Starling Law and the Origin of the Maximum Elastance

The qualitative and quantitative macroscopic description of the Starling law, which comes out of the single fiber mechanics utilized here, is of major interest from the bioengineering and physiological point of view. The Starling law relating the stroke work to the preload stems from the basic stress-length relationship of the sarcomere. The value of the maximum elastance is shown to have a direct relationship to the slope of the active stress-length relationship of the sarcomere. An increase in either fiber contractility (σ_{max}) or in the minimal sarcomere length necessary for stress development (SL_{0}) (Table 5) at zero active stress, increases the active sarcomere stress-length slope. Both are associated with an increased elastance value. Thus, the correspondence between the LV pressure-volume relationship, the well-known Starling law, and microstress-strain relationship is quantitatively demonstrated.

Model Perturbations—Pathology

A certain variability exists in the parameters which govern the performance of biological systems. The variability exists between individuals, and also in the same individual at different times. The effect of different parameter variations associated with various pathologies on some performance indices are summarized in Table 8. Note that a decrease in the electric propagation velocity occurs with a variety of drugs (β-blockers, slow calcium channel blockers, etc.). As shown by the calculations, significant slowing of the electrical propagation slows the pressure development rate (as evident by the lower values of dP/dt), decreases the maximum elastance, and slightly decreases the ejection fraction, thus mildly decreasing the cardiac function. The effects of non-uniform electrical propagation disturbances (conduction system disturbance) are not included in the current model. The increase in the unstressed volume, which usually is associated with cardiac failure, is clearly shown to be associated with a decrease in all the contractility parameters.

Hypertropy is easily simulated by increasing the unstressed wall thickness from 1.4 to 1.6 cm, corresponding to an increase in muscle volume from 172 to 232 ml. A corresponding increase in the value of dP/dt and a slight decrease in the value of the maximum elastance is also shown in Table 8, and an increase in the ejection fraction at normal afterload is predicted. Note that the ejection fraction calculated at higher afterloads (150 mm Hg) remains within its normal range.

Summary

The model of the LV presented here relates the complete systole mechanics to the LV geometry, fiber structure, sarcomere mechanics and dynamics, and the electrical activation propagation velocity from the endocard to the epicardium. The lack of detailed data on the time-dependent sarcomere function, the sarcomere length distribution, and the sarcomere's time-dependent stress-strain rate relationship is overcome by appropriate assumptions. The calculated results are consistent with experimental and clinical studies.

---

### Table 8

<table>
<thead>
<tr>
<th>Condition</th>
<th>Ejection Fraction (%)</th>
<th>dP/dt (mm Hg/sec)</th>
<th>Maximum Elastance (mm Hg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal parameters</td>
<td>69</td>
<td>1959</td>
<td>4.1</td>
</tr>
<tr>
<td>Increase in the unstressed volume (from 53 to 62 ml)</td>
<td>60</td>
<td>1715</td>
<td>3.6</td>
</tr>
<tr>
<td>Decreased electrical propagation velocity (from 30 to 15 cm/sec)</td>
<td>67</td>
<td>1900</td>
<td>3.8</td>
</tr>
<tr>
<td>Increase in the muscle volume, i.e., hypertrophy (increase in muscle volume from 172 to 232 ml)</td>
<td>80</td>
<td>219</td>
<td>3.7</td>
</tr>
</tbody>
</table>

* End-diastolic aortic pressure is 80 mm Hg.
The model can be used to calculate the energy utilization by the muscle in each particular layer, based on the stress-strain rate relationship. The coronary perfusion can then be interrelated to the stress distribution to yield the energy equations characterizing the different muscle layers.

Appendix A

Derivation and Normalization of the Circumferential and Meridional Stress Components

The stress in the fiber direction is defined by:

\[ \sigma_f = \frac{dF}{dA'} \]  (A-1)

where \( dF \) is the fiber force acting on a cross-section \( dA' \) which is normal to the direction of the fibers.

Assuming that the fiber is at an angle \( \alpha \) from the circumference, the force component \( dF_{\theta} \) which acts in the circumferential direction on the area element \( dA = dA' / \cos \alpha \) (which lies normal to the circumferential direction) is given by:

\[ dF_{\theta} = dF \cos \alpha \]  (A-2)

Combining Equations A-1 and A-2 yields (Van der Broek and Van der Broek, 1979) Equation 11:

\[ \sigma_{\theta} = \frac{dF_{\theta}}{dA} = \frac{dF \cos \alpha}{(dA') / \cos \alpha} \]

\[ = \frac{dF}{dA'} \cos^2 \alpha = \sigma_0 \cos^2 \alpha \]  (A-3)

A similar derivation is done for \( \sigma_{\phi} \), Equation 12.

Now consider a fixed number of fibers with the same angle of inclination \( \alpha \) undergoing uniform extension. Assume that the force per fiber is constant, i.e., the same force \( dF \) is resisted by the fibers having a cross-section \( dA_0 \) before the extension and a cross-section \( dA \) after the extension. Stress in the \( \theta \theta \) direction before extension is given by:

\[ \sigma = \frac{dF_{\theta}}{dA_0} \]

and, after the extension,

\[ \sigma_0 = \frac{dF \cos \alpha}{dA_0} \]  (A-5)

It is obvious that for identical \( dF \), \( \sigma \neq \sigma_0 \) as \( dA \neq dA_0 \). However, if we define \( \delta = \frac{dA}{dA_0} \) then:

\[ \sigma_0 = \delta \frac{dF \cos \alpha}{dA_0} = \sigma_0 \]

and

\[ \delta = \frac{dF \cos \alpha}{dA_0} \cdot \frac{dA}{dA_0} = \sigma_0 \]  (A-6)

Hence, it is obvious that \( \delta = \sigma_0 \). Obviously, \( \delta \) relates to the number of fibers rather than the force per cross-section. The analysis holds for the other direction, \( \phi \phi \), thus Equations 19–21 hold.

Appendix B

Calculation of the Effect of Twist on the Fibers' Extension Ratio

Consider the muscle layer at \( r = b + \gamma \) (Fig. 11A) and the triangle abc lying on this layer (Fig. 11B). Line ac represents the natural direction of the fiber (of length \( df \)), inclined by an angle \( \alpha \) to the transverse plane (Fig. 11C). The differential fiber length \( df \) is thus given by:

\[ df = \frac{d\gamma}{\sin \alpha} \]  (B-1)

and

\[ \tan \alpha = \frac{d\gamma}{r \, d\gamma} \]  (B-2)

Now allow the apex to twist \( \beta \) degrees around the longitudinal axis, relative to the fixed base. Assuming that the twisting gradient is uniform along the longitudinal axis yields:

\[ \frac{d\theta}{d\gamma} = \frac{\beta}{2a} \]  (B-3)

where \( \theta \) is the local twisting angle at a distance \( \gamma \leq 2a \) from the base. The twist produces a new differential fiber length \( df' \) at a new inclination angle, \( \alpha' \) (Fig. 11D). Thus,

\[ \tan \alpha' = \frac{\frac{d\gamma}{d\theta}}{r d\gamma + r d\gamma} \]  (B-4)

\[ \frac{d\gamma}{d\gamma} = \frac{d\gamma}{r d\gamma + r d\gamma} \]  (B-5)

It is obvious that for identical \( dF \), \( \sigma \neq \sigma_0 \) as \( dA \neq dA_0 \). However, if we define \( \delta = \frac{dA}{dA_0} \) then:

\[ \sigma_0 = \delta \frac{dF \cos \alpha}{dA_0} = \sigma_0 \]

and

\[ \delta = \frac{dF \cos \alpha}{dA_0} \cdot \frac{dA}{dA_0} = \sigma_0 \]  (A-6)

Hence, it is obvious that \( \delta = \sigma_0 \). Obviously, \( \delta \) relates to the number of fibers rather than the force per cross-section. The analysis holds for the other direction, \( \phi \phi \), thus Equations 19–21 hold.

Figure 11. The effect of twisting on the fibers' inclination angle \( \alpha \), and differential length \( df' \) for a thin shell with a semi-minor axis \( r = b + \gamma \).
and 
\[ \alpha' = \tan^{-1} \left( \frac{2a \tan \alpha}{2a + \beta \tan \alpha} \right) \]  
(B-5)

Now, 
\[ df' = \frac{dP}{\sin a'} \]  
(B-6)

and Equations B-1 and B-2 give the extension ratio, 
\[ \lambda = \frac{df'}{df} = \frac{\sin a}{\sin a'} \]  
(B-7)

Given the angle of twisting \( \beta \), the distribution of fiber lengths, the fiber stresses, and the related pressures can be calculated.

**Appendix C**

**Calculations of Transfer Fiber Stresses**

Consider a thin spheroidal shell within the LV wall, with fibers angled at \( \alpha \) to the equator. The stresses at the meridional (\( \phi \)) and circumferential (\( \theta \)) directions are given by

\[ \sigma_{\phi} = \phi_1 \cos^2 \alpha - \phi_5 \sin^2 \alpha \]  
(C-1)

\[ \sigma_{\theta} = \phi_5 \sin^2 \alpha + \phi_6 \cos^2 \alpha \]  
(C-2)

where \( \sigma_{\phi} \) and \( \sigma_{\theta} \) are the stresses along the normal to the fiber direction. Consider that each of the shells is balanced by the sum of forces operating on a transverse section through the equator. Assuming that no meridional shear stresses act between the layers yields:

\[ dP r_1^2 = \sigma_{\theta} \cdot 2 \pi r_1 \, dy \]  
(C-3)

Combining Equations C-3 and 10 yields:

\[ \frac{2 \sigma_{\theta}}{r_1} = \frac{\sigma_{\theta}}{r_1} + \frac{\sigma_{\phi}}{r_2} \]  
(C-4)

Incorporating Equations C-1 and C-2 into Equation B-4 gives:

\[ \sigma_n = \sigma_1 \cdot \frac{\sin^2 \alpha (2r_2 - r_1) - r_2 \cos^2 \alpha}{r_3 \sin^2 \alpha + \cos^2 (2r_2 - r_1)} \]  
(C-5)

Equation C-5 gives the equilibrium relation between \( \sigma_n \) and \( \sigma_1 \) for a given thin layer, and represents the maximum possible value of \( \sigma_n \) (assuming no meridional shear stresses between layers).

The existence of meridional shear stresses between the adjacent layers will diminish the value of \( \sigma_n \) to values smaller than those given by Equation C-5, hence its effect on the systolic LV performance will be much smaller.

For \( r_2 = k r_1 \) and \( k = 2 \), Equation C-5 gives positive values of \( \sigma_n \) (stretch) for \( \alpha < 37^\circ \), and negative values (compression) for \( \alpha > 37^\circ \).

The value of \( \sigma_n \) dictated by the material properties, in Equation 22, is used to calculate \( \sigma_n \). The value of \( F(y, t) \) can now be calculated, including the contribution of the calculated maximum value of \( \sigma_n \) (Eq. C-5) in Equations C-1 and C-2, and substituting in Equation 10.

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