Elasticity of soft tissues in simple elongation¹

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FUNG, Y. C. B. Elasticity of soft tissues in simple elongation. Am. J. Physiol. 213(6): 1532-1544. 1967.-Elasticity of living soft tissues is strongly nonlinear. Based on experimental results on rabbits' mesentery, a theoretical framework is presented in which the elastic properties of soft tissues can be described. It is shown that the mathematical formulation works well also in reducing published data on the series element of the heart and striated muscles, and the skin. In simple elongation the tensile stress is nearly an exponential function of the strain in the lower stress range. Based on this fact, it is shown that although we are dealing with the finite deformation of highly nonlinear materials, the elastic property of soft tissues in tension can be expressed quite simply in most cases. It is necessary, however, to give up the usual practice of trying to characterize the clasticity of a tissue by a representative Young's modulus, because this modulus varies over a very wide range, which is often zero at vanishing stress, and increases linearly as the stress increases, and therefore is meaningless unless the exact stress level is specified. New physical constants recommended are: the slope and curvature at the origin of the curve of $dT/d\lambda$ vs. T, where T stands for tension and λ stands for the extension ratio, and the tensile stress T^* , (based on the original crosssectional area) at a specific value of the extension ratio λ^* .

stress; strain; stress-strain-history law; constitutive equations

THERE ARE MANY PROBLEMS in physiology whose solutions require a detailed knowledge of the mechanical properties of the tissues involved. Hence the stress-strain relationship of living tissues is of fundamental interest. For example, when one speaks of hemodynamics, wave propagation in blood vessels, the distensibility of arteries and veins, etc., the normal and abnormal stress-strain relationship of the blood vessels and the surrounding tissues must be known. An understanding of the elastic property of blood vessels may serve as a tool for diagnosis in pathology. Information on mechanical action is necessary for a systems analysis of the autoregulation of blood flow, or of the contraction of the heart, or for an intelligent application of artificial prosthetics, etc.

Much work has been done on this problem, and con-

siderable amount of experimental data has been published, see the review by Frasher (9), and other authors (1, 4, 5, 12, 24, 34), but a degree of vagueness and uncertainty prevails. The main difficulty lies in the customary use of infinitesimal theory of elasticity to the media which normally exhibit finite deformations. The high degree of nonlinearity in the stress-strain relationship of living tissues is known to most authors, but a theoretical framework in which experimental results can be imbedded is lacking. The use of the concepts of the linear theory of elasticity to a highly nonlinear material leads to a certain inadequacy in data presentation. The practical difficulty of experimenting with small specimens of living tissue, and the limited ranges over which variables could be introduced in a given experiment, further cloud the issue. It seems obvious that a clarification of the basic approach would be worthwhile at this time.

The objective of this paper is to discuss the nonlinear stress-strain-history relationship in large deformations² of living tissues. The word "history" is added here to signify the dependence of stress on the history of strain, as is usually the case for biological materials. A framework is proposed which will be useful for quantitative research. Our method is theoretical, although in search for simplicity we shall be guided by experimental data. However, it is not the purpose of the present article to detail the biological data. Our scope is limited to the analytical aspects.

One may ask what is the merit of the theoretical approach? The answer is threefold: 1) To facilitate data

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² The classical linear theory of elasticity is strictly applicable only to infinitesimal strains (under the geometric requirement that the strain-displacement relations may be linearized), and only within the range of applicability of the Hooke's law. For engineering materials (metals, alloys, concrete, wood, structural plastics) these limitations are not severe, because the range of applicability of Hooke's law for the materials is limited to within the so-called "proportional limit," or, if that limit is too small, to the so-called "defined yield stress," which is conventionally set at a maximum strain of 0.002, or 0.2%. Strains beyond this range are "large" to engineers. It is remarkable that a theory of such severe restrictions has been sufficient for the design of most engineering structures. In contrast, we consider in this paper strains (extensions) of order 100% or more for the mesentery membranes, 30-70% for blood vessels, 10-40% for the skin, 140% for isolated striated muscle fiber and myosin fibres, and 5% for papillary heart muscles. These are indeed large compared with the familiar in structural engineering.

collection and data analysis. If an experimental curve can be characterized mathematically by a few parameters, then these parameters can be tabulated and be used to correlate the mechanical property of the tissues with other physical and physiological parameters, such as age, sex, injury, temperature, chemical environment, etc. 2) To derive three-dimensional stress-strain-history law under finite deformation. Such a law is needed for the analysis of any practical boundary-value problems, but is not yet available. Since it is very difficult to experiment with biological materials in three-dimensional stress fields, it is natural to turn to theoretical formulation and then derive solutions to appropriate problems which can be tested experimentally. In other words, a theoretical study may be used to formulate critical experiments to validate the basic hypotheses. 3) To unify different types of experiments, such as the static (very slow) elasticity, dynamic elasticity (finite strain rate), stress relaxation under fixed strain, creep deformation under fixed stress, strain-cycle hysteresis, and cyclic stress fatigue. A correct theoretical formulation should bring out the unity among these experiments. Only the formulation that is consistent with all the experimental results can be accepted.

A complete theoretical formulation is too long to be presented in one paper. The present article is concerned with one-dimensional stress field only. Extensions to three dimensions will be based on these one-dimensional results.

One of the results that will be shown in this paper is that the elastic stress for the mesentery is essentially an exponential function of the extension ratio. It follows that Young's modulus (or, more strictly, the tangential modulus, i.e., the slope of the tangent to the stress-strain curve, as opposed to the secant modulus, the slope of a line joining the origin to a point on the curve) varies exponentially with the strain. This variation is very broad: Young's modulus is almost zero at small strain but increases exponentially as the strain increases. Therefore it is meaningless to say what Young's modulus of a tissue is unless a strain level (or equivalently, a stress) is stated. For example, for the mesentery membrane Young's modulus can be anything between 0 and 5 \times 10⁶ dvnes/cm², and it is obviously necessary to specify at what point on the curve a slope is quoted for the number to have any meaning whatever.

This nonlinearity must have been obvious to all workers in the field. Many authors remarked about the fact that Young's modulus of soft tissues becomes larger and larger as strain increases. But when a numerical value is quoted, (for example, see 9, 24, 34) usually a single Young's modulus is given without an accompanying statement about the levels of stress and strain. An excuse for this situation perhaps is that the physiologist has a "typical" or "average" condition of the tissue in mind, and the quoted modulus refers to such a state. But without a suitable quantitative definition of the typical conditions, the vagueness and confusion of such an approach is obvious.

As an alternative, some authors publish entire experimental curves. The difficulties of this approach arc twofold: 1) cumbersome documentation, 2) no simple way to correlate these curves with other physical and physiological parameters. To overcome these difficulties we offer a second alternative: to characterize these experimental stress strain curves by a mathematical expression which contains two or three parameters, and can be used for systematic study of the tissue under varied conditions. We shall show that for the mesentery the most important parameter is the slope of the $dT/d\lambda$ vs. T curve at the origin, where T stands for stress (specifically, the "Lagrangian" stress, obtained by dividing tensile load by the original cross sectional area) and λ stands for the extension ratio (deformed length divided by the original length of specimen). This parameter, designated by the symbol a, happens to be dimensionless, (so that it has the same value in the cgs as in any other measuring systems), and is especially suitable a measure for the nonlinearity of the stress-strain law, (because the value of *a* is zero for all materials that obey the linear Hooke's law.)

Together with the exponential index a, an additional parameter $T^*(\lambda^*)$ specifies the whole elasticity curve. Here T^* is the stress at a specific extension ratio λ^* . Theoretically it is sufficient to choose any point (T^*, λ^*) on the stress-strain curve, but in practice it is advantageous to chose T^* and λ^* at a point which may be judged particularly significant from the point of view of physiology. In this way the physiological judgment of the experimenter can be recorded simply, precisely and without ambiguity, yet in a manner that will not jeopardize the presentation of the entire curve.

Further improvement of the accuracy of the elasticity curve presentation can be accommodated by taking into account the curvature of the $dT/d\lambda$ vs. T curve. Formulas for these improvements are presented in the paper. When these formulas are applied to the published data



FIG. 1. Sketch of the mesentery specimen for tension test.

on muscles and skin, reasonable agreement is obtained. Therefore it seems plausible that the mathematical form can be used for a fairly wide range of tissues.

Finally, we must specify the limitations of the mathematical expression. Again this can be made precise by a) an analytical presentation of the history-dependent part of the stress-strain relationship, b) by a statement of the range of λ within which the exponential law applies, and beyond which the curve flattens out, the material yields and fails.

The discussions above should justify the analytical approach as applied to one-dimensional experiments. However, in true perspective the value of the analytical approach lies in the analysis of two- and three-dimensional stress fields. It is to the general stress field that the analytical approach becomes truly nontrivial.

TENSILE TEST OF THE RABBIT MESENTERY

In an earlier study of the distensibility of the capillary blood vessels in the mesentery of the rabbit, the contribution of the surrounding tissue was evaluated by measuring the elasticity of the mesentery membrane in torsion, (13). It was shown that the shear modulus depends on the strain, so that the material is highly nonlinear. As an extension of this approach, a tension test was performed in which the mesentery membranes were taken from rabbits of approximately 3 kg wt, and tested in tension in the Instron testing machine. The tension-test program was more comprehensive, providing results suitable for theoretical treatment, and will be described in some detail below.

The test specimens were obtained as follows: The mesentery was spread out flat on a platform in the natural dimensions defined by the surrounding intestines and large blood vessels, to which no restraint other than gravity and friction on the platform was imposed (see Fig. 1). This was approximately the configuration under which most of the microcirculation measurements in the mesentery were made (35, 36), and it was also the extent to which the membrane was stretched in the torsion test (13). It will become clear from what is to be described below that the mesentery membrane was actually highly stretched in this configuration. The tensile stress was not small (of the order of 106 dynes/cm²) but owing to the comparative thinness of the tissue (about 6 \times 10⁻³ cm), the resultant force (of order 6 g/cm) was not large enough to move the intestines and large blood vessels. An area of the membrane free from fat and large blood vessels was selected. A special cutter which consisted of two parallel razor blades 1 cm apart was then dropped on this membrane, cutting two paralled slits 3.66 cm long. On lifting the cutter it was seen that the mesentery shrank immediately away from the cuts, leaving two large lenticular holes. The strip that was left at the center was then tied with fine silk threads at both ends and cut free. Again it shrank in length. The size of the final specimen was much smaller than that defined by the spreadout intestine.



FIG. 2. Load-deflection curve of a rabbit mesentery in tension. The state corresponding to the naturally spread-out mesentery is marked by the small circle. The point l_0 marks the relaxed length of the specimen.

Small hooks were attached to the specimen and the specimen was mounted onto the Instron testing machine (see Fig. 1). The machine has a load cell with a full scale range of 0–10 g, which can be changed electronically to scales of 2, 10, or 50 g, with a nominal error less than ± 0.5 %. The base can be moved at constant specific rates up and down. The recording pen moves horizontally in proportion to the load. The paper moves on drums rotating at chosen speeds. Altogether a great flexibility in the choice of strain and the strain rate can be obtained.

The excised mesentery was used as a tension specimen. As a folded thin membrane, the traction acting on the face of the membrane was zero. Since the lateral sides were free to deform, no stress was induced in a direction normal to the axis of tension. The only disturbing influence came from the ties at the ends. The influence of this evidently localized residual stress was unknown, but will be assumed to be negligible in view of the considerable length of the specimen.

TENSILE EXPERIMENTAL RESULTS

A variety of load-deflection curves was obtained. Typical results are shown in Figs. 2–7.

Figure 2 shows the load-deflection curve of a specimen when the rate of strain imposed was 0.254 cm/min. The ordinate shows the load in grams. The abscissa shows the deflection in centimeters. (The coordinates of the Instron records were interchanged in order to conform to the normal convention used in load-deflection curve presentation.) Note that the specimen was $l_0 = 1.22$ cm. This length was obtained by optical measurement of the specimen suspended in the saline, with a small hook tied to the lower end of the specimen with a silk thread. The weight of the hook and thread in saline was 8 mg. Hence the specimen was not entirely free, but was subjected to a stress of approximately 420 dynes/cm². Such a load would be too small to be seen in the scale of Fig. 2, but its influence on the relaxed length l_0 was unknown. If the specimen were left com-



FIG. 3. Hysteresis curves. Rabbit mesentery. Loading and unloading at a rate of 0.254 cm/min. The large loop shows the first complete cycle. The specimen was then stressed to an intermediate point and a cycle of small amplitude was performed. Note the difference in slope of the small dynamic loops from the large one and from each other.

pletely free, it would float and appear curved in the saline. Although the length of such a floating specimen could be measured photographically, such a procedure was not followed because of its lack of precision. Hence the basic problem of determining the length l_0 was yet unsolved, and must be given further attention in the future.

When the specimen was stretched from l_0 to $l_1 = 2.54$ cm, the corresponding tension induced was very small; in fact it was not readable in the chart illustrated in Fig. 2. Extension beyond $l_1 = 2.54$ cm, however, induced a rapidly increasing tension. The load-deflection relationship was definitely nonlinear. A small circle in Fig. 2 marks the state corresponding to the naturally spreadout mesentery. This point was located by the measured length L_{ph} of the specimen before it was cut. It is seen that considerable tensile stress must have existed in the specimen in this state which was often used in microcirculation observations, such as those reported in Zweifach (35, 36).

Figure 3 shows typical hysteresis curves of the specimen strained at a rate of ± 0.254 cm/min. The large loop shows the first complete cycle. It is seen that hysteresis existed, but was not very large. The nature of hysteresis in tension was very similar to that of the torsion tests reported in reference 13. Although it is not shown in Fig. 3, a completely unloaded specimen (free from the test machine but with the small hook attached as mentioned above) gradually returned to the length l_0 . In other words, the length l_0 was well defined, and there was no doubt that the material was elastic between l_0 and l_1 , although the modulus of elasticity was very small in that range.

The small loops in Fig. 3 were obtained by restressing the specimen to an intermediate point and performing a cycle of small amplitude at the same strain rate. Note the difference in slope of the small dynamic loops from the large one and from each other.

The effect of strain rate on the hysteresis is illustrated in Fig. 4. The curve marked "high" was produced at a strain rate 10 times faster than that marked "low." It is seen that the hysteresis loops did not depend very much on the rate of strain.

In Figs. 3 and 4 the extension (abscissa) was measured from an arbitrary point. Logically the extension should be measured from the relaxed length l_0 , but if this were done the origin would be located far to the left and the scale of the figure would be too small. Therefore, for the convenience of experimenting on hysteresis, an arbitrary starting point was taken.

Figure 5 shows a stress-relaxation curve. The specimen was strained at a constant rate until a tension T_1 was obtained. The length of the specimen was then held fixed and the change of tension with time was plotted.

Examination of a large number of such relaxation curves showed that the total amount of relaxation (i.e., T_1-T_{∞}) was roughly proportional to the total load T_1 .

Figure 6 shows the change in the stress-strain curve under repeated loading and unloading at a fixed rate of strain between two fixed limits of extension. In Fig. 6 the strain rate was ± 0.254 cm/min, and the stroke was 0.171 cm. The decrease of peak tension with the number of cycles resembled the relaxation curve of Fig. 5.

Finally, Fig. 7. shows the load-deflection curve, with a reduced scale for the coordinates, of a specimen strained up to failure. The failure was rather gradual. The ultimate strain at failure was large. The specimen failed by tearing at some unpredictable points.

In all these experiments the specimens were suspended in a physiological solution at room temperature. Cooling the fluid to 40 F did not change the load-deflection curve substantially. Exposure of the specimen to dry air, however, resulted in drastic changes in its mechanical property. Drying increased the tension at a fixed strain.

ELASTIC AND HISTORY-DEPENDENT PARTS OF THE STRESS-STRAIN RELATIONSHIP

To reduce the individual observations described in the previous section into objective constitutive equations, it is first necessary to consider the material nonhomogeneity and directional anisotropy. In the first place the mesentery membrane is covered with two layers of mesothelial cells with a total thickness about 6×10^{-4} cm, i.e., about 10% of the total thickness. The properties of the mesothelial cells are expected to be different from the bulk of the gel. However, lack of information prevents us from saying anything further about this.

Electron microscopic investigation of the mesentery shows that it is composed of randomly oriented collagen fibres buried in a gel. Hence in elements of dimension of the order of 100 A the medium is certainly nonhomogeneous. However, for elements with a linear dimension of order 10 μ the local nonhomogeneity will be averaged out and may be ignored. Hence, for the purpose of assessing the distensibility of the blood vessels, it is permissible to consider the medium as homogeneous.

It is almost axiomatic that biological material is anisotropic. However, again no quantitative information is



FIG. 4. Hysteresis curves of rabbit mesentery obtained at different strain rates. The high rate was 10 times that of the low rate. Only slight change in hysteresis curves was obtained. Some of the small difference is due to fatigue, some is due to strain rate.

available. It is hoped that the analysis of the present paper will lay the foundation for setting up a framework for future data collection with respect to anisotropy.

It is evident from the curves shown in Figs 2–7 that the stress-strain relationship for the mesentery and the arteries is nonlinear, that the stress does not depend on the strain alone, but also on the strain history. Let the stress-strain relationship be separated into two parts: an elastic part and a history-dependent part. The elastic part defines a unique stress-strain relationship, i.e., the "clasticity" of the material. The history-dependent part is time dependent; it is related to the hysteresis, stress relaxation, creep, and other nonconservative phenomena. Thus we may write:

$$\sigma(t) = F[\epsilon(t)] + F'[\epsilon(t - \tau); t, \tau]$$
(1)

where $\sigma(t)$ is the tensile stress at time t referred to the deformed state, $\epsilon(t)$ is the tensile strain at time t, $F[\epsilon(t)]$ is a function of the strain ϵ at time t; whereas $F'[\epsilon(t - \tau); t, \tau]$ is a function of the entire history of the strain, $\epsilon(t - \tau)$. The first elastic term $F[\epsilon(t)]$ represents a thermodynamically reversible part of the stress-strain relationship. The second term represents a thermodynamically irreversible processes. The first term states that at any instant of time t there is an elastic stress $\sigma^*(t) = F[\epsilon(t)]$ corresponding to the strain $\epsilon(t)$ at that instant. This correspondence is instantaneous, regardless of past history. The second term tells the influence of the past history.

It is difficult to represent the history-dependent portion of the stress-strain law analytically. The fact, as shown in Fig. 4, that the hysteresis loop is almost independent of the strain rate reflects a phenomenon which is well known in engineering structural analysis. It dispels at once the belief, popular in the literature, that the irreversible portion of the stress-strain law of biological material is linear viscoelastic. Indeed, many papers have been published listing the viscosity coefficients of tissues, arterial walls, etc. However, if the material were linear viscoelastic the hysteresis loop would vary with the strain rate. In fact, for damping of the Rayleigh viscous type the area of the hysteresis loop in a periodic motion would be directly proportional to the frequency, i.e., with the strain rate. This is certainly not the case found in biological experiments.

To account for the peculiar result that the hysteresis curves are rather insensitive to the strain rate, we have to assume either a nonlinear viscoelastic model or a model with a continuous relaxation spectrum. Analytically one can draw on past experience gained in the theory of aircraft vibration and flutter, in which a similar situation known as "hysteretic" damping occurs (see for example, ref. 11, p. 217, 227, 264, 375, 447-479 and references contained there in; see also Becker (2, 3)for a similar phenomenon in ferromagnetism). The unfortunate part about this type of damping is that thus far a simple analytical representation has been found only for harmonic oscillations. For transient motions Neubert (23) has shown that an approximate model can be obtained by a generalized Kelvin model with an infinite number of springs and dashpots representing a continuous distribution of relaxation spectrum.

Leaving the history-dependent portion of the stressstrain law to a separate article, we shall confine the rest of this paper to the elastic portion of the constitutive equation. Although strictly speaking such a separate treatment is not permissible, because unless we know both parts we will not be able to separate the measured total stress into elastic and inelastic parts. However, such a separate treatment has practical merits since not only is the elastic portion the main part (80 or 90% of the total) of the stress response, but also it is the much simpler portion, known with much greater precision and confidence than the history-dependent part.

ELASTIC EQUATION FOR THE MESENTERY

Let us now consider the reduction of the experimental data within the framework of equation 1. We speak of stress and strain. In an infinitestimal deformation these concepts are well known. In a finite deformation the description of these quantities has to be handled with care. Stress refets to force per unit area, but which area? An area of material composed of the same molecules changes with deformation. If a surface force is divided by the area in the deformed state, and is resolved into components along a system of coordinates imbedded in the deformed state, then the stress is referred to as Eulerian. If the term "deformed state" in the preceding sentence is replaced by an "initial" or a "reference" state, the stress is said to be Lagrangian. Similarly, a strain tensor describes the change of the metric between two states, the initial and the deformed, and several definitions can be chosen. The matter is fairly complex and cannot be described without lengthy treatment (12, 14, 15, 22, 25).

A uniform extension may be described as follows. Let a fixed rectangular Cartesian system of coordinates (x, y, z) be used to define the unstrained body. We consider a deformation in which a unit cube in the unstrained body whose sides are parallel to the axes is deformed into a



FIG. 5. Relaxation curve. Rabbit mesentery. The specimen was stressed at a strain rate of 1.27 cm/min to the peak. Then the moving head of the testing machine was suddenly stopped so that the strain remained constant. The subsequent relaxation of stress is shown.

cuboid of dimesions λ_1 , λ_2 , λ_3 parallel to the x, y, z axes, respectively. The coordinates of the particles in the strained body may be referred to a fixed Cartesian set of axes (ϵ , η , ζ) which coincide with the axes (x, y, z) so that:

$$\xi = \lambda_1 x, \quad \eta = \lambda_2 y, \quad \zeta = \lambda_3 z \qquad (2)$$

For this uniform extensional deformation the strain components may be written in the matrix form (see 14, p. 80, and note that $\gamma_{ij} = G_{ij} - g_{ij}$).

$$\begin{pmatrix} \gamma_{11} & \gamma_{12} & \gamma_{13} \\ \gamma_{21} & \gamma_{22} & \gamma_{23} \\ \gamma_{31} & \gamma_{32} & \gamma_{33} \end{pmatrix} = \begin{pmatrix} \frac{1}{2} \langle \lambda_1^2 - 1 \rangle & 0 & 0 \\ 0 & \frac{1}{2} \langle \lambda_2^2 - 1 \rangle & 0 \\ 0 & 0 & \frac{1}{2} \langle \lambda_3^2 - 1 \rangle \end{pmatrix}$$
(3)

The volume of the unit cube becomes $\lambda_1\lambda_2\lambda_3$ after deformation. The constancy of volume is expressed as a condition of incompressibility

$$\lambda_1 \lambda_2 \lambda_3 = 1 \tag{4}$$

Following the general practice in cardiovascular research, we shall consider the mesentery incompressible. Hence, on specializing *equation* 2 to describe a simple tension, for which $\sigma_{xx} = \text{const}$, $\sigma_{yy} = \sigma_{zz} = 0$, we have

$$\lambda_1 \lambda_2 \lambda_3 = 1, \, \lambda_2 = \lambda_3 \tag{5}$$

so that

$$\lambda_2 = \lambda_3 = \frac{1}{\sqrt{\lambda_1}} \tag{6}$$

We shall write λ for λ_1 in this case,

$$\lambda = \frac{\text{length of specimen under strain}}{\text{unstrained length}} = \frac{l}{l_0}$$
(7)

The corresponding tensile strain is

$$\epsilon = \gamma_{11} = \frac{1}{2}(\lambda^2 - 1) = \frac{1}{2}\left(\frac{l^2}{l_0^2} - 1\right)$$
 (8)

The cross sectional area of the specimen is decreased during extension by the ratio $\lambda_2 \lambda_3 = 1/\lambda$. Hence if the area at the unstrained state is A_0 , and the total tensile force is P, then the Eulerian stress in tension is

$$\sigma = \frac{P}{A} = \frac{P}{A_0}\lambda = T\lambda \tag{9}$$

Thus the simple tension can be described by a single component of stress σ and a single extension ratio λ .

In our experiments with rabbit mesentery, the specimen at the completely relaxed state was difficult to handle, and the measurements of the cross-sectional area of the specimen were made only when the mesentery was spread out on a platform under the dimensions defined by the intestine and large blood vessels. Let this state be indicated by a subscript *ph*. At this state in our tests the width of the specimen was 1 cm, the thickness of the rabbit mesentery was 60×10^{-4} cm $\pm 5\%$ (see ref. 13). Hence the area $A_{ph} = 60 \times 10^{-4}$ cm². The values of λ_{ph} , the ratio of the length before cutting to the cut-and-relaxed length, ranged over 2.0-3.2 for the 20 specimens examined. Of course, $A_0 = \lambda_{ph}A_{ph}$.

Now we can analyze the elastic part of the stress-strain equation for the rabbit mesentery. According to equation 1 the reversible portion of the elastic response can be obtained from an infinitely slow process of loading. However, since such an idealized experiment is impossible, we must derive the elastic relation from dynamic results. A simple procedure is as follows. For a given strain rate, a relaxation experiment is performed in which the specimen is loaded at the specified rate and then held fixed and the stress history is measured. Let the asymptotic stress be T_{∞} (see Fig. 5). An examination of many such curves indicates that T_{∞} is proportional to the peak stress T_1 . We assume that T_{∞} is the stress that would have been obtained had the load been applied slowly. Hence if the dynamic stress was reduced by the factor T_{∞}/T_{1} , the result would correspond to the elastic curve. This procedure was followed and the results will be discussed below.

The most striking feature of the elasticity of a living tissue as seen from Fig. 2 is the very small stress in response to a fairly large strain. In Fig. 2 an extension up to about 100 % of the relaxed length yields only a small, unmeasurable tension. However, for λ greater than 2 the stress rises rapidly, and indeed, exponentially.

When the elastic curve is determined from a typical hysteresis curve such as the one shown in Fig. 3, (using the segment corresponding to loading or increasing strain), the slope of the curve can be computed. Figure 8 shows an example of the slope of the elastic tension-deflection curve, $dT/d\lambda$, plotted against the elastic tension T. It is seen that a remarkable correlation exists. As a first approximation we shall fit the experimental

curve by a straight line:

$$\frac{\mathrm{d}T}{\mathrm{d}\lambda} = aT, \qquad (1 \leq \lambda \leq \lambda y) \quad (10)$$

An integration gives

$$T = \frac{1}{c} e^{a\lambda} \tag{11}$$

where *c* is an integration constant. If $T = T^*$ when $\lambda = \lambda^*$, then

$$c = \frac{1}{T^*} e^{a\lambda^*} \tag{12}$$

so that

$$T = T^* e^{a(\lambda - \lambda^*)}, \qquad (1 \le \lambda \le \lambda_y) \quad (13)$$

On substituting equation 9 into 13 we obtain

$$\sigma = T^* \lambda e^{a(\lambda - \lambda^*)}, \qquad (1 \le \lambda \le \lambda_y) \quad (14)$$

The range of applicability of these equations is the range in which *equation 10* is valid, which is indicated in the parentheses in *equations 13* and 14, with λ_y denoting the upper limit of validity.

By equation ϑ , the stress-strain relationship is obtained:

$$\sigma = T^* \sqrt{1+2\epsilon} \exp \left\{ a \left[\sqrt{1+2\epsilon} - \sqrt{1+2\epsilon^*} \right] \right\}$$
(15)

The strain energy per unit volume of the undeformed tissue, $W(\lambda)$, is equal to the work done by the load:

$$W\langle \lambda \rangle = \frac{1}{A_0} \frac{1}{l_0} \int_{l_0}^{l} T(l) A_0 \, \mathrm{d}l$$
$$= \frac{1}{l_0} \frac{l_0}{c} \int_{1}^{\lambda} e^{a\lambda} \, d\lambda = \frac{1}{A_0} \frac{1}{ca} [e^{a\lambda} - e^a] \tag{16}$$

$$= \frac{T^*}{a} \left[e^{a(\lambda - \lambda^*)} - e^{a(1 - \lambda^*)} \right], \quad (1 \le \lambda \le \lambda_y)$$

These simple relations are remarkable indeed. In mechanics, nonlinear material of an exponential type did not seem to have attracted any attention. Now it appears that the exponential type of materials is natural in the biological world.

A better fit to the elastic curve of the rabbit mesentery can be obtained by a quadratic expression instead of equation 10:

$$\frac{\mathrm{d}T}{\mathrm{d}\lambda} = aT(1 - bT) \tag{17}$$



FIG. 6. Fatigue curve. Rabbit mesentery. The specimen was first stressed to a peak, then a cyclic strain between two fixed displacements was imposed. All loading and unloading were at a constant rate of 0.254 cm/min. Note the reduction of stress amplitude in cycling.

The corresponding results are:

$$T = \frac{e^{a\lambda}}{C + be^{a\lambda}}, \qquad (1 \le \lambda \le \lambda_y) \quad (18)$$

$$C = \left(\frac{1}{T^*} - b\right) e^{a\lambda^*} \tag{19}$$

$$\sigma = \lambda \frac{\exp (a\lambda)}{C + b \exp (a\lambda)}, \qquad (1 \le \lambda \le \lambda_y) \quad (20)$$

$$W(\lambda) = \frac{1}{ba} \log \frac{1 + \frac{b}{C} e^{a\lambda}}{1 + \frac{b}{C} e^{a}}, \qquad (1 \le \lambda \le \lambda_b) \quad (21)$$

The strain energy may be expressed in terms of the strain ϵ by replacing λ with $\sqrt{1+2\epsilon}$ in equation 16 and 21. $W(\epsilon)$ is considerably more complex in appearance than $W(\lambda)$. Thus there is no particular advantage in expressing the strain energy in terms of ϵ .

To illustrate the usefulness of these formulas we have drawn in Fig. 8 a curve given by equation 17 with $l_0 =$ 0.864 cm, a = 12.4, $b = -7.29 \times 10^{-4}$ cm²/dyne. A good fit of the reduced result of Fig. 3 can be obtained by taking $T^*A_0 = 7.0$ gm, $\lambda^* = 3.21 = \lambda_y$, a = 12.4, b = 7.29×10^{-4} , $A_0 = 1.93 \times 10^{-2}$ cm². Thus the nonlinear elasticity law of the mesentery is well represented by four parameters.

It should be noted that T as given in equation 13 or 18 does not vanish unless $\lambda \to \infty$. By definition, however, we must have T = 0 when $\lambda = 1$, which defines the unstrained state. Hence a modification is necessary in order to account for this initial condition. This can be done by adding a small constant β to equation 10 or 17. For



FIG. 7. Failure curve. Rabbit mesentery. The specimen was stressed to failure. Note change of scale from Fig. 3. Failure appeared to be a gradual tearing.

example, replace 10 by

$$\frac{\mathrm{d}T}{\mathrm{d}\lambda} = a(T+\beta) \tag{22}$$

then

$$T + \beta = \frac{1}{c} e^{a\lambda} \tag{23}$$

If $T = T^*$ when $\lambda = \lambda^*$, then

$$T = (T^* + \beta)e^{a(\lambda - \lambda^*)} - \beta$$
(24)

Hence $T = 0, \lambda = 1$ implies

$$\beta = \frac{T^* e^{-a(\lambda^* - 1)}}{1 - e^{-a(\lambda^* - 1)}}$$
(25)

A small intercept $a\beta$ on the vertical axis does seem to exist in Fig. 8, but as a whole such a modification is quite unimportant.

Note that a rapid decrease of tension T is obtained for $\lambda < \lambda^*$. The tension is reduced 100-fold (i.e., to $T^*/100$) if the exponent $a(\lambda^* - \lambda) = 4.604$, whereas a 1,000-fold reduction is obtained if the exponent is 6.9. As an example, for a certain specimen, we have $l_0 = 1.27$ cm, and $A_0 dT/dl = 47.25$ g/cm at $\lambda^* = 2.1$, $A_0T^* = 7$ g, then $a = (120 \times 0.5)/7 = 8.57$, and tension of 0.07 g is obtained if $\lambda^* - \lambda = 4.604/8.57 = 0.537$; i.e., when $\lambda = 1.563$.

An alternative to the β factor introduced in (22) is to introduce a polynomial factor which vanishes at $\lambda = 1$. Guidance for such a modification can be obtained from the general theory of elasticity. It can be shown fairly easily that if the strain energy function $W(\lambda_1, \lambda_2, \lambda_3)$ of an isotropic incompressible elastic body is expressed in terms of the strain invariants I_1 and I_2 (see Green and Adkins, ref. 15, p. 299), then the Eulerian tensile stress in simple elongation is given by

$$\sigma = 2\left(\lambda^2 - \frac{1}{\lambda}\right)\left(\frac{\partial W}{\partial I_1} + \frac{1}{\lambda}\frac{\partial W}{\partial I_2}\right)$$
(26)

and the Langrangian stress, by

$$T = 2\left(\lambda - \frac{1}{\lambda^2}\right) \left(\frac{\partial W}{\partial I_1} + \frac{1}{\lambda}\frac{\partial W}{\partial I_2}\right)$$
(27)

When $\lambda \rightarrow 1$, the zero factor must be of the form $(\lambda - 1/\lambda^2)$ if the strain energy has no singularity at the unde formed state, i.e., if $\partial W/\partial I_1$, $\partial W/\partial I_2$ are finite and continuous at $\lambda = 1$. Adopting this zero factor, we modify equation 11 as follows:

$$T = \operatorname{const}\left(\lambda - \frac{1}{\lambda^2}\right)e^{\pi\lambda} \tag{28}$$

Evaluating the constant with the condition $T = T^*$ when $\lambda = \lambda^*$, we obtain

$$T = \frac{T^*}{\lambda^* - \frac{1}{\lambda^{*2}}} \left(\lambda - \frac{1}{\lambda^2}\right) e^{\overline{\alpha}(\lambda - \lambda^*)}, \qquad (1 \le \lambda \le \lambda_y) \quad (29)$$

By differentiation,

$$\frac{\mathrm{d}T}{\mathrm{d}\lambda} = T\left[\bar{a} + \frac{3\lambda^2}{\lambda^3 - 1} - \frac{2}{\lambda}\right] \tag{30}$$

it is seen that \bar{a} no longer has the same simple meaning as a, the slope of the $dT/d\lambda$ vs. T curve. However, the exponential factor in equation 29 is so powerful that as far as the mesentery is concerned, equations 29 and 30 plot out to be almost the same curves as those of equations 13 and 10, respectively, with only a slight difference between a and \bar{a} . In the arteries, for which λ^* is of order 1.6 and the significant range of λ is 1 to 2, the polynomial factor introduced in equation 29 become very important.

The same factor may be introduced into the more accurate formula 18 to obtain the Lagrangian stress

$$T = \left(\lambda - \frac{1}{\lambda^2}\right) \frac{e^{\overline{a}\lambda}}{\overline{C} + be^{\overline{a}\lambda}}, \qquad (1 \le \lambda \le \lambda_y) \quad (31)$$

where

$$\overline{C} = \left[\left(\lambda^* - \frac{1}{\lambda^{*2}} \right) \frac{1}{T^*} - b \right] e^{\overline{a}\lambda^*}$$
(32)

and the Eulerian stress

$$\sigma = \left(\lambda^2 - \frac{1}{\lambda}\right) \frac{e^{\bar{a}\lambda}}{\bar{C} + be^{\bar{a}\lambda}}, \qquad (1 \le \lambda \le \lambda_y) \quad (33)$$



FIG. 8. Tangential elastic modulus from hysteresis curves (specimen 3). Young's modulus (the slope of the load-deflection curve) of the rabbit mesentery plotted against the tension T. Note that the Young's modulus is not a constant as the linear theory assumes. For this figure, $l_0 = 0.865$ cm, $A_0 = 1.93 \times 10^{-2}$ cm², $\lambda_{ph} = 3.21$, T = 51.8 P dyncs/cm².

The comparison between these formulas, 13, 18, 24, 29, 31, and their appropriateness in the light of experimental results on other tissues, will be discussed in the section below. For the mesentery they are all applicable, with negligible differences between them.

King and Lawton (21) discussed the elasticity of body tissues in terms of statistical thermodynamics in analogy with polymer theory; hence it is of interest to compare the property of the mesentery with that of the rubbery material. We note that the molecular theory for rubberlike material yields as a first approximation a strain energy function of the form

$$W = C(I_1 - 3), \qquad I_1 = \lambda_1^2 + \lambda_2^2 + \lambda_3^2$$
 (34)

Hence the stress

$$\sigma = 2C\left(\lambda^2 - \frac{1}{\lambda}\right) \tag{35}$$

which is the polynomial factor in *equation 26* (see Treloar, 33). This same polynomial factor characterizes also a class of galvanized rubber known as the Mooney-Rivlin material, (see ref. 15, p. 26), for which the strain energy function is simply

$$W = C_1(I_1 - 3) + C_2(I_2 - 3), \qquad I_2 = \frac{1}{\lambda_1^2} + \frac{1}{\lambda_2^2} + \frac{1}{\lambda_3^2} \quad (36)$$

where C_1 , C_2 are constants, and the Eulerian stress in simple elongation is

$$\sigma = 2\left(\lambda^2 - \frac{1}{\lambda}\right)\left(C_1 + \frac{C_2}{\lambda}\right) \tag{37}$$

The Lagrangian stress is

$$T = 2\left(\lambda - \frac{1}{\lambda^2}\right)\left(C_1 + \frac{C_2}{\lambda}\right) \tag{38}$$

A more complex rubbery material was investigated by Rivlin and Saunders, (see ref. 15, p. 287 ff.), who proposed the strain energy function

$$W = C(I_1 - 3) + f(I_2 - 3)$$
(39)

where $f(I_2 - 3)$ is some function of the second invariant.

The absence of the characteristic exponential factor of *equation 29* from *equations 35* and *38* indicates that the mensentery is entirely different from vulcanized rubber.

APPLICATION TO OTHER TISSUES

The stress-strain law of the mesentery and blood vessels has much in common with other soft tissues. In the literature, definitive results on simple elongation are known for the skin, the tendons, and the muscles. Some of these will be reviewed below. Many other soft tissues, such as the lung, bladder, etc., have nonlinear load-deflection relationships that appear similar to what we have shown above, but experimental results on these whole organs cannot be compared with the results of simple elongation experiments.

Muscle. According to Hill (16–19), active muscle can be considered in terms of an active contractile element arranged in series with a passive (series elastic) element. The series element is functionally, but not necessarily structurally, separated from the contractile element. At rest, the contractile element is thought to be highly extensible and the resting tension is attributed primarily to another elastic component airanged in parallel with the contractile and passive elements named above. When activated, the contractile element develops tension and shortens at such a velocity that the power (rate of doing work) rapidly reaches a constant. As the contractile element shortens, the passive element is extended. The tension in the muscle is determined by the shortening of the contractile element, elasticity of the series elastic element, and the external end condition (whether fixed or moving). To separate and to measure these two elements require, of course, great ingenuity.

Aubert (1) has verified Hill's ideas and presented the exponential form $P = P_0 e^{-l/l_0}$ as the load-extension relation for the series element of the sartorius muscle. Here *l* is the instantaneous length of the muscle. Jewell



FIG. 9. The $dP/d\lambda$ vs. P plot the P vs. λ plot of the cat papillary muscle obtained by Sonnenblick (30). P = total tension.Note the similarity between these curves and those in Figs. 2 and 8. Interchange abscissa and ordinate in the right-hand figure before comparing with Fig. 2.

and Wilkie's (20) result on the frog's striated muscle (sartorius) was summarized by the equations

$$P = 7 e^{l/0.315} - 6 \text{ when } P < 15 \text{ g wt} P = 70 l - 9.2 \text{ when } P > 15 \text{ g wt}$$

Thus the exponential form of the stress-strain law has been known for some time with respect to the series element of the muscles.

Heart muscles. Quantitative study of the series (passive) elastic element of the heart muscle provides another example of the straight line relationship between dP/dland P, (or $dT/d\lambda$ vs. T). Sonnenblick's (30) result on cat's papillary muscle is reproduced in Fig. 9. whose similarity with Fig. 8 is evident. The integrated loaddeflection curve, as shown in Fig. 9 (right) does not go through the origin. This is necessarily the case if no modification such as those suggested in equation 24 or 29 were made. In the case of heart muscle the initial intercept may be identified with the preload. The diffculty of establishing the initial muscle length must be appreciated. Sonnenblick (30) determined it by applying a small initial force (40 g/cm² as against the developed isometric force of 600 g/cm^2). In view of the mesentery results, we believe that the details of the load-extension curve at small λ may very well have been masked by this small initial load.

Sonnenblick found that the $dT/d\lambda$ vs. T curve is was

independent of the initial muscle length. The series elastic element stretched to an amount of 8-10% of initial muscle length during the development of maximum isometric force (600 g/cm^2). (In a most recent revision (26), it was shown that the earlier data did not give full correction to the elasticity of the testing equipment. When proper corrections were made the figure on the stretching of the series elastic element of the cardiac muscle was reduced to 4-5%.)

Muscle fibers and myosin filaments. Dubuisson and Monnier (8) studied the elastic properties of myosin filaments. Their data are shown in Fig. 10. F_7 refers to freshly prepared myosin filaments placed in water buffered by phosphate (concentration 0.015_M) solution to pH 7.00 (normal pH of muscle at rest). A_7 refers to aged myosin filaments (aged 25 days at laboratroy temperature and exposed to daylight) at pH 7.00. $F_{5.5}$ and $A_{5.5}$ refer to fresh and aged filaments placed in water buffered to pH 5.5 (the isoelectric point). Also shown in Fig. 10 are Buchthal's data (7) for a tetanically contracted single striated muscle fiber (shown by \times) and a resting striated muscle fiber (shown by Δ). We tried to fit Dubuisson and Monnier's data with the theoretical equation 29 with the following constants:

for 1	$A_{5.5}$:	λ*	=	1.60	ā	=	0.61	T^*	=	8.45
for <i>i</i>	$F_{5.5}$:	λ*	=	1.40	ā	=	0.01	T^*	=	4.40
for <i>i</i>	F_7 :	λ*	=	2.20	ā	=	0.01	T^*	=	3.60

f



FIG. 10. Tension-elongation curves of myosin filament by Dubuisson and Monnier (8); F_7 , fresh filament placed in pH 7.00; A_7 , aged filament in pH 7.00; $F_{5.5}$, fresh filament placed in pH 5.50; $A_{5.5}$, aged filament in pH 5.50. Buchthal's (7) data for isolated striated muscle fiber stretched during tetanic contraction, and at rest. Solid curves, eq 29. Dotted curve, eq. 13.

The curves corresponding to equation 29 with these constants are plotted as solid lines in Fig. 10. The fit is reasonable, but some deviations exist. For Buchthal's tetanically contracted fiber the same constants as F_7 apply. For his resting muscle fiber the following equation 13 applies:

$T = 34.3 \ e^{-10.3(\lambda - 1.60)}$

This is shown as a dotted curve in Fig. 10. For Buchthal's data in Fig. 10 the ordinate should be regarded as tension in milligrams instead of kilograms per square centimeter as labeled.

King and Lawton (21) showed that a good fit to the F_7 curve in Fig. 10 for λ in the range 1–2 is obtained by the following equation derived from a statistical theory of polymer molecules:

$$T = 3.02 \left(\lambda^2 + \frac{2}{\lambda}\right)^{-2/5} \left(\lambda - \frac{1}{\lambda^3}\right) \text{ kg/cm}^2 \qquad (40)$$

Beyond $\lambda = 2$, King and Lawton's formula deviates greatly from the experimental data.

Skin. A typical load-extension curve for the skin from the abdomen of a 2-day-old male was given by Ridge and Wright (27), and reproduced in Fig. 11. This curve was obtained at a constant rate of 0.508 cm/min. The extension process could be divided into three phases, for which Ridge and Wright gave the following load-extension relations (when converted to our notations):

phase 1: (0-100 g):
$$\lambda = x + y \log T$$

 $T = e^{(\lambda-x)/y}$
phase 2: (100-1,000 g): $\lambda = c + kT^b$
phase 3: yielding and failure

where x, y, c, k, b are constants. The equation for the first phase may be identified with our *equation 11*. The second and the third phases are also similar to what we have shown in Fig. 7. However, whereas the second phase is relatively small in the mesentery, it is predominant in the skin.

DISCUSSION

From the point of view of mechanics, the next important step is to generalize the one-dimensional equations to three dimensions. This will be presented in a separate paper.

The specific results of the exponential elastic response and the exponential relaxation function are applicable to the mesentery and arteries only when the stresses are sufficiently small. Under unlimited stresses the specimen deviates from these laws and ultimately fails.

Aside from the usual measurements of the dimensions of the tension test specimen, it is important to obtain the relaxed length of the specimen, i.e., the length l_0 , when the specimen is unstressed. The extension ratio λ is based on l_0 .

The necessity of obtaining the natural relaxed state becomes evident when one tries to generalize the results of simple elongation to three-dimensional laws. For example, in simple elongation of the mesentery there exists a limiting large strain (of order 100-200% elongation) below which the stress is essentially zero. In a threedimensional stress field, there exist an infinite number of states of large strain (combinations of tensile strains and shear strain) within which the stress is negligibly small. One might think that any one of these strain states may be taken as a starting point for a stress-strain law, but if one did this the result will be very confused or cumbersome. The only state that has a unique claim as a starting point is the fully relaxed natural state. This is the natural unstrained state which fortunately exists for a soft tissue. However, how can we determine this state in a living tissue? I have no simple answer to this question. It is one of the most difficult questions to answer in biological experiments, and it is one that deserves the closest attention.

We note that, in general, the resting configuration of a soft tissue in the body is not the unstrained state. Anyone with the experience of cutting a major artery will find the vessel shrink away from the cut. The spreading hole in the cut mesentery as shown in Fig. 1 is another example.

CONCLUSION

A formulation of the stress-strain law applicable to simple elongation tests of some soft tissues is presented.



FIG. 11. Ridge and Wright's (27) load-extension curve of skin from the abdomen of 2-day-old male. Test has been carried to yielding and shows three phases. Gauge length = 1.0 cm.

This formulation may be used in the lower stress range. Since the proposed law is about the simplest possible that includes the known features of large deformation, it is suggested that other living tissues be tested against the same law in order to establish whether and how modifications are necessary.

For the mesentery, the series element of the heart muscle, and the skin at lower stress range, the elastic tension is approximately an exponential function of the extension ratio. Significant stress occurs only under a finite deformation. In the mesentery, an extension more than doubling the natural unstrained length of the specimen is necessary before significant stress response occurs.

According to these facts, it is elementary, but perhaps important, to point out that the usual practice of presenting a Young's modulus of elasticity for a blood vessel is meaningless. Young's modulus of a living tissue varies

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with the stress; and in the case of dynamic process, with the rate of change of stress; and finally, with the history of stress, if the specimen is tested in repeated loading and unloading. The literature on Young's modulus of living tissues could be salvaged only if it were possible to assign a stress level at which that modulus was obtained. Since this was practically never done, the significance of most of the published data is open to question.

On the other hand, the slope at the origin a and the curvature 2ab of the $dT/d\lambda$ vs. T curve are constant over the physiological range for many soft tissues. These parameters, together with a specific tension (or Lagrangian stress) T^* at a specific extension λ^* , completely characterize the elastic curve. They are the candidates for data collection and data presentation.

APPENDIX

List of Symbols

a	slope of the $dT/d\lambda$ vs. T curve, see eqs. 10, 17, and 22
ā	value of a modified by the zero factor, see eas. 28-33.
A, A_0, A_{nh}	cross-sectional area, at l , l_0 , and l_{nb} , respectively
h , , , , , , , , , , , , , , , , , , ,	curvature of $dT/d\lambda$ vs. T curve, see eq. 17
c C	integration constants see eas 12 19 respectively
F	Voung's modulus (tangential modulus)
$f(\lambda)$	elastic tension a function of)
F(z)	elastic tension, a function of x
$\Gamma(\epsilon)$	clastic stress, a function of strain e
lo	the relaxed length of test specimen (between bench marks)
1.	length of specimen at time when it was cut
ph D	force
1	
t T	time
	Lagrangian stress in specimen, tension/initial area
7*	Lagrangian stress in specimen when the extension ratio is λ^*
T_{π}	asymptotic value of Lagrangian stress at large time
$\widetilde{W(\lambda)}$	strain energy function
γ_{ii}	strain tensor components
e	strain
λ	extension ratio
λ*. λο	specific values of λ
λ_1 , λ_2 , λ_3	three principal extension ratios
λ	the upper limit of validity of the exponential stress
Λ_y	strain relationship
-	stress (Fulerian)
U _*	olostio stassa (Eulerian)
σ	clastic stress (Eulerian)
au	time

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