Elasticity of Keratin Fibers.   II.   Influence of Temperature

BY HENRY B. BULL

In a previous[1] paper we described experiments on the stress–strain relations of human hair fibers at a constant rate of loading and unloading. While such experiments are capable of yielding valuable and useful information, their utility in interpreting the fundamental nature of the elasticity of keratin is severely limited. In the present paper an attempt has been made to study the influence of temperature variations on the stress while maintaining a given stretch of the fiber. From these results an approximate calculation of the stress due to the internal energy and to the heat motion can be made.

Experimental.—The hair fibers were of a lot of natural human hair which had been exhaustively extracted with alcohol and ether and then electrodialyzed. About twenty individual hair fibers were made into a strand and the stress determined as a function of the temperature. By using a large number of hairs, the individual variations of the hairs were to a great extent eliminated and, second, the stress became large enough so that the comparatively small variation of the stress with the temperature could be measured with some accuracy. The diameter of each hair was measured with a microscope equipped with a micrometer and the total cross sectional area of the hair calculated on the assumption that each hair was a uniform cylinder; an assumption which is not far from true. This information allows the stress to be expressed in kilograms per square centimeter of hair cross section. It was further assumed that the hair undergoes no volume change during extension and that the cross sectional area at any given extension was inversely proportional to the stretch.

The tension apparatus was arranged so that the hair could be conveniently and accurately stretched to any desired extension and this extension maintained for any period of time. The hair was bathed in water while in the apparatus and the glass tube containing the hair under examination was surrounded by a water jacket through which water at any desired temperature between 15 and 60° could be circulated.

The stress on the hair, after the hair had been stretched to a given extent at 60°, decayed at a decreasing rate with time and at the end of about two hours the rate of decay had become very small. After this stress value was attained and recorded, the temperature was lowered by definite steps to about 17°. The adjustment of the stress to a change in temperature was very rapid and appeared to be complete as soon as the water-bath had come to temperature.

A second strand of 20 hairs was stretched to 25% extension at 60° and the temperature dependence of the stress measured as the hair was allowed to contract to 20, to 15, to 8 and to 4% extensions. In the case of the hair undergoing contraction, the stress increased with time. The temperature variation of the stress was studied after the rate of increase of the stress with time at 60° had become very small.

Results.—Table I shows the stress in kilograms per square centimeter of cross section of hair as a function of the temperature both for hair undergoing extension as well as for hair which is contracting.

Discussion.—What we are dealing with in the deformation of hair is evidently a very compli-

TABLE I

STRESS ON HAIR FIBERS AS A FUNCTION OF THE TEMPERATURE AND OF THE STRETCH

Extension			Contraction		
% Stretch	Temp., °C.	Load in kg./sq. cm.	% Stretch	Temp., °C.	Load in kg./sq. cm.
2	53	65.27	4	62	65.49
	40	68.20		38	69.67
	28	70.87		28	71.54
	17	72.40		18	72.09
5	53	181.72	8	58	93.89
	38	185.10		37	95.74
	28	186.41		28	95.93
	17	187.52		19	95.25
8	55	194.33	15	55	125.34
	38	195.67		38	125.76
	28	196.24		28	125.34
	17	196.45		18	124.71
15	56	212.31	20	56	161.01
	38	211.69		38	160.78
	28	211.46		28	160.45
	18	210.85		18	159.89
25	53	229.39	25	58	232.14
	37	229.30		38	229.76
	27	228.44		28	228.93
	18	227.39		18	228.45
35	58	246.50			
	38	244.00			
	28	243.10			
	17	242.40			

cated phenomenon; there are no doubt a number of elastic elements present and these elements probably act both in parallel and in series. For a single elastic element Maxwell's equation should be valid, i. e.

$$E = E_0 e^{t/\lambda} \qquad (1)$$

where E is the modulus of elasticity at any time, t, after the application of the stress, E_0 is the modulus of elasticity at zero time and λ is the mechanical relaxation time of the fibers. For a number of elastic elements in series, it should be possible to represent the stress–strain behavior by as many terms in equation 1 as there are elastic elements present.[2] The plot of the logarithm of the stress against the time does indeed yield a curve for hair which can be broken up into more or less straight lines but there is too much overlapping and too much uncertainty to allow even approximate evaluations of the separate λ values.

Having failed to obtain satisfactory analysis of the rate of decay of the stress in terms of the mechanical relaxation times, it was decided to measure the $^1/_5$-time of the stress of a hair fiber as

(1) Bull and Gutmann, THIS JOURNAL, **66**, 1253 (1944).

(2) Kuhn, Angew. Chem., **52**, 289 (1939).

a function of the stretch. The hair was stretched as rapidly as possible until the external load which had been fixed at a desired value was exactly counterbalanced by the hair. The hair was held at this stretch and the time in seconds required for the stress of the hair to decay to $^4/_5$ of the initial load measured. These results are shown in Fig. 1. From the above discussion it is clear that an equilibrium load for a hair fiber is meaningless because the load decays with time and while the rate of decay constantly diminishes, at infinite time the load at any stretch would be zero. While it is not shown in this paper, the rate of decay of the stress at higher temperatures is very much greater than it is at lower temperatures.
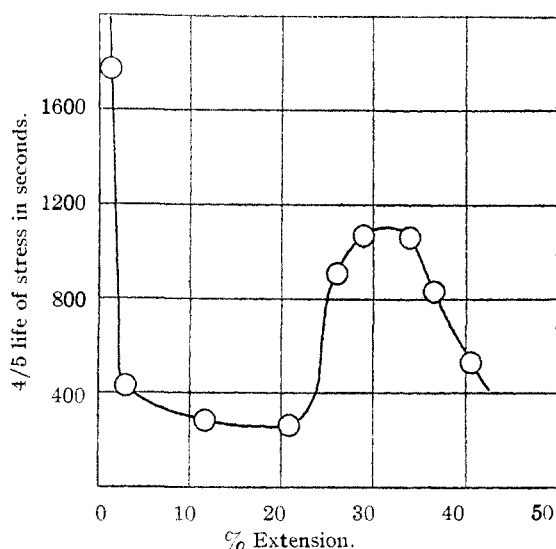

Fig. 1.—Four-fifths time of the stress of a single hair fiber as a function of the stretch at 25°.

The situation described above for hair is, in general, true of all elastic bodies. It is then a question as to how far one can go in the analysis of the thermal data reported in Table I in terms of the conventional thermodynamic methods. Wiegand and Snyder[3] have reported an equation based upon thermodynamics which enabled them to separate the stress of an elastic body into that part due to internal energy and into the part due to the entropy change. This equation has been used by Guth[4] and by others to analyze the thermal data on rubber and by Wöhlisch[5] on similar data from the study of the elastic properties of muscle, collagen and elastin. Perhaps the only justification for the use of the Wiegand-Snyder equation is that the change of the stress in response to temperature is very much greater than the corresponding decay of the stress during the time required for a measurement. According to

(3) Wiegand and Snyder, Trans. Instn. Rubber Ind., 1, 141 (1925).
(4) Guth, "Surface Chemistry," Am. Assoc. Sci. Pub. No. 21, p. 103 (1940).
(5) Wöhlisch, Arch. Ges. Physiol. Pflügers, 246, 469 (1942); Kolloid-Z., 104, 14 (1943).

Wiegand and Snyder the load can be resolved as follows

$$F = F_u + F_s \qquad (2)$$

where F is the total force exerted by the elastic body, F_u is the force due to the internal energy and F_s is the entropy term. The entropy term F_s is given by the relation

$$F_s = T(\delta F/\delta T)_L \qquad (3)$$

Accordingly, if we plot the stress against the temperature and multiply the slope of the line by the absolute temperature, we obtain F_s. When this value is subtracted from the total stress on the fiber, the difference is the force due to the internal energy F_u.

The data given in Table I have been plotted in this manner and F_s and F_u calculated. The variations of F, F_s and F_u with the stretch of the fiber at 25° are shown in Fig. 2 both for the hair undergoing extension as well as for hair being contracted from a 25% initial stretch.

The plot of the stress against temperature (data from Table I) leaves something to be desired as far as all of the experimental points for any given stretch falling exactly on a straight line. In no case, however, could the observed experimental variation change the final results as shown in Fig. 2 in any significant respect.

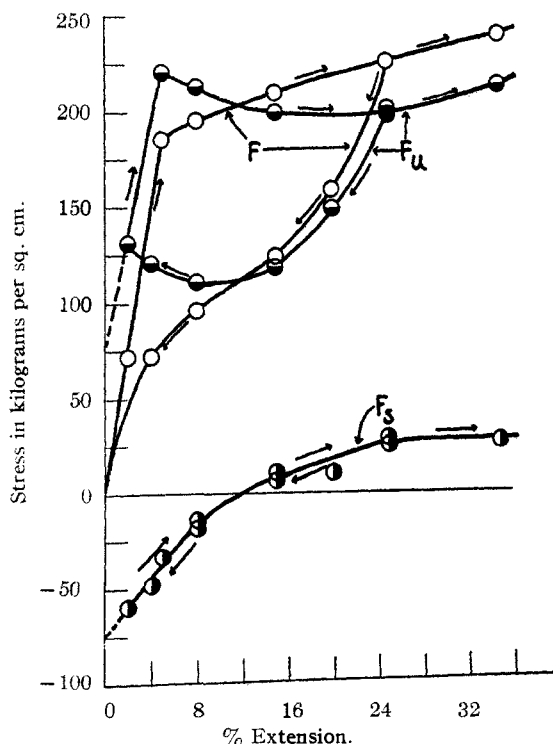As with the stress–strain curve at a constant rate of loading[1] there is a break in the curve at

Fig. 2.—Total stress (F), entropy term (F_s) and the stress due to the internal energy (F_u) as a function of the stretch both for extension and for contraction (indicated by directed arrows) at 25°.

about 5% extension. In the present study, however, the break is much sharper. There is likewise a large area of irreversibility between the extension and the contraction curves. In short, the qualitative resemblance between the stress-strain curve as determined by the present method and that at a constant rate of loading and unloading is marked.

The force due to the internal energy undergoes a very sharp break at about 5% extension and actually decreases from this point on to an extension of about 20%. The sharpness of this break indicates a phase transition which we have previously intrepreted[1] to be in the nature of a thixotropic gel → sol transformation. The present data are in keeping with such an interpretation. The internal energy of contraction exhibits a considerable area of irreversibility and the stress–strain curve shows a minimum at a stretch of about 12%. The deviation of the contraction curve of the internal energy from that of the extension curve is probably a reflection of a decrease in the number of secondary chemical bonds acting.

It is reassuring that the entropy term is apparently reversible in respect to both extension and contraction. This fact may be considered as additional support for the use of the Wiegand–Snyder equation in the analysis of our present problems. At zero extension the entropy has a large negative value and as such actually favors extension of the fiber. This probably means that the hair exists in nature in an ordered arrangement and it becomes more disordered as it is stretched, at least up to an extension of about 12% where the entropy term becomes zero. Beyond 12% extension, the hair becomes more ordered as it is stretched, i. e. the entropy term becomes positive and reaches more or less a constant value at about 25% extension.

Drawing a tangent to the entropy stress–strain curve at 12% extension, we find that the modulus of elasticity which is due entirely to the entropy change is 3.6×10^8 dynes per square centimeter of hair. We must remember, however, that about 20% of a human hair is composed of cuticle[6] which presumably does not take part in the long range elasticity of hair which we are describing. We must also bear in mind that at saturation of water vapor, keratin takes up about 40% of water.[7] The modulus of elasticity which is due to the entropy change and which involves only the dry weight of the cortex of the hair is then about 7.5×10^8 dynes per square centimeter. In a statistical analysis of elasticity, Flory and Rehner[8] derived the equation

$$E_s = 3RT\rho/M_c \qquad (4)$$

In the above equation E_s is the modulus of elasticity which arises from the entropy change, R is the gas constant, T is the absolute temperature,

ρ is the density of the elastic body, and M_c is the molecular weight of one chain. Substituting the appropriate data in equation 4, we find that the molecular weight of the molecular chain is about 135. This value is extraordinarily small and is not much greater than the average residue weight of keratin[9] which is 112. Even allowing for a very generous margin for error, this indicates a very tightly bound network structure for hair with frequent cross links between peptide chains.

Our results present some resemblances to and some contrasts with similar calculations for rubber. Referring again to Guth's[4] paper, we see that for a given stretch the corresponding stress for hair is very much greater than it is for rubber. In fact, the two stresses are almost of a different order of magnitude. Both the internal energy and the entropy terms are much larger for hair than for rubber. For hair, the largest positive entropy term amounts to only 14% of the force due to the internal energy while for rubber the entropy term is about four times larger than the force due to the internal energy.

We can conclude that the principal elastic element of hair involves the internal energy and that the entropy change or the force due to the Brownian motion of the peptide chains is, relatively, of minor importance. Hair behaves as a very much more imperfect "gas" than does rubber.

As pointed out by Guth[4] it is not possible to resolve the internal energy or the entropy term into their kinetic and potential energy parts on the basis of thermodynamics alone and our information concerning the molecular structure of keratin is too limited to enable us to attempt this resolution on the basis of molecular structure; we have tentatively and implicitly assumed in this paper that the entropy term is principally of a kinetic nature and is due to the heat motion of the molecules while the internal energy is mainly due to intermolecular forces.

Exposure of hair to a temperature of 60° would not be expected to break disulfide or other covalent bonds but no doubt the stress–strain characteristics have been changed by exposure to this temperature. It is believed, however, that a study of such fibers has an inherent interest even though they are not identical with "natural" hair.

.It is a pleasure to acknowledge the critical comments of Drs. E. Guth and M. L. Huggins.

Summary

1. The stress on human hair has been measured over a temperature range of from 17 to 60° at various stretches both for extension and for contraction.

2. The four-fifths life of the stress on a human hair at various stretches is reported.

3. The stress on hair has been resolved into that due to internal energy and that due to heat motion.

(6) Rudall, Proc. Leeds Philos. Soc., 4, 13 (1941).

(7) Bull, THIS JOURNAL, 66, 1499 (1944).

(8) Flory and Rehner, Ann. N. Y. Acad. Sci., 44, 423 (1943).

(9) Bailey, "Advances in Protein Chemistry," ed. by Anson and Edsall, Academic Press, Inc., New York, N. Y., 1944.

4. It is found that the force of contraction due to the internal energy is, in general, very much larger than that due to the entropy change. It is therefore concluded that the elastic element of hair involves principally the internal energy. In this respect the elasticity of hair is in sharp contrast with that of rubber.

CHICAGO, ILL.   RECEIVED DECEMBER 26 ,1944

The Synthesis of Arsenicals Containing Certain Heterocyclic Nuclei

BY E. J. CRAGOE, JR., AND CLIFF S. HAMILTON

Within the past few years organo-arsenic compounds which contain a heterocyclic nucleus have gained considerable interest as therapeutic agents.[1,2,3] Particular interest has been attached to those derivatives in which the heterocyclic nucleus is linked through an amino group to an aromatic ring bearing an arsenic atom. Since only a few heterocyclic types had been studied, it was the purpose of this investigation to extend the study to other heterocyclic nuclei. Hatlelid[2] had previously prepared 2-(p-arsonoanilino)-5-nitropyridine (I) and the corresponding m-derivative (II) by condensing p- or m-phenylenediamine with 2-chloro-5-nitropyridine (III) followed by the Bart[4] reaction on the resulting aminoanilino-5-nitropyridine.

In this investigation these compounds, (I) and (II), have been produced by the condensation of p- or m-arsanilic acid with 2-chloro-5-nitropyridine, (III), using aqueous media containing one equivalent of acid.[5] Reaction has also been successful between o-arsanilic acid and (III) to produce 2-(o-arsonoanilino)-5-nitropyridine (IV), which could not be prepared by the method used by Hatlelid to synthesize the p- and m-isomers.

Similar condensations occur when (III) is allowed to react with 3-amino-4-hydroxyphenylarsonic acid or 2-hydroxy-4-aminophenylarsonic acid. Like reactions have been observed between m-arsanilic acid and 2-bromopyridine, 2-bromothiazole, or 2-chloro-4-methylthiazole. p-Arsanilic acid reacts with these same haloheterocycles and also with 2-chlorobenzothiazole.

The reaction also has been extended to include haloheterocycles with a halogen atom gamma to the ring nitrogen. 4-Chlorobenzo(h)quinoline reacts with m- or p-arsanilic acid and 1-chlorobenzo(f)quinoline reacts with these same amines and also 3-amino-4-hydroxyphenylarsonic acid. With 3-bromopyridine, where the halogen atom is beta to the ring nitrogen, no reaction occurs with p- or m-arsanilic acid.

Binz and co-workers[6] reported the preparation

of a few N-substituted derivatives of 2-amino-5-arsonopyridine and indicated these compounds to be of therapeutic value. However, derivatives in which an aromatic or heterocyclic residue was substituted on the amino nitrogen had received little or no attention. 2-(Arylamino)-5-arsonopyridines are produced readily by the action of 2-chloro-5-arsonopyridine (V) upon aromatic amines using aqueous media under acidic conditions. Reaction is also successful when (V) is condensed with γ-aminopyridines such as 2-N-morpholino-5-aminopyridine (VI) or 2-N-thiomorpholino-5-aminopyridine (VII); however, with heterocycles containing an amino group in the position alpha to the ring nitrogen, such as 2-aminopyridine and 2-aminothiazole no condensation product is isolated. Since all of these reactions belong to the same general type described by Banks,[5] the results obtained serve further to verify and extend the application of this acid catalyzed reaction.

A review of earlier work[7] reveals that a labile halogen atom such as that in 3-nitro-4-bromophenylarsonic acid (VIII) will condense with strong amines in aqueous solution containing alkali. Although this reaction had previously been applied to only two heterocyclic amines, piperidine and piperazine, it is readily extended to include both morpholine and thiomorpholine.

The catalytic method, using molecular hydrogen and Raney nickel, has been applied successfully to the preparation of 2-(o-arsonoanilino)-5-aminopyridine (IX) from the corresponding 5-nitro- derivative, (IV); however, this method is found unsatisfactory for the reduction of 4-N-morpholino- (X) and 4-N-thiomorpholino-3-nitrophenylarsonic acid (XI). Likewise, reduced iron powder and water give unsatisfactory results, but by using ferrous hydroxide, the corresponding 3-amino- derivatives, (XII) and (XIII), are obtained in low yields.

N-(p-Arsonobenzenesulfonyl)-thiomorpholine (XIV) is prepared by conventional methods.

Experimental[8]

The preparation of o-arsanilic acid[9] (70%), 2-bromopyridine[10] (b. p. 97–99° (35 mm.), 52%), 2-chloro-5-

(1) Friedheim, Schweiz. med. Wochschr., 71, 116 (1941); C. A., 36, 1676 (1942).

(2) Hatlelid, Doctor's thesis, University of Nebraska, 1942.

(3) Banks, Gruhzit, Tillitson and Controulis, THIS JOURNAL, 66, 1771 (1944).

(4) Bart, Ann., 429, 55 (1922).

(5) Banks, THIS JOURNAL, 66, 1127, 1131 (1944).

(6) Binz and Rath, Ann., 455, 127 (1927); Binz and Maier-Bode Angew. Chem., 49, 486 (1936).

(7) Maclay and Hamilton, THIS JOURNAL, 54, 3310 (1932).

(8) The melting points of all arsenicals were taken by the method of Morgan and Hamilton, THIS JOURNAL, 66, 874 (1944).

(9) Kalb, Ann., 423, 39 (1921).

(10) Craig, THIS JOURNAL, 56, 231 (1934).