

MODELLING AND SIMULATION OF CERTAIN ASPECTS  
OF THE DYNAMIC BEHAVIOUR OF THE  
ISOLATED PAPILLARY MUSCLE OF THE RAT

BY

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ABSTRACT

The problem of formulating a model for the tension generating mechanism in the papillary muscle of a rat under the condition of periodic electrical stimulus, is considered. The model formulation is oriented around the movement of calcium among various compartments presumed to exist within the papillary muscle. A parameter of particular significance in the study is the calcium concentration in the Tyrode solution bath in which the muscle is suspended during experimentation.

Two particular model configurations are considered and it is demonstrated that the first is inadequate because of its substantial deviation from available Omega response (tension-frequency) data. The second model, which essentially incorporates the first as one of two subsystems, is shown to yield Omega responses which are in close agreement with the general trends of the available data.

In the course of study, the notion of dynamic equilibrium is introduced and conditions for its existence in the mathematical characterization of the system are developed. The generation of the necessary Omega response data for the models considered is considerably facilitated using the derived conditions.

A set of model parameters which minimizes the

deviation between the given Omega response data and model Omega responses is found by performing a series of computational experiments on the model.

NOMENCLATURE

- $\alpha_1$  : The fluid level in the tank  $T_s$  or  $T_{s_1}$ , after the occurrence of a pulse, meters.
- $\alpha_2$  : The fluid level in the tank  $T_r$  or  $T_{r_1}$ , after the occurrence of a pulse, meters.
- $\alpha_3$  : The fluid level in the tank  $T_{s_2}$ , after the occurrence of a pulse, meters.
- $\alpha_4$  : The fluid level in the tank  $T_{r_2}$ , after the occurrence of a pulse, meters.
- $A_\Lambda$  : The cross-sectional area of the tank  $T_\Lambda$  (where  $\Lambda$  can have the values  $r, r_1, r_2, s, s_1$  or  $s_2$ ), meter<sup>2</sup>.
- $B$  : The constant component of the flow rate,  $P_R(t)$ , through the pump  $P$ , meter<sup>3</sup>/sec.
- $\beta$  : The feed-back factor.
- $[Ca^{++}]_i$  : The intracellular concentration of free calcium after an electrical stimulus, MOLS/millilitre.
- $[Ca^{++}]_0$  : Calcium ion concentration in the external fluid bath, MOLS/millilitre.
- $Ca_F$  : Free calcium, MOLS.
- $Ca_0$  : Calcium in the external fluid bath, MOLS.

- $Ca_r$  : The rapidly releasable calcium, MOLS.
- $Ca_{r_1}$  : The fast filling component of  $Ca_r$ , MOLS.
- $Ca_{r_2}$  : The slow filling component of  $Ca_r$ , MOLS.
- $Ca_s$  : The stored calcium, MOLS.
- $Ca_{s_1}$  : The fast filling component of the stored calcium, MOLS.
- $Ca_{s_2}$  : The slow filling component of the stored calcium, MOLS.
- $\Delta$  : The interpulse interval, seconds.
- $e$  : The exponent factor associated with  $Q_R$ .
- $f$  : The frequency of stimulation, pulses/min.
- $f_1$  : The optimum frequency, (the frequency at which the peak of the Omega response occurs), pulses/min.
- $f_2$  : The least favourable frequency, (the frequency at which the minimum of the Omega response occurs), pulses/min.
- $h_\Lambda$  : The fluid level in the tank  $T_\Lambda$  (where  $\Lambda$  can have the values 0, r,  $r_1$ ,  $r_2$ , s,  $s_1$  or  $s_2$ ) meters.
- $\bar{h}_\Lambda$  : The steady state value of the fluid level  $h_\Lambda$  (where  $\Lambda$  can have the values 0, r,  $r_1$ ,  $r_2$ , s,  $s_1$  or  $s_2$ ), meters.

- $K_1$  : The fluid flow constant between the tanks  $T_s (T_{s_1})$  and  $T_r (T_{r_1})$ , meter<sup>2</sup>/sec.
- $K_2$  : The fluid flow constant between the tanks  $T_0$  and  $T_s (T_{s_1})$ , meter<sup>2</sup>/sec.
- $K_3$  : The fluid flow constant associated with the fluid flow,  $P_R(t)$ , of the pump P, meter<sup>2</sup>/sec.
- $K_1$  : The fluid flow constant between the tanks  $T_{s_2}$  and  $T_{r_2}$ , meter<sup>2</sup>/sec.
- $K_2$  : The fluid flow constant between the tanks  $T_0$  and  $T_{s_2}$ , meter<sup>2</sup>/sec.
- $K_3$  : The fluid flow constant associated with the fluid flow,  $P_R(t)$ , of the pump P', meter<sup>2</sup>/sec.
- $\lambda_\Lambda$  : The decay time constant for the tank  $T_\Lambda$  (where  $\Lambda$  can have the values s,  $s_1$  or  $s_2$ ), seconds.
- $\lambda_\Lambda$  : The recovery time constant of the tank  $T_\Lambda$  (where  $\Lambda$  can have the values r,  $r_1$  or  $r_2$ ), seconds.
- $M_\Lambda$  : The volume of the tank  $T_\Lambda$  (where  $\Lambda$  can have the values r,  $r_1$ ,  $r_2$ , s,  $s_1$  or  $s_2$ ), meter<sup>3</sup>.
- $\bar{M}_\Lambda$  : The steady state value of volume  $M_\Lambda$  (where  $\Lambda$  can have the values r,  $r_1$ ,  $r_2$ , s,  $s_1$  or  $s_2$ ), meter<sup>3</sup>.
- $Q_C$  : The calcium gated from the surrounding solution (outside calcium) to the  $C_s$  compartment, MOLS.

- $Q_h$  : The fluid gated from the tank  $T_0$  to the tank  $T_s(T_{s_1})$ , meter<sup>3</sup>.
- $t_p^j$  : Time of occurrence of the  $j^{\text{th}}$  pulse; seconds.
- $T_f$  : The normalized tension of the papillary muscle.
- $V_A$  : The volume of the compartment  $C_A$  (where  $A$  can have the values  $r, r_1, r_2, s, s_1$  or  $s_2$ ), millilitre.

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CHAPTER 1

INTRODUCTION

## 1.0 GENERAL COMMENTS

The challenge of biomedical research is to enhance understanding of biological systems and to apply this understanding as directly as possible to living systems. Increased comprehension of these systems can be obtained by observing the performance of the intact organism. Alternately, mathematical modelling and simulation methods are playing an increasingly important role in these activities. Engineers and medical doctors are working together to design and construct mathematical models which relate to the functions and operations of such organs as the heart, the kidneys, the limbs etc. A particular problem of this class is investigated in this thesis.

### 1.1 PROBLEM DESCRIPTION

The system under investigation is an isolated papillary muscle (cardiac muscle) of a rat suspended in a "Tyrode solution" bath and subjected to an electrical stimulus (a pulse train with a fixed interval between the pulses). The output of the system is the tension of cardiac muscle which is measurable. Figure 1.1 provides a block diagram representation for the system.

---

\* Tyrode solution is a solution of similar ionic composition to that of blood plasma. Although it contains a variety of components its calcium content is the only variable component considered in these experiments.

The relation between the frequency of the electrical pulse train and the resulting tension developed by the muscle once a steady state condition has been reached, is called the Tension-frequency relationship (referred to herein as the Omega relationship). It has been noted [1-3] that the tension-frequency relationship of cardiac muscle encompasses all influences which the interval between electrical pulses has on the strength of contraction.

It is desired to develop a model of the cardiac muscle system shown in Figure 1.1, such that its Omega responses correspond to experimental data obtained from an actual system using a papillary muscle of a rat.

A parameter associated with the Omega response of the cardiac muscle is the concentration of the calcium in the Tyrode solution (the "outside" calcium concentration). Hence a further criteria in formulating the model is that of obtaining satisfactory model responses (i.e. Omega curves) for four distinct outside calcium concentrations; namely:

- |                                    |                       |                 |
|------------------------------------|-----------------------|-----------------|
| a) Very low calcium concentration, | $0.25 \times 10^{-6}$ | Mols/milliliter |
| b) Low calcium concentration,      | $0.5 \times 10^{-6}$  | Mols/milliliter |
| c) Medium calcium concentration,   | $1.0 \times 10^{-6}$  | Mols/milliliter |
| d) High calcium concentration,     | $2.5 \times 10^{-6}$  | Mols/milliliter |

The effect of other system parameters on the time and frequency responses of various model components or compartments and on the Omega relationship is also of interest.

The electrical stimulus applied to cardiac muscle appears to act by causing a rapid discharge of calcium within the cells [1, 2]. The stimulus strength (volts) which is just needed to produce this effect is called the "Threshold of Excitation".

The evolution of the modelling process under consideration is guided by experimental data obtained from experiments performed on Male Sprague Dawley rats and Male Guinea pigs. The experiments were conducted in the Department of Physiology at the University of Ottawa. In these experiments, the muscle was stimulated through parallel platinum plate electrodes suspended in the bath on each side of the muscle and connected to a stimulator (GRASS Model s-4). Stimulation voltage was maintained at 50% above the threshold of excitation. The stimulator was controlled from a Devices Digitimer Programmable unit (Model 3290). The data provided from these experiments consisted of the Omega curves for the isolated papillary muscle of a rat at various calcium concentrations in the surrounding bath. These curves (obtained from Forester [12]) are shown in Figure 1.2.

Calcium is generally considered to be a principle link between excitation and contraction of cardiac muscle and it is well known [4] that the heart beat becomes stronger when the calcium ion concentration  $[Ca^{++}]_0$  in the surrounding fluid is increased.

When the muscle is stimulated at a constant pulse

frequency, the muscle contractions also assume a periodic behaviour after passing through an initial transient phase. Once the periodic mode has been obtained, (peak amplitude invariant from cycle to cycle) the peak tension developed is a function of the frequency of electrical stimulation and the calcium concentration in the fluid bath.

The shape of the Omega curve is dependent upon the outside calcium concentration. At high calcium concentrations (e.g.  $2.5 \times 10^{-6}$  MOLS/milliliter or more), the amplitude of tension decreases continuously as the frequency increases. At low calcium concentrations, the Omega relation is characterized by a valley whose minimum occurs at a stimulation frequency  $f_1$  (10-20 pulses/min.) followed by a peak occurring at a stimulation frequency  $f_2$  (60-80 pulses/min.). The stimulation frequencies  $f_1$  and  $f_2$  are often referred to the "least favourable frequency" and the "optimum frequency" respectively. Experimental evidence [1] has furthermore demonstrated that the frequency separation,  $(f_2 - f_1)$ , is dependent on the calcium concentration of the fluid bath. At lower calcium concentrations  $(f_2 - f_1)$  increases and vice versa.

### 1.2- PREVIOUS MODELLING EFFORTS

It is generally accepted [2] that  $[Ca^{++}]_i$ , the intracellular concentration of free calcium after an electrical stimulation, determines the tension development of the

cardiac muscle. It is, therefore, generally accepted that the changes in contractile strength of the heart muscle may be reflected in changes in  $[Ca^{++}]_i$  after stimulations. In order to explore this possibility Manring and Hollander [2] proposed a model for predicting changes in the contractile strength of cardiac muscle based on calcium movement between contractions.

Figure 1.3 shows a schematic diagram of their model. The arrows represent the flow of calcium, and  $n_1$  and  $n_2$  are two calcium storage compartments. The strength of contraction is proportional to the calcium content in  $n_1$  at the moment of stimulation. After a contraction,  $n_2$  acquires calcium from the contractile mechanism. Between beats calcium is transferred from  $n_2$  to  $n_1$ . The flow  $F_p$  is due to an active calcium pump which maintains the intracellular level [5].

In this model, feed-back effects are omitted and interaction of only two storage calcium compartments is considered. Tracer studies [6-9] have, however, suggested the existence of several compartments. These additional compartments may be important under certain conditions.

In 1970, a conceptual model of intracellular calcium movement was proposed by Mainwood and Lee [10]. In their model shown in Figure 1.4, the papillary muscle under the influence of the electrical stimulus and the outside calcium concentration, is represented by three compart-

ments. These are (i) the  $C_S$  compartment which contains stored or bound calcium ( $Ca_S$ ), (ii) the  $C_R$  compartment which contains rapidly releasible calcium ( $Ca_R$ ), and (iii) the  $C_F$  compartment which contains free calcium ( $Ca_F$ ).

The flow of calcium between the  $C_S$  compartment and the fluid bath has three components; namely:

- (i)  $F_0$ , a gated flow of calcium into the  $C_S$  compartment which occurs at the instant of electrical stimulus.
- (ii)  $F_b$ , a continuous flow phenomenon resulting from a difference in the calcium concentration between the  $C_S$  compartment and the fluid bath.  $K_2$  represents the associated flow rate constant.
- (iii)  $F_p$ , forced transfer of calcium from the  $C_S$  compartment into the fluid bath resulting from an active "Calcium Pump".

The calcium transfer between the  $C_R$  and  $C_S$  compartments is a continuous phenomenon resulting from a difference in the calcium concentrations within these two compartments. This transfer takes place under the influence of the flow rate constant  $K_1$ .

At the instant of an electrical stimulus, the total amount of calcium within the  $C_R$  compartment is transferred to  $C_F$  compartment where the actual contractile mechanism is assumed to reside. The calcium transferred to the  $C_F$

compartment generates the muscle contraction, and a portion of it is returned to  $C_S$  compartment, via the flow denoted by  $F_2$ . The latter transfer, which takes place over a relatively short interval of time, can be viewed as a feed-back effect.

In the subsequent considerations, the  $C_F$  compartment is removed from basic Mainwood-Lee model for the following reasons:

- (i) The calcium flow  $F_2$  from the  $C_F$  compartment to the  $C_S$  compartment has the form of a pulse whose duration, relative to the time constants of the system, is very short. The effect of the transfer can, therefore, be adequately incorporated by simply considering an instantaneous adjustment of calcium level in the  $C_S$  compartment by an appropriate amount.
- (ii) As described above the muscle contraction results from calcium transferred to the  $C_F$  compartment from  $C_R$  compartment at the instant of the electrical stimulus and the amount transferred is the total amount of calcium in  $C_R$  compartment. The strength of the contraction is proportional to the amount of calcium transferred. In effect then, the strength of the contraction can be determined directly from information about the calcium in

the  $C_r$  compartment at the time of the stimulus. From an operational point of view, therefore, the modelling of the system can proceed without reference to the  $C_F$  compartment.

### 1.3 GENERATION OF TENSION

As noted above, the tension generating mechanism in the Mainwood-Lee model is localized in the  $C_F$  compartment. However, the actual process which produces the tension from the calcium received from the  $C_r$  compartment is not a part of the model. Since tension is the only experimentally measurable output quantity of the papillary muscle system under study, the modelling procedures can be related to reality only via this particular variable. It is, therefore, necessary to generate a variable in the modelling process which is the analog of tension. The basis for achieving this is via available experimental data referred to as the "rested-state-contraction-tension" relationship.

This data is derived from experiments conducted on the papillary muscle in which the electrical stimulus pulse rate is sufficiently low to allow steady-state conditions to be attained between pulses. Under such conditions, the tension developed at steady-state is only a function of the outside calcium concentration,  $[Ca_0]$ .

Data of this type, applicable to the papillary muscle of the rat is given by Forester [12]. By normalizing

this data and investigating possible analytic expressions which provide a fit to it, Forester proposes the following analytic model

$$T = \frac{7.2 \times 10^{12} [Ca_0]^2}{1 + 7.2 \times 10^{12} [Ca_0]^2} \dots\dots\dots 1.1$$

where T represents normalized tension (non-dimensional) and  $[Ca_0]$  is the outside calcium concentration (MOLS/milliliter). A plot of the relation given in equation 1.1 is provided in Figure 1.5.

It is reasonable to assume that a functional relationship exists between  $[Ca_0]$  and  $Ca_r$  (at the pulse time) when the electrical pulse rate is low. Furthermore, this relation could be viewed as equally valid for any stimulation pulse rate. Under such assumptions a relationship between T and  $Ca_r$  can be inferred. This matter is investigated further in Chapter 2 and leads to a mechanism for generating a variable analogous to tension in the hydraulic analog to be formulated.

#### 1.4 APPROACH TAKEN IN PRESENT WORK

In order to evaluate and experiment with the Mainwood-Lee model, it was convenient to translate it into a physical analog based on the flow of fluid among tanks. This hydraulic model (Figure 1.6) serves to provide a link which enables the formulation of the mathematical model for the Mainwood-Lee proposal.

The investigations carried out in this thesis are concerned with studying and refining this physical analog

in order that its behaviour (or more precisely, that of its mathematical characterization) correspond to the experimental data obtained from experiments on the actual cardiac muscle.

The hydraulic analog shown in Figure 1.6 is intended to represent the situation only during the interpulse interval. The tanks  $T_0$ ,  $T_s$ , and  $T_r$  correspond to the compartments of outside calcium, stored calcium and rapidly releasable calcium.  $(h_0, M_0, A_0)$ ,  $(h_s, M_s, A_s)$ , and  $(h_r, M_r, A_r)$  represent the fluid levels, volumes and cross-sectional areas of the  $T_0$ ,  $T_s$ , and  $T_r$  tanks respectively. In this hydraulic analog the following assumptions are made:

- (i) All the tanks have constant cross-sectional areas, and so the volume of fluid in tanks  $T_s$ , and  $T_r$  is respectively

$$M_s(t) = A_s h_s(t)$$

$$M_r(t) = A_r h_r(t).$$

- (ii) The volume of tank  $T_0$  is substantially larger than both tanks  $T_s$ , and  $T_r$  and on this basis, it is assumed that the height of fluid in tank  $T_0$  never really changes during the course of investigation, i.e.  $h_0 = \text{constant}$ .

A summary of the correspondence between the various quantities of interest in the Mainwood-Lee Model and the hydraulic analog is given in Table 1. Throughout the

computational experiments, the following correspondence between the fluid height in tank  $T_k$  ( $k = 0, r, s$ ) and the calcium concentration within the corresponding compartment was used;

$$1 \text{ unit(meter)} + 0.25 \times 10^{-6} \text{ Mols/milliliter}$$

### 1.5 SUMMARY OF THE CONTENTS OF THESIS

Chapter 2 deals with the hydraulic analog of the basic Mainwood-Lee model and the results of the computational experiments carried out on the hydraulic analog. Chapter 3 deals with a modification of the basic Mainwood-Lee model together with its corresponding hydraulic analog and the results of computational experiments carried out on the hydraulic analog.

Appendices I and II describe the computer program used in carrying out the various computational experiments for producing the model response data.

Mainwood-Lee Model	Hydraulic Analog
The surrounding fluid bath	Tank $T_0$
Compartment $C_s$	Tank $T_s$
Compartment $C_r$	Tank $T_r$
Amount of calcium in the $C_s$ compartment ( $Ca_s$ )	Volume $M_s$
Amount of calcium in the $C_r$ compartment ( $Ca_r$ )	Volume $M_r$
Volume of the $C_s$ compartment ( $V_s$ )	Area of cross-section $A_s$
Volume of the $C_r$ compartment ( $V_r$ )	Area of cross-section $A_r$
Calcium concentration [ $Ca_0$ ]	Height $h_0$
Calcium concentration [ $Ca_s$ ]	Height $h_s$
Calcium concentration [ $Ca_r$ ]	Height $h_r$
$Ca_s = V_s [Ca_s]$	$M_s = A_s h_s$
$Ca_r = V_r [Ca_r]$	$M_r = A_r h_r$

TABLE 1.1

Correspondence between the Mainwood-Lee Conceptual Model and its Hydraulic Analog.

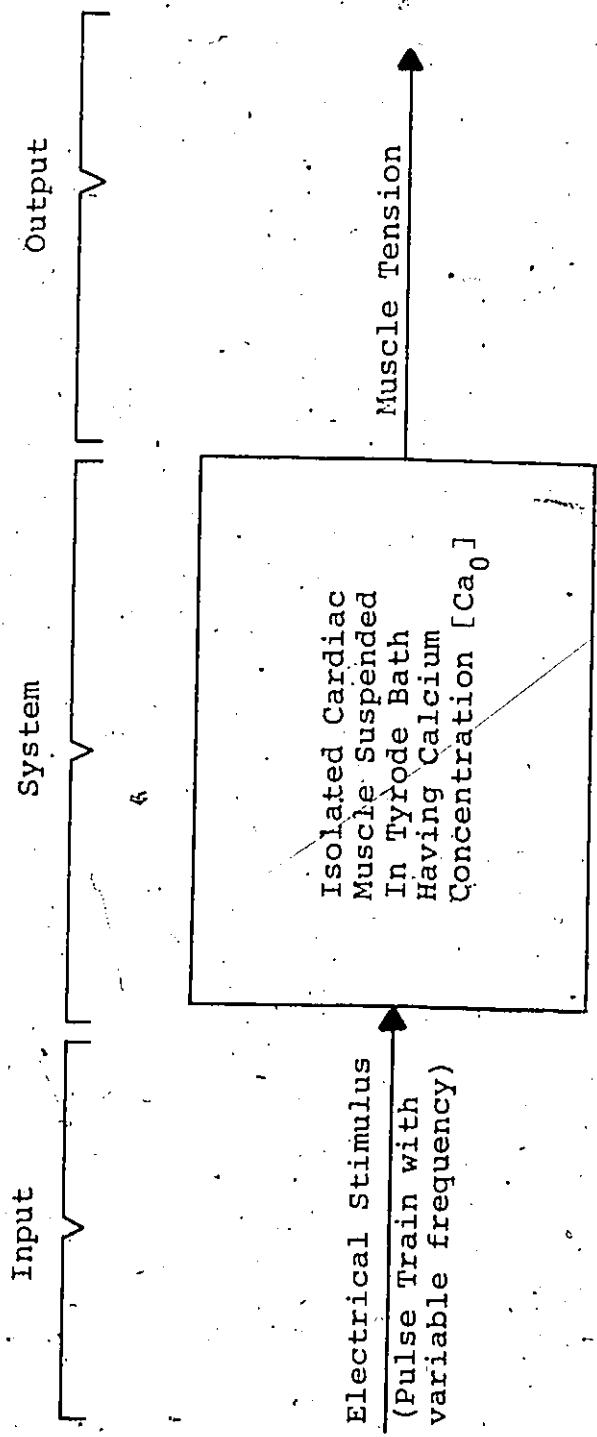


Figure 1.1

Isolated Papillary Muscle System Under Study.

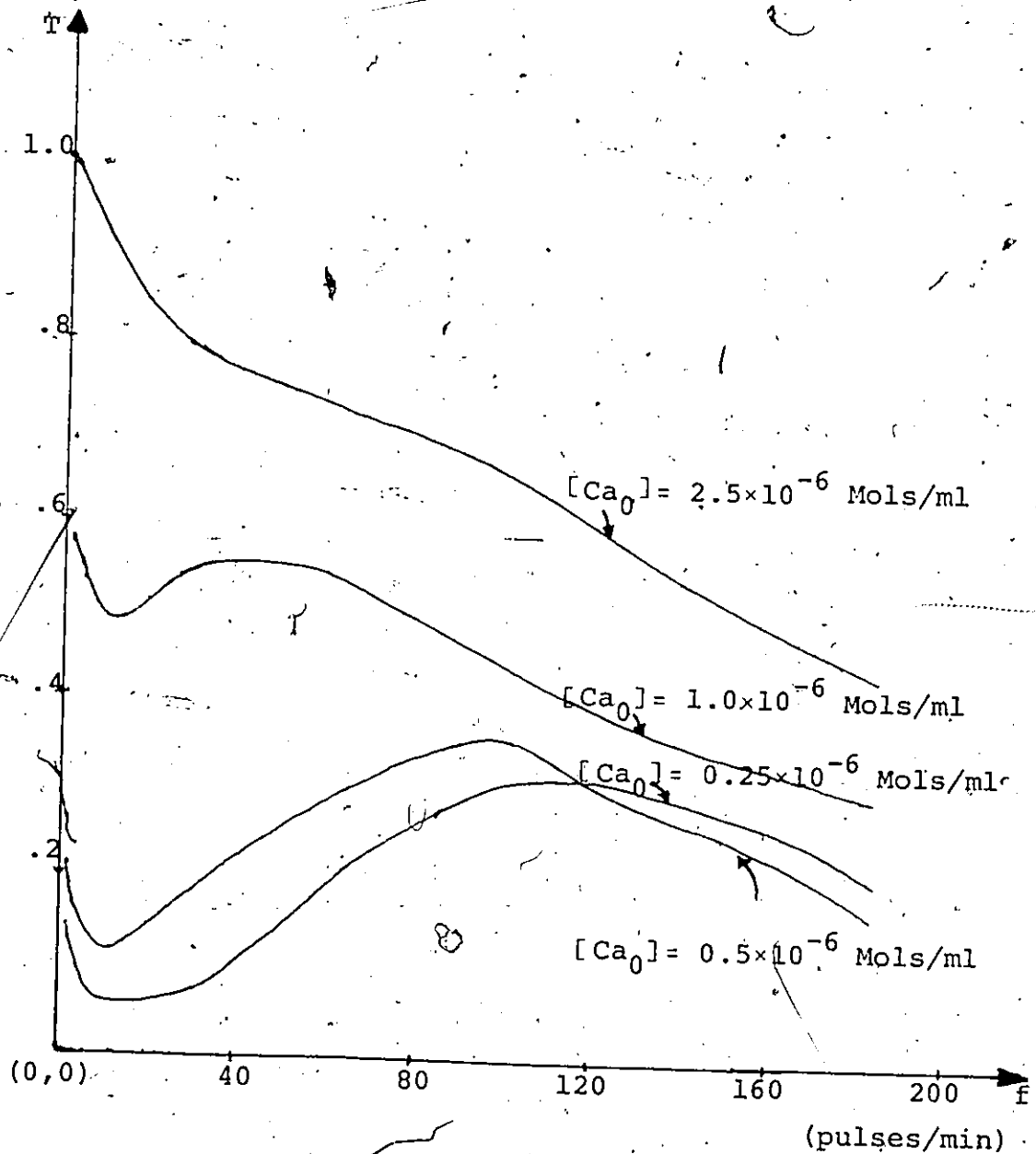


FIGURE 1.2

The Experimental Omega Responses for the Isolated Papillary Muscle of the Rat at Different Outside Calcium Concentrations.

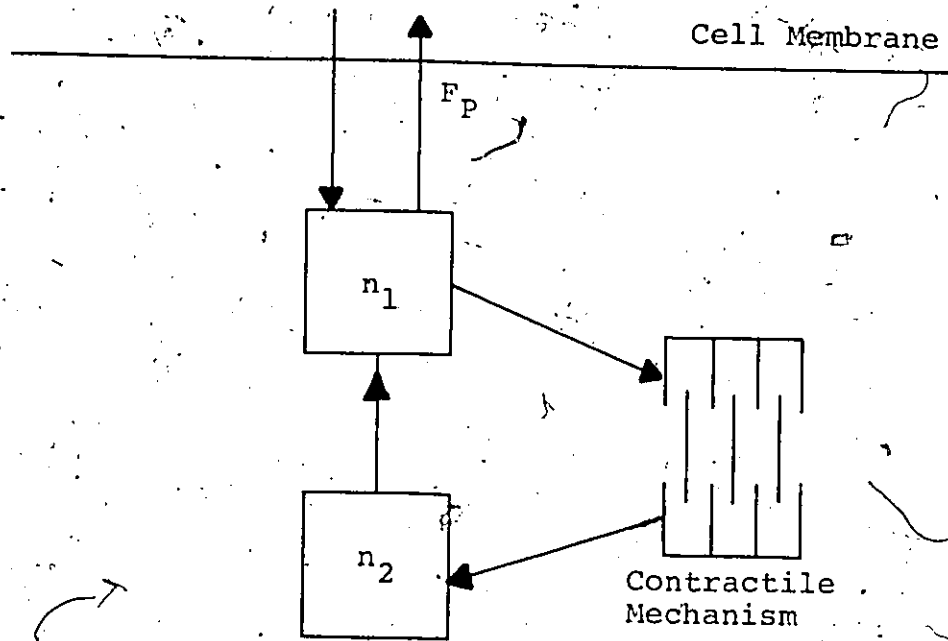


Figure 1.3

Schematic Diagram of the Manning and Hollander Model.

External Fluid bath having  
Calcium Concentration  $[Ca_0]$

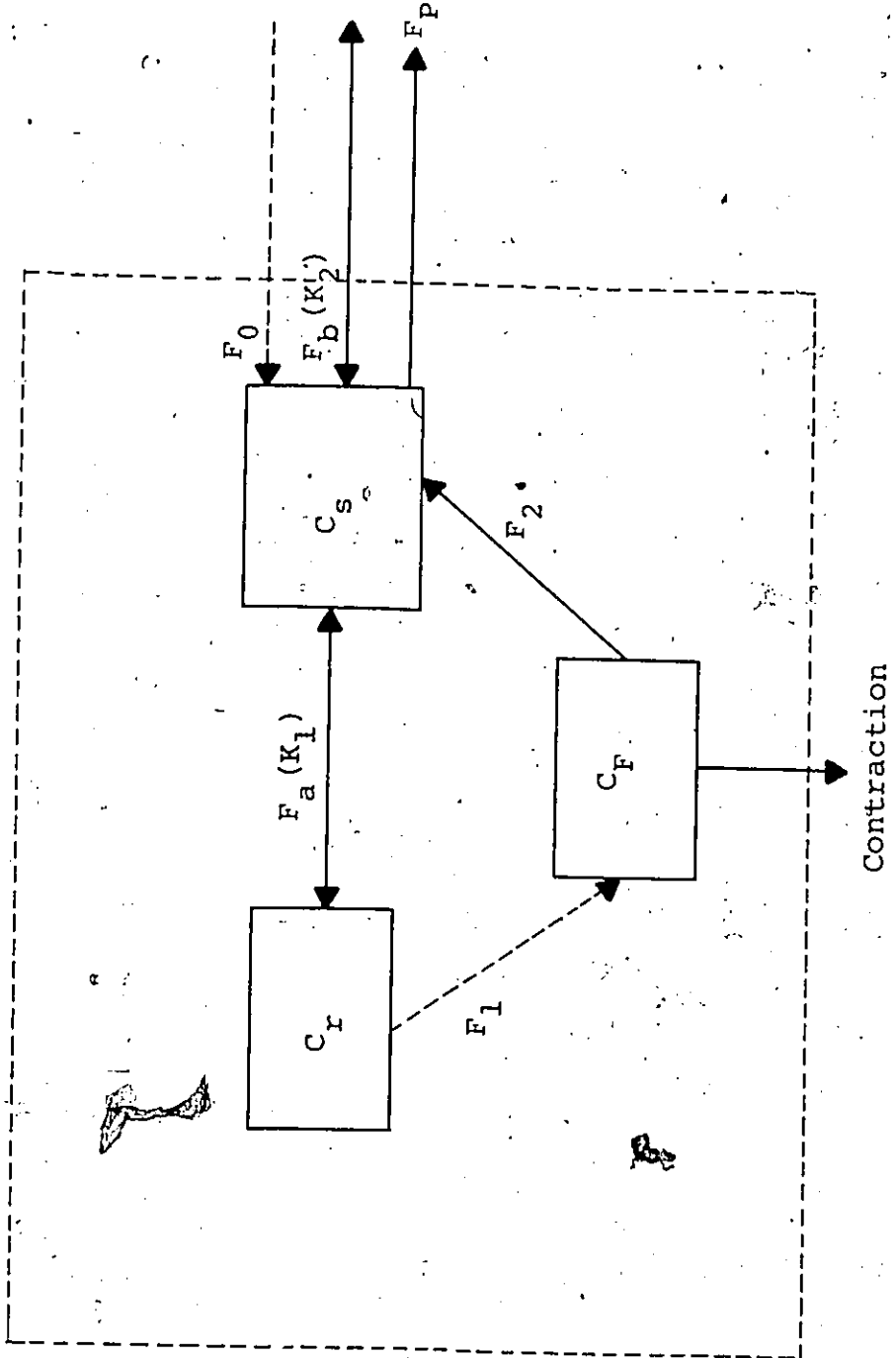


Figure 1.4

The Conceptual Model of Intracellular Calcium Movement Suggested by Mainwood and Lee.

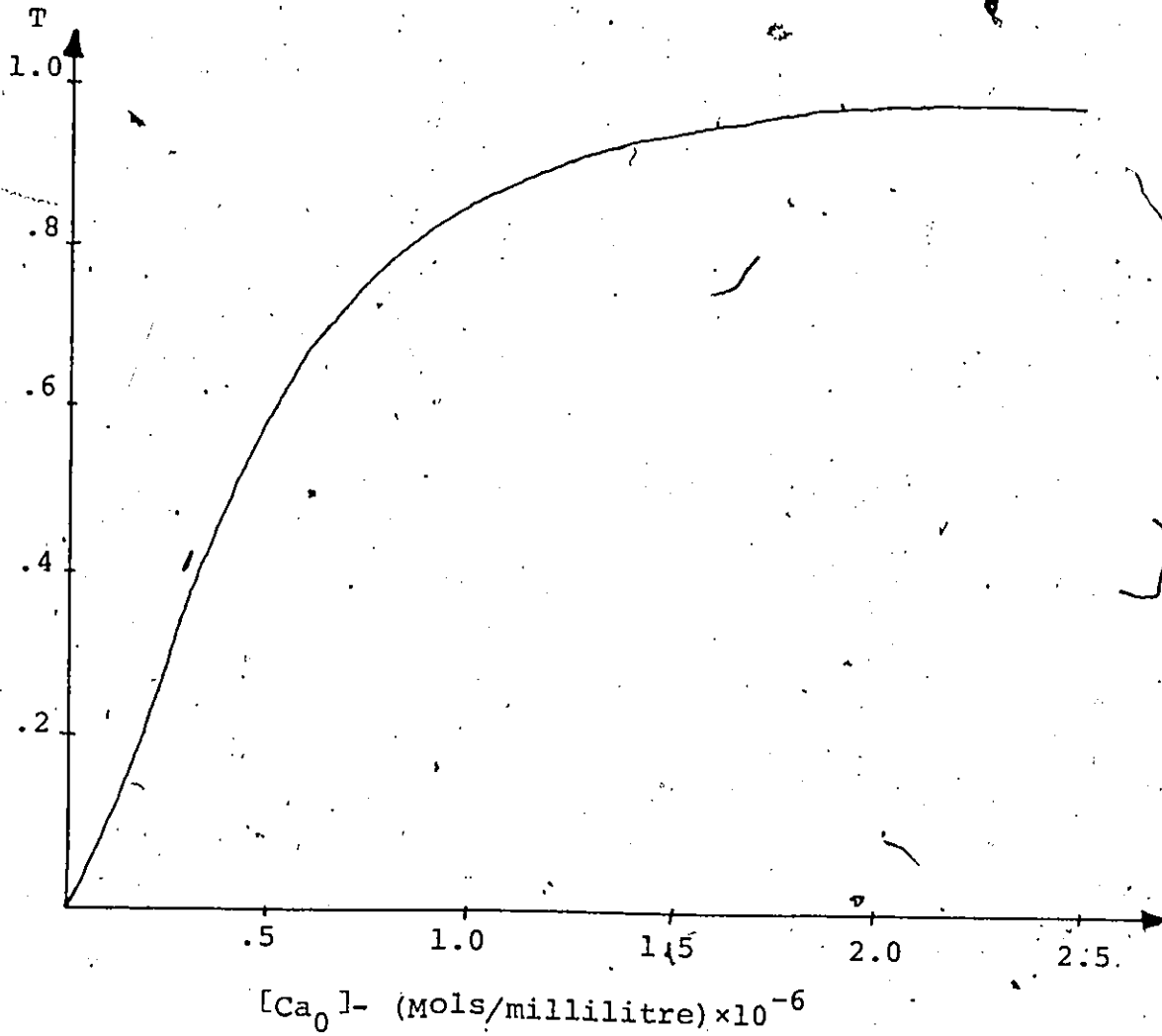


FIGURE 1.5

Effect of Outside Calcium Concentration on Steady State Tension in Isolated Papillary Muscle of the Rat.

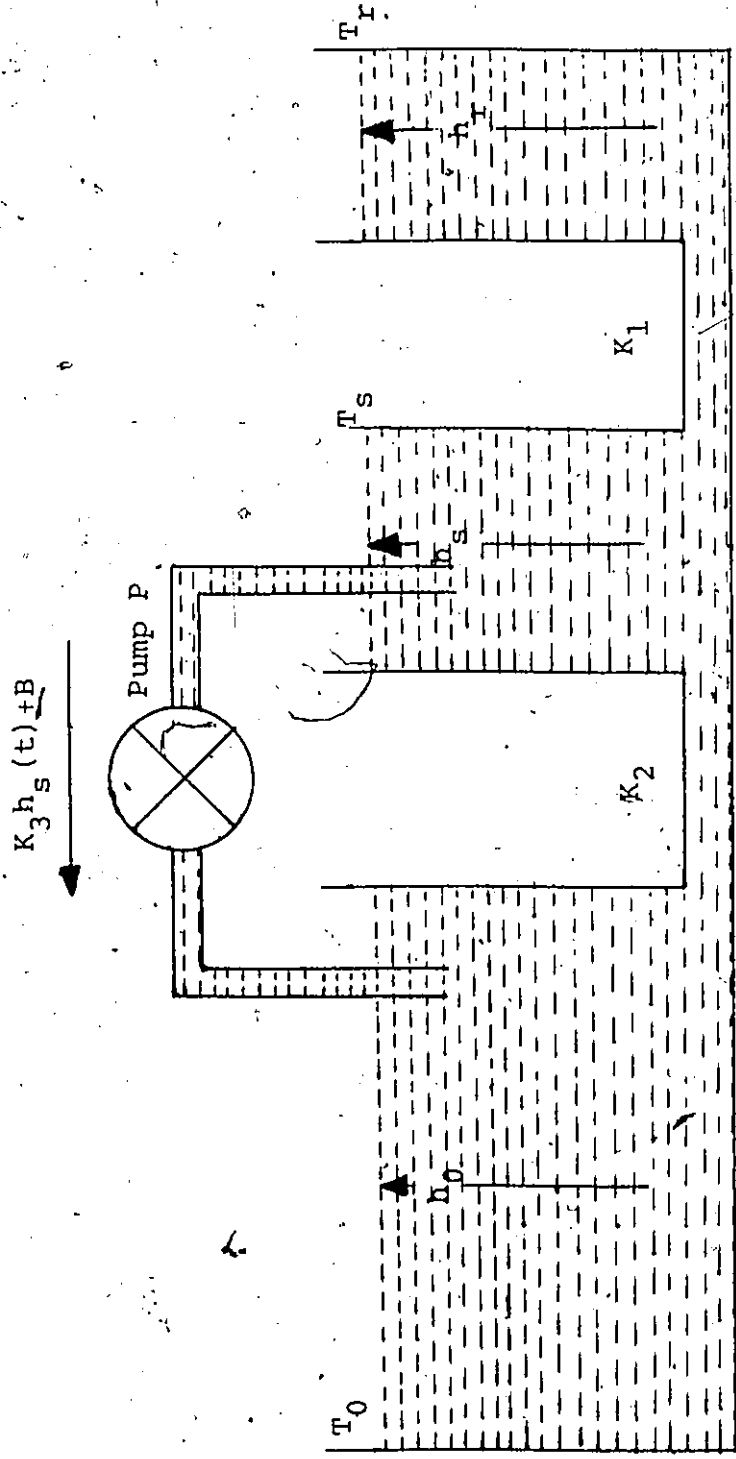


FIGURE 1.6

Hydraulic Analog of the Mainwood-Lee Model.

## 2.1 MATHEMATICAL MODEL FOR HYDRAULIC ANALOG

A hydraulic analog for the basic Mainwood-Lee model was developed in Chapter 1. The fluid levels in tanks  $T_S$  and  $T_R$  (Figure 1.6) are determined by the flow rate constant of the pump and flow rate constants among the reservoirs. A mathematical model describing the behaviour of the hydraulic analog during the interpulse interval and at the pulse times is given in the following sections.

### 2.1.1 INTERPULSE INTERVAL

The equation for the rate of change of fluid volume in tank  $T_S$  can be written as:

$$\frac{dM_S(t)}{dt} = K_2(h_0 - h_S(t)) - K_1(h_S(t) - h_R(t)) - P_R(t) \dots\dots 2.1$$

where  $K_1$  and  $K_2$  denote the flow rate constants between tanks  $T_S$  and  $T_R$ , and between tanks  $T_S$  and  $T_0$  respectively.

The flow rate through the pump P is denoted by  $P_R(t)$  and is given by:

$$P_R(t) = K_3 h_S(t) + B \dots\dots\dots 2.2$$

$P_R(t)$  is composed of two components, namely:

- (i) The  $h_S$  dependent component,  $K_3 h_S(t)$ , which depends on the flow rate constant  $K_3$  (meter<sup>2</sup>/sec.) and the fluid level  $h_S(t)$ .
- (ii) The constant component,  $B$  (meter<sup>3</sup>/sec.).

Rearranging and using the relation  $h = M/A$ , equation 2.1 is written as:

CHAPTER 2

BASIC MAINWOOD-LEE MODEL

$$\frac{dM_s(t)}{dt} = -(K_1 + K_2 + K_3) \frac{M_s(t)}{A_s} + K_1 \frac{M_r(t)}{A_r} + K_2 h_0 - B \dots\dots\dots 2.3$$

The rate of change of volume in tank,  $T_r$  can similiarly be written as:

$$\frac{dM_r(t)}{dt} = K_1 (h_s(t) - h_r(t)) \dots\dots\dots 2.4$$

or equivalently as:

$$\frac{dM_r(t)}{dt} = K_1 \frac{M_s(t)}{A_s} - K_1 \frac{M_r(t)}{A_r} \dots\dots\dots 2.5$$

Physiological considerations in context of the Mainwood-Lee model suggest that the following steady state conditions hold:

$$\begin{aligned} [Ca_s] &= [Ca_r] \\ [Ca_0] &= 5[Ca_s] \end{aligned}$$

In view of the correspondence between calcium concentration and fluid height (Table I), these conditions correspond to the constraints:

$$\left. \begin{aligned} \bar{h}_s &= \bar{h}_r \\ \bar{h}_0 &= 5\bar{h}_s \end{aligned} \right\} \dots\dots\dots 2.6$$

where the bar superscript is used to denote steady-state values.

The steady-state relations of equation 2.6 are directly satisfied by equation 2.4. However, when imposed on equation 2.3 (with  $B = 0$ ), the following constraint results:

$$h_0 = \left( \frac{K_2 + K_3}{K_2} \right) \bar{h}_s \dots\dots\dots 2.7$$

Equation 2.7 indicates that the required steady-state condition is satisfied when:

$$K_3 = 4K_2 \text{ (steady-state constraint) } \dots\dots\dots 2.8$$

Incorporation of this constraint into the system equations (2.3 and 2.5) yields:

$$\frac{dM_s(t)}{dt} = - \left( \frac{K_1 + 5K_2}{A_s} \right) M_s(t) + \left( \frac{K_1}{A_r} \right) M_r(t) + K_2 h_0 - B \dots\dots\dots 2.9$$

$$\frac{dM_r(t)}{dt} = \left( \frac{K_1}{A_s} \right) M_s(t) - \left( \frac{K_1}{A_r} \right) M_r(t) \dots\dots\dots 2.10$$

The time functions of  $M_s(t)$  and  $M_r(t)$  can assume negative values for certain combinations of initial conditions and values for the constant B. Such values are inadmissible from physical considerations and care must be taken to avoid such circumstances. This matter is considered further in section 2.3.

The decay time constant,  $\lambda_s$ , of tank  $T_s$  (or compartment  $C_s$ ) and recovery time constant,  $\lambda_r$ , of tank  $T_r$  (or compartment  $C_r$ ) play an important role in the simulation study.

In terms of the hydraulic analog, these parameters are defined as:

$$\lambda_s = \frac{A_s}{4K_2} \dots\dots\dots 2.11$$

$$\lambda_r = \frac{A_r}{K_1} \dots\dots\dots 2.12$$

### 2.1.2 REINITIALIZATION AT PULSE TIMES

The calcium concentration in the  $C_s$  compartment, after the occurrence of a pulse is comprised of three components; namely,

- (i) The amount of calcium in the  $C_s$  compartment at the time of the pulse.
- (ii) The amount of calcium obtained from the external fluid bath due to a gating phenomenon caused by the electrical stimulus.
- (iii) The amount of calcium fed back from the  $C_r$  compartment to the  $C_s$  compartment.

As noted earlier, at the pulse time, the  $C_r$  compartment empties and its calcium content causes the muscle contraction. However, as noted in iii) above, a portion of this calcium is retained in the system and is passed back to the  $C_s$  compartment as a feed-back effect.

After the occurrence of a pulse, the calcium contained in the  $C_s$  compartment (denoted by  $Ca_s^+$ ) can be written as:

$$Ca_s^+ = Ca_s(t_p) + Q_c + \beta Ca_r(t_p) \dots\dots\dots 2.13$$

- where
- i)  $t_p$  denotes the time at which pulse occurs,
  - ii)  $\beta$  denotes the feed-back factor,
  - iii)  $Q_c$  represents the calcium gated from the surrounding solution (outside calcium).

Experimental evidence suggests that the component  $Q_c$  depends on the stimulation frequency  $f$  and the outside calcium

concentration  $[Ca_0]$ . Very little can, however, be said about the specific nature of this functional dependency. During preliminary simulation experiments with the model a variety of relationships were considered and on the basis of the results obtained the following form was selected:

$$Q_c = C_1(f) \cdot C_2([Ca_0])$$

with

$$C_1(f) = Q_1(1 - e^{-b_1/f})$$

and

$$C_2([Ca_0]) = (1 - e^{-b_2[Ca_0]})$$

The above effects at the instant of the stimulation pulse are incorporated into the hydraulic analog by forcing a periodic re-initialization of the describing differential equations (namely equations 2.9 and 2.10). The time interval between the re-initialization is equal to the stimulation pulse period. Equations 2.9 and 2.10 are therefore considered to be relevant only in interval,  $[t_p^j, t_p^{j+\Delta})$ , where  $\Delta$  is the interpulse interval (secs.) and  $t_p^j$  is the time of occurrence of  $j^{th}$  pulse. The "initial" conditions which apply at the beginning of each such interval are determined in part by the conditions existing at the end of preceding interval, specifically

$$M_s(t_p^j) = \alpha_1 = M_s(t_p^{j-1} + \Delta) + Q_h + \beta M_r(t_p^{j-1} + \Delta) \dots\dots\dots 2.14$$

$$M_r(t_p^j) = \alpha_2 = 0 \dots\dots\dots 2.15$$

where  $Q_h$  corresponds to the gating effect and is taken as:

$$Q_h = 0.1(1 - e^{-120/f})(1 - e^{-\epsilon h_0}) \dots\dots\dots 2.16$$

where  $\epsilon$ , the exponent factor, is in the range [0.1, 0.3], and  $f$  is the stimulation frequency (pulses/min.).

## 2.2 CONDITIONS FOR DYNAMIC EQUILIBRIUM

### 2.2.1 DYNAMIC EQUILIBRIUM

The volumes  $M_s$  and  $M_r$  assume a periodic behaviour after passing through an initial transient phase when the hydraulic analog of the papillary muscle system is re-initialized at constant time intervals. Once a periodic mode has been attained (the time trajectories of  $M_s$  and  $M_r$  are invariant from cycle to cycle), the system is said to be in dynamic equilibrium.

Referring to Figure 2.1, the system is said to be in dynamic equilibrium if  $S_1 = S_2$  and consequently  $R_1 = R_2$ .

The experimental data available (Figure 1.2) correspond to this periodic mode, i.e., dynamic equilibrium. Because of this, a comparison of the model behaviour with the available data requires that the model be forced into a mode of dynamic equilibrium. A convenient method for achieving this is therefore imperative. This matter is considered in the following section.

### 2.2.2 MATHEMATICAL ANALYSIS FOR DYNAMIC EQUILIBRIUM

When the system is started from an arbitrary initial condition, the volumes  $M_s$  and  $M_r$  assume a periodic behaviour after passing through an initial transient phase. As the initial transient mode is not of interest, computing time, which is of major consideration, can be minimized by establishing a set of initial conditions for the system equations 2.9 and 2.10 which ensures that the system will attain periodic behaviour immediately without passing through this initial transient phase. The initial conditions for dynamic equilibrium are determined as follows: The equations 2.9 and 2.10 describing the system behaviour of the hydraulic analog of the basic Mainwood-Lee model, during the interpulse interval can be expressed in the standard form of a system of linear, first order differential equation; namely,

$$\dot{x}(t) = Ax(t) + b \dots\dots\dots 2.17$$

where

$$A = \begin{bmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{bmatrix} \quad \text{and} \quad b = \begin{bmatrix} b_1 \\ b_2 \end{bmatrix}$$

and

$$a_{11} = -\left(\frac{K_1 + 5K_2}{A_s}\right)$$

$$a_{12} = K_1/A_r$$

$$a_{21} = K_1/A_s$$

$$a_{22} = -K_1/A_r$$

$$b_1 = K_2 h_0 - B$$

$$b_2 = 0$$

In this representation  $x_1(t)$  and  $x_2(t)$  correspond to  $M_{Sc}(t)$  and  $M_r(t)$  respectively.

The general solution of the system described in 2.17 can be written as:

$$x(t) = e^{At} x(t_p^{j-1}) + r(t) \dots\dots\dots 2.18$$

where:

$$r(t) = \int_{t_p^{j-1}}^t e^{A(t-\tau)} b d\tau = \begin{bmatrix} r_1(t) \\ r_2(t) \end{bmatrix}$$

and  $t_p^{j-1}$  denotes the time of occurrence of the  $(j-1)^{th}$  pulse. For convenience, denote  $e^{At}$  for the present case where  $A$  is  $2 \times 2$ , by:

$$E(t) = \begin{bmatrix} E_{11}(t) & E_{12}(t) \\ E_{21}(t) & E_{22}(t) \end{bmatrix}$$

Let the initial condition of the system equations after the occurrence of the pulse at time  $t_p^{j-1}$  be  $x_1(t_p^{j-1}) = \alpha_1$  and  $x_2(t_p^{j-1}) = \alpha_2 = 0$ . The responses for  $x_1(t)$  and  $x_2(t)$  for  $t > t_p^{j-1}$  follow from equation 2.18 as:

$$x_1(t) = E_{11}(t)\alpha_1 + r_1(t) \dots\dots\dots 2.19$$

$$x_2(t) = E_{21}(t)\alpha_1 + r_2(t) \dots\dots\dots 2.20$$

As a result of the pulse occurring at time  $t_p^j$ , the initial conditions for the subsequent interpulse interval as given by equations 2.14 and 2.15 are:

$$\alpha_1 = x_1(t_p^{j-1+\Delta}) + Q_h + \delta x_2(t_p^{j-1+\Delta}) \dots\dots\dots 2.21$$

$$\alpha_2 = 0 \dots\dots\dots 2.22$$

Substituting 2.19 and 2.20, ( $\bar{t} = t_p^{j-1+\Delta}$ ), we obtain:

$$\alpha_1 = E_{11}(t_p^{j-1+\Delta})\alpha_1 + r_1(t_p^{j-1+\Delta}) + Q_h + \beta[E_{21}(t_p^{j-1+\Delta})\alpha_1 + r_2(t_p^{j-1+\Delta})] \dots\dots\dots 2.23$$

In order that the dynamic equilibrium conditions exist, it is necessary that  $\alpha_1 = \alpha_1$ . Hence equation 2.23 yields the required condition that

$$\alpha_1 = \frac{Q_h + r_1(t_p^{j-1+\Delta}) + \beta r_2(t_p^{j-1+\Delta})}{1 - E_{11}(t_p^{j-1+\Delta}) - \beta E_{21}(t_p^{j-1+\Delta})} \dots\dots\dots 2.24$$

Since each of the three terms in the numerator of the rational expression on the right hand side of equation 2.24 are well-defined, it follows that  $\alpha_1$  exists as long as the denominator,  $1 - E_{11}(t_p^{j-1+\Delta}) - \beta E_{21}(t_p^{j-1+\Delta})$ , is not zero.

### 2.3 GENERATION OF THE ANALOG OF TENSION

In view of correspondence between the basic Mainwood-Lee model and its hydraulic analog (see Table I), the relationship given by equation 1.1 can be written as:

$$T_f = \frac{Kh_0^2}{1+Kh_0^2} \dots\dots\dots 2.25$$

where  $K = 0.45$

In the above equation, the normalized tension,  $T_f$ , corresponds to the situation where there is a long duration between the pulses; that is, the interpulse interval is sufficiently long so that steady state conditions are attained. The steady state values implied by equations 2.1, 2.2 and 2.4 are:

$$\bar{h}_r = \bar{h}_s = \left(\frac{K_2}{K_2+K_3}\right)h_0 - \frac{B}{K_2+K_3} \dots\dots\dots 2.26$$

where, as before, the bar superscript is used to imply steady state conditions. Since physical considerations require that  $\bar{h}_s \geq 0$ , it follows that equation 2.32 implies the constraint that  $K_2h_0 - B \geq 0$  (assuming that  $K_2$  and  $K_3$  are positive).

The steady state model of the system given in Figure 2.2 suggests that the problem is to find the form of the function  $G = G(\bar{M}_r, B)$  in order that equation 2.25 is satisfied.

As a candidate for  $G$  choose:

$$G(\bar{M}_r, B) = \frac{K(a\bar{M}_r + B/K_2)^2}{1+K(a\bar{M}_r + B/K_2)^2} \dots\dots\dots 2.27$$

$$\text{with } a = \frac{K_2 + K_3}{A_r K_2}$$

Substitution of  $\bar{M}_r = A_r \bar{h}_r$  and equation 2.26 then yields the result that

$$T_f = G(\bar{M}_r, B) = \frac{Kh_0^2}{1 + Kh_0^2}$$

which has the desired form.

Having obtained the function  $G$  using known information pertinent to the special case of long interpulse interval, the function  $G$  will continue to be used for arbitrary interpulse intervals and will thus serve as the mechanism for generating  $T_f$  or rather its fictitious hydraulic analog.

## 2.4 COMPUTATIONAL APPROACH AND RESULTS

### 2.4.1 A COMMENT ON THE COMPUTATIONAL PROCEDURE

The quantities  $E_{11}(t_p^{j-1} + \Delta)$ ,  $E_{21}(t_p^{j-1} + \Delta)$  needed in equation 2.24 are obtained as the solutions  $x_1(\Delta)$  and  $x_2(\Delta)$  of the system equations when  $x_1(0) = 1$  and  $x_2(0) = b_1 = b_2 = 0$ . The quantities  $r_1(t_p^{j-1} + \Delta)$  and  $r_2(t_p^{j-1} + \Delta)$  needed in equation 2.24 are obtained as the solutions  $x_1(\Delta)$  and  $x_2(\Delta)$  of the system equation when  $x_1(0) = x_2(0) = b_2 = 0$  and  $b_1 = K_2 h_0 - B$ .

### 2.4.2 COMPUTATIONAL RESULTS

The following computational experiments were performed:

- (i) Effect of frequency of stimulation (increasing in steps from 1 pulse/min. to 180 pulses/min.) on the dynamic equilibrium values of  $M_r$ , and  $M_s$  volumes.
- (ii) Effect of following parameters on the Omega response:
- Recovery time constant,  $\lambda_r$
  - Decay time constant,  $\lambda_s$
  - Variation in  $h_0$  levels, ( $[Ca_0]$ )
  - Exponent factor,  $\epsilon$
  - Feed-back factor,  $\beta$ .

Table 2.1 shows the range of various parameters.

The values of interest are based on data suggested by experiments carried out with real papillary muscle of a rat.

The areas of cross-section,  $A_s$  and  $A_r$ , are taken as 1. and 0.08 respectively.

The time trajectories of  $M_r(t)$  and  $M_s(t)$  at dynamic equilibrium over a typical interpulse interval are shown in Figures 2.3 and 2.4. The value of  $M_r(t)$  starts from zero at the beginning of the interpulse interval and reaches its maximum rapidly (3 seconds for  $h_0 = 4$ ). It then decreases gradually with increasing time. The value of  $M_s(t)$  starts from its peak value at the beginning of interpulse interval and decreases with increasing time.

Omega responses for the hydraulic analog of the basic Mainwood-Lee model are shown in Figures 2.5 through 2.9.

In general, they are characterized by an increase of

tension at low frequencies of stimulation (peak occurrence at about 40-80 pulses/min.), followed by a decrease of tension at high frequencies of stimulation.

The stimulation frequency at which the peak of tension occurs, shifts towards the high frequency range if:

(i) Fluid level,  $h_0$ , is decreased (Figure 2.5)

or

(ii) Recovery time constant,  $\lambda_r$ , is decreased (Figure 2.6)

or

(iii) Feed-back factor,  $\beta$ , is increased (Figure 2.8)

The peak amplitude of tension decreases if:

(i) Fluid level  $h_0$ , is decreased (Figure 2.5)

or

(ii) Recovery time constant,  $\lambda_r$ , is increased (Figure 2.6)

or

(iii) Decay time constant,  $\lambda_s$ , is decreased (Figure 2.7)

or

(iv) Feed-back factor,  $\beta$ , is decreased (Figure 2.8)

or

(v) Exponent factor,  $\epsilon$ , is decreased (Figure 2.9)

From the Omega responses shown in Figures 2.5 through 2.9 it is clear that the behaviour of the basic Mainwood-Lee model is not in particularly close agreement with the reference experimental data shown in Figure 1.2. Re-examination and modification of this model therefore in order. This matter is considered in the following Chapter 3.

Parameter	Parameter value		Comments
	Minimum	Maximum	
$\beta$	0.3	0.95	
$\lambda_R$	0.2 seconds	1.0 seconds	
$\lambda_S$	20 seconds	30 seconds	
$\dot{f}$	1 pulse/ min.	180 pulses/ min.	
$h_0$	1 meter	10 meters	only four values of $h_0$ (i.e. 1, 2, 4, 10) are considered corresponding to calcium concentrations of $0.25 \times 10^{-6}$ , $0.5 \times 10^{-6}$ , $1.0 \times 10^{-6}$ , $2.5 \times 10^{-6}$ Mols./millilitre

TABLE 2.1

Ranges Considered for Various Parameters

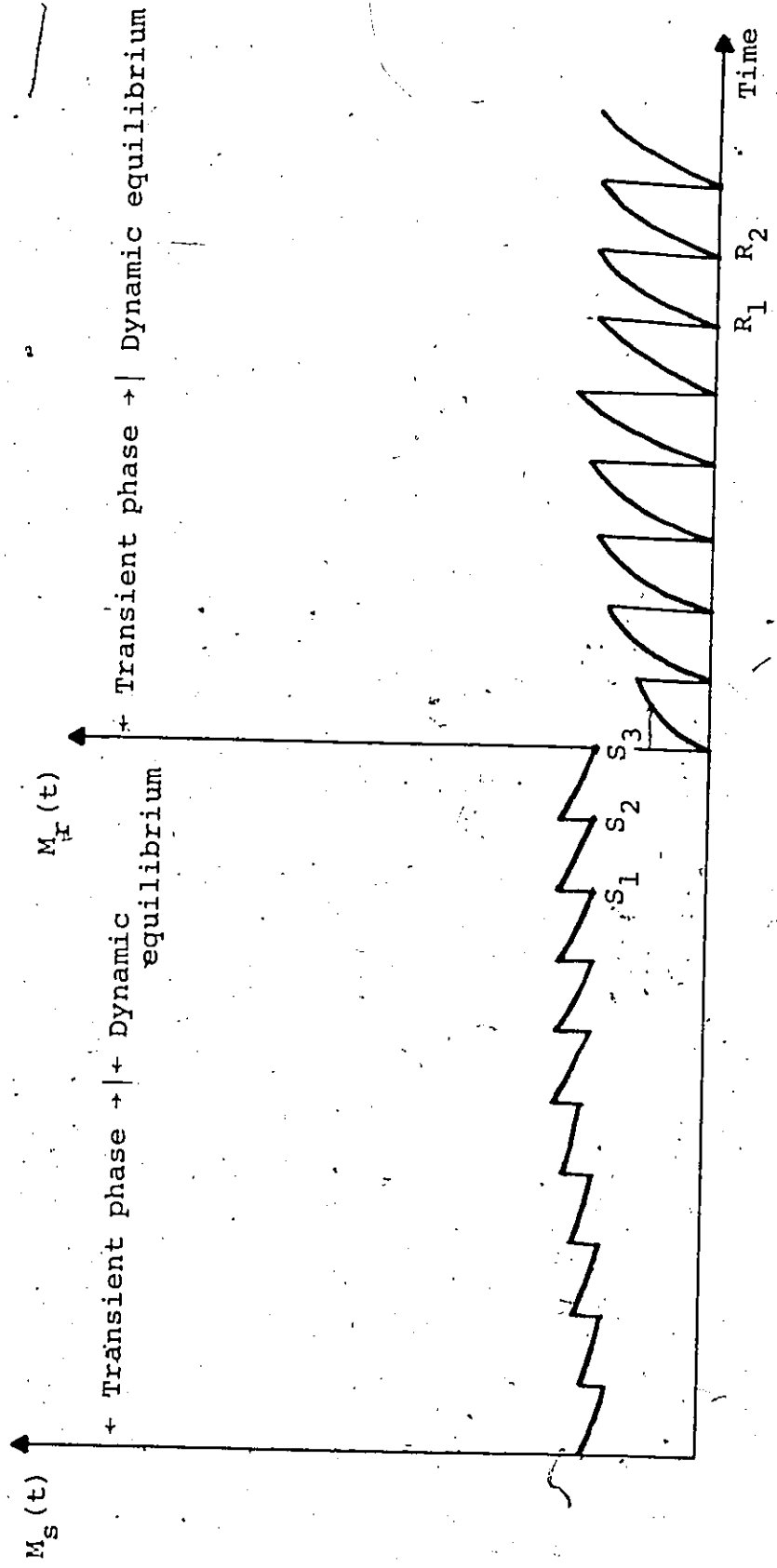


Figure 2.1

Time Responses of  $M_S$  and  $M_I$  Volumes.

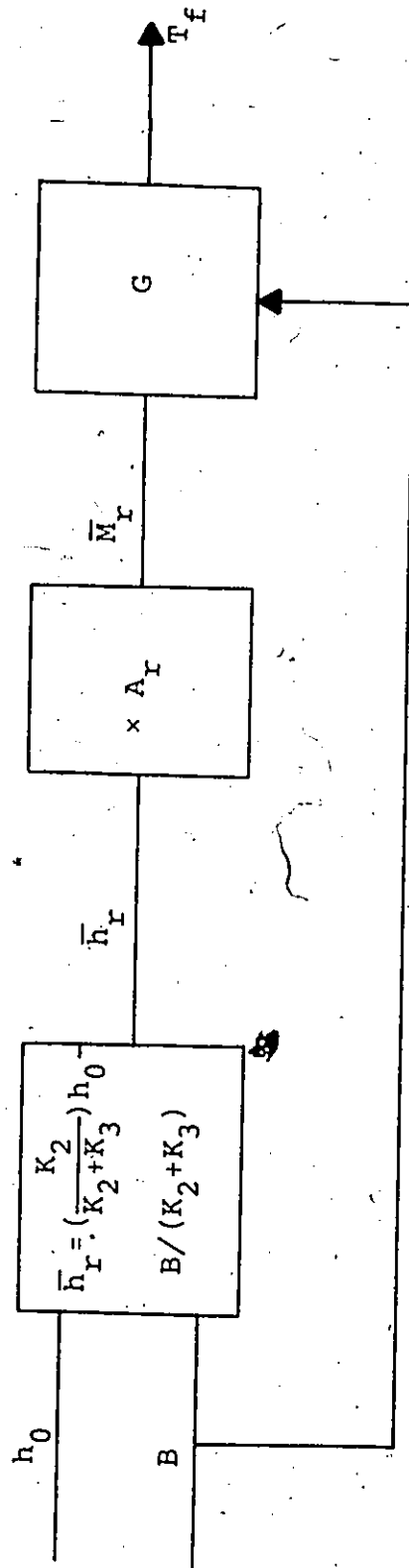


Figure 2.2

Steady State Model of the System Under Consideration.

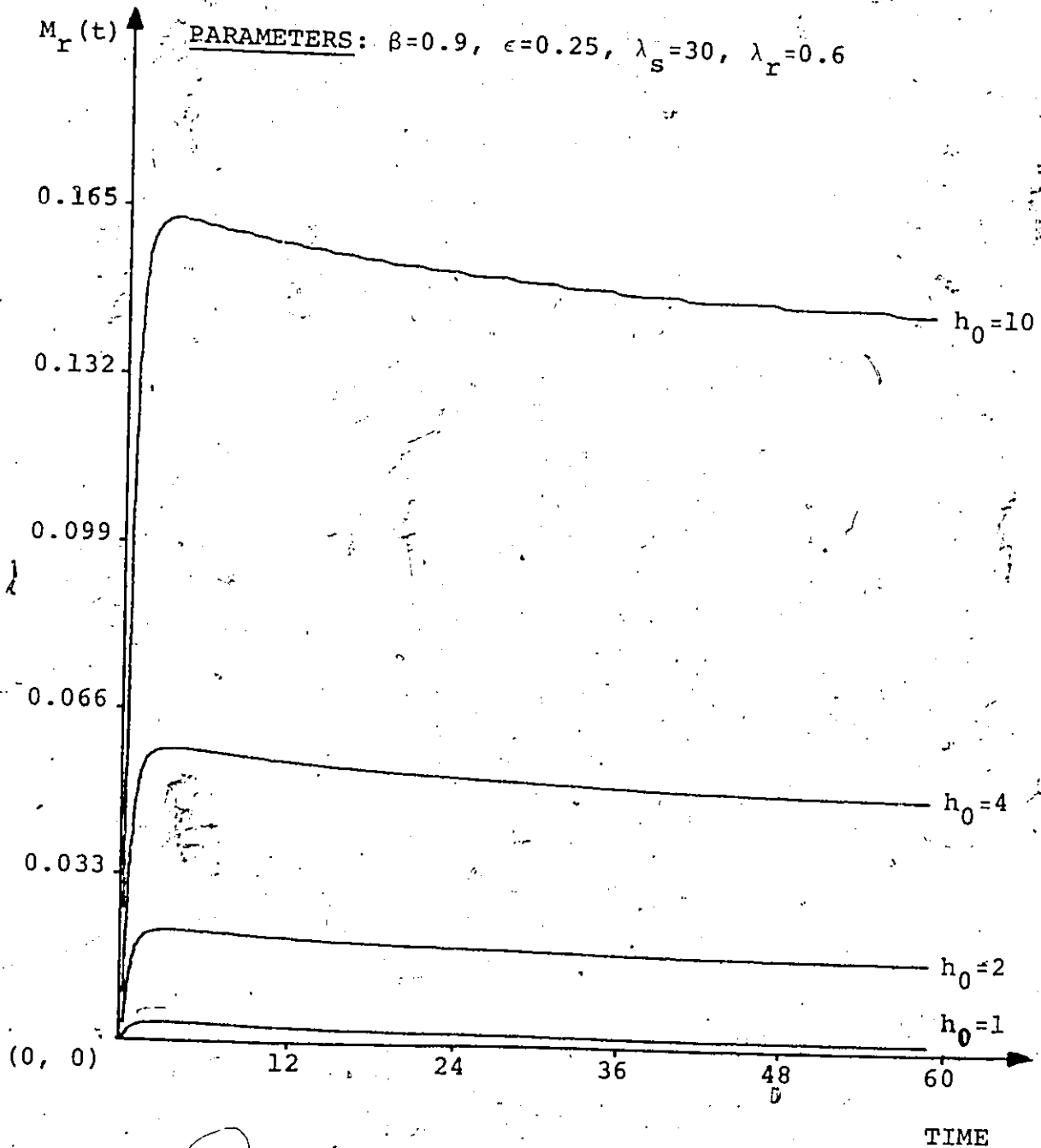


Figure 2.3

Time Trajectories of  $M_r(t)$  for Various  $h_0$  Levels  
 (Initial Conditions Are those for Dynamic  
 Equilibrium when  $\Delta=60$  secs.)

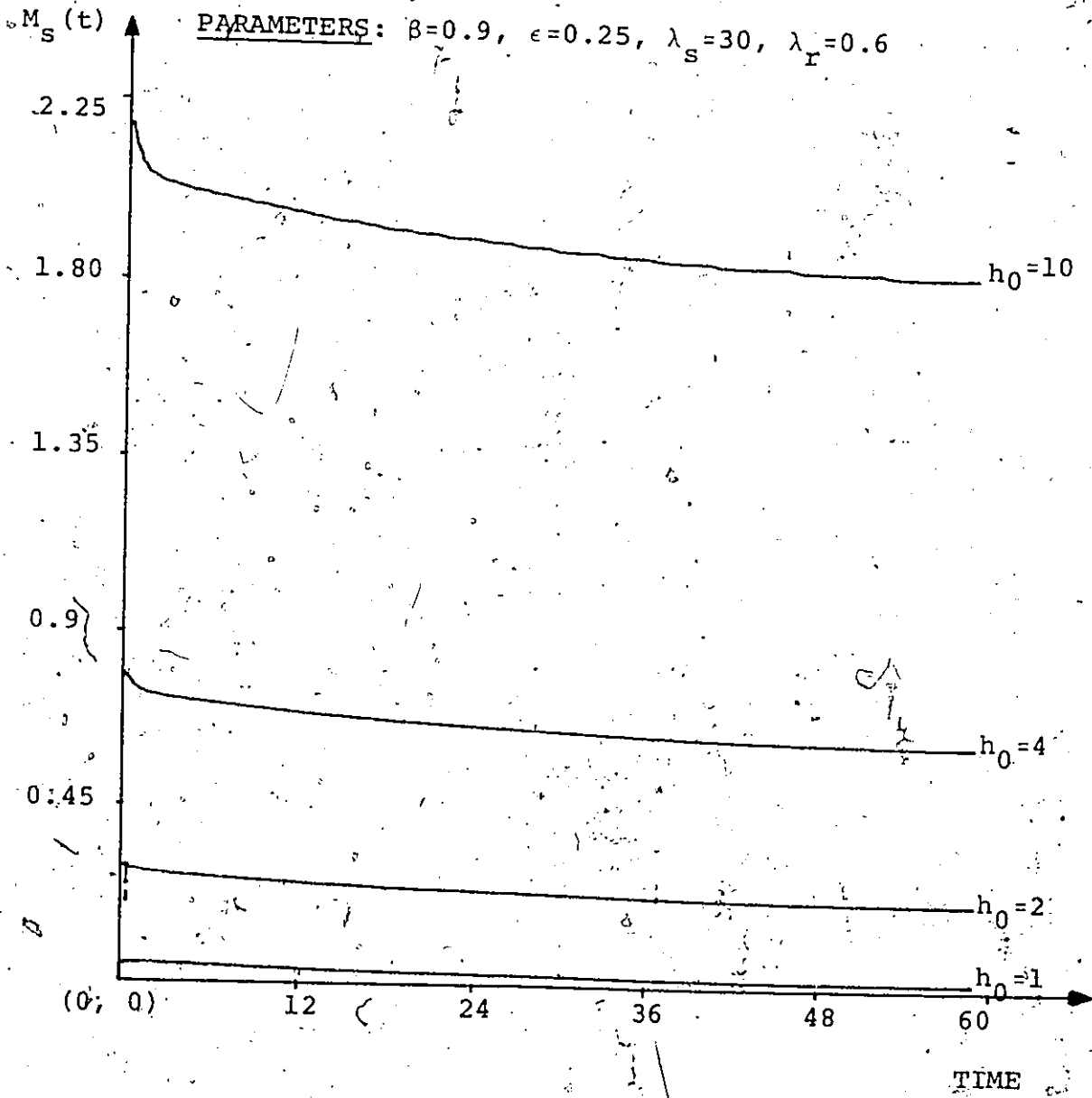


Figure 2.4

Time Trajectories of  $M_s(t)$  for Various  $h_0$  Levels.  
(Initial Conditions are those for Dynamic Equilibrium  
when  $\Delta=60$  seconds)

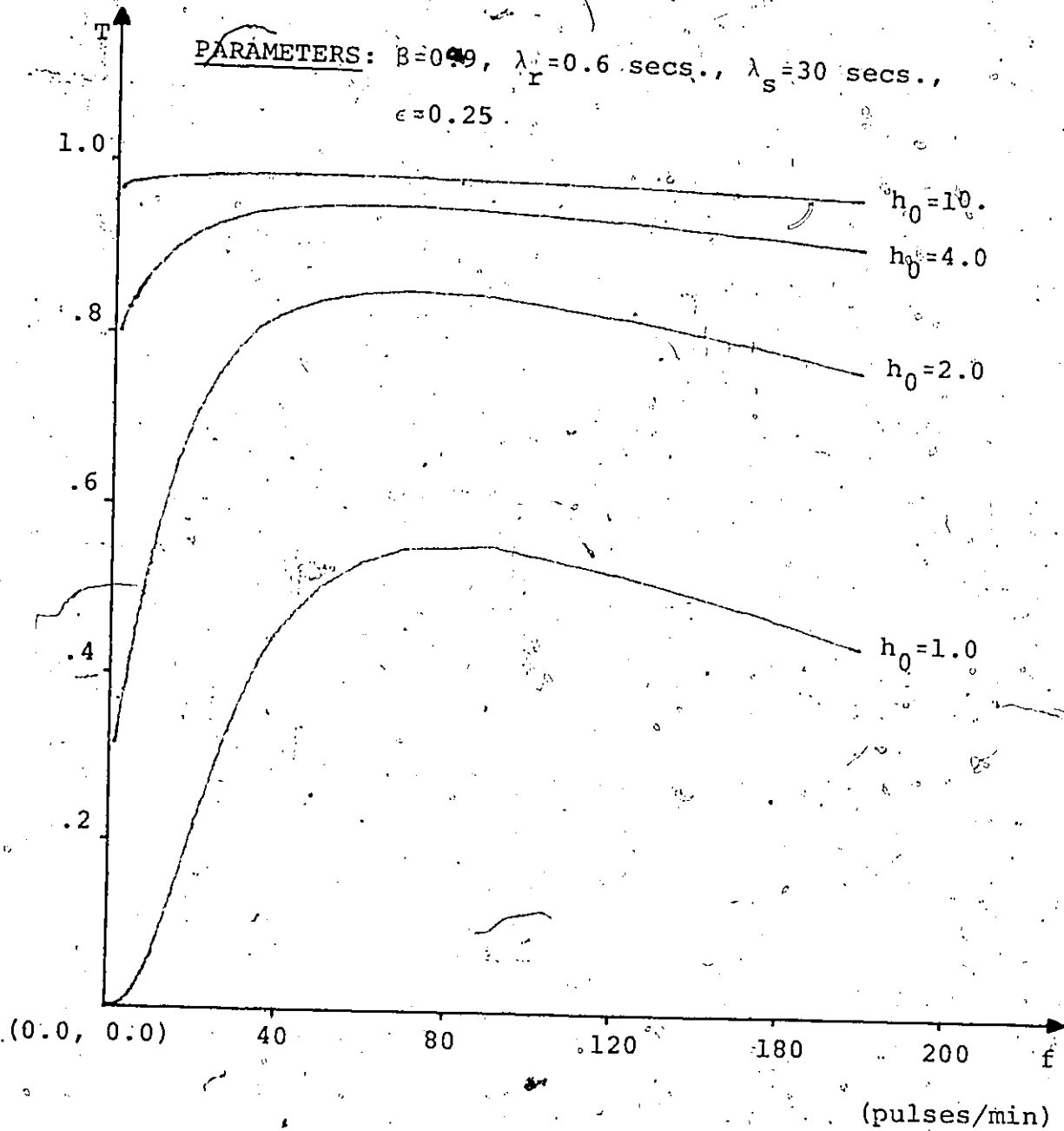


Figure 2.5

Omega Responses for Various Values of  $h_0$

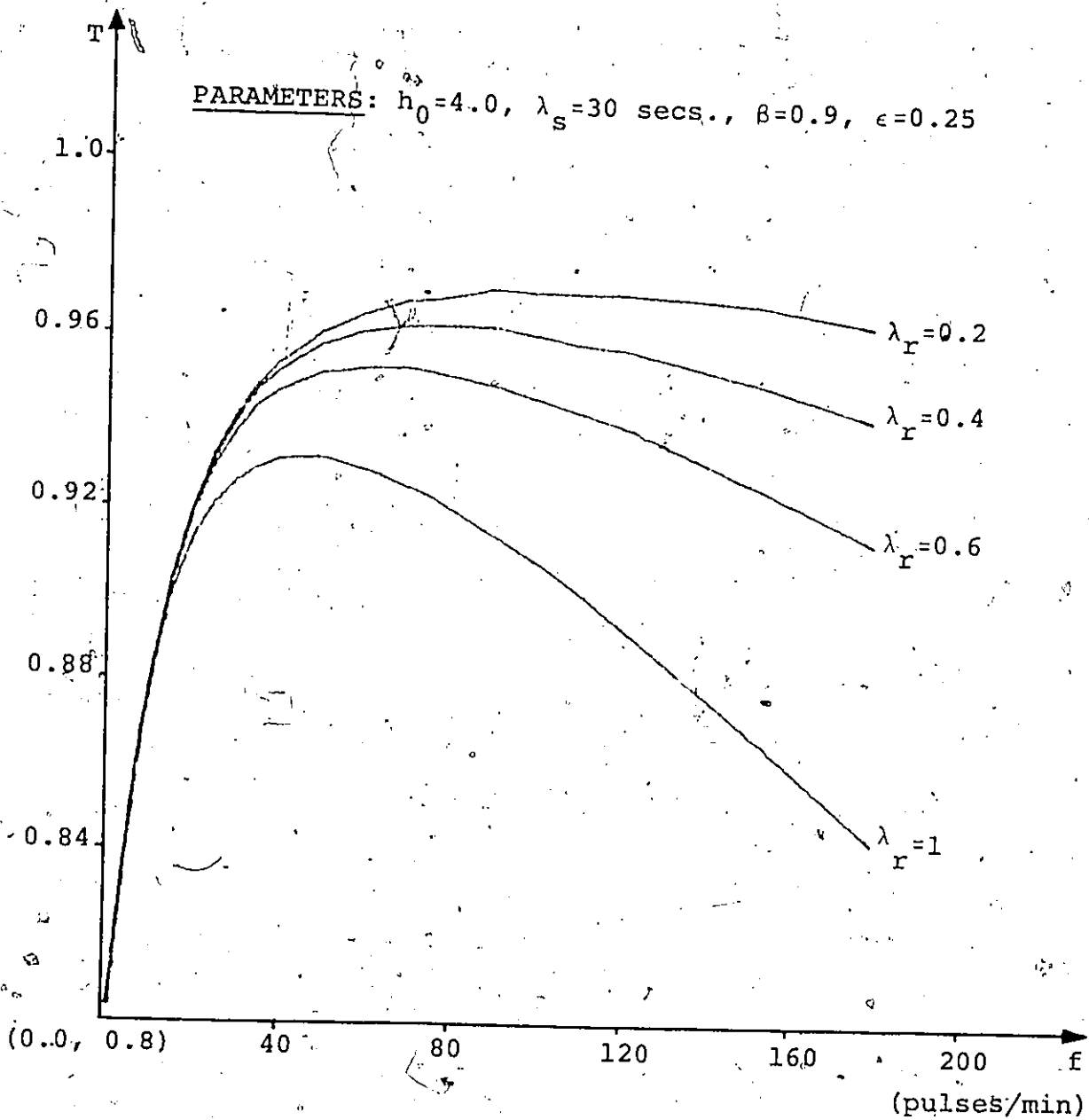


Figure 2.6

Omega Responses for Various Values of Recovery Time Constant,  $\lambda_r$ .

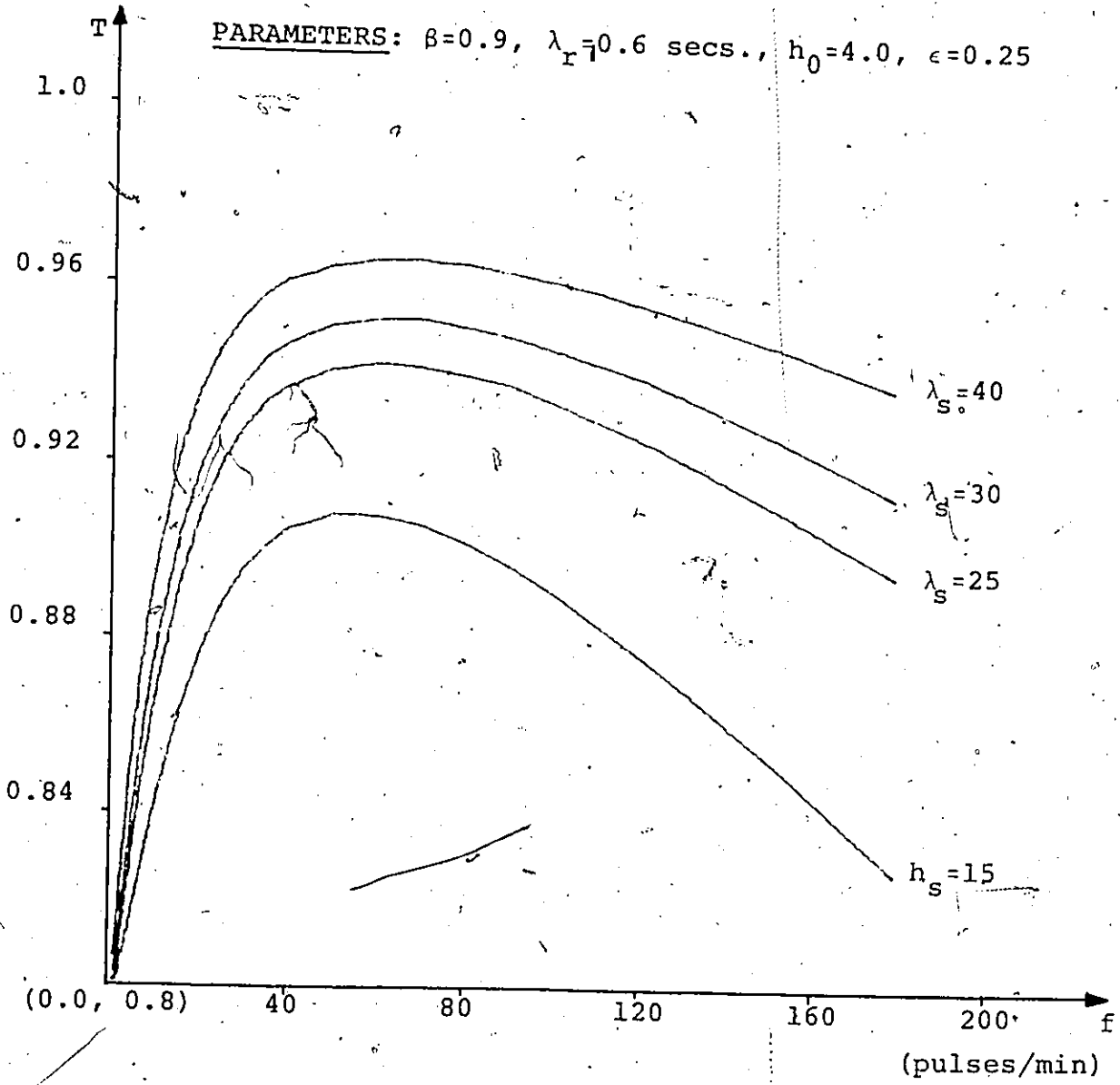


Figure 2.7

Omega Responses for Various Values of Decay Time Constant,  $\lambda_s$ .

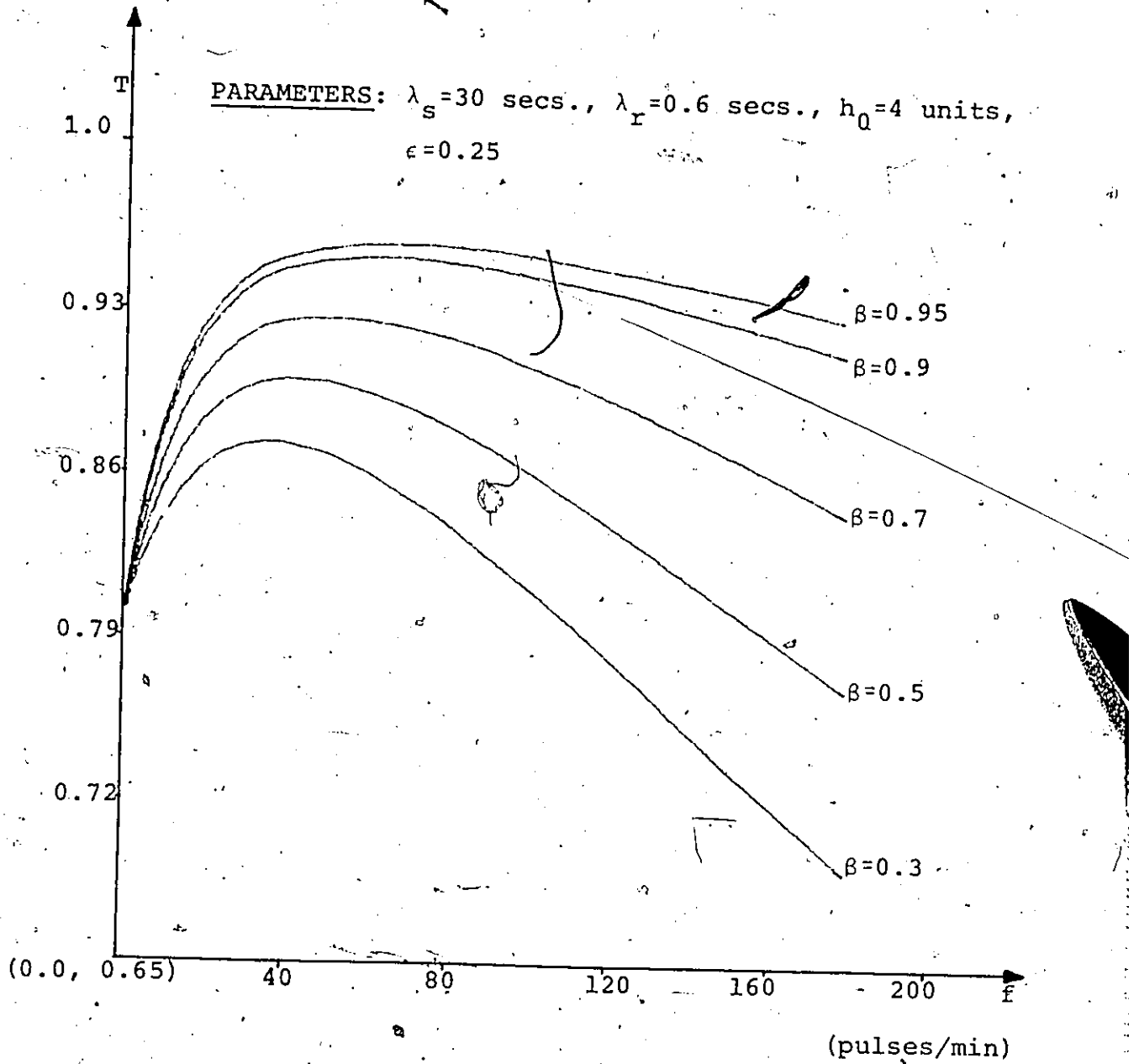


Figure 2.8

Omega Responses for Various Values of  
Feed-back Factor,  $\beta$ .

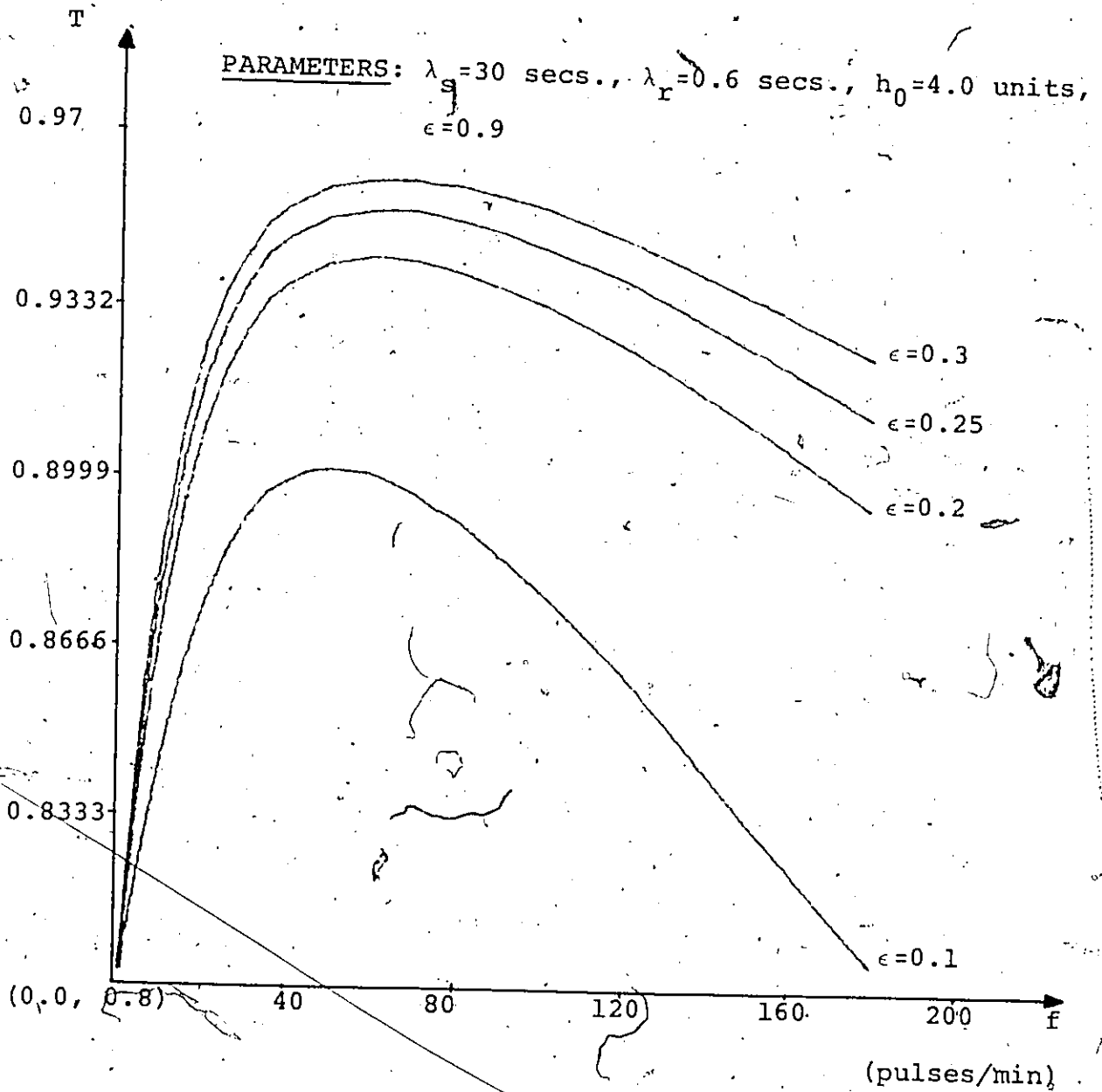


Figure 2.9

Omega Responses for Various Values of  
 Exponent Factor,  $\epsilon$ .

CHAPTER 3

MODIFICATIONS OF BASIC MAINWOOD-LEE MODEL

### 3.1 INTRODUCTION

As it can be noted from Figures 2.5-2.9, the Omega responses for the basic Mainwood-Lee model differ substantially from the given experimental data. On the basis of these results, one can conclude that the basic Mainwood-Lee model is inadequate and modification of this model is required.

The modification of the model in order to obtain better Omega response agreement was guided by the nature of deviation between the given data and the model responses. Various modifications were attempted and although improved Omega response agreement was often achieved, some difficulties in justifying the model from a physiological point of view were encountered. Continued efforts, however, finally led to the 'dual subsystem model' described in this chapter. The Omega responses for this model are satisfactory and its physiological basis is also acceptable.

### 3.2 THE DUAL SUBSYSTEM MODEL

As its name suggests, this model is comprised of two subsystems operating in parallel as shown in Figure 3.1.

Its components can be described as follows:

#### (i) Subsystems 1:

This subsystem is comprised of compartments  $C_{s_1}$  and  $C_{r_1}$  and can be viewed as being a direct counterpart of the basic Mainwood-Lee model.

(ii) Subsystem 2:

This subsystem is comprised of compartments  $C_{s_2}$  and  $C_{r_2}$ . It has a similar structure to that of subsystem 1 but differs in the following respects:

- (a) There is no feed-back flow from the  $C_{r_2}$  compartment to the  $C_{s_2}$  compartment.
- (b) There is assumed to be no gating effect to cause a flow of calcium from the external fluid bath to the  $C_{s_2}$  compartment.

The subsystem 1 and the subsystem 2 of the model respectively are often referred to as the 'fast filling subsystem' and the 'slow filling subsystem' because of their relative time constants.

The overall dual subsystem model can be viewed as having three compartments; namely:

- (i) The  $C_{s_1}$  compartment, which contains the stored calcium,  $Ca_{s_1}$ .
- (ii) The  $C_{s_2}$  compartment, which contains the stored calcium,  $Ca_{s_2}$ .
- (iii) The  $C_r$  compartment containing the releasable calcium,  $Ca_r$ , is comprised of the two compartments,  $C_{r_1}$  which contains the releasable calcium,  $Ca_{r_1}$ , and  $C_{r_2}$  which contains the releasable calcium,  $Ca_{r_2}$ .

The flow among the various compartments is similar to the description given in section 1.4 and the feed-back flow is from the  $C_r$  compartment to the  $C_{s_1}$  compartment.

At the instant of an electrical stimulus, the calcium in the  $C_r$  compartment (the total of the calcium in the  $C_{r_1}$  and the  $C_{r_2}$  compartments) generates the muscle contraction and a portion of this calcium is transferred to the  $C_{s_1}$  compartment via the feed-back flow,  $F_2$ .

### 3.3 HYDRAULIC ANALOG OF THE DUAL SUBSYSTEM MODEL

In order to study the dynamic behaviour of the dual subsystem model and the correspondence between the characteristics of this model and relevant characteristics of the real papillary muscle system, a hydraulic analog of the dual subsystem model is formulated (see Figure 3.2). As before, this hydraulic analog is intended to represent the model behaviour only during the interpulse interval.

The tank  $T_0$  represents the external fluid bath. The tanks  $T_{s_1}$  and  $T_{r_1}$  constitute the fast filling subsystem and represent the compartments  $C_{s_1}$  and  $C_{r_1}$  respectively.

The tanks  $T_{s_2}$  and  $T_{r_2}$  constitute the slow filling subsystem and represent the compartments  $C_{s_2}$  and  $C_{r_2}$  respectively.

The volume, cross-sectional area, and the fluid levels of tank  $T_\Lambda$  are represented by  $M_\Lambda$ ,  $A_\Lambda$ , and  $h_\Lambda$  respectively, (where  $\Lambda$  can have the value  $s_1$ ,  $s_2$ ,  $r_1$ , and

$r_2$ ). This hydraulic analog of the dual subsystem model incorporates the following assumptions:

- (i) All the tanks have constant cross-sectional area.
- (ii) The volume of the tank  $T_0$  is substantially larger than the volume of the other tanks and on this basis, it is assumed that the height of fluid in the tank  $T_0$  never really changes during the period of investigation, i.e.  $h_0 = \text{constant}$ .

The pumps P and P' force the transfer of fluid from the tank  $T_{s_1}$  to the tank  $T_0$  and from the tank  $T_{s_2}$  to the tank  $T_0$  respectively. Note that the flow rate through the pump P' does not have a constant component.

### 3.4 MATHEMATICAL MODEL OF THE DUAL SUBSYSTEM MODEL

The fluid levels in the various tanks are determined by the flow rates through the pumps and the flow rate constants among the reservoirs. A mathematical model describing the behaviour of the dual subsystem model both during the interpulse interval and at the pulse time is given in the following sections.

#### 3.4.1 INTERPULSE INTERVAL

An analysis of the hydraulic configuration shown in Figure 3.2 using arguments analogous to those used in Chapter 2, yields the following equations for the rate of change of the fluid volume in the tanks  $T_{s_1}$ ,  $T_{r_1}$ ,  $T_{s_2}$ ,

and  $T_{r_2}$ :

$$\frac{dM_{s_1}(t)}{dt} = -(K_1 + K_2 + K_3) \frac{M_{s_1}(t)}{A_{s_1}} + K_1 \frac{M_{r_1}(t)}{A_{r_1}} + K_2 h_0^{-B} \dots 3.1.a$$

$$\frac{dM_{r_1}(t)}{dt} = K_1 \frac{M_{s_1}(t)}{A_{s_1}} - K_1 \frac{M_{r_1}(t)}{A_{r_1}} \dots 3.1.b$$

$$\frac{dM_{s_2}(t)}{dt} = -(K'_1 + K'_2 + K'_3) \frac{M_{s_2}(t)}{A_{s_2}} + K'_1 \frac{M_{r_2}(t)}{A_{r_2}} + K'_2 h_0 \dots 3.1.c$$

$$\frac{dM_{r_2}(t)}{dt} = K'_1 \frac{M_{s_2}(t)}{A_{s_2}} - K'_1 \frac{M_{r_2}(t)}{A_{r_2}} \dots 3.1.d$$

As in the earlier analysis, the model must satisfy certain steady state conditions consistent with physiological considerations. In the context of the dual subsystem model, these are taken to have the following form:

$$\bar{h}_{s_1} = \bar{h}_{r_1} \dots 3.2.a$$

$$\bar{h}_{s_2} = \bar{h}_{r_2} \dots 3.2.b$$

$$\bar{h}_0 = 5\bar{h}_{s_1} = 5\bar{h}_{s_2} \dots 3.2.c$$

where, as before, the bar superscript is used to denote a steady state value.

The steady state relations of equation 3.2 are directly satisfied by equations 3.1.b and 3.1.d. However, when imposed on equations 3.1.a (with  $B = 0$ ) and 3.1.c, the following steady state constraints result:

$$h_0 = \left(\frac{K_2+K_3}{K_2}\right) \bar{h}_{s_1} = \left(\frac{K_2+K_3}{K_2}\right) \bar{h}_{s_2} \dots\dots\dots 3.3$$

Equation 3.3 indicates that the required steady state conditions are satisfied under the following circumstances

$$K_3 = 4K_2 \dots\dots\dots 3.4.a$$

$$K_3 = 4K_2' \dots\dots\dots 3.4.b$$

Incorporation of these constraints into the system equation 3.1 yields:

$$\frac{dM_{s_1}(t)}{dt} = -\left(\frac{K_1+5K_2}{A_{s_1}}\right) M_{s_1}(t) + \left(\frac{K_1}{A_{r_1}}\right) M_{r_1}(t) + K_2 h_0 - B \quad 3.5.a$$

$$\frac{dM_{r_1}(t)}{dt} = \left(\frac{K_1}{A_{s_1}}\right) M_{s_1}(t) - \left(\frac{K_1}{A_{r_1}}\right) M_{r_1}(t) \dots\dots\dots 3.5.b$$

$$\frac{dM_{s_2}(t)}{dt} = -\left(\frac{K_1+5K_2}{A_{s_2}}\right) M_{s_2}(t) + \left(\frac{K_1}{A_{r_2}}\right) M_{r_2}(t) + K_2' h_0 \dots\dots 3.5.c$$

$$\frac{dM_{r_2}(t)}{dt} = \left(\frac{K_1}{A_{s_2}}\right) M_{s_2}(t) - \left(\frac{K_1}{A_{r_2}}\right) M_{r_2}(t) \dots\dots\dots 3.5.d$$

Using similar arguments to those given in section 2.3, it can be shown that a necessary condition for the time functions

$M_{s_1}(t)$  and  $M_{r_1}(t)$  not to assume negative values is that:

$$B \leq K_2 h_0$$

The decay time constants,  $\lambda_{s_1}$  and  $\lambda_{s_2}$ , of tanks  $T_{s_1}$  (compartment  $C_{s_1}$ ) and  $T_{s_2}$  (compartment  $C_{s_2}$ ) and the

recovery time constants,  $\lambda_{r_1}$  and  $\lambda_{r_2}$ , of the tanks  $T_{r_1}$  (compartment  $C_{r_1}$ ) and  $T_{r_2}$  (compartment  $C_{r_2}$ ), play an important role in the simulation study. In terms of the hydraulic analog, these parameters are defined as:

$$\lambda_{s_1} = \frac{A_{s_1}}{4K_2} \dots\dots\dots 3.6.a$$

$$\lambda_{s_2} = \frac{A_{s_2}}{4K_2} \dots\dots\dots 3.6.b$$

$$\lambda_{r_1} = \frac{A_{r_1}}{K_1} \dots\dots\dots 3.6.c$$

$$\lambda_{r_2} = \frac{A_{r_2}}{K_1} \dots\dots\dots 3.6.d$$

The time constants associated with the fast filling component,  $\lambda_{s_1}$  and  $\lambda_{r_1}$ , are much smaller than their counterparts associated with the slow filling component, i.e.

$$\lambda_{s_1} < \lambda_{s_2} \text{ and } \lambda_{r_1} < \lambda_{r_2}$$

#### 3.4.2 REINITIALIZATION AT PULSE TIMES

The calcium concentration in the  $C_{s_1}$  compartment, after the occurrence of a pulse, is comprised of three components; namely,

- (i) The amount of calcium in the  $C_{s_1}$  compartment at the time of the pulse.
- (ii) The amount of calcium obtained from the external

fluid bath due to the gating phenomenon caused by the electrical stimulus.

- (iii) The amount of calcium fed back from the  $C_R$  compartment to the  $C_{S_1}$  compartment.

As noted earlier, at the pulse times, the  $C_R$  compartment empties and its calcium content causes the muscle contraction. However, as noted in (iii) above, a portion of this calcium is retained in the system and is passed back to the  $C_{S_1}$  compartment as a feed-back effect.

After the occurrence of a pulse, the calcium contained in the  $C_{S_1}$  and  $C_{S_2}$  compartments (denoted by  $Ca_{S_1}^+$  and  $Ca_{S_2}^+$ ) can be written as:

$$Ca_{S_1}^+ = Ca_{S_1}^+(t_p) + Q_c + \beta Ca_R(t_p) \dots\dots\dots 3.7.a$$

$$Ca_{S_2}^+ = Ca_{S_2}^+(t_p) \dots\dots\dots 3.7.b$$

$$\text{where } Ca_R(t_p) = Ca_{R_1}(t_p) + Ca_{R_2}(t_p) \dots\dots\dots 3.8$$

and  $t_p$ ,  $\beta$ , and  $Q_c$  denote respectively the time at which the pulse occurs, the feed-back factor, and the calcium gated from the surrounding solution (outside calcium).

The component  $Q_c$  is described in section 2.1.2. The above effects at the instant of the stimulation pulse are incorporated into the hydraulic analog by forcing a periodic re-initialization of the describing differential equations (namely equation 3.5). The time interval between the re-initialization is equal to the stimulation pulse

period. Equation 3.5 is, therefore, considered to be relevant only in interval  $[t_p^j, t_p^{j+\Delta})$ , where  $\Delta$  is the interpulse interval (seconds) and  $t_p^j$  is the time of occurrence of the  $j^{\text{th}}$  pulse. The initial conditions which apply at the beginning of each such interval are determined in part by the conditions existing at the end of the preceding interval, specifically:

$$M_{s_1}(t_p^j) = \alpha_1 = M_{s_1}(t_p^{j-1+\Delta}) + Q_h + \beta M_r(t_p^{j-1+\Delta}) \dots 3.9.a$$

$$M_{r_1}(t_p^j) = \alpha_2 = 0 \dots 3.9.b$$

$$M_{s_2}(t_p^j) = \alpha_3 = M_{s_2}(t_p^{j-1+\Delta}) \dots 3.9.c$$

$$M_{r_2}(t_p^j) = \alpha_4 = 0 \dots 3.9.d$$

$$\text{where } M_r(t_p^{j+\Delta}) = M_{r_1}(t_p^{j+\Delta}) + M_{r_2}(t_p^{j+\Delta}) \dots 3.10$$

and  $Q_h$  corresponds to the gating effect and is taken as:

$$Q_h = C_N (1 - e^{-120/f}) (1 - e^{-\epsilon h_0}) \dots 3.11$$

The exponent factor,  $\epsilon$ , is in the range  $[0.1 - 0.3] C_N$ , the nominal value of the stimulating factor, is 0.1, and  $f$  is the stimulation frequency (pulses/min.).

### 3.5 CONDITIONS FOR DYNAMIC EQUILIBRIUM

#### 3.5.1 MATHEMATICAL ANALYSIS FOR DYNAMIC EQUILIBRIUM

Similar to the situation with the basic Mainwood-Lee

model, the state variables,  $M_{s_1}(t)$ ,  $M_{s_2}(t)$ ,  $M_{r_1}(t)$ , and  $M_{r_2}(t)$ , of the dual subsystem model assume a periodic behaviour after passing through an initial transient phase when the dual subsystem model is started from an arbitrary initial condition. As the initial transient mode is of no interest, computing time, which is of major consideration, can be minimized by establishing a set of initial conditions for the system equation 3.5 which ensure that the system will attain a periodic behaviour immediately without passing through an initial transient phase.

The system equation 3.5 can be expressed in the standard form of a system of linear, first order differential equation, namely,

$$\dot{x}(t) = Ax(t) + b \dots\dots\dots 3.12$$

where:

$$A = \begin{bmatrix} a_{11} & a_{12} & a_{13} & a_{14} \\ a_{21} & a_{22} & a_{23} & a_{24} \\ a_{31} & a_{32} & a_{33} & a_{34} \\ a_{41} & a_{42} & a_{43} & a_{44} \end{bmatrix} \text{ and } b = \begin{bmatrix} b_1 \\ b_2 \\ b_3 \\ b_4 \end{bmatrix}$$

and

$$a_{11} = -\left(\frac{K_1 + 5K_2}{A_{s_1}}\right)$$

$$a_{12} = \frac{K_1}{A_{r_1}}$$

$$a_{21} = \frac{K_1}{A_{s_1}}$$

$$a_{22} = \frac{K_1}{A_{r_1}}$$

$$a_{13} = a_{14} = a_{23} = a_{24} = 0$$

$$a_{31} = a_{32} = a_{41} = a_{42} = 0$$

$$a_{33} = -\left(\frac{K_1 + 5K_2}{A_{s_2}}\right)$$

$$a_{34} = \frac{K_1}{A_{r_2}}$$

$$a_{43} = \frac{K_1}{A_{s_2}}$$

$$a_{44} = \frac{K_1}{A_{r_2}}$$

$$b_1 = -K_2 h_0 - B$$

$$b_3 = K_2 h_0$$

$$b_2 = b_4 = 0$$

In this representation  $x_1(t)$ ,  $x_2(t)$ ,  $x_3(t)$ , and  $x_4(t)$  correspond to  $M_{s_1}(t)$ ,  $M_{r_1}(t)$ ,  $M_{s_2}(t)$ , and  $M_{r_2}(t)$  respectively.

The general solution of the system, described by equation 3.12, can be written as:

$$x(t) = e^{At} x(t_p^{j-1}) + r(t) \dots \dots \dots 3.13$$

where

$$r(t) = \int_{t_p^{j-1}}^t e^{A(t-\tau)} b d\tau = \begin{bmatrix} r_1(t) \\ r_2(t) \\ r_3(t) \\ r_4(t) \end{bmatrix}$$

and  $t_p^{j-1}$  denotes the time of occurrence of the  $(j-1)$ <sup>th</sup> pulse. For convenience, denote  $e^{At}$  for the present case when  $A$  is  $4 \times 4$  by:

$$E(t) = \begin{bmatrix} E_{11}(t) & E_{12}(t) & E_{13}(t) & E_{14}(t) \\ E_{21}(t) & E_{22}(t) & E_{23}(t) & E_{24}(t) \\ E_{31}(t) & E_{32}(t) & E_{33}(t) & E_{34}(t) \\ E_{41}(t) & E_{42}(t) & E_{43}(t) & E_{44}(t) \end{bmatrix}$$

> Since  $A$  is block diagonal, it follows that  $E(t)$  is also a block diagonal and can therefore be written as:

$$E(t) = \begin{bmatrix} E_{11}(t) & E_{12}(t) & 0 & 0 \\ E_{21}(t) & E_{22}(t) & 0 & 0 \\ 0 & 0 & E_{33}(t) & E_{34}(t) \\ 0 & 0 & E_{43}(t) & E_{44}(t) \end{bmatrix}$$

Let the initial condition of the system equations after the occurrence of the pulse at time  $t_p^{j-1}$  be:

$$x_1(t_p^{j-1}) = \alpha_1 \dots\dots\dots 3.14.a$$

$$x_3(t_p^{j-1}) = \alpha_3 \dots\dots\dots 3.14.b$$

$$x_2(t_p^{j-1}) = x_4(t_p^{j-1}) = 0 \dots\dots\dots 3.14.c$$

The responses of  $x_1(t)$ ,  $x_2(t)$ ,  $x_3(t)$ , and  $x_4(t)$  for  $t > t_p^{j-1}$  follows from equation 3.13 as:

$$x_1(t) = E_{11}(t)\alpha_1 + r_1(t) \dots\dots\dots 3.15.a$$

$$x_2(t) = E_{21}(t)\alpha_1 + r_2(t) \dots\dots\dots 3.15.b$$

$$x_3(t) = E_{33}(t)\alpha_3 + r_3(t) \dots\dots\dots 3.15.c$$

$$x_4(t) = E_{43}(t)\alpha_3 + r_4(t) \dots\dots\dots 3.15.d$$

As a result of the pulse occurring at time  $t_p^{j-1}$ , the initial conditions for the subsequent interpulse interval as given by equation 3.9 are:

$$\alpha_1 = x_1(t_p^{j-1+\Delta}) + Q_h + \beta(x_2(t_p^{j-1+\Delta}) + x_4(t_p^{j-1+\Delta})) \dots\dots\dots 3.16.a$$

$$\alpha_2 = 0 \dots\dots\dots 3.16.b$$

$$\alpha_3 = x_3(t_p^{j-1+\Delta}) \dots\dots\dots 3.16.c$$

$$\alpha_4 = 0 \dots\dots\dots 3.16.d$$

Substitution of equation 3.15 at  $t = (t_p^{j-1+\Delta})$ , yields:

$$\alpha_1 = E_{11}(t_p^{j-1+\Delta})\alpha_1 + r_1(t_p^{j-1+\Delta}) + Q_h + \beta[E_{21}(t_p^{j-1+\Delta})\alpha_1 + r_2(t_p^{j-1+\Delta}) + E_{43}(t_p^{j-1+\Delta})\alpha_3 + r_4(t_p^{j-1+\Delta})] \dots\dots\dots 3.17.a$$

and

$$\alpha_3 = E_{33}(t_p^{j-1+\Delta})\alpha_3 + r_3(t_p^{j-1+\Delta}) \dots\dots\dots 3.17.b$$

In order that the dynamic equilibrium conditions exist, it is necessary that  $\alpha_1 = \alpha_1'$  and  $\alpha_3 = \alpha_3'$ . Hence equation 3.17 yields the required conditions that:

$$\alpha_1 = \frac{Q_h + r_1(t_p^{j-1+\Delta}) + \beta[r_2(t_p^{j-1+\Delta}) + E_{43}(t_p^{j-1+\Delta})\alpha_3 + r_4(t_p^{j-1+\Delta})]}{1 - E_{11}(t_p^{j-1+\Delta}) - \beta E_{21}(t_p^{j-1+\Delta})} \dots\dots 3.18.a$$

$$\alpha_3 = \frac{r_3(t_p^{j-1+\Delta})}{1 - E_{33}(t_p^{j-1+\Delta})} \dots\dots\dots 3.18.b$$

Since all the terms in the numerators of the rational expressions on the right hand sides of equation 3.18 are well defined, it follows that  $\alpha_1$  and  $\alpha_3$  exist as long as the denominators,  $1 - E_{11}(t_p^{j-1+\Delta}) - \beta E_{21}(t_p^{j-1+\Delta})$  and  $1 - E_{33}(t_p^{j-1+\Delta})$ , are not zero.

3.6 GENERATION OF THE ANALOG OF TENSION

The steady state values for the fluid levels can be readily established from the system equation 3.5 as:

$$\bar{h}_{r1} = \bar{h}_{s1} = \left(\frac{K_2}{K_2+K_3}\right)h_0 - \frac{B}{K_2+K_3} \dots\dots\dots 3.19.a$$

and

$$\bar{h}_{r2} = \bar{h}_{s2} = \left(\frac{K_2}{K_2+K_3}\right)h_0 \dots\dots\dots 3.19.b$$

The steady state model of the system shown in Figure 3.3 suggests that the problem is to find the form of the function  $G = G(\bar{M}_r)$  in order that the known steady state relation given in equation 2.25 is satisfied.

Proceeding as in Chapter 2, we consider the following form for G:

$$G(\bar{M}_r, B) = \frac{K(a_1\bar{M}_r + a_2)^2}{1 + K(a_1\bar{M}_r + a_2)^2} \dots\dots\dots 3.20$$

with  $a_1 = \frac{K_2 + K_3}{A_r K_2} = \frac{5}{A_r}$

$$a_2 = \frac{B}{K_2} \cdot \frac{A_{r1}}{A_r}$$

Since  $M_r = M_{r1} + M_{r2}$ , it follows that

$$\bar{M}_r = A_{r1} \bar{h}_{r1} + A_{r2} \bar{h}_{r2} \dots\dots\dots 3.21$$

Incorporating equation 3.19, and the fact that

$A_r = A_{r1} + A_{r2}$ , equation 3.21 can be written as:

$$\bar{M}_r = \frac{1}{5} h_0 A_r - \frac{B}{K_2} \cdot \frac{A_{r1}}{A_r} \dots\dots\dots 3.22$$

Substitution of  $\bar{M}_r$  into equation 3.20 then yields:

$$T_f = G(\bar{M}_r, B) = \frac{Kh_0^2}{1 + Kh_0^2} \dots\dots\dots 3.23$$

which is the desired result.

As discussed in Section 2.3, although the validity of the function G holds only for the case where there is a long duration between the pulses, it will continue to be used for arbitrary interpulse intervals. It thus serves as the mechanism for generating  $T_f$ , or rather its fictitious hydraulic analog.

### 3.7 COMPUTATIONAL APPROACH AND RESULTS

#### 3.7.1 COMPUTATIONAL APPROACH

The quantities  $E_{11}(t_p^{j-1} + \Delta)$  and  $E_{21}(t_p^{j-1} + \Delta)$  needed

in equation 3.18 are obtained as solutions  $x_1(\Delta)$  and  $x_2(\Delta)$  of equation 3.12, when  $x_1(0) = 1$  and

$x_2(0) = x_3(0) = x_4(0) = b_1 = b_2 = b_3 = b_4 = 0$ . The

quantities  $E_{33}(t_p^{j-1} + \Delta)$  and  $E_{43}(t_p^{j-1} + \Delta)$  needed in

equation 3.18 are obtained as the solutions  $x_3(\Delta)$  and

$x_4(\Delta)$  of equation when  $x_3(0) = 1$  and

$x_1(0) = x_2(0) = x_4(0) = b_1 = b_2 = b_3 = b_4 = 0$ . The

quantities  $r_1(t_p^{j-1} + \Delta)$ ,  $r_2(t_p^{j-1} + \Delta)$ ,  $r_3(t_p^{j-1} + \Delta)$ , and

$r_4(t_p^{j-1} + \Delta)$  needed in equation 3.17 are obtained as the

solutions  $x_1(\Delta)$ ,  $x_2(\Delta)$ ,  $x_3(\Delta)$ , and  $x_4(\Delta)$  of equation 3.12

when  $x_1(0) = x_2(0) = x_3(0) = x_4(0) = b_1 = b_4 = 0$ ,

$b_1 = K_2 h_0 - B$ , and  $b_3 = K_2 h_0$ .

### 3.7.2 EXPERIMENTAL RESULTS

The evaluation of the model was carried out by performing a sequence of computer runs in order to determine the influence of various system parameters on the Omega responses. Specifically, the influence of the following parameters was considered.

(a) Fluid level of tank  $T_0$ ,  $h_0$

(b) Recovery time constant,  $\lambda_{r1}$

(c) Recovery time constant,  $\lambda_{r2}$

(d) Decay time constant,  $\lambda_{s1}$

(e) Decay time constant,  $\lambda_{s2}$

(f) Feed-back factor,  $\beta$

(g) Exponent factor,  $\epsilon$

Table 3.2 shows the range considered for the various parameters. These values were suggested by experiments carried out with real papillary muscle of a rat.

In all the experiments, the areas of cross-section,  $A_{s_1}$ ,  $A_{s_2}$ ,  $A_{r_1}$ , and  $A_{r_2}$  were taken as 1.0, 1.0, 0.08 and 0.12 meter<sup>2</sup> respectively.

The time trajectories obtained for  $M_{s_1}(t)$  and  $M_{r_1}(t)$  at dynamic equilibrium over a typical interpulse interval are almost identical to those shown in Figures 2.4 and 2.5. This is a natural consequence of the fact that the fast filling subsystem of the present model corresponds to the basic Mainwood-Lee model. The time trajectories obtained for  $M_{s_2}(t)$ ,  $M_{r_2}(t)$ , and  $M_r(t)$  at dynamic equilibrium over a typical interpulse interval are shown in Figures 3.4 - 3.6.

The trajectory of  $M_{s_2}(t)$  starts from its initial value, passes through a valley (at approximately  $t = 12$  seconds for  $h_0 = 10$ ), and then increases with increasing time. The value of  $M_{r_2}(t)$  starts from zero at the beginning of the interpulse interval and then increases with increasing time; this increase is initially rapid and then becomes slower. The value of  $M_r(t)$  (Figure 3.6) starts from its zero value at the beginning of the interpulse interval and then increases with increasing time; this increase is initially very rapid (an increase of about 90% of peak value in first 16 seconds) and then becomes slower

(an increase of about 10% in remaining 44 seconds).

Omega responses for the hydraulic analog of the dual subsystem model are shown in Figures 3.7 through 3.13. In general, they are characterized by a valley whose minimum occurs at about (10-20) pulses/min. followed by a peak occurring at a stimulation frequency of (60-90) pulses/min.

The valley and the peak of the Omega response shifts to the left and the ratio of minimum value of tension to maximum value of tension decreases when:

(i) The recovery time constant,  $\lambda_{r1}$ , is decreased  
(Figure 3.8)

or

(ii) The decay time constant,  $\lambda_{s1}$ , is decreased (Figure 3.7).

or

(iii) The feed-back factor,  $\beta$ , is decreased (Figure 3.13)

or

(iv) The exponent factor,  $\epsilon$ , is decreased (Figure 3.12)

or

(v) The fluid level,  $h_0$ , is increased (Figure 3.11)

The valley and the peak of the Omega response shifts to the left, and the ratio of minimum value of tension to the maximum value of tension increases when:

(i) The decay time constant,  $\lambda_{s2}$ , is increased (Figure 3.9).

or

(ii) The recovery time constant,  $\lambda_{r2}$ , is increased

(Figure 3.10).

The stimulation frequency at which the peak tension occurs shifts towards the high frequency range and the stimulation frequency at which minimum of the tension occurs, shifts towards the low frequency range when:

(i) The decay time constant,  $\lambda_{r1}$ , is decreased (Figure 3.7)

or

(ii) The recovery time constant  $\lambda_{r1}$ , is decreased (Figure 3.8)

or

(iii) The feed-back factor,  $\beta$ , is increased (Figure 3.13)

or

(iv) The exponent factor,  $\epsilon$ , is decreased (Figure 3.12)

or

(v) The fluid level,  $h_0$ , is decreased (Figure 3.11).

From the Omega responses shown in Figures 3.7 through 3.13, it is clear that the behaviour of the dual subsystem model, while not in exact agreement with the given experimental data, does follow important trends of the experimental responses. It is noted in particular that when the external influence ( $h_0$  in the hydraulic analog,  $[Ca_0]$  in the experimental data) is reduced, the following general effects occur in both the experimental results and the simulated results.

(i) The optimal frequency (frequency at which the peak tension occurs),  $f_1$ , moves towards the high frequency

range.

- (ii) The least favourable frequency (frequency at which the minimum tension occurs),  $f_2$ , moves towards the low frequency range.
- (iii) The ratio  $\left(\frac{T_{\max}}{T_s}\right)$  increases, where  $T_{\max}$  is the value of the peak tension and  $T_s$  is the starting value of tension.
- (iv) The ratio  $\left(\frac{T_{\max}}{T_{\min}}\right)$  increases, where  $T_{\min}$  is the minimum value of tension (Note also that the valley and the peak of the Omega response disappear for high values of  $h_0$  ( $[Ca_0]$ )).
- (v) The ratio  $\left(\frac{T_s}{T_E}\right)$  decreases, where  $T_E$  is the tension value corresponding to the highest stimulation frequency considered (namely 180 pulses/min.).

The effect of stimulation frequency on the stimulus factor,  $c$ , as described by equation 3.24, is shown in Figure 3.14.

$$c = 0.1(1 - e^{-120/f}) \dots\dots\dots 3.24$$

### 3.8 A FUNCTIONAL DEPENDENCY FOR THE FEED-BACK FACTOR

By studying the various Omega responses of the dual subsystem model shown in Figures 3.4 - 3.13, it was felt that these responses could be improved if a functional relationship between  $\beta$  and  $h_0$  could be formed. Various analytic relations between  $\beta$  and  $h_0$  were investigated. On the basis of the computational results obtained, the

analytic relation which appeared to be the most promising was the following:

$$\beta = (1 - e^{-\delta/\sqrt{h_0}}) \dots\dots\dots 3.25$$

where  $\delta$  is in the range [2.-3.]

Incorporation of this relation in the dual subsystem model results in somewhat better Omega responses. Of the various values of  $\delta$  tested, the value of 2.65 provided the best results and they are shown in Figure 3.15.

The Omega responses for the cases  $h_0 = 10$  and  $h_0 = 4$ , shown in Figure 3.15, deviates towards the x-axis relative to the results given in Figure 3.11. The starting points remain unaltered. For the cases of  $h_0 = 1$  and  $h_0 = 2$ , the responses shown in Figure 3.15 are essentially the same as shown in Figure 3.11.

Dual Subsystem Model	Hydraulic Analog
The surrounding fluid bath	Tank $T_0$
Compartment $C_{s_1}$	Tank $T_{s_1}$
Compartment $C_{r_1}$	Tank $T_{r_1}$
Compartment $C_{s_2}$	Tank $T_{s_2}$
Compartment $C_{r_2}$	Tank $T_{r_2}$
Amount of calcium in the compartment $C_{s_1}$ ( $Ca_{s_1}$ )	Volume $M_{s_1}$
Amount of calcium in the compartment $C_{r_1}$ ( $Ca_{r_1}$ )	Volume $M_{r_1}$
Amount of calcium in the compartment $C_{s_2}$ ( $Ca_{s_2}$ )	Volume $M_{s_2}$
Amount of calcium in the compartment $C_{r_2}$ ( $Ca_{r_2}$ )	Volume $M_{r_2}$
Volume of the $C_{s_2}$ compartment ( $V_{s_1}$ )	Area of cross-section, $A_{s_1}$
Volume of the $C_{r_2}$ compartment ( $V_{r_1}$ )	Area of cross-section, $A_{r_1}$
Volume of the $C_{s_2}$ compartment ( $V_{s_2}$ )	Area of cross-section, $A_{s_2}$
Volume of the $C_{r_2}$ compartment ( $V_{r_2}$ )	Area of cross-section, $A_{r_2}$
Calcium concentration [ $Ca_{s_1}$ ]	Height $h_{s_1}$
Calcium concentration [ $Ca_{r_1}$ ]	Height $h_{r_1}$
Calcium concentration [ $Ca_{s_2}$ ]	Height $h_{s_2}$
Calcium concentration [ $Ca_{r_2}$ ]	Height $h_{r_2}$
Calcium concentration of the surrounding fluid bath	Height $h_0$

TABLE 3.1

Table of Correspondence between Quantities in the Dual Subsystem Model and its Hydraulic Analog.

PARAMETER	RANGE		SPECIAL COMMENTS OR VALUES OF SPECIAL INTEREST
	FROM	TO	
$h_0$	1 unit	10 units	Only four values of $h_0$ , 1, 2, 4, 10 units, corresponding to calcium concentrations of $(0.25, 0.5, 1.0, 2.5) \times 10^{-6}$ Mols/millilitre are considered.
$\lambda_{r1}$	0.2 secs.	1.0 secs.	$\lambda_{r1} = 0.6$ secs.
$\lambda_{r2}$	6.0 secs.	12.0 secs.	$\lambda_{r2} = 10.0$ secs.
$\lambda_{s1}$	20.0 secs.	40.0 secs.	$\lambda_{s1} = 30.0$ secs.
$\lambda_{s2}$	50.0 secs.	100.0 secs.	$\lambda_{s2} = 100.0$ secs.
$\beta$	0.3	0.9	$\beta = 0.7$
$c$	0.1	0.3	$c = 0.25$

TABLE 3.2.

Range Considered for Various Parameters.

External Fluid bath having Calcium Concentration  $[Ca_0]$ .

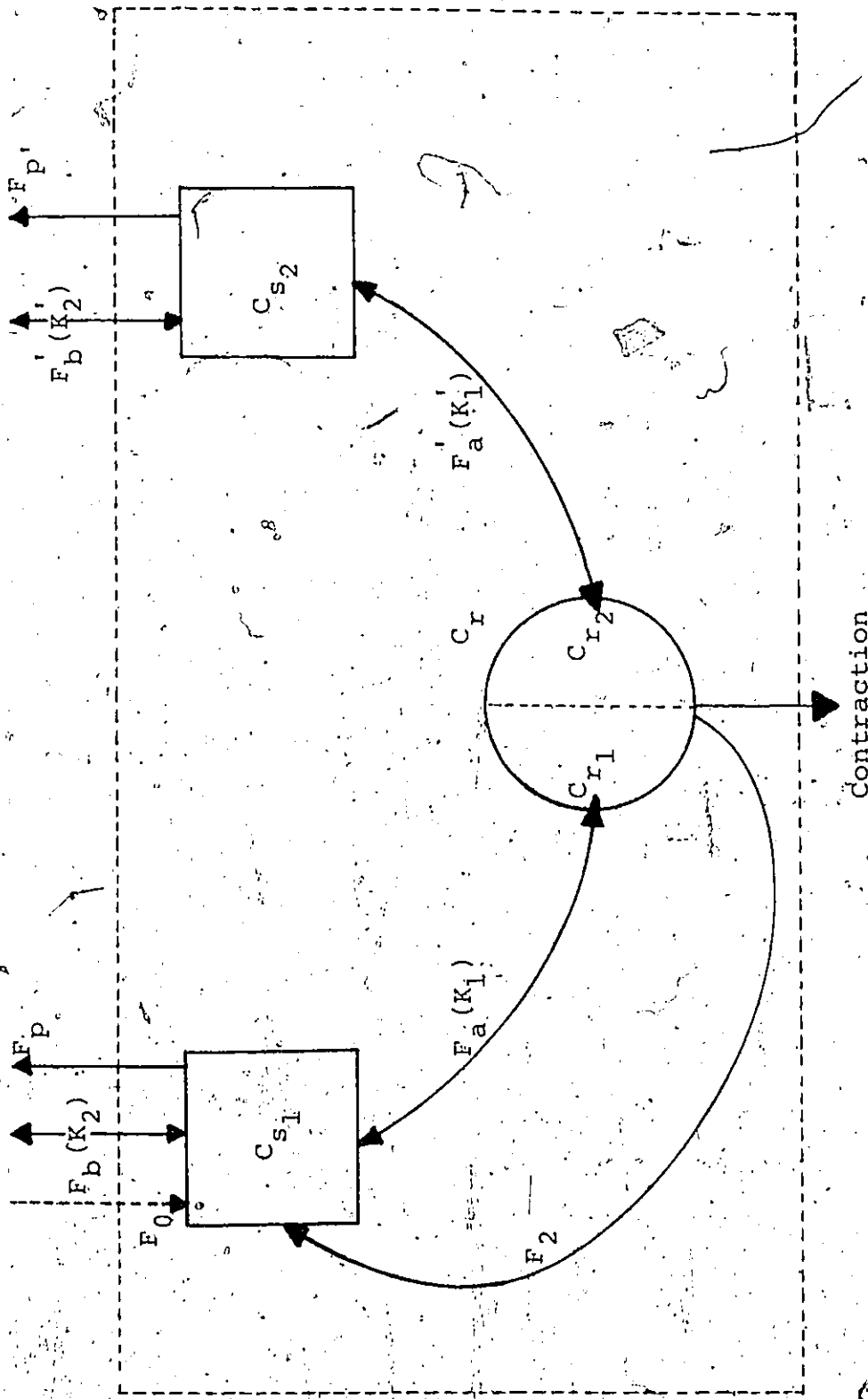


FIGURE 3.1

The Dual Subsystem Model

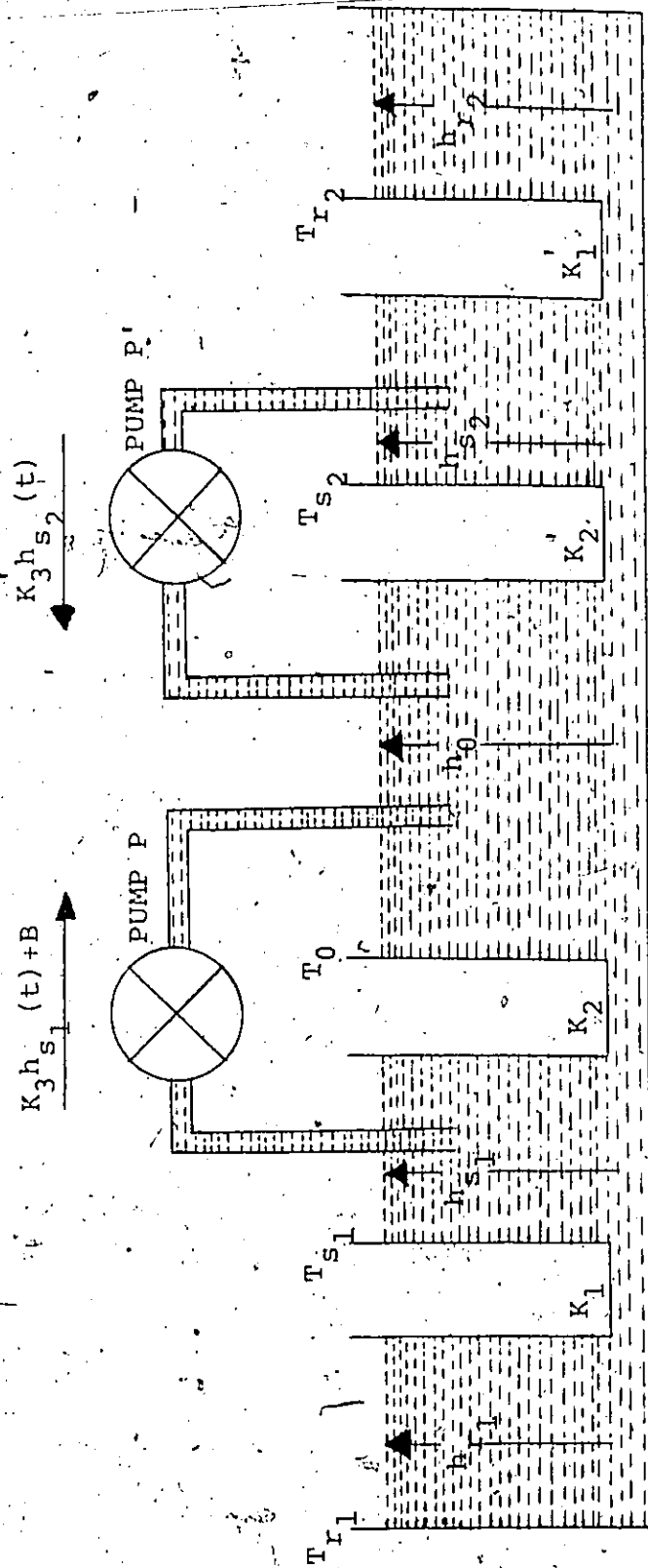


FIGURE 3.2

Hydraulic Analog of the Dual Subsystem Model

G

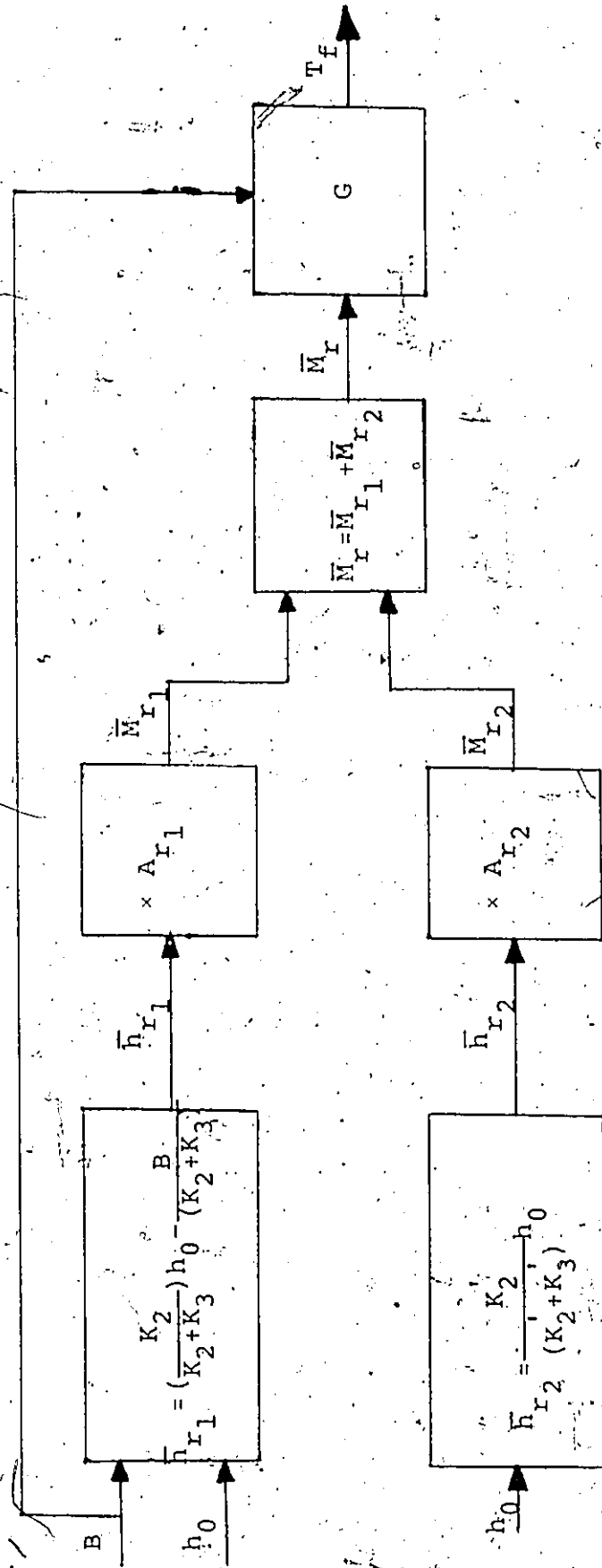


FIGURE 3.3

Steady State Model of the Dual Subsystem Model

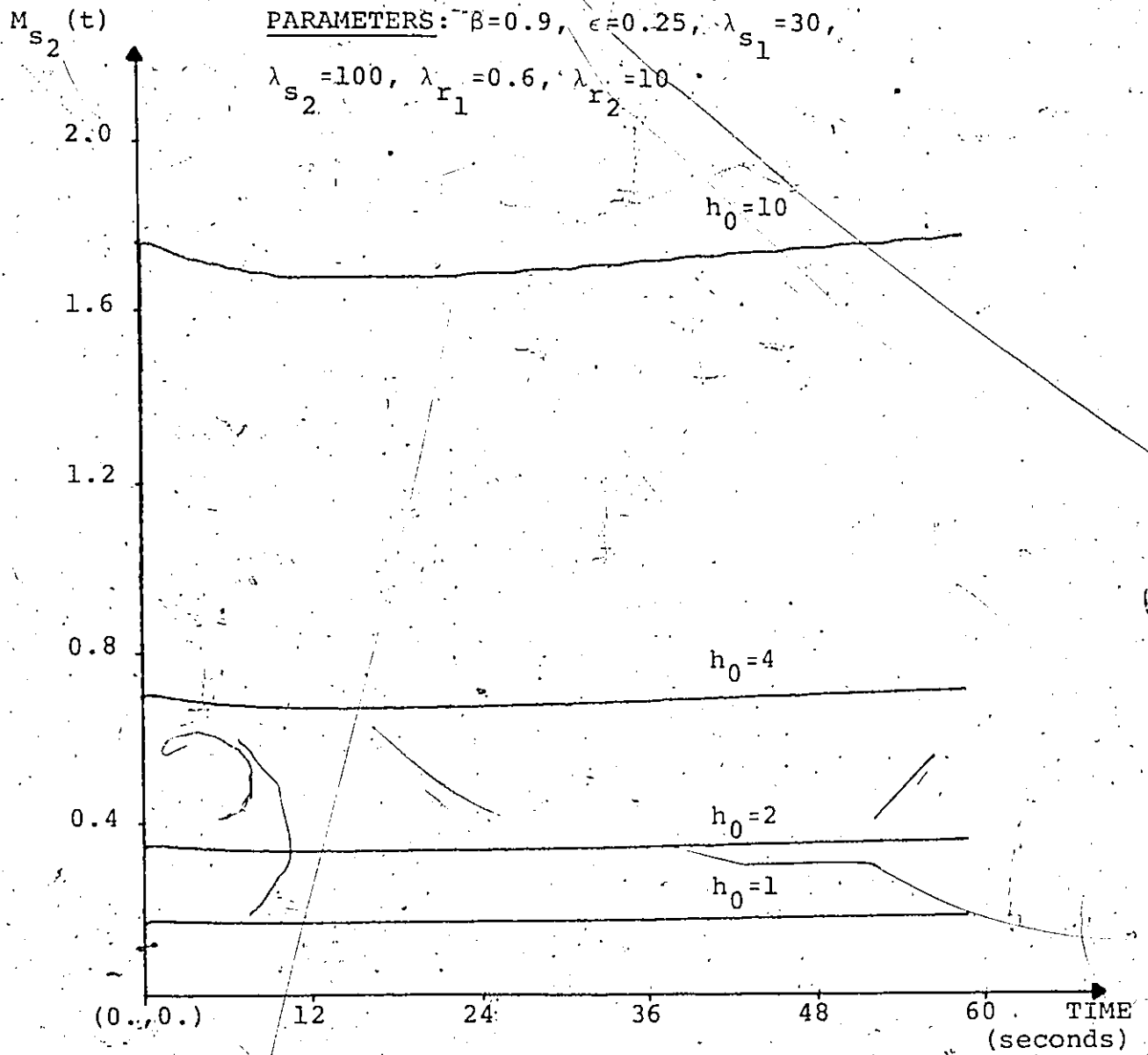


FIGURE 3.4

Time Trajectories of volume  $M_{s_2}(t)$  for Different  $h_0$  Fluid Levels  
 (Initial Conditions are those for Dynamic Equilibrium  
 with  $\Delta = 60$  secs.)

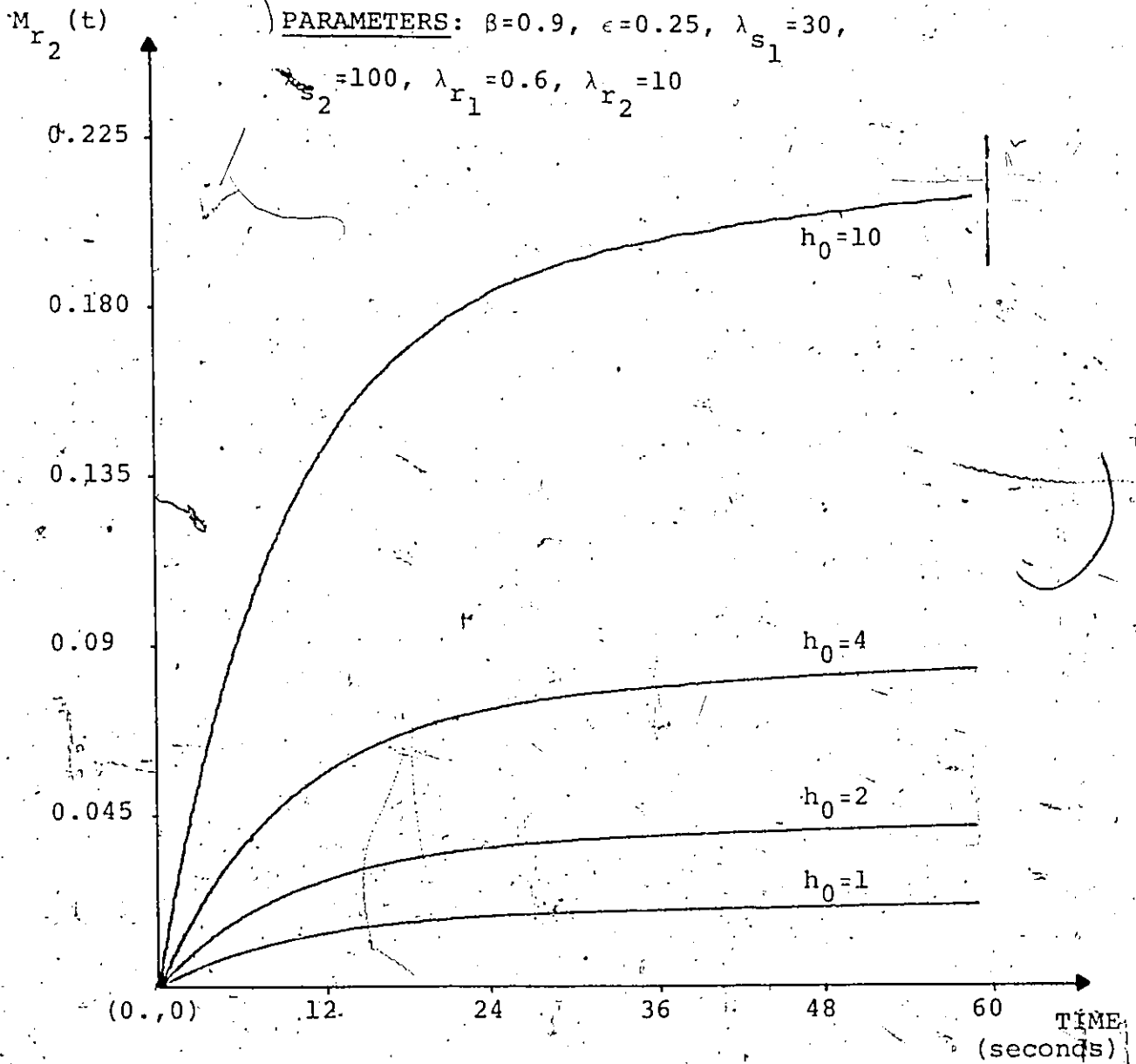


FIGURE 3.5

Time Trajectories of Volume  $M_{r_2}(t)$  for Different  $h_0$  Levels.

(Initial Conditions are those for Dynamic Equilibrium

with  $\Delta=60$  secs.)

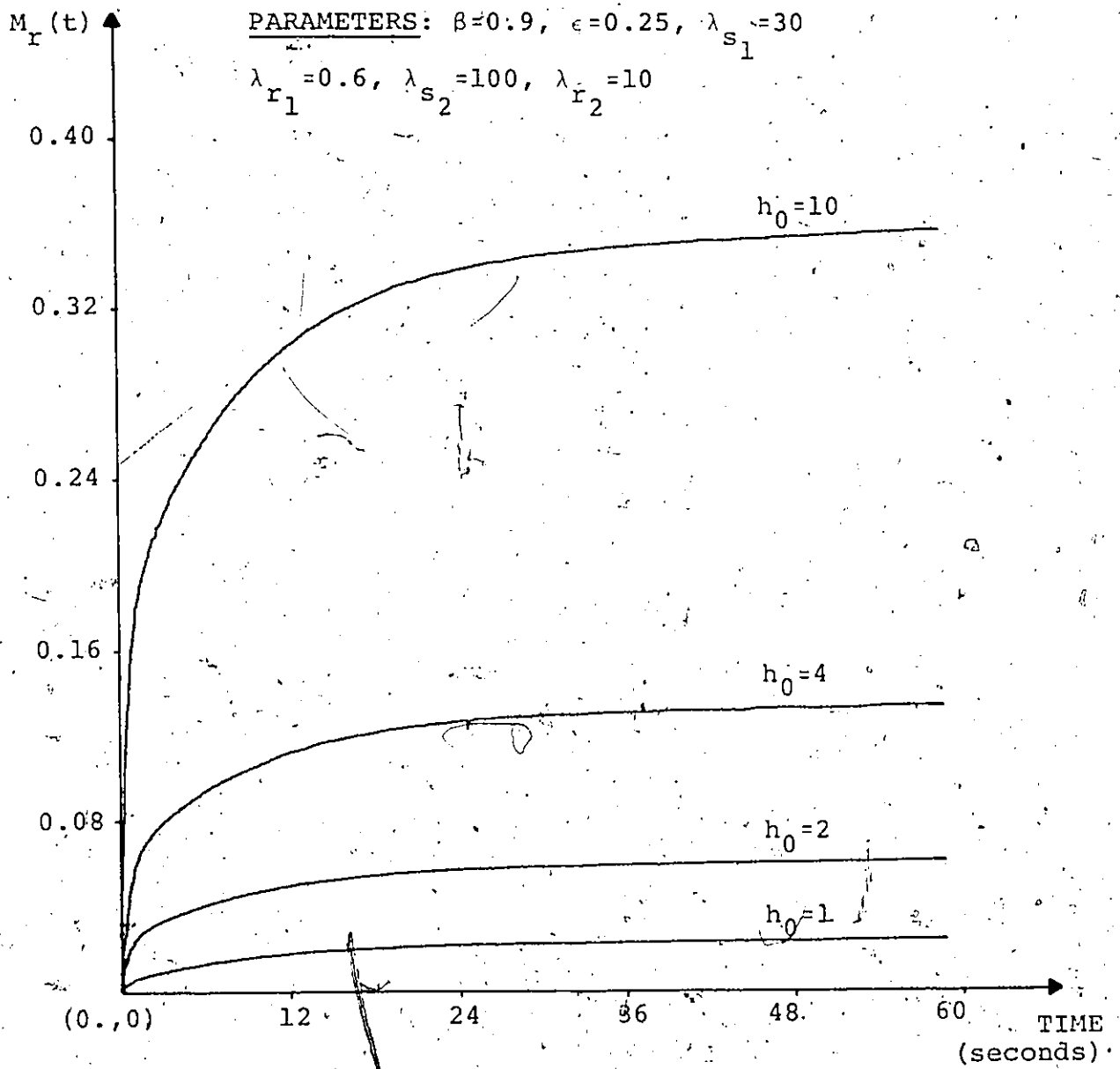


FIGURE 3.6

Time Trajectories of Volume  $M_r(t)$  for Different  $h_0$  Levels.

(Initial Conditions are those for Dynamic Equilibrium  
 with  $\Delta=60$  secs.)

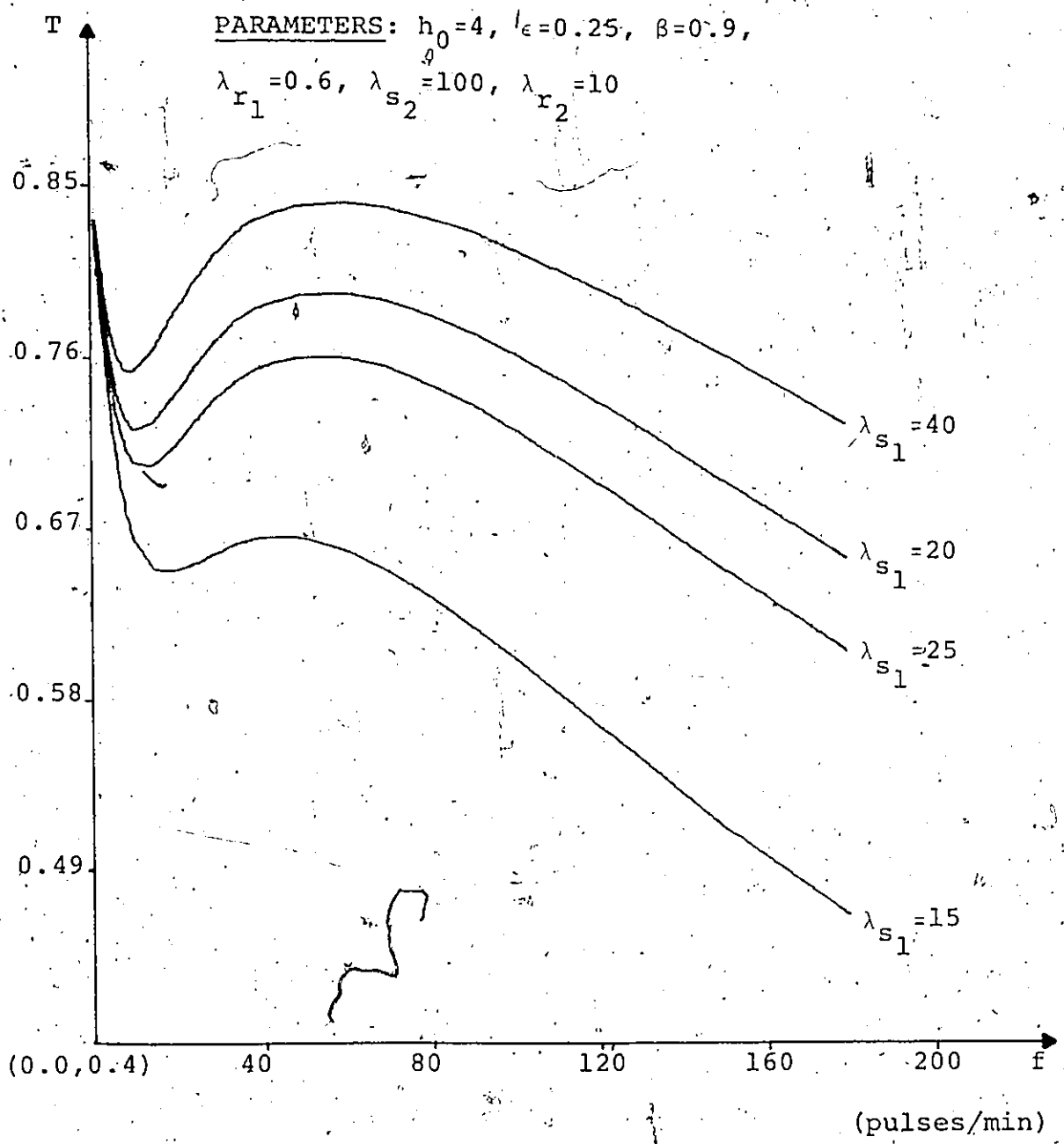


FIGURE 3.7

Omega Responses for Various Values of Decay Time Constant,  $\lambda_{s1}$

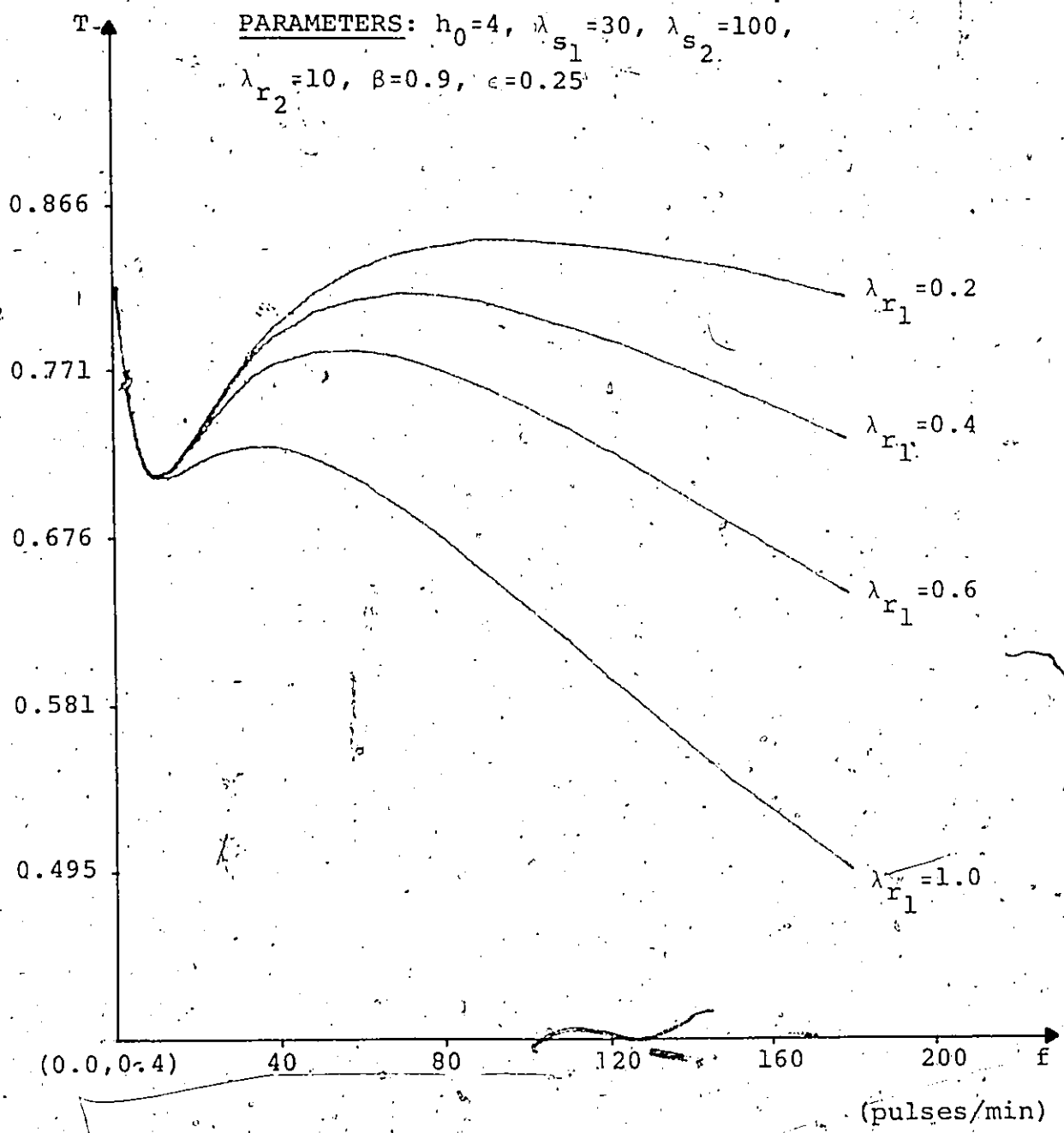


FIGURE 3.8.

Omega Responses for Various Values of Recovery Time Constant,  $\lambda_{r1}$ .

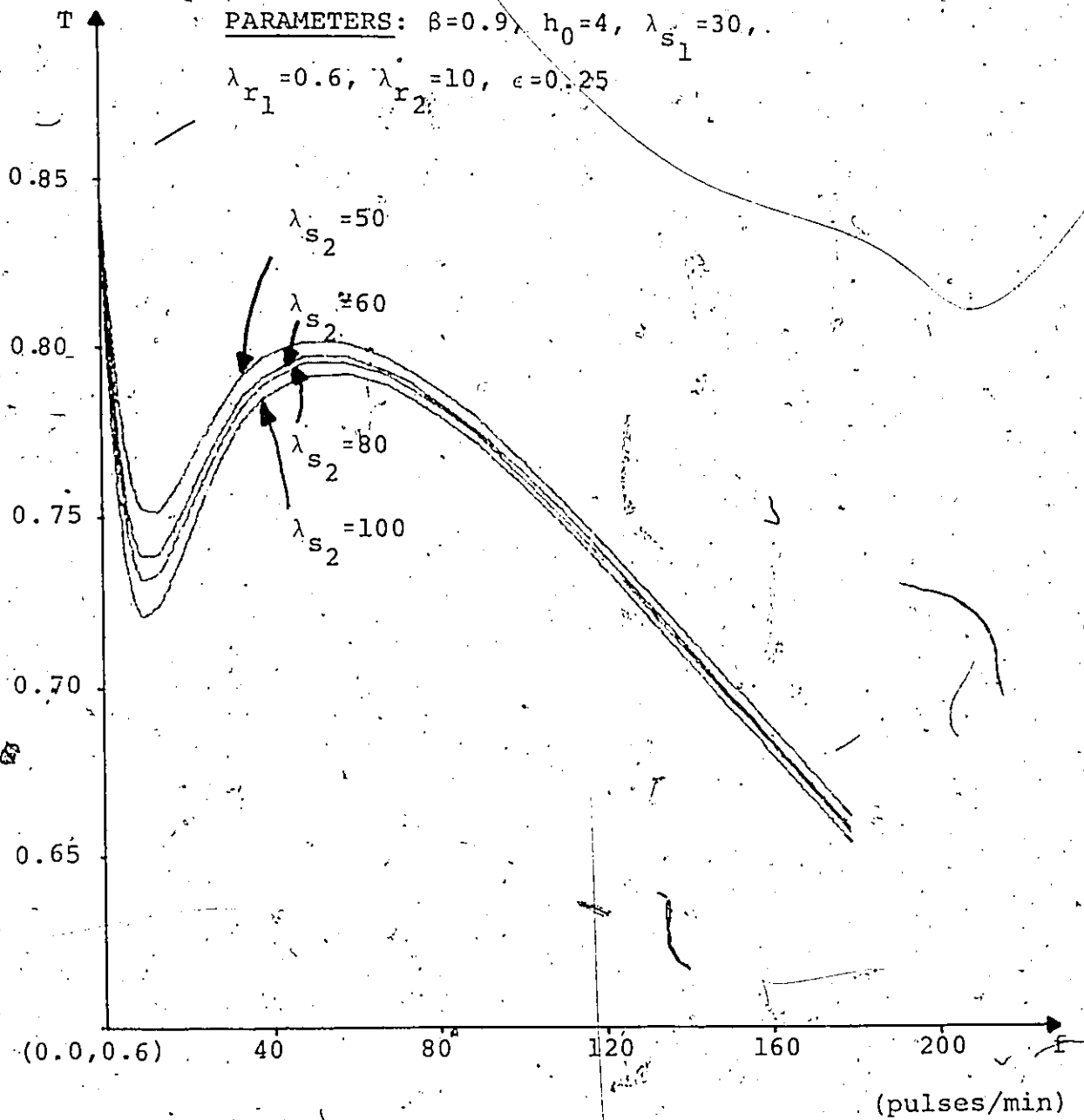


FIGURE 3.9

Omega Responses for Various Values of Decay Time Constant,  $\lambda_{s2}$ .

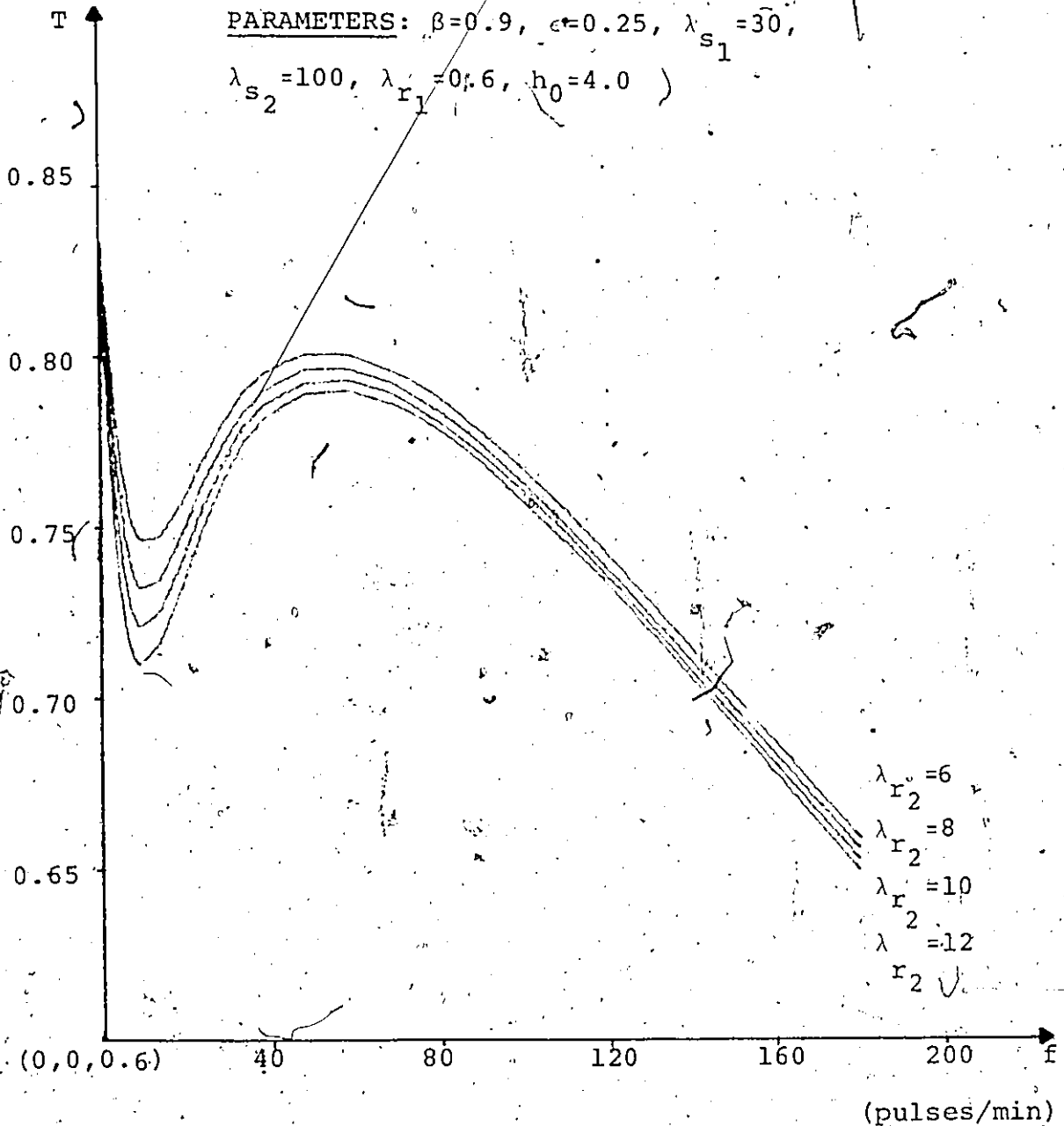


FIGURE 3.10

Omega Responses for Various Values of Recovery Time Constant  $\lambda_{r2}$ .

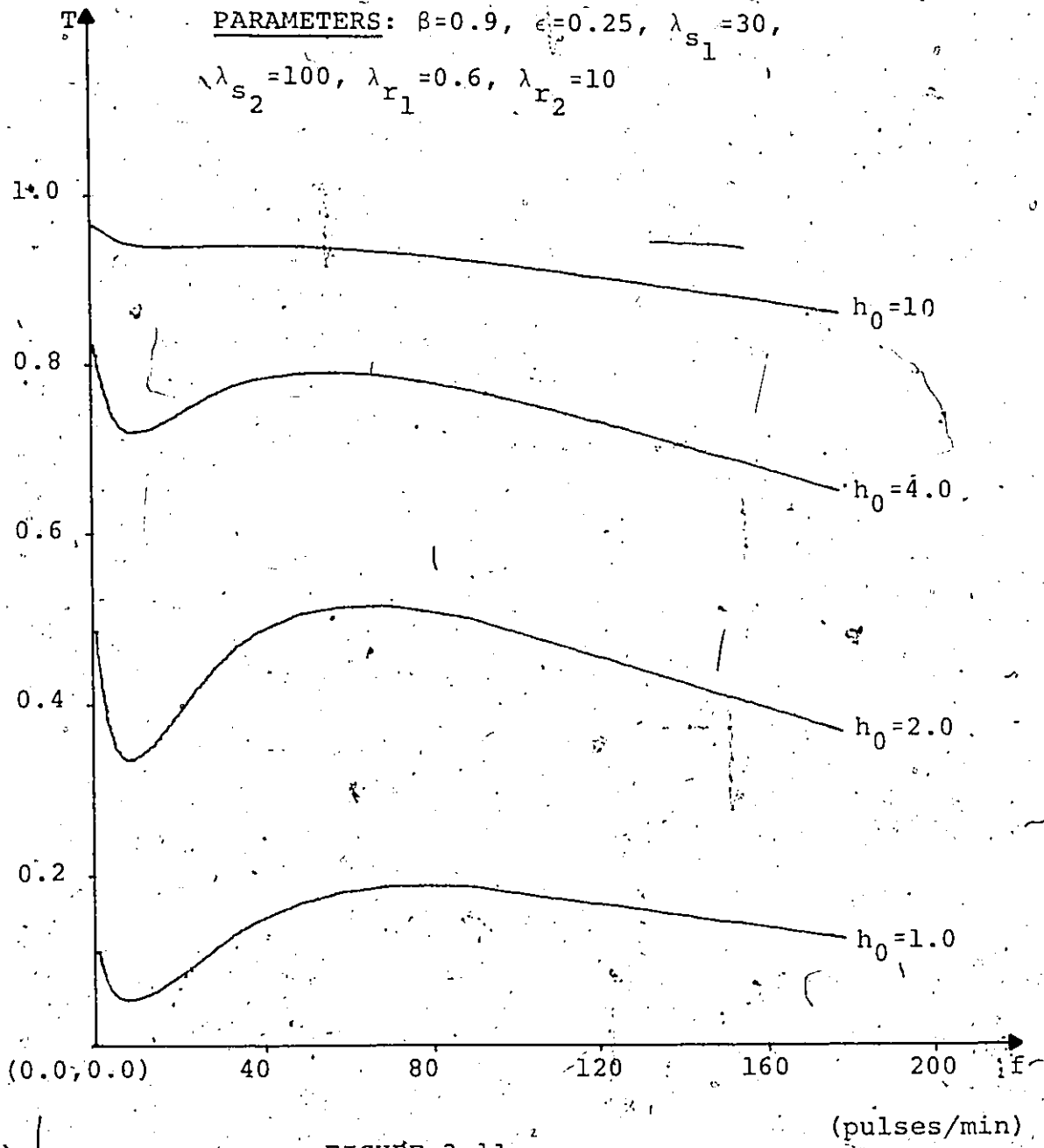


FIGURE 3.11

Omega Responses for Various Values of  $h_0$ .

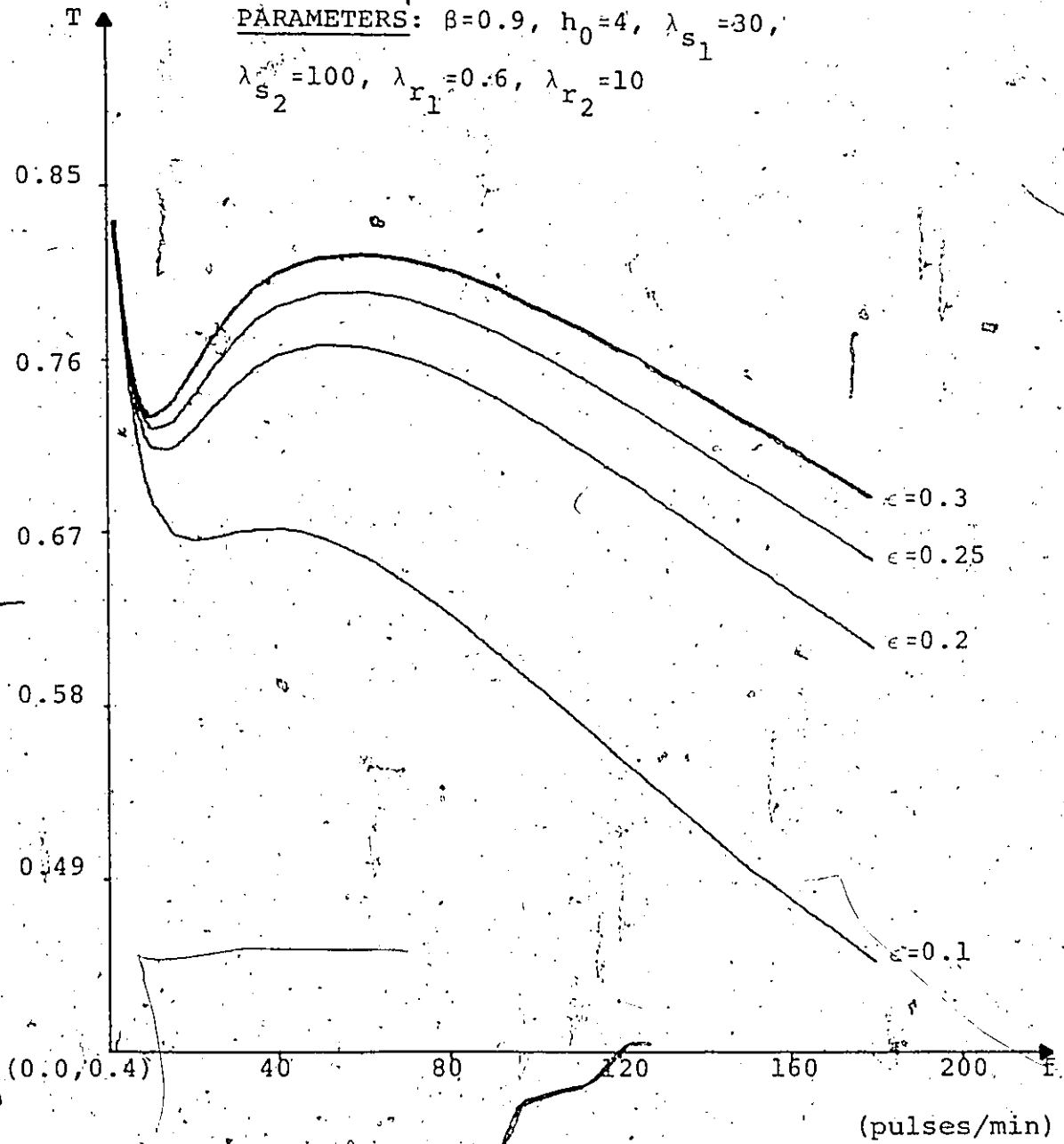


FIGURE 3.12

Omega Responses for Various Values of Exponent Factor,  $\epsilon$

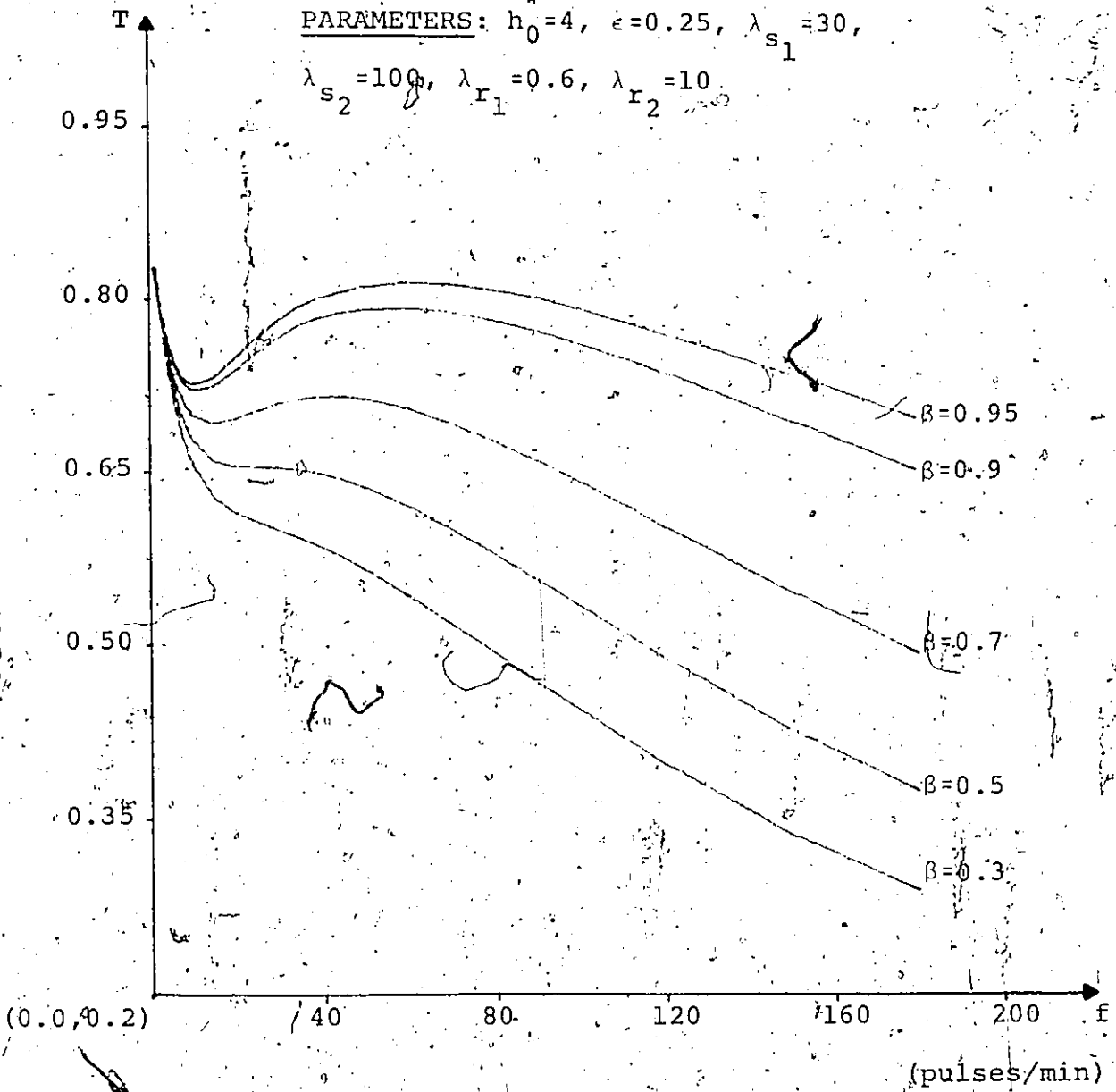


FIGURE 3.13

Omega Responses for Various Values of Feed-back Factor,  $\beta$

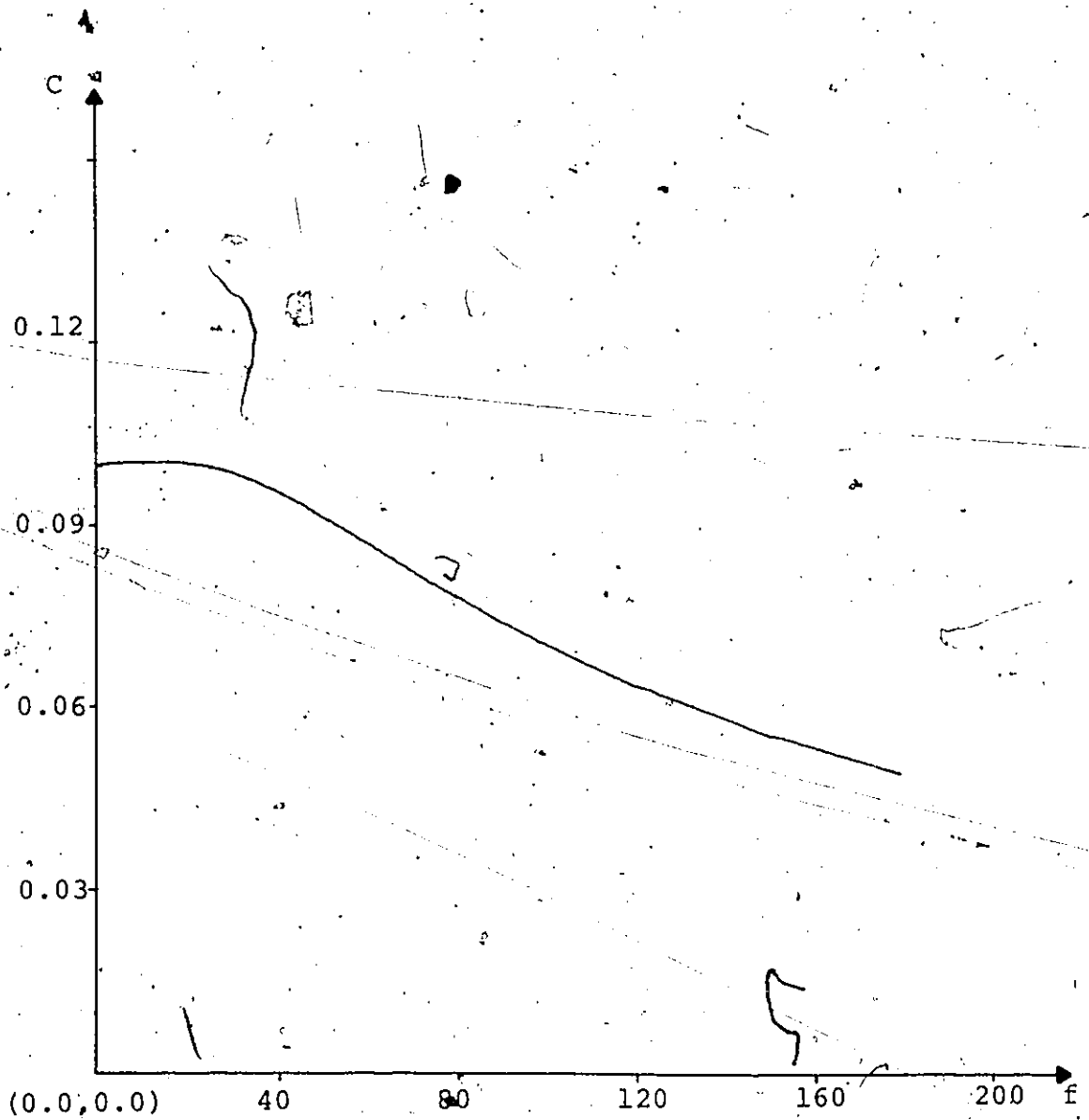


FIGURE 3.14 (pulses/min)

The Effect of Stimulation Frequency on the Stimulus Factor, C.

(See Equation 3.24)

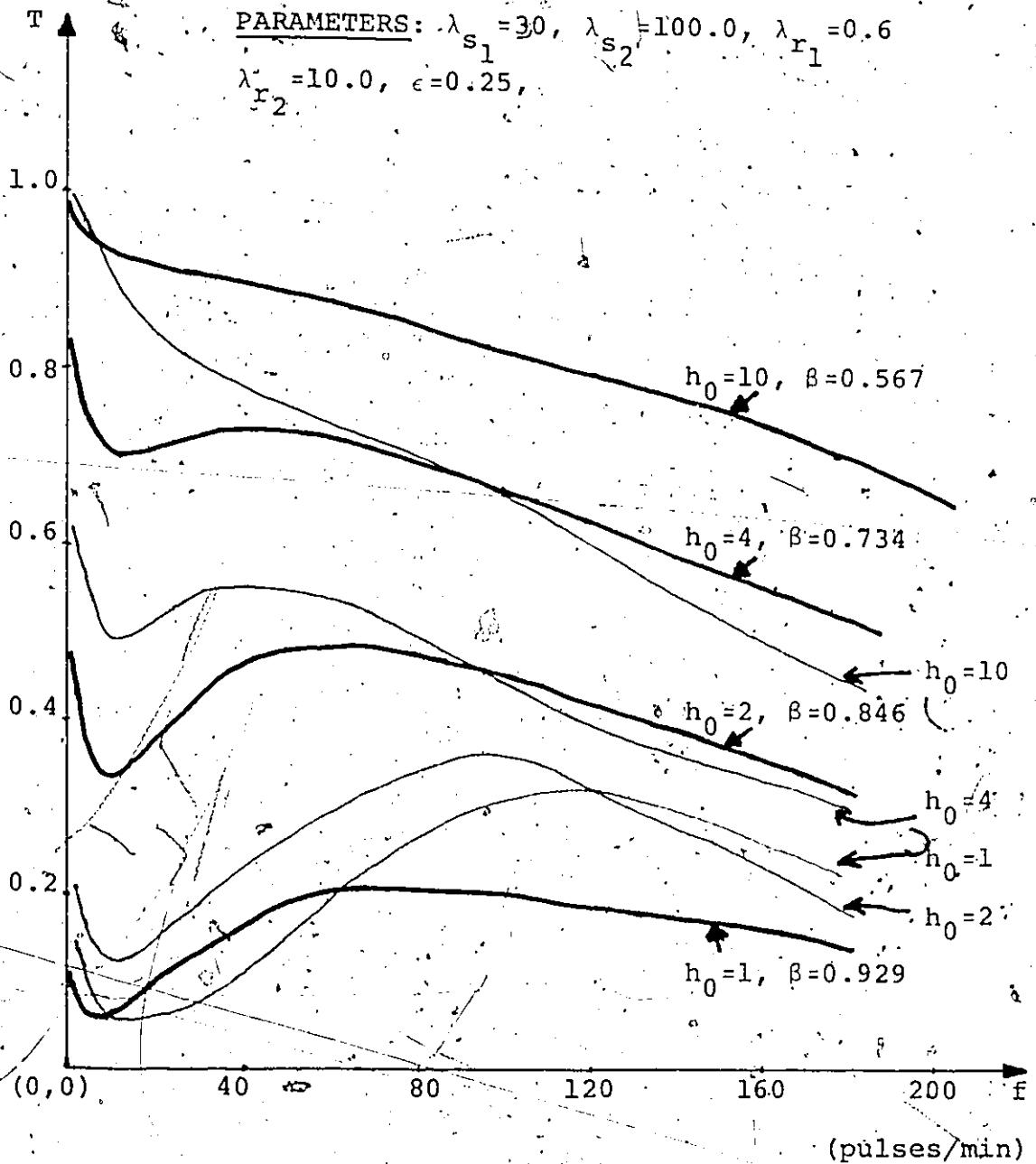


FIGURE 3.15

Omega Responses for Various Values of  $h_0$  with  $\beta$  Established by Equation 3.25 ( $\delta=2.65$ ).

SUMMARY AND CONCLUSIONS

A model for the calcium movement in the papillary muscle of a rat has been formulated based on the assumption that the calcium causing the muscle contraction is derived from three distinct calcium pools; namely, the outside calcium pool, the  $C_{s_1}$  compartment and the  $C_{s_2}$  compartment. In order to facilitate the development of a mathematical characterization for the configuration, a hydraulic analog for the model was formulated.

In the context of this mathematical configuration, the notion of dynamic equilibrium was defined and the conditions which force the model into this state were developed. The generation of the necessary Omega response data for the model was considerably facilitated using these results.

The effect of changes in various parameters on the Omega responses of the model was investigated through a series of computational experiments. The objective of these experiments was that of finding a set of model parameters which minimize the deviation between model Omega responses and Omega response data available from actual experiments (see Figure 1.2).

The best set of model Omega responses obtained (Figure 3.11) are in good agreement with the general trends in the given experimental data. Significant

deviations are, however, apparent. In order to possibly reduce the deviations in the context of the present model, various alterations can be explored. The most promising appear to be the following:

- (a) Removal of the constraint of a steady state gain of 5 between  $h_0$  and  $\bar{h}_{s1}$ , and  $h_0$  and  $\bar{h}_{s2}$  (see equation 3.2).
- (b) Alteration of the feed-back flow,  $F_2$ . In the present configuration, this flow is from the compartment  $C_r$  to the compartment  $C_{s1}$  (of the fast subsystem). An alternative would be to have this flow from the compartment  $C_r$  to the compartment  $C_{s2}$  (of the slow subsystem).
- (c) Alteration of the gated flow  $F_0$ . In the present configuration, this flow is from the outside bath to the compartment  $C_{s1}$ . An alternative would be to have this flow to the  $C_{s2}$  compartment.

It has been acknowledged that the reference experimental data being used (Figure 1.2) is not highly accurate and may in fact deviate as much as 20% from reality. This fact has complicated the search procedure for an acceptable set of parameters in the model.

It is noted also that the model responses can be improved somewhat when the feed-back factor,  $\beta$ , is made a function of  $h_0$ . Further investigations with this functional relation may prove fruitful.

The project has furthermore resulted in the creation of a documented Fortran program which can be used in further studies directed toward further refinement of the model.

APPENDIX 1

PROGRAM DOCUMENTATION

APPENDIX I.

This appendix describes the computer program used in carrying out the various computational experiments reported in the study. A brief synopsis of each of the subprograms contained in the program package is given. In addition, for certain of the critical subroutines, a flowchart is provided.

In order to facilitate the reading of the program, the various scalar and array variables used are summarized in Tables I.1 and I.2. A summary of the various COMMON blocks used to transfer information among the subprograms is given in Table I.3. Figure I.1 represents the subprogram interdependence, the modular information flow.

A complete listing of the Fortran program itself is given in the Appendix II and sample output is given in Appendix III.

I.1 MAIN PROGRAM

This program initializes the values of various parameters in data statements and acts as the control module. It calls various subprograms depending upon the type of function to be performed as follows:

- (i) Subroutine SETUP for setting up the numeric values of certain parameters.
- (ii) Subroutine SOLVE for solving the system equations with specially selected conditions.

- (iii) Subroutine GETCO for computing the fluid flow due to the gating effect of an electrical stimulus.
- (iv) Subroutine EVAL for computing the initial conditions for dynamic equilibrium.
- (v) Subroutine TENSION for computing the analog of tension.
- (vi) Subroutine GETCAR for computing the percentage error between the computational results and the reference data.
- (vii) Subroutine TRAJCT for solving the system equations using dynamic equilibrium initial conditions.
- (viii) Subroutine OUTPUT for outputting pertinent information.
- (ix) Subroutine PLTALL for plotting the Omega responses.
- (x) Subroutine PRCENT for computing the individually normalized Omega responses.

A flow chart of the Main Program is shown in Figure

I.2.

### I.2 SUBROUTINE ACES1

This subroutine is called by PCM and is used to extract information from the solution trajectories of the differential equations being solved. A flow chart of this subprogram is shown in Figure I.3.

### I.3 SUBROUTINE EIGEN

This subroutine computes the eigenvalues of coeffi-

cient matrix of the system equations (the Matrix A in equations 2.17 and 3.13) using subroutines from Scientific Subroutines Package (SSP). It then prints the elements of the A matrix and the eigenvalues associated with it.

#### I.4 SUBROUTINE EVAL

This subroutine computes the initial conditions for dynamic equilibrium (see equations 2.24 and 3.18) and using these initial conditions, it computes the corresponding final values for the system state variables at the end of the interpulse interval.

#### I.5 SUBROUTINE GETATR

This subroutine determines various critical (canonical) values associated with a given Omega curve and stores these values in the "Attribute Matrix" VATRBT. The canonical values determined for each Omega curve are:  $T_s$  (the initial value),  $T_E$  (the final value),  $T_{min}$  (the value at the least favourable frequency),  $T_{max}$  (the value at the optimum frequency),  $f_1$  (the least favourable frequency), and  $f_2$  (the optimum frequency). In addition, the following ratios are computed and stored,  $\frac{T_{min}}{T_s}$ ,  $\frac{T_{max}}{T_s}$ ,  $\frac{T_{min}}{T_{max}}$ ,  $\frac{T_E}{T_s}$  and  $\frac{T_E}{T_{max}}$ .

#### I.6 SUBROUTINE GETCAR

This subroutine calls GETATR to form the Attribute

Matrix for both computed results and the given experimental data. It also computes the percentage error between the computed results and the reference experimental data.

#### I.7 SUBROUTINE GETCQ

This subroutine computes the values of  $c$  (stimulating factor) and  $Q$  (see equation 2.16) corresponding to various values of stimulation frequency stored in vector PPM.

#### I.8 SUBROUTINE GETFBF

This subroutine computes the values of the feed-back factor corresponding to the different values of  $h_0$  stored in vector CA (see equation 3.25). It has relevance only in these experiments where  $\beta$  is taken to be a function of  $h_0$ .

#### I.9 SUBROUTINE NEGCHK

This subroutine examines the values of the system state variables under dynamic equilibrium conditions at all time points prior to the current interpulse time. It calls REJECT if it uncovers a system state variable with a negative value.

#### I.10 SUBROUTINE OUTPUT

This subroutine is the main output subroutine and provides a summary of the results pertaining to a particular Omega curve. The tabular output of the pertinent

information is preceded by a summary of the values of the parameters associated with it.

#### I.11 THE DESOLR PACKAGE

This package consists of three subroutines; namely PCM, STARTR and RHS. This package solves the system differential equations by using a predictor-corrector method.

#### I.12 SUBROUTINE PLTALL

This subroutine generates a group of four superimposed Omega response curves on a line printer plot. These curves correspond to four distinct values of any one of the following system parameters:  $\lambda_{s1}$ ,  $\lambda_{s2}$ ,  $\lambda_{r1}$ ,  $\lambda_{r2}$ ,  $h_0$ , and  $\epsilon$ .

#### I.13 SUBROUTINE PLTINF

This subroutine generates a line printer plot of the time trajectory of any system variable of interest.

#### I.14 SUBROUTINE PLTOUT

This subroutine generates a line printer plot of the dynamic equilibrium values of any system variable plotted against frequency of stimulation.

I.15 SUBROUTINE PPPINF

On the basis of the user specified value for the control parameter KOUT1, this subroutine calls one (or more) of the subroutines PRTINF, PUNINF, PLTINF in order to generate a time trajectory output having the desired format. A flow chart of this subroutine is given in Figure I.4.

I.16 SUBROUTINE PPPOUT

On the basis of the user specified value for the control parameter KOUT2, this subroutine calls one (or more) of the subroutines PUNOUT, PLTOUT in order to generate an output of the dynamic equilibrium values of the system variables. A flow chart of this subroutine is given in figure I.5.

I.17 SUBROUTINE PPRCENT

This subroutine plots a group of four superimposed and individually normalized Omega curves. These curves correspond to four distinct values of any of the following parameters:  $\lambda_{s1}$ ,  $\lambda_{s2}$ ,  $\lambda_{r1}$ ,  $\lambda_{r2}$ ,  $h_0$ , and  $\epsilon$ .

I.18 SUBROUTINE PRCENT

This subroutine computes the normalized tension at dynamic equilibrium corresponding to the various stimulation frequencies stored in the vector PPM.

### I.19 SUBROUTINE PRTINF

This subroutine provides a tabular output of the time trajectories of any specified system variable.

### I.20 SUBROUTINE PUNINF

This subroutine provides a punched card output of the same data printed in subroutine PRTINF.

### I.21 SUBROUTINE PUNOUT

On the basis of the user specified value for the control parameter KOUT2, this subroutine provides a punched card output of the same data printed in subroutine OUTPUT (or a portion of this data).

### I.22 SUBROUTINE QUAD

This subroutine performs a quadratic curve fitting operation on given discrete data. Specifically, it determines the values for the coefficients  $a$ ,  $b$ , and  $c$  in the quadratic function,  $ax^2 + bx + c$ , so that the quadratic function passes through three specific data points. The routine is used to establish the location of extreme values on a given Omega curve.

### I.23 SUBROUTINE REJECT

This subroutine prints the values of the various parameters associated with a negative excursion in any one of the system state variables at dynamic equilibrium.

It also maintains a count of the total number of negative occurrences.

#### I.24 SUBROUTINE SCAN

The data for a particular Omega curve is transferred from the T array into the CAR vector and is scanned for three entries bracketing an extreme value. This information is then passed to QUAD for use in the quadratic curve fitting procedure. A flow chart for the scanning procedure is given in Figure I.6.

#### I.25 SUBROUTINE SETUP

This subroutine computes the values of the flow constants  $K_1$ ,  $K_1'$ ,  $K_2$  and  $K_2'$ , and establishes the numerical values of elements of A matrix. It also establishes the correct value for the forcing function to be applied during the solution of the system equations.

#### I.26 SUBROUTINE SOLVE

This subroutine generates a set of basic solutions to the system equations (see equations 2.17 and 3.13) which correspond to a specially selected set of conditions.

#### I.27 SUBROUTINE STORE

This subroutine stores the values of the system state variable (the elements of E matrix and r vector) when the system equations are solved with specially

selected conditions.

#### I.28 SUBROUTINE TENSON

This subroutine computes the dynamic equilibrium values of tension (see equations 2.27 and 3.20) and stores these values in the array T.

#### I.29 SUBROUTINE TJCTST

This subroutine stores the time trajectories of the system variables,  $M_{s_1}$ ,  $M_{s_2}$ ,  $M_{r_1}$ ,  $M_{r_2}$ , and  $M_r$ , in the array MATCAL. The time points at which data is stored are contained in the vector TIME.

#### I.30 SUBROUTINE TRAJCT

This subroutine generates a set of solutions to equations 2.17 and 3.13 using initial conditions which correspond to dynamic equilibrium conditions.

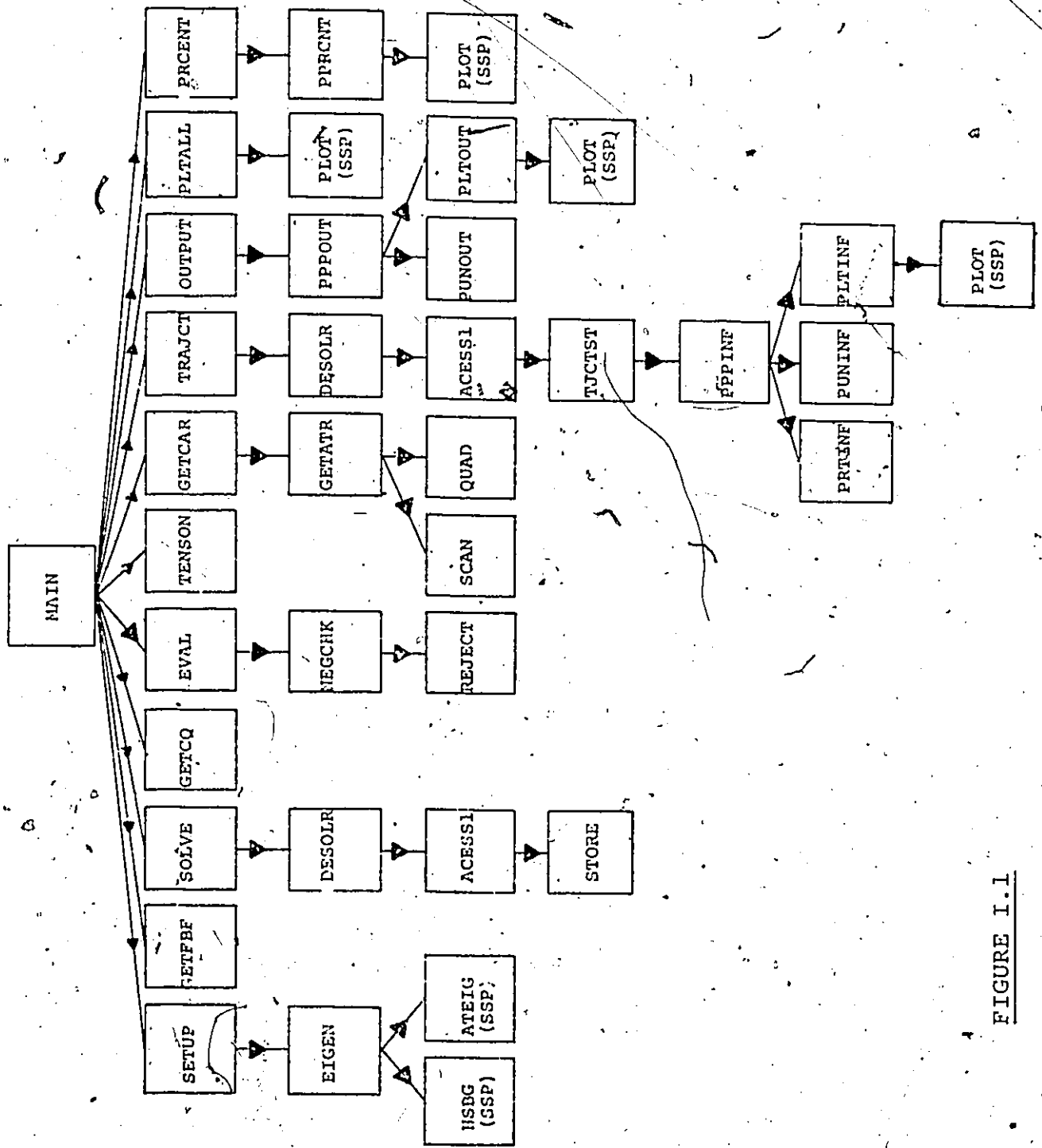


FIGURE I.1

A Schematic diagram of Subprogram Interdependence

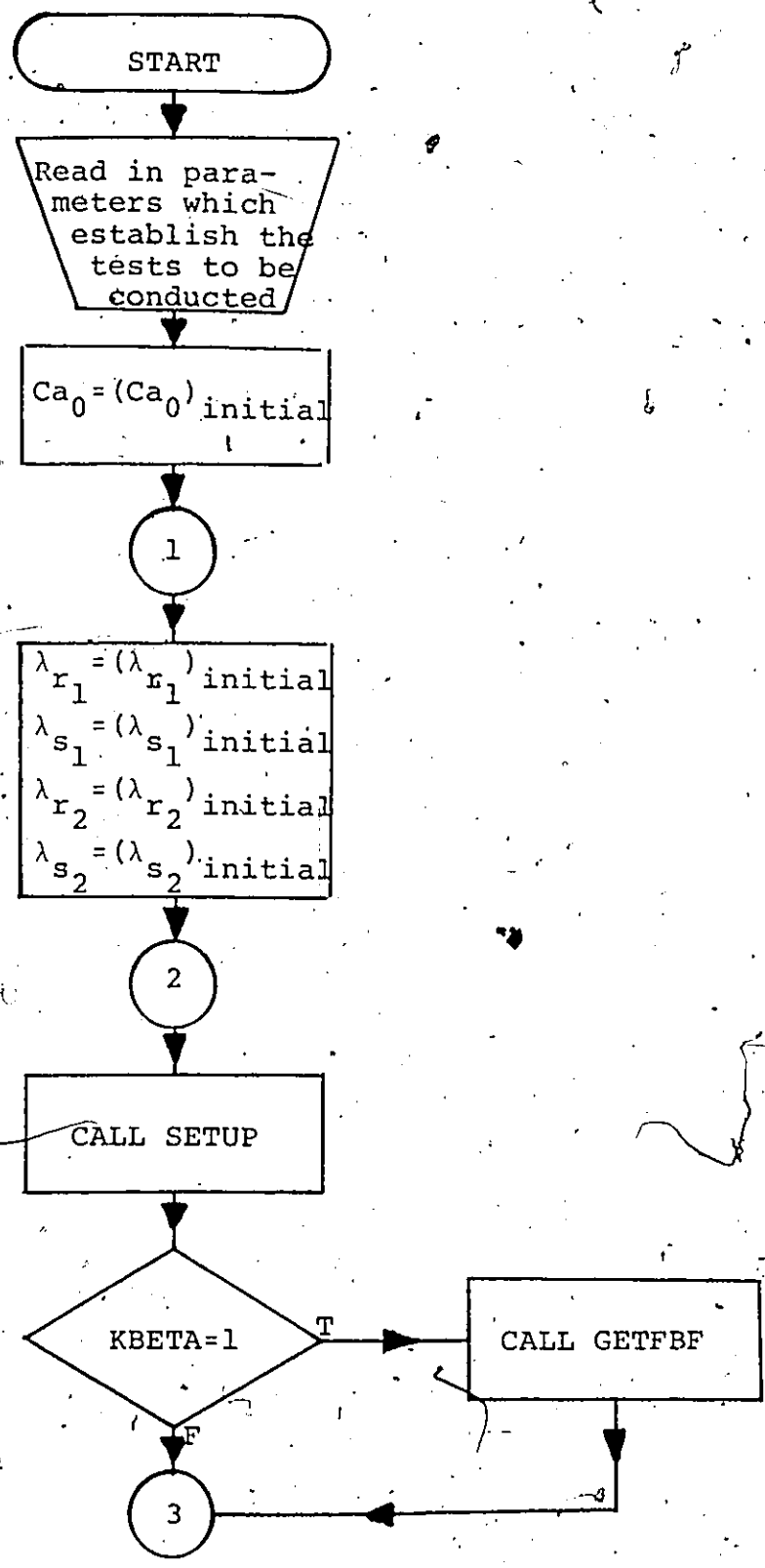


FIGURE I.2

Flow Chart of the Main Program

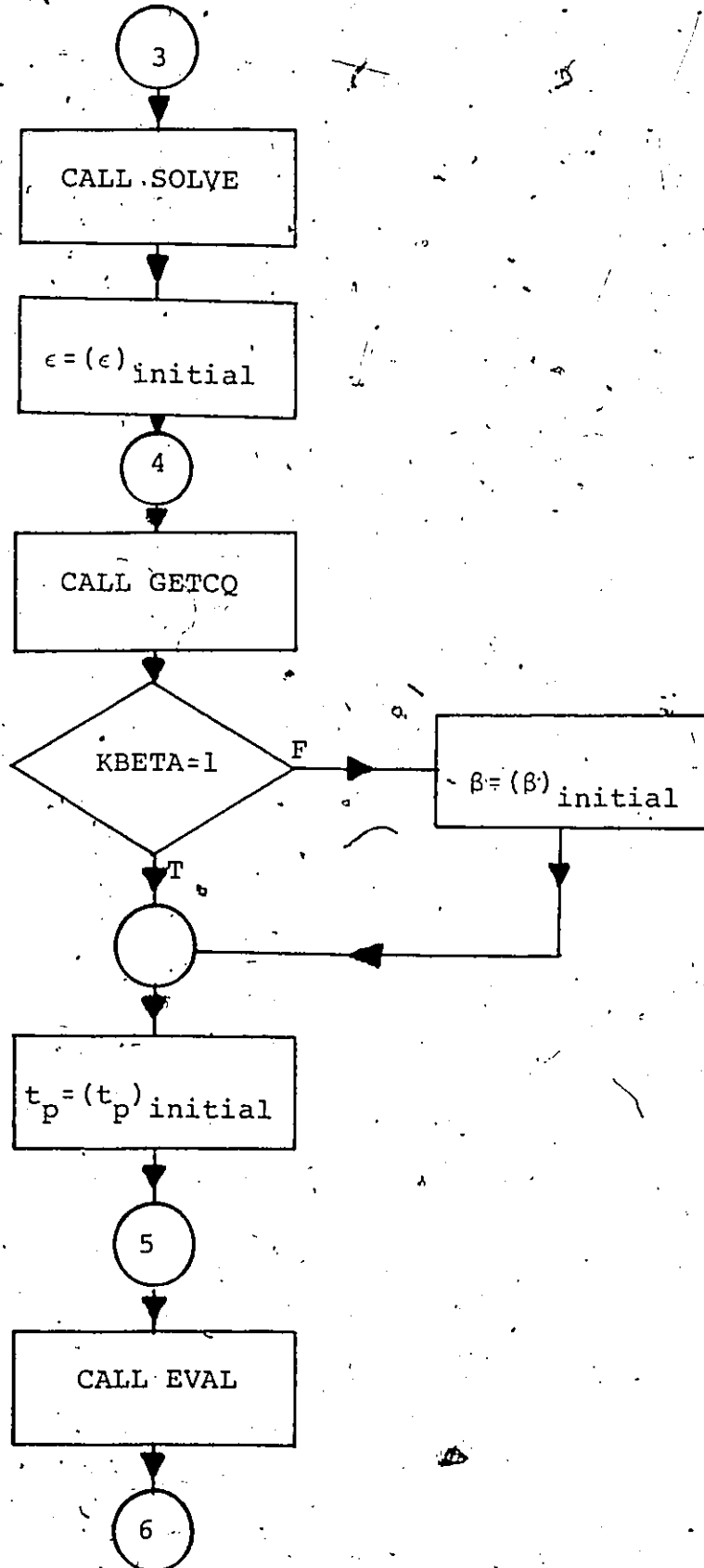


FIGURE I.2 (Cont'd)

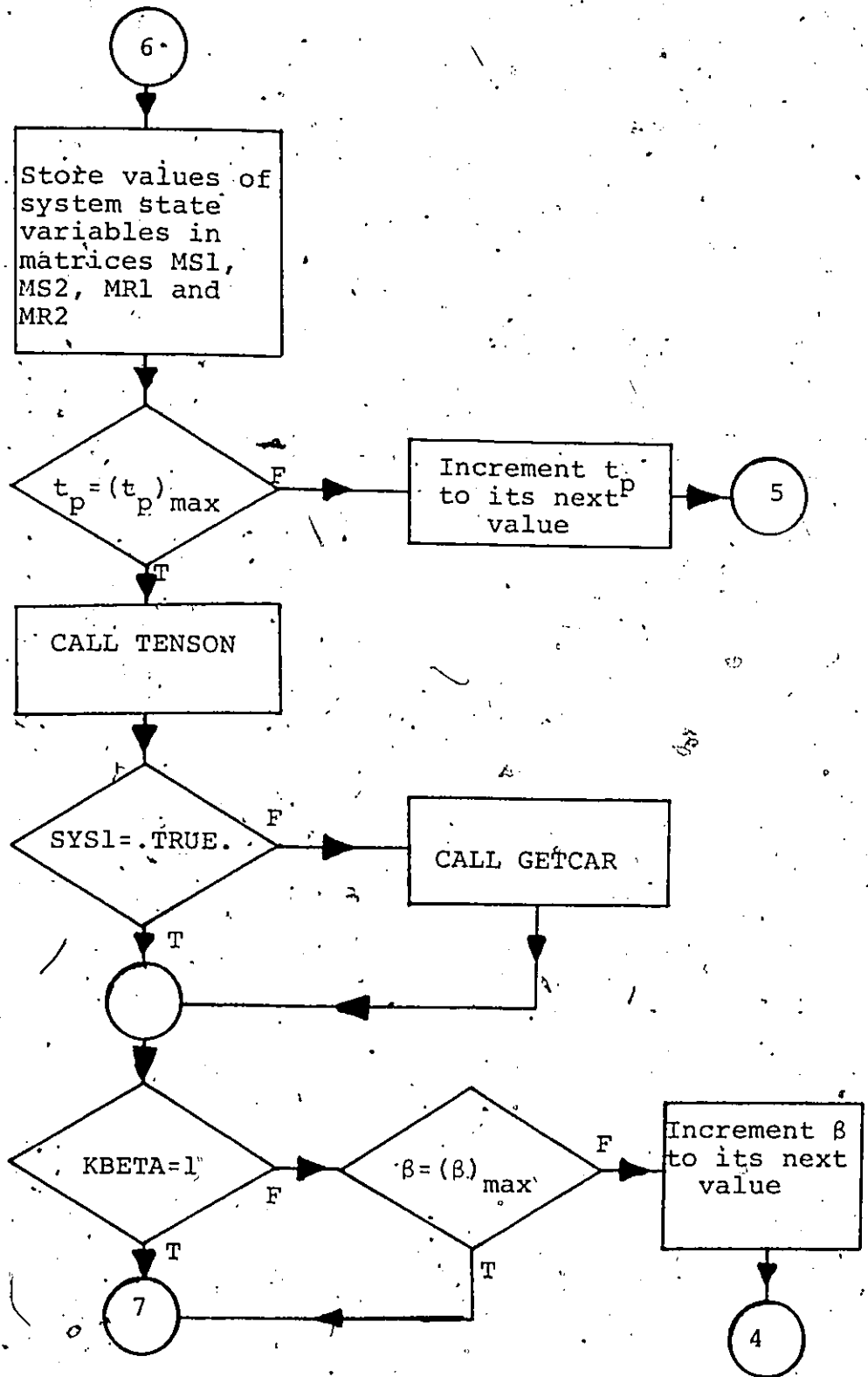


FIGURE I.2 (Cont'd)

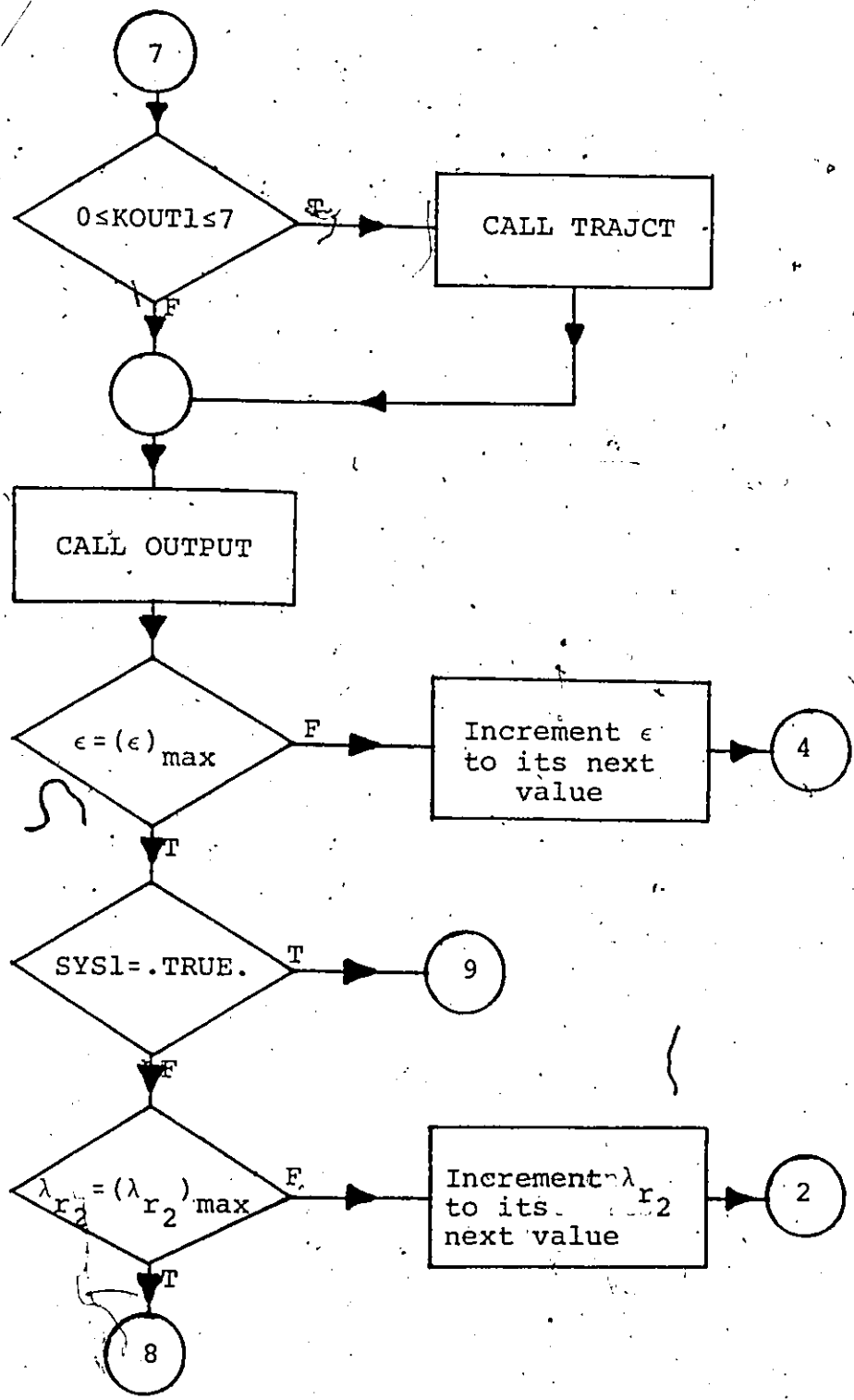


FIGURE I.2 (Cont'd)

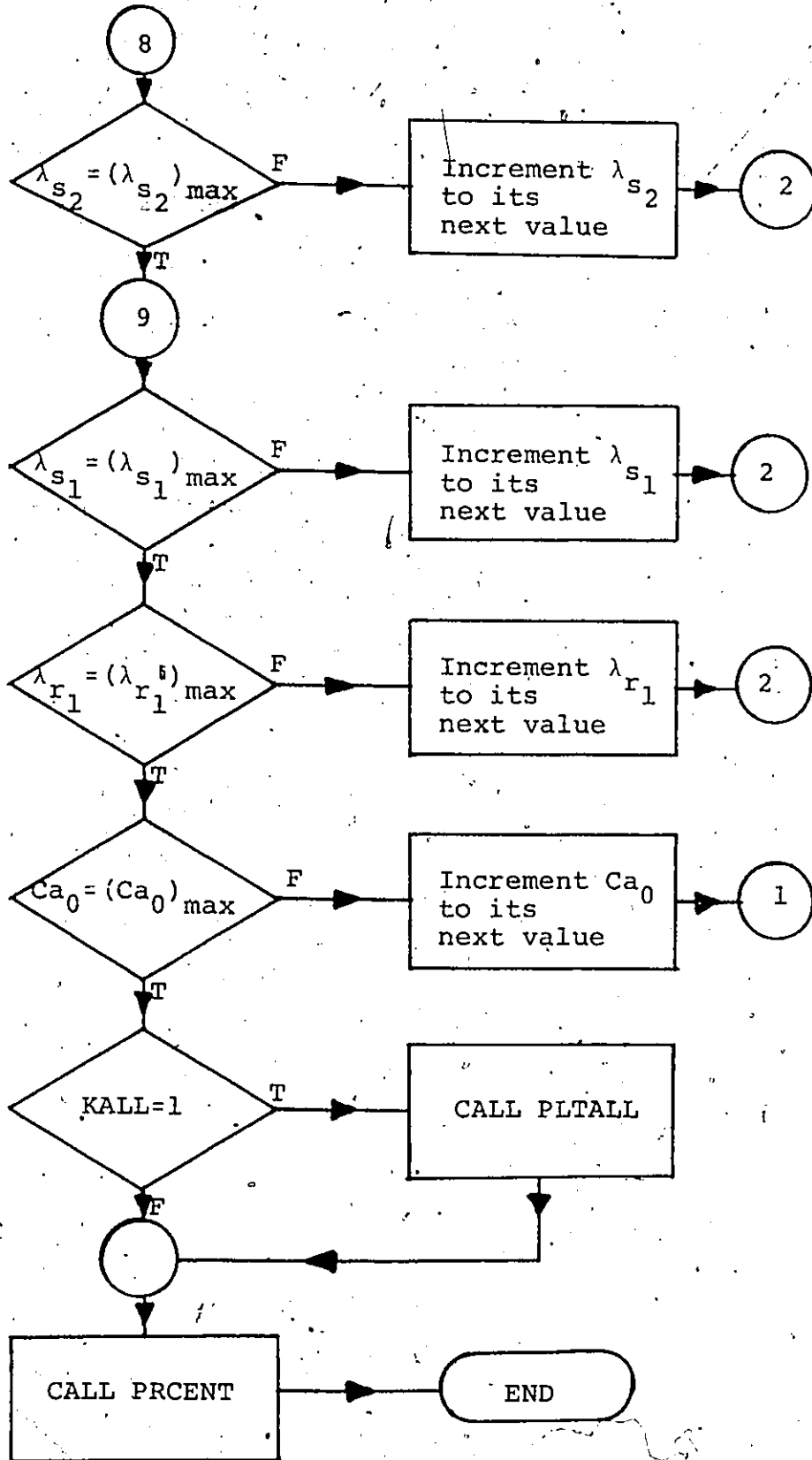


FIGURE I.2 (Cont'd)

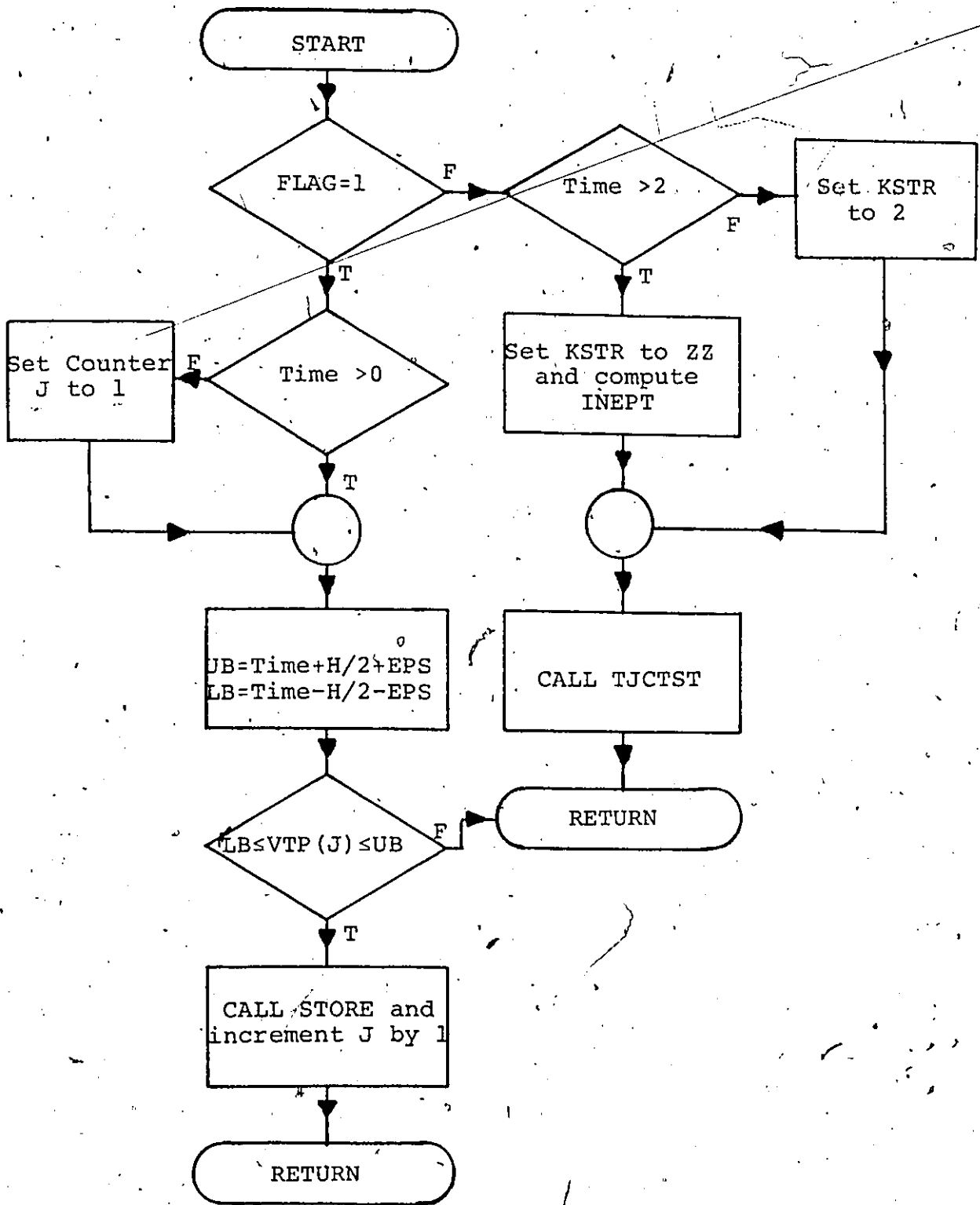


FIGURE I.3.

Flow Chart of the ACCESS1 Subroutine.

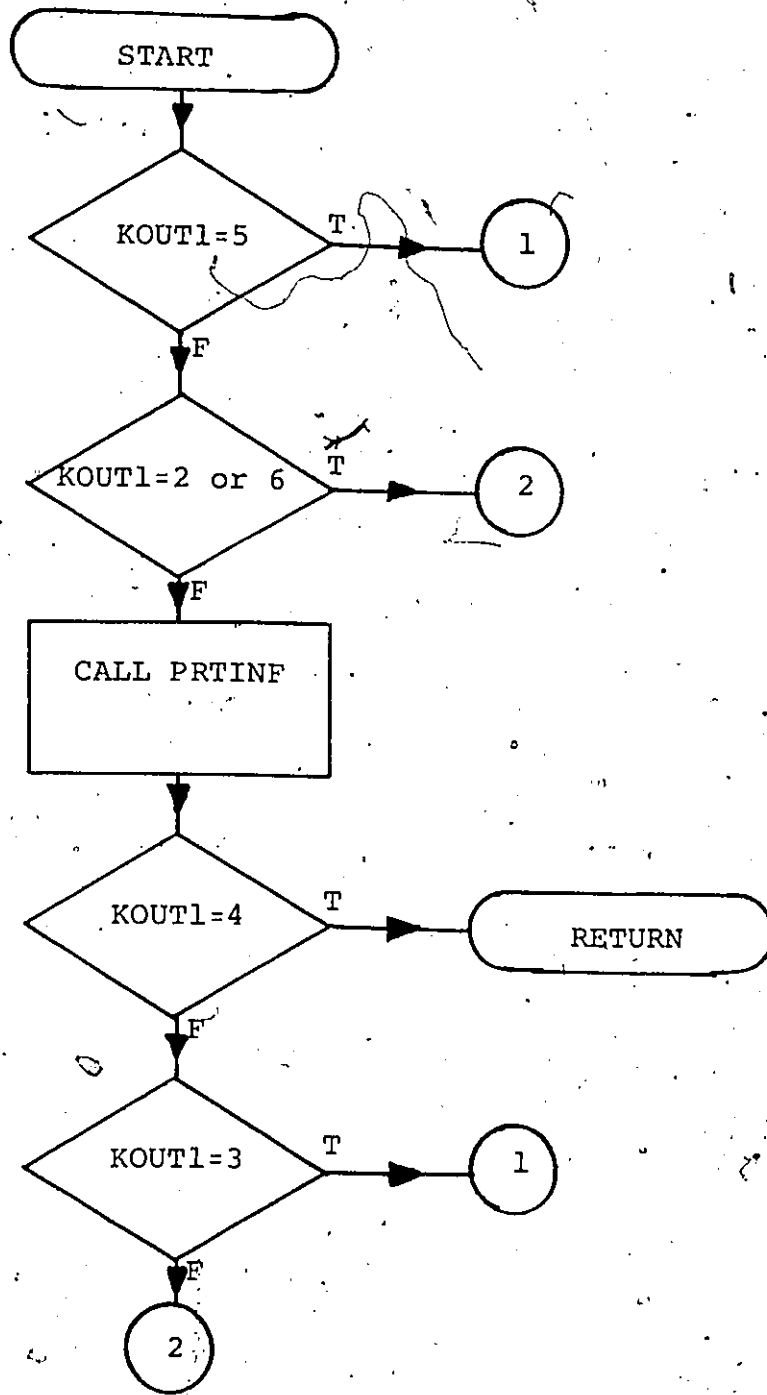


FIGURE I.4

Flow Chart of the PPPINF Subroutine

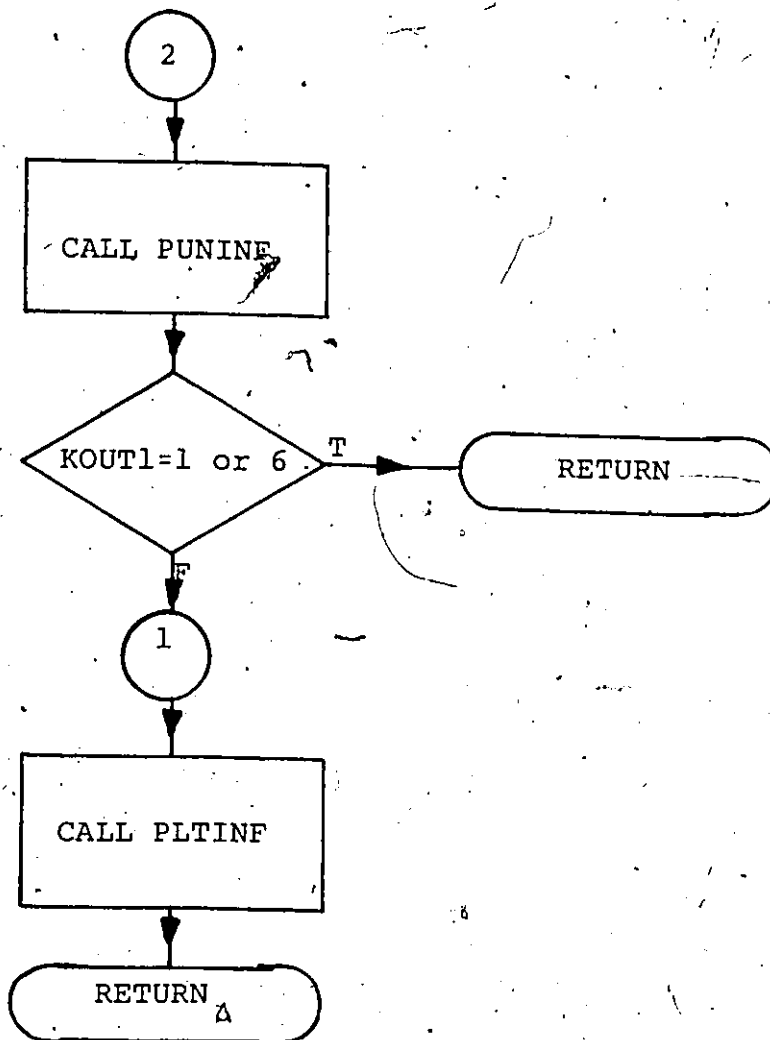


FIGURE I.4 (Cont'd).

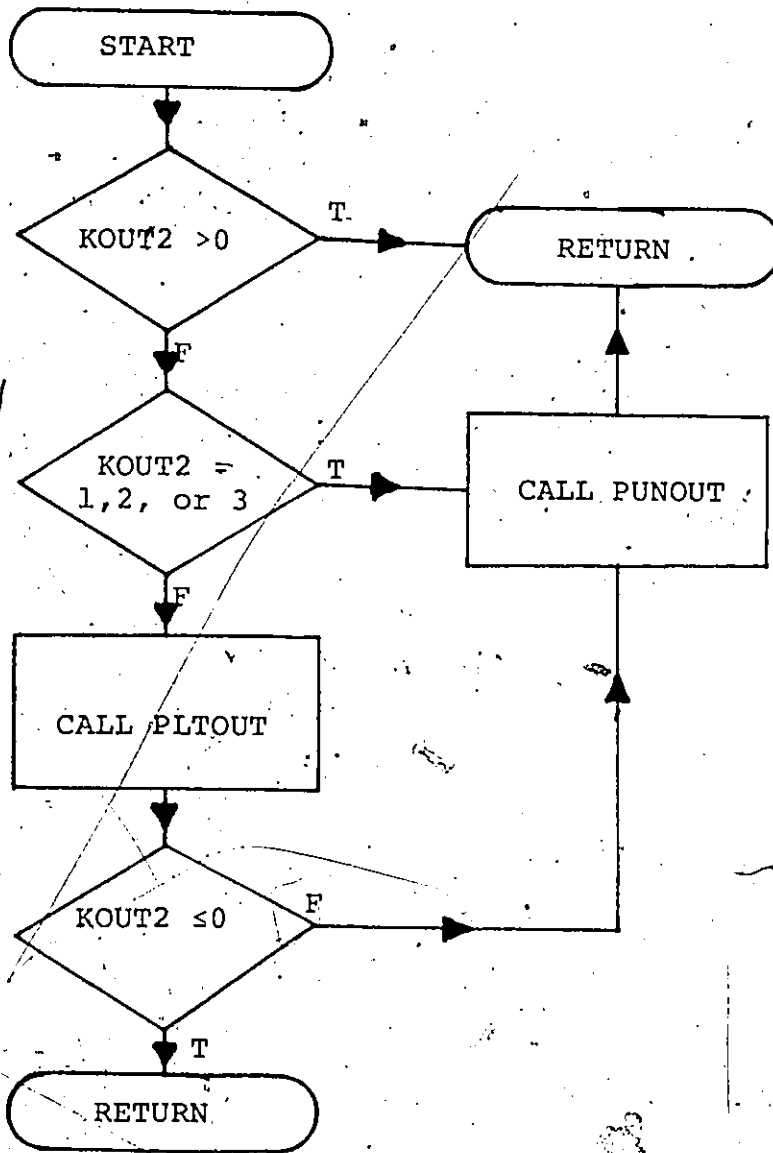


FIGURE I.5

Flow Chart of the PPOUT Subroutine.

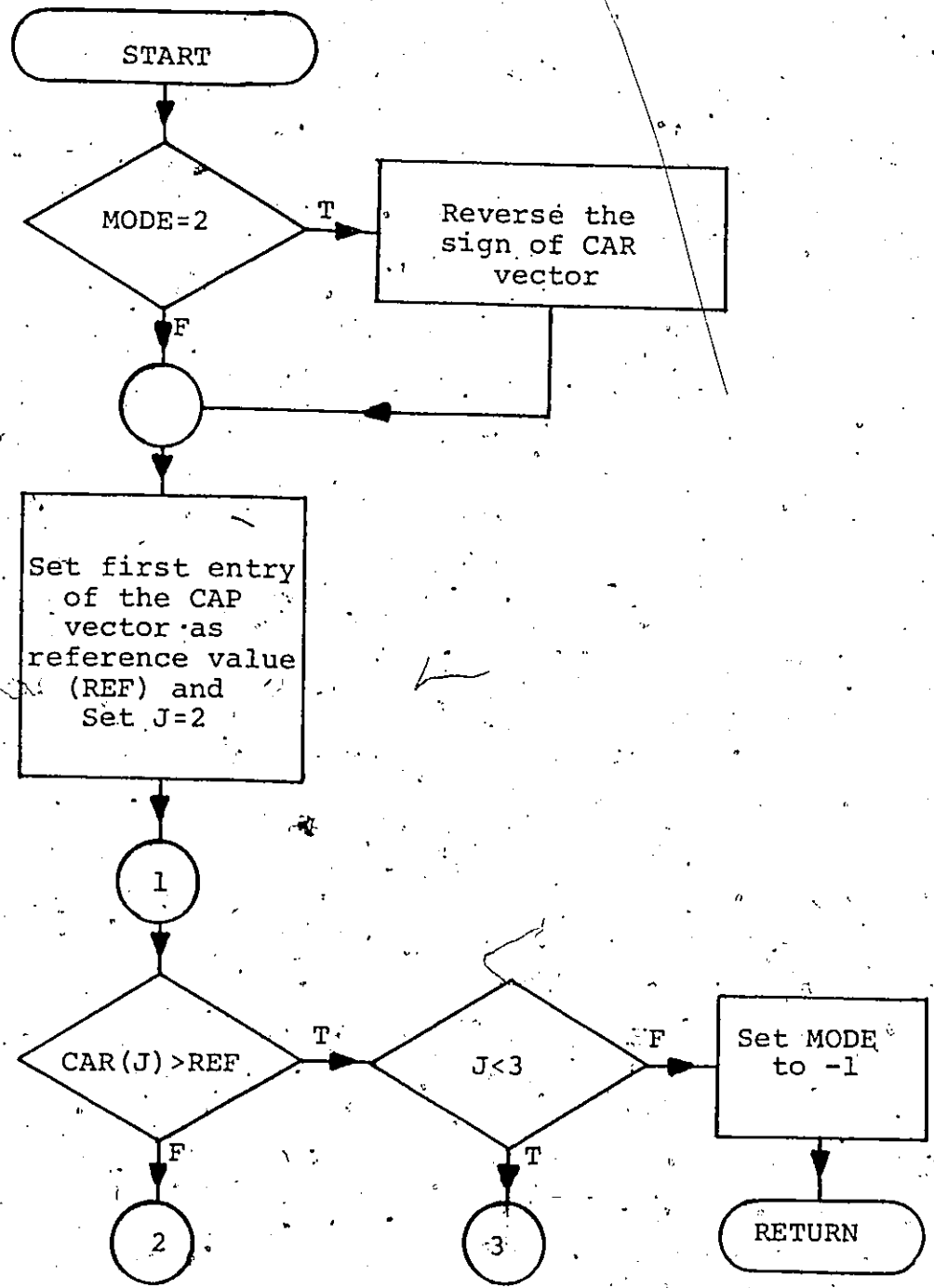


FIGURE I.6

Flowchart of the SCAN subroutine

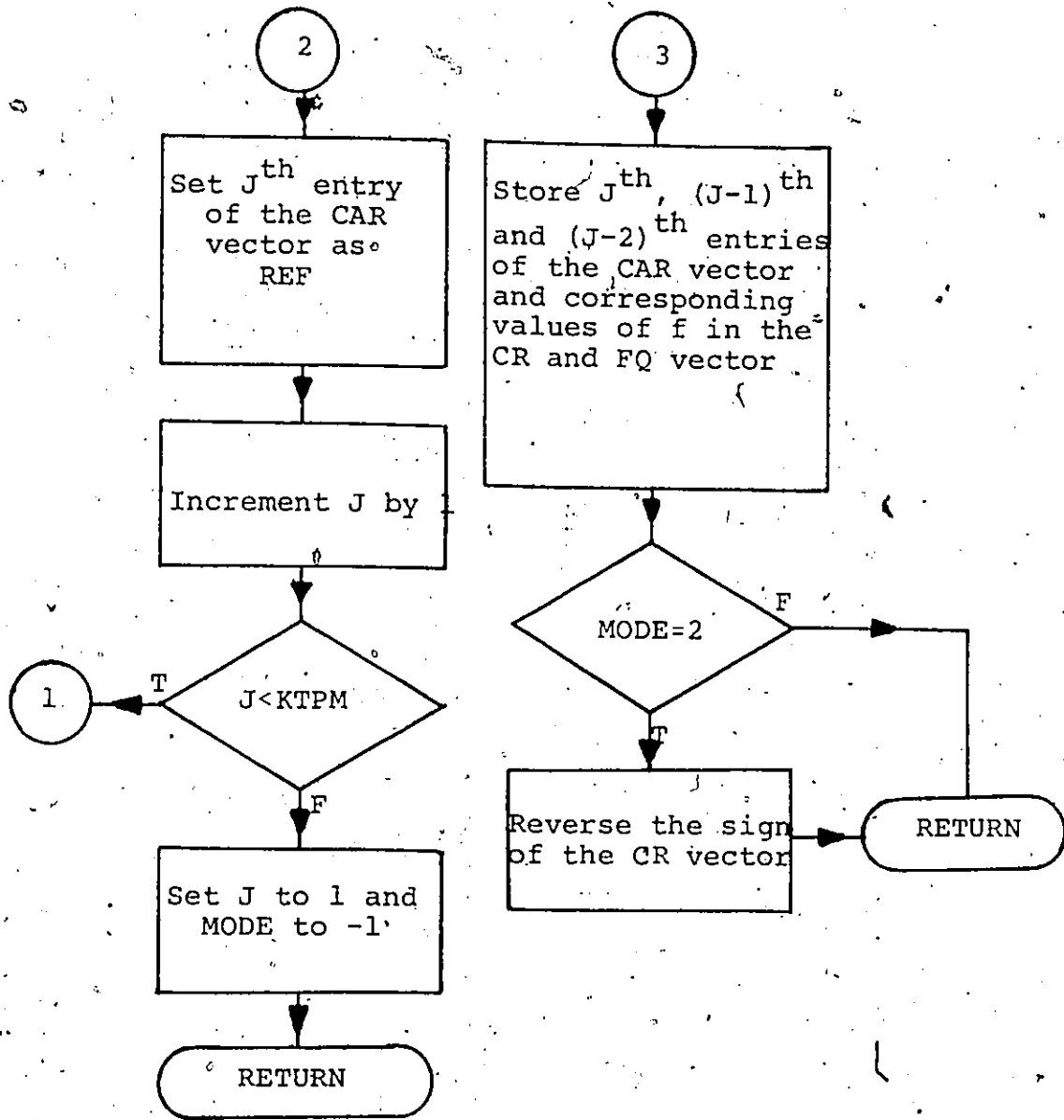


FIGURE I.6 (Cont'd).

DATA SET NAME	DECLARED DIMENSIONS	PURPOSE	SUBROUTINE (S) WHERE CREATED AND/OR ALTERED	SUBROUTINE (S) WHERE PRINCIPAL USE OCCURS
A	(5,5)	Stores the co-efficients of the system state equations (see eq'ns 2.9, 2.10 and eq'n 3.5)	SETUP	EIGEN, RHS
ALPHAM	(4,25)	Stores the computed initial conditions for dynamic equilibrium which correspond to the values of f stored in PPM.	EVAL	TRAJCT
CA	5	Stores the four standard values of $h_0$ ( $[Ca_0]$ ).	MAIN	MAIN
CAR	25	Stores the values of the T array corresponding to the current value of $h_0$ ( $[Ca_0]$ ) and $\beta$ .	GETCAR	SCAN

TABLE I.1

Table of Vectors and Matrices Used in the Program

DATA SET NAME	DECLARED DIMENSIONS	PURPOSE	SUBROUTINE (S) WHERE CREATED AND/OR ALTERED	SUBROUTINE (S) WHERE PRINCIPAL USE OCCURS
CASE	10	Stores the given experimental data for the current value of $h_0$ ([Ca <sub>0</sub> ]).	GETCAR, GETATR	SCAN
CR	3	Stores three entries of the CAR vector for use in the quadratic fitting procedure.	SCAN	QUAD
CSTD	(4,10)	Stores the given experimental data for the four standard values of $h_0$ ([Ca <sub>0</sub> ]) at the values of stimulation frequency stored in F.	GETCAR	GETCAR
DXZ	5	Stores the values of the system initial conditions to initialize the differential equation solving procedure.	SOLVE, TRAJCT, ACCESS1	PCM

TABLE I.1 (cont'd)

DATA SET NAME	DECLARED DIMENSIONS	PURPOSE	SUBROUTINE(S) WHERE CREATED AND/OR ALTERED	SUBROUTINE(S) WHERE PRINCIPAL USE OCCURS
EMAT1	(4,25)	Stores the values of $E_{11}(t)$ , $E_{21}(t)$ , $E_{12}(t)$ , and $E_{22}(t)$ (for $t=t_k$ , $k=1,2,\dots,25$ , where $t_k=60/f_k$ and $f_k$ is the $k$ th entry of PPM).	STORE	EVAL, NEGCHK
EMAT2	(4,25)	Stores the values of $E_{33}(t)$ , $E_{43}(t)$ , $E_{34}(t)$ and $E_{44}(t)$ (for $t=t_k$ , $k=1,2,\dots,25$ , where $t_k=60/f_k$ and $f_k$ is the $k$ th entry of PPM).	STORE	EVAL, NEGCHK
EXPF	5	Stores the values of exponent factors (see eq'n 2.16).	MAIN	MAIN

TABLE I.1 (cont'd)

DATA SET NAME	DECLARED DIMENSIONS	PURPOSE	SUBROUTINE(S) WHERE CREATED AND/OR ALTERED	SUBROUTINE(S) WHERE PRINCIPAL USE OCCURS
F	10	Stores the stimulation frequencies (pulses/min.) at which experimental tension data is available.	GETCAR, GETATR	SCAN
FQ	3	Stores the three values of stimulation frequency which correspond to the three values of tension stored in the CR vector.	SCAN	QUAD
MATCAL	(5,100)	Stores the values of various system state variables at the times stored in the TIME vector.	TJCTST	PRTINF, PUNINF, PLTINF, TENSION
MR	(5,25)	Stores dynamic equilibrium values of $M_I(t)$ ( $Ca_I$ ) at the frequencies contained in PPM which correspond to the values of $\beta$ stored in VB.	MAIN	TENSION, OUTPUT, PUNOUT

TABLE I.1 (cont'd)

DATA SET NAME	DECLARED DIMENSIONS	PURPOSE	SUBROUTINE (S) WHERE CREATED AND/OR ALTERED	SUBROUTINE (S) WHERE PRINCIPAL USE OCCURS
MR1	(5,25)	Stores dynamic equilibrium values of $M_{I_1}(t)$ ( $Ca_{I_1}$ ) at the frequencies contained in PPM which correspond to the values of $\beta$ stored in VB.	MAIN	OUTPUT, PUNOUT, PLTOUT
MR2	(5,25)	Stores dynamic equilibrium values of $M_{I_2}(t)$ ( $Ca_{I_2}$ ) at the frequencies contained in PPM which correspond to the values of $\beta$ stored in VB.	MAIN	OUTPUT, PUNOUT, PLTOUT
MS1	(5,25)	Stores dynamic equilibrium values of $M_{S_1}(t)$ ( $Ca_{S_1}$ ) at the frequencies contained in PPM which correspond to the values of $\beta$ stored in VB.	MAIN	OUTPUT, PUNOUT

TABLE I.1 (cont'd)

DATA SET NAME	DECLARED DIMENSIONS	PURPOSE	SUBROUTINE(S) WHERE CREATED AND/OR ALTERED	SUBROUTINE(S) WHERE PRINCIPAL USE OCCURS
MS2	(5,25)	Stores dynamic equilibrium values of $M_s(t)$ ( $Ca_s$ ) at the frequencies contained in PPM which correspond to the values of $\beta$ stored in VB.	MAIN	OUTPUT, PUNOUT
PPM	25	Stores the values of stimulation frequencies (pulses/min,) which are of interest.	MAIN	GETCQ, SCAN, OUTPUT, PUNOUT, PLTOUT, MAIN
RMAT	(4,25)	Stores the values of $r_1(t)$ , $r_2(t)$ , $r_3(t)$ , and $r_4(t)$ (for $t=t_k$ , $k=1,2,3,\dots,25$ , where $t_k=60/f_k$ , and $f_k$ is the $k$ th entry of PPM.	STORE	EVAL, NEGCHK

TABLE I.1 (cont'd)

DATA SET NAME	DECLARED DIMENSIONS	PURPOSE	SUBROUTINE (S) WHERE CREATED AND/OR ALTERED	SUBROUTINE (S) WHERE PRINCIPAL USE OCCURS
T	(5,5,25)	Stores the dynamic equilibrium values of tension at the frequencies contained in PPM which correspond to the values of $\beta$ stored in VB and to one other Parameter (One of $\lambda_{s1}, \lambda_{s2}, \lambda_{r1}, \lambda_{r2}, \epsilon, \text{or } h_0$ ).	TENSON	OUTPUT, PUNOUT, PLTOUT, PLTALL
TIME	100	Stores the values of time at which the values of various system variables are stored in MATCAL.	TJCTST	PRTINF, PUNINF, PLTINF
TMR	(5,5,25)	Stores data similar to that in T except each curve is individually normalized.	PRCENT	OUTPUT, PUNOUT, PPRCNT

TABLE I.1 (cont'd)

DATA SET NAME	DECLARED DIMENSIONS	PURPOSE	SUBROUTINE (S) WHERE CREATED AND/OR ALTERED	SUBROUTINE (S) WHERE PRINCIPAL USE OCCURS
VATRB	(6,8)	Stores certain numeric Parameters of the Omega responses corresponding to the values of $\beta$ stored in VB, and the given experimental data.	GETATR	GETCAR, OUTPUT
VB	5	Stores the values of the feed-back factor, $\beta$ .	MAIN	MAIN, OUTPUT PUNOUT
VLAMRF	5	Stores the values of the recovery time constant, $\lambda_{r1}$ .	MAIN	MAIN, SETUP
VLAMRS	5	Stores the values of the recovery time constant, $\lambda_{r2}$ .	MAIN	MAIN, SETUP
VLAMSF	5	Stores the values of the decay time constant, $\lambda_{s1}$ .	MAIN	MAIN, SETUP

TABLE I.1 (cont'd)

DATA SET NAME	DECLARED DIMENSIONS	PURPOSE	SUBROUTINE (S) WHERE CREATED AND/OR ALTERED	SUBROUTINE (S) WHERE PRINCIPAL USE OCCURS
VLAMSS	5	Stores the values of the decay time constant, $\lambda$ s <sup>2</sup>	MAIN	MAIN, SETUP
VC	25	Stores the values of stimulus factor, C, which correspond to the stimulation frequencies stored in PPM.	GETCQ	OUTPUT, PUNOUT, PLTOUT
VEERROR	(5,8)	Stores the percentage error between the computed and experimental data corresponding to the values of $\beta$ stored in VB.	GETCAR	OUTPUT
VQ	25	Stores the values of $Q_h$ (eq'n 2.16) which correspond to the stimulation frequencies stored in PPM.	GETCQ	EVAL

TABLE I.1 (cont'd)

DATA SET NAME	DECLARED DIMENSIONS	PURPOSE	SUBROUTINE(S) WHERE CREATED AND/OR ALTERED	SUBROUTINE(S) WHERE PRINCIPAL USE OCCURS
VP	6	Stores the maximum, minimum, starting and final values of tension along with the frequencies at which maximum and minimum of tension occurs.	GETATR	GETATR
VTP	25	Stores the interpulse interval length corresponding to the stimulation frequencies stored in PPM.	MAIN	ACCESSI, REJECT

TABLE I.1 (cont'd)

SCALAR	PURPOSE	SUBPROGRAM WHERE SCALAR IS INITIALIZED OR ALTERED	SUBPROGRAMS WHERE PRINCIPAL USE OCCURS
ALPHA1	Value of $\alpha_1$ , an initial condition for dynamic equilibrium	EVAL	NEGCHK
ALPHA3	Value of $\alpha_3$ , an initial condition for dynamic equilibrium	EVAL	NEGCHK
B	The constant component of pump flow, $P_R(t)$	SETUP	OUTPUT, REJECT, TENSION
BC	Exponent factor of the $\beta$ expression (see eq'n 3.25)	SETUP	GETFBF
BETA	The feed-back factor, $\beta$	GETFBF	MAIN, EVAL
CAO	Current value of $h_0$ ( $[Ca_0]$ )	MAIN	GETCQ, OUTPUT, REJECT
CAOMIN	The smallest entry stored in CA vector	MAIN	SETUP
CN	Nominal value of stimulus factor, (0.1)	SETUP	GETCQ

TABLE I.2

Table of Scalars Used in the Program

SCALAR	PURPOSE	SUBPROGRAM WHERE SCALAR IS INITIALIZED OR ALTERED	SUBPROGRAMS WHERE PRINCIPAL USE OCCURS
F	The frequency at which an extreme value (i.e. a minimum or a maximum value) of the Omega curve occurs	QUAD	GETATR
FLAG	FLAG is set to 0 to indicate that the system eq'ns are being solved from a set of initial conditions which correspond to dynamic equilibrium. For a solution from any other set of initial conditions, FLAG is set to 1.	SOLVE, TRAJCT	ACCESS1
K1	The flow constant between tanks $T_s$ or $T_{s1}$ and $T_r$ or $T_{r1}$	SETUP	OUTPUT
K2	The flow constant between $T_0$ and $T_s$ or $T_{s1}$	SETUP	TENSON
K1P	The flow constant between tanks $T_{s1}$ and $T_{r1}$	SETUP	OUTPUT

TABLE I.2 (CONT'D)

SCALAR	PURPOSE	SUBPROGRAM WHERE SCALAR IS INITIALIZED OR ALTERED	SUBPROGRAMS WHERE PRINCIPAL USE OCCURS
K2P	The flow constant between tanks $T_0$ and $T_{S1}$	SETUP	SETUP
KALL	KALL is set to 1 to indicate that a plot of the Omega responses for different values of some parameters is desired; otherwise it is set to 0	MAIN	PRCENT
KB	Pointer to the component of VB which contains the current value of $\beta$ .	MAIN	MAIN, EVAL, GETATR, OUTPUT, REJECT, SETUP, TENSION
KBETA	KBETA is set to 1 to indicate that $\beta$ is $h_0$ dependent, otherwise it is set to 0	MAIN	MAIN
KBM	Number of values of $\beta$ stored in VB	MAIN	MAIN, ACCESS1, EVAL, GETATR, OUTPUT, PLTALL, PRCENT
KBS	Starting value assigned to pointer KB	MAIN	MAIN, OUTPUT, PLTALL, PRCENT
KCA	Pointer to the component of CA which contains the present value of $h_0$	MAIN	MAIN, GETCAR, OUTPUT, PLTINF

TABLE I.2 (CONT'D)

SCALAR	PURPOSE	SUBPROGRAM WHERE SCALAR IS INITIALIZED OR ALTERED	SUBPROGRAMS WHERE PRINCIPAL USE OCCURS
KCAM	Number of values of $h_0$ stored in CA	MAIN	MAIN, ACCESS1, EVAL, GETCAR, OUTPUT, REJECT,
KLRF	Pointer to the component of VLAMRF which contains the present value of $\lambda_{r1}$	MAIN	MAIN, OUTPUT, SETUP
KLRFM	Number of values of $\lambda_{r1}$ stored in VLAMRF	MAIN	MAIN, OUTPUT
KLRS	Pointer to the component of VLAMRS which contains the present value of $\lambda_{r2}$	MAIN	MAIN, SETUP
KLRSM	Number of values of $\lambda_{r2}$ stored in VLAMRS	MAIN	MAIN
KLSSF	Pointer to the component of VLAMSF which contains the present value of $\lambda_{s1}$	MAIN	MAIN, SETUP
KLSPM	Number of values of $\lambda_{s1}$ stored in VLAMSF	MAIN	MAIN
KLSS	Pointer to the component of VLAMSS which contains the present value of $\lambda_{s2}$	MAIN	MAIN, SETUP

TABLE I.2 (CONT'D)

SCALAR	PURPOSE	SUBPROGRAM WHERE SCALAR IS INITIALIZED OR ALTERED	SUBPROGRAMS WHERE PRINCIPAL USE OCCURS
KLSSM	Number of values of $\lambda_s^2$ stored in VLAMSS	MAIN	MAIN
KOUT1	KOUT1 is a parameter whose value indicates the type of output (i.e. print, punch, or plot) for time trajectories. The significance of the various values is given at the beginning of the program listings.	MAIN	PPPIPE
KOUT2	A parameter whose value indicates the type of output for dynamic equilibrium values of system variables of interest. The significance of the various values is given at the beginning of the program listing.	MAIN	PPPOUT
KSTMF	Pointer to the component of VEXPF which contains the present value of $\epsilon$ .	MAIN	MAIN, OUTPUT
KSTMFM	Number of values of $\epsilon$ stored in VEXPF.	MAIN	MAIN, OUTPUT

TABLE I.2 (CONT'D)

SCALAR	PURPOSE	SUBPROGRAM WHERE SCALAR IS INITIALIZED OR ALTERED	SUBPROGRAMS WHERE PRINCIPAL USE OCCURS
KTP	Pointer to the component of PPM which contains the present value of stimulation frequency.	MAIN	MAIN, EVAL, NEGCHK, OUTPUT, REJECT, TRAJCT
KTPM	Number of values of stimulation frequency, stored in PPM.	MAIN	MAIN, ACCESS1, EVAL, GETATR, GETCAR, GETCQ, OUTPUT, PLTOUT, REJECT, SETUP, TENSION
KVAR	Pointer to the components of T which are currently being used.	MAIN	OUTPUT, PLTOUT, PRCENT, TENSION
LAMR1	Current value of recovery time constant, $\lambda_{r1}$	SETUP	OUTPUT, REJECT, SETUP
LAMR2	Current value of recovery time constant, $\lambda_{r2}$	SETUP	OUTPUT, REJECT, SETUP
LAMS1	Current value of decay time constant, $\lambda_{s1}$	SETUP	OUTPUT, REJECT, SETUP
LAMS2	Current value of decay time constant, $\lambda_{s2}$	SETUP	OUTPUT, REJECT, SETUP

TABLE I.2 (CONT'D)

SCALAR	PURPOSE	SUBPROGRAM WHERE SCALAR IS INITIALIZED OR ALTERED	SUBPROGRAMS WHERE PRINCIPAL USE OCCURS
MODE	A parameter which governs the type of computation to be carried out in QUAD.	GETATR, SCAN	GETATR, QUAD
N	Number of system equations.	SETUP	SETUP, SOLVE, STORE, TJECTST, TRAJCT
NEGCNT	A counter which counts the number of occurrences of negative values for $h_s$ or $h_r$ or $h_{r1}$ or $h_{r2}$ .	MAIN	OUTPUT
SYS1	SYS1 is set to .TRUE. to indicate that system 1 is under study, otherwise SYS1 is set to .FALSE..	MAIN	EIGEN, EVAL, NEGCHK, OUTPUT, PLTINF, PLTOUT, REJECT, RHS, SOLVE, STORE, TJECTST
UDUM	Dummy value of forcing function.	SOLVE	RHS, STORE
VALU	Stores an extreme value of the Omega curve.	QUAD	GETATR
VR1	Area of cross-section of tank T <sub>1</sub> .	SETUP	OUTPUT, SETUP, TENSION

TABLE I.2 (CONT'D)

SCALAR	PURPOSE	SUBPROGRAM WHERE SCALAR IS INITIALIZED OR ALTERED	SUBPROGRAMS WHERE PRINCIPAL USE OCCURS
VR2	Area of cross-section of tank $T_{r2}$ .	SETUP	OUTPUT, SETUP, TENSION
VS1	Area of cross-section of tank $T_{s1}$ .	SETUP	OUTPUT, SETUP
VS2	Area of cross-section of tank $T_{s2}$ .	SETUP	OUTPUT, SETUP
ZZ	Number of data points to be skipped while storing the time trajectories of various system variables.	TRAJCT	ACCESS1

TABLE I.2 (CONT'D)

NAME OF BLOCK	VARIABLES WHICH FORM THE BLOCK	SUBPROGRAMS WHERE VARIABLE VALUES ARE INITIALIZED OR ALTERED	SUBPROGRAMS USING BLOCK
ATTVEC	VATBTR	GETATR	OUTPUT
BIAS	B	SETUP	OUTPUT, REJECT, TENSION
BETAGP	KBS, KBETA	MAIN	OUTPUT, PLTALL, PRCENT, PUNOUT
CADETL	MATCAL, TIME	TJCTST	PLTINF, PRNTNF, PUNINF
COEF	A, U1, U2, UDUM	SETUP	RHS, SOLVE, STORE
CONSTM	KCAM, KBM, KTPM, KSTMF, KLRFM, KLSEFM, KLSSM, KLRS	MAIN	ACCESS 1, EVAL, GETCQ, OUTPUT, PLTALL, PLTOUT, PERCENT, PUNOUT, REJECT, TENSION
CONSTS	KTP, KB, KLRF, KCA, KSTMF, KLSF, KLSS, KLRS	MAIN	EVAL, NEGCHK, OUTPUT, PLTINF, PUNOUT, REJECT, SETUP
CVECT	VC, VQ	GETCQ	EVAL, OUTPUT, PLTOUT, PUNOUT
DECOND	ALPHAM	EVAL	TRAJECT

TABLE I.3

Summary of COMMON Blocks Used

NAME OF BLOCK	VARIABLES WHICH FORM THE BLOCK	SUBPROGRAMS WHERE VARIABLE VALUES ARE INITIALIZED OR ALTERED	SUBPROGRAMS USING BLOCK
ER	EMAT1, EMAT2, RMAT	STORE	EVAL, NEGCHK
ERRVEC	VERROR	GETCAR	OUTPUT
EXPBC	BC	SETUP	GETFBF
FBF	BETA	GETFBF	MAIN, PUNOUT
FLOWCT	K1, K1P, K2, K2P	SETUP	OUTPUT, TENSION
INTGER	N	SETUP	SOLVE, STORE, TJCTST, TRAJCT
NEGSUM	NEGCNT	MAIN, REJECT	OUTPUT
OUTPT	FLAG, ZZ	SOLVE, TRAJCT	ACESS1
OUTPAR	KOUT1, KOUT2	MAIN	OUTPUT, PPPINF, PPOUT, PUNOUT
OUTCAL	CAO, CN, CAOMIN	MAIN, SETUP	GETCQ, GETFBF, OUTPUT, PUNOUT
PERT	TMR	PRCENT	OUTPUT, PPRCNT, PUNOUT
PRTPTS	INFPT	ACESS1	PLTINF, PRTINF, PUNINF, TJCTST

TABLE I.3 (CONT'D)

NAME OF BLOCK	VARIABLES WHICH FORM THE BLOCK	SUBPROGRAMS WHERE VARIABLE VALUES ARE INITIALIZED OR ALTERED	SUBPROGRAMS USING BLOCK
PRTRW	M	PRTINF	PUNINF, TJCTST
RST	T	TENSION	OUTPUT, PLTALL, PLFOUT, PRCENT, PUNOUT
STTVAR	MR1, MR2, MR, MS1, MS2	MAIN	OUTPUT, PLFOUT, PUNOUT, TENSION
SYSTEM	SYS1	MAIN	EIGEN, EVAL, NEGCHK, OUTPUT, PLTINF, PLFOUT, PRTINF, PUNOUT, REJECT, RHS, SETUP, SOLVE, STORE, TJCTST
TCONST	LAMR1, LAMR2, LANS1, LAMS2	SETUP	OUTPUT, PUNOUT, REJECT
TIMES	VTP	MAIN	ACCESS1, OUTPUT, REJECT
VAR	KVAR	MAIN	OUTPUT, PLFOUT, PRCENT, PUNOUT, TENSION
VOLMS	VR1, VR2, VS1, VS2	SETUP	OUTPUT, TENSION
WDVICE	KWD, KWDD	MAIN	EIGEN, OUTPUT, PRTINF, PUNINF, PLFOUT, QUAD, REJECT, SETUP, TJCTST

TABLE I.3 (CONT'D)

APPENDIX 2

LISTING OF THE FORTRAN PROGRAM

TITLE

SIMULATION AND MODELLING

THE PAPILLARY MUSCLE (CARDIAC MUSCLE) OF THE RAT UNDER THE EFFECTS OF ELECTRICAL PULSE TRAIN AND OUTSIDE CALCIUM CONCENTRATION.

THIS PROGRAM DESIGNED FOR STUDYING THE DYNAMIC BEHAVIOUR OF THE PAPILLARY MUSCLE OF THE RAT CAN COMPUTE THE INFLUENCES OF :

- 1. OUTSIDE CALCIUM CONCENTRATION IN THE EXTERNAL FLUID.
- 2. FREQUENCY OF STIMULATION (1 PULSE PER MIN. TO 180 PULSES PER MIN.).
- 3. RECOVERY TIME CONSTANT OF CAR1.
- 4. RECOVERY TIME CONSTANT OF CAR2 (ONLY IN DUAL SUBSYSTEM MODEL).
- 5. DECAY TIME CONSTANT OF CAS1.
- 6. DECAY TIME CONSTANT OF CAR2 (ONLY IN DUAL SUBSYSTEM MODEL).
- 7. EXPONENT FACTOR.
- 8. THE FEED-BACK FACTOR.

ON THE OMEGA RESPONSE (TENSION-FREQUENCY RELATION) OF THE CARDIAC MUSCLE

THIS PROGRAM CAN ALSO COMPUTE THE TIME TRAJECTORIES OF VARIOUS SYSTEM STATE VARIABLES.

THIS PROGRAM CAN OUTPUT THE REQUESTED INFORMATION ON :

- 1) LINE PRINTER, 2) COMPUTER CARDS, 3) PLOTTER (FOR PLOTTING).

\*\*\*\*\*  
 \* OUTPUT MODE CONTROL PARAMETERS \*  
 \*\*\*\*\*

KOUT1 IS A PARAMETER WHICH CONTROLS THE OUTPUT MODE OF TIME TRAJECTORIES AND ITS VARIOUS VALUES HAVE THE FOLLOWING SIGNIFICANCE :

VALUE OF KOUT1	OUTPUT MODE
NEGATIVE	NONE
0	LINE PRINTER, CARD PUNCH, PLOTTER
1	LINE PRINTER, CARD PUNCH
2	CARD PUNCH, PLOTTER
3	LINE PRINTER, PLOTTER
4	LINE PRINTER
5	PLOTTER
6	CARD PUNCH
>6	NONE

KOUT2 IS A PARAMETER WHICH CONTROLS THE OUTPUT MODE AND ITS VARIOUS VALUES HAVE THE FOLLOWING SIGNIFICANCE :

VALUE OF KOUT2	OUTPUT MODE
NEGATIVE	LINE PRINTER
0	LINE PRINTER, PLOTTER
1	LINE PRINTER, CARD PUNCH (ALL STATE VARIABLES)
2	LINE PRINTER, CARD PUNCH (ONLY T)
3	LINE PRINTER, CARD PUNCH (C, CAR)

\*\*\*\*\*  
 \* SYSTEM DECIDING PARAMETER \*  
 \*\*\*\*\*

KSYS1 IS A SYSTEM DECIDING PARAMETER AND ITS VARIOUS VALUES HAVE THE FOLLOWING SIGNIFICANCE :

VALUE OF KSYS1	SYSTEM UNDER STUDY
0	SYSTEM 1 (BASIC MAINWOOD-LEE MODEL)
1	SYSTEM 2 (DUAL SUBSYSTEM MODEL)

KBETA IS ANOTHER PARAMETER WHICH DECIDES WHETHER THE FEED-BACK FACTOR IS CAO DEPENDENT OR NOT.

.....  
 VALUE OF KBETA .

SIGNIFICANCE  
 .....

0 .

BETA IS NOT CAO DEPENDENT.

1 .

BETA IS CAO DEPENDENT.  
 .....

\*\*\*\*\*

MAIN PROGRAM

\*\*\*\*\*

REAL\*4 PPM(25),VTP(25),MS1(5,25),MS2(5,25),MR1(5,25),CA(5),  
 \*MR2(5,25),VLAMRF(5),ALPHAM(4,25),VB(5),EXPF(5),VLAMSS(5),VLAMSF(5)  
 \*,VLAMRS(5),MR(5,25),T(5,5,25)

LOGICAL SYS1

COMMON/CONSTM/KCAM,KRM,KTPM,KSTMFM,KLRFM,KLSFM,KLSSM,KLRSM

COMMON/CONSTS/KTP,KB,KLRF,KCA,KSTMF,KLSF,KLSS,KLRS

COMMON/TIMES/VTP

COMMON/OUTCAL/CAO,CN,CAOIN

COMMON/STTVAR/MP1,MR2,MR,MS1,MS2

COMMON/SYSTEM/SYS1

COMMON/OUTPAR/KOUT1,KOUT2

COMMON/BETAGP/KBS,KBETA

COMMON/RST/T

COMMON/EBF/BETA

COMMON/VAR/KVAP

COMMON/NFGSUM/NFGCNT

COMMON/WDVICE/KWD,KWDD

DATA CA/1.,2.,4.,10./

DATA VLAMRF/0.,2.,4.,6.,1./

DATA VLAMRS/6.,8.,10.,12./

DATA EXPF/0.,1.,2.,0.25,0.3/

DATA VB/0.3,0.5,0.7,0.9,0.95/

DATA VLAMSF/15.,25.,30.,40./

DATA VLAMSS/50.,70.,80.,100./

DATA VLAMRS/6.,8.,10.,12./

DATA PPM/1.,2.,4.,6.,8.,10.,15.,20.,25.,30.,35.,40.,45.,50.,  
 60.,70.,75.,80.,90.,100.,110.,120.,150.,180.,240./

THE NUMERICAL VALUES 1.,2.,4.,10.,AS INITIALIZED IN CA VECTOR ABOVE

CORRESPOND TO THE FOUR STANDARD VALUES OF 'OUTSIDE CALCIUM CONCENTRATIONS'

RESPECTIVELY.

CAOIN = CA(1)

KWD = 6

KWDD = 9

KALL = 1

NFGCNT = 0

KVAP = 0

```

READ(1,2) KCAM,KLRFM,KSTMF,M,KBM,KLSFM,KLSSM,KLRSM
PFAD(1,2) KCAS,KLRFS,KSTMFS,KBS,KLSFS,KLSSS,KLRSS
READ(1,2)KSYS1,KOUT1,KOUT2,KBETA

```

```

2 FORMAT(7I5)

```

```

IF(KSYS1.EQ.1) SYS1 = .TRUE.

```

```

KTPM=25

```

```

KTPMP1 = KTPM+1

```

```

DO 5 J=1,KTRM

```

```

JJ=KTPMP1-J

```

```

VTP(J)=60./PPM(JJ)

```

```

5 CONTINUE

```

```

KCA = KCAS

```

```

4 CAD = CA(KCA)

```

```

KLRS = KLRSS

```

```

KLSS = KLSSS

```

```

KLSF = KLSFS

```

```

KLRF = KLRFS

```

```

10 CALL SETUP(VLAMRF,VLAMRS,VLAMSF,VLAMSS)

```

```

IF(KBETA.EQ.1) CALL GETFBF

```

```

CALL SOLVE

```

```

KSTMF = KSTMFS

```

```

20 STIME = EXPF(KSTMF)

```

```

CALL GETCQ(PPM,STIME)

```

```

KB = KBS

```

```

KVAR = KVAR+1

```

```

30 IF(KBETA.EQ.0) BETA = VB(KB)

```

```

KTP=1

```

```

40 TP=VTP(KTP)

```

```

CALL EVAL(BETA,CAS1,CAS2,CAR1,CAR2)

```

```

KPT = KTPMP1-KTP

```

```

MS1(KB,KPT) = CAS1

```

```

MS2(KB,KPT) = CAS2

```

```

MR1(KB,KPT) = CAR1

```

```

MR2(KB,KPT) = CAR2

```

```

MP(KB,KPT) = CAR1+CAR2

```

```

IF (KTP.EQ.KTPM) GO TO 50

```

```

KTP=KTP+1

```

```

GO TO 40

```

```

50 CALL TENSOR(KB)

```

```

IF(SYS1) GO TO 55

```

```

CALL GETCAR(PPM)

```

```

55 IF(KBETA.EQ.1) GO TO 60

```

```

IF (KB.EQ.KBM) GO TO 60

```

```

KB=KB+1

```

```

GO TO 30

```

```

60 IF((KOUT1-GE.0).AND.(KOUT1.LT.7)) CALL TRAJCT

```

```

CALL OUTPUT(VB,PPM,STIME)

```

```

IF(KSTMF.EQ.KSTMFM) GO TO 70
KSTMF = KSTMF+1
GO TO 20

```

```

70 IF(SYS1) GO TO 90
IF(KLRS.EQ.KLPSM) GO TO 80
KLRS = KLRS+1
GO TO 10

```

```

80 IF(KLSS.EQ.KLSSM) GO TO 90
KLSS = KLSS+1
GO TO 10

```

```

90 IF(KLSF.EQ.KLSFM) GO TO 100
KLSF = KLSF+1
GO TO 10

```

```

100 IF(KLRF.EQ.KLRFM) GO TO 110
KLRF = KLRF+1
GO TO 10

```

```

110 IF(KCA.EQ.KCAM) GO TO 120
KCA = KCA+1
GO TO 4

```

```

120 IF(KALL.EQ.1) CALL PLTALL(PPM)
CALL FRCENT(PPM,KALL)
CONTINUE
STOP
END

```

```

SUBROUTINE ACESS1(X,F,T,D,H)
REAL*4 X(1),F(1),D(1),VTP(1)
COMMON/TIMES/VTP
COMMON/CONSTM/KCAM,KBM,KTPM
COMMON/OUTPT/FLAG,ZZ
COMMON/PRTPTS/INFPT

```

```

DATA EPS/1.E-4/
STT = 2.
IF(FLAG.GT.0.5) GO TO 10
IF(T.GT.STT) GO TO 30
KSTR = STT
GO TO 31
20 KSTR = ZZ+0.1

```

COMPUTE NUMBER OF DATA POINTS (INFPT) TO BE STORED FOR A TIME TRAJECTORY.

```

INFPT = (1/H)+(VTP(KTPM)-STT)/(ZZ*H)+0.1
71 CALL TJCTST(X,T,KSTR)
RETURN
10 IF(T.GT.1.E-20) GO TO 20
J = 1

```

CHECK WHETHER ANY OF THE SPECIAL TIMES GIVEN IN VECTOR VTP LIE IN THE

PERMISSIBLE RANGE OF THE PRESENT TIME.

```

20 TRET+H/2+EPS
   TRET-H/2-EPS
   IF((VTP(J).LT.TPI).AND.(VTP(J).GT.TM)) GO TO 25
   RETURN
25 CALL STORF(X,D,J)
   J = J+1
   RETURN
   END

```

```

SUBROUTINE EIGEN(A,N)
  REAL*4 A(5,5),A1(2,2),VR(2),VI(2),VD(2)
  LOGICAL SYS1
  COMMON/SYSTEM/SYS1
  COMMON/WDVICE/KWD
  WRITE(KWD,101)
101 FORMAT('---',20X,'THE A MATRIX OF THE SYSTEM',/20X,
  $'-----',//)
  DO 10 J=1,N
    WRITE(KWD,100) (A(J,K),K=1,N)
10 CONTINUE
  J1 = 0
  K1 = 0
15 DO 20 J = 1,2
  DO 20 K = 1,2
  JJ = J+J1
  KK = K+K1
20 A1(J,K) = A(JJ,KK)
  CALL HSBG(2,A1,2)
  CALL ATEIG(2,A1,VR,VI,VD,2)
  IF(SYS1) GO TO 60
  IF(J1.EQ.0) GO TO 50
  WRITE(KWD,500)
500 FORMAT('---',5X,'EIGEN VALUES OF THE SLOW SUB-SYSTEM',/5X,
  $'-----')
100 FORMAT('---',5X,4E15.4)
  WRITE(KWD,501) ((VR(J),VI(J)),J = 1,2)
  RETURN
  50 WRITE(KWD,502)
502 FORMAT('---',5X,'EIGEN VALUES OF THE FAST SUB-SYSTEM',/5X,
  $'-----')
  WRITE(KWD,501) ((VR(J),VI(J)),J = 1,2)
  J1 = 2
  K1 = 2
  GO TO 15
  60 WRITE(KWD,503)
503 FORMAT('---',5X,'EIGEN VALUES OF THE SYSTEM ARE : ')
  WRITE(KWD,501) ((VR(J),VI(J)),J = 1,2)
501 FORMAT('0',2E15.4)
  RETURN
  END

```

```

SUBROUTINE EVAL(BETA,CAS1,CAS2,CAR1,CAR2)
REAL*4 FMAT1(4,25),FMAT2(4,25),RMAT(4,25),ALPHAM(4,25),
*VC(25),VQ(25)
LOGICAL SYS1
COMMON/CONSTM/KCAM,KBM,KTPM
COMMON/CONSTS/KTP,KB
COMMON/ER/EMAT1,EMAT2,RMAT
COMMON/SYSTEM/SYS1
COMMON/DECOND/ALPHAM
COMMON/CVECT/VC,VQ
KPT = KTPM+1-KTP
E11=EMAT1(1,KTP)
E21=EMAT1(2,KTP)
R1=RMAT(1,KTP)
R2=RMAT(2,KTP)
E33 = 0.0
E43 = 0.0
R3 = 0.0
R4 = 0.0
ALPHA3 = 0.0
IF(SYS1) GO TO 30.
E33=EMAT2(3,KTP)
E43=EMAT2(4,KTP)
R3=RMAT(3,KTP)
R4=RMAT(4,KTP)

COMPUTE INITIAL CONDITIONS FOR DYNAMIC EQUILIBRIUM EXISTENCE

ALPHA3=R3/(1.-E33)
70 Q = VQ(KPT)
Q1 = 1.-E11-BETA*E21
Q2 = R1+Q+BETA*(R2+R4)+BETA*E43*ALPHA3
ALPHA1 = Q2/Q1

STORE THE VALUES OF SYSTEM INITIAL CONDITIONS FOR DYNAMIC EQUILIBRIUM
IN MATRIX ALPHAM.

ALPHAM(1,KTP) = ALPHA1
ALPHAM(2,KTP) = 0.0
ALPHAM(3,KTP) = ALPHA3
ALPHAM(4,KTP) = 0.0
CALL NEGCHK(ALPHA1,ALPHA3,BETA)

COMPUTE DYNAMIC EQUILIBRIUM VALUES OF STATE VARIABLES

CAS1=E11*ALPHA1+R1
CAR1=E21*ALPHA1+R2
CAS2=E33*ALPHA3+R3
CAR2=E43*ALPHA3+R4
RETURN
END

```

```

SUBROUTINE GETATR(CAR,PPM,KB,KTPM)
REAL*4 PPM(25),CAR(25),VP(6),FQ(3),CR(3),VATRBT(6,8)
COMMON/ATTVEC/VATRBT
MODE = 1
K = 1
CALL SCAN(CAR,MODE,KTPM,K,PPM,J,FQ,CR)
IF(MODE.LT.0) GO TO 20
CALL QUAD(FQ,CR,F,VALU)
VP(3) = CAR(1)
VP(4) = CAR(KTPM)

```

STORE THE MINIMUM VALUE OF CAR AND CORRESPONDING STIMULATION FREQUENCY.

```

VP(1) = F
VP(2) = VALU
MODE = 2
K = J

```

```

CALL SCAN(CAR,MODE,KTPM,K,PPM,J,FQ,CR)
IF(MODE.LT.0) GO TO 30
CALL QUAD(FQ,CR,F,VALU)

```

STORE THE PEAK VALUE OF CAR AND THE CORRESPONDING STIMULATION FREQUENCY.

```

31 VP(5) = F
VP(6) = VALU
GO TO 35
20 F = -1
VALU = -1
GO TO 21
30 F = -1
VALU = -1
GO TO 31

```

FORM A ROW OF ATTRIBUTE MATRIX

```

35 VATRBT(KB,1) = VP(3)
VATRBT(KB,2) = VP(2)/VP(3)
VATRBT(KB,3) = VP(6)/VP(3)
VATRBT(KB,4) = VP(2)/VP(6)
VATRBT(KB,5) = VP(4)/VP(3)
VATRBT(KB,6) = VP(4)/VP(6)
VATRBT(KB,7) = VP(1)
VATRBT(KB,8) = VP(5)
RETURN
END

```

```

SUBROUTINE GETCAR(PPM)
REAL*4 T(5,5,25),PPM(25),CAR(25),CASE(10),F(10),CSTD(4,10),
*VATRBT(6,8),VEERRR(5,8)
COMMON/CONSTM/KCAM,KBM,KTPM
COMMON/RRST/T
COMMON/CONSTS/KTP,KB,KLRF,KCA
COMMON/VAR/KVAR
COMMON/ERRVEC/VEERRR
COMMON/ATTVEC/VATRBT

```

## EXPERIMENTAL DATA

DATA F/2.,5.,12.,30.,60.,95.,120.,150.,180./

DATA CSTD/14.,21.,62.,100.,6.5,11.5,52.,95.5,5.,10.5,48.,88.,  
\$7.,19.,55.5,78.,20.,28.5,54.5,73.5,31.,35.5,44.,67.5,32.,30.,38.5,  
\$58.5,28.,26.,50.,21.,21.5,31.,44./

DATA KCAOLD/0/

DO 10 J=1,KTPM

10 CAP(J) = T(KVAR,KB,J)

COMPUTE ATTRIBUTE VECTOR FOR COMPUTED RESULTS

CALL GETATR(CAR,PPM,KB,KTPM)

IF(KCA,EQ,KCAOLD) GO TO 11

COMPUTE ATTRIBUTE VECTOR FOR EXPERIMENTAL RESULTS

DO 20 J = 1,9

20 CASE(J) = CSTD(KCA,J)

CALL GETATR(CASE,F,6,9)

KCAOLD = KCA

11 CONTINUE

COMPUTE PERCENTAGE ERROR

DO 30 K = 1,8

30 VERROR(KB,K) = ((VATRBT(KB,K)-VATRBT(6,K))/VATRBT(6,K))\*100.

END

SUBROUTINE GETCQ(PPM,STIME)

REAL\*4 VC(25),PPM(1),VQ(25)

COMMON/OUTCAL/CAO,CN

COMMON/CVECT/VC,VQ

COMMON/CONSTM/KCAM,KBV,KTPM,KSTMF,M,KLRFM,KLSFM,KLSSM,KLRSM

CHAT = 1.-EXP(-STIME\*CAO)

DO 10 J=1,KTPM

CKNEE = -120./PPM(J)

C = CN\*(1.-EXP(CKNEE))

VC(J) = C

10 VQ(J) = C\*CHAT

RETURN

END

SUBROUTINE GETFBF

COMMON/FBF/BETA

COMMON/EXPBG/BC

COMMON/OUTCAL/CAO,CN

BEXP = (BC/CAO)\*\*.5

BETA = 1.-EXP(-BEXP)

RETURN

END

```

SUBROUTINE NEGCHK(ALPHA1,ALPHA3,BETA)
REAL*4 EMAT1(4,25),EMAT2(4,25),RMAT(4,25)
LOGICAL SYS1
COMMON/ER/EMAT1,EMAT2,RMAT
COMMON/CONSTS/KTP
COMMON/SYSTEM/SYS1
EP = -1.E-4

```

```

C COMPUTE THE VALUES OF SYSTEM STATE VARIABLES AT ALL SPECIAL TIMES (AS
C GIVEN IN VECTOR VTP) PRIOR TO THE PRESENT ONE AND CHECK FOR THE NEGATIV
C VALUES OF STATE VARIABLES.

```

```

DO 10 I = 1,KTP
X1 = FMAT1(1,KTP)*ALPHA1+RMAT(1,KTP)
X2 = FMAT1(2,KTP)*ALPHA1+RMAT(2,KTP)
IF(SYS1) GO TO 5
X3 = FMAT2(3,KTP)*ALPHA3+RMAT(3,KTP)
X4 = EMAT2(4,KTP)*ALPHA3+RMAT(4,KTP)
IF((X3.LT.EP).OR.(X4.LT.EP)) GO TO 20
5 IF((X1.LT.EP).OR.(X2.LT.EP)) GO TO 20
10 CONTINUE
RETURN
20 CALL REJECT(BETA,X1,X2,X3,X4)
RETURN
END

```

```

SUBROUTINE OUTPUT(VB,PPM,STIME)
REAL*4 MS1(5,25),MS2(5,25),MR1(5,25),MR2(5,25),MR(5,25),T(5,5,25)
*,PPM(1),VB(1),VTP(1),VC(1),VATRBT(5,8),VERRO(5,8)
LOGICAL SYS1
COMMON/VOLMS/VR1,VR2,VS1,VS2
COMMON/FLOWCT/K1,K1P
COMMON/ATTVEC/VATRBT
COMMON/VAR/KVAR
COMMON/CONSTS/KTP,KB,KLRF,KCA,KSTMF
COMMON/CONSTM/KCAM,KBM,KTPM,KSTMF,M,KLRFM,KLSFM,KLSSM,KLRSM
COMMON/STTVAR/MR1,MR2,MR,MS1,MS2
COMMON/SYSTEM/SYS1
COMMON/OUTCAL/CAO,CN
COMMON/NEGSUM/NEGCNT
COMMON/TCONST/LAMR1,LAMS1,LAMR2,LAMS2
COMMON/CVECT/VC,VO
COMMON/ERRVEC/VERRO
COMMON/BETAGP/KBS,KBETA
COMMON/ADVCE/KWD,KWDD
COMMON/PERT/TMF
COMMON/RIAS/B

```

```

COMMON/PST/T
DATA NUM/1/
KTPMFI=KTPM+1
DO 20 K = KBS,KBM
WRITE(KWD,90) CA0
90 FORMAT('1',30X,'*',5X,'HEIGHT HO (CAO CONC.) = ',F7.3,5X,'*')
IF(KBETA.EQ.0) WRITE(KWD,100) VB(K)
IF(KBETA.EQ.1) WRITE(KWD,100) BETA
100 FORMAT(/,30X,'*****',/
$50X,'BETA = ',F10.2,/30X,
$'*****')
WRITE(KWD,110) B,STIMF
110 FORMAT('-',10X,'*',5X,'THE VALUE OF ZERO-BIAS = ',2X,F10.3,5X,'*',
$'EXPONENT FACTOR = ',F5.3,5X,'*')
WRITE(KWD,150) LAMR1,LAMS1,VS1,VR1,K1
IF(SYS1) GO JD 30
WRITE(KWD,200) LAMR2,LAMS2,VS2,VR2,K1P
150 FORMAT('-',4X,'-----',
*
*/5X,'LAMR1 = ',F10.2,5X,'LAMS1 = ',F10.2,5X,'VS1 = ',F10.3,5X,
$'VR1 = ',F10.3,5X,'K1 = ',F10.3)
200 FORMAT('-',4X,'LAMR2 = ',F10.2,5X,'LAMS2 = ',F10.2,5X,'VS2 = ',
$F10.3,5X,'VR2 = ',F10.3,5X,'K1P = ',F10.3,/
$'-----',
*
WRITE(KWD,250)
250 FORMAT('-',3X,'PULSES/MIN.',6X,'CAS1',8X,'CAS2',7X,'CAR1',8X,
$'CAP2',7X,'CAR',7X,'TENSION',7X,'C')
DO 10 J=1,KTPM
10 WRITE(KWD,300) PPM(J),MS1(K,J),MS2(K,J),MR1(K,J),MR2(K,J),MR(K,J),
$T(KVAR,K,J),VC(J)
WRITE(KWD,101)
101 FORMAT('-',9X,
$/10X,'THE CANONICAL VALUES AND RATIOS OF OMEGA CURVE',/10X,
$'-----')
WRITE(KWD,302)
302 FORMAT(' ',10X,'*****')
WRITE(KWD,11)
-----
THE QUANTITIES Z,V,P, AND L CORRESPOND TO TS,TMIN,TMAX,AND TE (DEFINED
IN TEXT) RESPECTIVELY.
-----
11 FORMAT(/,13X,'Z',8X,'V/Z',5X,'P/Z',4X,'V/P',4X,'L/Z',4X,'L/P',4X,
$'F1',5X,'F2')
WRITE(KWD,12) (VATRB(T(K,I),I=1,8),(VATRB(6,I),I=1,8)
12. FORMAT(/,10X,8F7.3,5X,'* ----- EXPERIMENTAL
$VALUES',/10X,8F7.3,5X,'* ----- REFERENCE
$VALUES')
WRITE(KWD,13) (VERROR(K,I),I=2,8)
13 FORMAT(/,17X,7F7.3,5X,'* ----- PERCENTAGE
$ERROR')
WRITE(KWD,303)
303 FORMAT(' ',10X,'*****')

```

```

GO TO 20
70 WRITE(KWD,260)
260 FORMAT(' ',1X,'PULSES/MINT.',6X,'CAS',8X,'CAR',10X,'TENSION',10X,
*'C')
DO 111 J=1,KTPN
111 WRITE(KWD,301) PPM(J),MS1(K,J),MR1(K,J),T(KVAR,K,J),VC(J)
20 CONTINUE
CALL PPOUT(PPM,NUM,VB)
IF((KCA.EQ.KCAM).AND.(KLRP.EQ.KLRM).AND.(KSTMF.EQ.KSTMFM))
*WRITE(3,555) NEGNT
RETURN
555 FORMAT(' ',5X,'TOTAL NO. OF OCCURENCES OF A NEGATIVE CALCIUM
*CONTENT = ',I5)
700 FORMAT(1X,F12.2,7E12.3)
701 FORMAT(1X,F12.2,5E12.3)
END

```

```

SURROUTINE PCM(DXZ,NINT,N,IA,T1,X)
RFAL*4 XZ(5),XNM3(5),XNM2(5),XNM1(5),XN(5),XNP1(5),CN(5),CNP1(5),
$PN(5),PNP1(5),MCD(5),FMOD(5),FNM2(5),FNM1(5),FN(5),FNP1(5),X(5),
$FZ(5),XP(5),DXZ(5),F(5)

```

```

DO 21 K=1,N
21 XZ(K) = DXZ(K)
TZ=0.0

H=T1/NINT
NM3 = NINT-3

DO 10 J=1,N
10 XNM3(-J)=XZ(J)

CALL RHS(XZ,TZ,FZ)
IF(IA.EQ.1) CALL ACES1(XZ,FZ,TZ,DXZ,H)

11 ISW = 0

CALL STARTR(XZ,TZ,H,N,ISW,XNM2,T)
CALL PHS(XNM2,T,FNM2)
IF(IA.GT.0) CALL ACES1(XNM2,FNM2,T,DXZ,H)
CALL STARTP(XNM2,TZ,H,N,ISW,XNM1,T)
CALL PHS(XNM1,T,FNM1)
IF(IA.GT.0) CALL ACES1(XNM1,FNM1,T,DXZ,H)
CALL STARTR(XNM1,TZ,H,N,ISW,XN,T)
CALL PHS(XN,T,FN)
TN = T
IF(IA.GT.0) CALL ACES1(XN,FN,T,DXZ,H)
DO 8 J=1,N
CN(J)=0.0
PN(J)=0.0
DO 50 MASTER=1,NM3
DO 14 J=1,N

PREDICTOR

```

```
PNP1(J)=XNM3(J)+4.0*H*(2.0*FN(J)-FNM1(J)+2.0*FNM2(J))/3.0
```

0000

```
MODIFIER
```

```
4 MOD(J)=PNP1(J)-112.E0*(PN(J)-CN(J))/121.E0
```

```
TNP1=TN+H
```

```
CALL RHS(MOD,TNP1,FMOD)
```

```
DO 15 J=1,N
```

```
CORRECTOR
```

```
CNP1(J)=(9.F0*XN(J)-XNM2(J)+3.E0*H*(FMOD(J)+2.E0*FN(J)-FNM1(J)))/81.F0
```

```
FINAL VALUE, ITS DERIVATIVE, AND ERROR TEST
```

```
15 XNP1(J)=CNP1(J)+9.E0*(FNP1(J)-CNP1(J))/121.E0
```

```
CALL RHS(XNP1,TNP1,FNP1)
```

```
TN=TNP1
```

```
DO 20 J=1,N
```

```
FNM2(J)=FNM1(J)
```

```
FNM1(J)=FN(J)
```

```
FN(J)=FNP1(J)
```

```
XNM3(J)=XNM2(J)
```

```
XNM2(J)=XNM1(J)
```

```
XNM1(J)=XN(J)
```

```
XN(J)=XNP1(J)
```

```
X(J)=XN(J)
```

```
PN(J)=PNP1(J)
```

```
20 CN(J)=CNP1(J)
```

```
IF(IA.GT.0) CALL ACFS1(X, FN, TN, DXZ, H)
```

```
50 CONTINUE
```

```
RETURN
```

```
END
```

```
SUBROUTINE PLTALL(PPM)
```

```
REAL*4 T(5,5,25),P(25,6),PPM(1)
```

```
COMMON/BETAGP/KBS
```

```
COMMON/CONSTM/KCAM,KBM,KTPM
```

```
COMMON/RST/T
```

```
DO 10 K = KBS,KBM
```

```
DO 20 J = 1,25
```

```
P(J,1) = PPM(J)
```

```
P(J,2) = 0.0
```

```
P(J,3) = T(1,K,J)
```

```
P(J,4) = T(2,K,J)
```

```
P(J,5) = T(3,K,J)
```

```
20 P(J,6) = T(4,K,J)
```

```
CALL PLOT(K,P,25,6,120,0)
```

```
10 CONTINUE
```

```
RETURN
```

```
END
```

```

SUBROUTINE PLTINF
REAL*4 MATCAL(5,100),TIME(100),C(100,7)
LOGICAL SYS1
COMMON/PRTPTS/INFPT
COMMON/CADETL/MATCAL,TIME
COMMON/CONSTS/KTP,KB,KLRF,KCA,KSTMF
COMMON/SYSTEM/SYS1
DO 10 J = 1,INFPT
C(J,1) = TIME(J)
C(J,2) = 0.0
C(J,3) = MATCAL(1,J)
C(J,4) = MATCAL(2,J)
IF(SYS1) GO TO 10
C(J,5) = MATCAL(3,J)
C(J,6) = MATCAL(4,J)
C(J,7) = MATCAL(5,J)
10 CONTINUE
CALL PLOT(KCA,A,INFPT,5,0,0)
RETURN
END

```

```

SUBROUTINE PLTOUT(PPM,K,NUM)
REAL*4 PPM(1),MR1(5,25),MR2(5,25),A(25,6),VC(1),T(5,5,25)
LOGICAL SYS1
COMMON/CVECT/VC,VQ
COMMON/SYSTEM/SYS1
COMMON/CONSTM/KCAM,KBV,KTPM
COMMON/STTVAR/MR1,MR2
COMMON/VAR/KVAR
COMMON/RST/T
KTPM1 = KTPM + 1
IF(SYS1) GO TO 30
DO 10 J=1,25
A(J,1) = PPM(J)
A(J,2) = 0.
A(J,3) = MR1(K,J)
A(J,4) = MR2(K,J)
A(J,5) = A(J,3) + A(J,4)
10 A(J,6) = T(KVAR,K,J)
CALL PLOT(NUM,A,25,6,0,0)
GO TO 40
20 DO 11 J=1,25
A(J,1) = PPM(J)
A(J,2) = 0.
A(J,3) = MR1(K,J)
11 A(J,4) = T(KVAR,K,J)
CALL PLOT(NUM,A,25,4,0,0)
40 DO 20 J = 1,KTPM
A(J,1) = PPM(J)
A(J,2) = 0.0
20 A(J,3) = VC(J)
IF(NUM.EQ.1) CALL PLOT(NUM,A,25,3,0,0)

```

```

NUM = NUM + 1
RETURN
END

```

```

SUBROUTINE PPPINF -
COMMON/OUTPAR/KOUT1
IF(KOUT1.EQ.5) GO TO 50
IF((KOUT1.EQ.6).OR.(KOUT1.EQ.2)) GO TO 40
CALL PRTINF
IF(KOUT1.EQ.4) RETURN
IF(KOUT1.EQ.3) GO TO 50
40 CALL PUNINF
IF((KOUT1.EQ.1).OR.(KOUT1.EQ.6)) RETURN
50 CALL PLTINF
RETURN
END

```

```

SUBROUTINE PPPOUT(PPM,NUM,VB)
REAL*4 PPM(1),VB(1)
COMMON/OUTPAR/KOUT1,KOUT2
IF(KOUT2.LT.0) RETURN
IF((KOUT2.EQ.1).OR.(KOUT2.EQ.2).OR.(KOUT2.EQ.3)) GO TO 10
CALL FLTOUT(PPM,K,NUM)
IF(KOUT2.LE.0) RETURN
10 CALL FUNOUT(PPM,NUM,VB)
RETURN
END

```

```

SUBROUTINE PPPCNT(PPM,K)
REAL*4 PPM(1),P(25,6),TMR(5,5,25)
COMMON/PEPT/TMR
DO 30 J = 1,25
P(J,1) = PPM(J)
P(J,2) = 0.0
P(J,3) = TMR(1,K,J)
P(J,4) = TMR(2,K,J)
P(J,5) = TMR(3,K,J)
30 P(J,6) = TMR(4,K,J)
CALL PLOT(K,P,25,6,120.0)
RETURN
END

```

```

SUBROUTINE PRCENT(PPM,KALL)

```

```

REAL*4 T(5,5,25),TMR(5,5,25),PPM(1)
COMMON/PERT/TMR
COMMON/RST/T
COMMON/VAP/KVAR
COMMON/BETAGP/KBS
COMMON/CONSTM/KCAM,KBM,KTPM
IF(KALL.EQ.1) RETURN
DO 20 N = KBS,KBM
DO 22 M = 1,KVAR
DO 25 K = 2,KTPM
J = K-1
IF(T(M,N,J).LT.T(M,N,K)) GO TO 10
25 CONTINUE
TREF = T(M,N,1)
GO TO 15
10 TREF = T(M,N,K)
J = K-1
K = K+1
IF((TREF.GT.T(M,N,K)).AND.(TREF.GT.T(M,N,J))) GO TO 16
GO TO 10
16 IF(T(M,N,1).GT.TREF) TREF = T(M,N,1)
15 DO 30 L = 1,KTPM
30 TMR(M,N,L) = T(M,N,L)/TREF
22 CONTINUE
CALL FPRCNT(PPM,N)
20 CONTINUE
STOP
END

```

```

SUBROUTINE PRTIME
REAL*4 MATCAL(5,100),TIME(100)
LOGICAL SYS1
COMMON/WDVCE/KWD,KWDD
COMMON/SYSTEM/SYS1
COMMON/CADETL/MATCAL,TIME
COMMON/PRTPTS/INFPT
COMMON/PRTROW/M
IF(SYS1) GO TO 10
WRITE(KWD,102)
102 FORMAT('-',5X,'TIME',9X,'CAS1',10X,'CAR1',10X,'CAS2',10X,'CAR2',
$10X,'CAR')
GO TO 20
10 WRITE(KWD,101)
101 FORMAT('-',5X,'TIME',10X,'CAS1',10X,'CAR1')
20 DO 30 J = 1,INFPT
30 WRITE(KWD,100) TIME(J),(MATCAL(I,J),I = 1,M)
100 FORMAT('-',5X,F7.3,5E15.4)
RETURN
END

```

```

SUBROUTINE PUNINF

```

```

REAL*4 MATCAL(5,100),TIME(100)
COMMON/PRTPTS/INFPT
COMMON/CADETL/MATCAL,TIME
COMMON/WDVCE/KWD,KWDD
COMMON/PRTROW/M
WRITE(KWDD,10)
10 FORMAT(20X,'TIME')
WRITE(KWDD,50) (TIME(J),J = 1,INFPT)
WRITE(KWDD,20)
20 FORMAT(5X,'1,2,3,4,5 ROWS OF MATCAL MATRIX ARE :',/5X,
5 'CAS1,CAR1,CAS2,CAR2,CAR RESPECT.')
DO 40 I = 1,M
WRITE(KWDD,30) I
30 FORMAT(10X,'ROW NO. OF MATCAL' = ',I5)
WRITE(KWDD,50) (MATCAL(I,J),J = 1,INFPT)
40 CONTINUE
50 FORMAT(8F10.3)
RETURN
END

```

```

SUBROUTINE PUNCUT(PPM,NUM,VB)
REAL*4 PPM(1),MR1(5,25),MR2(5,25),MS1(5,25),MS2(5,25),MR(5,25),
VB(5),VC(25),T(5,5,25),TMR(5,5,25)
LOGICAL SYS1
COMMON/CONSTS/KTP,KB,KLRF,KCA,KSTMF
COMMON/CONSTM/KCAM,KBM,KTPM
COMMON/STTVAR/MR1,MR2,MR,MS1,MS2
COMMON/VAR/KVAR
COMMON/BETAGP/KBS,KBETA
COMMON/WDVCE/KWD,KWDD
COMMON/SYSTEM/SYS1
COMMON/OUTCAL/CAO,CN
COMMON/TCONST/LAMR1,LAMS1,LAMR2,LAMS2
COMMON/CVECT/VC,VQ
COMMON/OUTPAR/KOUT1,KOUT2
COMMON/FBF/BETA
COMMON/PERT/TMR
COMMON/RST/T
WRITE(KWDD,500) CAO,LAMS1,LAMR1,LAMS2,LAMR2
WRITE(KWDD,69)
60 FORMAT(20X,'PULSES PER MINT.')
WRITE(KWDD,600) (PPM(J),J = 1,25)
WRITE(KWDD,700)
DO 33 K = KBS,KBM
WRITE(KWDD,900) VB(K),LAMR1,CAO,LAMS1,LAMS2,LAMR2
900 FORMAT(2X,'B,LAMR1,CAO,LAMS1,LAMS2,LAMP2',6F6.2)
IF(KBETA.EQ.1) WRITE(KWDD,70) BETA
70 FORMAT('FEED-BACK FACTOR = ',F5.3)
IF((KOUT2.EQ.2).OR.(KOUT2.EQ.3)) GO TO 20
WRITE(KWDD,121)
121 FORMAT('VALUE OF CAS1')
WRITE(KWDD,600) (MS1(K,J),J = 1,25)
WRITE(KWDD,700)
WRITE(KWDD,123)
123 FORMAT('VALUE OF CAR1')

```

```

WRITE(KWDD,600) (MR1(K,J),J=1,25)
WRITE(KWDD,700)
IF(SYS1) GO TO 30
WRITE(KWDD,122)
122 FORMAT('VALUE OF CAS2')
WRITE(KWDD,600) (MS2(K,J),J = 1,25)
WRITE(KWDD,700)
WRITE(KWDD,124)
124 FORMAT('VALUE OF CAR2')
WRITE(KWDD,600) (MR2(K,J),J = 1,25)
WRITE(KWDD,700)
WRITE(KWDD,125)
125 FORMAT('VALUE OF CAP')
WRITE(KWDD,600) (MR(K,J),J = 1,25)
WRITE(KWDD,700)
20 IF(KOUT2.EQ.2) GO TO 30
WRITE(KWDD,100)
300 FORMAT('VALUE OF C')
WRITE(KWDD,600) (VC(J),J = 1,25)
WRITE(KWDD,700)
30 WRITE(KWDD,126)
126 FORMAT(20X,'TENSION OF THE MUSCLE')
WRITE(KWDD,600) (T(KVAR,K,J),J = 1,25)
WRITE(KWDD,700)
WRITE(KWDD,600) (TMR(KVAR,K,J),J = 1,25)
33 CONTINUE
600 FORMAT(8E10.3)
700 FORMAT('SUB DATA END')
RETURN
800 FORMAT('I.D',6F10.3)
END

```

```

SUBROUTINE QUAD(FQ,CR,F,VALU)

```

```

REAL*4 FQ(3),CR(3)

```

```

COMMON/WDVICE/KWD

```

```

DN = (FQ(1)-FQ(2))*(FQ(2)-FQ(3))*(FQ(1)-FQ(3))

```

```

A=(CR(1)*(FQ(2)-FQ(3))+CR(2)*(FQ(3)-FQ(1))+CR(3)*(FQ(1)-FQ(2)))/DN

```

```

BD = (CR(2)-CR(3))/(FQ(2)-FQ(3))

```

```

B = BD-A*(FQ(2)+FQ(3))

```

```

CD = (FQ(3)*CR(1)-FQ(1)*CR(3))/(FQ(1)-FQ(3))

```

```

C = A*FQ(1)*FQ(3)-CD

```

```

COMPUTE MINIMUM VALUE OF CAR AND CORRESPONDING STIMULATION FREQUENCY

```

```

(QUADRATIC FITTING TECHNIQUE)

```

```

XSTAR = -B/(2.*A)

```

```

IF((XSTAR.GE.FQ(1)).AND.(XSTAR.LE.FQ(3)))GO TO 10

```

```

DEFAULT OPTION

```

```

F = FQ(2)

```

```

VALU = CR(2)

```

```

WRITE(KWD,99)

```

```

99 FORMAT(/,80X,'ERROR----- DEFAULT OPTION (MIDDLE POINT)')

```

```

GO TO 20
10 F = XSTAR
   VAI U = (A*(XSTAR**2)+B*XSTAR+C)
20 CONTINUE
   RETURN
   END

```

```

SUBROUTINE REJECT(BETA,X1,X2,X3,X4)
REAL*4 VTP(25)
LOGICAL SYS1
COMMON/TCONST/LAMR1,LAMS1,LAMR2
COMMON/TIMES/VTP
COMMON/NEGSUM/NEGCNT
COMMON/CONSTS/KTP,KB,KLRF,KCA,KSTMF
COMMON/WDVICE/KWD,KWDD
COMMON/SYSTEM/SYS1
COMMON/CONSTM/KCAM,KBM,KTPM
COMMON/BIAS/B

```

COUNT THE NEGATIVE CALCIUM OCCURENCES.

```

NEGCNT = NEGCNT+1
WRITE(KWD,10)
10 FORMAT('!', '*****', 5X, 'ERROR--- NEG.CAL.'
  & //10X, 'CAL. IN ONE OF THE COMPTS HAS GONE NEGATIVE')
   IF(SYS1) GO TO 5
   WRITE(KWD,20) X1,X2,X3,X4
20 FORMAT('-', 10X, 'THE PRESENT VALUES OF CAL. ARE AS FOLLOWS :-',
  & //10X, 'CAS1 = ', F10.3, 10X, 'CAR1 = ', F10.3, /
  & 10X, 'CAS2 = ', F10.3, 10X, 'CAR2 = ', F10.3)
   GO TO 7
5 WRITE(KWD,6) X1,X2
6 FORMAT('-', 10X, 'THE PRESENT VALUES OF CAL. ARE AS FOLLOWS :-',
  & //10X, 'CAS1 = ', F10.3, 10X, 'CAR1 = ', F10.3)
7 KK = KTPM-KTP+1
  F = 60./VTP(KK)
  WRITE(KWD,30) BETA,B,LAMR1,LAMR2,F
30 FORMAT('-', 20X, 'THE CURRENT PARAMETER VALUES ARE : ', /20X,
  & '-----', /5X, 'BETA = ', F9.3, /5X, 'B = ',
  & F9.3, /5X, 'LAMR1 = ', F9.3, /5X, 'LAMR2 = ', F9.3, /5X, 'F = ', F9.3)
  RETURN
  END

```

```

SUBROUTINE RHS(X,T,F)
REAL*4 F(1),X(1),A(5,5)
LOGICAL SYS1
COMMON/COEF/A,U1,U2,UDUM
COMMON/SYSTEM/SYS1
F(1)=A(1,1)*X(1)+A(1,2)*X(2)+U1*UDUM
F(2)=A(2,1)*X(1)+A(2,2)*X(2)
IF(SYS1) RETURN

```

```

F(3)=A(3,3)*X(3)+A(3,4)*X(4)+U2*UDUM
F(4)=A(4,3)*X(3)+A(4,4)*X(4)
RETURN
END

```

```

SUBROUTINE SCAN(CAR,MODE,KTPM,K,PPM,J,FQ,CR)
REAL*4 CAR(25),PPM(1),FQ(1),CR(1)
IF(MODE.EQ.2) GO TO 10
GO TO 20
10 DO 30 I = 1,KTPM
30 CAR(I) = -CAR(I)
20 CREF = CAR(K)
J = K+1
40 IF(CAR(J).GT.CREF) GO TO 50
CREF = CAR(J)
J = J+1
IF(J.LE.KTPM) GO TO 40
J=1
60 MODE = -1
RETURN
50 IF(J.LT.3) GO TO 60

```

STORE THREE VALUES OF CAR AND CORRESPONDING FREQUENCIES OF STIMULATION  
FOR QUADPATIC FITTING.

```

CR(1) = CAR(J-2)
CR(2) = CAR(J-1)
CR(3) = CAR(J)
FQ(1) = PPM(J-2)
FQ(2) = PPM(J-1)
FQ(3) = PPM(J)
IF(MODE.EQ.2) GO TO 70
RETURN
70 DO 80 I=1,3
80 CR(I) = -CR(I)
RETURN
END

```

```

SUBROUTINE SETUP(VLAMRF,VLAMRS,VLAMSF,VLAMSS)
REAL*4 A(5,5),K1,K1P,K2,K2P,LAMS1,LAMS2,LAMR1,LAMR2,VLAMRF(1),
*VLAMRS(1),VLAMSF(1),VLAMSS(1)
LOGICAL SYS1
COMMON/COEF/A,U1,U2,UDUM
COMMON/OUTCAL/CA0,CN,CA0MIN
COMMON/CONSTS/KTP,KB,KLRF,KCA,KSTMF,KLSF,KLSS,KLRS
COMMON/TCONST/LAMR1,LAMS1,LAMR2,LAMS2
COMMON/INTGER/N
COMMON/VOLMS/VR1,VR2,VS1,VS2
COMMON/FLDWCT/K1,K1P,K2,K2P
COMMON/CONSTS/CA0,CN,CA0MIN

```

```

COMMON/EXPBC/BC
COMMON/BIAS/B
COMMON/WDVICE/KWD
N = 2
CN = 0.1
RC = 0.
IF(SYS1) GO TO 5
N = 4

```

```

5 DO 10 J=1,N
DO 10 K=1,N
10 A(J,K) = 0.

```

```

IF(SYS1) GO TO 30

```

```

SLOW COMPONENT OF SYSTEM 2.

```

```

VS2 = 1.0
VR2 = 0.12
LAMS2 = VLAMSS(KLSS)
LAMR2 = VLAMRS(KLRS)
K1P = VR2/LAMR2
K2P = VS2/(4.*LAMS2)
A(3,3) = -(K1P+5*K2P)/VS2
A(3,4) = K1P/VR2
A(4,3) = K1P/VS2
A(4,4) = -K1P/VR2
U2 = K2P*CA0

```

```

FAST COMPONENT OF SYSTEM 2 (SYSTEM1)

```

```

20 VR1 = 0.08
VS1 = 1.
LAMR1 = VLAMRF(KLRF)
LAMS1 = VLAMSF(KLSF)
K1 = VR1/LAMR1
K2 = VS1/(4.*LAMS1)
A(1,1) = -(K1+5*K2)/VS1
A(1,2) = K1/VR1
A(2,1) = K1/VS1
A(2,2) = -K1/VR1
B = 1.00*K2*CA0MIN
U1 = K2*CA0-B
WRITE(KWD,100) LAMR1
IF(.NOT.SYS1) WRITE(KWD,200) LAMR2
CALL EIGEN(A,N)
RETURN
300 FORMAT('1', 'LAMR1 = ', F12.2)
400 FORMAT('0LAMR2 = ', F12.2)
END

```

```

SUBROUTINE SOLVE
REAL*4 DXZ(5), A(5,5), X(5)
LOGICAL SYS1
COMMON/COEF/A, U1, U2, UDUM

```

```

COMMON/DUTPT/FLAG,ZZ
COMMON/INTGER/N
COMMON/SYSTEM/SYS1
FLAG = 1.
T1=60.
NINT = 1200
IA=1.
IF(SYS1) GO TO 20

```

```

CALL THE DIFFERENTIAL EQUATION SOLVING PACKAGE WITH SPECIALLY SELECTED
CONDITIONS FOR SYSTEM 2.

```

```

DXZ(1)=1.0
DXZ(2)=0.0
DXZ(3)=0.0
DXZ(4)=0.0
UDUM=0.0
CALL PCM(DXZ,NINT,N,IA,T1,X)
DXZ(1)=0.0
DXZ(2)=0.0
DXZ(3) = 1.0
DXZ(4)=0.0
UDUM=0.0
CALL PCM(DXZ,NINT,N,IA,T1,X)
DXZ(1)=0.0
DXZ(2)=0.0
DXZ(3) = 0.0
DXZ(4)=0.0
UDUM=1.0
CALL PCM(DXZ,NINT,N,IA,T1,X)
RETURN

```

```

CALL THE DIFFERENTIAL EQUATION SOLVING PACKAGE WITH SPECIALLY SELECTED
CONDITIONS FOR SYSTEM 1.

```

```

20 DXZ(1) = 1.0
DXZ(2) = .0.0
UDUM = 0.0
CALL PCM(DXZ,NINT,N,IA,T1,X)
DXZ(1) = 0.0
DXZ(2) = 0.0
UDUM = 1.0
CALL PCM(DXZ,NINT,N,IA,T1,X)
RETURN
END

```

```

SUBROUTINE STARTR(XZ,TZ,H,N,ISW,X,T)
REAL *4 A(4),B(4),C(4),X(5),XZ(5),F(5),Q(6)
DATA A/.5,,.9289321,1.7071067,.1666666/,B/2.0,1.0,1.0,2.0/,C/.5,.2
.9289321,1.7071067,.5/
IF(ISW)1,1.3
T=TZ
LL=N+1

```

```

DO 2 I=1,LL
Q(I)=0.0
ISW=1
TT=T
DO 10 J=1,N
  X(J)=XZ(J)
10 CONTINUE
DO 4 J=1,4
CALL PHS(X,TT,F)
DO 5 I=1,N
W=A(J)*(F(I)-B(J)*Q(I))
X(I)=X(I)+H*W
5 Q(I)=Q(I)+3.E0*W-C(J)*F(I)
W=A(J)*(1.E0-B(J)*Q(N+1))
TT=TT+H*W
4 Q(N+1)=Q(N+1)+3.E0*W-C(J)
T=TT
RETURN
END

```

SUBROUTINE STORF(X,D,J)

REAL\*4 D(1),EMAT1(4,25),EMAT2(4,25),RMAT(4,25),A(5,5),X(1)

LOGICAL SYS1

COMMON/COFF/A,U1,U2,UDUM

COMMON/ER/EMAT1,EMAT2,RMAT

COMMON/SYSTEM/SYS1

COMMON/INTGER/N

IF(SYS1) GO TO 50

STORE THE VALUES OF SYSTEM 2 STATE VARIABLES.

IF (UDUM.LT.0.5) GO TO 30

RMAT(1,J)=X(1)

RMAT(2,J)=X(2)

RMAT(3,J)=X(3)

RMAT(4,J)=X(4)

RETURN

30 IF(D(1).LT.0.5) GO TO 40

EMAT1(1,J)=X(1)

EMAT1(2,J)=X(2)

EMAT1(3,J)=X(3)

EMAT1(4,J)=X(4)

RETURN

40 EMAT2(1,J)=X(1)

EMAT2(2,J)=X(2)

EMAT2(3,J)=X(3)

EMAT2(4,J)=X(4)

RETURN

STORE THE VALUES OF SYSTEM 1 STATE VARIABLES.

50 IF(UDUM.LT.0.5) GO TO 60

RMAT(1,J) = X(1)

RMAT(2,J) = X(2)

RETURN

```

60 EMAT1(1,J) = X(1)
   EMAT1(2,J) = X(2)
   RETURN
   END

```

```

SUBROUTINE TENSION(KB)
  REAL*4 MR(5,25),T(5,5,25),MR1(5,25),MR2(5,25)
  COMMON/RST/T
  COMMON/STTVAR/MR1,MR2,MR
  COMMON/FLOWCT/K1,K1P,K2,K2P
  COMMON/VAR/KVAR
  COMMON/VOLMS/VR1,VR2
  COMMON/BIAS/B
  COMMON/CONSTM/KCAM,KBM,KTPM
  AR = VR1+VR2
  G1 = 5./AP
  P = 0.45
  G2 = (B/K2)*(VR1/AP)
  DO 20 KK = 1,KTPM
  HOS = ((G1*MR(KB,KK)+G2)**2)*R
  T(KVAR,KB,KK) = HOS/(1.+HOS)
20 CONTINUE
  RETURN
  END

```

```

SUBROUTINE TJCTST(X,T,KSTR)
  REAL*4 X(1),MATCAL(5,100),TIME(100)
  LOGICAL SYS1
  COMMON/CADETL/MATCAL,TIME
  COMMON/PRTPTS/INPT
  COMMON/INTGER/N
  COMMON/PRTROW/M
  COMMON/WDVICE/KWC,KWDD
  COMMON/SYSTEM/SYS1
  M = N+1
  IF(SYS1) M=N
  IF(T.GT.1.E-20) GO TO 5
  KNT=1
  KNTR = 1
5. IF(KNT.EQ.KSTR) GO TO 20
  KNT=KNT+1
  RETURN
20 CAP = X(2)+X(4)
  IF(SYS1) CAP = X(2)
  TIME(KNTR) = T

```

STORE TIME TRAJECTORIES OF SYSTEM STATE VARIABLES.

```

MATCAL(1,KNTR) = X(1)
MATCAL(2,KNTR) = X(2)
IF(SYS1) GO TO 30

```

```
MATCAL(3,KNTR) = X(3)
MATCAL(4,KNTR) = X(4)
MATCAL(5,KNTR) = CAR
70 IF(KNTR.EQ.INFRT)CALL PPPINF
KNTR = KNTR+1
KNT=1
RETURN
END
```

```
SUBROUTINE TRAJCT
REAL *4 DXZ(5),ALPHAM(4,25),X(5)
COMMON/DECOND/ALPHAM
COMMON/CONSTS/KTP,KB,KLRF,KCA,KSTMF
COMMON/CUTPT/FLAG,ZZ
COMMON/INTGER/N
FLAG = 0
ZZ = 7
T1=60
NINT=600
IA=1
```

```
CALL THE DIFFERENTIAL EQUATION SOLVING PACKAGE WITH DYNAMIC EQUILIBRIUM
CONDITIONS.
```

```
DO 20 J=1,N
20 DXZ(J)=ALPHAM(J,KTP)
CALL PCM(DXZ,NINT,N,IA,T1,X)
RETURN
END
```

APPENDIX 3

A SAMPLE OF THE COMPUTER OUTPUT

LAMP1 = 0.60

LAMP2 = 10.00

-----  
THE A MATRIX OF THE SYSTEM  
-----

-0.1750E 00	0.1667E 01	0.0	0.0
0.1733E 00	-0.1667E 01	0.0	0.0
0.0	0.0	-0.2450E-01	0.1000E 00
0.0	0.0	0.1200E-01	-0.1000E 00

-----  
EIGEN VALUES OF THE FAST SUB-SYSTEM  
-----

-0.1407E 01 0.0  
-0.7451E-01 0.0

-----  
EIGEN VALUES OF THE SLOW SUB-SYSTEM  
-----

-0.1135E 00 0.0  
-0.1101E-01 0.0

HEIGHT HO (CAD CONC.) = 1.000

BETA = 0.90

THE VALUE OF ZERO-BIAS = 0.008 \*EXPONENT FACTOR = 0.250

LAMP1 = 0.60 LAMS1 = 30.00 VS1 = 1.000 VRI = 0.080 K1 = 0.133  
 LAMP2 = 10.00 LAMS2 = 100.00 VS2 = 1.000 VR2 = 0.120 K1P = 0.012

PULSFS/MIN.	CAS1	CAS2	CAS1	CAR2	CAR1	CAR2	CAR	TENSION	C
1.00	0.416F-02	0.17RE 00	0.341F-03	0.210F-01	0.214E-01	0.114E 00	0.100E 00	0.114E 00	0.100E 00
2.00	0.160F-01	0.157F 00	0.131F-02	0.176F-01	0.182E-01	0.911E-01	0.100E 00	0.911E-01	0.100E 00
4.00	0.389F-01	0.135F 00	0.318F-02	0.125E-01	0.156E-01	0.644E-01	0.100E 00	0.644E-01	0.100E 00
6.00	0.589F-01	0.125F 00	0.483F-02	0.044F-02	0.143E-01	0.541E-01	0.100E 00	0.541E-01	0.100E 00
8.00	0.775F-01	0.120F 00	0.645E-02	0.756E-02	0.139E-01	0.516E-01	0.100E 00	0.516E-01	0.100E 00
10.00	0.952F-01	0.116F 00	0.779E-02	0.629E-02	0.141E-01	0.528E-01	0.100E 00	0.528E-01	0.100E 00
15.00	0.177E 00	0.112F 00	0.112F-01	0.442E-02	0.156E-01	0.642E-01	0.100E 00	0.642E-01	0.100E 00
20.00	0.176E 00	0.100F 00	0.143F-01	0.340E-02	0.177E-01	0.812E-01	0.992E-01	0.812E-01	0.992E-01
25.00	0.217F 00	0.104F 00	0.171E-01	0.276E-02	0.199F-01	0.119E 00	0.982E-01	0.119E 00	0.982E-01
30.00	0.281F 00	0.107F 00	0.195F-01	0.233E-02	0.219F-01	0.137E 00	0.968E-01	0.137E 00	0.968E-01
35.00	0.404F 00	0.106F 00	0.233F-01	0.177E-02	0.237E-01	0.150E 00	0.950E-01	0.150E 00	0.950E-01
40.00	0.431F 00	0.105F 00	0.244F-01	0.142E-02	0.251F-01	0.160E 00	0.931E-01	0.160E 00	0.931E-01
45.00	0.450F 00	0.105F 00	0.250E-01	0.119E-02	0.270E-01	0.171E 00	0.909E-01	0.171E 00	0.909E-01
50.00	0.402F 00	0.105F 00	0.269F-01	0.102E-02	0.281E-01	0.182F 00	0.865E-01	0.182F 00	0.865E-01
60.00	0.442F 00	0.104F 00	0.276E-01	0.102E-02	0.286E-01	0.187E 00	0.820E-01	0.187E 00	0.820E-01
70.00	0.455F 00	0.104F 00	0.276F-01	0.940E-03	0.285E-01	0.186E 00	0.798E-01	0.186E 00	0.798E-01
75.00	0.455F 00	0.104F 00	0.276F-01	0.940E-03	0.285E-01	0.186E 00	0.777E-01	0.186E 00	0.777E-01
80.00	0.507F 00	0.104F 00	0.276F-01	0.783E-03	0.284F-01	0.185E 00	0.736E-01	0.185E 00	0.736E-01
90.00	0.515E 00	0.104F 00	0.270E-01	0.723E-03	0.277E-01	0.177E 00	0.699E-01	0.177E 00	0.699E-01
100.00	0.535E 00	0.103F 00	0.264F-01	0.644E-03	0.270E-01	0.170E 00	0.664E-01	0.170E 00	0.664E-01
110.00	0.556E 00	0.103F 00	0.258E-01	0.604E-03	0.264E-01	0.164E 00	0.632E-01	0.164E 00	0.632E-01
120.00	0.596E 00	0.103F 00	0.238F-01	0.485E-03	0.243E-01	0.143E 00	0.551E-01	0.143E 00	0.551E-01
150.00	0.659E 00	0.103F 00	0.217E-01	0.425E-03	0.221E-01	0.121E 00	0.487E-01	0.121E 00	0.487E-01
180.00	0.601E 00	0.103F 00	0.217E-01	0.425E-03	0.221E-01	0.121E 00	0.487E-01	0.121E 00	0.487E-01
240.00	0.671F 00	0.103F 00	0.186E-01	0.304E-03	0.189E-01	0.133E-01	0.393E-01	0.133E-01	0.393E-01

EXPERIMENTAL VALUES  
 REFERENCE VALUES  
 PERCENTAGE ERROR

THE CANONICAL VALUES AND RATIOS OF OMEGA CURVE

\*\*\*\*\*

7	V/Z	P/Z	V/P	L/Z	L/P	F1	F2
0.114	0.453	1.647	0.275	0.804	0.488	8.350	71.052
14.000	0.736	2.296	0.147	1.500	0.654	16.732	13.846
34.762-28.228	87.764-46.422	25.349-50.097	37.589				

HEIGHT HO (CAO CONC.) = 2.000

\*\*\*\*\*  
 BETA = 0.90  
 \*\*\*\*\*

\* THE VALUE OF ZERO-BIAS = 0.000 \* EXPONENT FACTOR = 0.250 \*

LAMP1 = 0.60 LAMSI = 30.00 VSI = 1.000 VRI = 0.080 K1 = 0.133  
 LAMP2 = 10.00 LAMSP = 100.00 VS2 = 1.000 VR2 = 0.120 KIP = 0.012

PULSES/MIN.	CAS1	CAS2	CARI	CAR2	CAR	CAR	TENSION	C
1.00	0.209F 00	0.354E 00	0.166E-01	0.420E-01	0.586E-01	0.492E 00	0.100E 00	
2.00	0.229F 00	0.313E 00	0.184E-01	0.351E-01	0.535E-01	0.446E 00	0.100E 00	
4.00	0.270E 00	0.270E 00	0.217E-01	0.249E-01	0.466E-01	0.379E 00	0.100E 00	
6.00	0.305E 00	0.250E 00	0.246E-01	0.189E-01	0.434E-01	0.347E 00	0.100E 00	
8.00	0.337E 00	0.240E 00	0.272E-01	0.151E-01	0.423E-01	0.335E 00	0.100E 00	
10.00	0.367E 00	0.237E 00	0.297E-01	0.126E-01	0.422E-01	0.334E 00	0.100E 00	
15.00	0.439E 00	0.224E 00	0.354E-01	0.881E-02	0.443E-01	0.355E 00	0.100E 00	
20.00	0.504E 00	0.219E 00	0.407E-01	0.690E-02	0.475E-01	0.388E 00	0.998E-01	
25.00	0.566E 00	0.214E 00	0.453E-01	0.552E-02	0.508E-01	0.421E 00	0.992E-01	
30.00	0.625E 00	0.214E 00	0.492E-01	0.465E-02	0.539E-01	0.449E 00	0.982E-01	
35.00	0.682E 00	0.212E 00	0.526E-01	0.398E-02	0.565E-01	0.473E 00	0.968E-01	
40.00	0.728E 00	0.211E 00	0.548E-01	0.353E-02	0.583E-01	0.489E 00	0.950E-01	
45.00	0.769E 00	0.211E 00	0.564E-01	0.319E-02	0.556E-01	0.500E 00	0.931E-01	
50.00	0.816E 00	0.210E 00	0.580E-01	0.285E-02	0.608E-01	0.510E 00	0.909E-01	
60.00	0.860E 00	0.209E 00	0.593E-01	0.239E-02	0.617E-01	0.517E 00	0.865E-01	
70.00	0.958E 00	0.208E 00	0.597E-01	0.204E-02	0.617E-01	0.517E 00	0.820E-01	
75.00	0.980E 00	0.208E 00	0.597E-01	0.192E-02	0.612E-01	0.513E 00	0.798E-01	
80.00	0.101E 01	0.208E 00	0.590E-01	0.180E-02	0.608E-01	0.509E 00	0.777E-01	
90.00	0.107E 01	0.207E 00	0.582E-01	0.157E-02	0.588E-01	0.501E 00	0.736E-01	
100.00	0.109E 01	0.207E 00	0.566E-01	0.149E-02	0.580E-01	0.486E 00	0.699E-01	
110.00	0.112E 01	0.207E 00	0.550E-01	0.133E-02	0.564E-01	0.472E 00	0.664E-01	
120.00	0.116E 01	0.207E 00	0.536E-01	0.119E-02	0.548E-01	0.458E 00	0.632E-01	
150.00	0.123E 01	0.206E 00	0.489E-01	0.970E-03	0.498E-01	0.411E 00	0.551E-01	
180.00	0.121E 01	0.206E 00	0.445E-01	0.849E-03	0.453E-01	0.366E 00	0.487E-01	
240.00	0.136E 01	0.205E 00	0.375E-01	0.608E-03	0.381E-01	0.290E 00	0.393E-01	

THE CANONICAL VALUES AND RATIOS OF OMEGA CURVE

Z	V/Z	P/Z	V/P	L/Z	F1	F2	EXPERIMENTAL VALUES	REFERENCE VALUES	PERCENTAGE ERROR
0.092	0.670	1.054	0.644	0.591	9.273	6.717			
21.000	0.500	1.694	0.295	1.024	11.403	91.786			

HEIGHT HO (CAD CONC.) = 4.000

BETA = 0.90

THE VALUE OF ZERO-BIAS = 0.008 \* EXPONENT FACTOR = 0.250 \*

LAMP1 = 0.60 LAMS1 = 30.00 VS1 = 1.000 VR1 = 0.080 K1 = 0.133  
 LAMP2 = 10.00 LAMS2 = 100.00 VS2 = 1.000 VR2 = 0.120 KIP = 0.012

PULSES/MIN.	CAS1	CAS2	CAR1	CAR2	CAR	TENSION	C
1.00	0.617E 00	0.712E 00	0.491F-01	0.840E-01	0.132E 00	0.833E 00	0.100E 00
2.00	0.651F 00	0.627E 00	0.522E-01	0.702E-01	0.132E 00	0.808E 00	0.100E 00
4.00	0.719E 00	0.540E 00	0.577E-01	0.498E-01	0.100E 00	0.765E 00	0.100E 00
6.00	0.776E 00	0.501E 00	0.624E-01	0.378E-01	0.100E 00	0.739E 00	0.100E 00
8.00	0.826F 00	0.479E 00	0.665E-01	0.302E-01	0.968E-01	0.725E 00	0.100E 00
10.00	0.874F 00	0.446F 00	0.704E-01	0.251E-01	0.956F-01	0.720E 00	0.100E 00
15.00	0.944F 00	0.447E 00	0.794F-01	0.177E-01	0.970E-01	0.726E 00	0.100E 00
20.00	0.106F 01	0.438F 00	0.874F-01	0.136E-01	0.101E 00	0.741E 00	0.998E-01
25.00	0.119F 01	0.432E 00	0.942F-01	0.110E-01	0.105E 00	0.757E 00	0.992E-01
30.00	0.127F 01	0.428E 00	0.999F-01	0.930E-02	0.109E 00	0.770E 00	0.982E-01
35.00	0.136F 01	0.425E 00	0.105E 00	0.797E-02	0.113F 00	0.781E 00	0.968E-01
40.00	0.143F 01	0.427E 00	0.108E 00	0.707E-02	0.115E 00	0.787E 00	0.950E-01
45.00	0.149F 01	0.421E 00	0.109E 00	0.639E-02	0.116E 00	0.790E 00	0.931E-01
50.00	0.157F 01	0.420E 00	0.111F 00	0.570E-02	0.117E 00	0.793E 00	0.909E-01
60.00	0.169F 01	0.418F 00	0.112F 00	0.477E-02	0.117E 00	0.793E 00	0.865E-01
70.00	0.179F 01	0.417E 00	0.111F 00	0.407E-02	0.115E 00	0.789E 00	0.820E-01
75.00	0.182F 01	0.416E 00	0.110E 00	0.348E-02	0.114E 00	0.785E 00	0.798E-01
80.00	0.184F 01	0.416F 00	0.109E 00	0.360E-02	0.113E 00	0.781E 00	0.777E-01
90.00	0.197F 01	0.415E 00	0.107E 00	0.313E-02	0.110E 00	0.772E 00	0.736E-01
100.00	0.200F 01	0.414E 00	0.103F 00	0.289E-02	0.106E 00	0.761E 00	0.699E-01
110.00	0.204F 01	0.414E 00	0.100F 00	0.266E-02	0.103F 00	0.749E 00	0.664E-01
120.00	0.210F 01	0.413F 00	0.971F-01	0.242E-02	0.995E-01	0.736E 00	0.632E-01
150.00	0.221F 01	0.412E 00	0.879F-01	0.194E-02	0.899E-01	0.694E 00	0.551E-01
180.00	0.222F 01	0.412E 00	0.799F-01	0.170E-02	0.816F-01	0.652E 00	0.487E-01
240.00	0.241F 01	0.411F 00	0.668E-01	0.122E-02	0.680E-01	0.565E 00	0.393E-01

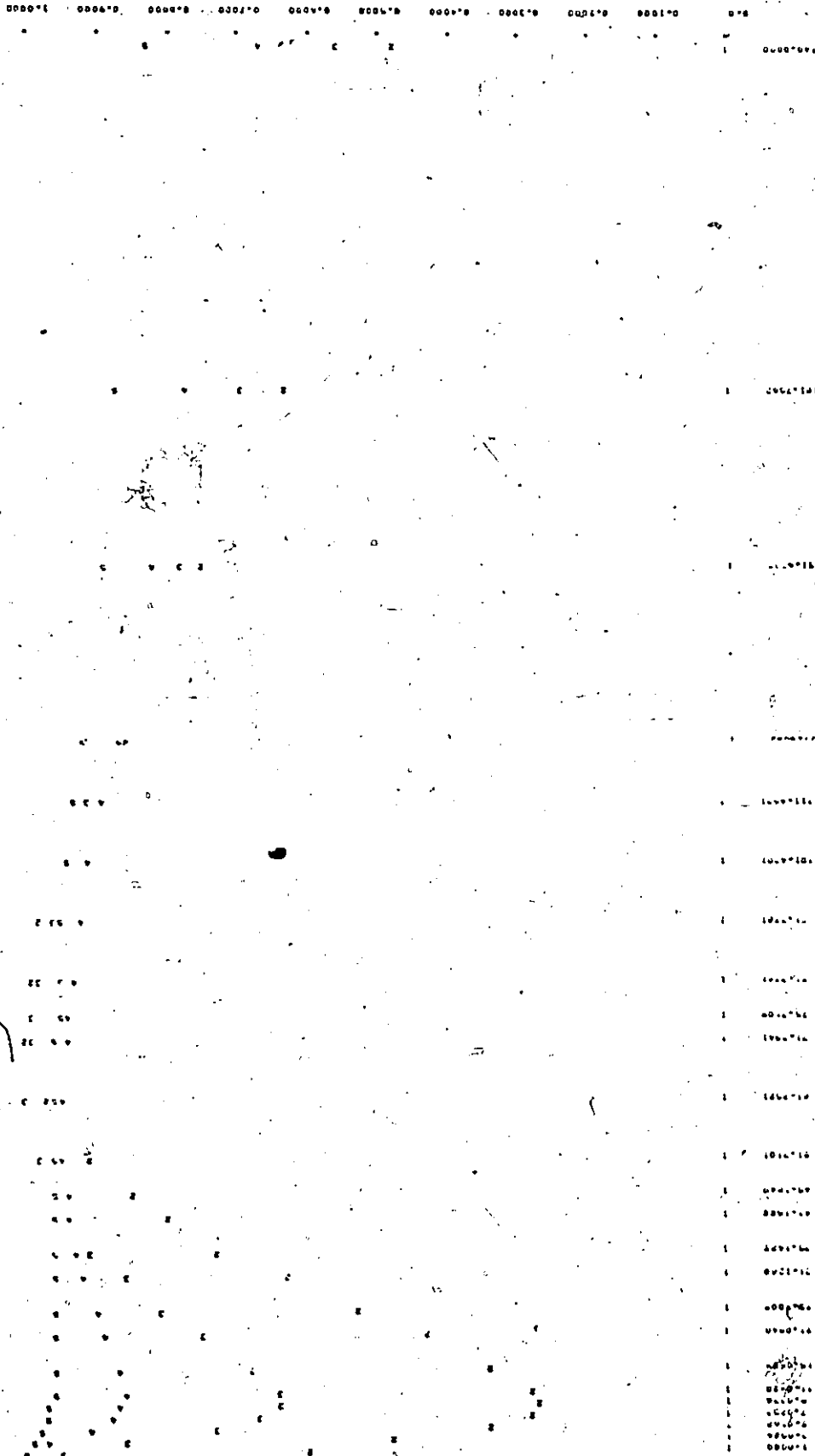
THE CANONICAL VALUES AND RATIOS OF OMEGA CURVE

Z	V/Z	P/Z	V/P	L/Z	L/P	F1	F2	EXPERIMENTAL VALUES	REFERENCE VALUES	PERCENTAGE ERROR
0.833	0.863	0.954	0.909	0.678	0.711	11.357	54.821			
67.000	0.765	0.922	0.830	0.500	0.543	15.720	43.222			





Omega Responses Individually Normalized Omega Responses



REFERENCES

- 1) Forester, G. V., and Mainwood, G. W., "The Effect of Calcium Ion Concentration on the Mechanical Properties of the Isolated Cardiac Muscle of the Rat, Submitted for Publication.
- 2) Manring, A., and Hollander, P. B., "The Interval Strength Relationship in Mammalian Atrium: A Calcium Exchange Model", Biophysical Journal, Vol. II: 483-501, (1971).
- 3) Kruta, V., and Braveny, P., "Potentiation of Contractility in the Heart Muscle of the Rat and Some Other Mammals", Nature, 187: 327-328, (1960).
- 4) Niedergerke, R., and Lüttgau, H. C., "Calcium and the Contraction of the Heart", Nature, 173: 1066-1067, (1957).
- 5) Kelly, J. J., and Hoffman, B. F., "Mechanical Activity of Rat Papillary Muscle", American Journal of Physiol., 199: 157-162, (1960).
- 6) Langer, G. A., and Brady, A. J., "Effect of Temperature upon Contractile Tension and Ionic Exchange in Rabbit Ventricle", Journal of Gen. Physiol., 52: 682, (1966).

- 7) Shelburne, J. C., Serens, S. D., and Langer, G. A., "The Rate-Tension Staircase in Rabbit Ventricular Muscle: Relation to Ionic Exchange", American Journal of Physiol., 213: 1115-1125, (1967).
- 8) Langer, G. A., "Ion Fluxes in Cardiac Excitation and Contraction and their Relation to Myocardial Contractility", Physiol., Rev. 48: 708-757, (1968).
- 9) Winegrad, S., and Shanes, A. M., "Calcium Flux and Contractility in Guinea-Pig Atria", Journal of GEN. Physiol., 45: 371-394, (1962).
- 10) Lee, S. L., Mainwood, G. W., and Korecky, B., "The Electrical and Mechanical Response of Rat Papillary Muscle to Paired Pulse Stimulation", Canadian Journal of Physiol. Pharmacol., 48: 216-225, (1970).
- 11) Brady, A. J., "Active State in Cardiac Muscle", Physiol. Rev. 48: 570-600, (1968).
- 12) Forester, G. V., "The Effect of Calcium Ion Concentration on the Interval-Strength Relationship of Isolated Papillary Muscle of the Rat: Correlation with a Model of Calcium Movement", Ph.D. Thesis, Dept. of Physiology, Univ. of Ottawa, Feb. 1974.

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