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# RIGIDITE ET PLASTICITE DU MUSCLE STRIE EN CONTRACTURE IODOACETIQUE

PAR

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# RIGIDITY AND PLASTICITY OF STRIATED MUSCLE IN IODOACETIC CONTRACTURE

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(6 figures)

## Introduction

After vigorous tetanic excitation, a muscle poisoned by mono-iodoacetic acid (IAA) enters into contracture and, if maintained at a constant length, develops an important fraction of its tetanic tension (SANDOW and SCHNEYER, 1955, MARÉCIIAL, 1958) . Although the phenomenon is irreversible, inasmuch as it is impossible to obtain a new contracture on the muscle, this tension disappears spontaneously within a few hours. In this case, MAURIELLO and SANDOW (1959) have made various arguments to show that the development and disappearance of contracture would correspond to the evolution of an active state comparable to that which was used during the muscular twitch but at very long time scale.

Although the chemical determinism of contracture has been the subject of much research (cf. GODEAUX, 1950 and MARÉCIIAL, 1958), relatively little is known about the physical properties of the muscle in this state (PETIT, 1931b, AUBERT, 1956 SANDOW et al., ). Rheological methods make it possible to obtain certain information on the structure of high polymers. Applied not only during the contracture plateau. as AUBERT (1956) did, but also during the phase of the disappearance of tension, they illuminate the nature of this apparent relaxation

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The experiments reported in this work do not support the hypothesis of SANDOW and his collaborators. They demonstrate that at every moment of the contracture cycle the muscle remains characterized by a great stiffness and that the relief of tension is explained by phenomena of plastic and viscous glides. The discussion of these results shows that the evolution of the isometric contracture resembles much more the tonic contraction of the muscles of Lamellibranchs than the muscular twitch of the striated muscle,

## Techniques

The experiments were performed on sartorius muscles of frog (Rana Temporaria). Muscle length $l_o$ is measured placing the thighs in abduction at 90°; This length is the reference length, $l_o$, the length *in situ*. The two muscles are dissected up to the coxal bone, to which they remain attached. The pair of muscles is mounted on an assembly that carries six platinum electrodes for each muscle of the pair; the coxal is fixed by a forceps, and the two distal tendons are connected to the tensionmeter by a glass tube. The muscles were immersed for 1 hour in vigorously oxygenated Ringer (NaCl, 115.5 mM, KCl, 2.0 mM, $CaCl^2$, 1.8 mM and a mono-sodium and bisodic phosphate buffer1.9 mM adjusted to pH 7.3, T°: 18 ° C). They are then extended to a length of 10 2 mm for the measurement of the tetanic tension $P_o$, which is maximum at this length (AUBERT, ROQUET and VAN DER ELST, 1951). To the Ringer is added sodium monoiodoacetate at a final concentration of 0.4 mM. After one hour, the toxic solution is removed and the preparation is henceforth suspended in an humid atmosphere, and oxygenated during the remainder of the experiment.

The muscle is excited directly. An electronic Morse key key allows to charge and to discharge alternatively, a capacitor of 0.5 microfarad through a resistance of 6000 ohms. at a frequency of 25 per second. The six electrodes are connected in parallel to the 6000 ohm resistor, through a resistance of 37,000 ohms in series. The six electrodes laying on each muscle of the pair are alternatively cathodes and anodes. The duration of the tetanus is controlled by a manual key

The tension developed by the muscle deforms a steel blade on which are attached four strain gauges Phillips PR 9214. The stiffness of the tensionmeter system is 2 kg / cm. These gauges form the arms of a bridge whose unbalance is measured by a "Multiplex" galvanometer of Lange. A spot tracker ("Nachlaufsehreiber" by Lange) records the deflection of the galvanometer.

The elongation of the muscle is obtained by vertical displacement of the tensionmeter. In the majority of experiments, the tensionmeter was attached to the movable arm of an ergometer lever of the type described by LEVIN and WYMAN (1927). This lever is perfectly suited to lengthen the muscle at a constant and regular speed between 10 cm per s. and 1 mm in 14 s. In some experiments, the tensionmeter was connected to a sliding plate on an Archimede screw set in motion by an electric motor; The movement of this apparatus is not absolutely regular, which leads to the appearance of an artifact in the trace of tension. For example, it can be seen in fig 3.

## Results

### 1. - THE SPONTANEOUS DISAPPEARANCE OF THE CONTRACTURE

After a prolonged tetanization at constant length, a muscle intoxicated by monoiodoacetic acid develops a contracture which reaches its maximum amplitude in two to three minutes (Figure 1). Then the tension begins to decrease and disappears completely within a few hours. In five experiments at 18° C. the contracture tension had fallen 60 % in two hours and disappeared in four hours. But in another case, it disappeared much more slowly, and it still reached 10% of its maximum value after a dozen hours. The rate of disappearance of the tension varies greatly during a same experiment, and does not appear to obey any determinate law. Finally, it should be pointed out that if the muscle is plunged into Ringer instead of being stored in a moist chamber as in the experiments mentioned, the disappearance of the contracture tension is much more rapid and is complete in an hour. LIPPAY and PATZL (1935) had already pointed out the effect of the bath on the contracture, which is perhaps related to the leakage of phosphates in the Ringer (HERMANS, 1956)

This gradual disappearance of tension could be interpreted, by analogy with the relaxation of the normal contraction, as a diminution of the bonds between the structural proteins. This should be accompanied by a fall of the modulus of elasticity. This is the hypothesis suggested by SANDOW and SCHNEYER (1955), and quite recently again, by MAURIELLO and SANDOW (1959).

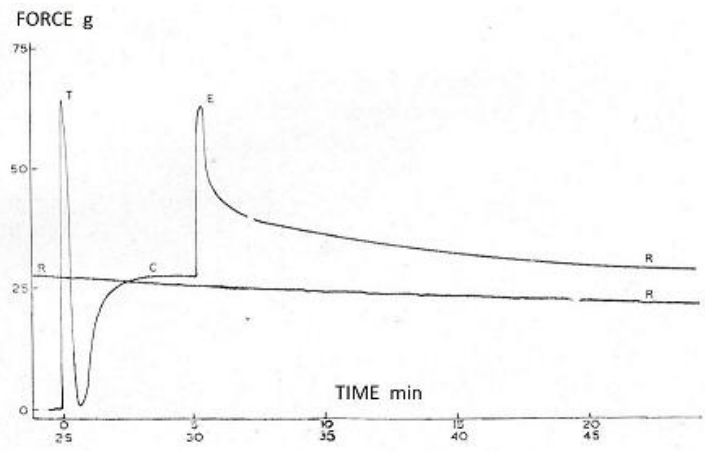


Figure 1. - Double frog sartorius; Weight: 120 mg. ; Length: 30 mm. ; T°: 18°C. - Poisoning for 1 h. by IAA 0.4 μM. - Tetanus conditioning (T), at length of 30 mm, followed by contracture (C), stretch of 1.38 mm in 14 seconds (E), stress-relaxation (R)

It is, however, remarkable that the intoxicated muscle thus "relaxed" is not at all comparable to a muscle at rest. As will be shown in paragraph 2, the great stiffness, very characteristic of the muscle in contracture, disappear undoubtedly much more slowly than the tension of contracture. In an experiment analogous to that of Fig. 1, the contracture tension reached 33 g, and a stretch of 2.18 mm. brought it to 85 g. Five and a half hours later the tension had dropped to 3 g, but a second stretch produced an increase in the tension to 40 g.

It is thus possible to ask whether the tension drop results from a creep, or more specifically, from an internal reorganization of the contractile proteins, certain connections broken under the effect of the tension reforms to a new position . The contractured muscle would therefore be just as rigid during its relaxation,

but its equilibrium length would have slightly increased. A similar phenomenon of internal slip has been reported in the case of the normal muscle in tetanic contraction: after a considerable stretch beyond the equilibrium length, the isometric tension-length diagram moved towards the long lengths without any appreciable change of the maximum tension or elastic modulus (AUBERT et al., 1953). A simple experiment, described in the following paragraph under the name of "intermittent tension", allows us to distinguish between the respective importance of the two mechanisms.

## 2. - INTERMITTENT TENSION

If the external constraint is nullified by sufficiently shortening the muscle in contracture so that it no longer exerts any tension, the reorganization of the contractile structure by internal sliding becomes improbable, while nothing opposes the possible chemical transformations characteristic of normal relaxation. A shortening of 1.5 mm, for example, is sufficient to cancel the tension of the muscle in contracture. If the muscle is brought back to its initial length thirty seconds every eight minutes, the maximum tensions of the successive stretches are almost equal (curve A, figure 2, table 1): it rises to 62% $P_o$ at the first, and 57% $P_o$ at the eighth, one hour after the beginning of contracture. Eleven hours later, a ninth stretch was still developing 57.5 g. or 47% $P_o$. If the deformity had been imposed continuously rather than only intermittently, the contracture would have completely disappeared at this time. In the experiments of Fig. 2, the external stress is applied for 4 minutes (curve B) or for 12.5 minutes (curve C ); The maximum tensions of the successive stretches decrease and decrease more rapidly when the duration of application of the strain is longer. Other experiments of the same type are reported in Table 1. It is evident that the ability to maintain a contracture tension at a determined length depends largely on external constrains. But it persists for a long time if this constrain is cancelled.

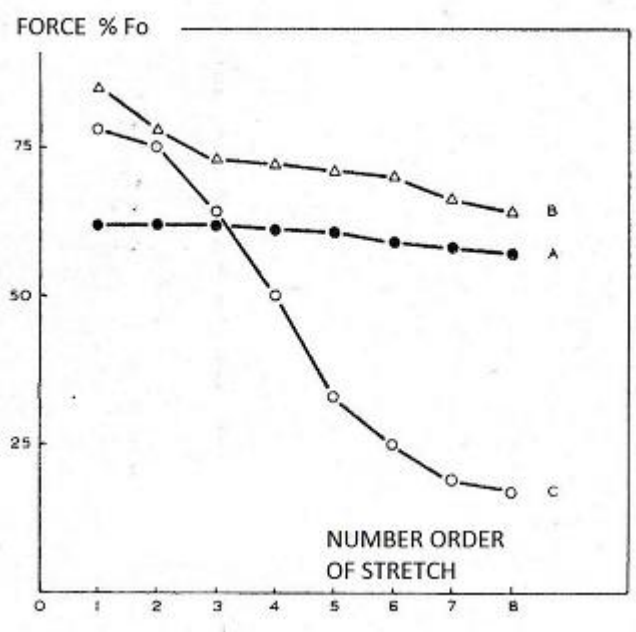


Fig. 2. Cycles of successive shortenings and stretches between two constant lengths of three contractured muscles. At short length, the muscle tension is zero; the maximum sustained tension is measured during a stretch of 1.38 mm. in 14 seconds. It remains constant in A, where the muscle is extended for thirty seconds every eight minutes; It decreases little in B, where the muscle is stretched four minutes every eight minutes, and collapses rapidly in C. where the muscle is stretched 12.5 min. every 25 minutes

**TABLE 1**

| Duration of stretch | Duration of relaxation | Number order of stretches | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 5 | 6 | 6 | 7 | 8 |
| 30 s. | 7.5 min. | 62 | 62 | 62 | 61 | 61 | 59 | 58 | 57 |
| 30 s. | 24 min. | 103 | 100 | 99 | 95 | 92 | 82 | 71 | 63 |
| 4 min. | 4 min. | 73 | 70 | 68 | 67 | 66 | 64 | 63 | 62 |
| 4 min. | 4 min. | 85 | 78 | 73 | 72 | 71 | 70 | 66 | 64 |
| 12.5 min. | 12.5 min. | 78 | 75 | 64 | 50 | 33 | 25 | 19 | 17 |
| 12.5 min. | 12.5 min. | 85 | 68 | 63 | 49 | 35 | 25 | 20 | 18 |

Force expressed in % $F_o$.

It thus appears impossible to assimilate the spontaneous disappearance of contracture to the relaxation which follows the normal contraction. It is similar to a phenomenon of creep. The experiments described in the following paragraphs will clarify this notion.

## 3. THE RESPONSE OF CONTRACTURED MUSCLE TO A STRETCH

The response of the contractured muscle to a stretch has two interesting characteristics: during stretching, the tension cannot exceed a certain limiting value; after stretching, the tension decreases according to a defined function of time. These two characters appear in Figure 1. An intoxicated muscle develops a maximum tetanic tension (point T, fig1) at length $l_0$. This tetanus causes the appearance of the contracture, which rapidly reaches its maximum in three to four minutes (point C, fig 1). Five minutes later, the muscle is extended by 1.38 mm. in 14 seconds. Despite the very low elongation velocity, the tension increases very rapidly from the beginning: the muscle is very rigid, and its Young's modulus varies from 7 to 30 kg./cm2 (30 determinations). When the tension during stretching approaches the tetanic tension Po, it does not increase much anymore, although the elongation continues: *a critical level is reached*, and this level is of the order of the maximum tetanic-tension. As soon as stretching ceases, the tension decreases following a regular curve. This regularity is all the more remarkable since the spontaneous tension of contracture disappears in a variable manner.

The existence of a *critical tension* is more clearly demonstrated by the experiment shown in Fig. 3. The muscle is contractured at a very short length, 65% $l_0$. and then it is stretched at a constant speed of 5 mm/min. The irregularities of the trace originate from the mechanical apparatus: because of the great stiffness of the muscle in contracture, very slight variations of the regime of the electric motor which extends the muscle are sufficient to provoke these artefacts. After an extension of 3 mm, the tension reaches 79% Po, and only increases to 89% Po during the following 7 mm extension. It is interesting to note that the critical tension depends less on the length of the muscle than the tetanic tension.

The diagram tension-length of this muscle, determined before intoxication, is shown in Fig. 3 by the dashed line. At short lengths, the critical tension (full line) is much higher than the local tetanic tension (dashed line). At the lengths around $l_0$.it is slightly lesser.

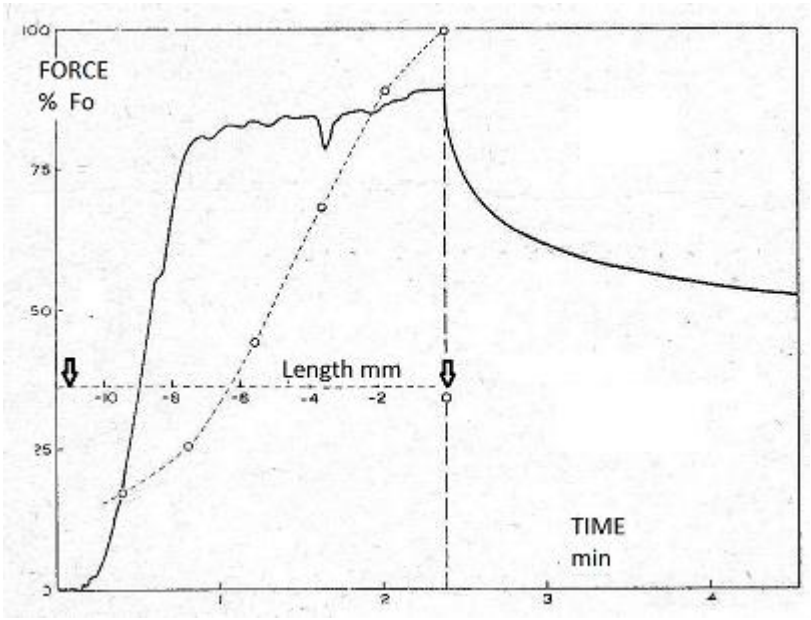


Figure 3. - Frog's double sartorius; Weight: 180 mg.; Length: 30 mm. ; T°: 18° C. Intoxication 1 h. IAA 0, 4 mM, Then shortened by 11 mm. - After a tetanus of 15 seconds and the development of the contracture (not reproduced), it is stretched 11 mm. at 5 mm./min. (between the two arrows). The left half of the figure (full line) represents the tension-length during the stretch. of contractured muscle. The white circles represent the tension-length diagram of the muscle stimulated isometrically before its intoxication (dashed line).

The existence of a critical tension is also very evident when the muscle is subjected to a series of successive stretches, as is the case for the experience shown in Fig. 4. The muscle contractured at 65% of its length $l_0$, is stretched 2-mm in 14 seconds eight times in succession, at 25 minute intervals. Its length increases from 19 to 35 mm ; The resting tension before intoxication was zero or very low between these length limits and it can therefore be assumed that the supporting elements do not contribute to the response observed during the stretching. These responses are similar, and by the maximum tension sustained during the stretches, and by the shape of the relaxation curves. In this experiment, the tension at the start of

Each stretch increases gradually for the simple reason that the 25 minute intervals between the successive stretches are not sufficient to allow the tension to regain its initial level just before the stretch. It will be noted that this increase in the tension at the start is compensated by a decrease in the tension increment caused by the stretching, which decreases by 112 g. for the first one, to 48 g. for the eighth one. As a result, the total tension at the end of the stretch is more constant than the strain induced by the stretch. In seven similar experiments, the *critical mean forces* of six successive stretches of 2 mm were 87, 104, 95, 84, 79 and 73% of Po

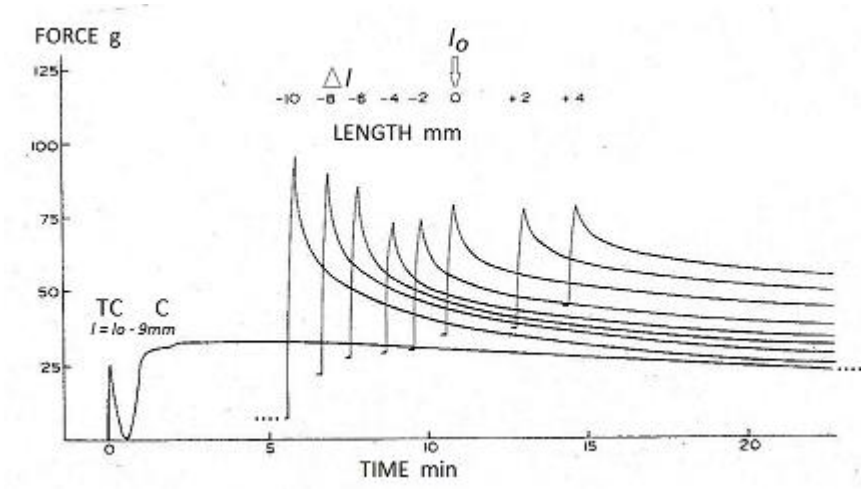


Fig 4. - Double frog sartorius; Weight: 165 mg, Length: 28 mm. ; T°: 18°C, poisoned 1 h. with 0.4 mM IAA. - The muscle is tetanized 12 sec. 100 / sec. (TC) at a length of 19 mm (=$l_o$.-9mm). Development of contracture (C). The muscle is shortened to 18 mm.(point -10)) and stretched 2 mm. in 14 sec. It is then stretched 2 mm at the same speed every 25 min. (points -Δ*l* = -10mm, -8, -6, -4, -2 0, +2 +4); The figures above each stretch indicate the muscle length. relative to the *in situ* length $l_o$.

In conclusion, the muscle in contracture cannot withstand a tension higher than the maximal tetanic tension Po. The great stiffness of the contractured muscle is not associated with an increased ability to sustain tension. Everything happens as if a phenomenon of plastic flow occurs at a force close to the maximum tetanic tension Po, whatever the length of the muscle

4. – RELAXATION AFTER A STRETCH.

The relaxation of the tension after stretching has a remarkable character: its form is largely independent of the muscle. The experiment of Fig. 4 represents the relaxations of eight successive step stretches at 25 minutes interval of a contractured muscle at 65% $l_o$. As soon as the stretching ends, the tension decreases according to a regular curve. The successive relaxations are very similar, and can be represented in first approximation by equation 1:

$$P = A \exp(-t/a) + C$$

In other words, log (P - C) decays according to a linear function of time.

Figure 5 (A) shows the relationship between the logarithm of the tension and the time after elimination of a constant C. Only four of the eight stretches have been represented so as not to overload the drawing. The four functions are linear and parallel, except for times less than 1 minute, the experimental points of which deviate significantly from the expected line. To account for this gap, it is necessary to postulate a faster exponential second of the form B exp (-t / b). This function is represented in FIG. 5 (B) for the four stretches already considered. The points are more dispersed, because they are obtained after two differences, but the functions are linear and practically parallel. The relaxation can thus be represented by an exponential double of the form (Equation 2) :

$$P = A \exp(-t/a) + B \exp(-t/b) + C$$

Where P is the contracture tension, A, B and C of the force constants; A and b of the time constants. Table 2 reproduces the results of the complete analysis of the experiment represented in Fig. 4. A second experiment of the same type led to similar results. The increase of the constant C reflects the increase of the tension at the start of each stretch. The constants A and B decrease on each stretch, which represents the corresponding decrease in the tension increment during the elongation. The sum A + B + C equals the tension

peak, which remains relatively constant. The time constants a and b, which characterize the shape of each exponential, vary little with the length of the muscle. A statistical analysis does not reveal any significant differences between the constants of the different successive stretches. *After the stretch, the tension disappears with the same velocity, whatever the length of the muscle.*

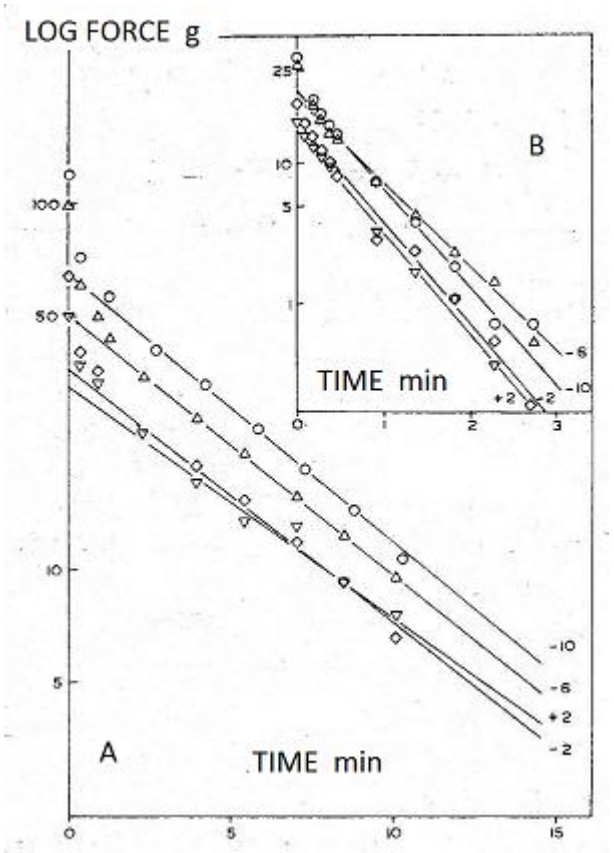


Fig 5. Analysis of tension relaxations after four of the eight stretches of the experiment illustrated in Fig 4. The figures (-10, -6, +2,+4) which indicate the length of the muscle in mm in relation to the length *in situ* $l_o$ , make it possible to identify the stretches. The straight lines are the theoretical curves whose parameters are set out in Table 1**. A**: first exponential (Equation 1) after elimination of constant C **B**: second exponential (Equation 2) after the elimination of constant C, and of the first exponential.

There is another representation of these facts, simpler but of less obvious interpretation. After a sudden extension, the tension of many biological materials diminishes in proportion to the logarithm of time, such as arteries

Table II

| △length mm | —10 | —8 | —6 | —4 | —2 | 0 | +2 | +4 |
|---|---|---|---|---|---|---|---|---|
| A | 64 | 56 | 48 | 41 | 36 | 34 | 33 | 31 |
| B | 48 | 44 | 46 | 28 | 25 | 27 | 18 | 17 |
| C | 62 | 66 | 70 | 74 | 78 | 92 | 99 | 104 |
| A + B + C | 174 | 166 | 164 | 143 | 139 | 153 | 160 | 152 |
| *a* | 320 | 370 | 380 | 390 | 470 | 410 | 390 | 600 |
| *b* | 20 | 23 | 21 | 19 | 30 | 21 | 34 | 25 |

Table II.- Analysis of the experiment illustrated in Fig 4 computed using Equation 2. Constants A, B and C in g ; a and b in sec. Δl is the muscle length relative to the reference length $l_{o.}$ at the start of each stretch.

(STAGY et al., 1952) and isolated muscle fibers (BUCHTHAL and KAISER, 1951) .The evolution of the tension for the four stretches already considered above is represented in Fig. 6 as a function of the logarithm of the time , the solid lines correspond to equation 3:

$$P = P_1 - p \log t$$

P is the contracture tension; $P_1$, the tension one second after the end of stretching, and *p* a force constant.

The time evolution of the tension after elongation is described both by equation 3 and by equation 2 but equation 3 requires two constants only, while equation 2 requires five. Unfortunately, this representation tends to mask the analogy of the shape of the relaxations: the two constants depend on the length of the muscle (see Table 3). P1 depends on the tension at the start of each stretch, and its variations are of little interest; the constant of force p decreases very significantly on each successive stretching.

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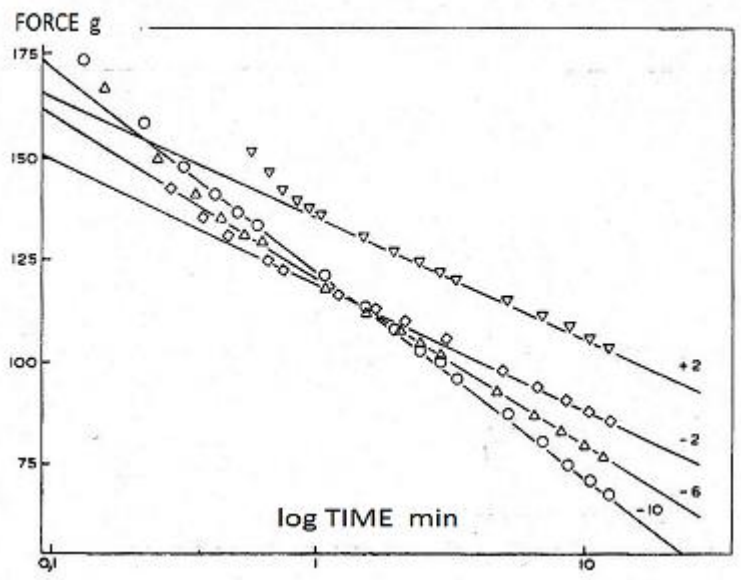


Fig. 6. Tension relaxation after four stretches (same experiment as in Figures 3, 4 and 5), analyzed with Equation 3.. The figures refer to the length of the muscle in mm at the start of each stretch, relative to the reference length $l_o$. The parameters of the theoretical solid lines are given in Table III

Table III

| △length mm | —10 | —6 | —2 | +2 |
|---|---|---|---|---|
| $p$ | 22 | 17 | 13 | 13 |
| $P_1$ | 169 | 157 | 128 | 128 |

$p$ and $P_1$ in g.. $\Delta 1$ is the length at the start of each stretch in mm relative to the reference length $l_o$.

It is not possible at this moment to specify whether this effect is correlated by the tension, or by the length of the muscle, which increases with each stretch, or even by the time elapsed since the beginning of the contracture.

## Discussion

1. The tension supported by the muscle in iodoacetic contracture seems to originate from the same protective structures that generate tetanic tension. Two main lines of argument support this point of view. First, a biochemical argument: the proteins electrophoretic diagram of muscle in contracture is more similar to that of muscle in contraction than it is to that of resting muscle (JACOB, 1947 DUBUISSON, 1950, CREPAX et al., 1950). Then there are various mechanical arguments: this work showed that the maximum tension that the muscle can undergo in contracture is close to the maximum tetanic tension; below this critical tension, the stiffness ($dP / dl$) is of the same order in contracture as in contraction; finally, the elasticity of the muscle in contracture is the same as that of the muscle in contraction (results of PETIT, 1931b, recalculated by AUBERT, 1956, page 269) or as determined by HILL's (1950) method of rapid releases (personal observations). It seems, therefore, that the muscle in iodoacetic contracture resembles a muscle in free contraction freezed in some static equilibrium.

2. SANDOW and his colleagues pushed this analogy even further by assimilating the temporal contraction to the appearance and evolution of an active state similar to that which causes the muscular twitch, but prodigiously slowed down. They note, for example, that the muscle in contracture, like the muscle in normal contraction, presents a phenomenon of tension re-development after rapid release (MAURIELLO and SANDOW, 1959), and that there is a hyperbolic relation between the lifted load and the rate of development of isotonic contracture (SANDOW and MAURIELLO, 1955, 1959). These, however, are only superficial analogies. After a rapid release just sufficient to cancel the tension of contracture, one observes effectively a re-development of the tension, but limited to 10 to 15% of the tension of contracture sustained by the muscle before the release. This redevelopment of the tension is too weak to be assimiled to the phenomenon described by GASSER and HILL (1924) under the name of *quick release recovery*. The resting muscle also exhibits a slight rebound in tension after release (PETIT, 1931a). The phenomenon reported by SANDOW could be attributed to a viscous hysteresis, as is found in many high polymers. As for the existence of a hyperbolic-type force relation, it is observed also for the muscle at rest (GASSNER and REICHEL, 1952), and it is not a proof of the existence of an active state.

Two consequences of the SANDOW hypothesis are susceptible to experimental verification. On the one hand, the existence of an active state must be accompanied by a metabolism, slowed doubtless, but superior to the metabolism of rest. On the other hand, if the progressive disappearance of the contracture corresponds to the relaxation which follows a normal contraction, it cannot have the stress-relaxation characteristics typical of high polymers.

The heat released by the muscle represents a faithful index of the intensity of its overall metabolism. In the hypothesis of SANDOW, one would expect the heat released during the development of the contracture to be at least equal to the heat of activation of a twitch. Unfortunately, the development is so slow that the expected heat flow becomes extremely low and cannot be accurately measured (personal observation). No decision could be drawn from this type of experiment, especially since the possible thermal effects are masked by the warming associated with the condensation of water vapor on a muscle whose osmotic pressure increases little by little (HILL And KUPALOV, 1930)

A second possible test of the hypothesis is based on the study of the disappearance of muscle tension in contracture, and the concomitant variations of stiffness: this is the very object of this work. In a normal muscle, stiffness increases during contraction, and disappears with tension: immediately after the twitch, the muscle becomes as supple as it was before contracting. The same cannot be said of muscle in contracture: the tension of contracture may disappear, whereas the stiffness persists (see § 1 of the results). This result can be explained simply by a stress-relaxation phenomenon, as shown by the high polymers, without having to resort to the radical change in the structure of the muscle, which characterizes the disappearance of the active state. A crucial experiment must distinguish between the two hypotheses: stress relaxation can only occur if the sample is solicited by a force which tends to stretch it.

The disappearance of the active state is accompanied by chemical transformations which alter the nature of the combinations between the contractile proteins, and which take place even if the muscle does not sustain any tension. The removal of any external stress can be achieved simply by shortening the muscle so as to cancel the tension it sustains. By intermittently returning the muscle to its initial length, we can observe the effect of the suppression of the external stress on the evolution of the tension maintained at this length: under these conditions no "*relaxation*" of the contracture is observed, The "*intermittent*" tension remains constant (see § 2).

The tension decrease of the contractured muscle maintained at constant length can therefore be explained by a phenomenon of plastic flow. A further argument is made after a series of successive stretches, pursued for several hours, the curves of the tension release are very similar (see § 4). This seems to exclude the existence of an evolutionary process, progressively modifying the structure of the muscle (hypothesis of the disappearance of an active state); On the contrary, the phenomenon is easily understood if we assume that the tension developed at each successive elongation leads to a new creep of the muscle.

3. The experiments reported in this paper lead us to the conclusion that the muscle in contracture does not appear to be the seat of processes analogous to the evolution of the state of activity. To explain the disappearance of contracture over time it is not necessary to invoke a radical change in the structure of the muscle, as would a return to the state of rest. It is sufficient to assimilate the muscle to a body which presents viscous and plastic phenomena. The viscous phenomena are betrayed by the almost exponential disappearance of stress (stress-relaxation), and by the gradual increase in the length of equilibrium of the muscle following a successive series of stretching. Plastic phenomena are manifested in the existence of a *critical tension* (Fig.3). It is important to note that these phenomena are irreversible to a very large extent.

A simple physical model can mimic some aspects of contractured muscle behavior. The exponential decay of the tension after stretching (Equation 2, § 4) leads us to consider a model consisting of two elements of Maxwell and an elastic element in parallel. It is interesting to note that the behavior of the muscle stretched at rest obeys analogous laws (ABBOTT and LOWY, 1957). However, this model correctly describes the tension drop only after a certain time after the end of stretching. At short times, experimental curves exceed the theoretical curves (see our Figure 5B, and also Figure 3b of ABBOT and LOWY, 1957). We could account for these differences by postulating three, four, or even infinitely exponential exponentials faster and faster. The equivalent physical model would then comprise an infinite number of Maxwell elements in parallel. If we admit, with Buchthal and Kaiser (1951), that the viscosities of all these elements are the same, and that the number of elements offering a high stiffness exceeds that of the elements with little rigidity, the mathematical expression of this model simplifies, and we get Equation 3: the logarithmic derivative of the tension is a constant. Under these conditions, Equation 3 becomes a generalization of Equation 2. The relationship thus established between the two equations remains fragile, however, since a consequence of the two hypotheses allowed to pass from one equation to the other is not verified: the force constant in equation 3 should increase in proportion to the length; In fact, this constant decreases as the length increases (see Table III). This assimilation of the muscle into a contracture to a simple physical model constituted by Maxwell's elements does not seem to be very fruitful, and a more realistic model would probably have to be used, taking into account new data on the protein structure.

4. The muscle in contracture is capable of maintaining for several hours a high tension, without showing the characteristic increase of the metabolism which is related to the maintenance of the tension during a tetanus. This behavior brings it closer to the smooth muscle, and particularly to certain muscles of the lamellibranch mollusks, such as the anterior byssus retractor muscle (ABRM) of, *Mytilus edulis*.

ABRM may present two different modes of relaxation after contraction, depending on the nature of the stimulation (WINTON, 1937). After stimulation by an alternating current of 50 cps, the relaxation of the muscle reaches 90% in 25 seconds. After stimulation by direct current, the release is much slower, and reaches 90% in 55 minutes. There has been much discussion about the nature of the tonic contraction which follows an excitation by a galvanic current. Some authors support the tetanic nature of this contraction (HOYLE and LOWY, 1956, LOWY and MILLMAN, 1959). Others believe that the muscle in tonic contraction is in a distinct state of both the state of rest, and the state of tetanic contraction (WINTON, 1937). JOHNSON and TWAROG (1960) show that the stiffness of the muscle increases strongly after galvanic stimulation, even if the muscle is shortened to a length at which it hardly develops tetanic tension. Since it is known that an increase in stiffness is the first characteristic of a striated muscle in iodoacetic contracture, one may wonder whether the tonic state of the smooth muscle is equivalent to a state of contracture.

The mechanical behavior of the smooth muscle in tonic contraction, as described in several recent publications, presents remarkable analogies with the contracture, as described in this work. During stretching, the tension of the smooth muscle rises in two phases, like that of the muscle in contracted stretch (see Fig 3): the tension rises at first rapidly because of the great stiffness of the muscle and then remains stationary, or grows slowly when the critical tension level is reached; As is the case of the striated muscle in contracture, this critical tension of smooth muscle is of the order of maximum tension: it reaches 84% Po in the case described by LOWY and MILLAN (1959). The stiffness of the smooth muscle depends very little on the length at which the muscle has been stimulated (JOHNSON and TWAROG, 1960): the stiffness of the muscle in contracture also depends little on the length of the muscle (see Fig 4). Smooth muscle also presents the phenomenon of "intermittent" tension, that is to say that the relaxation of the tonic contraction is stopped during the time that the muscle is shortened and does not support any tension (JOHNSON and TWAROG1960; JEWELL, 1959). The series-elasticity of the smooth muscle in tonic contraction is identical to that of the muscle in tetanic contraction (JEWELL, 1959);

we have said above that the series-elasticity of the sartorius muscle is not modified by contractility. After a rapid release, tension redevelopment is very weak if the smooth muscle is in the state of tonic contraction (JEWELL, 1959, JOHNSON and TWAROG, 1960), and is very much less than that observed when the muscle is released during a tetanic contraction; These authors concluded that there was no active state during the tonic phase of contraction. The contractured sartorius also exhibits a slight redevelopment of tension after release (MAURIELLO and SANDOW, 1959, personal observation).

In short, the analogies between the smooth muscle in tonic contraction and the sartorius in iodoacetic contracture are numerous. It would be interesting to investigate whether the stiffness of the muscle in tonic contraction remains elevated when its tension has disappeared spontaneously, in order to complete the parallelism between the two types of muscle. However, iodoacetic contracture is almost completely irreversible, and cannot be obtained twice on the same muscle, whereas tonic contraction disappears under the influence of faradic excitation (WINTON, 1937) or 5-hydroxytryptamine (TWAROG , 1954), and can be repeated on the same muscle. One might conceive that the smooth muscle should have a physiological mechanism which allows it to enter in a reversible manner in a state identical with that of the muscle in iodoacetic contracture.

This leads us to discuss the still obscure mechanism of contracture by monoiodoacetic acid. At the doses used herein, the latter selectively inhibits triosephosphate dehydrogenase. The blocking of glycolysis no longer allows the resynthesis of the adenosine triphosphoric acid (ATP) and the phosphocreatine (PC). In addition, the glycerolated muscular fibers enter into rigor if deprived of ATP, which plays the role of plasticizer for muscle proteins (WEBER and PORTZEHL, 1954). We conclude that the iodoacetic contracture is explained by the depletion in ATP caused by intoxication, an hypothesis that does not explain the kinetics of the appearance of contracture (MARECHAL, 1958). If the tonic contraction of mussel smooth muscle is equivalent to the contracture of frog sartorius, it may be that this smooth muscle has a mechanism for temporarily suspending ATP resynthesis or to maintain this substance off the contractile proteins, a possible function for the water-insoluble tropomyosin (paramyosin) characteristic of these tonic muscles (see Hanson and Lowy, 1960).

**Summary**

1) Frog sartorius muscles were intoxicated by 0.4 mM monoiodoacetic acid.to block glycolysis, attached to a tensionmeter to measure isometrically their force their and tetanically stimulated isometrically for 10 sec. by an isometric tetanus of 10 seconds at 18°C, at reference length $l_o$ .They relaxed completely, but after a latency of a few seconds, they developed spontaneously a contracture, which peaked after a few minutes to 40-60% of the maximal tetanic force. The contracture disappeared in a few hours.

2) Their capacity to resist an elongation remains considerable, very superior to that of a normal unpoisened muscle at rest. even when the contracture of the muscle has disappeared,

(3) If muscles are kept at a short length under zero load, the contracture was evaluated by bringing back the muscles to $l_o$ tsuch that they shortened between the measurements of the tension at a given length, this tension may persist for several hours: the tension only disappears to the extent that the external stress causes a plastic elongation.

4) During stretch that does not bring the muscle beyond the in situ length, the muscle tension does not exceed a critical level, which is of the order of the maximum tetanic tension that the muscle could develop Before intoxication. This level is largely independent of the length of the muscle.

5) After stretching, the tension disappears according to a definite law, the shape of which does not depend on the length of the muscle.

6) These elastic and plastic properties bring the muscle in contracture to the smooth muscle of the lamellibranch in contraction tonic.

**Summary**

1) The tension of a frog sartorius muscle intoxicated by 0.4 mM monoiodoacetic acid. And contracted by an isometric tetanus of 10 seconds disappears in a few hours.

2) Even when the tension of the muscle has disappeared, its capacity to resist an elongation remains considerable, very superior

Has a muscle at rest.

(3) If the muscle is shortened between the measurements of the tension at a given length, this tension may persist for several hours: the tension only disappears to the extent that the external stress causes a plastic elongation.

4) During stretching that does not bring the muscle beyond the in situ length, the muscle tension does not exceed a critical level, which is of the order of the maximum tetanic tension that the muscle could develop Before intoxication. This level is largely independent of the length of the muscle.

5) After stretching, the tension disappears according to a definite law, the shape of which does not depend on the length of the muscle.

6) These elastic and plastic properties bring the muscle in contracture to the smooth muscle of the lamellibranch in contraction tonic.

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