MODEL FOR LEFT VENTRICULAR CONTRACTION COMBINING THE FORCE LENGTH VELOCITY RELATIONSHIP WITH THE TIME VARYING ELASTANCE THEORY

R. BEYAR AND S. SIDEMAN
The J. Silver Institute of Biomedical Engineering, Technion, Israel Institute of Technology, Haifa 32 000, Israel

ABSTRACT A model for the contraction of the left ventricle (LV) is developed for a spheroidal geometry. The classical force-length-velocity relationship for a single muscle fiber is assumed. The linear maximum pressure volume relationship (maximum elastance), a measure of muscle contractility, is further extended into a time-varying function. This is achieved by utilizing a mechanical activation function, assumed as half a sinusoidal wave, to describe the time-dependent isometric stress for the activated cardiac muscle. This, in turn, results in the time-varying elastance function and represents the instantaneous activity of the muscle contractile proteins. The model is tested for a set of boundary conditions that determine preload, afterload, and the inherent properties of the muscle, i.e., the contractility. The computed results of the isovolumic contraction, auxotonic contraction, and isovolumic relaxation are in agreement with the expected behavior of the LV. The relations between the simulated variations on preload, afterload, and contractility, and the set of performance indexes of the LV, are presented and discussed.

INTRODUCTION

The intact heart is constructed of muscle fibers, arranged in a given pattern, which are connected to the ligamentous structures like the valves and their related rings. Numerous investigators have tried to characterize the heart muscle behavior and the function of the left ventricle (LV). The motivation for such investigations is the clinical need for a reliable and meaningful index with which one can measure the functional status of the heart muscle, i.e., the contractility. The main approaches to this problem can be divided into the following categories.

(*a*) The force-velocity relationship, schematically shown in Fig. 1 for a given length of fiber, was introduced by Hill (1938, 1970) and later extended to describe the behavior of an isolated strip of muscle as well as that of the whole LV (Parmley et al., 1969, 1972; Sonnenblick et al., 1962). According to this theory, the velocity of fiber shortening is a function of the instantaneous length and force against which the muscle contracts.

(*b*) Characterization of the total LV behavior is done using a time-varying elastance function with a maximum value that relates to the contractility. The maximum elastance value defines a linear relationship that exists between the maximum pressure and volume of the LV (Suga et al., 1973; Suga and Sagawa, 1974; Suga et al., 1976). This theory presents a smooth function describing the force development throughout the cycle, as opposed to the "all or none" theory that has only two discrete situations, "active" and "passive," of the cardiac muscle.

The maximum and the passive pressure-volume relationships are shown as lines 1 and 4 in Fig. 2. The instantaneous elastance value of the LV can be formalized throughout the systole by a pressure-volume relationship that is described at each moment by a line which lies between these two constraints.

From an overall point of view, the mechanical function of the heart depends on three major factors:

(*a*) The initial conditions at the beginning of systole are usually denoted in the clinical and physiological language as "preload," and are characterized by indexes like the initial wall stress, the ventricular end diastolic pressure, or the initial length of the fibers.

(*b*) The load against which the heart pumps is known as the "afterload." Although this term is commonly used, its precise definition is not unanimously accepted, and circumferential wall stress, LV pressure during systole, or LV transmural pressure are some of the physiological quantities used to describe the afterload.

(*c*) The "contractility" of the heart muscle is an ill-defined concept meant to provide a measure of the ability of the muscle to develop force in a setup that is independent of the preload and afterload. The contractility of the

Address reprints requests to R. Beyar, Dept. of Biomedical Engineering, Technion IIT, Haifa 32 000, ISRAEL.

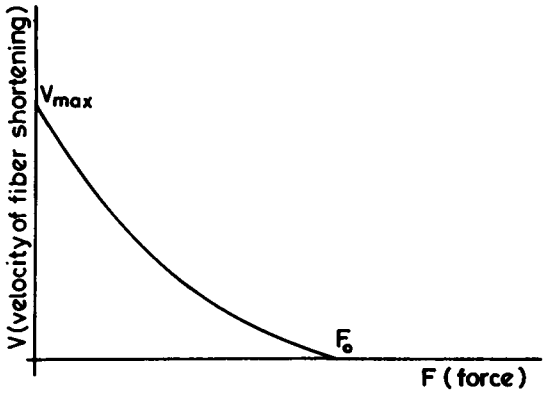

FIGURE 1 A characteristic force-velocity curve.

muscle can be modified in various physiological states and in different pathological situations and can be altered by pharmacological interventions. Quantification of this phenomenon is difficult due to the incomplete definition of this concept. Thus, a great number of indexes have been suggested and tested, based on experimental and clinical studies. Some of these will be discussed below.

As the above concepts of preload, afterload, and contractility are ambiguous and ill defined, it is desirable to relate the heart's functional characteristics to well-defined quantities such as fiber length and velocity of contraction, LV volume, wall stress, intraventricular pressure, etc. Thus, to understand the performance of the LV, one has to have a good description and a clear definition of the contractile behavior of a single isolated strip of muscle.

The work presented here is an attempt to combine the various approaches to the contraction mechanics of the LV into a single, all-inclusive model. The model is based on a simplified geometry of the LV and combines an "activation function," defined by the isovolumic time-varying elastance, together with the force-velocity-length relationship of the muscle.

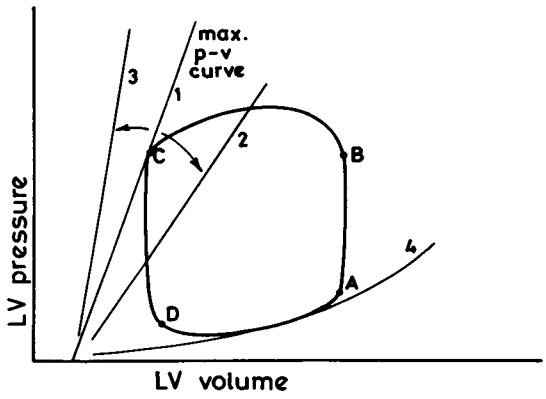

FIGURE 2 The maximum pressure volume curves: (*1*) the normal state, (*2*) decreased contractility, (*3*) increased contractility, (*4*) the passive pressure volume curve. Loop *A*, *B*, *C*, *D*, represents the classical pressure volume loop for the LV cycle: *AB*, isovolumic contraction; *BC*, ejection phase; *CD*, isovolumic relaxation; *DA*, LV filling.

PHYSIOLOGICAL BACKGROUND

The contractile element of the muscle was studied extensively by numerous investigators (Hill, 1938; Parmley et al., 1972; Sonnenblick, 1962). It seems that the instantaneous velocity of contraction depends on the force and the instantaneous fiber length. The typical force vs. velocity curve at a certain contractility, as shown in Fig. 1, indicates that the maximum velocity of contraction, V_{max}, occurs when the muscle is at zero load, while the (maximum) force, F_0, which develops in the contracting muscle occurs when the velocity of contraction, V_{cf}, approaches zero. The force-velocity curve can be fitted by a hyperbolic function of type

$$(F + a)V_{cf} = b(F_0 - F) \quad (1)$$

where F is the force against which the muscle contracts and a and b are constants. Different lengths of the muscle yield different curves (Dehmer et al., 1981), but the zero force intersection (V_{max}) remains constant. This explains why V_{max}, though frought with problems (Pollack, 1970) is suggested as a parameter to characterize the LV function, independent of the preload or afterload (Gault et al., 1968; Parmley et al., 1970; Sonnenblick, 1964). It has clearly been shown experimentally (Sonnenblick, 1964) that the ratio (F_0/a) is constant for identical contractility values and that the values of b and F_0 are strongly affected by changing the contractility. It is important to note that the simple fiber velocity-force relationship was recently shown to represent the performance of the whole heart (Weber and Janicki, 1977). It has also been found that the overall force-length-time relationship is transformable to force-velocity-length relationship, which is valid under all loading conditions (Piene and Covell, 1981).

A different approach to characterize the contraction mechanics of the LV is known (Suga et al., 1973; Suga and Sagawa, 1974; Suga et al., 1976). A time-dependent, pressure-volume relationship, the elastance $E(t)$, is defined by

$$E(t) = P(t)/[V(t) - V_0] \quad (2)$$

where $P(t)$ denotes the instantaneous LV pressure, $V(t)$ is the instantaneous LV volume, and V_0 is the volume at zero pressure, an experimental constant, corresponding to the sarcomere length in which an active pressure (see below) cannot be developed. Note that in the above representation $E(t)$ does not depend on the strain rate.

As shown by Suga and Sagawa, the time-dependent elastance curve is almost totally independent of the preload or afterload. However, the magnitude and shape of $E(t)$ are strongly dependent on the heart rate and contractility (as modified by epinephrine injection) (Suga et al., 1973). The maximum elastance value, which represents a certain contracility state, defines a linear end systolic pressure-volume relationship, Fig. 2. The end systolic pressure-

volume values for differently preloaded and afterloaded beats determine a unique line, and its slope (equivalent to maximum elastance defines an index of the contractility, independent of the preload and the afterload (Suga and Yamakoshi, 1977). The time-dependent capacitance, the reciprocal of the time-dependent elastance, was calculated (Deswysen, 1977) by using flow and pressure measurements in dogs and applying an electrical model for the heart and circulation. The calculated $E(t)$ was thus found to depend on the contractile state of the LV. The slope that defines the maximum elastance value decreases with different diseases of the myocardium and can be increased by epinephrine injection. Intensive recent work (Dehmer et al., 1981; Schüler et al., 1981; Schüler et al., 1982; Slutzky et al., 1980; Grossman et al., 1977) supports the potential clinical value of this parameter and indicates its advantage over the classical ejection fraction parameter (Nivatpumin et al., 1979).

The characterization of heart muscle mechanics by "derived" relationships such as force-length, stress-length, or tension-length relationships is preferred by a number of investigators (Reichek et al., 1982; Peterson et al., 1973; Weber and Janicki, 1977, 1978, 1979; Weber et al., 1976*a* and *b*), to the pressure-volume relationships. Linear correlations were reported for every one of these relationships, and the slopes were assumed to characterize contractility states of the muscle.

The various procedures suggested to characterize contractility can easily be related. The linear maximum isovolumic pressure-volume relationship is represented by

$$P_{0(\max)} = \alpha(V - V_0) \tag{3}$$

where α is the maximum elastance, and V is the LV volume under consideration. Assuming the LV to be represented by a sphere with a thin shell, the force F that acts to stretch the shell at the circumference is given by

$$F = P(t)\,\pi r^2 = P(t) \cdot \pi \left[\frac{\ell_c(t)}{2\pi}\right]^2 \tag{4}$$

where r is the LV internal radius and equals $\ell_c(t)/2\pi$, where $\ell_c(t)$ is the instantaneous length of the circumference. Obviously, a highly nonlinear force-length relationship emerges from the initial pressure-volume relation, hence either the latter or the former is erroneous. However, as the experimental environment does not provide us with accurate measurements for the whole range of the parameters involved, one must assume that within the narrow range of the measured parameters that can actually be determined under physiological conditions, the nonlinearities of the maximum pressure volume (P-V) curve are negligible in relation to the large variations in the measurements.

The above two-coordinate correlations were extended into a three-dimensional space made of the force-length-velocity coordinates (Weber and Janicki, 1980) shown in Fig. 3. This approach can be utilized to describe the contractile states of the heart, accounting for all the possible combinations between the preload and the afterload. Thus, isometric force-velocity curves are obtained on a plane perpendicular to the length axis, while the force-velocity curves can be similarly derived for different velocities. An auxotonic contraction, the normal physiological contraction against a variable aortic pressure occurs within the particular surface defined by the muscle contractility (Weber and Janicki, 1980). It should, however, be noted that the surface within this three-dimensional space represents the maximum force that develops within the muscle during the systole. As the pressure-volume relationship, i.e., the elastance, is time-dependent during a heart cycle, it is clear that the time coordinate is required for the complete description of the mechanics of a single beat of the heart. The end-point of the LV systole is defined as the closure point of the aortic valve. The factors that dictate this endpoint are attributed to the maximum elastance value. The ejection ends once this value is reached at the maximum pressure-volume relationship (Reicheck et al., 1982). This description of the end systole state seems rather simple in view of the electrical activation of the heart muscle which dictates the duration of systole. Note that although the relationship between the electrical and mechanical activities of the muscle fibers is rather complicated, it is usually agreed that the relaxation process of an activated fiber begins after repolarization (Berne et al., 1979). Hence, the maximum force of an isometric contraction of an isolated strip of muscle is experimentally reached towards the end of the electrical activation. Thus, an assumption that the duration of the action potential of the muscle determines the duration of the ascending limb of the isovolumic beat, as well as the ascending part of the elastance curve for an auxotonic contraction is used here. However, this assumption should be assessed experimentally in the future for a better characterization of the mechanical systole.

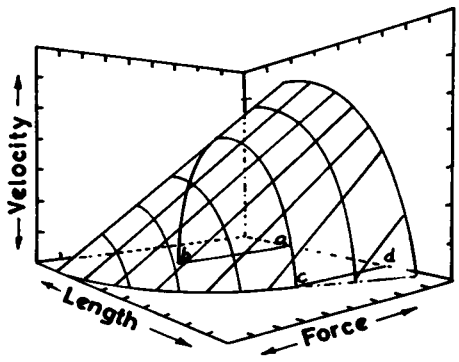

FIGURE 3 Schematic representation of the three-dimensional plane describing the force-length-velocity characteristics for a given contractile state (from Weber and Janicki, 1977).

PROPOSED LV MODEL

Physiological Assumptions

To study the ejection characteristics of the LV, a computer model describing the LV systole at different preloading, afterloading, and contractility conditions is developed, utilizing the following assumptions. (*a*) The LV has a spheroidal geometry. (*b*) The time varying elastance for an isovolumic contraction is approximated by half a cycle of a sine function. The duration of the rising limb of the elastance curve is equal to the "action potential" duration, seen in Fig. 4. The activation function of the cardiac muscle has a similar pattern and ranges between 0 and 1. (*c*) The maximum isovolumic pressure developed within the LV is a given function of the volume and contractility. Also, the maximum pressure-volume curve is linear. (*d*) The passive pressure volume relationship obeys an exponential curve low (Diamond et al., 1971). (*e*) The relationship between the pressure within the LV and the circumferential wall stress is described by Laplace's law which relates the LV transmural pressure to the average stress and geometry (Mirsky et al., 1974). (*f*) The velocity of contraction of the muscle is a function of the instantaneous wall stress at the specific volume, determined by the volume and elastance function, and the actual wall stress which can be calculated from the LV pressure and geometry.

Mathematical Formulae

The pressure within the spheroidal LV, Fig. 5, with an internal short semiaxis r_1, a long semiaxis r_2, and a wall of thickness h, is related to the radius and circumferential wall stress $\sigma(t)$ by

$$\sigma(t) = \frac{P(t)\, r_1}{h}\left(1 - \frac{r_1^2}{2r_2^2}\right). \tag{5}$$

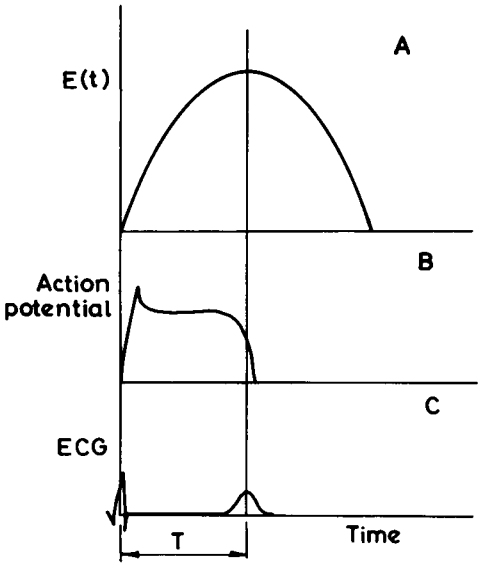

FIGURE 4 (*A*) Assumed time varying elastance function, (*B*) a representative cardiac muscle action potential, and (*C*) the ECG. All are plotted against a common time scale. Note that the duration of the action potential, T, is half the duration of the total mechanical activity.

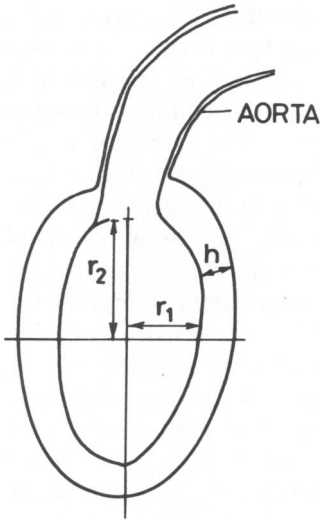

FIGURE 5 The assumed LV geometry: a prolate spheroid with a short semiaxis r_1, long semiaxis r_2, and wall thickness h.

The maximum pressure which develops within the LV is the sum of the maximum active pressure $P_{a(max)}$ and the passive pressure P_d within the ventricle. The latter is due to the stretching of passive elements, such as the collagen and elastin fibers, and is correlated by

$$P_d = A\{e^{C[V(t) - V_0]} - 1\} \tag{6}$$

where A and C are empirical constants.

The maximum active pressure $P_{a(max)}$ achieved for each specified volume is due to the contractile mechanism and is evaluated by the difference between the two empirical curves given by Eqs. 3 and 6

$$P_{a(max)} = P_{0(max)} - P_d = \alpha(V - V_0) - A[e^{C(V - V_0)} - 1]. \tag{7}$$

Note that, as a first approximation, an identical value of V_0 is assumed for both the passive and the total pressures. The active pressure function is represented by half a sine function, based on an activation function approximated by the isovolumic elastance curve:

$$P_a(t) = P_{a(max)} \cdot \sin\frac{\pi}{2T}t \tag{8}$$

where T is the duration of the action potential (Fig. 4). The total time-dependent isovolumic pressure in the LV, $P_0(t)$, is the sum of the instantaneous active and passive pressures

$$P_0(t) = P_a(t) + P_d. \tag{9}$$

The above equations suffice to describe the isovolumic contraction. However, to describe nonisovolumic contrac-

tion, we must introduce the velocity of fiber shortening. The relationship between the circumferential fiber velocity V_{cf} in the ejecting heart and the wall stress, $\sigma(t)$, which is determined by the afterload, is given by modifying Eq. 1 to read

$$[\sigma(t) + a]V_{cf} = b[\sigma_0(t) - \sigma(t)] \tag{10}$$

where a and b are constants, numerically different from those in Eq. 1, and $\sigma_0(t)$ is the instantaneous isometric wall stress developed by the contractile mechanism. $\sigma_0(t)$ depends on the geometry and instantaneous isovolumic pressure and can be calculated by using $P_0(t)$ instead of $P(t)$ in Eq. 5. Combining Eqs. 5–9 yields

$$\sigma_0(t) = \left\{\alpha(V - V_0)\sin\frac{\pi}{2T} - A(e^{C(V-V_0)} - 1)\left(\sin\frac{\pi}{2T}t - 1\right)\right\} \cdot \frac{r_1}{h}\left(1 - \frac{r_1^2}{2r_2^2}\right). \tag{11}$$

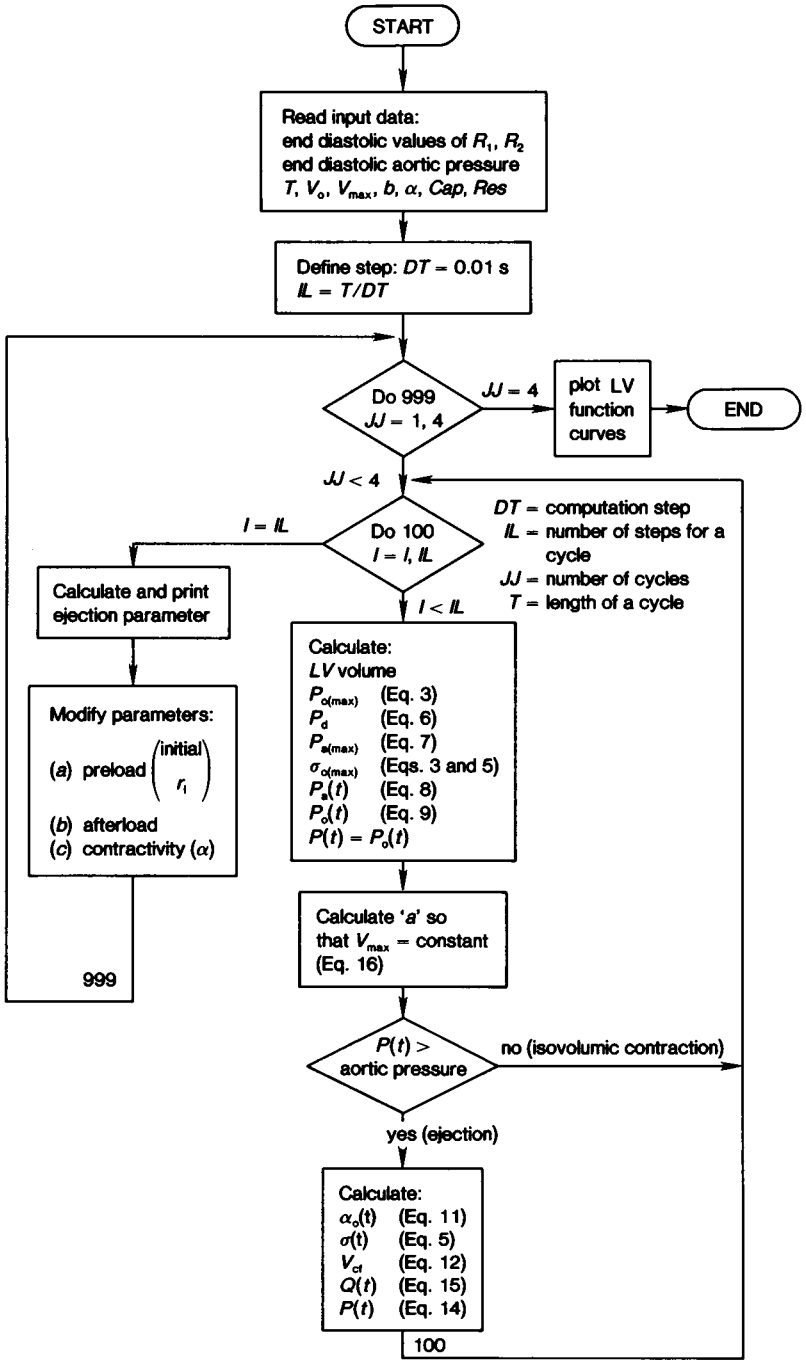

FIGURE 6 A schematic flow chart of the computer program simulating LV contraction.

The circumferential fiber shortening rate, V_{cf} is given by

$$V_{cf} = 2\pi \frac{dr_1}{dt}. \quad (12)$$

Utilizing Eq. 10 yields

$$\frac{dr_1}{dt} = \frac{b[\sigma_0(t) - \sigma(t)]}{2\pi[\sigma(t) + a]}. \quad (13)$$

Because $\sigma_0(t)$ and $\sigma(t)$ are functions of r_1 and r_2, Eq. 13 is a nonlinear, first-order differential equation. This equation is used to calculate the rate of change of the LV geometry from the calculated values of $\sigma_0(t)$ (Eq. 11) and $\sigma(t)$ (Eq. 5).

The value of the LV pressure is approximated by the aortic pressure (the pressure gradient across the aortic valve is assumed negligible) and can be calculated, according to the Windkessel approach (Noodergraaf, 1978) by

$$P(t) = e^{-t/Res \cdot Cap}\left[P_0 - \frac{1}{Cap}\int_0^t e^{t/Res \cdot Cap}\, Q(t)dt\right] \quad (14)$$

where *Res* is the peripheral resistance and *Cap* is the capacitance of the arterial system.

Assuming that the valvular system of the heart is intact, we can relate the LV outflow $Q(t)$ to the change of r_1 with time by

$$Q(t) = \frac{dV}{dt} = \frac{d\left(\frac{4}{3}\pi r_2 r_1^2\right)}{dt} = \frac{4}{3}\pi\left(r_1^2\frac{dr_2}{dt} + 2r_2 r_1\frac{dr_1}{dt}\right). \quad (15)$$

Computation Methods and Parameter Estimation

The computer program, in Fortran, was run on an IBM 370 (IBM Instruments, Inc., IBM Corp., Danbury, CT). The block diagram of the program is presented in Fig. 6. The calculations are performed in steps of 0.01 s. Four heart beat cycles are calculated at each run; i.e., four different values are taken for the preloading, afterloading, and contractility variations. The different parameters of the LV contraction [$P(t)$, $\sigma(t)$, etc.] are then calculated for the isovolumic contraction. Once the aortic valve is "opened," the LV is coupled with the aorta according to Eqs. 12, 14, 15. After "closing" the aortic value, the isovolumic relaxation values are computed. The calculated parameters of the LV function are printed and a graphic output of the variables is obtained by utilizing graphic subroutines. The time for one compute run varies between 5 and 15 s. The system parameters which are used in the model are listed in Table I. Included in Table I are the corresponding normal values, as taken from the literature, and their physiological meaning and dependence.

RESULTS

An auxotonic contraction of the LV is described by the solution of the above equations representing the characteristics of the LV model. The mechanics of the LV contraction is shown below by sets of "function curves": pressure-volume, force-length, stress-length, pressure-time, and volume-time curves. The calculated effects of changing the

TABLE I
THE MODEL CONSTANTS AND THEIR REPRESENTATIVE VALUES IN THE PRESENT MODEL OF THE LV

Parameter	Physical meaning	Normal value	Dependence on	Equation number	Reference
α	maximum elastance	4 mm Hg/ml	contractility	3, 4, 7, 11	Grossman et al. 1977 Dehmer et al. 1981
V_{max}	unloaded velocity of shortening	3 circumferences/s	contractility	10 [$\sigma(t) = 0$]	Pollack, 1970
T	duration of active state	400 ms	heart rate	8, 11	Altman and Dittmer, 1971
a	empirical constant	determined so that σ_0/a is constant	volume	10	
b	empirical constant	100 cm/s	contractility	10	chosen to fit Pollack's force-velocity relationship
v_0	LV volume at zero pressure*	10 ml	myocardial changes	2–4, 6, 7, 11	Mirský et al., 1974
A	experimental constant	1 mm Hg	passive P-V relationship	6, 7, 11	chosen to fit passive P-V relationship reported by Gaash et al., 1972
C	experimental constant	0.025	passive P-V relationship	6, 7, 11	
Res	peripheral resistance	2 mm Hg/ml/s	humoral factors, nervous system	15	Noordegraaf, 1978
Cap	arterial capacitance	1 ml/mm Hg	humoral factors, nervous system.	15	Noordegraaf, 1978

*Note that no active pressure is generated at zero pressure. Also, the values of V_0 for the passive and active pressures might differ from each other. However, the difference does not exceed a few milliliters and can be neglected.

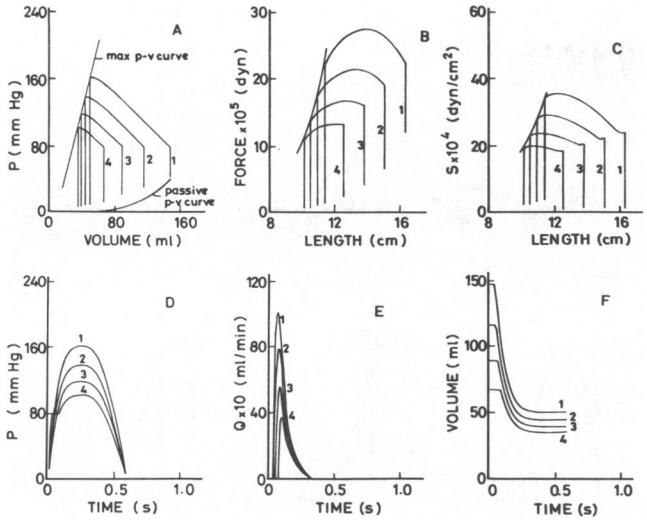

FIGURE 7 LV function curves obtained for different preloads; *1*, r_1 = 2.6 cm; *2*, r_1 = 2.4 cm; *3*, r_1 = 2.2 cm; *4*, r_1 = 2.0 cm.

preload, afterload, and contractility are shown as a family of curves for each case.

Effect of Changes in Preloading Conditions

The preload is represented here by the LV initial volume or radius. This, in turn, can be easily expressed in terms of the initial pressure, based on the experimental exponential passive pressure-volume relationship, Eq. 6. Fig. 7 shows a family of "function curves" for four different preloading conditions. The curve in Fig. 7 *A* connecting all the end systolic pressure-volume values at different auxotonic ejections is practically linear, representing the maximum elastance. The slope of the line is dictated by the contractile behavior. Note that the corresponding curves connecting the end systolic values of the force-length as well as the stress-length relationship (Fig. 7, *B* and *C*) are not linear. Increasing the LV initial volume leads to more powerful ejections shown by the pressure-time and flow-time relationship (Fig. 7, *D* and *E*). This increase in blood flow corresponds to greater stroke volumes and greater ejection fraction values (Fig. 7 *F*). The classical Starling mechanism relating the dependence of the stroke volume on the end diastolic volume, is clearly demonstrated by these results.

Table II lists the calculated ejection parameters for the four different preloading conditions. An increase in the initial short axis, which can be translated to an increase in end diastolic volume, is followed by a moderate increase in the ejection fraction, and by major increases in the end systolic pressure, the stroke volume, and stroke work, the ejection velocities and the accelerations. The contractility index $[(1/p)\ (dp/dt)]_{max}$ is moderately increased even with a major increase in the preload. An increase in the ejection time follows an increase in preload.

Effect of Changes in the Afterloading Conditions

The aortic pressure is used here to represent the afterload. This is a common physiological measurement, used both clinically and experimentally to define the afterloading conditions of the LV. These afterloading conditions are not identical with the afterload concept used in the isolated muscle experiments, but it is nevertheless directly related to the engineering stress. The aortic pressure curve is determined here by the initial conditions at the aorta, i.e., the end diastolic aortic pressure, and the arterial impedance (composed of a capacitance and resistance values in the Windkessel model used here). The resulting function curves for successive increase in the end diastolic arterial pressure are illustrated in Fig. 8. The pressure-volume curves approach the same maximum pressure-volume relationship, shown in Fig. 7, for the differently preloaded beats.

The corresponding force-length and stress-length relationships, at different ejections, approach nonlinear curves that represent their maximum values (Fig. 8, *B* and *C*). However, it is quite obvious that it is difficult to identify the character of these curves in the narrow range of experimental conditions and they can only be approximated by linear curves. Higher pressures in Fig. 8 *D* correspond to lower flow rates (Fig. 8 *E*). Lower volume changes (Fig. 8*F*) occur with an increase in the afterload.

Table III summarizes the calculated ejection parameters of the differently afterloaded ejections. No change in

TABLE II
EJECTION PARAMETERS CALCULATED FOR DIFFERENT PRELOADS

Initial short semiaxis r_1	End diastolic volume	End systolic volume	Stroke volume	Ejection fraction	End systolic pressure	Stroke work	Maximum flow	Maximum volume acceleration	$[(dp/dt)/P]$ max	Ejection time
cm	*ml*	*ml*	*ml*	*%*	*mmHg*	*erg · 10⁷*	*ml/s*	*ml/s²*	*s⁻¹*	*ms*
2.0	67.0	35.3	31.7	47.3	99.6	0.39	379.4	$24.0 \cdot 10^3$	49.3	260
2.2	89.2	39.3	46.9	55.9	115.5	0.67	563.1	$31.9 \cdot 10^3$	54.3	280
2.4	115.8	44.2	71.5	61.8	135.0	1.06	791.8	$49.5 \cdot 10^3$	57.4	290
2.6	147.2	50.1	97.1	65.9	157.9	1.61	1017	$59.6 \cdot 10^3$	59.4	300

α = 4 mmHg/ml; V_{max} = 45 cm/s; time of active tension = 600 ms. End diastolic aortic pressure = 80 mmHg.

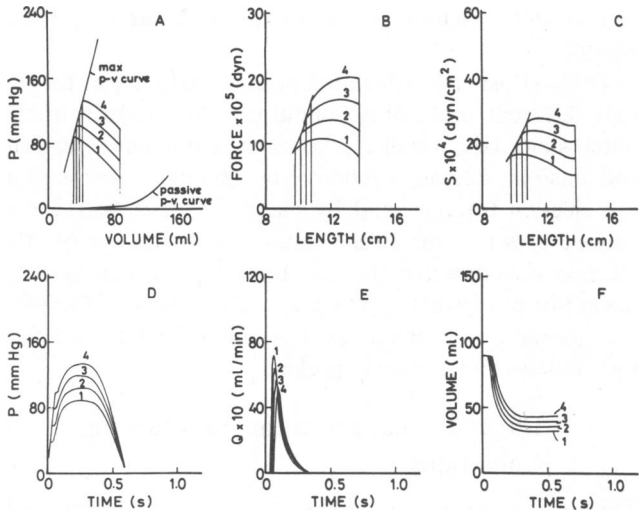

FIGURE 8 LV function curves obtained for different afterloads represented by different end diastolic pressures; *1*, 40 mm Hg; *2*, 60 mm Hg; *3*, 80 mm Hg; *4*, 100 mm Hg.

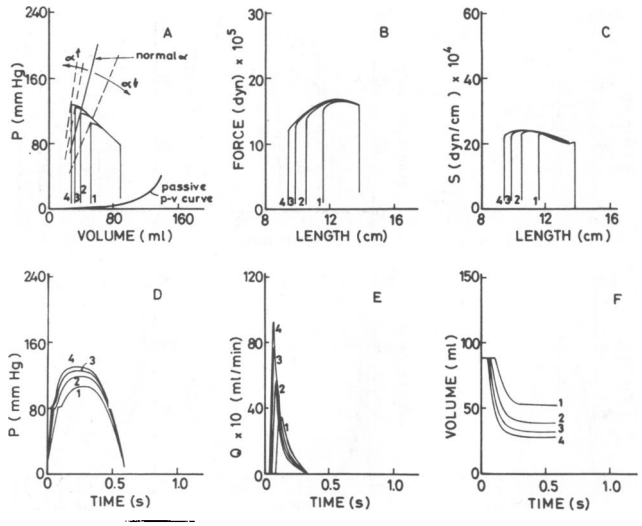

FIGURE 9 LV function curves for different contractile state represented by different values of α[mmHg/ml]; 1, α = 2.5; *2*, α = 4 (normal); *3*, α = 5.5; *4*, α = 7.

contractility is noted by the values of V_{max} and, $[(1/p)\ (dp/dt)]_{max}$. A moderate decrease in the flow velocities with the increased afterload is shown. The stroke volume and ejection fraction are moderately decreased with an increase in the afterload. However, the corresponding stroke work is moderately increased. An increase in afterload shortens the ejection time moderately.

Effect of Changes in Contractility

An increase in contractility is simulated by an increase in the value of the maximum elastance parameter α. A characteristic family of function curves is depicted in Fig. 9.

The pressure-volume curves (Fig. 9 *A*) show an increase in the stroke volume and an increase in end systolic pressure-volume relationship with increased contractility. The maximum pressure-volume curves shown in Fig. 9 *A* (dashed lines) indicate higher slopes for higher contractile states. A similar trend is shown by the force-length and stress-length relationships (Fig. 9, *B* and *C*). The pressure-time relationship (Fig. 9 *D*) shows that the LV pressure as well as the values of an isovolumic pressure-time derivative $(dp/dt)_{max}$ are increased contractility. As contractility increases the flow across the aortic valve increases (Fig. 9 *E*) resulting in greater volume changes, as reflected in the volume-time curves (Fig. 9 *F*).

Table IV summarizes the calculated ejection parameters for the different contractile properties of the muscle. Increasing the contractility, expressed by an increase in α and V_{max}, yields higher maximum flows with higher maximum accelerations, and a large increase in the ejection fraction, with a large increase in stroke work. The well-known parameter of contractility $[(1/p)\ (dp/dt)]_{max}$ is shown to increase when the contractile state is enhanced. A dependence on the contractility is clearly demonstrated.

DISCUSSION

This study represents an attempt to obtain a single all-embracing characterization of the functional behavior of the LV. The elastance value represents a relationship between the instantaneous values of the pressure and the volume while the force-velocity-length concept combines the LV volume, and the ejection flow, with the LV pressure. The model presented here combines the pressure,

TABLE III
CALCULATED EJECTION PARAMETERS FOR DIFFERENT AFTERLOADS

End diastolic aortic pressure	End systolic volume	Stroke volume	Ejection fraction	End systolic pressure	$[(dp/dt)/P]$ max	Stroke work	Maximum flow	Maximum acceleration	Ejection time
mmHg	*ml*	*ml*	*%*	*mmHg*	s^{-1}	$erg \cdot 10^7$	*ml/s*	*ml/s*	*ms*
40	32.0	57.2	64.1	86.7	57.4	0.5	716.3	$47.3 \cdot 10^3$	300
60	35.6	53.5	60.0	101.1	57.4	0.60	634.7	$39.6 \cdot 10^3$	290
80	39.3	49.9	55.9	115.5	57.4	0.67	563.1	$31.9 \cdot 10^3$	280
100	43.0	46.2	51.7	130.1	57.4	0.73	499.7	$24.2 \cdot 10^3$	270

End diastolic volume = 89.2 ml; end diastolic radius = 2.2 cm; α = 4 mmHg/ml; V_{max} = 45 cm/s; time of active tension = 600 ms.

TABLE IV
CALCULATED EJECTION PARAMETERS DUE TO CHANGE IN CONTRACTILITY

α	V_{max}	$[(dp/dt)/P]$ max	Maximum flow	Maximum volume acceleration	End systolic volume	Stroke volume	Ejection fraction	Stroke work	End systolic pressure	Ejection time
mmHg/ml	*cm/s*	s^{-1}	*ml/s*	ml/s^2	*ml*	*ml*	%	$erg \cdot 10^7$	*mmHg*	*ms*
2.5	28.1	53.0	351.7	18.6×10^3	52.5	36.6	41.0	0.46	104.7	250
4	45	57.4	563.1	31.9×10^3	39.3	49.8	55.9	0.67	115.5	280
5.5	61.9	59.7	778.5	55.2×10^3	32.4	56.8	63.6	0.80	123.0	280
7	78.7	61.0	931.0	59.4×10^3	28.1	61.1	68.5	0.88	125.5	290

Time of active tension = 600 ms; End diastolic aortic pressure = 80 mmHg; end diastolic volume = 89.2 ml; end diastolic short axis = 2.2 cm.

volume and fiber velocity with specific patterns of muscle "activation function," approximated by the time varying elastance. This approach leads to a satisfactory description of the isotonic, isometric, and auxotonic contractions. These correspond to the appropriate plane selected in the multidimensional space defined by the pressure, volume, velocity, and time. To complete the description of the ejecting LV, the passive diastolic characteristic of the heart muscle is introduced by an exponential pressure-volume curve, and the LV is assumed to eject into a Windkessel arterial model. A spheroidal geometry, with an even intramural stress distribution, is assumed. The time varying elastance is assumed to be half of a sine wave, with a peak value occurring at the onset of the T wave (Fig. 4). This is a fair assumption, giving a reasonable first approximation of the elastance curve. However, different curves can easily be incorporated into the model.

The above assumptions were derived from the classical biophysical theories for the isolated and global cardiac muscle behavior. However, the elastance function indicates the existence of an "activation function" of the cardiac muscle. This activation function is the result of the complex metabolic processes which lead to cardiac muscle contractions. This function determines the instantaneous active isovolumic stress which develops within the muscle fibers. This stress $[\sigma_o(t)]$, which corresponds to an isometric contraction of the fiber, is modified by the velocity of fiber shortening to a smaller value $[\sigma(t)]$, which relates to the instantaneous LV pressure by Laplace law. The main justification for the use of this approach is that the classical "all or none" phenomena of the mechanical cardiac activation is an inaccurate description of the myocardial contraction process. As the classical force-length-velocity relationship is derived for a maximum activity of the muscle (the active state), the need for an instantaneous force-length-velocity relationship which depends on the instantaneous magnitude of the activation function is rather obvious.

The related model parameters can be roughly divided into two groups: the first (A, V_0, C) characterizes the passive properties of the muscle, while the second (α, F_0, a, b, V_{max}) includes the active characteristics of contraction.

The passive state parameters that appear in Eq. 7 represent the passive pressure-volume relationship of the heart. Changes in contractility should not affect these parameters. However, chronic changes in heart volume, hypertrophy of muscle, and changes in the fraction of collagen and elastin within the muscle significantly affect these parameters. Changes in the elasticity of the pericardium, which acts as a stiff constraining envelope of the heart, modifies these parameters and affects the interaction between the left and right ventricular passive pressure-volume curves.

The active parameters are those related to the time varying elastance, i.e., α, and those related to the force-velocity-length curves, i.e., σ_0, a, b, and V_{max}. As we distinguish between loading conditions of the heart and its contractile behavior, we would like to derive a single parameter to characterize and quantify this concept. Intensive work has been reported and many parameters were suggested as contractility indexes some of them have profound physiological meaning and others show vague relationship to physiology, V_{max} and α are the commonly accepted contractility indexes. Based on the physiological meaning of the contractile state, it is reasonable to expect that these two parameters should be interrelated. Both V_{max} and α have been shown to be relatively independent of the loading conditions. V_{max} can be derived from Eq. 1 which, for a zero force, reduces to

$$V_{max} = \frac{bF_0}{a}. \tag{16}$$

It has been found experimentally that the ratio (F_0/a) remains constant when the volume is changed and the constant b is sensitive to contractility changes (Noordergraff, 1978). The maximum force at zero velocity, F_0, is related to the LV volume by the constant α via Eq. 3. An increase in contractility is reflected by an increase in α which, for a given LV volume or fiber length, causes an increase in F_0. Increasing F_0, without changing the value of α, increases V_{max}. This change, in turn, can be used as another (interrelated) index of contractility. Obviously, if V changes then, by Eq. 3, the values of F_0 and hence σ_0 change too. However, a similar, but inverse, dependence of a on V keeps F_0/a unchanged and V_{max} remains constant under these conditions. The same interrelations are kept

when the stress (σ) is used instead of the force (F) in Eq. 10.

The above analysis shows that based on the physiological characteristics of heart muscle, the contractility index α can be transformed to another index V_{max}. It is interesting to find out whether these two indexes (α, V_{max}) are independent of each other under certain conditions. This would mean that the contractility which is a unique property of the heart muscle, might require several parameters for description. The answer, however, is still unknown, though it is presently common to characterize the contractility only by a single parameter.

The calculated function curves under different loading and contractility conditions, Figs. 7–9, are similar to the reported experimental function curves. The end systolic points of the ejection phase on the pressure-volume curves are situated on the maximum pressure-volume line dicated by the value of α, and thus define the contractility. The isovolumic contraction, followed by the auxotonic contraction and the isovolumic relaxation, describe the classical pressure-volume loop. The force length and stress-length relationship are equivalent relationships. These curves also tend to approach lines which, for a limited experimental range, can be assumed to be linear though, in truth, are nonlinear. The calculation shows that an increase in the initial volume of the LV increases the stroke volume, the LV stroke work and the pressure, in accordance with the classic Frank Starling mechanism. It is clearly shown by Table II, that the ejection fraction — a common clinical index of contractility — $[(1/p)\ (dp/dt)]_{max}$, and the velocity parameters, are strongly preload dependent. However, as is well-known from clinical experience, it is shown by the theoretical model that both the ejection fraction and $[(1/p)\ (dp/dt)]_{max}$ are quite satisfactory as contractility indexes when only minor preload changes are considered.

The changes in the afterloading conditions were induced by decreasing the end diastolic arterial blood pressure. The same maximum elastance line is approached by different contractions which start from the same initial volumes. As is well-known, ejection fraction increases with a decrease in the afterload. The flows which develop at lower pressures are obvious and are related to force-velocity curves. As expected, the contractility index $[(1/p)\ (dp/dt)]_{max}$ is completely afterload independent.

Changes in contractility were induced by changing α which in turn determines the value of V_{max}. It is shown in Table IV that all the clinical parameters commonly used to estimate contractility are sensitive to these contractility changes. Clearly, a change in the contractile state affects the maximum pressure-volume relationship.

The termination of ejection is a common subject of debate and ambiguity. Some investigators (Reichek et al., 1982) claim that the contraction ceases once the pressure-volume curve approaches the maximum elastance line (Figs. 7 *A*, 8 *A*, and 9 *A*). This statement does not comply with the fact that the duration of the time varying elastance curve is somehow related to the length of the action potential. Once the time-dependent elastance curve passes its maximum value, the flow across the aorta deccelerates, and the ejection ends when the LV outflow reverses directions. However, the maximum elastance value is nearly approached when sufficient time is available for the heart to eject. It should be noted that the maximum elastance curve is actually an upper limit to the pressure-volume (P-V) relationship at the specific contractile state and cannot be exceeded. However, for normal heart beats which are long enough, the end systolic point on the P-V loops is practically on the maximum P-V curves.

The model presented here includes almost all the parameters needed to characterize ejection. However, some simple assumptions were used to make this highly complicated phenomenon tractable. Future work should include the stress distribution within the wall of a thick spheroid, and the variations in the velocity of contraction within the wall should be accounted for. The anisotropic electrical activation signal throughout the muscle is also expected to have a significant effect. The different time durations of the action potentials at different locations within the LV wall should be kept in mind. Eventually, real geometries should be used by utilizing appropriate imaging techniques.

SUMMARY

A model of the LV that combines the force-velocity-length relationship of the muscle to the time-varying elastance creates a four-dimensional space in which the velocity of contraction at each point in the systole stage depends on the pressure, volume, and time from the onset of contraction. The computed results, based on relatively simple assumptions, show that the functional status of the LV and its dependence on the contractile state, afterload and preload can be conveniently described by this relatively simple model, in good agreement with experimental evidence.

This study was supported by a special grant from the Kennedy-Leigh Foundation. The trust and support of Mr. Michael Kennedy-Leigh are highly appreciated.

Received for publication 23 June 1983 and in final form 26 October 1983.

REFERENCES

Altman, P. L., and D. S. Dittmer. 1971. Respiration and Circulation. Federation of American Societies for Experimental Biology, Bethesda, MD. 282.

Berne, R. M., N. Sperelakis, and S. R. Geiger. 1979. Handbook of Physiology. The cardiovascular system. American Physiological Society, Bethesda, MD. Vol. 1:411.

Dehmer, G., S. E. Lewis, L. D. Hillis, J. Corbett, R. W. Parkey, and J. T. Willerson. 1981. Exercise-induced alternations in left ventricular volumes and the pressure volume relationship: a sensitive indicator of left ventricular dysfunction in patients with coronary disease. *Circulation.* 63:1008–1068.

Deswysen, B. 1977. Parameter estimation of a simple model of the left

ventricle and of the systemic vascular bed with particular attention to the physical meaning of the left ventricular parameters. *IEEE (Inst. Electr. Electron. Eng.) Trans. Biomed. Eng.* BME-14:1:29–38.

Diamond, G., J. S. Forrester, J. Hargis, W. W. Pamley, R. Danzig, and H. J. C. Swan. 1971. Diastolic pressure-volume relationship of the canine left ventricle. *Circ. Res.* 23:267–275.

Frank, O. 1899. Die Grundform des arterielen pulses. *Z. Biol.* 37:483.

Gaash, W. A., W. E. Battle, A. A. Oboler, J. J. Banes, and N. J. Levine. 1972. Left ventricular stress and compliance in man. *Circulation.* 45:746–762.

Gault, J. H., J. Ross, Jr., and E. Braunwald. 1968. Contractile state of the left ventricle in man. Instantaneous tension-velocity length relations in patients with and without disease of the left ventricular myocardium. *Circ. Res.* 22:451–463.

Grossman, W., E. Braunwald, T. Mann, L. Mclauren, and L. Green. 1977. Contractile state of the left ventricle in man as evaluated from end systolic pressure volume relationship. *Circulation.* 56:845–852.

Hill, A. V. 1938. The heat of shortening and dynamic constants of muscle. *Proc. R. Soc. Lond. Ser. B. Biol.* 126:136–152.

Mirsky, I., D. N. Ghista, and H. Sandler. 1974. Cardiac Mechanics: Physiological, Clinical and Mathematical Considerations. John Wiley & Sons, Inc., New York. 389.

Nivatpumin, T., S. Katz, and J. Scheuer. 1979. Peak left ventricular systolic pressure/end diastolic volume ratio. A sensitive detector of left ventricular disease. *Am. J. Cardiol.* 43:969–974.

Noordegraff, A. 1978. Circulatory System Dynamics. Academic Press, Inc., New York. 213.

Parmley, W. W., D. L. Brutsaert, and E. H. Sonnenblick. 1969. Effect of altered loading on contractile events in isolated cat papillary muscle. *Circ. Res.* 24:521–529.

Parmley, W. W., L. A. Yeatman, and E. H. Sonnenblick. 1970. Difference between isotonic and isometric force velocity relations in cardiac and skeletal muscle. *Am. J. Physiol.* 219:546–550.

Parmley, W. W., L. Chuck, and E. H. Sonnenblick. 1972. Relations of V_{max} to different models of cardiac muscles. *Circ. Res.* 30:34–43.

Peterson, K. L., J. B. Uther, R. Shabetai, and E. Braunwald. 1973. Assessment of left ventricular performance in man. Instantaneous tension-velocity-length relations obtained with the aid of an electromagnetic velocity catheter in the ascending aorta. *Circulation.* 47:924–935.

Piene, H., and J. W. Covell. 1981. A force length time relationship describes the mechanics of left venticular wall segments during auxotonic contractions. *Circ. Res.* 49:70–79.

Pollack, G. H. 1970. Maximum velocity of an index of contractility in cardiac muscle. A critical evaluation. *Circ. Res.* 26:111–127.

Reicheck, N., J. Wilson, M. J. Sutton, M. B. Theodore, A. Plappest, S. Goldberg, and J. W. Hirshfeld. 1982. Noninvasive determination of left ventricular end systolic stress: validation of the method and initial application. *Circulation.* 65:99–108.

Schuler, G., K. V. Olshausen, H. Mehmel, F. Schwarz, H. J. Herman, and W. Kübler. 1981. Noninvasive determination of the end systolic pressure volume relation in patients with aortic regurgitation. *Am. J. Cardiol.* 47:427. (Abstr.)

Schuler, G., K. Olshausen, F. Schwarz, H. Mehmel, M. Herman, H. J. Herman, D. Lange, and W. Kübler. 1982. Noninvasive assessment of myocardial contractility in asymptomatic patients with severe aortic regurgitation and normal left ventricular ejection fraction at rest. *Am. J. Cardiol.* 50:45–52.

Slutzky, R., F. Karliner, K. Gerber, A. Battler, V. Fraelicher, E. Peterson, and W. Ashburn. 1980. Peak systolic blood pressure/end systolic volume ratio: assessment at rest and during exercise in normal subjects and patients with coronary heart disease. *Am. J. Cardiol.* 46:813–820.

Sonnenblick, E. H. 1962. Force velocity relations in mammalian heart muscle. *Am. J. Physiol.* 202:931–939.

Sonnenblick, E. H. 1964. Series elastic and contractile elements in heart muscle. Change in muscle length. *Am. J. Physiol.* 207:1330–1338.

Suga, H., K. Sagawa, and A. Shoukas. 1973. Load independence of the instantaneous pressure volume ratio of the canine left ventricle and effects of epinephrine and heart rate on the ratio. *Circ. Res.* 32:314–322.

Suga, H., and K. Sagawa. 1974. Instantaneous pressure-volume relationships and their ratio in the exercised supported canine left ventricle. *Circ. Res.* 35:117–126.

Suga, H., K. Sagawa, and D. P. Koustuik. 1976. Controls of ventricular contractility assessed by pressure-volume ratio, E_{max}. *Cardiovasc. Res.* 10:582–592.

Suga, H., and D. Yamakoshi. 1977. Effects of stroke volume and velocity of ejection on end systolic pressure of canine left ventricle. *Circ. Res.* 40:445–450.

Weber, K. T., J. S. Janicki, and L. L. Hefner. 1976*a*. Left ventricular force-length relations of isovolumic and ejecting contractions. *Am. J. Physiol.* 231:337–343.

Weber, K. T., J. S. Janicki, R. C. Reeves, and L. L. Hefner. 1976*b*. Factors influencing left ventricular shortening in isolated canine heart. *Am. J. Physiol.* 230:419–426.

Weber, K. T., and J. S. Janicki. 1977. Instantaneous force-velocity relations isolated dog heart. *Am. J. Physiol.* 232:H241–H249.

Weber, K. T., and J. S. Janicki. 1978. Interdependence of cardiac function, coronary flow and oxygen extraction. *Am. J. Physiol.* 285:H784–H793.

Weber, K. T., and J. S. Janicki. 1979. The heart as a muscle pump system and the concept of heart failure. *Am. Heart J.* 98:371–384.

Weber, K. T., and J. S. Janicki. 1980. The dynamic of left ventricular contraction force-length and shortening. *Fed. Proc.* 39:188–195.