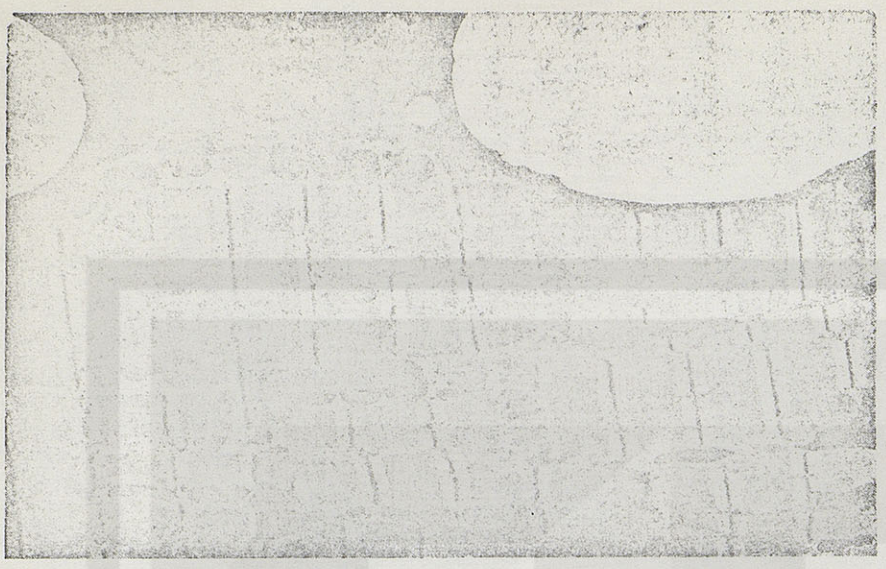


Electronmicrograph shows a longitudinal section of the right ventricle of dog heart. The repetitious pattern of the sarcomeres "in register" is readily visible, as are such features as the intercalated disks (jagged lines) and the numerous mitochondria.

but are harder to discern than in skeletal muscle. The result of the dissociation of sarcomere length and muscle length in overstretched heart muscle is a distortion in the relationship of the fibrils. Normally, in myocardium, the fibrils are arranged to register – much as though they were freight cars in a railroad yard in which there were several trains on parallel tracks, with the cars of each train so aligned that all their couplings were exactly opposite one another. One could then look across the arrayed trains and see daylight between the cars from track to track.

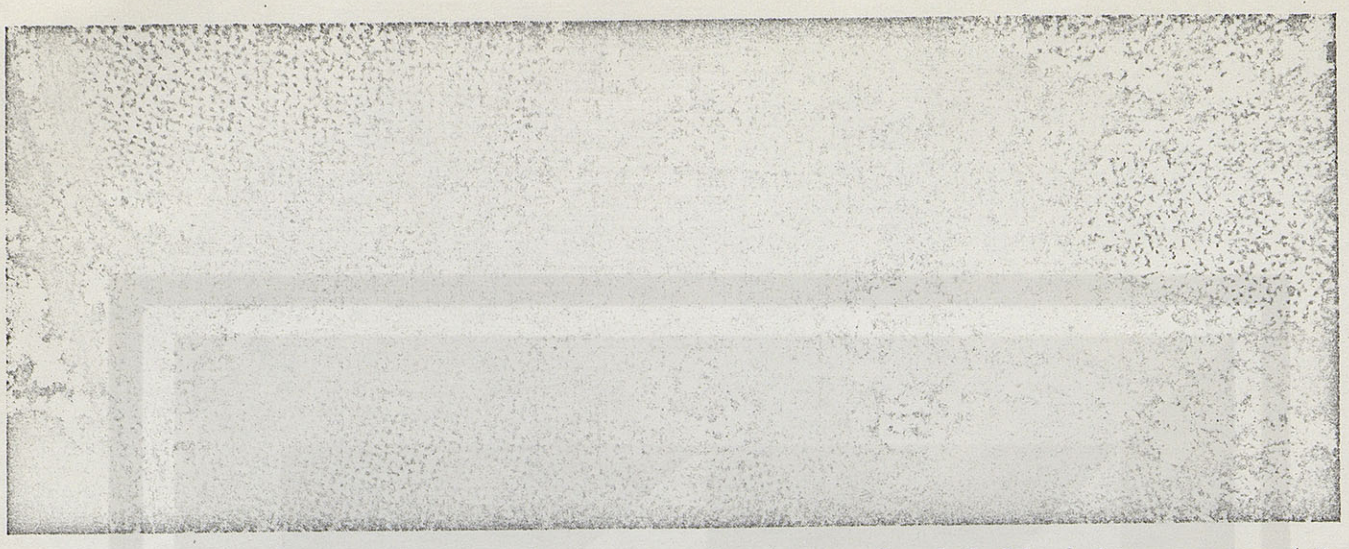
But when myocardial muscle is significantly overstretched, the fibrils, instead of being in register, begin to describe an irregular zigzag pattern. One cell can become longer than its individual components by allowing one of its parts to slide in one direction, another in another. That this slippage could be most important as a factor in chronic failure and dilatation is apparent. While the sarcomere is limited in its ability to stretch, possibly because of membrane containment, the cell apparently can become enlarged through distortions in register beyond the limits permitted by stretch. Clinically, the result is a permanently deformed cell and a large, "baggy" heart without a very high filling pressure. Thus, while the impact of slippage on myocardial function has not been established, there is good reason to suspect that it is quite important.

What has been established is that at the lengths at which cardiac muscle ordinarily functions not only is there a direct relationship between sarcomere and muscle lengths, but sarcomere lengths in the midwall of the heart can be correlated quite exactly with the filling pressures and diastolic stresses in the wall of the heart. Catheterization has shown that the upper limit to the filling pressure of the normal heart ranges between 10 and 15 mm Hg, and at this pressure, sarcomere length is 2.2μ.

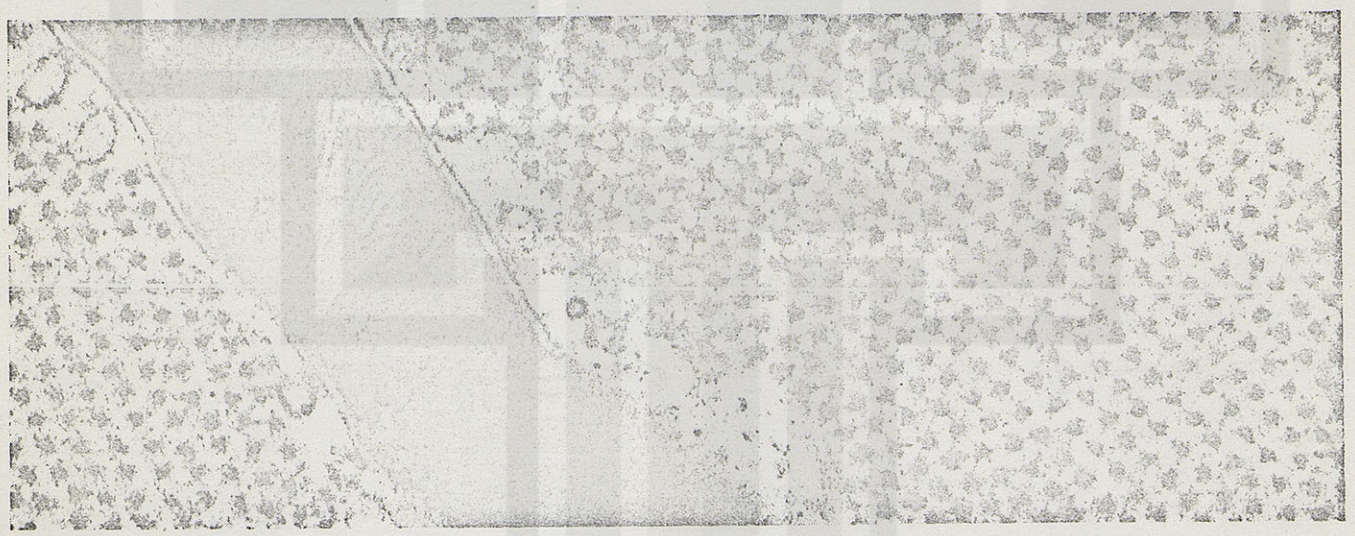
In a teleologic sense, then, the circle is complete. The cardiac pump is designed so that the upper limit to normal filling pressure is achieved exactly at the optimal length of the heart's basic contractile structure – the sarcomere. As heart volume is reduced, the sarcomeres get shorter, the tension they produce is reduced, and the force generation is lessened. Experimental support for this statement has come from studies in which the dog heart has been fixed in systole or diastole by rapidly injecting fixative into the coronary arteries, and sarcomeres have been measured. These studies have shown that the normal diastolic sarcomere length is between 2.05μ and 2.15μ, while the normal systolic sarcomere length is about 1.9μ. The difference in sarcomere lengths between systole and diastole explains the amount of blood pumped by the heart, i.e., stroke volume.

Now let us turn to some of the problems confronted if cardiac dilatation supervenes either as a consequence of myocardial weakness and/or overload. In the normal heart, wall tension falls during the course of ejection as the volume decreases substantially. In the dilated heart wall tension remains elevated since initial volume is augmented and does not decrease markedly in systole since stroke volume is reduced. In this sense dilatation and decreased stroke volume place an added tension load on the sarcomere, which may already be pushed to the apex of its length-tension curve. If the end-diastolic size is increased, the tension must rise to maintain output. However, when the muscle begins to become overstretched, the tension cannot increase further. In terms of the length-tension curve, we are now approaching a descending limb. In functional terms, the heart must continue to dilate as a compensatory mechanism. Cardiac function gets progressively worse, further dilatation supervenes, and the heart loses its ability to maintain a steady state. This is one of the critical ways in which cardiac failure can be related directly back to sarcomere length.

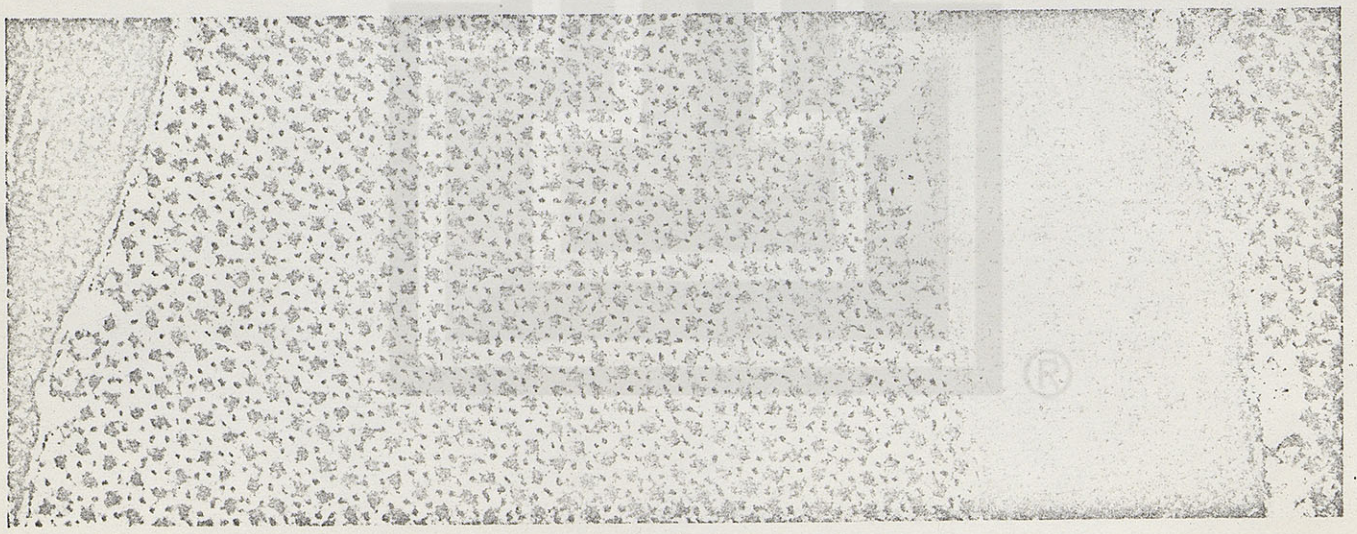
In both acute and chronic dilatation, there is an increase in sarcomere length. In the chronically dilated heart, sarcomere lengths are found to be right at the peak of the length-active tension curve, i.e., around 2.2μ or 2.25μ. There is no reserve capacity since any further lengthening would place the heart on the descending limb of the length-active tension curve. At the same time, slippage may be occurring so that a larger heart results without a further significant increase in filling pressure. It should be noted that the increased sarcomere length is known from direct observation. The enlargement of the heart beyond the size that could be predicted from increased sarcomere length is similarly documented. Slippage is a plausible but not proved explanation for the disparity. At any rate, when ventricular volume is increased beyond this optimal sarcomere length, increased diastolic tension will be required, but this increased tension will not be rewarded with increased pumping capacity. Without increased developed



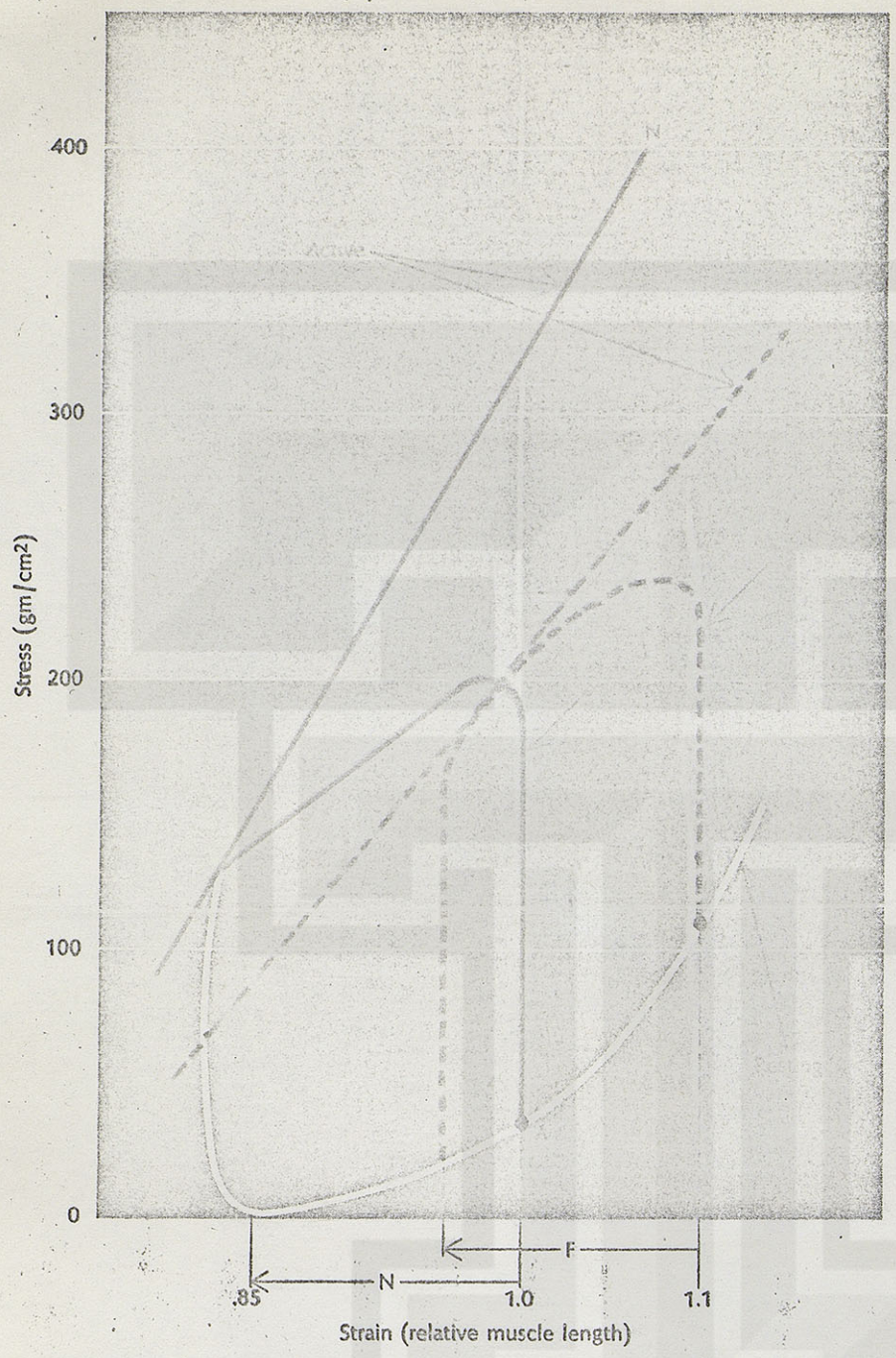
The Z line, which appears as a darkened orthogonally patterned area running horizontally through this EM, is a prominent feature of a section cut through the I band of two sarcomeres. Actin filaments are seen on both sides of the Z line.



In this electronmicrograph of a transverse section made across the center of the A band, one sees only the thick myosin filaments. No thin actin filaments are to be found. Bridges between many of the thick filaments are clearly visualized.



Another transverse section, this one across the lateral portion of the A band, shows both thick and thin filaments. The hexagonal lattice, with six thin filaments rotating around each thick filament, can be discerned. Parts of two mitochondria also appear.



The curves represent the relationships between stress (force in the ventricular wall) and strain (change of length for the shortening muscle). The lowest curve shows the relationship between the resting force on the muscle and initial muscle length. The upper curves (N for normal and F for failing) depict the maximum forces generated by an activated muscle as a function of length. At point A, normal muscle begins contracting from the resting curve. Force development proceeds until arrow, when shortening or, in the intact heart, ejection of blood occurs. Force rises slightly beyond this point and then begins to fall as the ventricle gets smaller. Ultimately, relaxation takes place as the shortening curve approaches the normal isometric tension curve. Point B marks the start of shortening for the failing ventricular muscle. The muscle is longer to begin with in compensation for depressed function, represented by the movement of dashed-line curve to the right. At any given length, less force can be generated by the failing muscle. After ejection (arrow) there is some fall in stress within the wall, but it is less than in the normal heart. Line N can now be compared with line F and the point is made that failing ventricular muscle has a larger load and shortens to a lesser degree. Hence the failing muscle has a depressed curve relating stress development to length and an abnormally large stress load during systole, thus further limiting the extent of muscle shortening.

tension in the wall, increased volume will lower the ejection fraction. This might be termed an important functional lesion in chronic dilatation. At this stage all the heart can do to make up for the deficit in output is to dilate further.

What are some of the factors leading to deterioration of myocardial performance and what ultrastructural changes, if any, are associated with these phenomena? First it should be recognized that functional abnormalities may not be reflected by any obvious structural changes. In hypertrophy of the myocardium, myofibrils appear larger in diameter, leading to an enlargement of cells rather than an increase in their number. Nuclei enlarge considerably while mitochondria increase in number so that the ratio of mitochrondrial mass to myofibrillar mass remains about the same.

In the presence of ischemia attendant on loss of coronary blood flow, changes in the activation system, in the mitochondria, and in the sarcomeres occur in the course of time. However, loss of contractile function precedes these apparent structural change, and in the early stages the structure may appear normal.

If one examines the surface membranes as ischemia is prolonged, one may see disruptions and breaks. The possibility exists that these disruptions increase membrane permeability so that normal gradients for electrolytes cannot be maintained. At the same time, elements of the activation mechanism – the T system – become dilated. The reason for this is not clear, but it is possible that the metabolic inadequacies resulting from ischemia could lead to breakdown of bits and pieces of the cell. In turn this may increase osomotic pressure, allowing fluid to enter and dilate the cell.

Even greater morphologic damage is seen in the mitochondria subsequent to ischemia. Vacuolation occurs and water droplets appear inside the mitochondria. They lose their normal crystalline structure, become loosely packed, swell, and tend to dissolve. These events, which take place under the influence of hypoxia, may also be observed in tissue from animals with severe congestive failure. However, it is important to distinguish between structural and biochemical damage. In

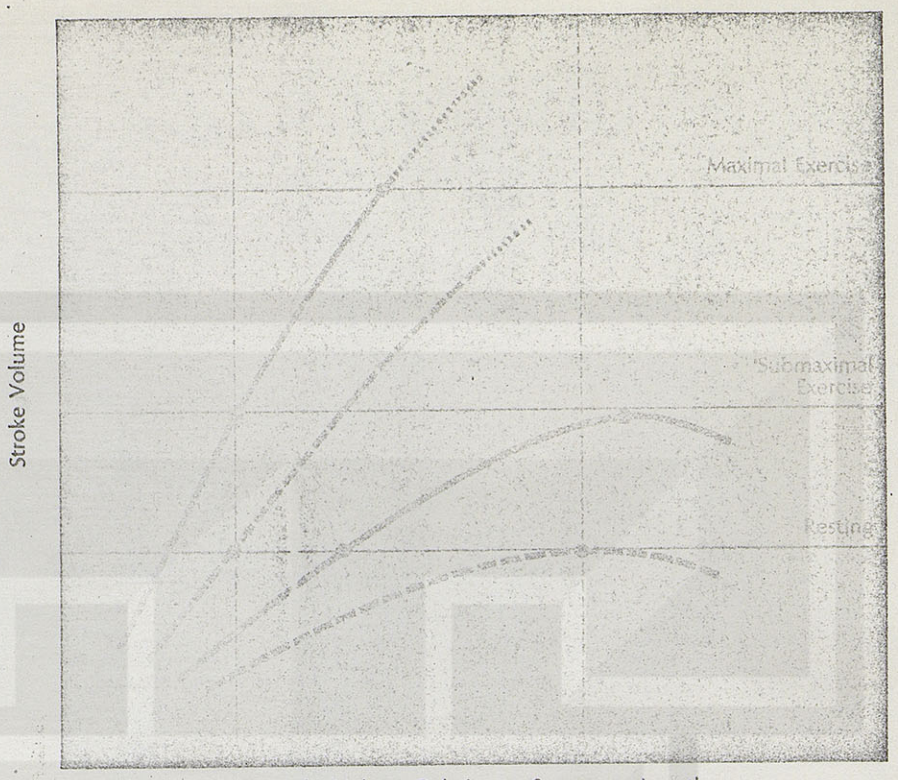
fact, although the mitochondria may appear to be extremely ragged and disrupted, there may be little evidence that their function is seriously compromised until quite late. Further, some of the ischemic changes in the appearance of the mitochondria may also be artifactual and occur as a result of fixation methods. This is especially true in the fixation of tissue that is already compromised.

With ischemia, the sarcomeres begin to manifest contraction bands in which some of the myofibrils contract and then do not relax. Thus, one sees areas in which the sarcomeres are jammed together and the sarcomere distribution becomes irregular in relation to their length.

What is quite remarkable in the picture of ischemic changes is their total reversibility. If blood flow is restored within 30 or even 45 minutes of interruption, most of the changes – disruption of surface membranes, swollen, vacuolated mitochondria, sarcomere irregularities – may disappear. Even the mitochondria, which may take a long time to recover morphologically, seem to regain their functional integrity very rapidly. This reversibility serves to warn us that great caution is needed if one is seeking to relate directly what one sees to deficits in function of the organism. The history of medicine and medical research is replete with situations in which investigators have found an abnormality and considered it responsible for the disorder being studied. In fact the abnormality may be merely an associated event or a result of the disease process and not causative. Relative to ultrastructure, artifacts of fixation must also be considered. On the other hand, some morphologic or biochemical alteration so slight as to be overlooked or ignored may be of much more importance. Before one can make meaningful correlations of cause and effect, an evaluation system must be established in which the generalized effects of cellular disorders and possible specific events can be weighed. However, studies of myocardial ultrastructure have not yet progressed to the stage at which such a system can be defined.

When a child's heart is overloaded, the child is able to handle that overload because the reserves intended to last a lifetime are virtually intact. But with the passage of time, function deteriorates and superimposed loads become ever more burdensome. In the absence of valvular heart disease or damage secondary to ischemia, one may live until 90 before load exceeds function. This provides some understanding about the true meaning of myocardial failure. Failure is not a dilated heart. On the contrary, the dilated heart is the compensation for the occurrence of myocardial failure, but as dilatation progresses, the function of the dilated heart fails.

To me, these are the reasons why one has to study the contractility of muscle and why ultrastructural studies are vital to our eventual understanding of cardiac function and dysfunction. A promising start has been made here in elucidating the ultrastructural landmarks of contractility. But there are still important gaps. More knowledge about the force-generating sites on the contractile protein filaments is needed. Further, added attention must focus on the system that controls activation and relation, and its contribution to cardiac contractility. Ultrastructural studies may also afford a means of understanding the role of the right ventricle in relationship to both function and failure. It appears that the techniques that will make it possible to acquire this information are now available. □



Curves represent the relationship between cardiac output and diastolic volume, which is related in turn to sarcomere length, in normal hearts and in hearts in mild and severe failure. A key point is that in the severe failure situation, exertion would produce increased diastolic volume but a fall in stroke volume.

Additional Reading

Huxley, HE: The mechanism of muscular contraction: Scientific American 213: 18-27, 1965

Sonnenblick, EH: Correlation of myocardial ultrastructure and function. Circulation 38: 29-44, 1968

Braunwald, E, Ross Jr., J, and Sonnenblick, EH: Mechanism of Contraction of the Normal and Failing Heart. Boston, Little Brown and Co. 1968

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

Departments of Electrical and Mechanical Engineering

6.022J/2.792J: Quantitative Physiology: Organ Transport Systems

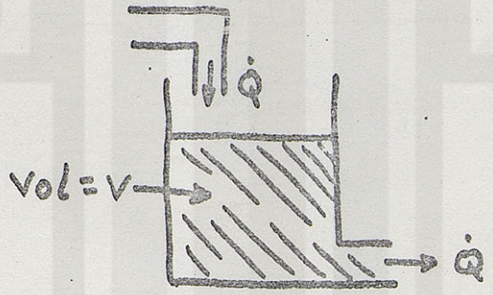
PROBLEM SET #3

Problem 1

A simplified model of the sudden-injection indicator dilution technique which helps to understand the shape of the tail of the concentration curve is illustrated in the following problem.

Consider a reservoir containing fluid of volume V into which fluid flows at a rate $\dot{Q}$ cc/min. Fluid leaves the reservoir at the same rate. (See Figure 1.)

Figure 1

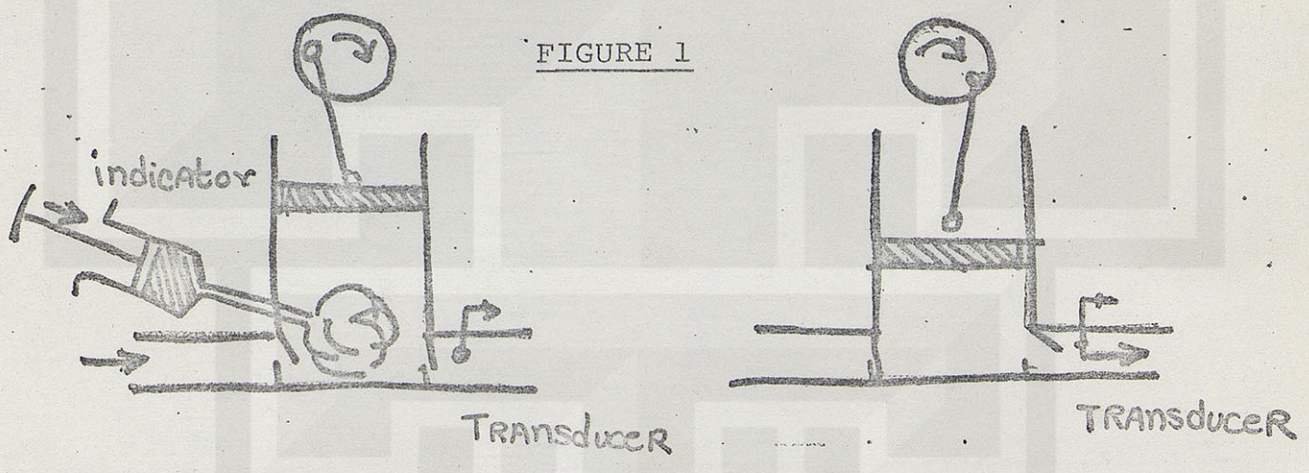


At t = 0, a quantity I_o of an indicator is suddenly added to the reservoir and is instantly mixed uniformly throughout the fluid. (This ideal mixing action continues for all t.) Derive an expression for the concentration of indicator substance c(t) in the exit stream. Sketch the function and show how it will change with changes in $\dot{Q}$ and V.

Problem #2

Assume that the heart can be modeled as a reciprocating piston pump as shown in Figure 1.

FIGURE 1



The output of this pump is measured in the following manner. An indicator is injected during early diastole such that it mixes thoroughly during this first diastole with the incoming fluid. A detector placed in the outflow tract reads concentration of indicator as a function of time. The response time of the transducer is very fast, so sudden changes in indicator concentration are faithfully reproduced. The total amount of indicator injected was 10mgm.

The concentration of dye as a function of time at the output detector is shown in Figure 2.

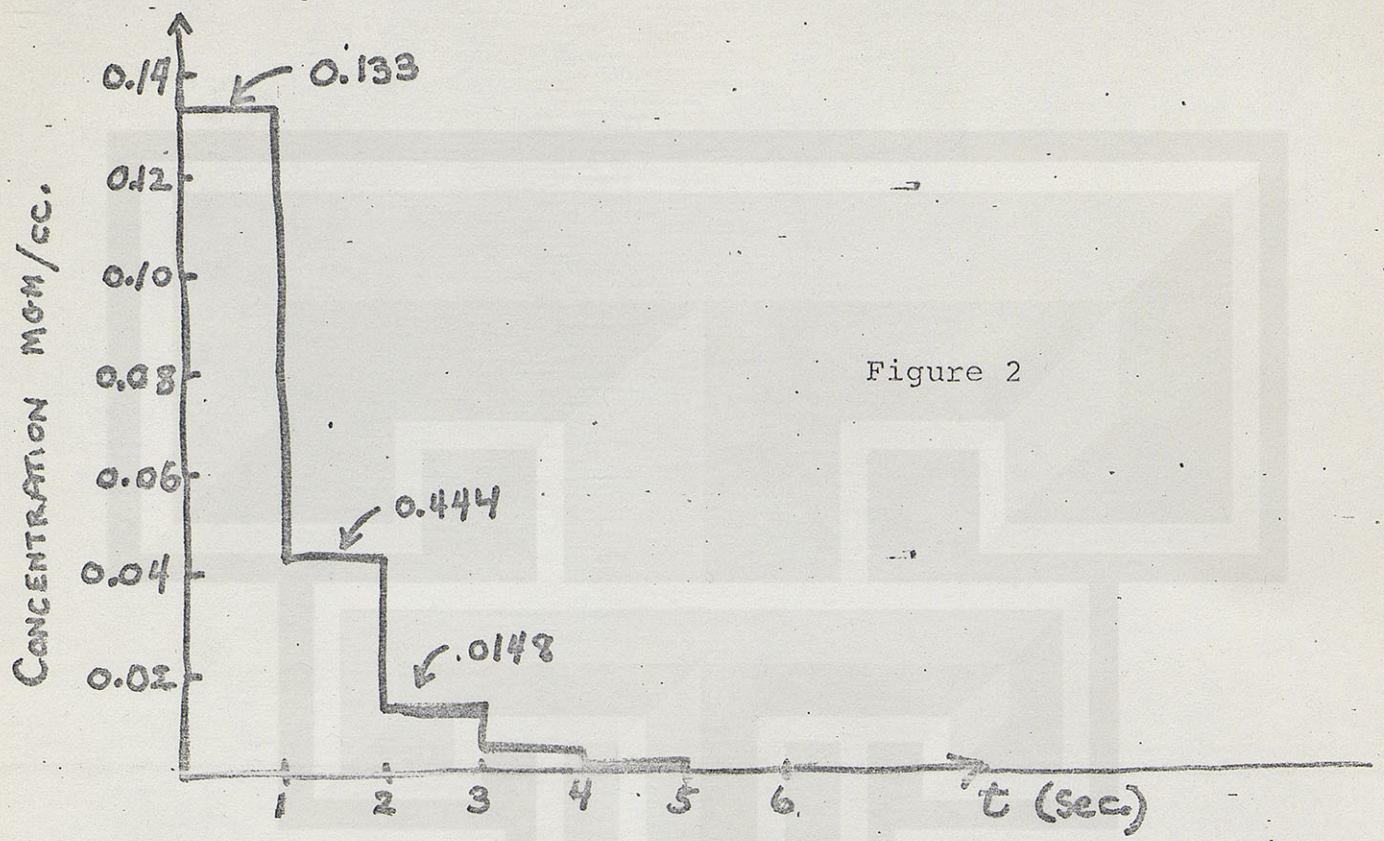


Figure 2

The concentration of dye as a function of time at the output detector is shown in Figure 2.

(a) Derive the equation of the curve in terms of:

V_s - the end-systolic pump volume .
V_d - the end-diastolic pump volume
I_o - the total amount of indicator injected.
T - the pump cycle length.

(b) Calculate the following:

1. Cardiac output
2. Stroke volume
3. End diastolic volume
4. End systolic volume.

Problem 3

Consider the following clinical data:

History

Mr. J. H., a 56-year old white male with no past history of rheumatic fever, was admitted to the hospital because of two fainting episodes prior to admission. One episode occurred while pushing a car, the other while chasing his daughter's cat.

Physical Examination

Blood Pressure: 100/80, Pulse rate: 80 beats/min.
Heart not enlarged. Slow rising arterial pulse.
Systolic murmur in the aortic area with a decreased second heart sound.

Laboratory Data

Chest x-ray: within normal limits. (Heart not enlarged, no calcified heart valves.) EKG: Normal electrical axis, no evidence of left ventricular hypertrophy.

The Clinical Problem

Are the symptoms on the basis of aortic stenosis, or are they due to other causes (cerebral vascular insufficiency, cardiac arrhythmia, etc.)?

A cardiac catheterization was performed to resolve the clinical problem, and to provide basis for rational therapy for the patient. Catheters were placed in the left ventricle (LV) and aorta (Ao) and pressure recorded. In addition, a catheter was placed in the right pulmonary artery in order to obtain samples of mixed venous blood for Fick output studies. The data obtained are as follows:

Oxygen capacity of blood (pH 7.4, T37°C) =
20 ml O_2/100 ml blood

During a three-minute collection time, a total volume of 408cc. of oxygen were consumed by the patient. During this period, the patient was resting comfortably and was assumed to have been in a steady state with respect to cardiac output. Samples of arterial blood showed an average O_2 saturation of 95%, and samples of mixed venous blood from the pulmonary artery showed an average O_2 saturation of 75%.

Question

Using the Fick data, calculate the resting cardiac output in liters/min.

The estimated body surface area of this patient was 2.9 m^2. What is the cardiac index? How does this compare with normal values?

Pressure data is shown in Figures 1 and 2 and the appropriate calibration curves are in Figure 3.

Measure LV pressure:

a) Systolic
b) Diastolic
c) End-diastolic (use high sensitivity scale)

Comment on significance of these values, particularly on the end-diastolic pressure. Can you relate this LVED pressure to the "operating point of this man's heart on the ventricular function curve discussed in class?

Measure the aortic pressure:

a) Systolic
b) Diastolic
c) Up-stroke rate in mmHg/sec (Normal 600-1000)

In the clinical observation of the pulse wave, the carotid artery in the neck is usually chosen for palpitation. Would you expect the slow-rising pulse of aortic stenosis to

be more apparent at a more peripheral location, such as the radial artery at the wrist? Why?

From the catheterization data, measure the pressure gradient (peak and mean), and then calculate the aortic valve area.

What is your clinical assessment and diagnosis of this patient?

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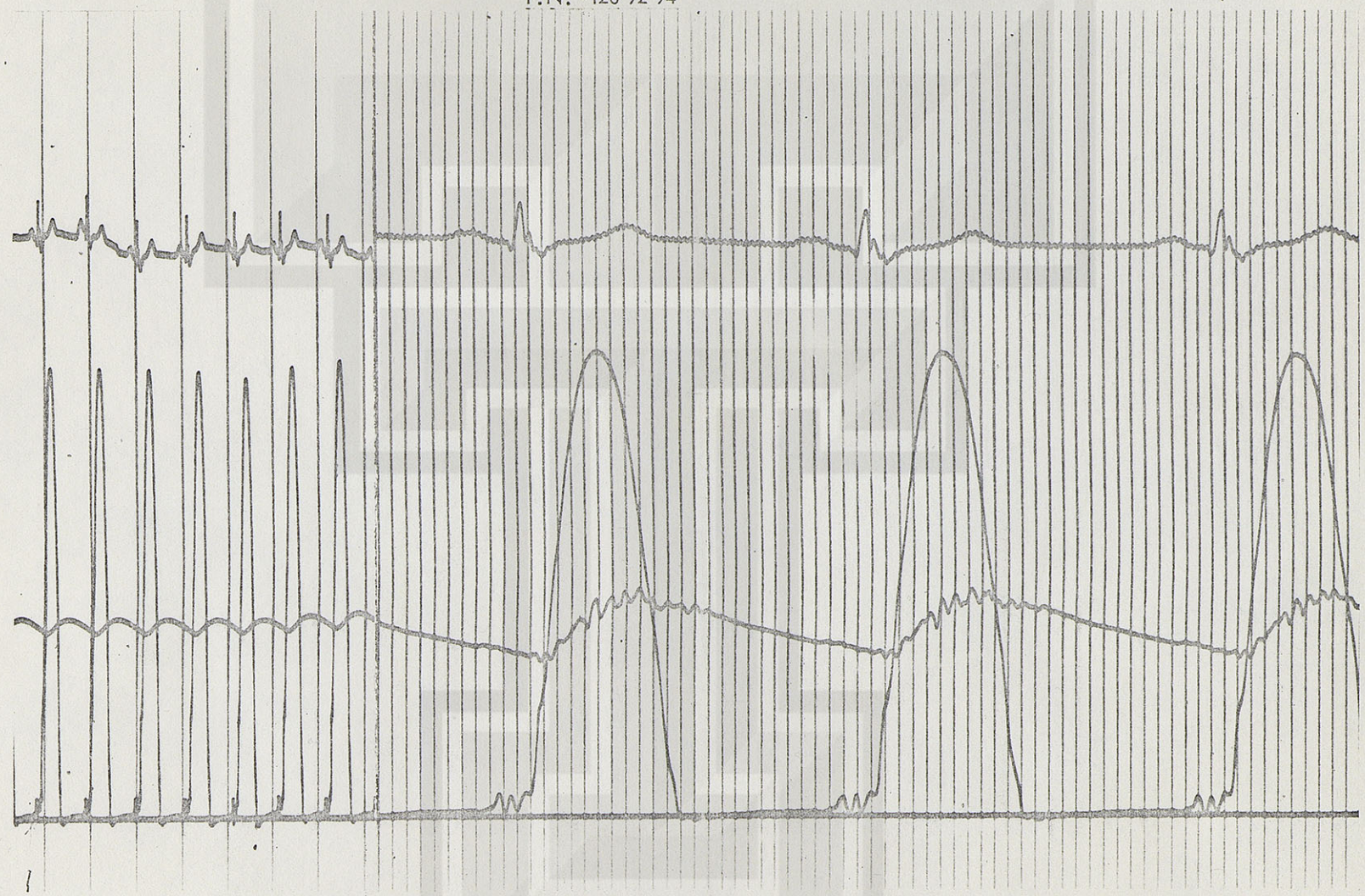

LV/Aorta Low Sensitivity
Time Line Interval = 0.04 second

FIGURE 1

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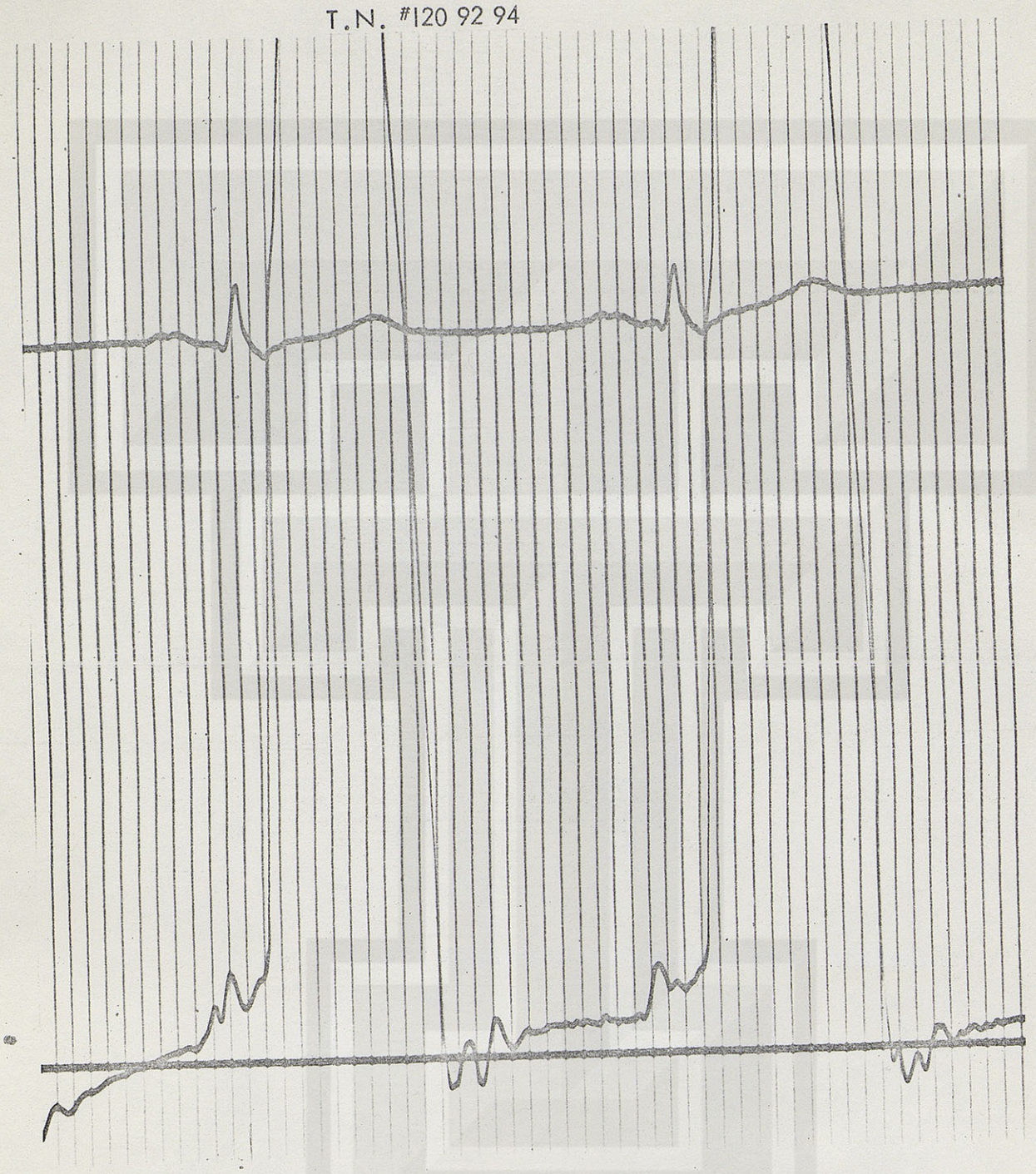

LV. High Sensitivity
Time Line Interval = 0.04 second

FIGURE 2

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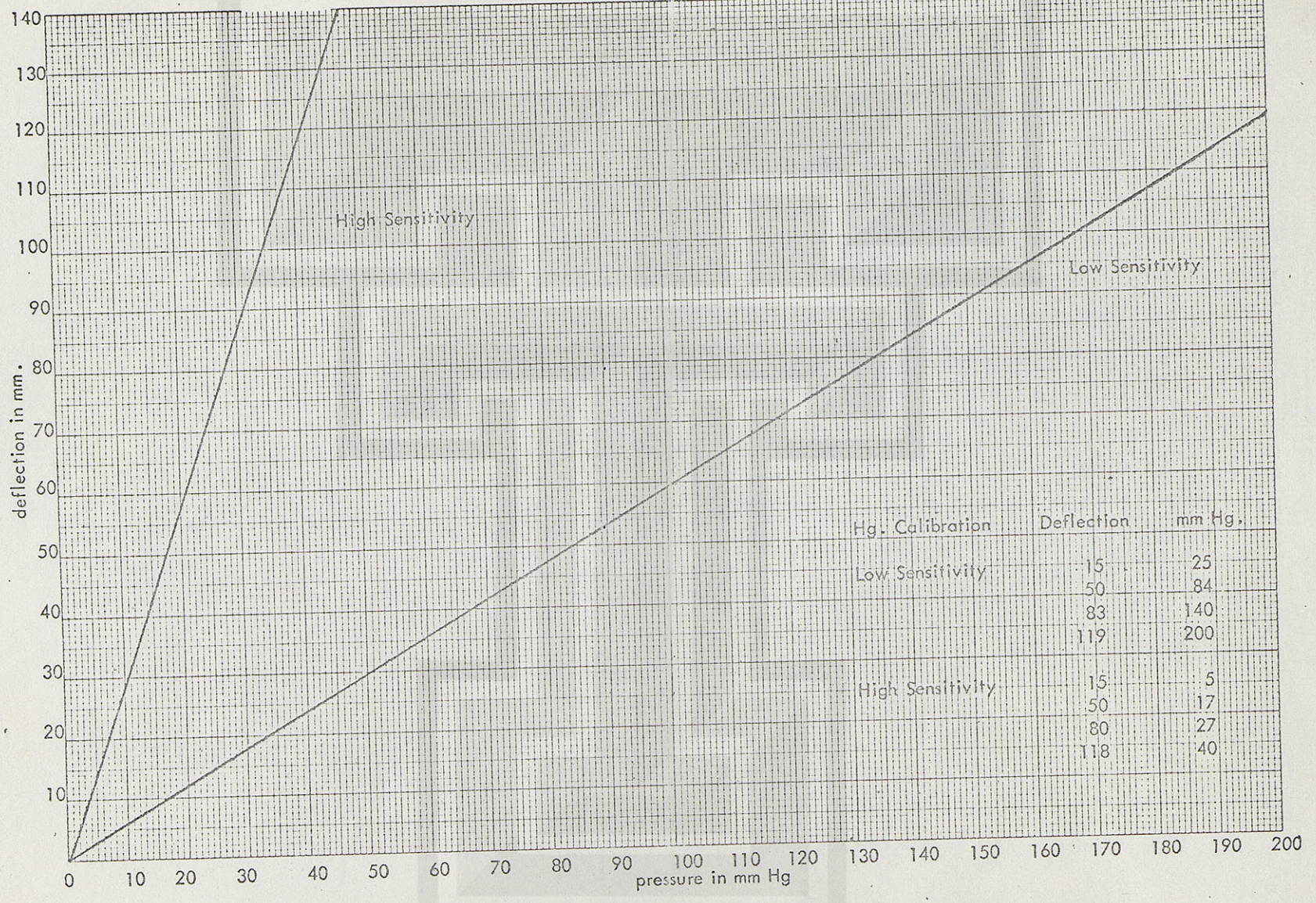
FIGURE 3



Hg. Calibration	Deflection	mm Hg.
Low Sensitivity	15	25
	50	84
	83	140
	119	200
High Sensitivity	15	5
	50	17
	80	27
	118	40

MASSACHUSETTS INSTITUTE OF TECHNOLOGY
Departments of Electrical and Mechanical Engineering
6.022J/2.792J: Quantitative Physiology: Organ Transport Systems

The Autonomic Nervous System

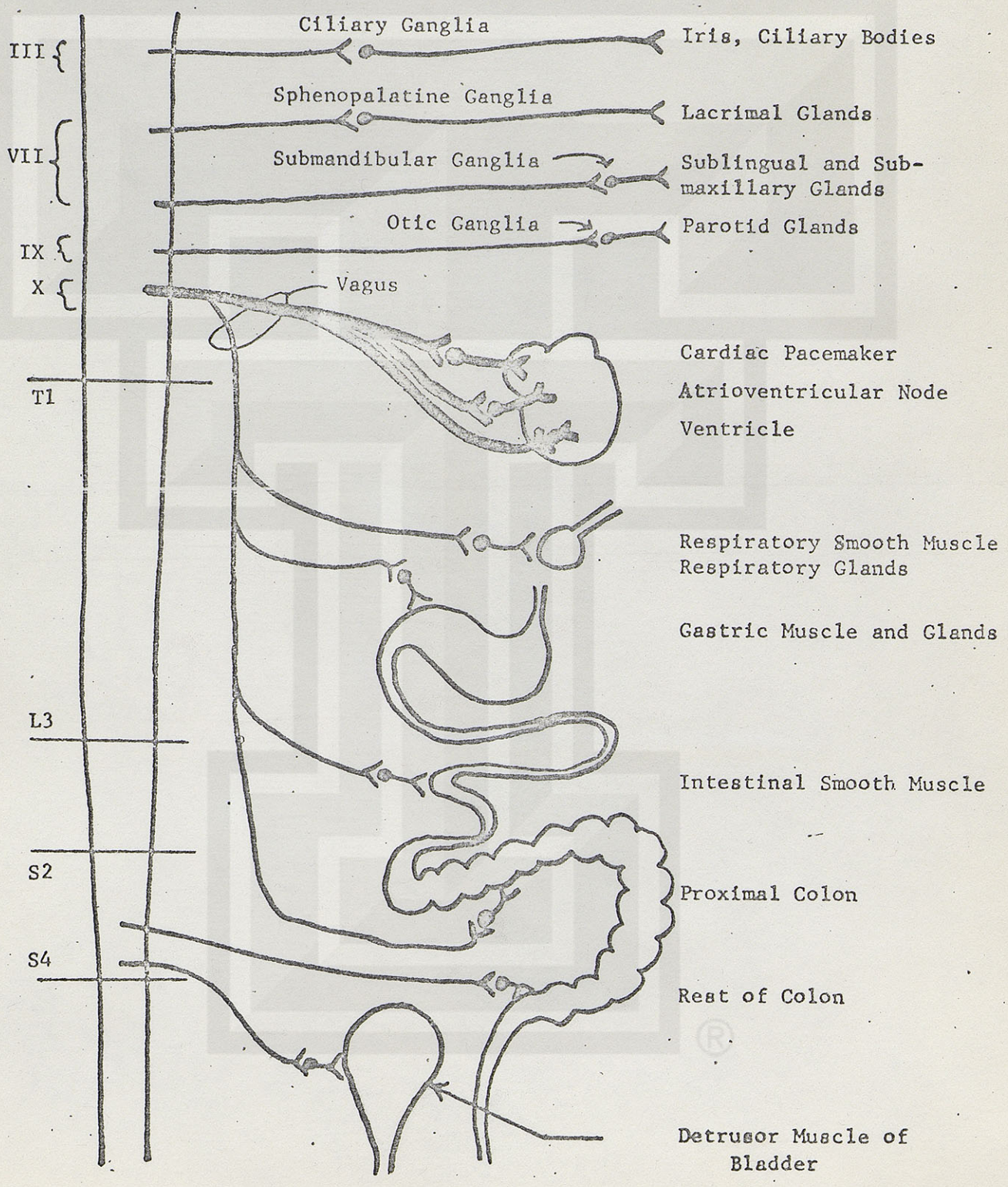
The autonomic nervous system coordinates and regulates many of the body's organ systems, and its operation is usually at an unconscious level. The autonomic nervous system can be divided into 1)afferent pathways, which carry information from organs to the brain, 2) centers in the central nervous system (spinal column or brainstem) which integrate autonomic responses, and 3) efferent pathways which carry information to the various organs. The efferent pathways have been subdivided into two sections--the sympathetic system and the parasympathetic systems. A rough generalization would assign the base-line negative functions of the body to the parasympathetic nervous system, and the mobilization of the body for emergency situations to the sympathetic system. Thus parasympathetic activity increases GI motility, gastric secretion, etc. Sympathetic stimulation leads to increase in heart rate, rise in arterial pressure, and in general opposes parasympathetic effects. In general many organs are innervated by both systems, and the net balance of nervous activity determines the behavior of the organ.

The following sketches outline the arrangement of the autonomic nervous system. They were prepared by Dr. Waud of Harvard Medical School.

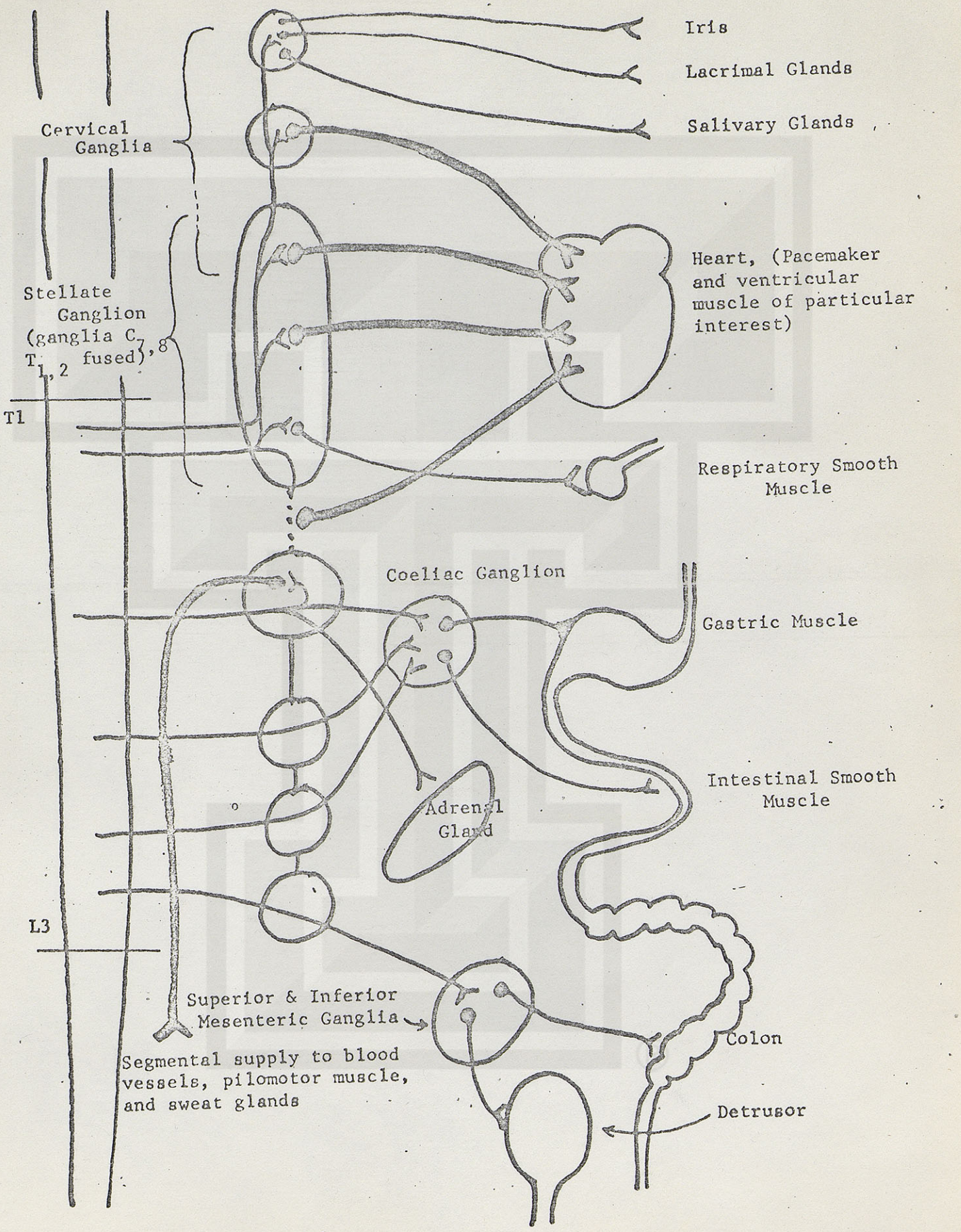
2. THE WIRING DIAGRAM

The parasympathetic and sympathetic outflows are shown schematically in the following two diagrams. The pathways of particular relevance to the cardiovascular system are shown bold face.

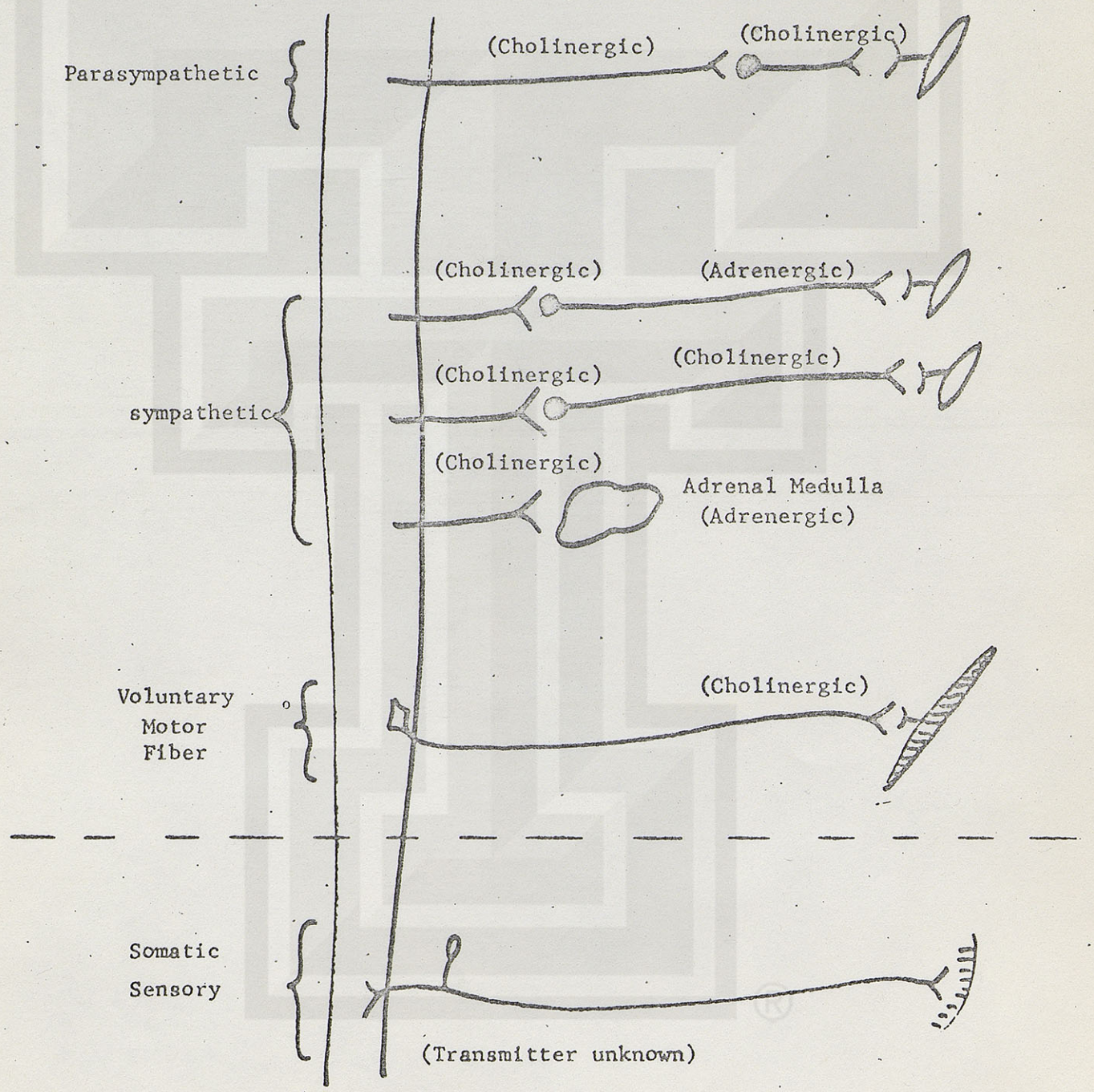
A. The parasympathetic outflow



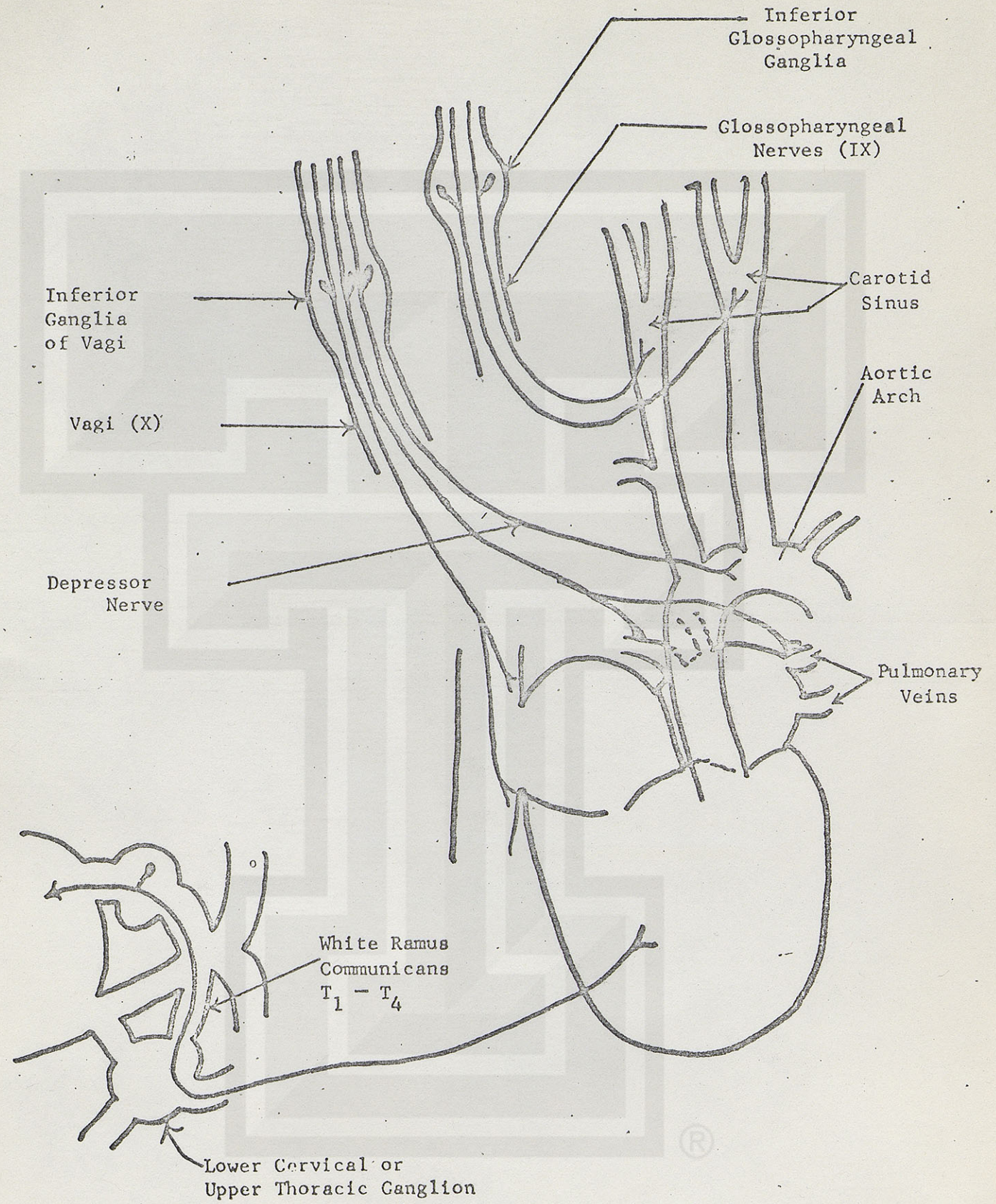
THE SYMPATHETIC OUTFLOW



Somatic sensory nerves are represented at the bottom of the diagram. This is done to emphasize that not all "ganglia" contain synapses. Ganglion just means a swelling, usually on a nerve trunk.



Afferent autonomic pathways of relevance to the cardiovascular system



MASSACHUSETTS INSTITUTE OF TECHNOLOGY

Departments of Electrical and Mechanical Engineering

6.022J/2.792J: Quantitative Physiology: Organ Transport Systems

MUSCLE PHYSIOLOGY AND VENTRICULAR FUNCTION

A. Structure of Muscle

1. Myocardium - composed of fibers (cells) approximately 10 x 50μ, branched, connected via tight junctions of low resistivity to form functional syncitium.

2. Contractile Machinery -

   a. Fibrils - run from one intercelated disc to the other - consists of sarcomeres in series.

   b. Sarcomere - basic contractile unit composed of 2 sets of myofilaments of constant length which interdigitate. Thick filaments of myosin, 1.5μ long; and thin filaments of actin 1.0μ long, arranged in double helix.

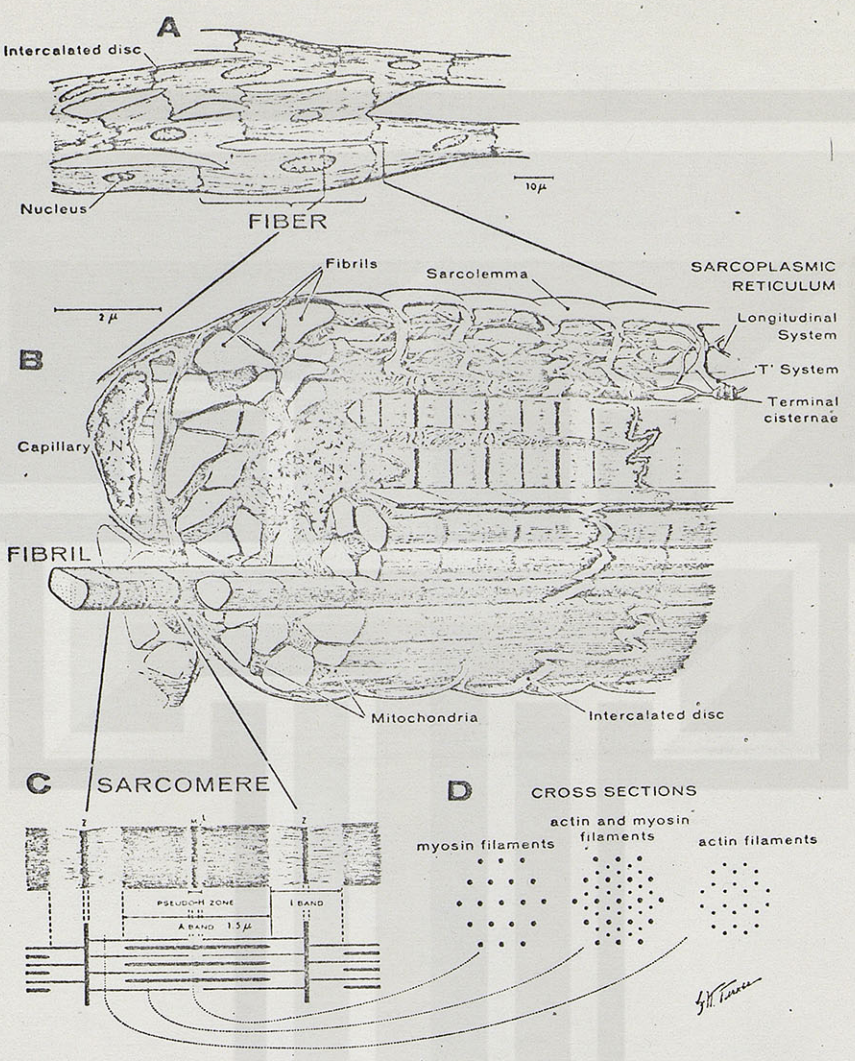
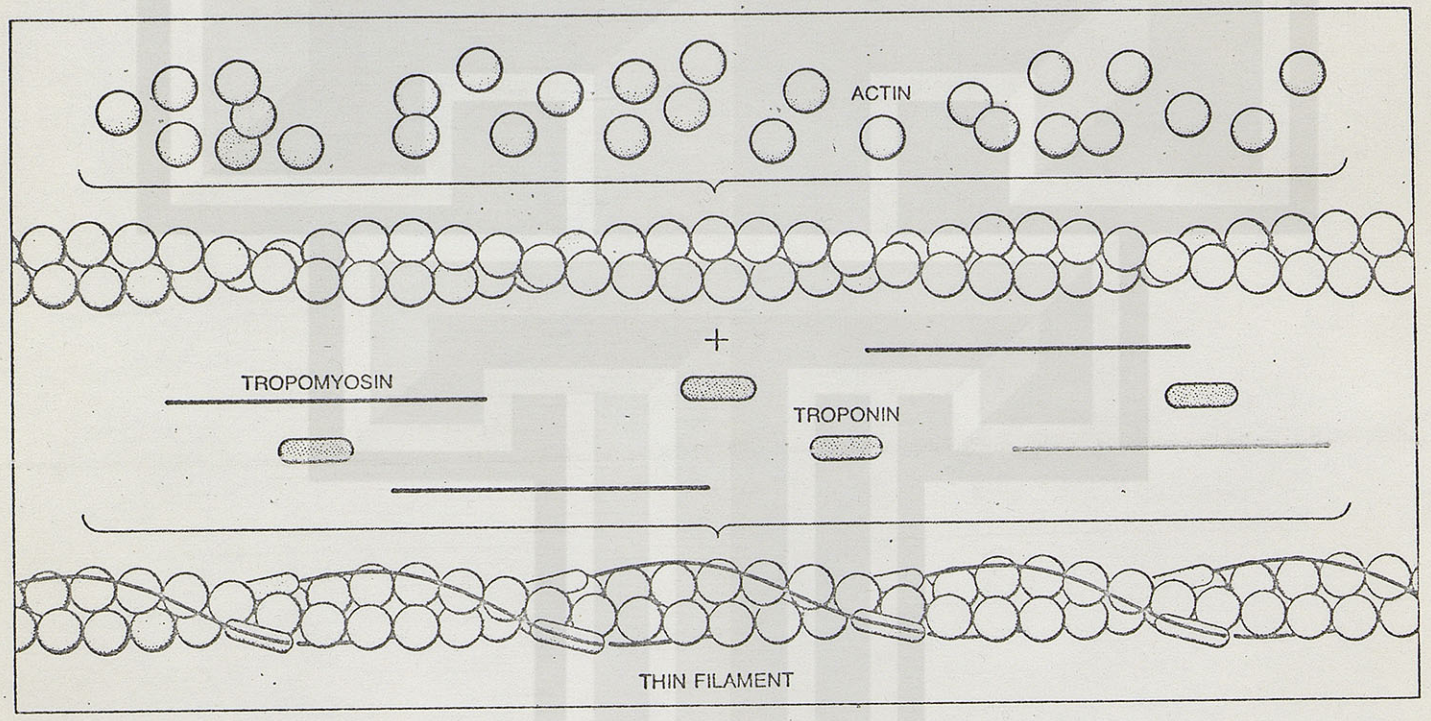


FIGURE 1. *The Microscopic Structure of Heart Muscle.*
A. *Myocardium as seen under the light microscope. Branching of fibers is evident, each containing a centrally located nucleus.* B. *A myocardial cell or fiber reconstructed from electron micrographs, showing the arrangement of the multiple parallel fibrils that compose the cell and of the serially connected sarcomeres that compose the fibrils. N = nucleus.* C. *An individual sarcomere from a myofibril. A diagrammatic representation of the arrangement of myofilaments which make up the sarcomere is shown below. Thick filaments, 1.5 μ in length, composed of myosin, form the A band, while thin filaments, 1.0 μ in length, composed primarily of actin, extend from the Z line through the I band into the A band, ending at the edges of the H zone. An H zone exists in the central area of the A band where thin filaments are absent. An overlapping of thick and thin filaments is seen only in the A band.* D. *Cross sections of the sarcomere, showing the specific lattice arrangements of the myofilaments. In the center of the sarcomere (left) only the thick (myosin) filaments arranged in a hexagonal array are seen. In the distal portions of the A band (center) both thick and thin (actin) filaments are found with each thick filament surrounded by 6 thin filaments. In the I band (right) only thin filaments are present.*

From Braunwald, Ross + Sonnenblick, 1968

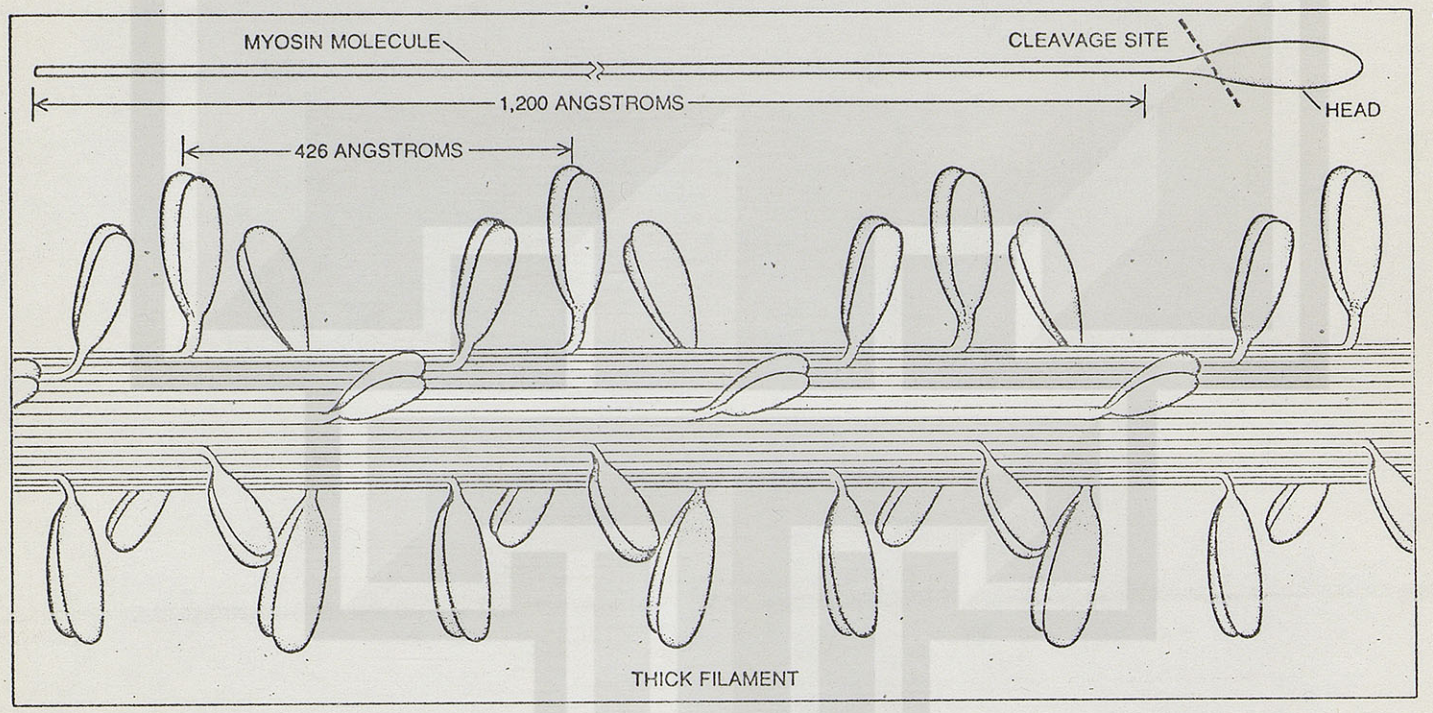
c. Tropomyosin - strands run in grooves of actin helix with a more globular troponin molecule located every 7 actins.

Figure 2



THIN FILAMENT is an assembly of actin, tropomyosin and troponin molecules. The actins, present in the largest amount, are small spheroidal molecules that are linked to form a double helix. Tropomyosin, a long, thin molecule, forms a continuous strand that sits on the string of actins alongside each groove of the double helix. A globular troponin molecule is affixed near one end of each tropomyosin. One tropomyosin extends over seven actin molecules and there are from 300 to 400 actins in the micron-long filament.

Figure 2 Continued



THICK FILAMENT is an assembly of myosin molecules, long rods with a double "head" at one end. The head has an active site where the chemical events involved in muscle contraction take place; purified heads are prepared for experiments by cleaving the molecule with an enzyme. In thick filaments myosins are bundled into a sheaf about 1.5 microns long with heads projecting in groups of three. Filament drawing includes pertinent aspects of a new model developed by John M. Squire of Imperial College London.

d. Role of tropomyosin and troponin as inhibitors of actin-myosin bonding. Role of Ca++ as an inhibitor of the troponin inhibitor.

3. The Activation System -

The cell membrane (sarcolemma) with transverse tubules (T-system).

The sarcoplasmic reticulum (SR), relation to T-System, role in Ca++ binding and release. In relaxed state, myoplasmic Ca++ is low (pCa>7.5), and Ca++ is stored in SR.

Activation: electrical depolarization→influx of Ca++ across cell membrane→Ca++ release from SR→increased Ca++ (pCa~ 6.0).
Relaxation: Ca++ bound by SR

B. Tension Development

Depends on number of interacting sites between thick and thin filaments {(a) myofilament overlap, and (b) Ca++ available.}

Ca++ released from SR→enters myofilment area and binds to troponin, inhibiting the inhibition of actin site. Myosin head binds with actin in presence of Mg++ and ATP to form "high energy bond". Conformational change of myosin head→displacement and later breaking of bridge. "Rigor" bonds between actin and myosin possible in absence of ATP. See Figure 3.

Figure 3

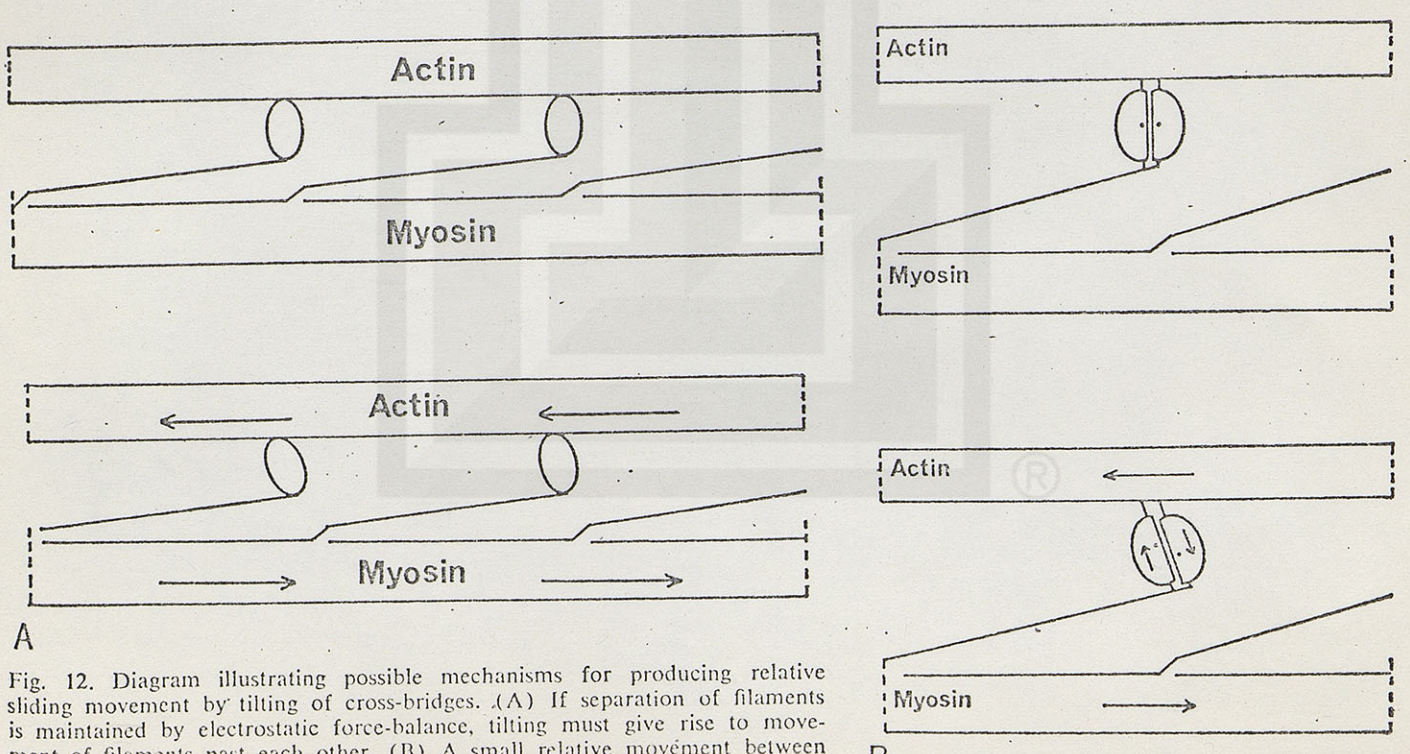


Fig. 12. Diagram illustrating possible mechanisms for producing relative sliding movement by tilting of cross-bridges. (A) If separation of filaments is maintained by electrostatic force-balance, tilting must give rise to movement of filaments past each other. (B) A small relative movement between two subunits of myosin could give rise to a large change in tilt, by the mechanism shown.

From H.E. Huxley, 1969

C. Relation of Structure to Function (Length-Tension)

The length-tension relationship is dependent upon sarcomere myofilament overlap.

Figure 4

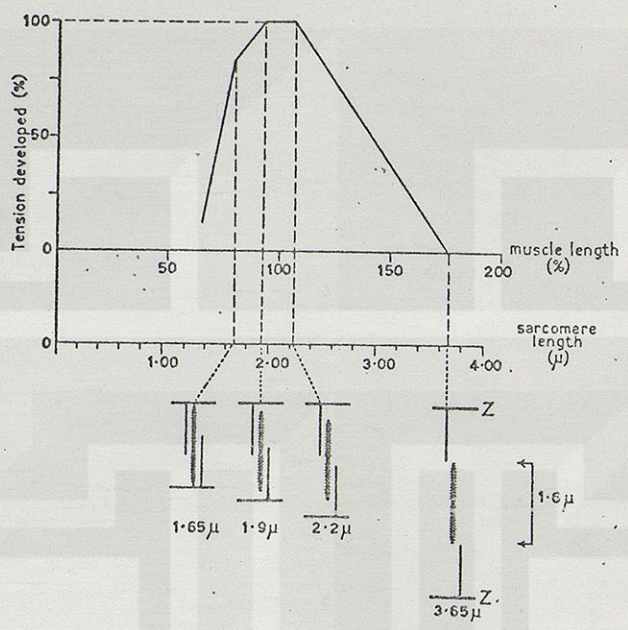


FIGURE 5. *Relation between Sarcomere Length and Relative Tension Development for Single Skeletal Muscle Fiber Preparations (Reproduced from Hanson and Lowy[36] with the Permission of the Publishers).*

The extent of thick and thin filament overlap in relation to developed tension is shown. Developed tension is constant between sarcomere lengths of 2.0 and 2.2 μ and decreases as sarcomeres shorten below 2.0 μ or elongate beyond 2.2 μ.

REFERENCES

1. Vandor, Sherman & Luciano, Human Physiology Ch.9, This chapter will provide a reasonably good introduction to the physiology of skeletal muscle.

2. Braunwald, E., Ross, J., and Sonnenblick, E., Mechanisms of Contraction of the Normal and Failing Heart, Little, Brown, 1968.
A very readable monograph covering the structure and function of heart muscle both at the ultra-structural and gross level.

3. Huxley, H.E. The mechanism of muscular contractions., Science, 164: 1356, 1969.
A classic paper describing the sliding filament hypothesis.

4. Langer, G., and Brady A. The Mammalian Myocardium, Wiley, 1974.

A collection of review articles on a variety of key issues including myocardial ultrastructure, cardiac energetics, the contractile proteins, myo-cardial mechanics, etc. An excellent up-to-date resource for the student who wishes to dig deeper.

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

Departments of Electrical and Mechanical Engineering

6.022J/2.792J: Quantitative Physiology: Organ Transport Systems

ANSWERS TO PROBLEM SET #2

Problem 1:

In the Hemodynamics notes (pp 32-35) when we derived the momentum equation (eq. 24, Newton's 2nd law for a nonviscous, incompressible fluid in a pipe, we neglected the nonlinear convective velocity term $\rho(\vec{v}\cdot\nabla)\vec{v}$. The justification for this omission was given as ' to a first approximation the axial vel. is small compared to the wave vel., i.e. the net flux of momentum into our control volume is assumed to be small compared to the time rate of change of momentum within the control volume. In this problem, we examine this approximation in more detail: first we obtain the momentum equation with the nonlinear acceleration term included, then we make a dimensional analysis argument as to the order of magnitude of this term, finally we examine some reasons why we might expect our estimate to be too high or too low. (Note: $Q \triangleq$ flow rate, $\dot{Q}$ in our previous notation)

a) 1) $\frac{\partial Q}{\partial x} + \frac{\partial A}{\partial t} = 0$

2) $\frac{\partial v}{\partial t} + v\frac{\partial v}{\partial x} = -\frac{1}{\rho}\frac{\partial p}{\partial x}$ } given

let $v(x,t) = \frac{Q(x,t)}{A(x,t)}$, now plug in eq. 2.

2') $\frac{\partial}{\partial t}\left(\frac{Q}{A}\right) + \frac{Q}{A}\frac{\partial}{\partial x}\left(\frac{Q}{A}\right) = -\frac{1}{\rho}\frac{\partial P}{\partial x}$

but i) $\frac{\partial}{\partial t}\left(\frac{Q}{A}\right) = \frac{A\frac{\partial Q}{\partial t} - Q\frac{\partial A}{\partial t}}{A^2} = \frac{1}{A}\frac{\partial Q}{\partial t} - \frac{Q}{A^2}\frac{\partial A}{\partial t}$

ii) $\frac{\partial}{\partial x}\left(\frac{Q}{A}\right) = \frac{1}{A}\frac{\partial Q}{\partial x} - \frac{Q}{A^2}\frac{\partial A}{\partial x}$

substituting i) and ii) into 2'), we have

2'') $\frac{1}{A}\left\{\frac{\partial Q}{\partial t} - \frac{Q}{A}\boxed{\frac{\partial A}{\partial t}} + \frac{Q}{A}\frac{\partial Q}{\partial x} - \frac{Q^2}{A^2}\frac{\partial A}{\partial x}\right\} = -\frac{1}{\rho}\frac{\partial P}{\partial x}$

multiplying both sides by A, and using the continuity eq.(1) to evaluate the boxed term:

$$\frac{\partial Q}{\partial t} + \underbrace{\frac{Q}{A}\frac{\partial Q}{\partial x} + \frac{Q}{A}\frac{\partial Q}{\partial x}}_{2\frac{Q}{A}\frac{\partial Q}{\partial x}} - \left(\frac{Q}{A}\right)^2\frac{\partial A}{\partial x} = -\frac{A}{\rho}\frac{\partial P}{\partial x}$$

Finally noting

$$\frac{\partial}{\partial x}\left(\frac{Q^2}{A}\right) = 2\frac{Q}{A}\frac{\partial Q}{\partial x} - \left(\frac{Q}{A}\right)^2\frac{\partial A}{\partial x},$$

we have our desired result

3) $$\boxed{\frac{\partial Q}{\partial t} + \frac{\partial}{\partial x}\left(\frac{Q^2}{A}\right) = -\frac{A}{\rho}\frac{\partial P}{\partial x}}.$$

1. b) While one approach might be in trying to bound our nonlinear term in eq. 3. through estimating Q/A in eq. 3 with the nonlinear term omitted, and then evaluating R using our linear estimate, we shall 1st try a direct dimensional analysis.

i) $\frac{\partial}{\partial x}\left(\frac{Q^2}{A}\right) \simeq \frac{\bar{Q}^2}{\bar{A}\,\Delta L}$, where $\bar{Q}$ represents a "spatial averaged" flow rate, $\bar{A}$ is an average area, ΔL is the length of the aorta.

ii) $\frac{\partial Q}{\partial t} \simeq \frac{\langle Q \rangle}{\Delta t}$, where $\langle Q \rangle$ is a "time averaged" flow rate, $\Delta t \simeq 1$ sec. is a heart period.

The above approximations are valid in the sense that if we double Q, we expect i) to increase by a factor of 4, and ii) to increase by a factor of 2. Doubling A should half i), and likewise for the other variables. Now we assume $\bar{Q} \simeq \langle Q \rangle$, and consider the ratio R for $\Delta L = 40\text{cm}$, $A \simeq 6\text{cm}^2$ $\Delta t \simeq 1\text{sec}$, $\bar{Q} = 80\ \text{cc/sec}$.

$$R = \frac{\frac{\partial}{\partial x}\left(\frac{Q^2}{A}\right)}{\frac{\partial Q}{\partial t}} \simeq \frac{\Delta t\,\bar{Q}}{\bar{A}\,\Delta L} = \frac{1(80)}{6(40)} = \frac{1}{3}$$

So our 2nd term in eq. 3. is of the same order of magnitude as the 1st term. Thus $\frac{\partial}{\partial x}\left(\frac{Q^2}{A}\right)$ can't be neglected as extremely small.

1.c The measured ratio R is some factor of 10 smaller than the value we computed in part b. In part b we were averaging over the whole length of the aorta and over a whole period. At, locally things might be somewhat different. In particular, Q is not steady w.r.t. time, we have a high Q when the valve opens, so a smaller Δt, & thus a smaller R, might be more appropiate for our average of $\frac{\partial Q}{\partial t}$, Our Linear estimate for $\frac{\partial}{\partial x}\left(\frac{Q^2}{A}\right)$ has assumed we go from some value $\frac{\bar{Q}^2}{A}$ at x=0 to 0 at x=L. but we know $\frac{\bar{Q}^2}{A} \neq 0$ at the distal end, and using $\bar{Q} = 80 cc/sec$ might be too high a value for the initial value.

Problem 2:

a) given $\begin{cases} \tau_0 \simeq \mu \frac{v_0}{\delta_0} \\ \tau_1 \simeq \mu \frac{v_1}{\delta_1} \end{cases}$,

by continuity of mass

$$v_0 R_0^2 = 2 v_1 R_1^2$$

$$\frac{v_0}{v_1} = 2\left(\frac{R_1}{R_0}\right)^2$$

so $$K = \frac{\tau_0}{\tau_1} = \frac{v_0}{v_1}\frac{\delta_1}{\delta_0} = 2\left(\frac{R_1}{R_0}\right)^2 \frac{\delta_1}{\delta_0}$$

but $\delta_0 = \delta_1$, since δ is given as independent of radius.

Thus $\boxed{K = 2\left(\frac{R_1}{R_0}\right)^2}$, and

$K \geq 1$ if $R_1 \geq \frac{1}{\sqrt{2}} R_0$,

In human arteries, as we examine in problem 6,

$R_1 \simeq \frac{1}{2.4} R_0$, so we expect $K > 1$

b) For Poiseuille flow

$$u(r) = \frac{2Q}{\pi R^2}\left(1 - \frac{r^2}{R^2}\right)$$

$$\left.\frac{\partial u(r)}{\partial r}\right|_{r=R} = \left.\frac{2Q}{\pi R^2}\left(-\frac{2r}{R^2}\right)\right|_{r=R} = -\frac{4Q}{\pi R^3}$$

thus

$$K = \frac{\tau_0}{\tau_1} = \frac{\mu\left(\frac{\partial u}{\partial r}\Big|_{R_0}\right)}{\mu\left(\frac{\partial u}{\partial r}\Big|_{R_1}\right)} = \frac{\mu \frac{-4Q_0}{\pi R_0^3}}{\mu \frac{-4Q_1}{\pi R_1^3}} = \frac{Q_0}{Q_1}\left(\frac{R_1}{R_0}\right)^3$$

but $Q_0 = 2Q_1$

$$\therefore \boxed{K = 2\left(\frac{R_1}{R_0}\right)^3}$$

$K = 1$ for $R_1 \simeq \frac{1}{2^{.33}} R_0$, a bigger radius than above.

Problem 3: given: $A = C_u (p - p_{ref})$

a) $$\int_0^L \left(\frac{\partial Q}{\partial t} + \frac{\partial}{\partial z}\left(\frac{Q^2}{A}\right)\right) dz = -\frac{A}{\rho}\int_0^L \frac{\partial p}{\partial z}\, dz$$

$$L\left(\overline{\frac{\partial Q}{\partial t}}\right) + \left(\frac{Q^2}{A}\right)_L - \left(\frac{Q^2}{A}\right)_0 = -\frac{C_u}{\rho}\int_{p_0}^{p_L} (p - p_{ref.})\, dp$$

but

$$\int_{p_0}^{p_L} (p - p_{ref})\, dp = \frac{p_L^2}{2} - p_L p_{ref.} - \frac{p_0^2}{2} + p_0 p_{ref.}$$

$$= -\frac{(p_L^2 - p_0^2)}{2} + p_L^2 - p_0^2 - p_L p_{ref} + p_0 p_{ref.}$$

$$= -\frac{(p_L^2 - p_0^2)}{2} + p_L(p_L - p_{ref}) - p_0(p_0 - p_{ref})$$

$$= -\frac{(p_L^2 - p_0^2)}{2} + p_L \frac{A_L}{C_u} - p_0 \frac{A_0}{C_u}$$

$$= -1\left\{ \frac{A_0}{A_0}\frac{(p_L^2 - p_0^2)}{2} + \frac{A_0}{C_u}\left(p_0 - p_L\left(\frac{A_L}{A_0}\right)\right)\right\}$$

thus

$$-\frac{C_u}{\rho}\int_{p_0}^{p_L} (p - p_{ref})\, dp = \frac{A_0}{\rho}\left\{ \frac{C_u}{A_0}\frac{(p_L^2 - p_0^2)}{2} + p_0 - p_L\left(\frac{A_L}{A_0}\right)\right\},$$

whence

$$\boxed{(1)\quad p_0 - p_L\left(\frac{A_L}{A_0}\right) = \frac{\rho L}{A_0}\left[\left(\overline{\frac{\partial Q}{\partial t}}\right) + \frac{1}{L}\left(\frac{Q^2}{A}\right)_L - \frac{1}{L}\left(\frac{Q^2}{A}\right)_0\right] - \frac{C_u}{A_0}\frac{(p_L^2 - p_0^2)}{2}}$$

this differs from the expression given in the problem by the boxed term.

b) Assume $A_0 \cong A_1$, $Q \cong$ const., we want to show that $p_0 - p_L = (\text{const.})\left(\overline{\frac{\partial Q}{\partial t}}\right)$ in analogy to ~~$i = \frac{V}{\mathcal{L}}$~~

$$V = \mathcal{L}\frac{di}{dt}$$

$A_0 \simeq A_1$, $Q \simeq$ const $\Rightarrow$

$$\frac{1}{L}\left(\frac{Q^2}{A}\right)_L \simeq \frac{1}{L}\left(\frac{Q^2}{A}\right)_0 \quad , \quad \frac{A_L}{A_0} \simeq 1 \quad ;$$

also if the boxed term, was not included.

$$\frac{p_L - p_0}{L-0} \simeq \frac{\partial p}{\partial x} \quad ; \quad \frac{1}{A_0}\left(\frac{\partial Q}{\partial t}\right) \simeq \frac{\partial v}{\partial t}$$

which would give us $\frac{\partial p}{\partial x} = -\rho \frac{\partial v}{\partial t}$, the form of the desired result, we now show that with the boxed term, we get a solution of the same form but with a ρ' to be determined.

Eq. 1 (for $A_0 \simeq A_1$, $Q \simeq$ const.) becomes.

$$p_0 - p_L = \frac{\rho L}{A_0}\left[\left(\frac{\partial Q}{\partial t}\right)\right] - \frac{C_u}{A_0}(p_L - p_0)\frac{(p_L + p_0)}{2}$$

$$= \frac{\frac{\rho L}{A_0}\left(\frac{\partial Q}{\partial t}\right)}{1 + \frac{C_u}{A_0}\left(\frac{p_L + p_0}{2}\right)} = \underbrace{\frac{\rho}{1 + \frac{C_u}{A_0}\left(\frac{p_L + p_0}{2}\right)}}_{\rho'} \frac{L}{A_0}\left(\frac{\partial Q}{\partial t}\right)$$

$$\frac{p_L - p_0}{L} = -\rho' \frac{1}{A_0}\left(\frac{\partial Q}{\partial t}\right)$$, which is approximately at least for quasi-linear changes.

$$\frac{\partial p}{\partial x} = -\rho' \frac{\partial v}{\partial t}$$

Now to show ρ' is roughly a constant. The crux of the argument lies in the fact that p_L and p_0 represent small deviations from a relatively large p_{ref}. So $\frac{p_L + p_0}{2}$ is about $\frac{2p_{ref}}{2} \simeq p_{ref}$.

Let $A(x) = A_0 + \alpha x$ with αx small compared to A_0, since $A_L \simeq A_0$.

$$\left.\begin{aligned} \text{Thus } A_L &\simeq A_0 + \alpha L = C_u(p_L - p_{ref.}) \\ A_0 &= C_u(p_0 - p_{ref}) \end{aligned}\right\} \text{ Adding}$$

$$2A_0 + \alpha L = C_u(p_0 + p_L) - 2C_u p_{ref.}$$

So solving for $\frac{C_U}{2A_0}(p_0+p_L)$,

$$\frac{C_U}{A_0}\,p_{ref.} + 1 + \frac{\alpha L}{2A_0} = \frac{C_U}{2A_0}(p_0+p_L).$$

Now by our original assumption $\frac{\alpha L}{A_0}$ is small compared to 1 so we may neglect this term. C_U and A_0 are constants in this part of the problem, so

$$\rho' = \frac{\rho}{1+\frac{C_U}{A_0}\left(\frac{p_L+p_0}{2}\right)} \simeq \frac{\rho}{1+1+\frac{C_U}{A_0}p_{ref.}} = \frac{\rho}{2+\frac{C_U}{A_0}p_{ref.}}$$

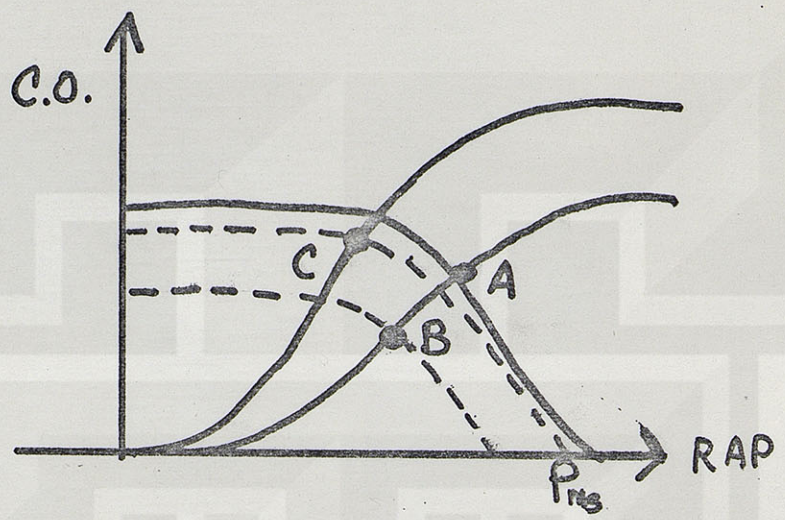
$$= \text{const.}$$

so $\frac{\partial p}{\partial x} = -\rho'\frac{\partial v}{\partial t}$ as desired.

Note: we have already assumed A_0 was roughly const. with respect to time, anyway, when we said.

$\frac{1}{A_0}\left(\frac{\partial Q}{\partial t}\right) \simeq \frac{\partial v}{\partial t}$, so no new assumptions were required.

4. Hemorrhage→drop in blood volume→drop in Pms initially. Operating point A→B. (Figure 2.)

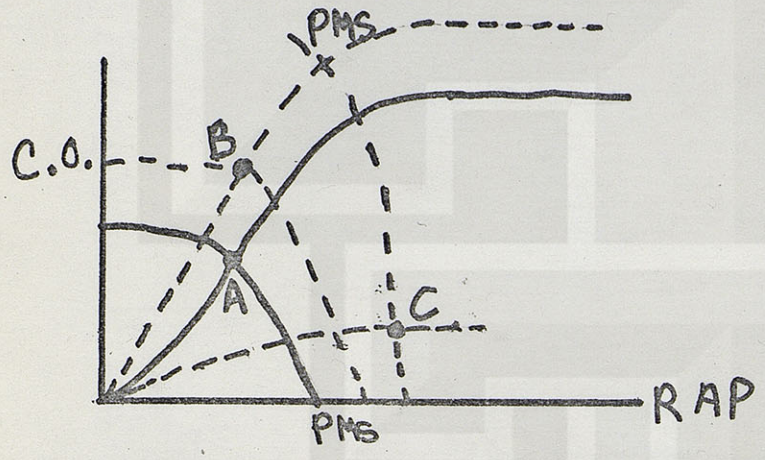


The drop in pressure→baroreceptor reflex→increased cardiac contractility, ↑heart rate causing some restoration of Pms. Operating point moves to C. In addition, other control loops cause increased fluid transfer from interstitial fluid to intravascular compartment, and later actual retention of fluid by the kidneys. Furthermore, the liver will replenish serum protein, and the marrow will increase its production of blood cells.

5. Asphyxia

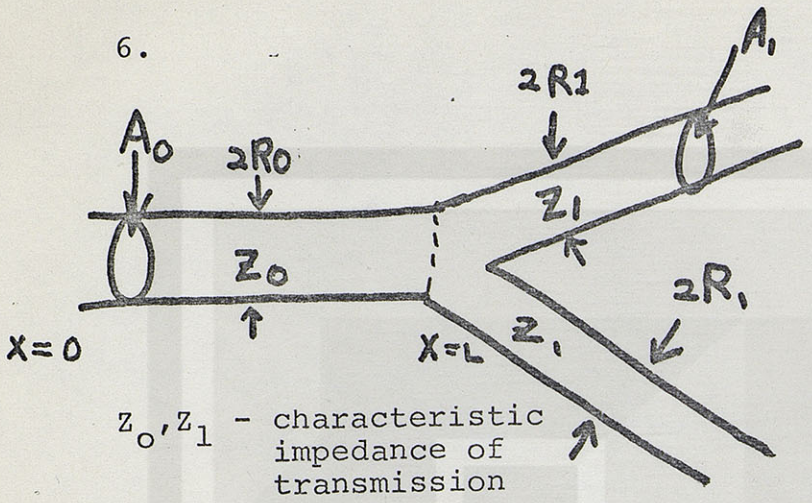
Initially brain and tissue hypoxia cause vasodilation throughout, and the resistance to venous return decreases, causing a shift in the venous return curve slope. In addition there will be sympathetic stimulation causing a shift in the C.O. curve, and an increase in Pms.

The original operating point would move from A B.



As hypoxia worsens, vasodilation increases, but severe damage is done to the contraction of the heart. Hence the VR curve continues to change more, but the C.O. curve drops way down. Hence the late operating point would be C.

6.



Z_o, Z_1 - characteristic impedance of transmission line.

Assume

1) modulus of elasticity doesn't change across bifurcations.

2) Compliance is

$$C_u \simeq \frac{2\pi r^3}{E_k}$$

We want to find the relationship between R_o and R_1 such that there is no reflection at X = L. Treating the vessels as lossless transmission lines, we know insofar as the input end in conerned, a <u>finite</u> line terminated in its characteristic impedance behaves as if it wereinfinitely long, in particular we expect no reflections. From class notes, we know the reflection coef. Γ is:

$$\Gamma = \frac{Z_L - Z_o}{Z_L + Z_o} \quad \text{(eq.33, Feb.14notes) w/} Z_L = \text{impedance at termination}$$

so if $Z_L = Z_o$, we have no reflections. Also from notes.

$$Z_o = \sqrt{\frac{L_u}{C_u}} = \sqrt{\frac{\rho}{A_o C_u}} = \sqrt{\frac{\rho}{(\pi R_o^2)\,\frac{2\pi R_o^3}{E_k}}} = C_1 R_o^{-5/2}$$

$$Z_1 = C_1 R_1^{-\frac{5}{2}}$$

and $$Z_L = Z_1 \| Z_1 = \frac{Z_1^2}{Z_1 + Z_1} = \frac{Z_1}{2},$$

Thus we have as our constraint $Z_o = \frac{Z_1}{2}$ or $\frac{Z_o}{Z_1} = \frac{1}{2}$

$$\text{so} \left(\frac{R_1}{R_o}\right)^{\frac{5}{2}} = \frac{1}{2} \Rightarrow R_1 = \frac{1}{2^{\frac{2}{5}}} R_o$$

$$2^{-.4} = \text{antilog } (-.4 \log_{10} 2)$$
$$= \text{antilog } (-.1204)$$
$$= .758$$

$$R_1 = .758\ R_o$$
$$3/4\ R_o$$

Experimentally, we find that the sum of the lumen <u>areas</u> of the daughter vessels to be about 1.2 times that of the parent vessel.

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6.022J/2.792J: Quantitative Physiology: Organ Transport Systems

CLINICAL HEMODYNAMICS

MASSACHUSETTS INSTITUTE OF TECHNOLOGY
Departments of Electrical and Mechanical Engineering
6.022J/2.792J: Quantitative Physiology: Organ Tranport Systems

CIRCULATORY MEASUREMENTS

Indicator Dilution Techniques

Indicator dilution techniques are frequently employed clinically to measure cardiac output. The types of indicators which may be used include oxygen and other gases, heat, electrical conductivity, dyes, etc. The rationale for the indicator methods is as follows:

A. Constant Infusion Rates

Consider a non-recirculating fluid flowing in a conduit at a flow rate Q ml/min (see Figure 1). An indicator is introduced at point A at a constant rate of $\Delta I/\Delta t$ mg/min. We will assume that the addition of the indicator does not significantly change the volume of the fluid. [We do not have to make this assumption if it is unreasonable in a given case, see problem below.] The concentration of the indicator upstream from point A is c_1, and downstream it is c_2. If we assume steady-state conditions, the net increase in the amount of indicator in the fluid in a time Δt must exactly equal the amount of indicator added during that period. The volume of fluid passing point A in Δt would be $Q\Delta t$, and hence the increase in

the amount of indicator would be $(c_2 - c_1)Q\Delta t$. In the time Δt, an amount of ΔI of indicator was added, hence

$$\Delta I = (c_2 - c_1)Q\Delta t$$

Rearranging, and solving for Q we have

$$Q = \frac{\Delta I/\Delta t}{c_2 - c_1} \qquad (1)$$

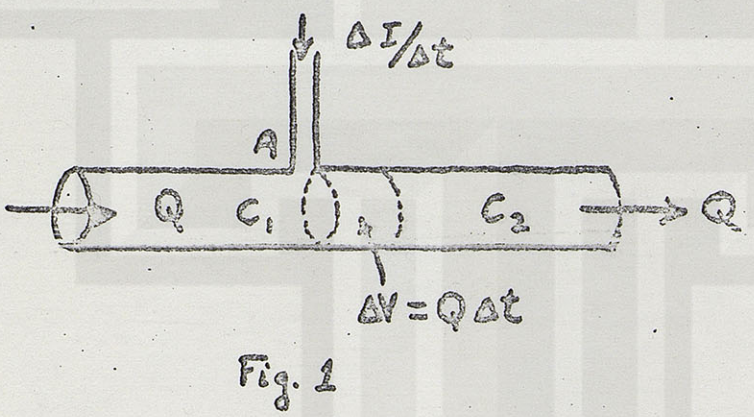


Fig. 1

In practical cases, one generally samples the concentration of the indicator c(t) at a point downstream from the additon of the indicator. If the rate of indicator injection is a step function, then c(t) will appears as shown in Figure 2. It will be c_1 at first, but then will rise to its final value c_2. The flow rate may be derived from equation 1. The cardiovascular system, however, is a <u>circulation</u>, hence the arterial blood

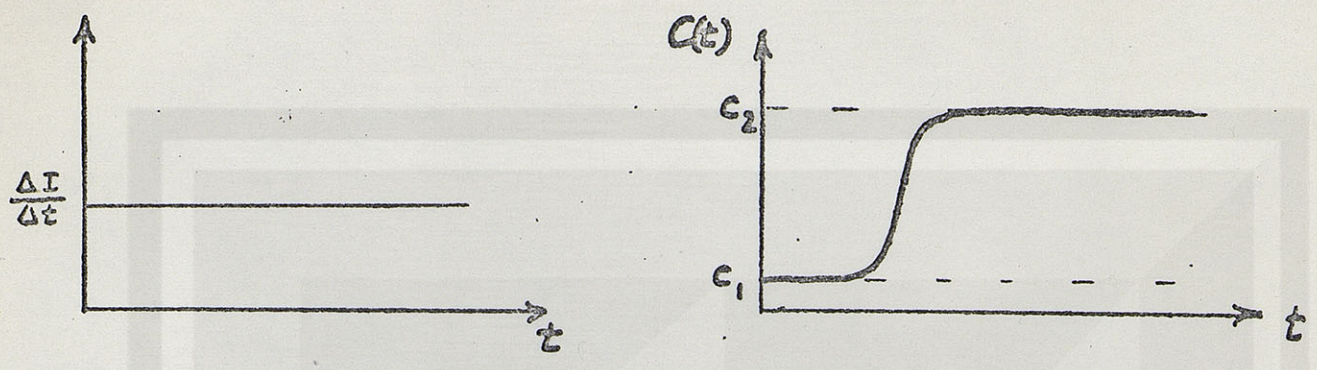


Fig. 2

eventually recirculates, and the indicator concentration curve will no longer remain at a stable plateau value of c_2 but will eventually begin to increase (see Figure 3).

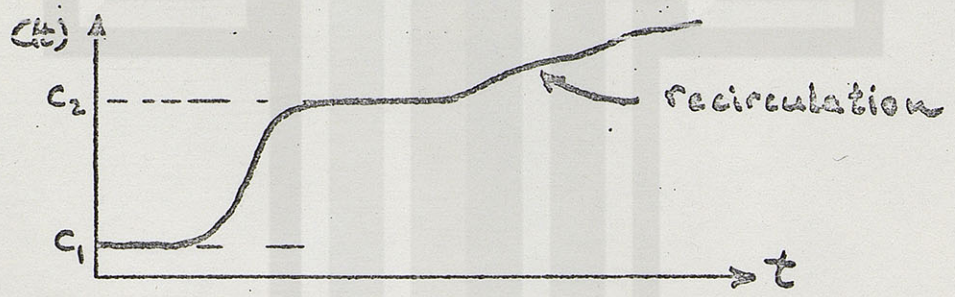


Fig. 3

Generally, one can identify the plateau at c_2, however, and this is the value to use

B. Impulse or Bolus Injection Methods

It is often desirable from the point of view of convenience to inject all the indicator substance suddenly in a negligibly short time. Consider Figure 4 which illustrates the sudden injection method. At time t = 0, a quantity of indicator I mg is injected suddenly into the stream of fluid flowing at a

flow rate of Q ml/min. At a point downstream, the indicator concentration c(t) is monitored. The general shape of c(t)

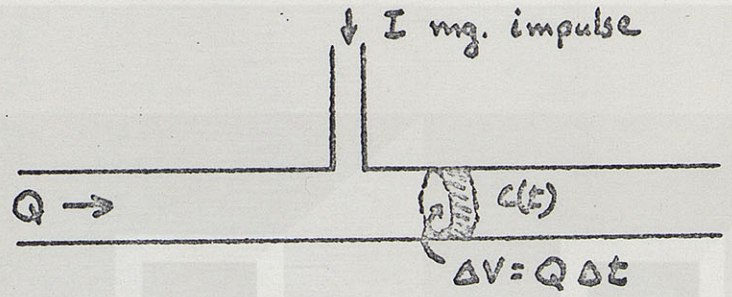


Fig. 4

assuming no recirculation is shown in Figure 5. Since all the indicator added must eventually pass the sampling point we have

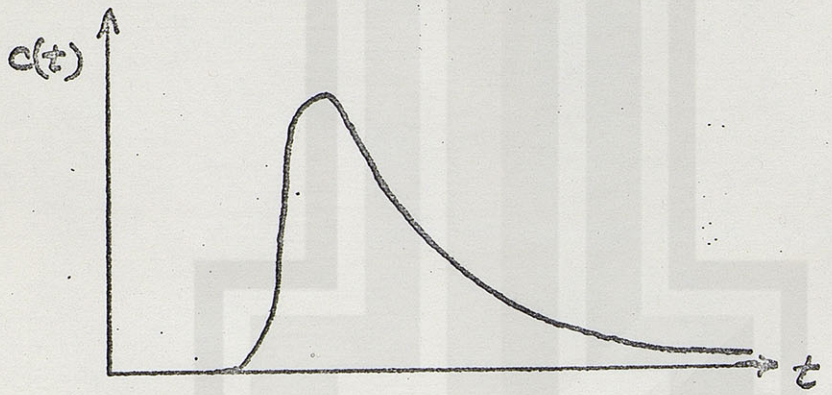


Figure 5

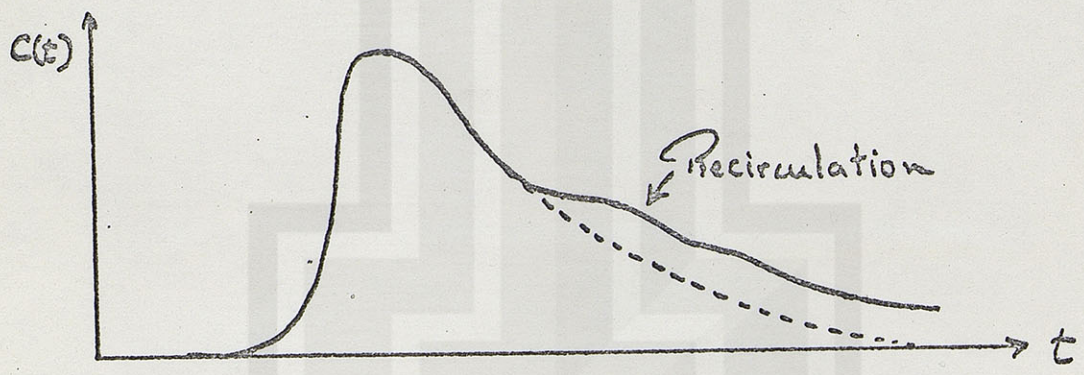
$$I = \int_0^\infty c(t)\, Q dt$$

Since Q is steady, we have by rearranging

$$Q = \frac{I}{\int_0^\infty c(t)\,dt} \qquad (2)$$

This equation is the one to use in cases of sudden dye injection, and is the one most commonly used clinically.

How does recirculation affect the shape of the c(t) curve, and how does one use equation 2 in the presence of recirculation? First of all, recirculation will introduce extra humps on the tail of the curve of Figure 5 and also the tail will never get to zero as $t \to \infty$ (Figure 6). It turns out that the tail of the curve in Figure 5 is exponential in the absence of recirculation.



In the presence of recirculation, one must extrapolate the tail of the curve to zero by fitting it to the best possible exponential. (The fitting is done before the recirculation effects appear.)

One way to do the curve-fitting is to use semi-logarithmic paper, ~~(See codes on "Basic Terms").~~ The area may then be calculated. The process of area calculation may be done by square counting, planimetry, etc.

DISCHARGE SUMMARY

Admitted: 7-20-64 Age: 15 7/12
Discharged: 8-8-64

DISCHARGE SUMMARY

This was the first CHMC admission for this 15 7/12-year-old white male.

CHIEF COMPLAINT: Heart disease.

PRESENT ILLNESS: There was never any question of heart disease in this boy until four months prior to admission when a heart murmur was found on a routine school physical examination. He was the product of a full term pregnancy and delivery. His growth and development was perfectly normal, and he was entirely asymptomatic. He is very active playing baseball and other sports. He admits to some tiredness if he runs a great deal. There is no history of syncope or chest pain. Recently he was seen in the Clinic here and felt to have severe aortic stenosis and, therefore, was admitted for catheterization and possible surgery.

PAST HISTORY: There is no history of rheumatic fever, severe tonsillitis, chorea, joint symptoms, or frequent sore throats. At age 11, four years ago, the patient was hospitalized for a bleeding duodenal ulcer and at this time he had transfusions, bed rest, and a medical regimen with complete remission of symptoms. There has been no recurrence of melena or ulcer symptoms since.

FAMILY HISTORY: His father died when he was very young of heart disease. There is no other known heart disease in the family. Family history is otherwise noncontributory.

PHYSICAL EXAMINATION: The patient appeared as a well-developed, well-nourished, white male in no distress. Blood pressure 90/60, pulse 90 and regular, respirations 20, temperature 98.6° P.O. Skin: Good hydration and color without clubbing, edema, or cyanosis. Head: Normocephalic. Eyes, ears, nose, and throat: Within normal limits. Chest: Clear to percussion and auscultation with good diaphragmatic excursion. Heart: Point of maximum impulse in the fifth intercostal space in the mid-clavicular line. The rhythm was regular. There was a Grade V/VI harsh, systolic, ejection murmur heard over the entire precordium and radiating to the neck and to the right side. There was a Grade I diastolic rumble at the apex. Abdomen: Soft and scaphoid without organomegaly. Genitalia: Normal male. Extremities: All pulses palpable and synchronous. The pulse was noted to be very diminished in amplitude.

LABORATORY DATA: Admission urinalysis was negative. Hematocrit was 41.5%. White blood count was 6,000 with a normal differential and platelets decreased on smear. Admission stool: Benzidine negative. Throat culture on admission revealed many hemolytic staphylococcus aureus coagulase positive. Urine revealed no growth. BUN 14. Following his admission, his hematocrit dropped to 31% and on his discharge was stable at 32% for some while. During his post-operative course, he had a number of guaiac positive stools but an upper GI series was negative. His initial cardiogram revealed left ventricular

hypertrophy with severe ST segment and T wave changes. Admission chest film revealed a heart within the normal limits of size and configuration. There was some prominence of the aortic arch, however. Post-operative films were consistent with a resolving post-thoracotomy state. An upper GI series on 8-4-64 showed a deformed duodenal bulb. No evidence of active ulceration. The blood type was A positive.

HOSPITAL COURSE: The patient had a cardiac catheterization performed on 7-21-64 which revealed severe valvular aortic stenosis with a gradiant of 125 mm of mercury. Thus, on 7-24-64, he had an aortic valvular plasty performed with cardio-pulmonary by-pass. He tolerated the procedure well and post-operatively had a very benign course. There remained a Grade II/III diamond shap ed, systolic murmur audible over the aortic area which radiated into the neck. The chest tube was removed on the second day, the skin sutures on the fifth day from the chest, on the seventh day from the remaining areas. His hematocrit dropped to 31% and the possibility of a occult bleeding from his known old duodenal ulcer was considered. Upper GI series was not consistent with an active ulcer. Nevertheless, he was placed on a strict medical ulcer regimen for the remainder of his stay. He was discharged two weeks post-operatively feeling quite well.

DIAGNOSIS: AORTIC STENOSIS, VALVULAR, SEVERE. 421.1

OPERATIONS: AORTIC VALVULAR PLASTY ON CARDIOPULMONARY BYPASS. 30.3
Dr. Gross, 7-24-64

MEDICATIONS: Maalox 30 cc P.O. q.i.d. between meals.
Bland diet.

COMPLICATIONS: NONE.

PROGNOSIS: Good.

DISPOSITION: The patient is to return home on a bland diet and limited activity and will return to the Thoracic Clinic in one month's time and to the Cardiology Clinic in two months.

DISCHARGE SUMMARY

Admitted: 11/5/72 Discharged: 11/8/72

This was the 2nd CHMC admission for this 24 year old male.

CHIEF COMPLAINT: Admitted for elective cardiac catheterization on a SNatural History Study.

PRESENT ILLNESS: The patient was thought to be well until about 16 years of age when on routine physical examination a murmur was heard. He was referred to the Central Maine Medical Center where the diagnosis of aortic stenosis was made. He was referred to CHMC for cardiac catheterization which showed a Gradient across the aortic valve of 125 mm. On the same hospitalization he had an aortic valvulotomy and had a benign postoperative course except for mild GI bleeding. He also developed serum hepatitis in the recuperative period. Subsequently he had been followed in the Cardiac Clinic where his electrocardiogram progressively improved. In retrospect he felt that he was quite symptomatic before the operation but since then has had absolutely no cardiac symptoms.

PHYSICAL EXAMINATION: Pulse 72, respirations 16, blood pressure 110/60. The patient was a well developed muscular male in no acute distress. HEENT were entirely within normal limits. The neck was supple without masses. The chest moved symmetrically with respirations, breath sounds were equal bilaterally and there were no rales or wheezes heard. Pulses were strong and equal in the upper extremities and slightly decreased in the lower extremities. The jugular venous pressure was not increased. There were no thrills, there was a left ventricular impulse and there were no heaves. S1 was normal, S2 was greatest at the base and with a very slight narrow split. There was no click heard. There was a Grade III/VI systolic ejection murmur along the upper left sternal border and the upper right sternal border radiating to the neck. There was a Grade I/VI decrescendo diastolic murmur on the upper right sternal border. No S3 or S4. Vasculature was normal and there was no cyanosis or edema. The abdomen and the rest of the examination were entirely within normal limits.

LABORATORY DATA: Electrocardiogram showed an axis of 0, mild left ventricular hypertrophy with upright T waves in all leads. There were ST-T waves changes in leads III and ADF and absent anterior forces. There were inversion of T waves in lead III. Chest xray was within normal limits. Complete blood count showed a hematocrit of 46, white blood cell count 6,200 with a normal differential.

HOSPITAL COURSE: The patient was admitted for elective cardiac catheterization on the Natural History Study. On the 3rd hospital day he had the cardiac catheterization which was normal and showed a gradient across the AV valve of 30 mm. of mercury. He tolerated the procedure well and was discharged home on the day following catheterization. He was advised to have some one drive him home rather than drive himself home.

DISCHARGE DIAGNOSIS: AORTIC STENOSIS, STATUS POST AORTIC VALVULOTOMY.

OPERATIONS AND SPECIAL PROCEDURES: LEFT AND RIGHT HEART CATHETERIZATION.

PROGNOSIS: GOOD.

FOLLOWUP: The patient will be seen in Cardiac Clinic in 1 year

DISCHARGE SUMMARY

Admitted: 11/5/72 Discharged: 11/8/72

Medications: None

CARDIAC CATHETERIZATION DATA

Finnan, J. Age 15 Body Surface area 1.79 m^2

I. Oxygen Saturations

	Percent	Content
Min Pulmonary Artery	81.2	
Right ventricle	80.6	
Right atrium	83.4	
Superior Vena Cava	85.6	
Main Pulmonary Artery	82.5	
Aorta	99.2	17.1
Pulmonary Artery	81.4	14.2
Aorta	100.0	17.2
Pulmonary Artery	83.4	14.3

II. Fick Data

O_2 Consumption	226	$\frac{ml}{min.}$
A-V Difference	2.9	$\frac{ml.}{100cc}$
Cardiac Output	7.8	L/min.
Cardiac Index	4.3	L/min./m^2

III. Valve Area

Peak systolic gradient	125 mmHg.
Mean systolic gradient	76 mmHg.
HR	79
SEP	0.33 sec.
AVF	300 cc/sec
AVA	0.76. cm^2

CASE STUDY

Patient:

15 Years Old

Procedure:

The patient was lightly sedated, quiet and cooperative throughout the porcedure. A #6, 125 Lehman catheter was inserted into the rt. brachial vein and passed to the superior vena cava, rt. atrium, rt. ventricle and pulmonary artery. A #7 100 NIH catheter was then inserted into a small artery which was medial to the rt. brachial artery. The catheter was passed retrograde into the ascending aorta and from there down into the lt. ventricle. A biplane angiogram was performed with an injection of 45cc of renovist into the lt. ventricle at 800 psi just above the aortic valve.

Oxygen consumption was measured with simultaneous aortic and pulmonary artery sampling.

Discussion:

The pressures on the rt. side of the heart and in the pulmonary artery were normal and there was no significant change in oxygen saturation to indicate a lt. to rt. shunt.

The systemic arterial blood was fully saturated.

There was an extremely marked elevation of the lt. ventricular pressure to a level of 260 systolic. There was a slight drop in systolic pressure as the catheter was withdrawn towards the aortic valve with the level dropping from 260 to 210-235 and then a sudden, sharp decrease in pressure as the catheter passed the valvar stenosis with the pressure level in the aorta at 95-100. The slight change in systolic pressure just below the aortic valve in all probability represents a muscular hypertrophy with some degree of functional narrowing in systole. The biplane angiograms of the lt. ventricle did not show any

fixed constriction below the aortic valve. The very tight valvar stenosis is illustrated in the cineangiogram with renovist injection into the ascending aorta. A fixed dome-like stenosis with a very narrow orifice and a small jet of blood getting through the dye column can be seen.

With the cardiac output calculated at 4.3 L/min/M^2, the aortic valve index area was calculated at 0.37 cm^2/M^2.

Diagnosis:

Aortic stenosis, valvar, severe, probably with some additional functional element.

Biplane angiogram.

Cineangiogram.

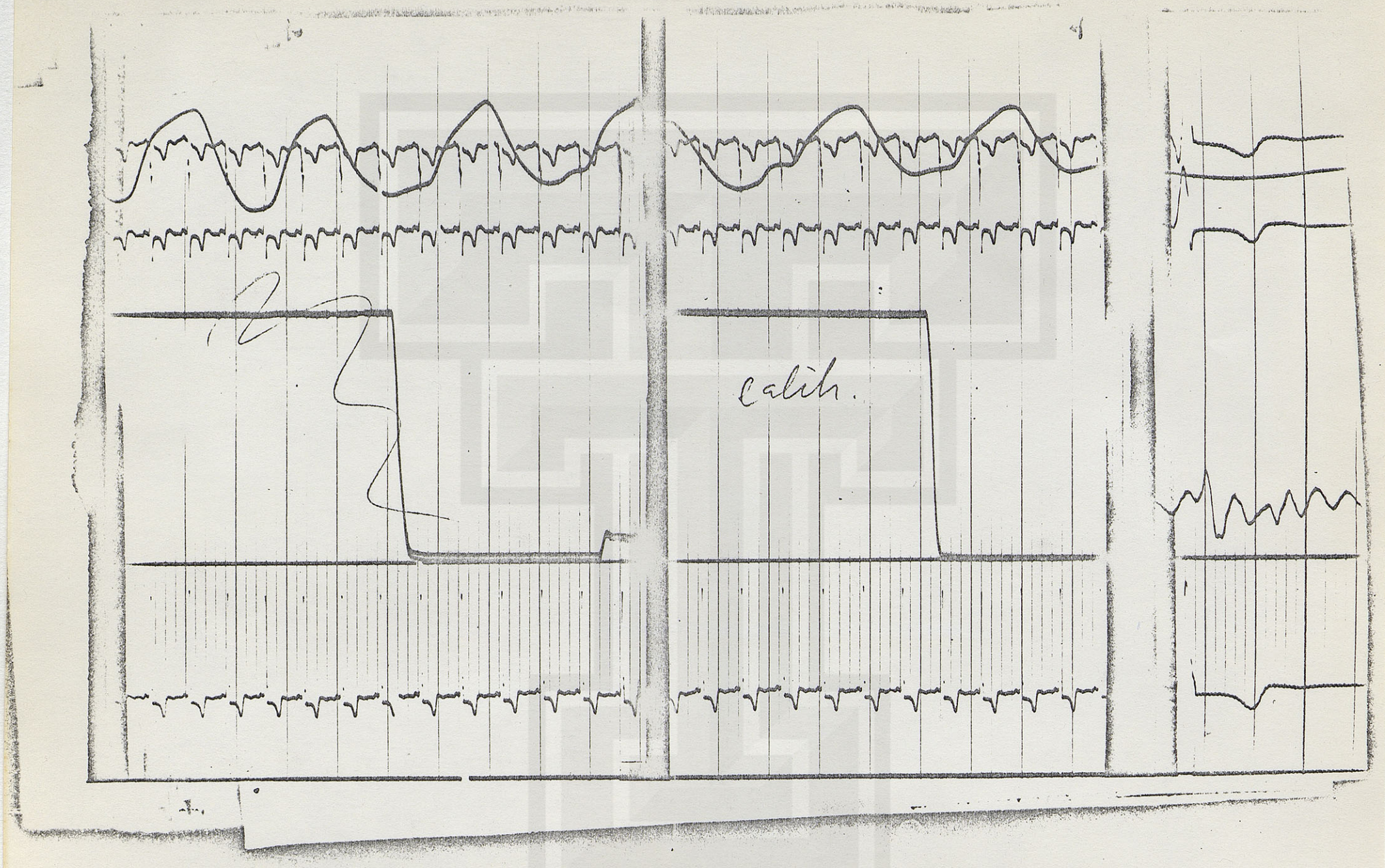
Retrograde arterial study.

Catecholamine study.

Catecholamine study.

Frank vectorcardiogram.

M.D.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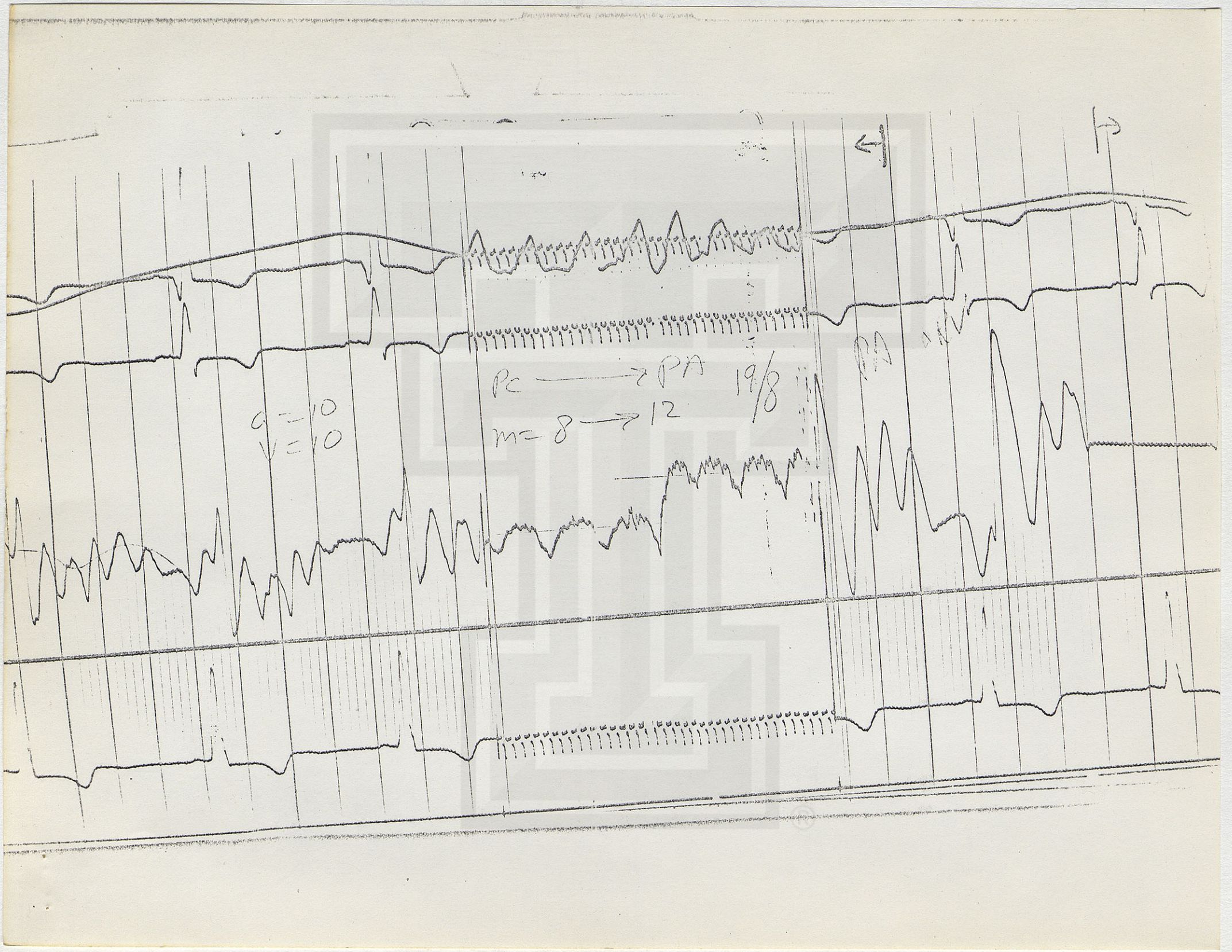
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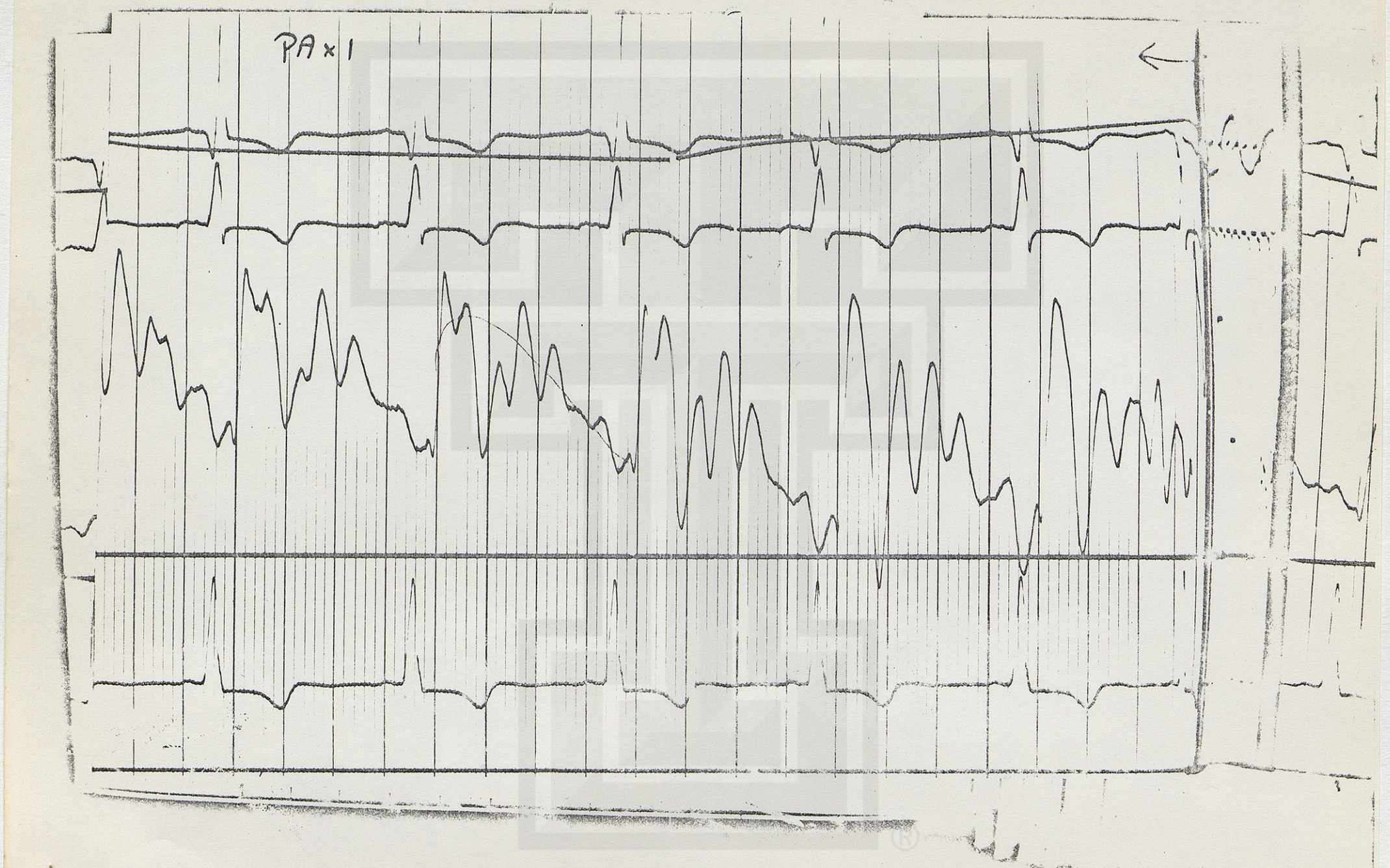
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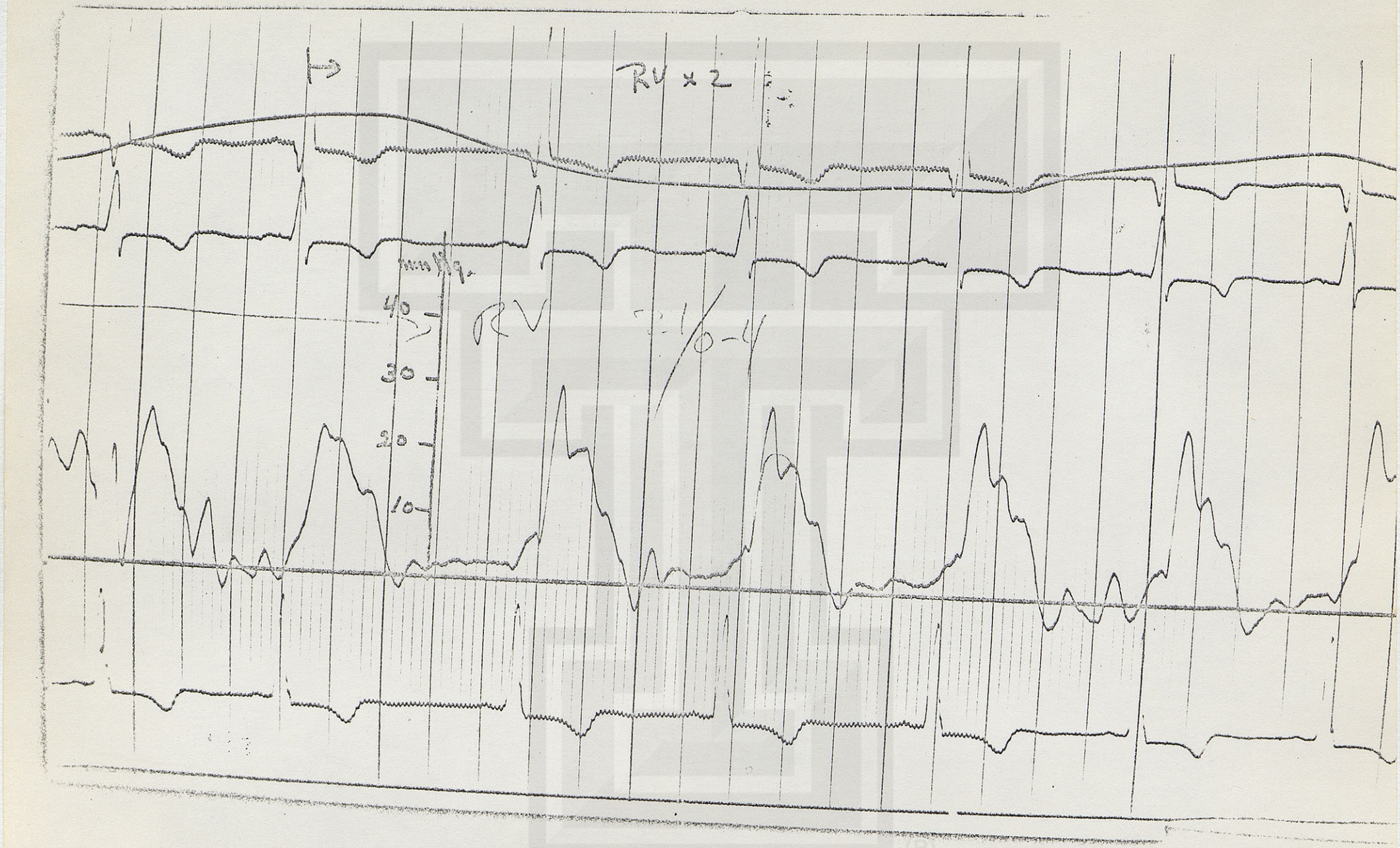
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