A CONTROL SYSTEM FOR ISOLATED MUSCLE EXPERIMENTS

by

Jerry Israel Kleinbaum

SUBMITTED IN PARTIAL FULFILLMENT OF THE

REQUIREMENTS FOR THE DEGREES OF

BACHELOR OF SCIENCE

and

MASTER OF SCIENCE

at the

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

August, 1972

Signature of Author Signature redacted
Department of Electrical Engineering, August 14, 1972

Certified by Signature redacted
Thesis Supervisor

Accepted by Signature redacted
Chairman, Departmental Committee on Graduate Students

A CONTROL SYSTEM FOR ISOLATED MUSCLE EXPERIMENTS

BY

Jerry Israel Kleinbaum

Submitted to the Department of Electrical Engineering on August 14, 1972 in partial fulfillment of the requirements for the Degrees of Bachelor of Science and Master of Science.

ABSTRACT

An experimental system at the Circulation Laboratory of Boston City Hospital allows the study of isolated cardiac muscle. Trabecular muscle of rat hearts are dissected and mounted from a lever arm.in the muscle chamber. The muscle can be stimulated and made to contract against varying loads determined by weights hung from the lever arm.

It is desired to have the isolated muscle perform the same contraction-relaxation sequence as the intact muscle performs in the beating heart. This is approximated by a four state sequence of events: isometric contraction; isotonic shortening; isometric relaxation; and isotonic lengthening. This requires the ability to change loads against which the muscle contracts in mid-cycle. To accomplish this, the system is modified so that the lever arm is driven by a motor whose current can be electrically controlled.

During each of the four states of the sequence, one of the two variables is constant. This is achieved through the use of an active feedback network. Stable feedback compensation is derived for both displacement and tension. A logic network determines which variable should be held constant, at any given time, and switches that variable into the feedback loop. Comparator circuits analyze the tension and displacement waveforms and provide the input signals to the logic network.

Using this system, a controlled contraction-relaxation sequence can be obtained for the isolated muscle. Flexibility is provided by the ability to preset points at which state changes are to occur. This allows modelling of a wide range of in vivo type contractions. Results obtained for the system are good.

THESIS SUPERVISOR: Roger G. Mark, M.D.
TITLE: Assistant Professor of Electrical Engineering

ACKNOWLEDGEMENTS

I wish to express my sincere appreciation to all those who helped in the performance of this thesis. To Doctors Roger Mark and Oscar Bing for their ideas, guidance, and patience. To the staff and fellow students of the Biomedical Engineering Lab at Boston City Hospital: Donald Zimmerman, Richard Middlekauff, Doug Belli, Chester Conrad, Seymour Freidel, and David Sulman. To Wesley Brooks for doing much of the dissecting work. To the National Institute of Health and the Research Lab of Electronics for their support with funds and equipment. And to my wife Nancy for her typing, her encouragement, and her confidence in my ability.

TABLE OF CONTENTS

I. Introduction

The experimental study of isolated muscle began in 1924 with the work of A.V. Hill.[1] Since that time, scores of physiologists have performed hundreds of different experiments on both cardiac and skeletal muscle. Although many different aspects of muscle dynamics have been studied, the experimental apparatus used in a great majority of these experiments remains essentially the same as that developed by Hill 50 years ago.

The typical experimental apparatus consists of a chamber containing a constant-temperature and well-oxygenated saline solution in which the muscle being studied is suspended. One end of the muscle is connected to a lever arm by a short gold chain; the other end is fastened to a tension transducer by another short chain which passes through a mercury seal and out the bottom of the chamber. Various preloads and afterloads may be placed on the muscle by means of weights attached appropriately to the lever. A displacement transducer monitors the motion of the lever arm. The muscle is stimulated by a pair of electrodes mounted inside the chamber. Both tension and displacement are monitored during the contraction by the two transducers. A schematic diagram of the system is shown in figure 1.

After using a system similar to that described above to study the frog sartorius muscle, Hill suggested his three-component model for skeletal muscle shown in figure 2. Hill postulated that the contractile element is freely extensible and therefore the parallel elastic element (PE) supports the resting tension of the muscle. Thus, the role of the PE is characterized by the muscle length-resting tension curve. The contractile element (CE) is the dynamic element which is capable of shortening during muscle contraction. The observed action of the muscle depends on the interplay between the contractile element and the series elastic element (SE) to which it is attached. If the ends of the muscle are fixed, the muscle contracts isometrically; the shortening CE causes the SE to lengthen, resulting in a buildup in tension at the ends of the muscle.

Much research has been devoted to the physiological and biochemical basis of muscle contraction. Each cardiac muscle cell consists of a series of parallel myofibrils that run the length of the cell. The parallel stacking of the myofibrils forms a regular and repeating striated pattern. Each fibril is surrounded by a membrane, the sarcolemma, and a network of tubules, the sarcoplasmic reticulum, runs parallel to the myofibrils and between them. A second system of tubules runs transverse to the fibrils. These two communication systems are necessary for coordinated contraction.[2]

The sarcomere is the working unit of the muscle. It is the repeating unit formed by the regular stacking of myofibrils and proteins within each myofibril. The sarcomere is formed from two fibrous proteins, actin and myosin. The thicker myosin filaments are about 1.5u long, while the actin filaments are approximately 1.0u long. It is the arrangement of these two filaments that gives the muscle its characteristic striated appearance shown in figure 3.

The actin and myosin filaments are stacked in the regular pattern shown in figure 3 as well. The actin fibers intertwine at the ends of the sarcomere and project in toward the center. The myosin filaments appear bridged at their centers and lie in the center of the sarcomere sandwiched between the actin filaments. The regions of overlap and non-overlap cause the characteristic appearance shown in figure 3 and each region is given a different designation as indicated.

The sliding filament hypothesis explains the possible nature of muscle contraction. According to this hypothesis, both the actin and myosin filaments remain constant in length during contraction. When activated, however, interactions occur between adjacent sites on the actin and myosin filaments which somehow act to propel the two sets of protein fibers past each other. The detailed structure of actin and myosin seem to support the possibility of interaction between the two proteins. Contraction also requires the presence of Ca^{++}, thought to be delivered by the sarcoplasmic reticulum system, and the splitting of ATP.[3]

The Hill model discussed above was an attempt to explain observed experimental data with a mechanical model. As such, the components of that model do not relate to structural features of muscle physiology. The model remains useful, however, both as a framework for analyzing experimental data and as a basis for making predictions about the outcome of future experiments.

Interest in the study of the dynamics of muscle contraction has centered on the contractile element. But observation of the contractile element alone requires separation of the CE effects from those of the series elastic components. This has been accomplished by a technique known as the afterloaded contraction. In the apparatus described earlier, the muscle being studied can be made to contract against a given load by hanging the appropriate weight at the back end of the lever arm. In addition, an adjustable stop is positioned above the lever arm tip for added flexibility in load regulation.

A small weight, the preload, is first placed on the back of the lever arm to establish some resting tension on the muscle. This causes a stretch in the PE, while leaving the CE and the SE unaffected. The stop is then adjusted so that it just makes contact with the lever arm tip without changing the resting tension or position of the muscle. An additional weight, the afterload, may then be added to the back end of the arm without causing any change at the muscle, because the afterload is supported by the stop. The muscle is then stimulated, and the contractile element shortens, thus pulling on the series elastic element and building up force. The contraction remains isometric, however, until the force of contraction just equals the afterload. When this happens, the muscle begins to shorten, and the load is moved. Throughout the remainder of the contraction, the force exerted by the muscle remains equal to the load (neglecting accelerations), and the stretch of the SE remains constant supplying that constant force. The subsequent shortening of the muscle must, therefore, represent the shortening of the contractile element. The sequence of events is outlined for the Hill model in figure 4.

In a series of experiments in 1938, Hill discovered the force-velocity relation of the contractile element, the most important relationship in muscle dynamics. By performing afterload contractions using a series of different ~~over~~afterloads with a constant preload, it was found that the initial velocity of shortening varies inversely with the magnitude of the load. At some value of load, P_0, the shortening of the muscle becomes zero, and P_0 is the maximum isometric force of that muscle; as the afterload approaches zero, the velocity approaches its maximum value, V_{max}. Graphically, the force-velocity relation has the form of a displaced hyperbola, and it has been described by the Hill Equation: $(P + a)(V + b) = (P_0 + a)b$, where a and b are constants. A typical force-velocity relation is demonstrated in graphic form in figure 5.

The significance of the force-velocity relation is the fact that it succinctly represents the contractile capability of an individual muscle. Its application to clinical cardiology is perhaps typified best by an example. Starling's Law of the Heart has been long observed experimentally in animals and in human catheterization subjects. As ventricular end-diastolic pressure rises, causing greater filling of the ventricle, the ensuing beat becomes more forceful, ejecting the blood under a higher systolic pressure. This observation of behavior of the intact heart is reflected in studies on isolated cardiac muscle. The variation in filling during diastole causes varying degrees of stretch in the individual muscles comprising the ventricular walls. Thus, if we perform a series of afterloaded-contractions, using the range of afterloads needed to derive a force-velocity curve as described above, and repeating each afterload with a range of different preloads, we will obtain a series of force-velocity relations, each for a different initial muscle length as shown in figure 6. The result is an isolated muscle analog of Starling's Law; as the initial muscle length increases, V_{max} remains constant, but P_0, the maximum isometric force of which the muscle is capable, increases. Thus, as the initial length of the muscle increases, as it does during an increase in filling volume, the muscle becomes capable of more force during contraction, as observed for the heart in the ensuing systole.

The force-velocity relation for isolated cardiac muscle also reflects changes brought about by drugs and chemicals. Chemicals such as norepinephrine and calcium, and drugs such as digitalis and phenobarbital cause changes in the force-velocity relation, changing both V_{max} and P_0. Different types of heart disease would also be expected to alter the nature of the force-velocity relation. Thus, as can be seen, the isolated muscle system provides a useful model for studying problems in clinical cardiology.

An experimental apparatus such as that described above has been set up at the Circulation Lab of Boston City Hospital by Dr. Oscar Bing, a cardiologist. His studies have been aimed at exploring the nature of cardiac muscle hypertrophy to find the nature of the change it causes in muscle dynamics and the biochemical changes that occur to bring it about. The studies involve the induction of hypertrophy in rats' hearts, and then the determination of the force-velocity curve for the ventricular trabecular muscle of these rats and for a group of control rats. The experimentation also involves a comparative biochemical assay of the hypertrophied ventricular tissue as compared to ventricular tissue for the control group.

It was in the performance of these experiments that the idea developed for this thesis. During each heartbeat, the left ventricle, the chamber that supplies the systemic circulation, goes through a cycle of contraction and relaxation. At the start of the contraction phase, or systole, the ventricle has just been filled from the atrium. Both the mitral valve, connecting the ventricle to the atrium, and the aortic valve are closed. The ventricle thus contracts isovolumetrically (to a first approximation) causing pressure within the ventricle to rise. When the ventricular pressure exceeds the aortic pressure, the aortic valve is forced open and the blood is expelled. During this phase of the cycle, end systole, ventricular pressure and aortic pressure are identical and change much more slowly. Once the blood has been ejected, diastole begins and ventricular pressure begins to fall. When it dips below aortic pressure, the aortic valve closes again and the ventricle relaxes isovolumetrically. The pressure in the ventricle falls until it drops below the atrial pressure, allowing the mitral valve to open and the ventricle to fill from the atrium. We can once again make the approximation that during this filling phase ventricular pressure remains relatively constant. Once filling is completed, the cycle begins again. The actual variation of ventricular volume and pressure during each heart beat are shown graphically in figure 7, along with the approximations discussed.

The above scheme is idealized in that it makes various approximations. The ejection and filling phases are merely approximately constant in pressure, the pressure changes being fairly significant. The assumption of isovolumic phases neglects changes in chamber shape and wall thickness which occur. These approximations,however, make possible a simplified sequence of events in the isolated muscle experiment. An individual muscle in theventricular wall passes through four phases corresponding to those discussed above. The initial phase is an isometric contraction followed by an isotonic shortening during ejection, an isometric relaxation during early diastole, and finally, an isotonic lengthening during filling. This succession of states is shown graphically in figure 8.

The first two contractile phases of the cardiac cycle can be simulated in the isolated muscle system as has already been discussed in relation to the afterloaded contraction. The relaxation phase, that occurring between times t_2 and t_4, cannot, however, be simulated in an isolated muscle system of the nature described. During the isotonic contraction, beginning at time t_1, the muscle shortens against a relatively large load representing the aortic pressure. Isotonic lengthening beginning at the time t_3 occurs against a much smaller load representing the atrial pressure during filling. In the experimental system, changing loads between the contraction and relaxation phases to more realistically model the cardiac cycle requires the actual physical removal of the afterload from the back end of the lever arm at time t_2 during the cycle. Clearly, this is not a feasible approach.

The problem, then, is to modify the experimental system for isolated muscle experiments to enable the isolated cardiac muscle to be loaded in approximately the same sequence as it would during the beating of an in vivo heart. The derivation of a force-velocity relation for the muscle is still possible and at the same time provides a more valid system for the study of the effects of disease, drugs, etc. on the contractile activity of cardiac muscle.

The accomplishment of this goal implies the ability to achieve instantaneous regulation of the load against which the muscle works. To do this, it is proposed that the experimental system be revised so that the load be determined by an electric motor attached to the lever arm, rather than by the placement of weights of the back end of the lever arm. Note that during each of the phases of contraction and relaxation, previously displayed graphically, one of the two variables, either tension or displacement, is held constant. This is to be achieved by the use of a feedback control system, controlling each of the two variables at the appropriate values and for the appropriate times.

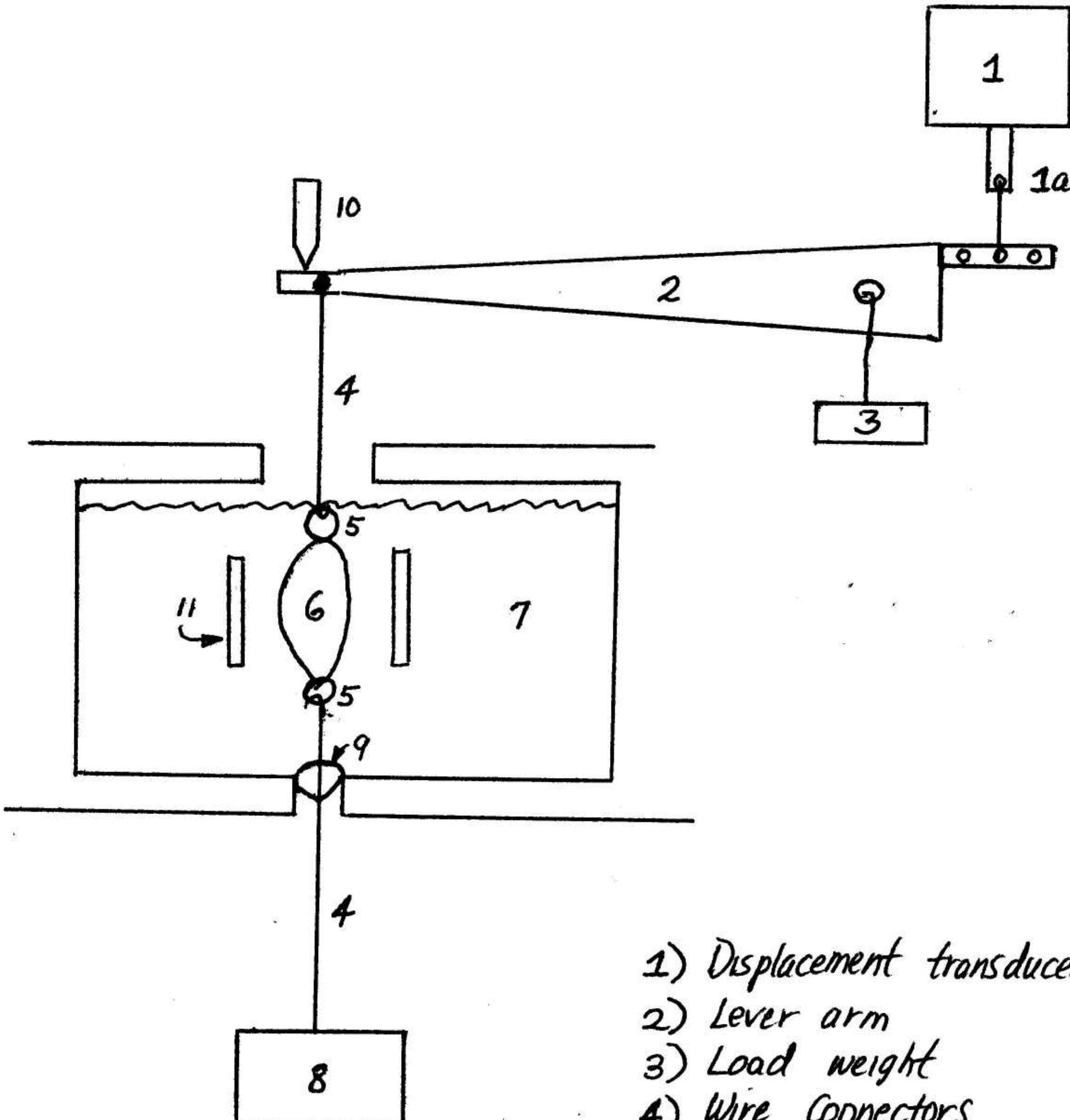
The broad outlines of the project are as follows: First, the redesigning of the mechanics of the experimental system to accomodate a motor-driven lever arm. Additionally, it is necessary to evaluate the transducers already in use in the system to determine their compatability with the revised system. Second, the characterization of the motor and its driver, the lever arm, the muscle, and the transducers in terms of the overall transfer function relating motor input to transducer output. Third, the design of a feedback control system for both tension and displacement which is stable and at the same time provides the required regulation and resolution. Fourth, the design of signal processing and logic circuitry to properly control the sequence of events which occur during a muscle contraction-relaxation cycle. Finally, the integration of all the circuitry into a working system.

---

[1]Hill, A. V., First and Last Experiments in Muscle Mechanics, Cambridge University Press, Cambridge, England, 1970.

[2]Curtis, H., Biology, Worth Publishers, Inc, New York, 1968.

[3]Braunwald, E, Ross J., and Sonnenblick, E., Mechanisms of Contraction of the Normal and Failing Heart, Little, Brown and Co., Boston, 1968.



1) Displacement transducer
2) Lever arm
3) Load weight
4) Wire Connectors
5) Metal rings
6) Muscle
7) Nutrient bath
8) Tension Transducer
9) Mercury seal
10) Adjustable stop
11) Electrode plates

Figure 1 – Schematic diagram of original experimental setup.

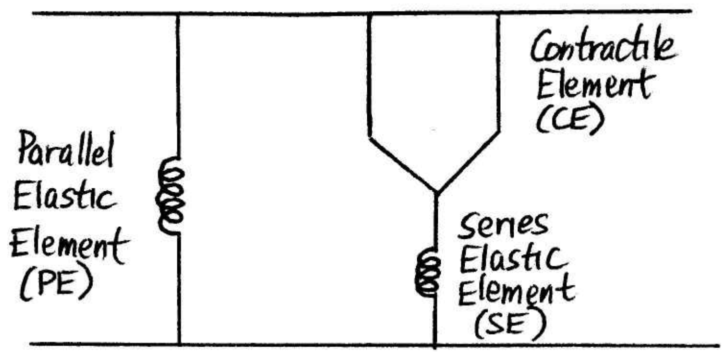


Figure 2 - Three-Component Muscle Model

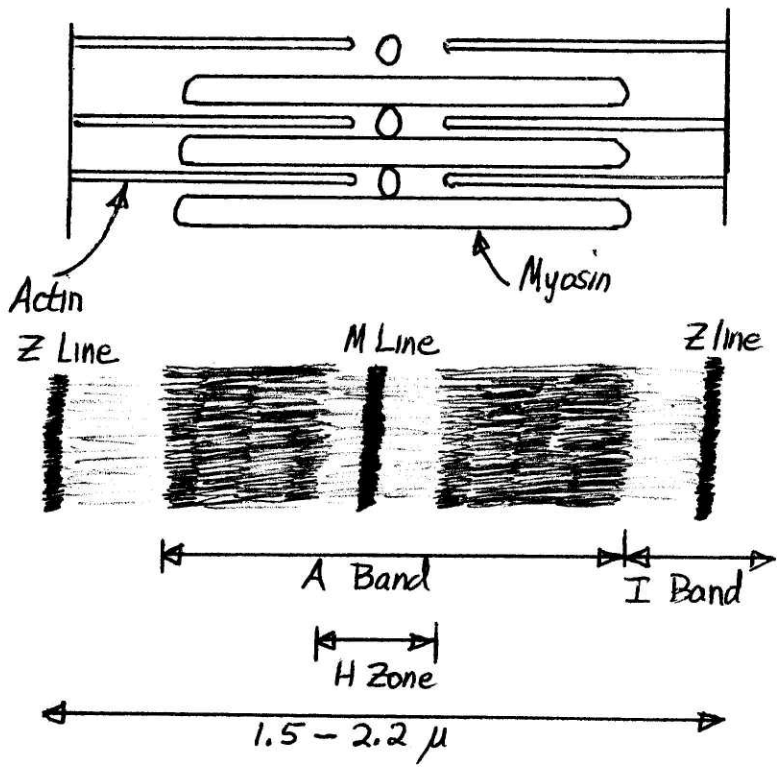


Figure 3 - Schematic Representation of Muscle Fiber

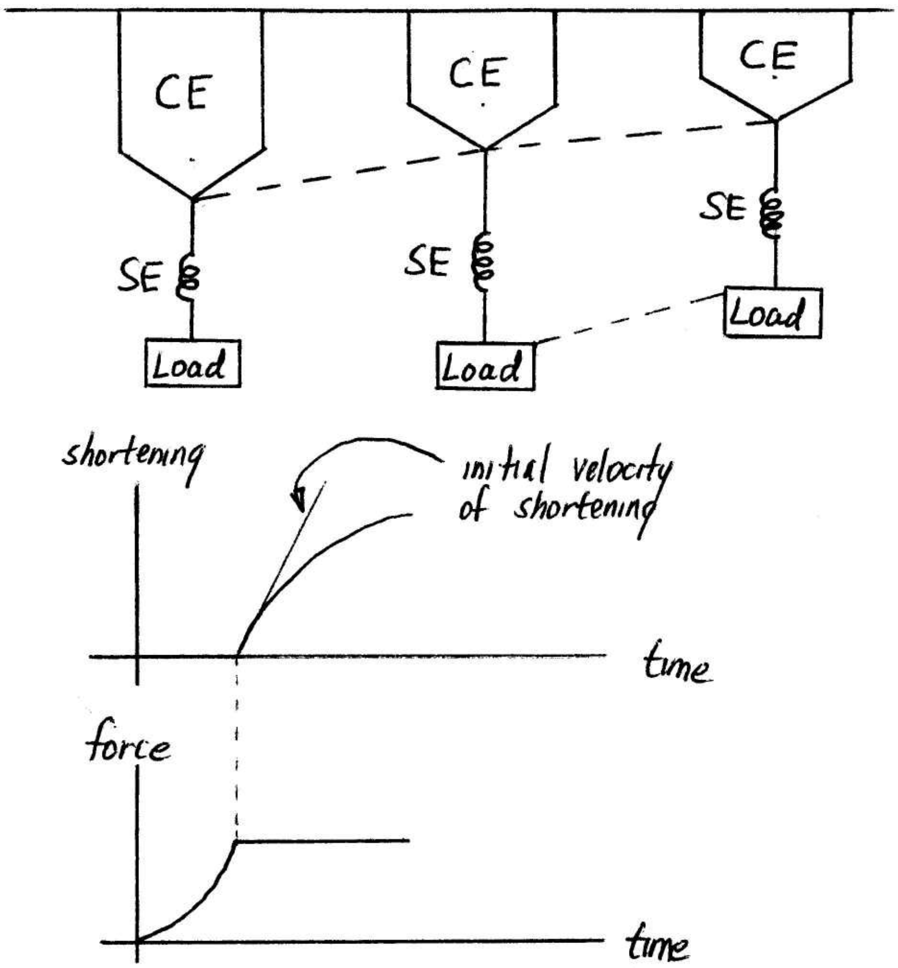


Figure 4 - Afterloaded Contraction

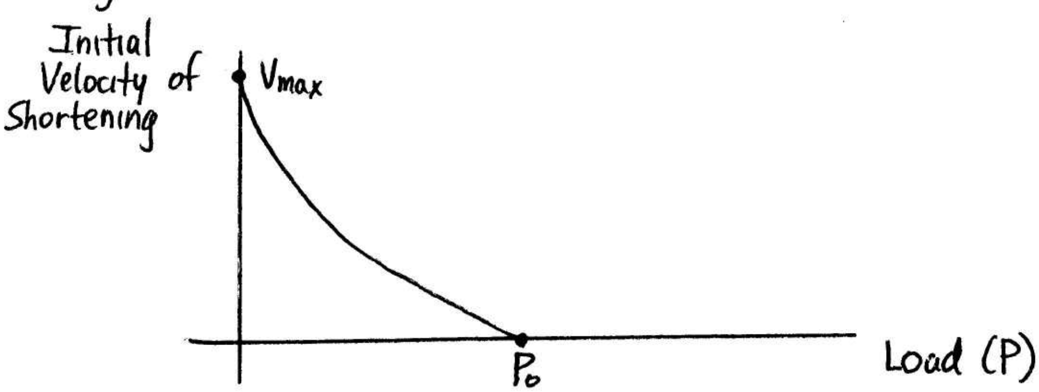


Figure 5 - Force-Velocity Relation

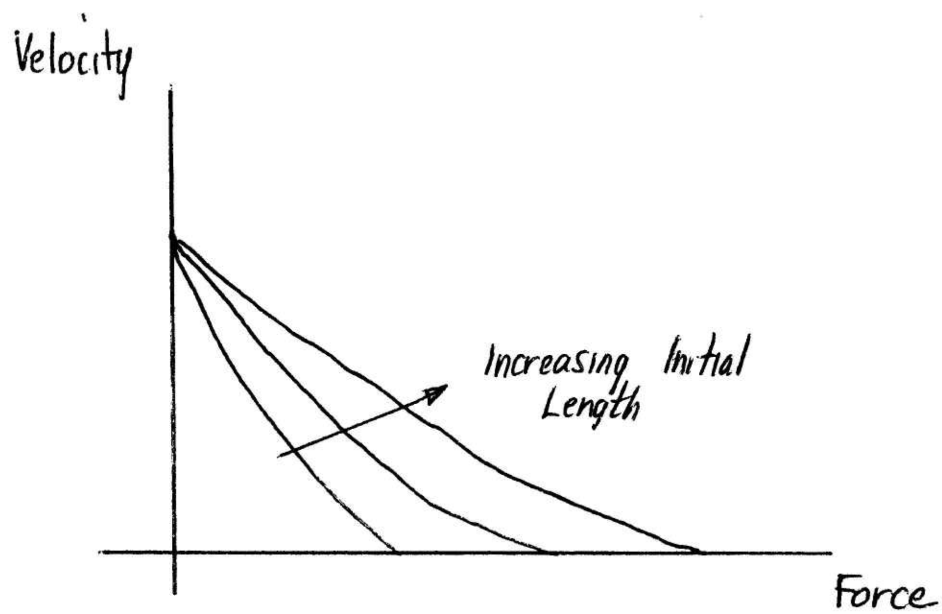


Figure 6 - The Variation of the Force-Velocity Relation with Resting Muscle Length.

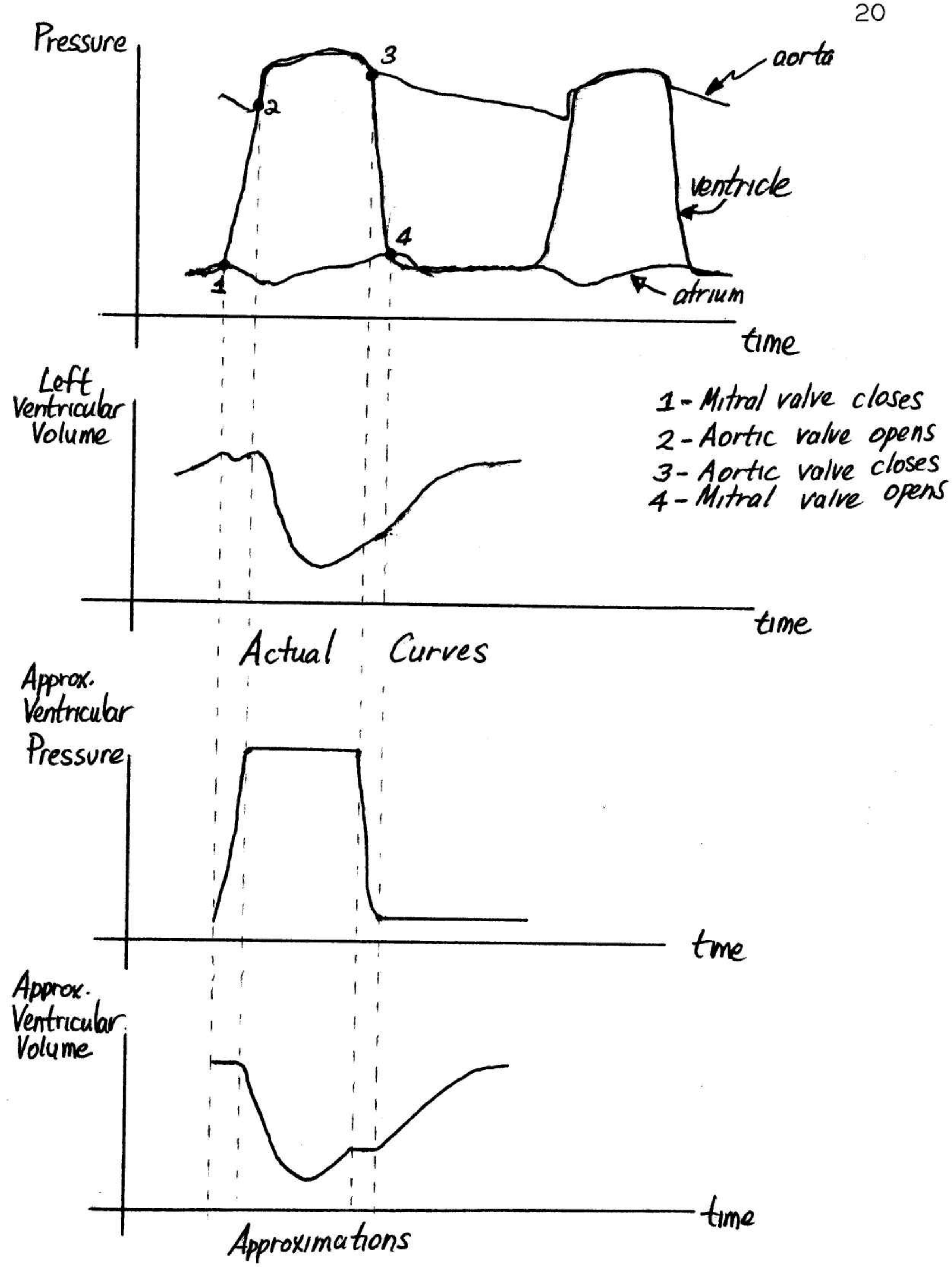


Figure 7 - Real and Approximate Ventricular Pressure & Volume During Heartbeat

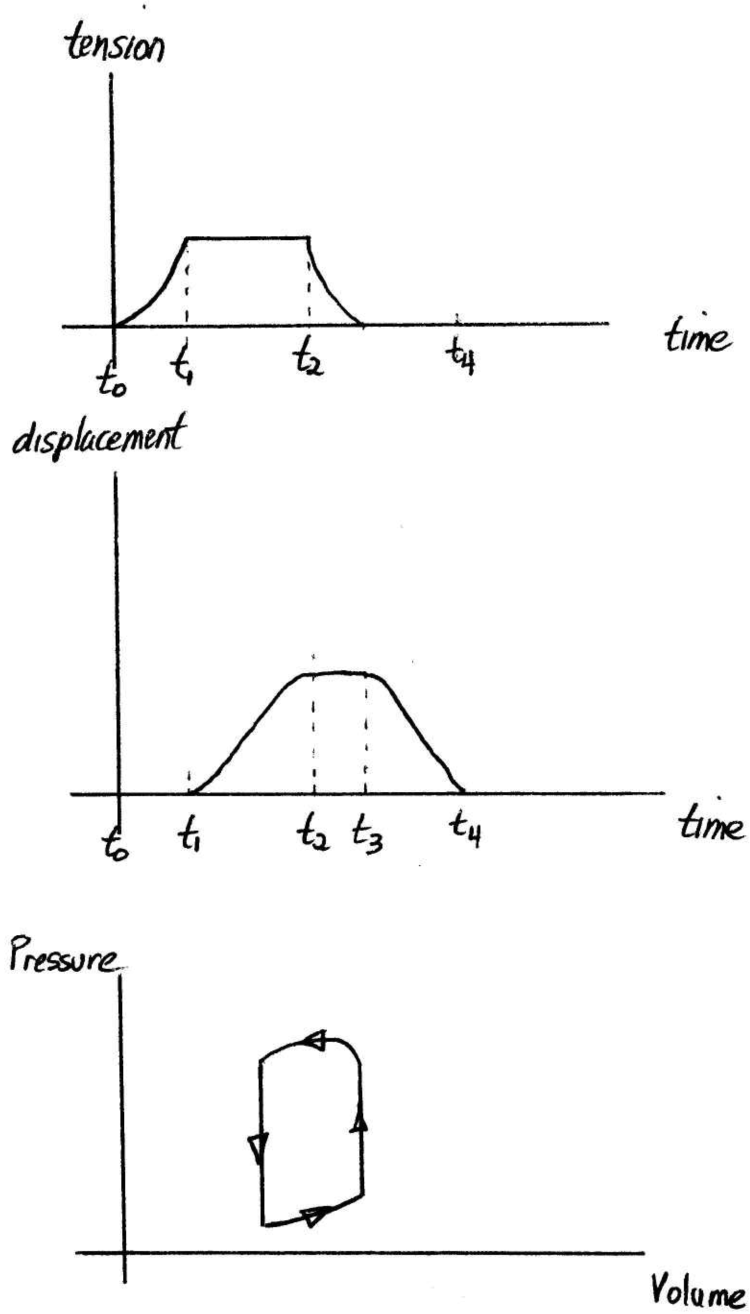


Figure 8 - Sequence of Events During Model of Ventricular Contraction.

II. The Experimental System

The arrangement of the experimental system before modification has already been discussed briefly. A schematic representation is shown in figure 1. The muscles used in these experiments are trabecular muscles from the rat ventricle. The muscle is dissected and mounted very rapidly, usually within ten minutes. All surgical work was done by Dr. Oscar Bing and by Wesley Brooks of the Circulation Lab staff. The muscle is maintained during the experiment in a nutrient solution, which is kept at a constant temperature of 28 degrees. The supply of oxygen in the solution is continuously replenished by an oxygen bubbler. Under these conditions, the contractile capability of the muscle remains intact for about six hours, more than enough time to complete a series of experiments.

The muscle is stimulated by a pair of mass electrodes driven by a Grass stimulator. The stimulator output pulse is variable both in frequency and duration with its amplitude set at 90 volts. The stimulation frequency is important in the survival of the muscle; the higher the stimulation frequency the more rapid the deterioration in the contractile properties. In our experiments, a frequency of 12 per minute is used, with a pulse duration of 10 milliseconds. The stimulator also provides a 1 microsecond pulse synchronized with the start of the stimulus pulse.

In the revised system, shown in figure 9, the weights at the end of the lever arm and the micrometer stop, both used to adjust the load against which the muscle contracts, are replaced by a motor. The motor specified was the General Scanning G-310. An important feature of this motor is its high natural frequency of 235 hertz. It is capable of a mechanical rotation of its shaft by 10°, enough to permit the maximum displacement required by the contracting muscle using a lever length of 3 centimeters. It requires 100 milliamps per degree of angular displacement, linear within 0.1 degrees or better. It provides a torque of approximately 1000 gm-cm. The motor is driven by the driver circuit shown in figure 10. The output transistors are both power transistors, and the feedback from the output to the inverting input of the second operational amplifier serves to eliminate the crossover distortion inherent in the push-pull configuration of the two transistors.

In order to achieve the maximum frequency response of the motor-lever arm system, the lever arm was kept short and holes were drilled along its length to lighten it. It was then mounted onto the motor shaft by the use of a hollow nail. The motor-lever arm assembly was then mounted on a support over the muscle chamber, with the entire support adjustable in its vertical position.

The displacement transducer is mounted above the back end of the lever arm and connected to it by a thin wire connector. The transducer used is the Hewlett Packard model 7DCDT-050. It consists of a linear, variable differential transformer, a moveable core which connects to the lever arm and moves up and down with the muscle, an oscillator and a demodulator. The oscillator requires a 6 volt, 20 milliamp DC excitation. The oscillator then excites the transformer primary. The position of the core, moving up and down axially, determines the amount of voltage induced in the secondaries of the transformer. The demodulator provides a DC output proportional to the displacement of the core. This is shown in figure 11.

The transducer has a full-scale output of 1.5 volts, and a displacement range of 2.30 millimeters. Its maximum nonlinearity is ±0.005 mm. Its output impedence is 2.2k and its natural frequency is 350 cycles per second. Since the natural frequency of the transducer is greater than the natural frequency of the motor, and the phase shift contributed by the displacement transducer is small at the natural frequency of the motor, it was decided that the transducer could be kept in the revised system.

The force developed by the muscle during contraction is measured by a force transducer mounted under the muscle chamber. The muscle is connected to the sensing element of the transducer by a thin wire running through a mercury seal and out of the bottom of the muscle chamber. The transducer used in the original system was a Statham bonded strain-gauge type transducer. This was unsuitable for use in the modified system because of the inherent slowness in response of the mechanical type transducer. The natural frequency of the transducer is 160 hertz, well below the natural frequency of the motor. Although strain-gauge type transducers can be found that are significantly faster than the one in use, and other types of mechanically coupled tension transducers having higher response frequencies are available, the cost of the transducer varies directly with the speed required.

In addition, the Statham transducer suffered a second fault. The tension transducer should have the smallest possible compliance; that is, there should be a minimum amount of motion at the sensing element of the transducer during a tension measurement. This is especially important during the measurement of the buildup of tension in an isometric contraction, when the lever arm position is kept constant, either by a weight in the original system or by position feedback in the new system. The compliance in the tension transducer permits the muscles to shorten during the buildup of tension, adding an error to the result. It should be noted that the tension transducer is not the only source of this type of error. There is a compliance in the wire connections between the muscle and the lever arm, and between the muscle and the tension transducer. However, these connections are chosen to have minimum compliance, and the tension transducer should not add significant error. This was not the case, however, for the Statham transducer. The motion involved in the sensing arm of the transducer was significant compared to the displacement changes actually observed in non-isometric experiments. For these reasons, it was decided that a new transducer was needed.

The transducer selected was the Pitran, a pressure sensitive transistor, having a high resonance frequency and a very low compliance. The Pitran is a silicon, NPN transistor in which the emitter-base junction is mechanically coupled to the surface of the transistor can. The transistor is first biased into its active region and a collector current thereby established. As pressure is applied to the surface of the can, the beta of the transistor changes, causing a consequent change in the collector current. The collector to emitter voltage, v_{ce}, is measured as the output. The model chosen, the PT22, provides a 2 volt full scale output for about 7 grams applied to its surface. Its sensitivity is 320 millivolts per gram, with linearity within 1%. Its resonant frequency is 150 kilohertz, and the maximum diaphragm displacement during a pressure measurement is less than 0.1 micron. A schematic diagram of the Pitran is shown in figure 12.

The Pitran is designed for measuring the force pressing on its surface. In this system, however, with the transducer mounted underneath the muscle chamber, as the muscle contracts, it pulls up on the transducer sensing element. This push-pull problem was solved by the design of the Pitran holder. The Pitran itself is mounted in the base of a plexiglass holder, recessed so that its pressure-sensitive surface is slightly below the surface level of the holder. It is epoxied in place with its leads projecting through the bottom of the holder. A small plexiglass lever was then positioned above the Pitran with one end rounded to contact the Pitran surface. The holder is positioned on its support to line up the eyelet in a vertical line with the lever arm tip. As the muscle shortens, it pulls up on the back of the arm, causing the front end to press down on the Pitran surface. This apparatus is shown in figure 13.

The Pitran is quite sensitive, and consequently it is also quite fragile. It is rated to withstand 500% of its maximum specified output before permanent damage occurs, but even this safety margin will not protect against the slip of a finger. For this reason, a second dowel was driven through the front end of the Pitran lever. This dowel holds the lever tip off the Pitran surface while it is not in use. It can be removed for pressure measurement at the beginning of each experiment.

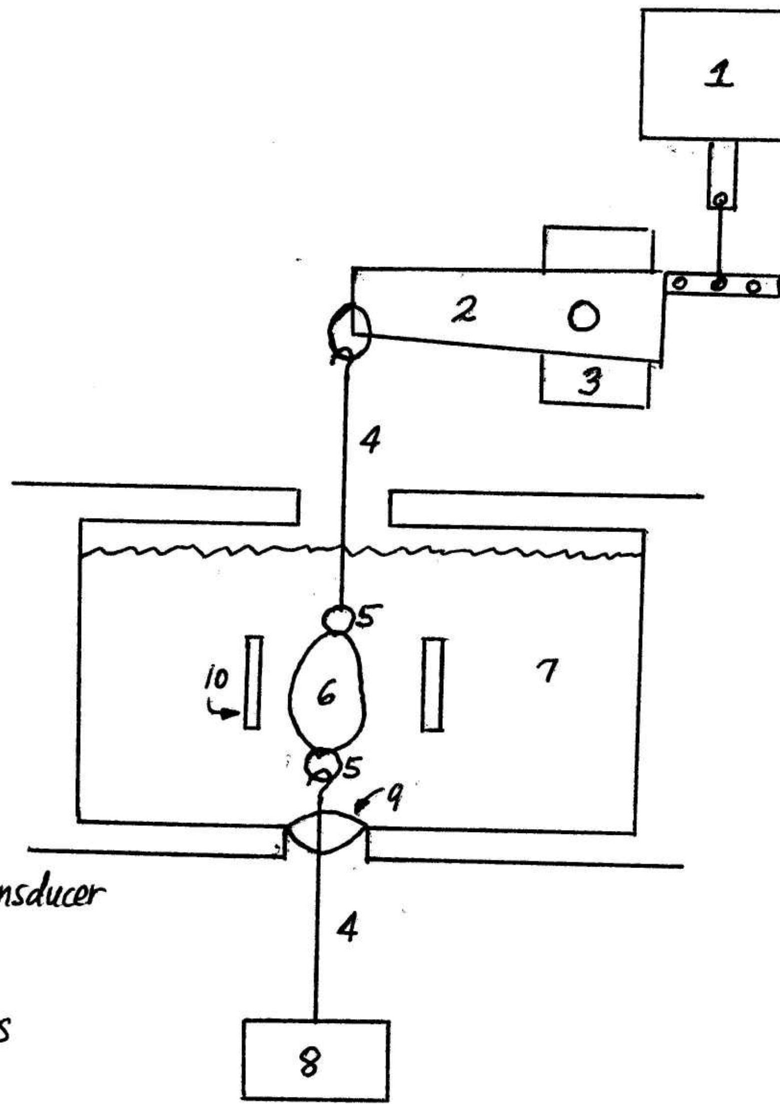
It is suggested in the Pitran specifications that the transistor be used in a simple common-emitter configuration. When this was attempted, however, it was found that the output drift, both during and between contractions, was unacceptably large. The output appeared to drift in a random fashion and the bias point has to be reset before each contraction by varying a potentiometer in order to zero the output voltage. This was unacceptable, and an inquiry was made into the nature of this instability. The Pitran has a large specified temperature coefficient, 150 millivolts v_{ce} per degree Centigrade. This is a drift of 7.5% of rated full-scale output per degree. It was also learned that the device has an inherent susceptibility to mechanical instability, and any flexibility in mounting will contribute to the drift. After conversations with the applications engineers of Stow Laboratories, manufacturers of the Pitran, it was determined that a signal conditioning circuit be used to minimize the drift.

The circuit used is shown in figure 14. The circuit operates in two modes. When the switch is closed, the feedback loop containing the Pitran is closed and the operating point is maintained at zero. Any drift effects, whether due to mechanical instability or to small temperature fluctuation, are cancelled by the feedback. In addition, however, any changes in output caused by the application of pressure are also cancelled out by the feedback network, the Pitran base current being continuously adjusted to maintain the collector voltage at zero. Thus, this mode of operation is used between contractions to keep the Pitran output drift-free and zeroed.

During contractions, the switch is opened, and the feedback loop is broken. In this mode, the capacitor, C, stores the voltage across it just prior to the switch opening. The mylar capacitor has low leakage current, as does the input amplifier, so that during the course of the contraction the baseline remains unchanged and no discontinuity is measured due to established resting tension. Now, however, with no feedback in the circuit, the Pitran responds to pressure changes on its surface. After the contraction is completed the switch is again closed and the Pitran output is again actively fixed at zero.

The switching between the two modes is done by the RCA CD4016, an integrated CMOS switch chosen for its low leakage during the "off" state. The switch is controlled by the circuit shown in figure 15. The stimulus synch pulse, 30 volts and 1 microsecond, is first converted to logic levels. This stimulus pulse then activates a TTL monostable producing a 2 second pulse. This pulse controls the CMOS switch. The switch is closed until a stimulus pulse triggers the monostable. The monostable then opens the switch for 2 seconds, long enough to allow a complete contraction. After the two seconds, the switch returns to the closed position.

The results obtained using this technique were excellent. The operating point between contractions is held at zero, and the drift observed during the two seconds the switch is open was limited to about 20 millivolts. Some pressure tracings obtained for isometric contractions using the Pitran are shown in figure 16.



1) Displacement transducer
2) Lever arm
3) Motor
4) Wire connectors
5) Metal rings
6) Muscle
7) Nutrient bath
8) Tension transducer
9) Mercury seal
10) Electrode plates

Figure 9 Schematic diagram of revised experimental setup.

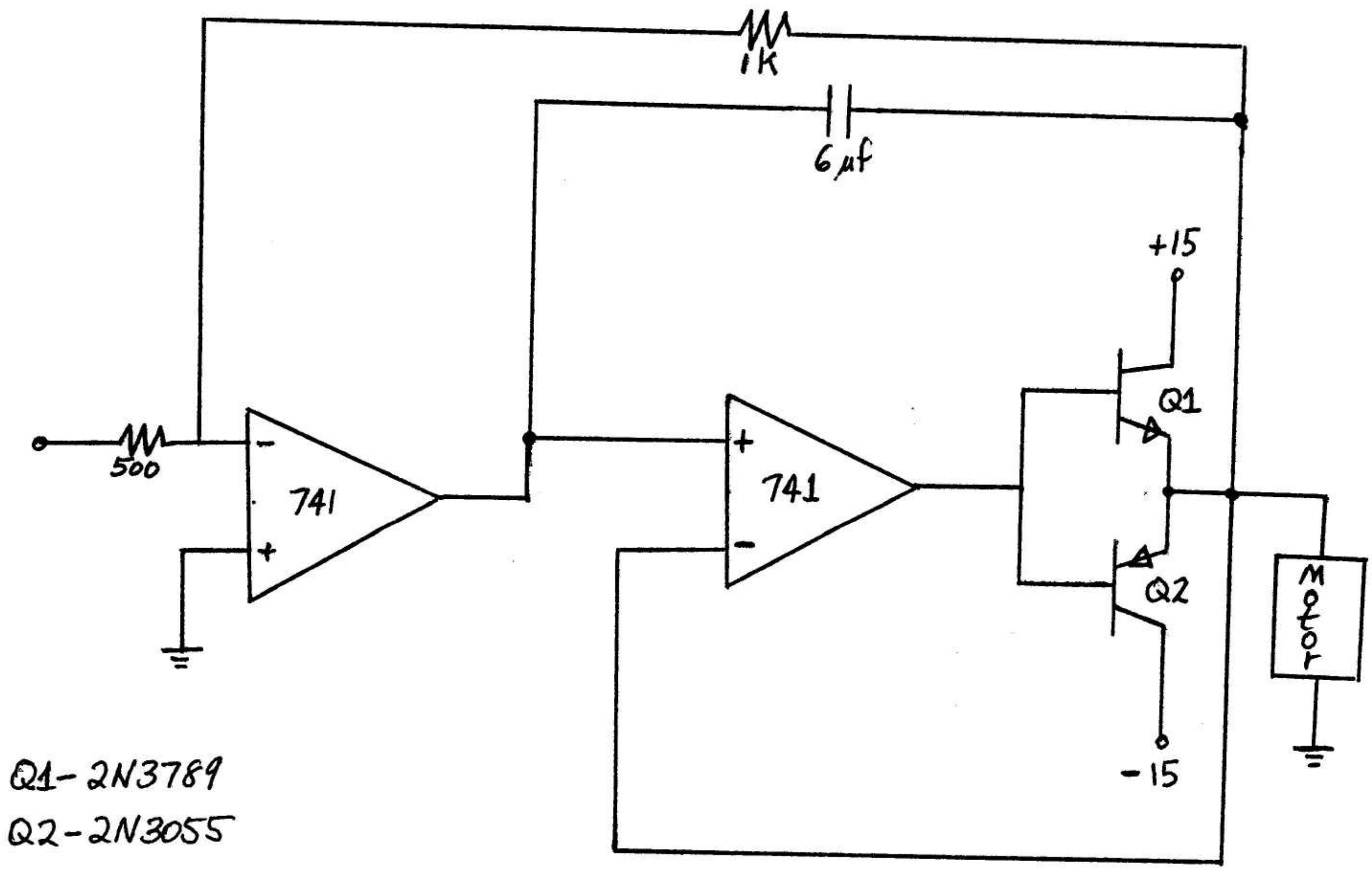


Figure 10 Motor driver circuit

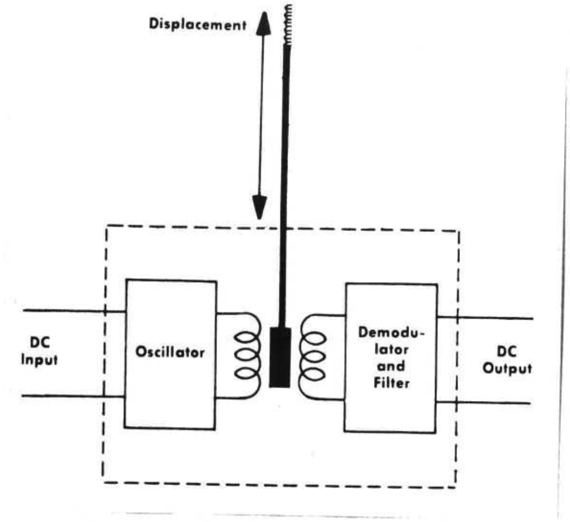


Figure 11 - Schematic Diagram of Hewlett-Packard Displacement Transducer

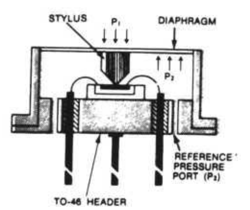


Figure -12- Schematic Diagram of Pitran Tension Transducer

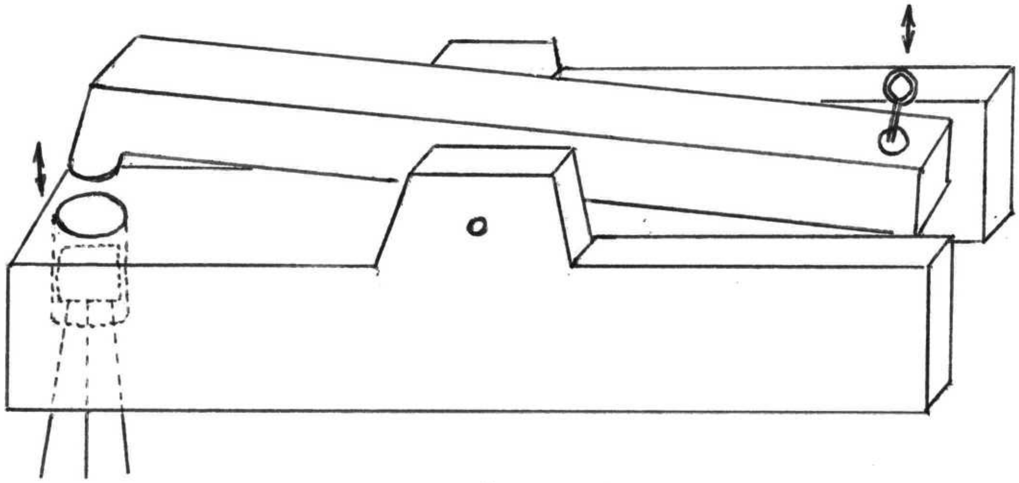
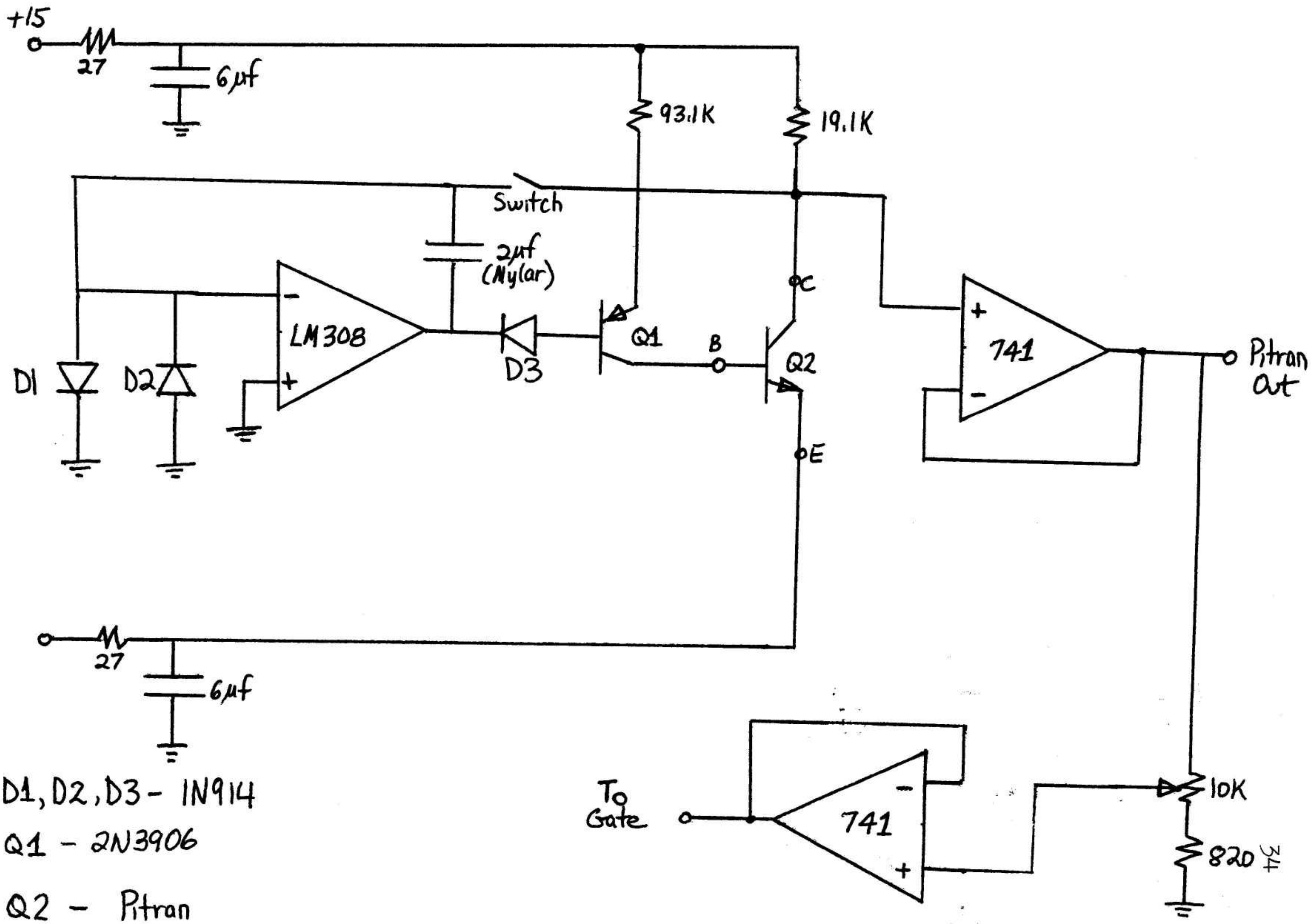


Figure 13- Pitran Apparatus



D1, D2, D3 - IN914

Q1 - 2N3906

Q2 - Pitran

Figure 14 Pitran Bias Circuit

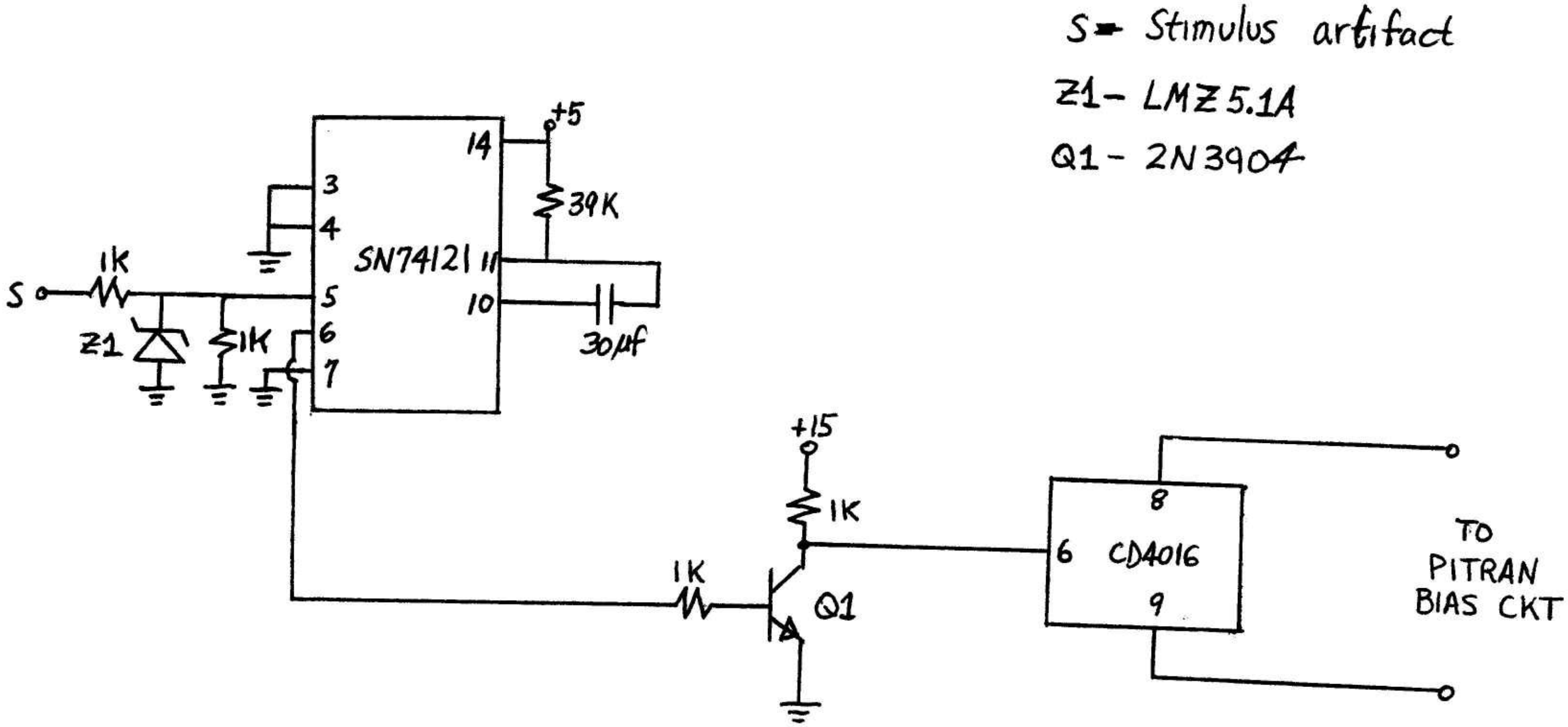
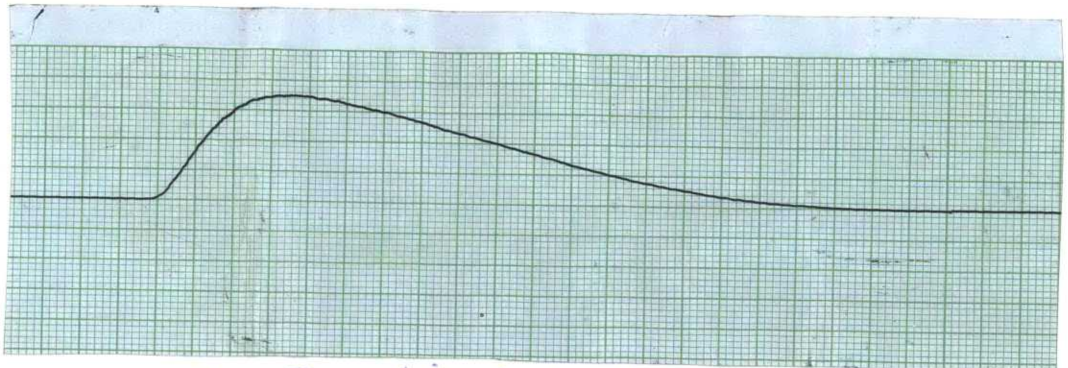
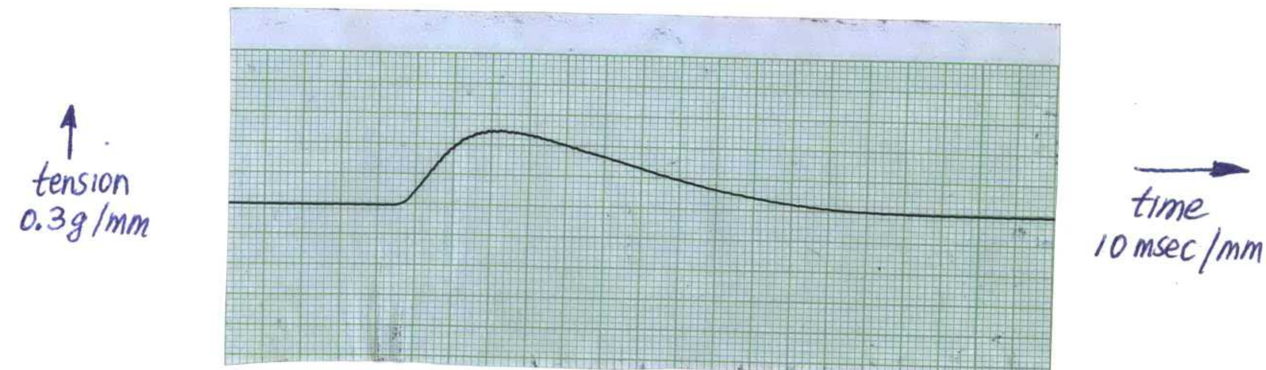


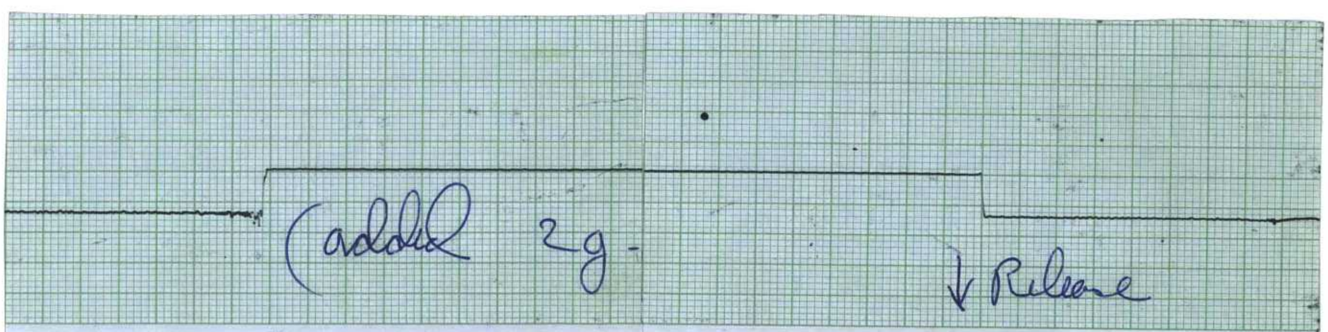
Figure 15 Pitran Bias Circuit Switch



1. Isometric Contraction



2. Isometric Contraction



3. Step Response (Loading & Unloading)

Figure 16 - Pitran Pressure Tracings

III. Frequency Response and Compensation

Following the reconstruction of the apparatus as described, the next task was the building of a feedback system allowing control of the two variables involved, displacement and tension. The requirements for such a system are that its steady state error and overshoot be small and that its response time be fast. For example, in control of displacement, the change in position of the lever arm when a maximum load of 5 grams is added at its tip should be negligible compared to the length changes of the muscle during a contraction, 1-3 millimeters. The settling time of the displacement transducer in response to a step change in load at the lever arm tip should be short relative to the length of time the displacement must be held constant, 100-300 milliseconds. And the overshoot observed during the settling time should be small as well.

The first step in the design of such a feedback control system is the characterization of the variable to be controlled in terms of its transfer function as a function of frequency. For the moment, consider controlling only the displacement variable. The displacement is determined by the position of the lever arm, which is measured by the position of the core within the differential transformer as it moves up and down. The lever arm position is in turn controlled by the contracting muscle and by the motor driving the arm. And the motor is controlled by the voltage exciting its driver circuit. We can thus lump together the motor and its driver, the lever arm and muscle, and the displacement transducer into a black box which is characterized by the ratio of the output voltage (the signal returned from the displacement transducer),to the input voltage (the excitation voltage of the motor driver.)

The frequency response of the "black box" was determined in the following manner: the motor-driver input was excited with a constant amplitude sinusoidal signal applied at the input, and the displacement transducer output was monitored over a range of frequencies. For these tests, the muscle was replaced by a short piece of rubber-band. This models the elasticity of muscle, and simplfies the experimental setup by eliminating the need for the muscle chamber with its nutrient bath and its constant-temperature and oxygen-bubbling apparatus. The validity of this substitution will be discussed in Chapter V.

The first observations made during these tests were for linearity. The motor-driver was driven by a sine-wave input, and it was verified that the motor input itself was sinusoidal. It should be expected, then, that the displacement transducer output also be sinusoidal. It was found, however, that significant distortion of the transducer output occurred, particularly at higher frequencies. It was apparent that this distortion was due to the small amount of backlash or hysteresis in the wire coupling between the lever arm and the core of the displacement transducer. This distortion problem was overcome by reinforcing this wire coupling with a layer of silastic. It was then observed that the rigidity of the coupling improved, the visible slack in the connection was gone, and the distortion was no longer present.

The frequency response determined for the system is shown in figure 17. The magnitude begins falling at about 10 cycles, reaching a local minimum at about 135 cycles. At that point the magnitude begins rising again toward a resonance that occurs at 230 cycles. The magnitude at resonance frequency is about 3.4 times the magnitude at 135 cycles and about 90% of the maximum in magnitude that occurs at 10 cycles. Beyond the resonance, the magnitude falls rapidly, so that by 400 cycles, the magnitude is less than half that observed at the local minimum at 135 cycles. The phase shift observed at the output, meanwhile, rises fairly slowly and in the positive direction until resonance frequency is approached. At about 170 cycles, the phase begins to rise very slowly, passing through 180° at the resonance frequency and continuing to rise beyond. Not until beyond 400 cycles does the phase begin to change more slowly.

The significant part of this frequency response is clearly the resonance at 230 cycles. It should be noted that this observed resonance frequency is near the specified natural frequency of the motor, 235 cycles. Using the original lever arm with the motor, a resonance frequency of 180 cycles was obtained. It was then decided to make the changes in the lever arm already described, to shorten and lighten it, so that the natural frequency of the motor could be more closely approached. The fact that the observed resonance approaches the motor resonance frequency so closely is an indication of the success of the procedure. The conclusion follows that the frequency response derived is due primarily to the motor and shows little contribution from the transducer or other components of the system. For this reason, it was not necessary to separately determine the frequency response of the system for measuring tension. Since the only difference in the two systems is the substitution of the Pitran for the displacement transducer, and since the Pitran has a natural frequency of 150 kilocycles, no additional phase shifts or magnitude changes would be expected due to the Pitran. Its magnitude curve is flat and its phase shift approximately zero over the range 0-400 cycles. The only change expected would be in the position of the magnitude curve, reflecting the different sensitivities of the Pitran and the displacement transducer.

The object of the feedback system is to achieve the desired control of the variable in question while maintaining its stability. The question of stability is answered by analysis of the open-loop magnitude and phase characteristics of the system. The important point in those characteristics is the point at which the phase shift observed equals 180^{o}, in this case at a frequency of 230 cycles. If the magnitude of the open loop gain at the frequency at which the phase shift is 180^{o} is greater than 1, the system will oscillate. Figure 17 indicates that at 230 cycles, where the phase shift of 180^{o} is observed, the magnitude of the gain is slightly less than 0.3. If we consider an amplifier whose gain is constant and whose phase shift is negligible below 400 cycles, the maximum gain we can tolerate and still have a stable feedback system is about 3.3. But although such a system would be stable, it would not permit enough gain to attain the control desired. The problem, then, is to provide a large amount of gain at low frequencies needed to provide the control function, a much smaller amount or no gain at the resonant frequency in order to maintain stability while leaving the phase characteristics unchanged. Or, alternatively, a circuit can be designed to alter the magnitude and phase characteristics of the overall system so that the resonance at 230 cycles is effectively removed and the 180^{o} phase shift point occurs higher in frequency.

The first attempts at compensation were along the lines of the second alternative above. By analyzing the location of the resonance frequency and the width of the resonance peak, it was possible to characterize the system in terms of its pole-zero plot. An attempt was then made to design an active filter which would, in effect, offer an anti-resonance which would cancel out the existing resonance peak. The attempt resulted in a design for an active filter whose frequency response was the compliment to that of the system, replacing poles for zeroes and zeroes for poles. When built, however, the filter itself was unstable in a marginal sense. While not breaking into gross oscillations, it did exhibit a sinusoidal ripple distortion superimposed on the output. When repeated attempts met with little success, the method was abandoned.

The goal then was to find a method to achieve a large gain at low frequencies while keeping the gain less than 1 at the point where the phase shift is 180°. The use of simple single or multiple pole amplifiers, whose gain is constant approximately until the pole location and then rolls off at 20 db per decade, was ruled out by the fact that each pole contributes 90° of phase shift. The solution to this problem was found in the form of the RC lag network. This network consists of a pole at some frequency f_1, followed by a zero at some higher frequency f_2. The magnitude of the gain is flat below f_1, then starts falling at 20 db per decade until f_2 is reached. At that point, the gain once again becomes flat, but at a much reduced level, as the pole and zero cancel each other out. The pole and zero likewise contribute phase shift in opposite directions, the pole adding negative phase shift and the zero positive. At f_1, the phase shift is due primarily to the pole. Between f_1 and f_2, the zero begins to exert its effect and the phase shift, already negative due to f_1, becomes less negative. By $10f_2$ the pole and zero completely cancel each other out in phase and the phase contribution of the entire network is zero. The distance between f_1 and f_2 determines how much attenuation is achieved at frequencies beyond f_2.

These guidelines were used to locate the positions of f_1 and f_2. Since it is required that negligible phase shift be added at the resonance frequency, 230 cycles, f_2 was chosen as 20 cycles. Thus, by $10f_2$, or 200 cycles, the phase shift contributed by the lag network is zero. f_1 is chosen to be 5 cycles. This is a compromise between the need for the largest possible attenuation, and the speed of response required. By making this choice, an attenuation by a factor of 4 is obtained. That is, below 5 cycles, the gain of the lag network is 1, while above 20 cycles, the gain is 0.25. The maximum phase shift occurs at about 10 cycles, and its magnitude is about 42°, and the phase shift drops off from there. The frequency response of the simple lag compensator is shown in figure 19.

The overall compensation is achieved by cascading three lag compensators, each identical in form. The effect on the magnitude of the compensation is multiplicative; the gain below 5 cycles is 1, while beyond 20 cycles, the gain is

(.25)(.25)(.25), or 0.016. The maximum phase shift occurs at 10 cycles, and is 126°. Above 200 cycles, the overall phase shift remains that of the mechanical system itself. Thus, the point of 180° phase shift remains at 230 cycles, but the overall magnitude curve has been changed drastically. Now, gain can be added at appreciable levels before the gain at 230 cycles reaches 1. The maximum possible gain that can now be applied before the danger of oscillation becomes evident is 263.

The overall compensation circuit is shown in figure 12. Each of the three lag networks is followed by the LM302 voltage follower. The three lag networks are followed by a non-inverting amplifier having a fixed gain of 23. This amplifier is followed by a second non-inverting amplifier having a variable gain from 1 to 20 and controlled by a 20 turn trim-pot. In operation, the feedback loop from the compensator to the motor is closed, and the adjustable gain amplifier turned up until the oscillation stops. This setting gives the maximum possible gain short of oscillation. When this was done, it was found that the control of the arm position was well within that required.

Finally, the differentiator circuit shown in figure 20 was added as compensation as well in order to speed up the transient response of the system. In the steady-state, the differentiator has no effect because the differentiator output is zero. During transitions, however, the differentiator provides an additional signal to the motor to speed its response to changes.

In achieving stable displacement feedback, it was found that the muscle was not a crucial element in the system. The stiffness of the motor spring was such that when a 7 gram weight, representing the maximum possible force a muscle is capable of exerting, is hung from the lever arm tip in the open-loop configuration, no downward displacement is observed. Thus, displacement feedback can be applied without a muscle in the system.

In the tension feedback mode, the muscle is an integral part of the system. Force measured by the Pitran is exerted through the muscle itself. In obtaining a stable feedback system for tension, a similar approach was used with a few modifications. Because of the high sensitivity of the Pitran, an attenuator was placed at its output. The same compensation circuit is used for both displacement and tension. The Pitran attenuator is turned down, giving a greatly reduced sensitivity, and the feedback loop closed. The attenuator is then adjusted by a pot until a stable response with maximum gain is obtained. In this way, stable feedback systems were obtained for both displacement and tension.

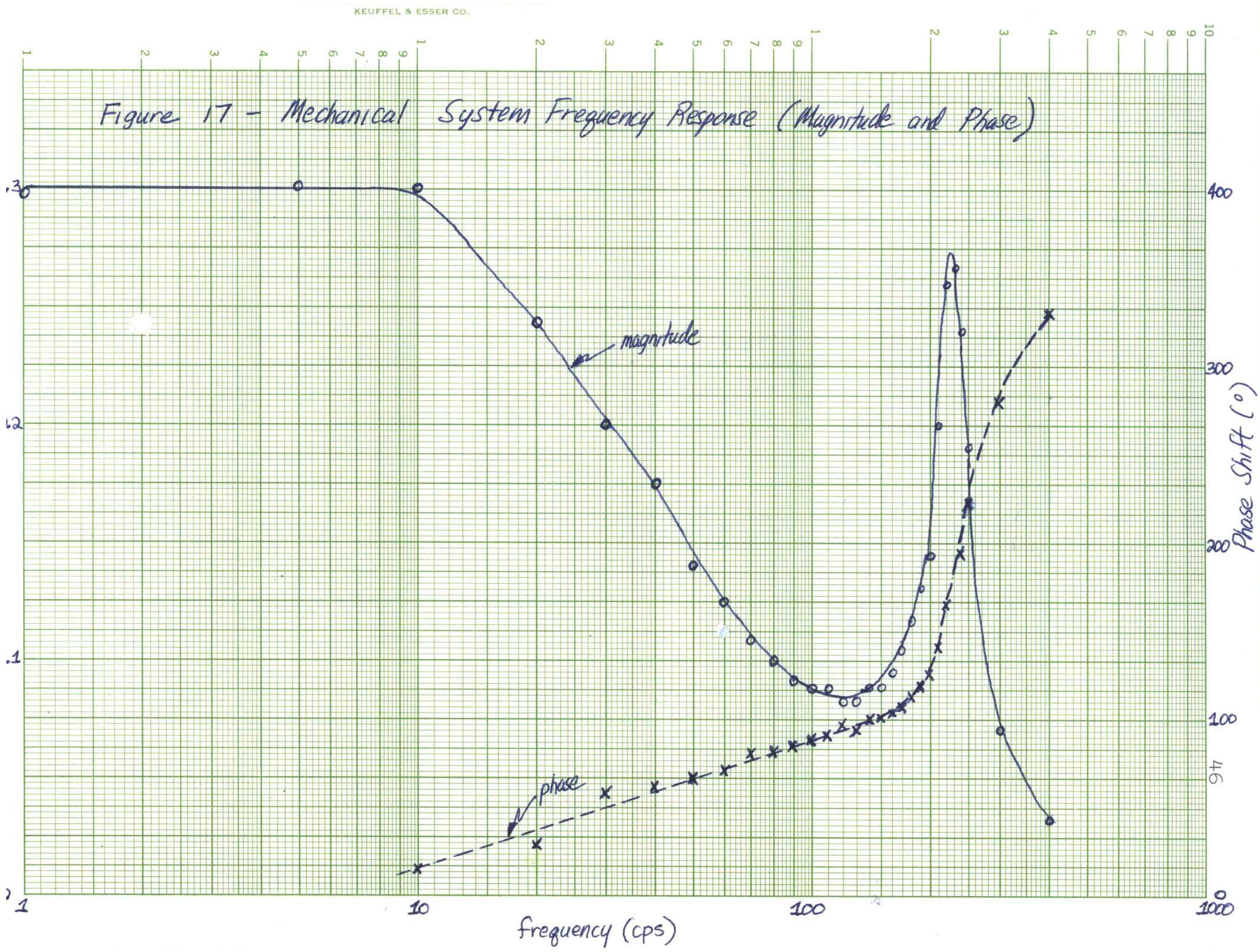
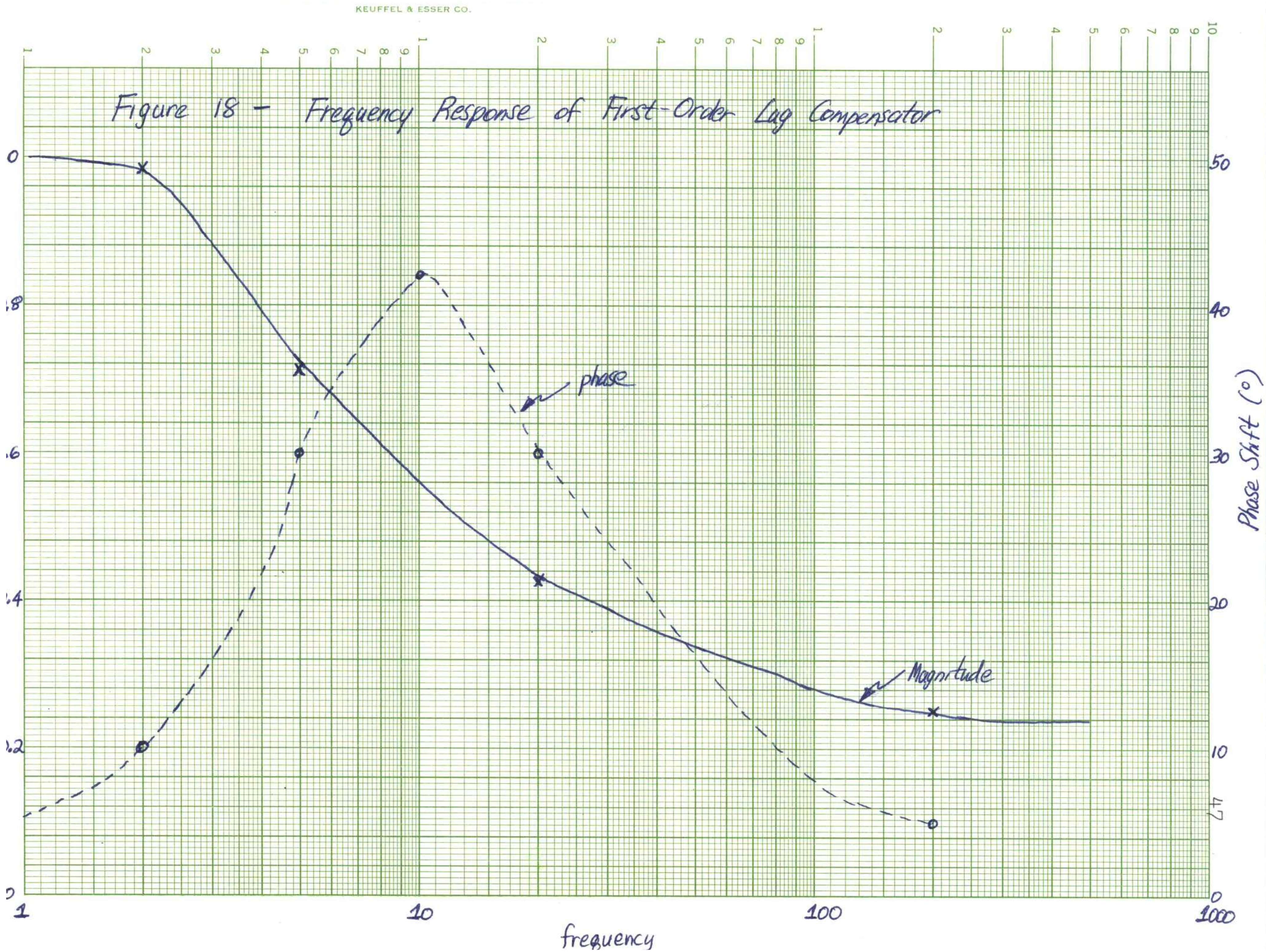


Figure 17 - Mechanical System Frequency Response (Magnitude and Phase)



KEUFFEL & ESSER CO.
Figure 18 - Frequency Response of First-Order Lag Compensator
phase
Magnitude
0
.8
.6
.4
.2
0
50
40
30
20
10
4.7
0
Phase Shift (°)
1
10
100
1000
frequency

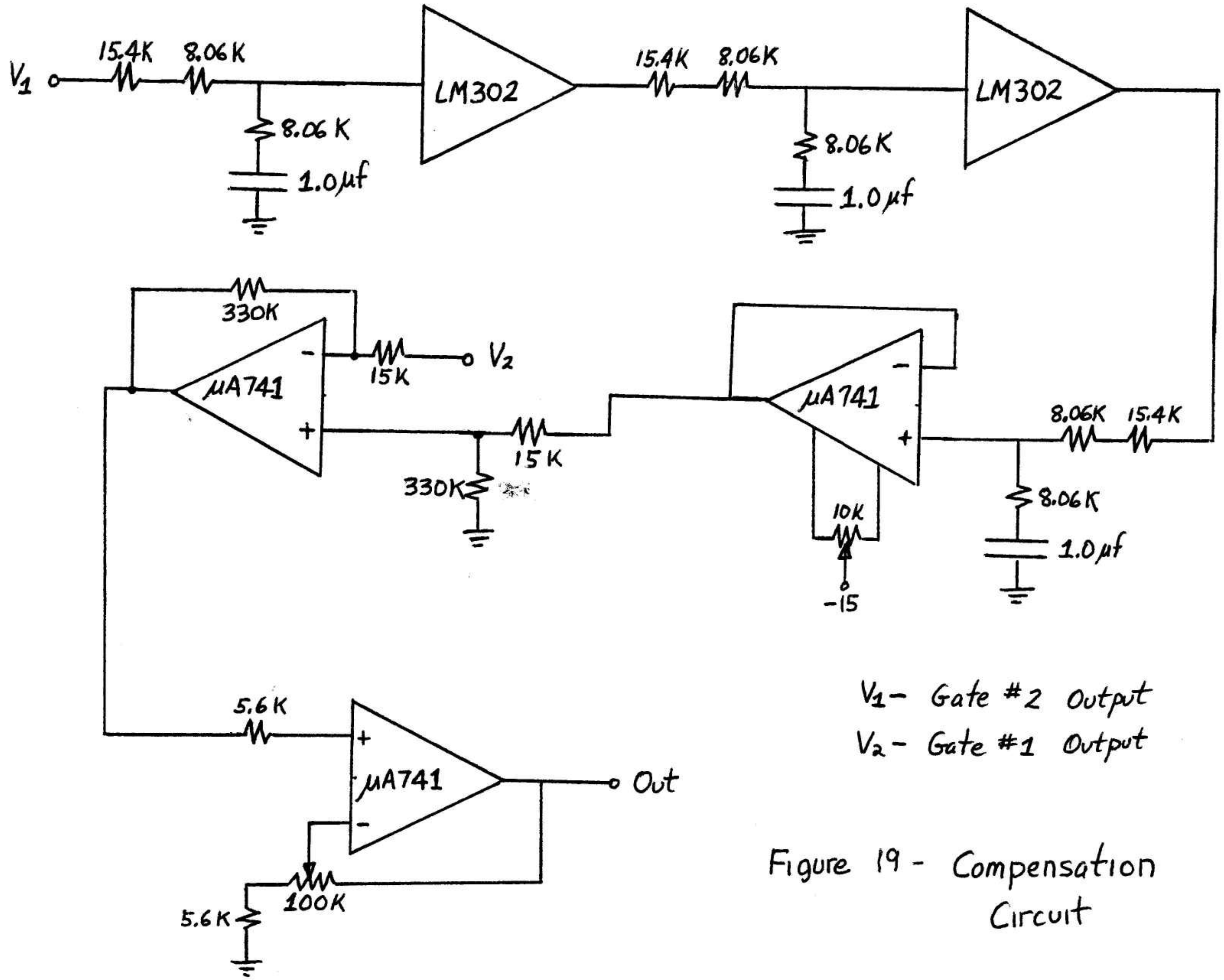


Figure 19 - Compensation Circuit

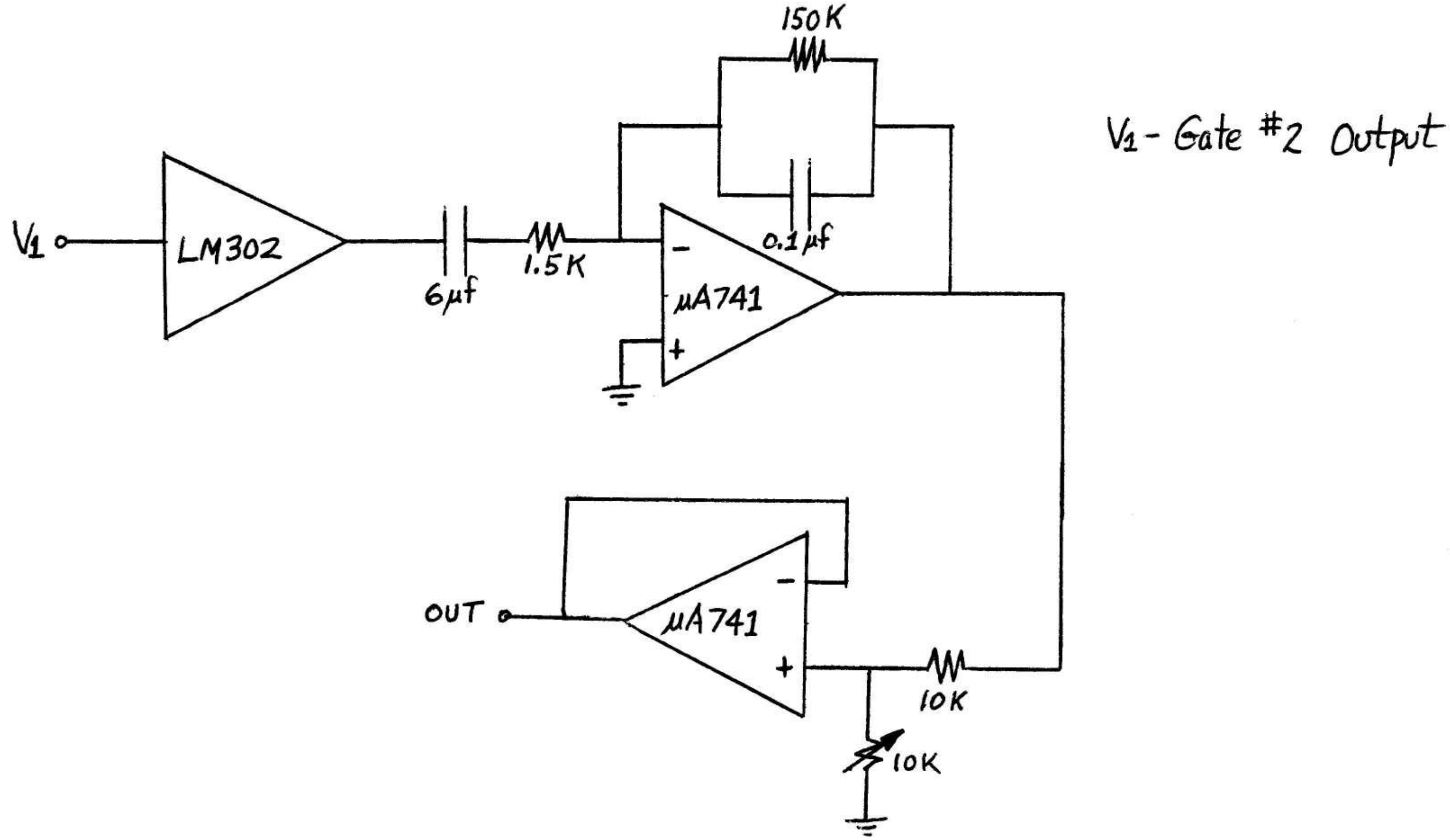


Figure 20 - Differentiator Circuit

IV. Logical Control

The desired sequence of events of muscle contraction and relaxation which approximate those actually occurring in the beating heart have been discussed in Chapter I. The sequence is reviewed graphically and divided into five states in figure 21. In state A, the muscle is waiting to be stimulated, and is maintained at some resting length and exerts some resting tension. When a stimulus pulse is received, the muscle is activated and enters state B. During this state, the muscle length is actively maintained ~~and~~ at its resting value by displacement feedback, and tension begins building up. When the tension exerted by the muscle reaches the load level desired, the muscle enters state C. The tension is held constant during this state, and the muscle shortens isotonically. When the muscle has shortened maximally, state D begins. The muscle length is held constant at its minimum value, and the muscle relaxes isometrically until tension returns to its resting level. When resting tension is once again achieved, the muscle is allowed to lengthen with tension held at the resting value during state E. When both displacement and tension have returned to their initial resting values, the muscle is once again in state A.

During each of the five states, one of the two variables, either displacement or tension, is held constant. This is accomplished by closing the feedback loop around the appropriate transducer. The second transducer is removed from the feedback lopp while the first variable is being controlled. For example, during state B, the displacement transducer is passed through the compensation circuit to the motor-driver circuit. As the muscle begins to contract, it pulls down on the lever arm, tending to drive the transducer output voltage away from zero. This small deviation is amplified by the large gain of the compensation circuit, and a large error-signal voltage, proportional to the amount by which the transducer output differs from zero, is fed to the motor-driver in the appropriate polarity to drive the arm back to its equilibrium value. Displacement must be held constant during states B and D, while tension is constant during states C and E. To accomplish this, both transducer outputs enter a gate, and during the appropriate states, one of the two transducer outputs is allowed to pass through the gate to the feedback compensation circuit.

Although one of the two variables is constant during each state, the value of the constant variable is not zero. During state B, the displacement is held at the resting value, some small but positive stretch. During state C, the tension is held at the value of load against which the muscle contracts. Both the resting displacement controlled during state B and the load tension controlled during state C should be adjustable over a wide range, to represent the variations in aortic pressure and atrial pressure which occur in the intact heart. During state D, the displacement is held constant at the value determined by the maximum shortening of the muscle. The tension is held at its resting value, some small, non-zero tension, during state E. As has already been explained, the feedback operates to keep the controlled variable at zero. In order to achieve some controlled but non-zero value of the variable, an additional input must be provided for the motor-driver circuit during each state. This input provides an offset for the motor, representing the constant value required during each state. The feedback then operates to keep the output constant at the value of offset provided. Thus, during each state an offset input must be provided to the motor. The switching of these offset inputs into the motor-driver from state to state is controlled by a second gate.

During state A, both tension and displacement are maintained at their resting values before a contraction begins. Since both variables are constant either one can be controlled by the feedback loop. Maintaining a constant resting tension establishes a resting displacement, or stretch of the muscle as well. Similarly, providing an initial stretch of the muscle and holding it establishes some resting tension. The more desirable approach is to control the level of resting tension rather than resting displacement. This corresponds to the specification of atrial pressure rather than ventricular volume as a starting point for the ensuing contraction. The former is certainly a more logical initial condition. Establishing an initial resting tension between contractions, however, was ruled out by the nature of the Pitran tension transducer. As explained in Chapter III, in order to achieve maximum stability and minimum baseline drift, the Pitran is used in a switched mode. Between contractions, the Pitran bias point is actively maintained at zero output. The application of a resting tension is actively compensated for by the biasing circuit and the resting tension does not appear in the Pitran output. The Pitran is capable of measuring tension only for a 2 second period following a stimulus pulse. During that time, only actively developed tension is measured. Thus, during state A the resting condition of the muscle is determined by switching the displacement transducer into the closed feedback loop and adjusting the resting position of the muscle. The resting displacement can be set at any desired value.

The use of resting displacement rather than resting tension, and the nature of the Pitran biasing scheme, simplifies some of the mechanics of the system. Since resting tension registers as zero at the Pitran output, the tension during state E must be held at zero by thefeedback loop rather than at the non-zero actual value of resting tension. This eliminates the need for the offset input to the motor-driver during state E. During state B, the muscle begins contraction and tension build-up occurs, but the muscle is held at its resting displacement value. Thus, both states A and B are constant displacement states with the feedback holding displacement at its resting value. This eliminates the need for switching from tension control to displacement control between states A and B, as would be required if state A were a state of resting-tension control.

Switching from one state to another requires processing of the two transducer output signals. Between contractions, the resting displacement of the muscle is determined by the setting of resting displacement potentiometer. The pot output is applied as the offset input to the motor-driver, and so directly determines the lever-arm position. A second potentiometer, the load pot, allows a predetermined after-load to be applied to the muscle. A stimulus pulse causes a change from state A to state B, and tension begins to develop. A comparator, comparator # 1, compares the tension voltage developed to the preset load pot voltage and when the two are equal, state C begins. During state C, the displacement transducer is processed by a peak detector. When the transducer output has risen to its peak, representing maximal shortening, and just begins to fall, the peak detector causes the transition to state D and at the same time holds the peak voltage and applies it as the motor offset input during state D. The tension transducer is compared to zero during state D, and when the output returns to zero, as determined by comparator #2, state E begins. During the final state, the displacement transducer output is processed by comparator #3, which has the value of the resting displacement pot as its threshold. When the displacement voltage returns to its resting level, the system returns to state A to await another stimulus pulse.

The entire system is integrated by a digital logic network. The network receives as its input the outputs of the peak detector and the three comparator circuits. The state of the three bits of a flip-flop register within the logic network determines the state which the muscle is in during the cycle. The change in comparator outputs as the contraction proceeds causes changes in the flip-flop register. The flip-flop register, in turn, provides output signals to the two gates which switch the proper output transducer into the feedback loop and apply the proper motor offset signals at the appropriate times. A block diagram of the complete system is shown in figure 22.

The three comparator circuits used to provide the inputs to the logic network are identical in nature and differ only in the thresholds which they are set to detect. All of the comparators have a small amount of hysteresis built into them to insure error-free switching independent of small levels of input noise. The Fairchild 741 operational amplifier is used as the level detector, and its output is + 15 volts when the input is below the threshold and switches to -15 volts when the input equals the threshold level set. The output remains at -15 volts as long as the input exceeds the threshold voltage. When the input returns to zero, again crossing through the threshold level, the output returns to +15 volts. The output of the amplifier is then passed to a logic-level converter consisting of a diode and a 5-volt zener diode. This circuit converts the plus and minus 15 volt levels of the comparators to the zero and 5 volt levels required as logic inputs. Finally, the output of this circuit is fed as input to the SN74121, an integrated circuit monostable. This circuit can be used to produce a variable-width pulse which can be triggered by either the positive- or negative- going edge of the input signal.

The three comparators are shown in figures 23, 24 and 25. Comparator #1 provides the signal for the switching from state B to state C. The threshold level is set by the load pot, and is variable from 0, or no afterload, to 2 volts, representing the maximum afterload of about 7 grams. The Pitran output is compared to this threshold voltage. Since tension rises to the load value set, we are interested in the negative to positive change in the comparator output, and the one-shot is programmed to deliver a 1 millisecond pulse on the positive-going input.

Comparator #2 is a tension zero-cross detector. It is responsible for the transition from state D to state E when the tension as measured by the pitran returns to zero. Due to the hysteresis in the comparator circuit, the voltage threshold must be set slightly positive by about 20 millivolts. Since ±15 millivolts of hysteresis is built into each comparator, switching actually occurs at $v_{th} + 0.015$ and $v_{th} - 0.015$. The error involved in this technique is insignificant, and it prevents the multiple switching of the comparator when the input is near the threshold level. If the threshold of comparator #2 were set at 0 volts, the negative-to-positive zero-cross detection desired would occur at some small negative voltage. But the muscle can only develop tension in a positive sense without changing the resting position. By keeping the threshold level slightly positive, the actual switching is done at a positive tension. Since the return from positive voltage to zero is being detected, the monostable is programmed to trigger on the positive-going edge.

Comparator #3 provides the input signal to the logic network required to cause the switching from state E to state

A. When the displacement returns to its resting value, the contraction-relaxation cycle is completed and the muscle is returned to the resting state. The displacement transducer output is compared to the resting displacement pot which was set at the beginning of the contraction. The state change occurs when the transducer output returns from a high output as the muscle is contracted, to its lower, resting output as the muscle relaxes. Thus, the monostable is programmed to give a pulse triggered by the positive-going edge of the input.

The transition between states C and D occurs when the muscle has shortened to its minimum length. Since shortening is registered as positive voltage from the displacement transducer, we wish to generate a signal indicating when the transducer output has reached a maximum. It has already been explained that during four of the five states, a second offset input must be applied to the motor to determine the non-zero control point at which the feedback circuit operates. Three of these four inputs are determined directly by pots set before the contraction begins: the resting displacement pot provides the offset inputs during states A and B, while the load pot provides the offset input during state C. During state D,however, the muscle is held at its maximally contracted displacement, a value characteristic of the individual muscle fiber and the given load. This value must be determined during the contraction.

The circuit shown in figure 26 serves two functions. It stores the peak value of the transducer output for application to the motor-driver as the offset input during state D, and it provides a signal to the logic circuit causing the transition from state C to state D. The peak holder is formed by the two operational amplifiers and the storage capacitator shown in the figure. As the displacement input begins to rise toward the peak, the storage capacitator is charged through the diode. As long as the input keeps rising, the capacitator keeps charging and the voltage is fed-back from the output to the inverting input of the input amplifier. When the displacement input reaches its peak and just begins its fall, the negative input, held fixed by the capacitator feedback, exceeds the positive input of the LM301 and the amplifier output switches to -15 volts, the saturation voltage of the amplifier. This turns the diode off, allowing the capacitator to hold its stored voltage. The voltage output of the LM302 remains at the peak value for the remainder of the contraction, providing the offset input signal to the driver during state D.

The input amplifier, the 301, follows the displacement transducer input until its peak is reached, and then the output of the amplifier switches to -15 volts. It is this transition to -15 volts that is detected by the comparator circuit shown as part of figure 26. The 301 output provides the input to the standard comparator circuit. The threshold level is set at -8 volts. Since the 301 saturates very fast, the setting of the threshold at any negative voltage would result in minimum delay. The saturation of the 301 causes a negative-to-positive transition in the comparator, and the one-shot is programmed to provide a pulse out on the positive-going edge of the input. Thus, the circuit shown provides both the displacement transducer peak output and a control signal for the logic network.

The final input to the logic network, causing the transition from the resting state, state A, to the beginning of the contraction-relaxation sequence, state B, is provided by the stimulus artifact. The Grass stimulator provides an excitation pulse to the muscle every 5 seconds. Since it may be necessary to make adjustments to the system between contractions requiring longer than 5 seconds, the circuit in figure 27 is used to gate the stimulus artifact to the logic network. A push-button switch, followed by a one-shot, is used to set a set-reset flip-flop. Once the flip-flop is set, the next stimulus artifact, obtained from the synch output of the stumulator, is gated to the logic network. The muscle then proceeds through states B,C,D, and E of the contraction-relaxation sequence and upon completion, returns to state A. The return to state A triggers a second monostable which resets the flip-flop and closes the output gate. The result is that activation of the push-button supplies one and only one stimulus artifact pulse to the logic network, despite the fact that the muscle is repeatedly being stimulated.

The logic network receives as inputs, then, the stimulus artifact, the three comparator outputs, and the peak detector output, all processed through 1 millisecond monostables. The logic network itself is designed as a finite state machine having the state transition diagram shown in figure 28. The five states of the system, each corresponding to the phase of the contraction indicated by the letter, are represented by the closed circle. For each state, all possible transitions to other states are indicated by arrows, along with the input required to cause that transition. When the system is in state A, for example, all possible transitions to other states are represented by arrows leading away from state A. If the value of the stimulus artifact input is a logic 1, transition from state A to state B occurs. If the stimulus artifact input is a logic 0, the system remains in state A. Since no other transitions from state A to any other state are programmed into the scheme, variations in any of the other input signals when the system is in state A are irrelevant and need not be taken into consideration.

The transition diagram for the most part follows the sequence of events already outlined. Transition from A to

B requires the stimulus input to be 1; transition from B to C requires the comparator #1 output to be 1; transition from C to D requires a 1 from the peak detector output; transition from D to E requires comparator #2 to have an output of 1; and transition from E to A requires an output of 1 from comparator #3. One other pathway exists which has not yet been discussed. It involves the isometric contraction of the muscle, which occurs when the load which the muscle is required to contract against is greater than the amount of tension which the muscle can actively develop. The result is that the contraction occurs without any motion of the muscle, and only a buildup of tension to a peak value and a return to resting state. While this type of contraction is not an analog to any physiologic activity of the muscle in an intact ventricle (it would correspond to a ventricular contraction inadequate to meet the aortic pressure and open the aortic valve), it is a useful experiment to perform to determine the maximum tension which the muscle is capable of exerting as a function of resting length. The method of achieving an isometric contraction in the original system is to put a very large weight as the afterload on the back of the lever arm. In the new system, this corresponds to setting the load pot to a very large voltage. The muscle is stimulated, and the system switches from state A to state B. But the transition to state C, which occurs when the tension reaches the threshold set by the load pot, is never attained, and the tension falls back to zero. At this event, the muscle should be returned to state A. This is accomplished by adding a second possible transition from state B. In addition to transferring to state C on a signal from comparator #1, a pathway back to state A is included on a signal from comparator #2.

Since there are five states involved in the design of the logic network, 3 flip-flops are required. Three flip-flops are capable of providing eight possible states, and the fact that three of these are unused helps simplify the design. The first task, then, is to assign a sequence of outputs of the three flip-flops to each state. This is shown with the state transition diagram in figure 28. From the state transition diagram, the truth table relating the J and K inputs to the flip-flop outputs, and the state assignments made, an eight-variable Karnaugh map can be derived for both the J and K inputs of each of the three flip-flops. While this magnitude of Karnaugh map may sound formidable, it should be realized that many of the entries of the map are "don't cares" corresponding to the three unused flip-flop states and the existence of only one or two inputs relevant to each state. In this manner, equations are derived for the J and K inputs of each flip-flop and realized in the logic diagram shown in figure 29. All logic used is TTL, and the flip-flops used are SN7474N, a JK flip-flop having gated J and K inputs. The flip-flop register is triggered by a 1 megacycle clock formed by appropriately connecting an integrated circuit Schmidt trigger.

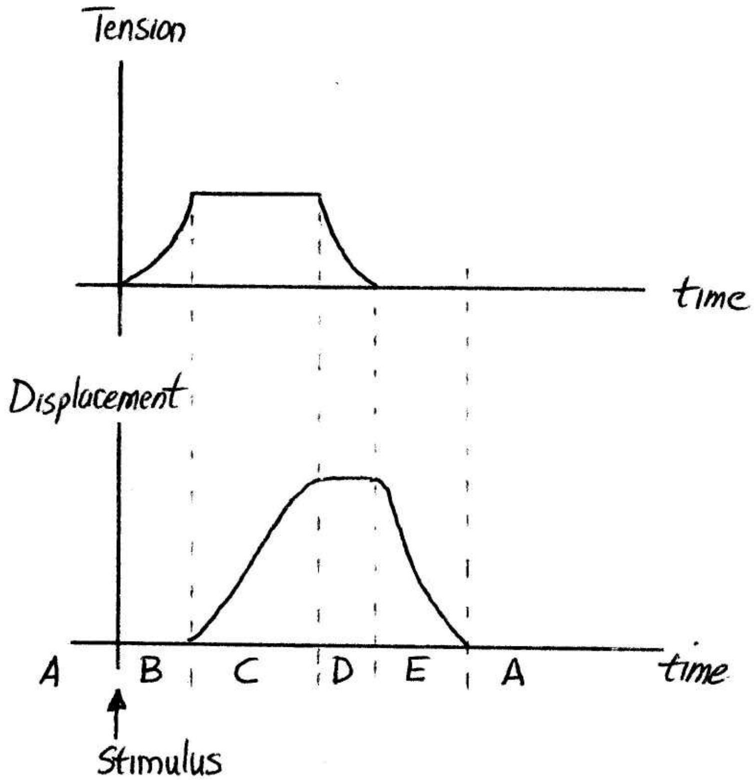
Thus, as the contraction-relaxation sequence proceeds, and the inputs are fed to the logic network, the flip-flops change state according to the transition diagram and the state assignments. The flip-flop outputs are then processed by the logic circuit shown in figure 30. This circuit translates the three flip-flop outputs into five output lines designated A, B, C, D, and E. Each output line corresponds to a state as indicated, and remains high for the duration of that state. These output lines provide the control functions in the feedback loop.

The logic network output serves two functions in the operation of the feedback loop. It switches the proper transducer into the feedback loop, and it provides the correct offset input to the motor driver. Gating of the two transducers is accomplished by using the RCA CD4016A, an integrated circuit containing 4 CMOS switches. Each of the four switches in the package consists of an input and output capable of a 0-15 volt range, and a control input. When the control input is at ground, the switch is open. The use of field-effect transistors in the switch insures very low leakage current when the switch is off. If the control input is at 15 volts, the switch is closed and the output is connected to the input. The gate is formed by the use of two switches as shown in figure 31. The displacement transducer is the input to switch 1 while the tension transducer is the input to switch 2. The outputs are isolated and then summed in the appropriate sense. The control inputs are driven by simple logic networks derived from lines A, B, C, D, and E. The logic levels are converted to the 0-15 volt levels required by the transistor switch. During states A, B, and D, switch 1 is turned on by a 15 volt level at its control input while switch 2 is turned off. The displacement transducer output is therefore passed through the gate to the compensation circuit. During states C and E, switch 2 is turned on while switch 1 is turned off, allowing the tension to pass through the gate to the compensation network.

A second gate controls the application of the required offset to the motor-driver during each state. The Harris Semiconductor HA2405 programmable amplifier is used for this function. This device is an integrated circuit having four identical input amplifiers and one output amplifier. Any one of the four input stages may be connected to the output stage based on the decode control inputs. The truth table for the device and the gate design are shown in figure 32. Three offset inputs are required. The resting displacement pot must be applied during states A and B, and this pot is applied as the input to channel 1. The load pot is required during state C, and this input is applied to channel 2. The output of the displacement-peak holder circuit, required during state D, goes to channel 3. During state E, the tension transducer is held at zero, and no offset input need be applied to the motor-driver. However, when the programmable amplifier is disabled, its output is put at 15 volts negative. For this reason, it is desirable to ground the input to channel 4, and apply it to the motor-driver during state E. All four input amplifiers are connected to the output amplifier in a follower mode. The truth table of the device, and the logic network output lines were used to derive the decode control inputs as shown. The result is that during states A and B, the device output is the resting displacement pot, during state C it is the load pot, during state D the peak displacement value, and during state E, zero. Both gates feature response times in the nanosecond range, fast enough to accomplish proper switching.

It is required that during each state, the transducer output be equal to the offset input and kept at that value. But the transducer outputs are multiplied by the large gain of the compensation circuit before being applied to the motor-driver. In order to maintain proper transducer outputs, the offset inputs must be multiplied by a gain equal to the DC gain of the compensation circuit. This is accomplished by providing the offset inputs to the motor-driver through the gain stage of the compensator. The gate output is provided as a summing input to the gain stage of the compensator as shown in figure 19.

Two separate input signals are provided to the motor-driver circuit: the two signals from the compensation circuit. These inputs are combined into a single input by the non-inverting adder shown in figure 33. Each of the inputs is given a weight of 1 by the adder, so that the output is simply the sum of the inputs. The output of the adder then goes directly to the driver circuit.



State A – Muscle waiting to be stimulated. Displacement held at resting value.

State B – Contraction begins. Position remains fixed at resting value; tension build-up occurs.

State C – Tension held at load value determined by pot. Muscle shortens.

State D – Displacement held at minimum value (maximum transducer output). Tension falls to zero.

State E – Tension remains at resting value (zero transducer output). Position returns to resting value.

Figure 21 – System State Definitions

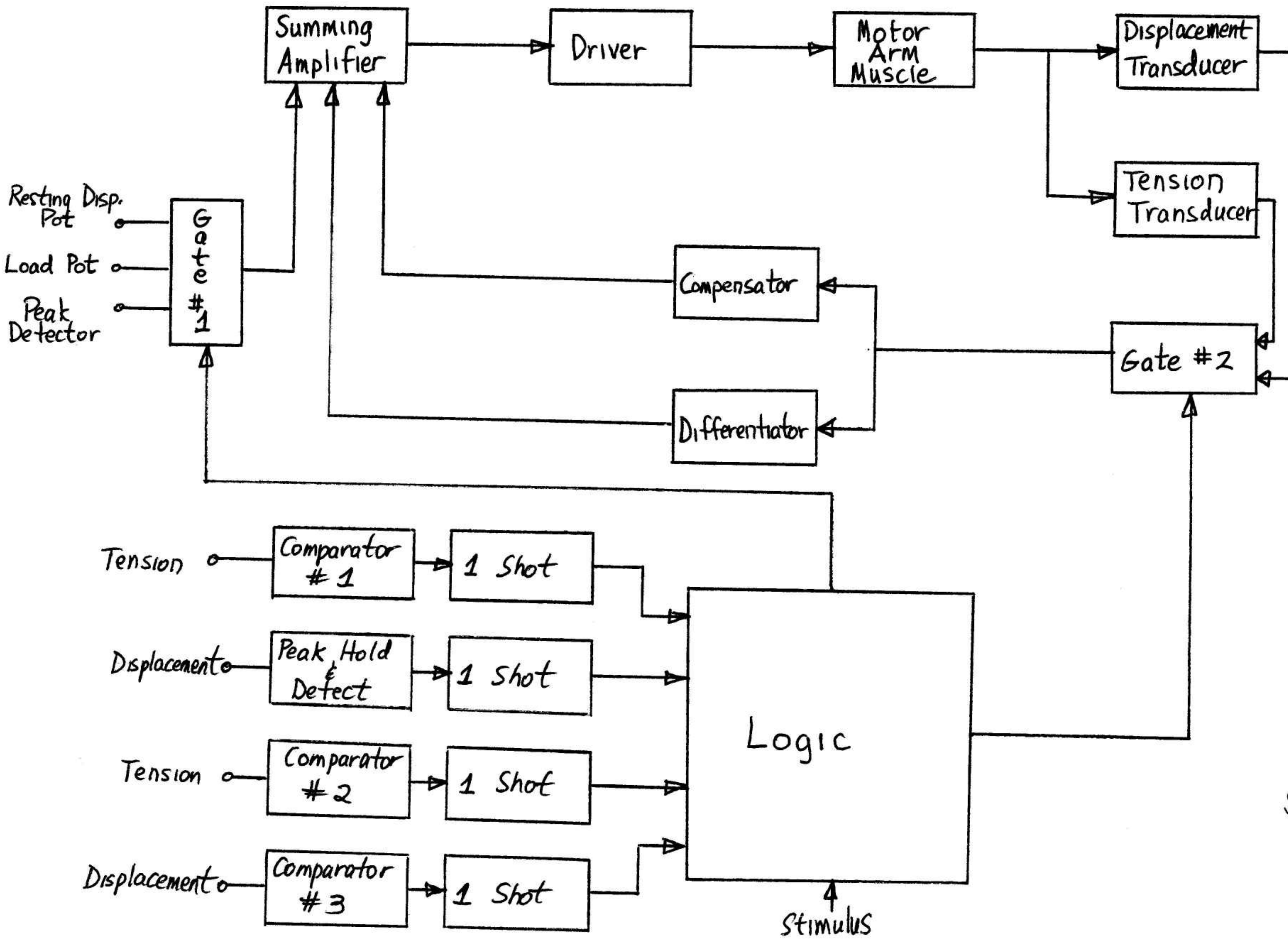


Figure 22 - System Block Diagram

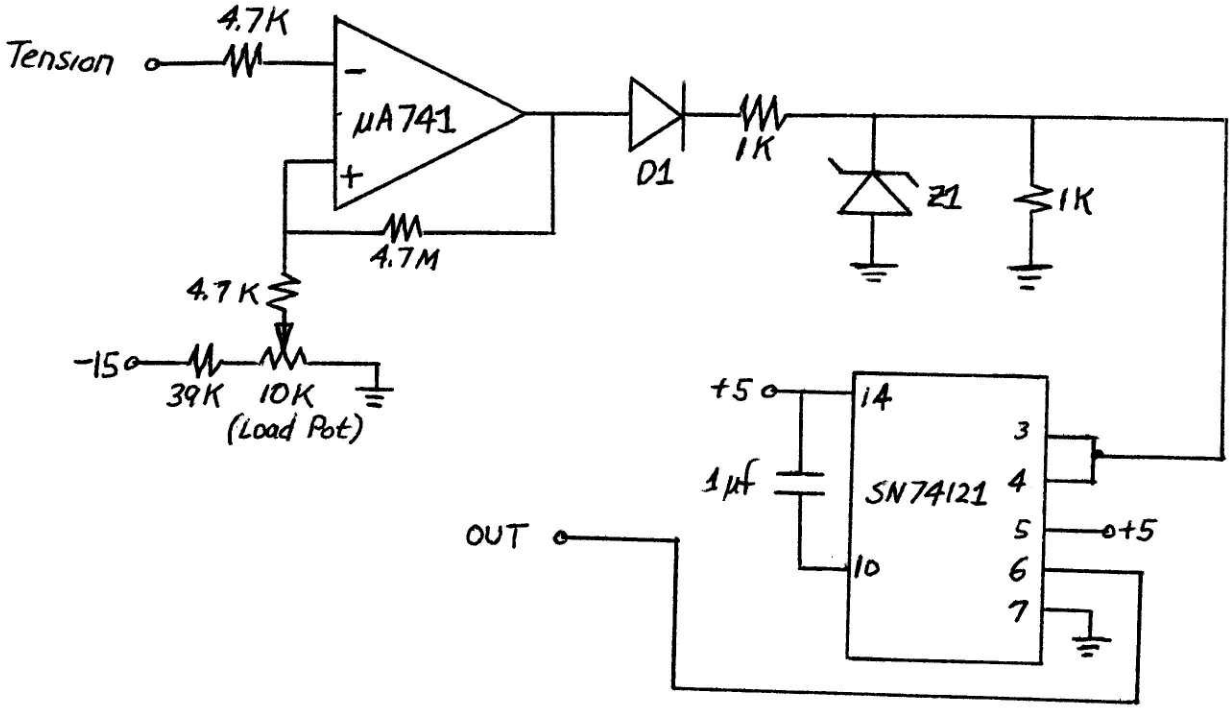


Figure 23 Comparator #1

D1 - 1N914
Z1 - LMZ5.1A

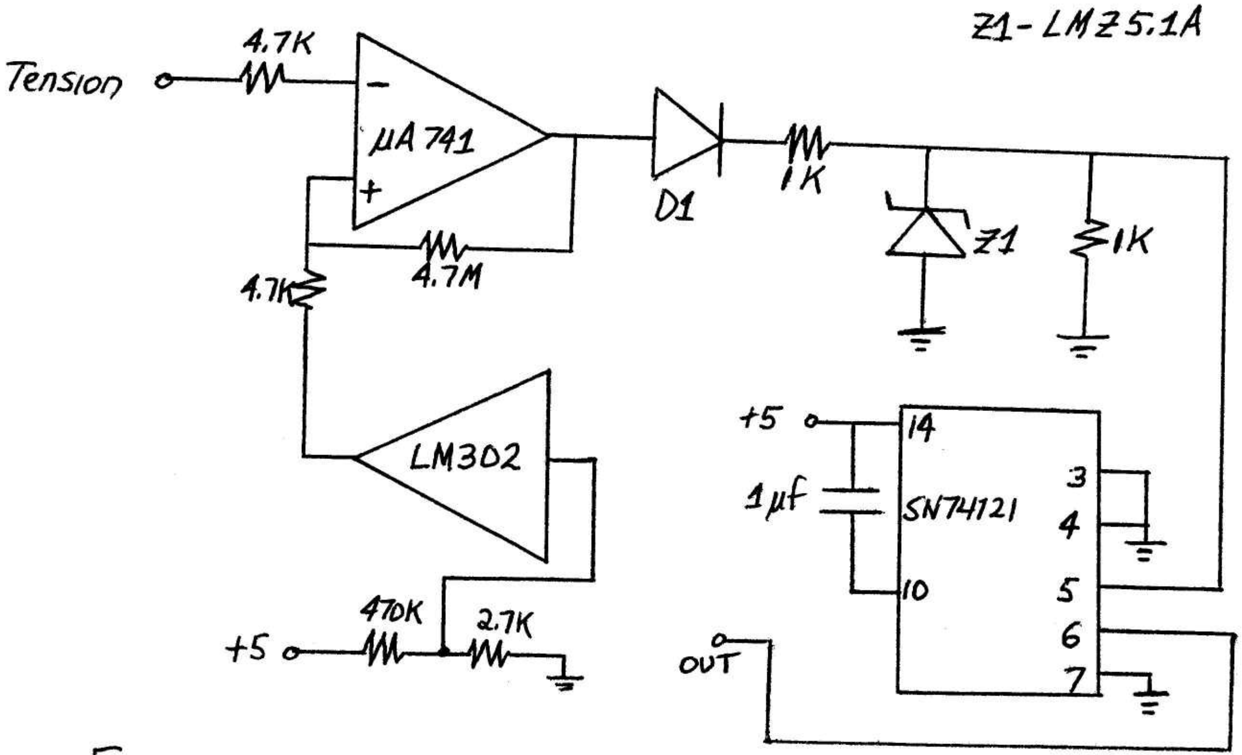


Figure 24 Comparator #2

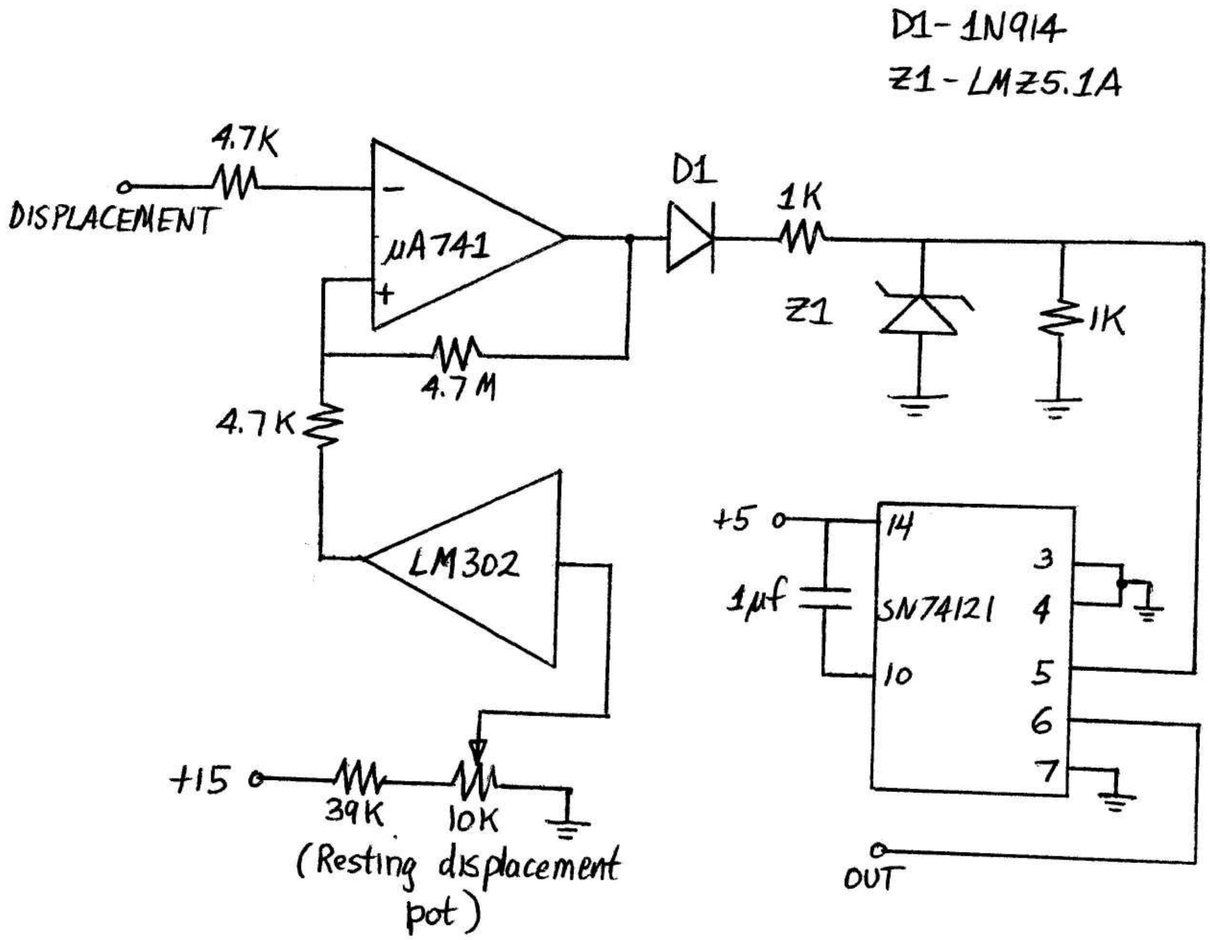


Figure 25 - Comparator #3

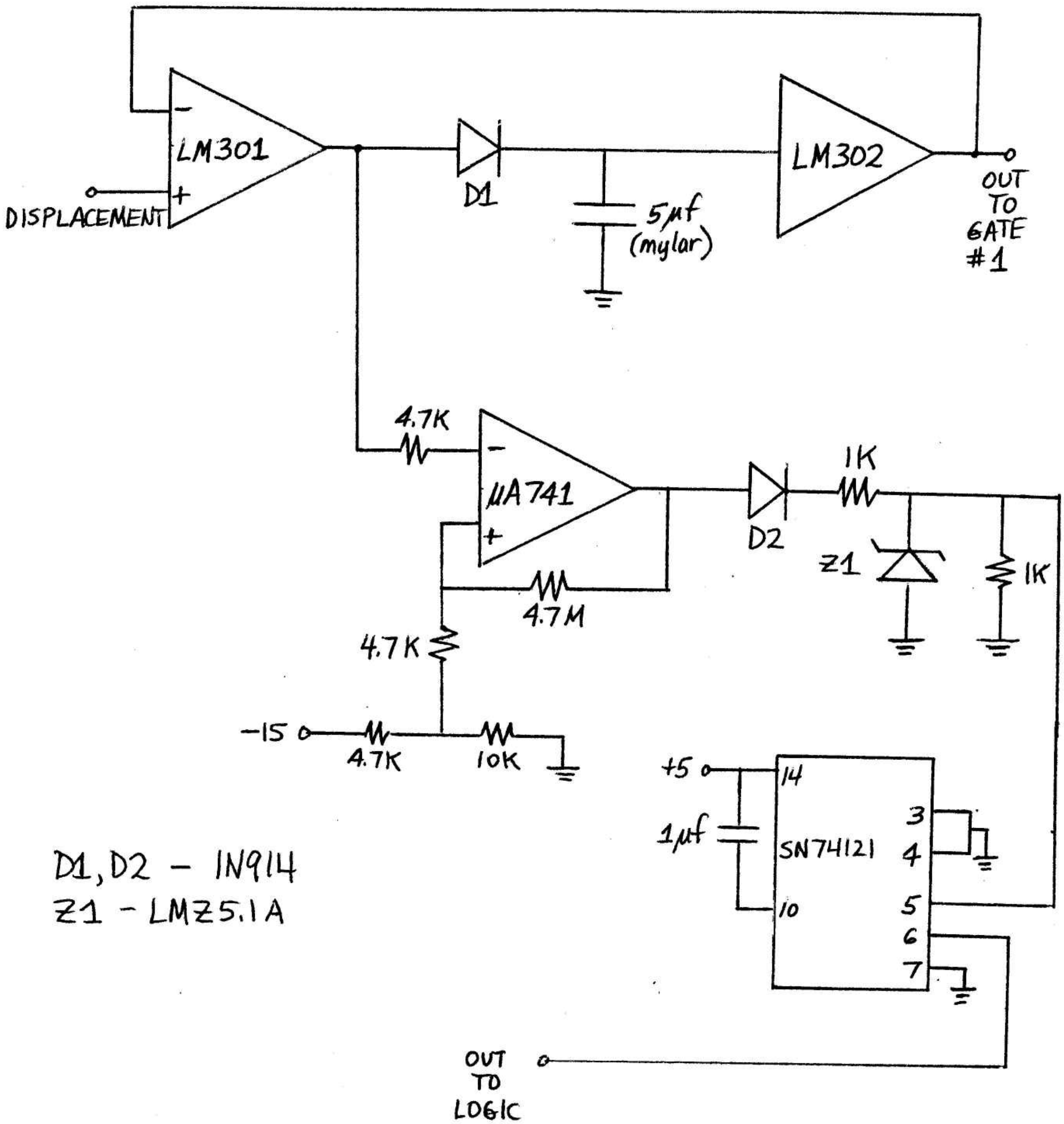


Figure 26 Peak Holder & Detector

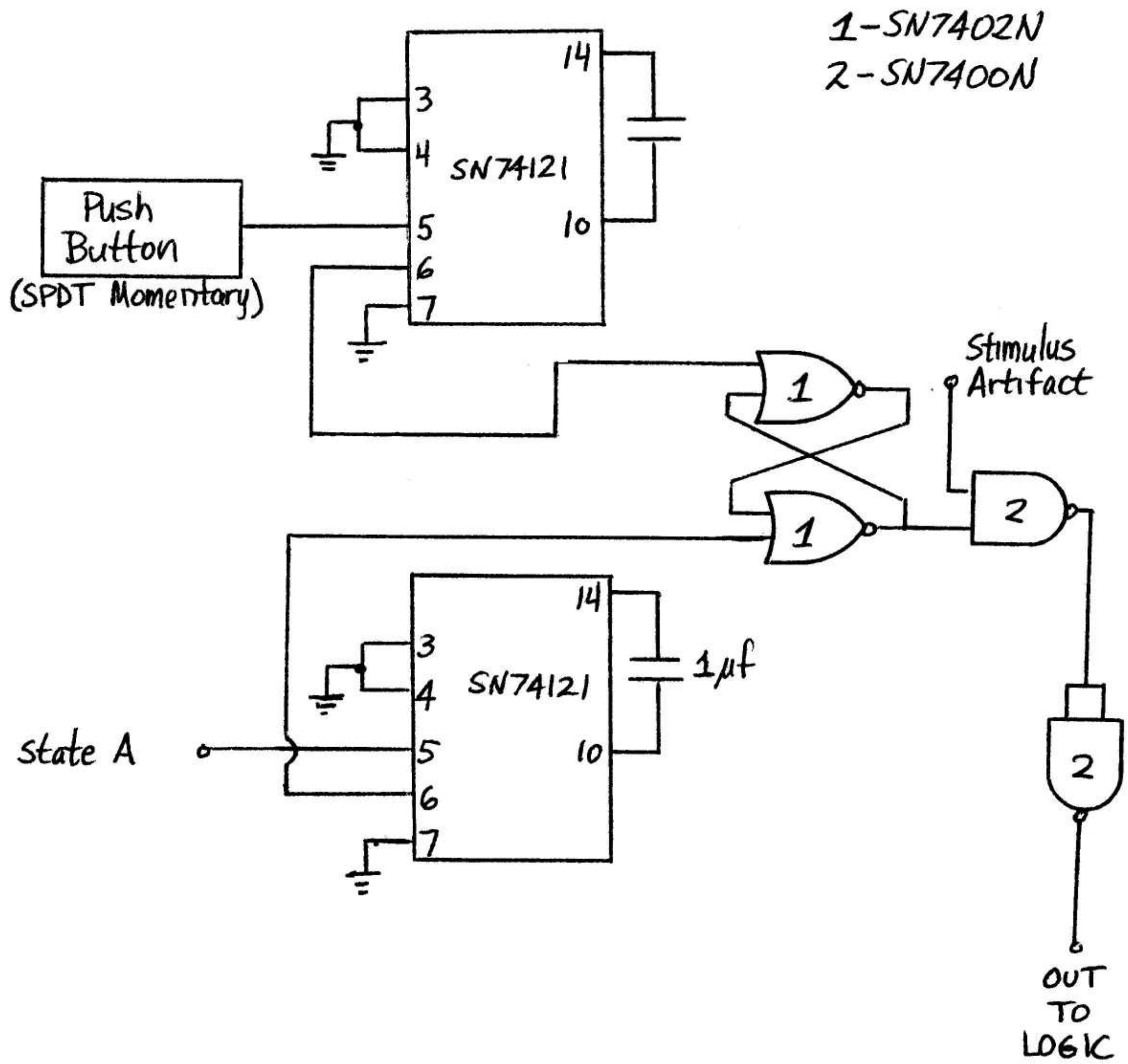
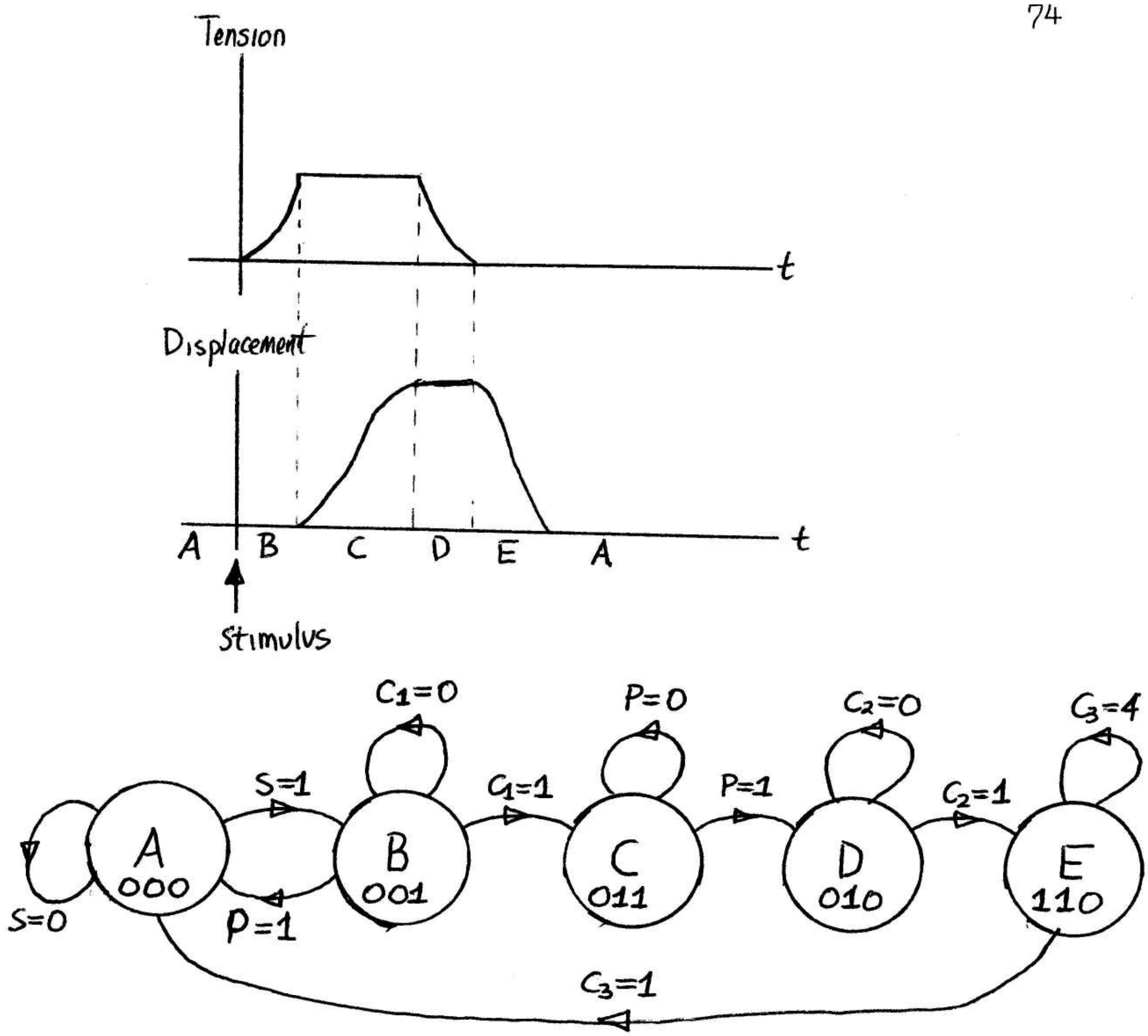


Figure 27 — Stimulus Artifact Circuit



S= Stimulus pulse

C_1= Comparator #1 output 1-shot

P= Peak detector output 1-shot

C_2= Comparator #2 output 1-shot

C_3= Comparator #3 output 1-shot

Figure 28 - State Transition Diagram & Assignments

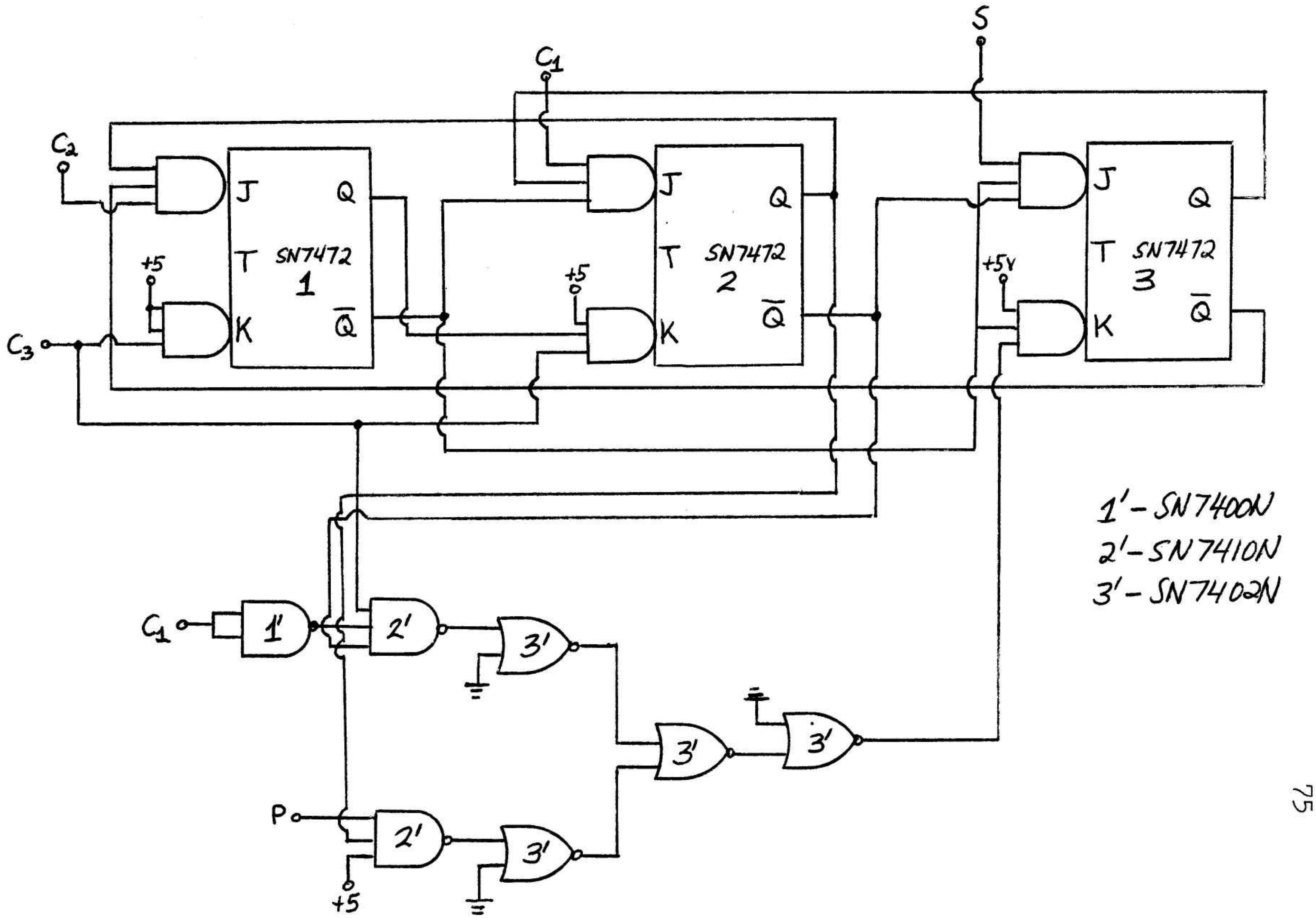


Figure 29 – Logic Circuit

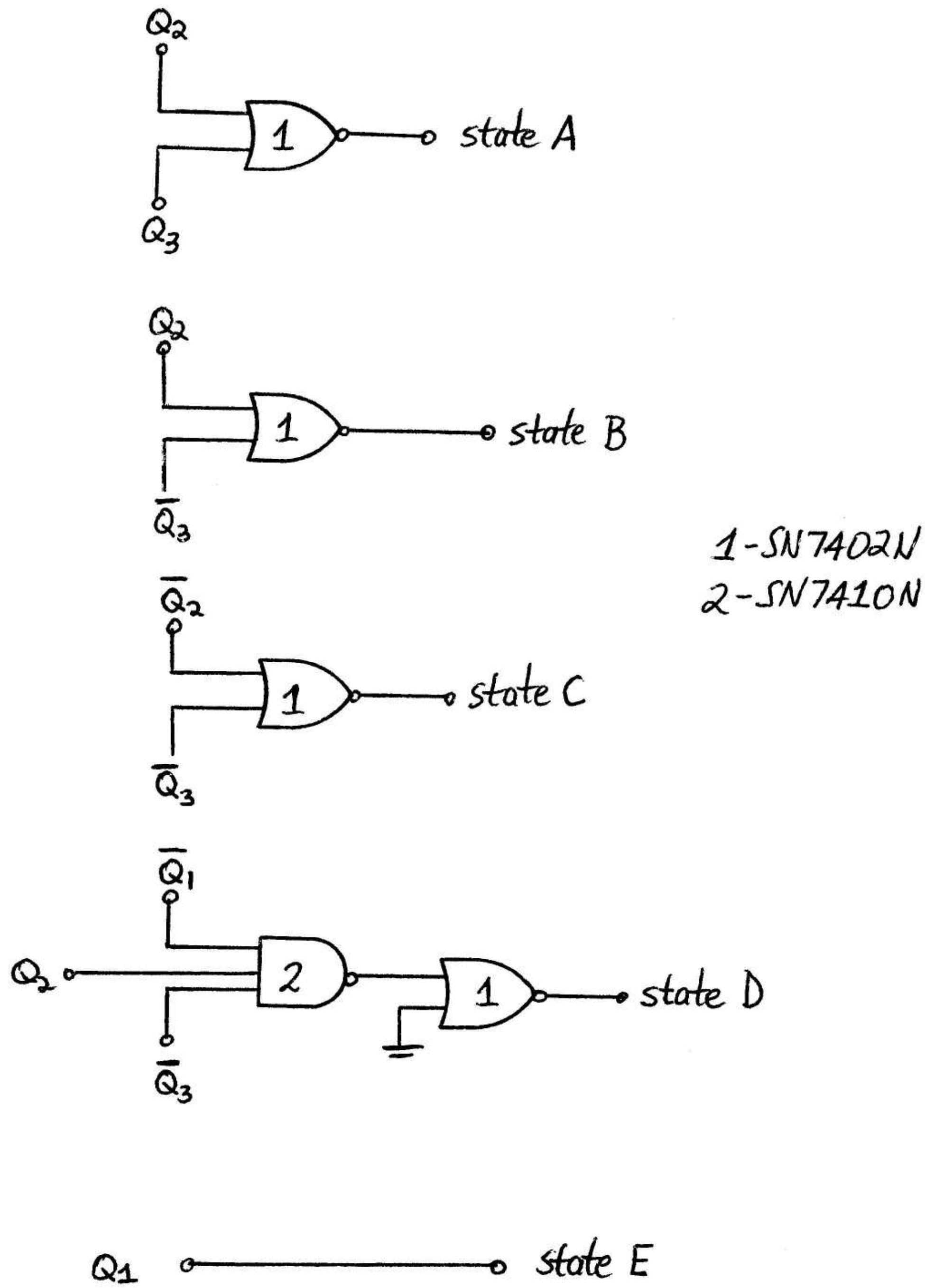


Figure 30 State Decoding Circuitry

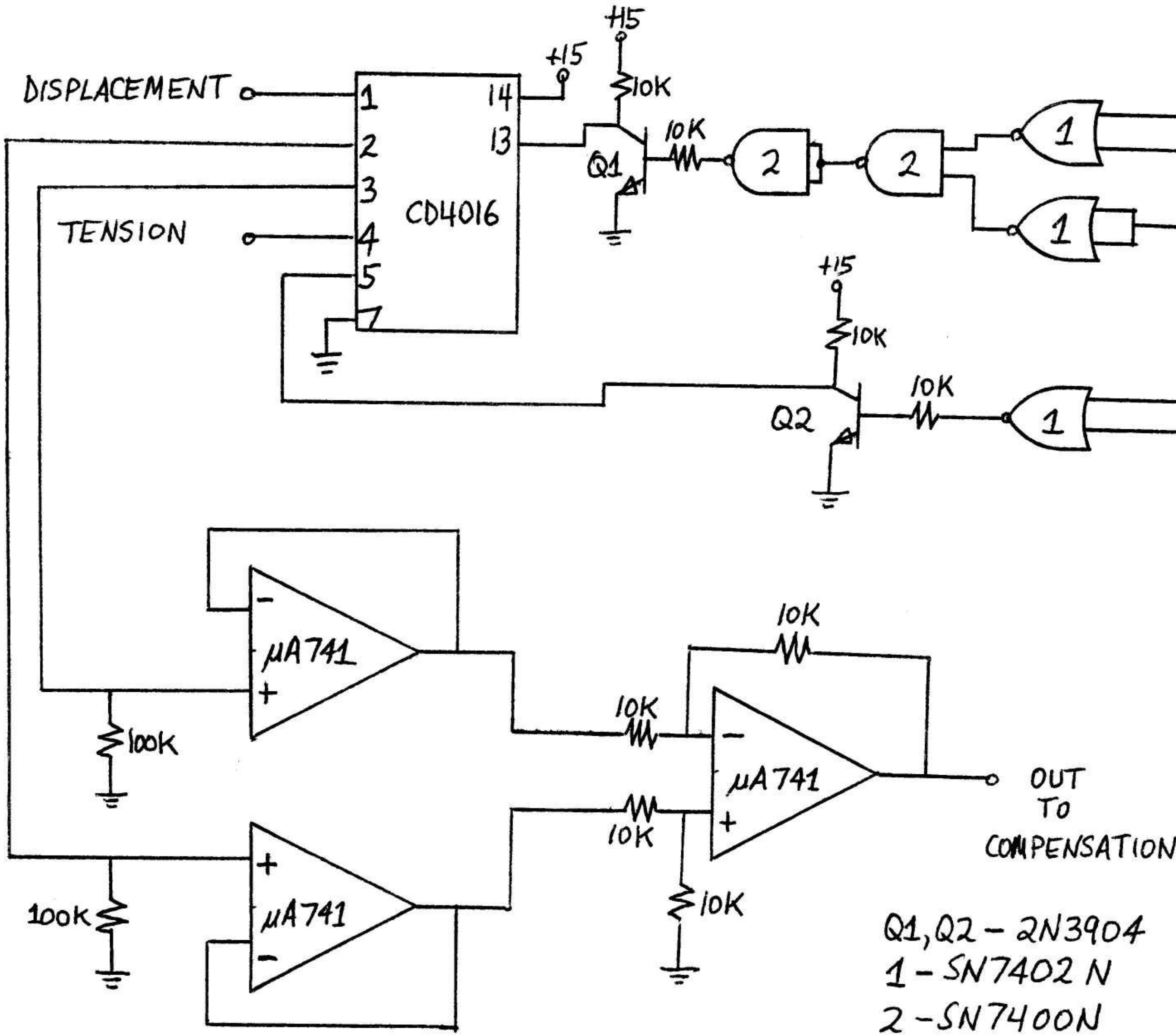
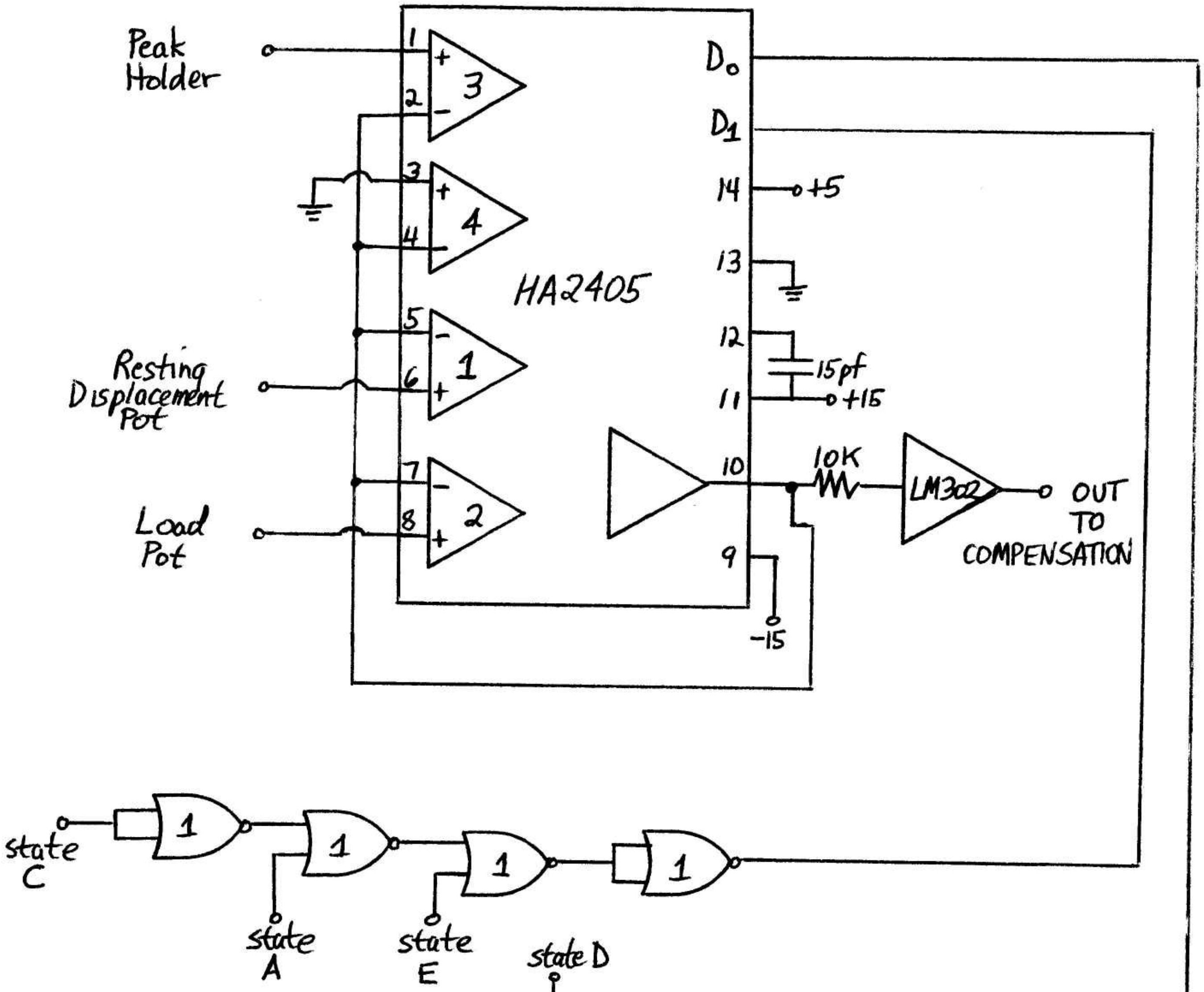
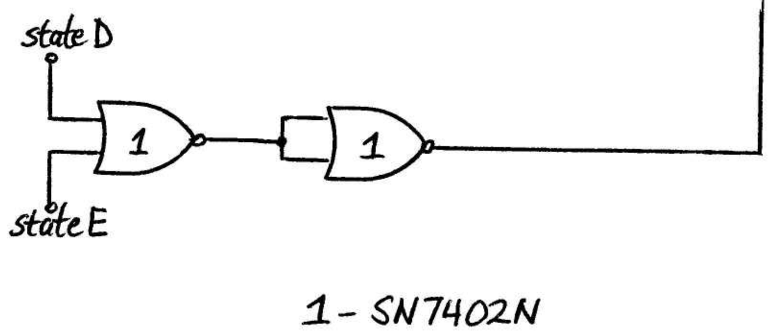


Figure 31 - Gate #2





D_0	D_1	Channel Selected
0	0	1
0	1	2
1	0	3
1	1	4

Figure 32 - Gate # 1

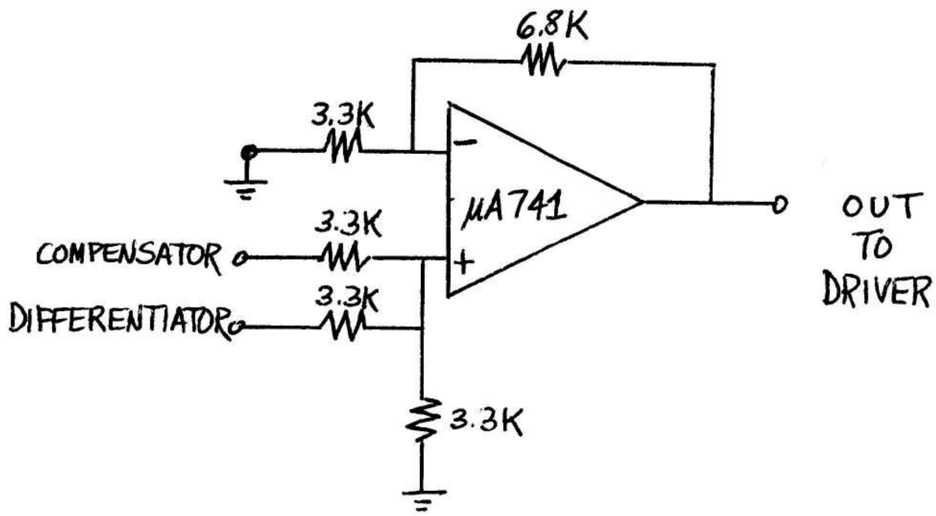


Figure 33 – Summing Amplifier

V. Results

Due to the complicated nature of the peripheral equipment required to maintain a muscle during an experiment (oxygen bubbler, constant temperature apparatus, etc.), it was desirable to first test as much of the system as possible without actually mounting a muscle. This also served to keep the supply of rats at adequate levels. This could easily be accomplished for the signal processing circuitry which provides the input to the logic network, and for the logic network itself. In testing these circuits, an RC circuit was used to generate a waveform of the approximate shape and duration of the isometric tension rise of the muscle. Using the muscle waveform simulator, the individual comparators and the peak detector were tested in sequence and their operations verified. The outputs of these circuits provided to the logic in the proper sequence was used to test and debug the logic network. Every possible input sequence to the logic network was tested to assure that the proper state changes occurred in the flip-flop register and that no improper state-changes occur. In this manner, it was verified that the comparator and logic circuitry functioned as designed.

As has already been described, the feedback compensation circuit was first tested using a short piece of rubber-band in place of a muscle. The displacement feedback was adjusted as previously described and its ability to maintain lever arm position at a constant value was tested by adding a 10 gram weight to the end of the arm. During this testing procedure, it was found that if the rubber-band was removed from the lever arm, it made no difference in setting the gain pot of the compensation circuit for maximum gain while maintaining stability. The stiffness of the motor is such that the small weight of the rubber-band and connectors attached to the lever arm presents about the same load as the arm alone. This indicated that in hanging a real muscle in the constant displacement mode, the compensation used for the rubber-band should be appropriate. This was indded found to be the case, as shown in the tracing of figure 34. This shows the isometric tension obtained for a muscle actively held at its resting position throughout the contraction. Also shown is the displacement transducer output during the contraction. Slight deflections of about 0.01mm occur at the beginning of the tension build-up and at the return to zero. This motion is very small, and the maintainance of the baseline throughout the contraction indicates that the deflections are probably artifacts of the mechanical connectors in the system.

The active control of tension was to be performed by the same compensation circuit used for displacement control, with a sensitivity adjustment pot for the tension transducer output.

Since the relative sensitivity of the Pitran is greater than that of the displacement transducer, the pot was to be used as an output attenuator. During the measurement of tension, the muscle is an integral part of the system. The use of the same compensation circuit for both tension and displacement depends on the assumption that the muscle, as an important element in the feedback loop during tension measurement, does not contribute significant phase shift to the open-loop response at frequencies below 230 cycles. An attempt to verify this fact was made by repeating the open-loop frequency response measurement relating motor-driver input voltage to Pitran output voltage with a muscle in place. This attempt was unsuccessful except at extremely small input signal levels to the motor due to severe non-linearities in the output. The properties of the muscle as an element in the feedback loop vary depending on its resting length and tension and also from muscle to muscle. For this reason, it was decided to apply tension feedback slowly, by turning the attenuator all the way down and then increasing it slowly. The attenuator was set far below the critical value for oscillations to allow for variations due to changing resting conditions and different muscles. The isometric tension developed by a muscle gave a 2 volt Pitran output. The Pitran was then connected in the feedback loop and the muscle restimulated. The maximum output observed was 50mv, 2½% of the full-scale output. For practical considerations, this control was considered adequate. In testing both feedback modes, gates 1 and 2 were bypassed and stimulus pulses were prevented from triggering the logic.

The final testing of the system involved the ability to switch the muscle between constant displacement and constant tension phases as described. Problems, both minor and major, arose during the testing. Minor problems concerning both gate #1 and gate #2 were solved. The integrated circuit used for gate #2, the CD4016A, repeatedly burned out until it was discovered that the control input of the unused single switch in the package of four had to be grounded. An error on the data sheet of the HA2405 led to improper programming of gate #1. Another relatively minor problem easily solved involved the proper polarity of the offset input signals to the motor-driver during each of the four states.

The most inportant modification required concerned the use of the peak detector to switch from state C to state D. During state C, the muscle tension is to be held constant at the predetermined load value set. The muscle should then contract isotonically until maximal shortening occurs. At that point, the peak detector circuit should trigger the transition from state C to state D. In practice, this sequence of events did not occur. The proper operation of the peak detector circuit requires a smoothly rising input signal. The displacement transducer output, however, is somewhat noisy, and small fluctuations in the transducer signal as the muscle begins to shorten cause false triggering of the peak detector circuit. As a result, the transition sequence required could not be obtained.

Modification of the peak-detector circuit to avoid false triggering by input noise is a subtle problem, one requiring more time than was available. For this reason, the peak detector circuit was replaced by a threshold comparator identical to the one shown in figure 24. A pot is used to set in advance the point in the displacement waveform at which the switch from state C to state D occurs. This pot can be adjusted to the peak value of the contraction empirically. If the pot is set too low, state D begins before the muscle reaches its maximum activity. When the tension is then released during state D, it rises to its peak before returning to resting value while the displacement is held at its cutoff value. Several tracings of this type, with various settings of cutoff value below the peak, are shown in figure 35. If the pot is set too high, the muscle is not capable of shortening sufficiently to reach the cutoff value and the system remains indefinitely in state C. Since state C is a constant tension state, this mode of operation can be used to demonstrate the ability of the system to keep tension constant. A tracing of this type is shown in figure 36.

Using these observations as guidelines, the peak displacement cutoff pot can be varied to the proper value for switching at the peak of the rising displacement waveform. Three representative tracings are shown in figure 37a, b, and c along with an isometric contraction in 37d for comparison. Certain characteristics of the waveform deserve note. First, the transitions occur as desired, and the states and transition points are indicated in figure 37a. Second, the duration of the contraction and relaxation sequence, from state A through state E, is the same as the time course of the isometric tension, 350 milliseconds. The rising and falling tension states, states B and D, parallel the rise and fall of tension during the isometric contraction. Both of these results are expected. Finally, the transient response of the motor is evident at each of the switching points. The settling time required is about 25 milliseconds. While at each of the switching points the tension and displacement are both continuous, the input to the compensation circuit, and thus to the motor as well, undergoes a step change at each state transition. The ability of the motor to respond to this step input is determined by the frequency cutoff of the compensation circuit at 5 cycles per second. Thus, the delay in the lag compensator is demonstrated for a step input to the compensator in figure 38.

In conclusion, certain observations should be made. The system works well within the speed limitations of the motor used. If a faster motor is used, then improved transient response characteristics can be obtained leading to smooth transitions from state to state. Such a system utilizing this faster motor would also require the replacement of the displacement transducer by one correspondingly faster as well. Finally, a peak detector that was noise-immune would be a useful replacement for the cutoff pot used in state D. This would eliminate the need for the rather careful adjustments required to set the pot at the peak of the displacement waveform.

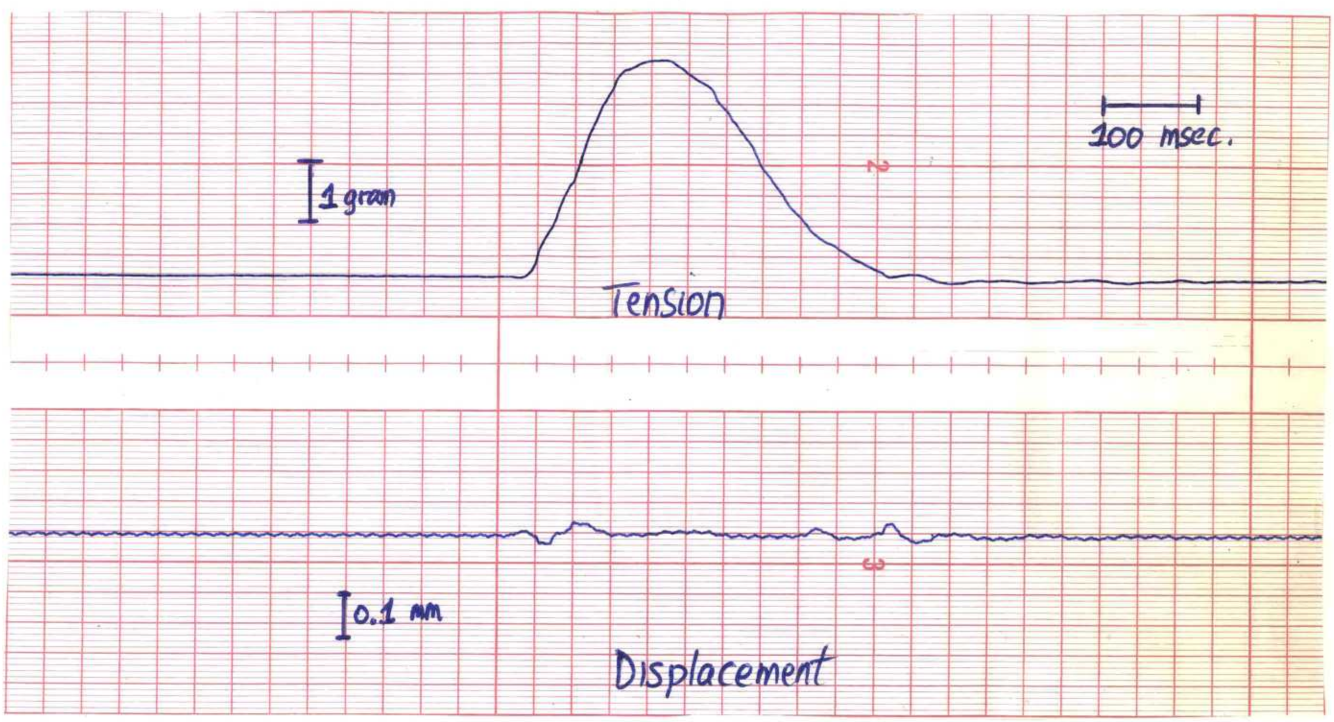


Figure 34 - Isometric Contraction

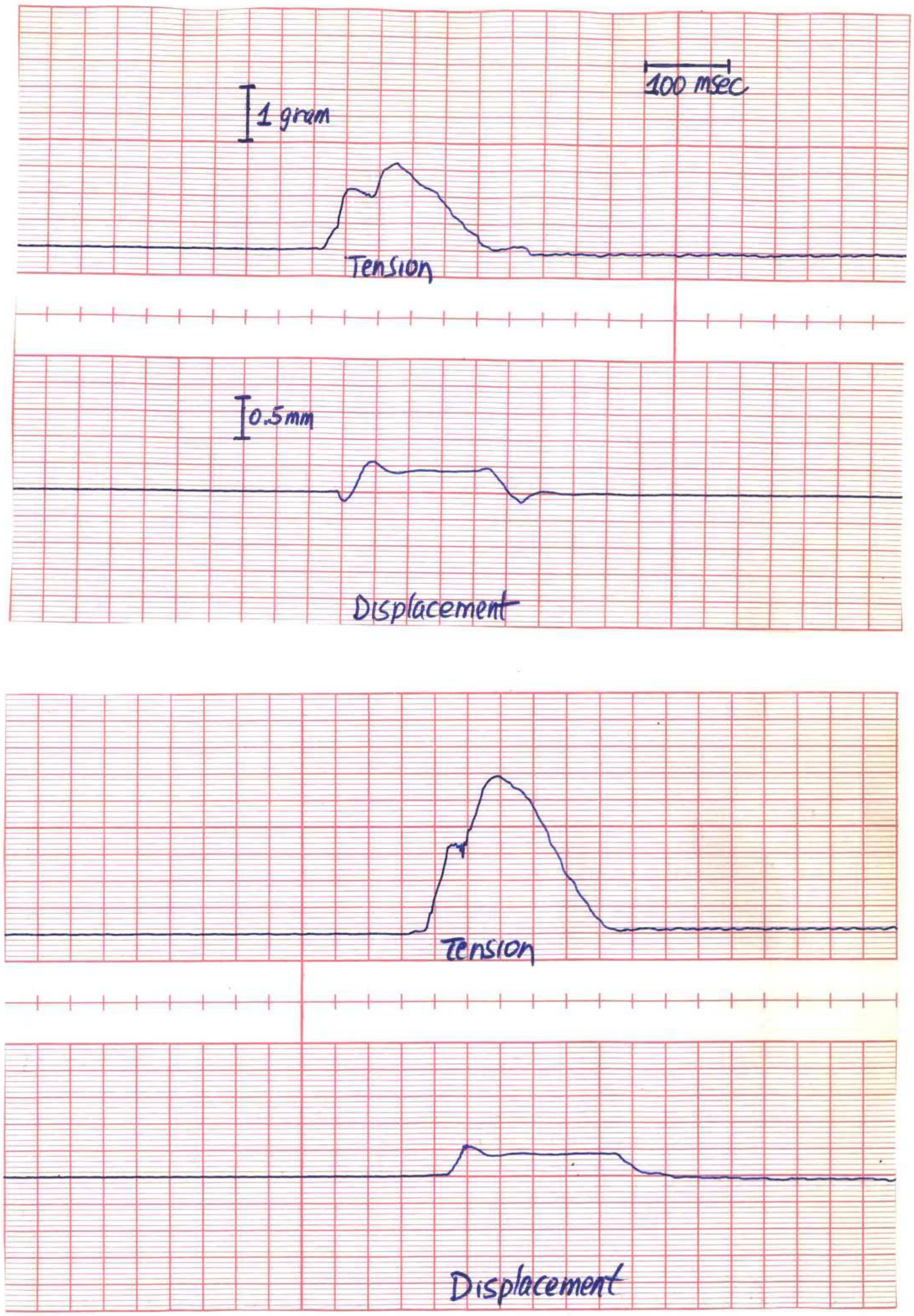


Figure 35 - Programmed Contraction with Displacement Cutoff Pot Set Low.

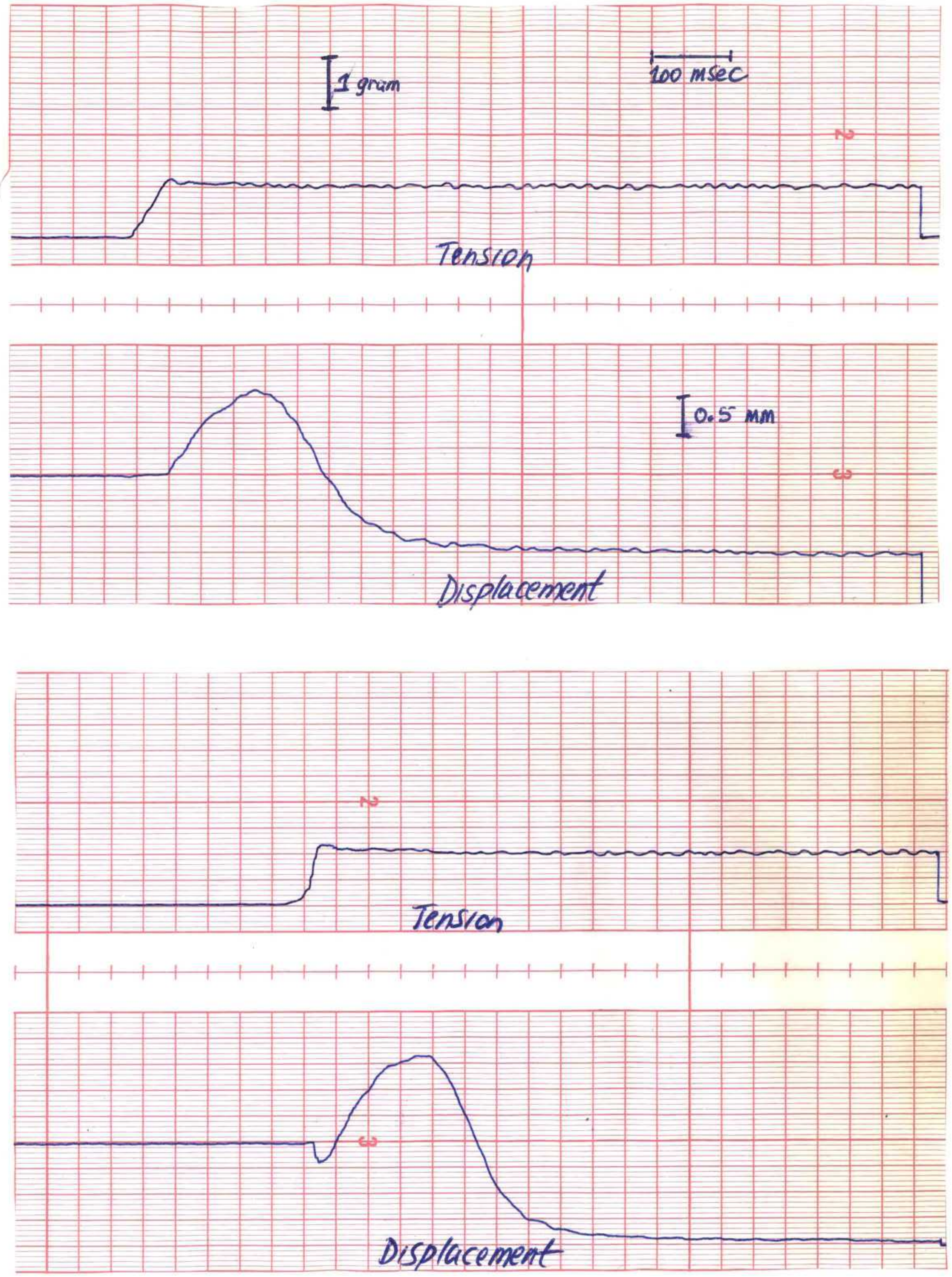


Figure 36 - Programmed Contraction with Displacement Cutoff Pot set High.

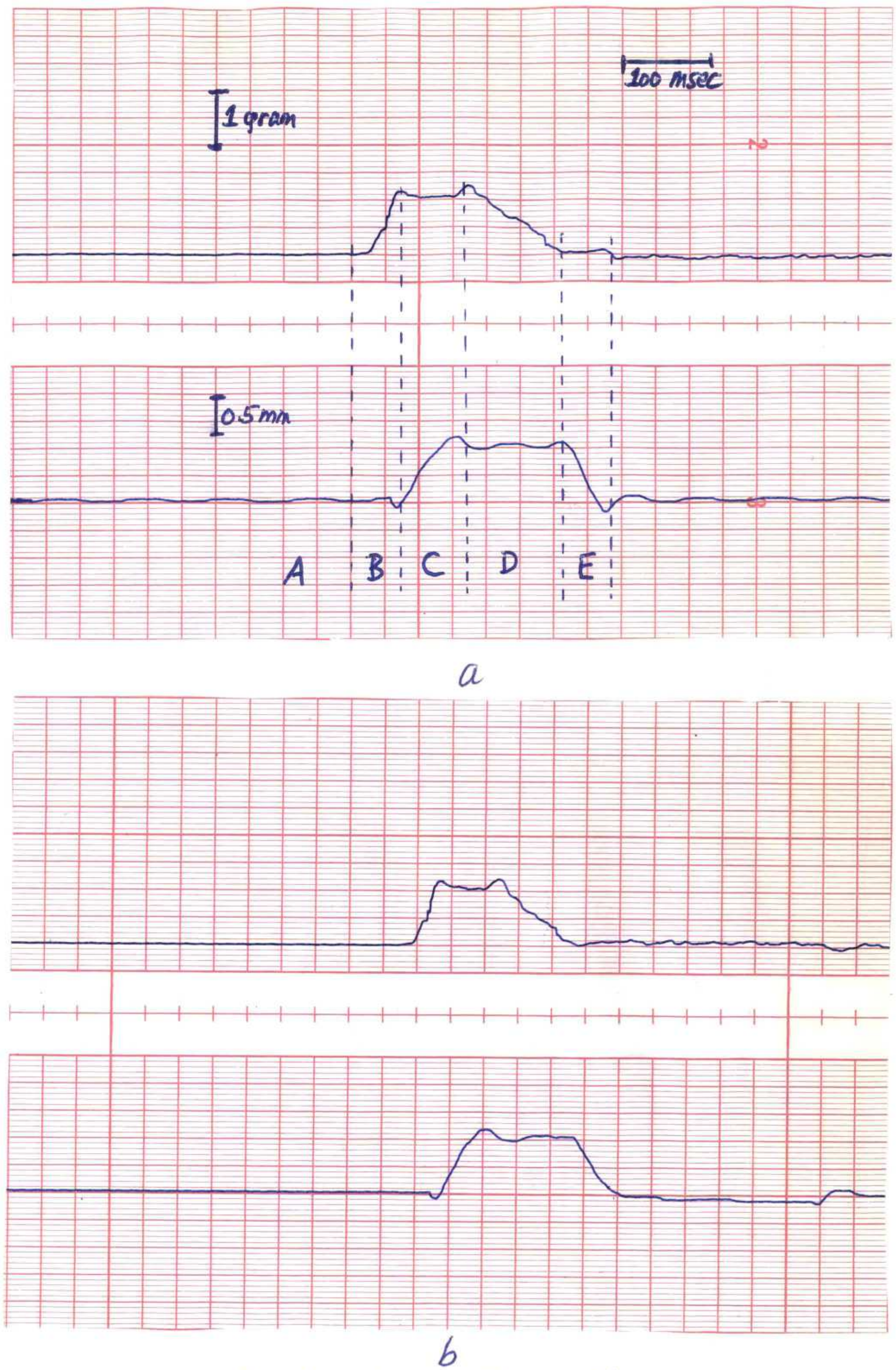
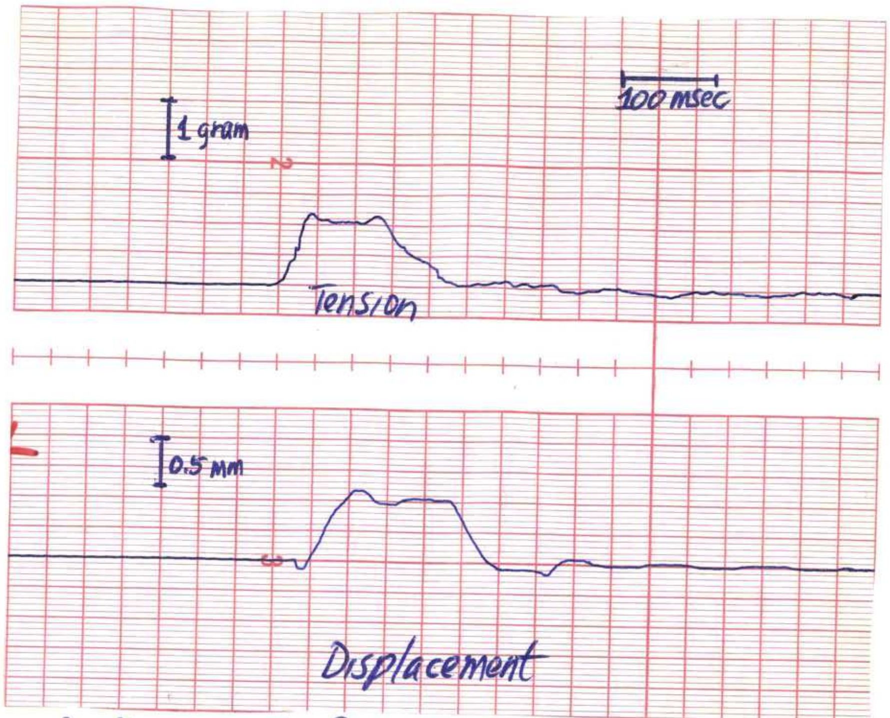
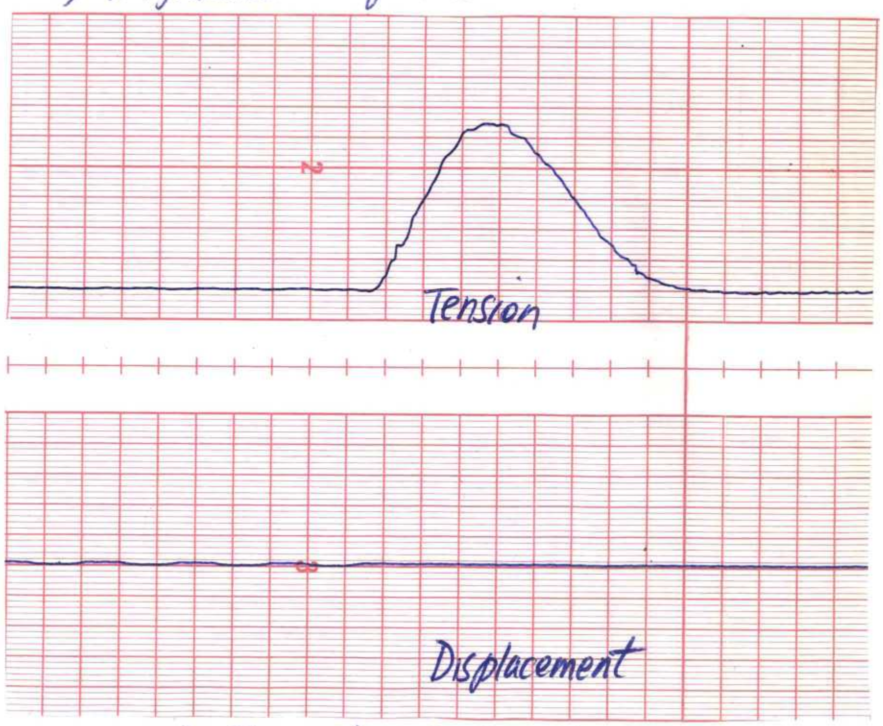


Figure 37 - Contraction Relaxation Sequence



c) Programmed Sequence



d) Isometric Contraction

Figure 37

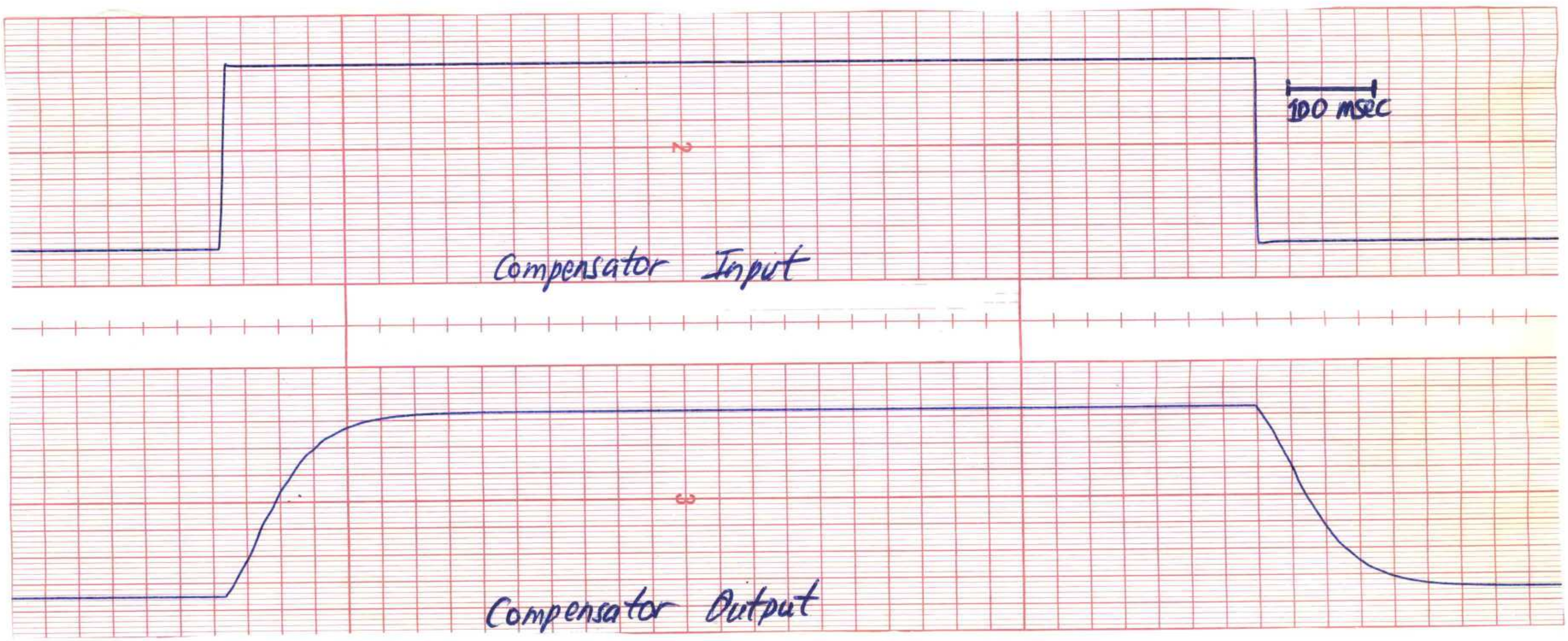


Figure 38 – Lag Compensator Step Response

BIBLIOGRAPHY

Braunwald, E., Ross, J., and Sonnenblick, E., Mechanisms of Contraction of the Normal and Failing Heart, Little, Brown, and Co., Boston, 1965.

Curtis, H., Biology, Worth Publishers, Inc., New York, 1968.

D'Azzo, J., and Houpis, C., Feedback Control: System Analysis and Synthesis, McGraw Hill, New York, 1966.

Hill, A. V., First and Last Experiments in Muscle Mechanics, Cambridge University Press, Cambridge, England, 1970.

Newton, G., Gould, L., and Kaiser, J., Analytical Design of Linear Feedback Controls, John Wiley and Sons, New York, 1967.