THE OSCILLATIONS OF THE AURICULAR TONUS IN THE BATRACHIAN HEART WITH A THEORY ON THE FUNCTION OF SARCOPLASMA IN MUSCULAR TISSUES.

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(From the Physiological Laboratory, under the direction of Prof. G. FANO, Florence.)

A GREAT many phenomena concerning the physiology of muscular tissue have not as yet received any satisfactory explanation. Such are, on the one hand: Bowditch's staircase phenomenon (Treppe), the "superposition" of two contraction curves described by Helmholtz—caused by two stimuli following each other within a short space of time; the phenomenon which Ranvier designated "tetanus of tonus"; the contracture described by Tiegel; the tetanus itself; the idiomuscular contraction, and generally speaking all those phenomena in which the summation ('addition' of Richet) of several contractions takes place; and on the other hand, the phenomenon of the "oscillations of the auricular tonus," which Fano first described in the heart of *Emys europæa.* The general fact to be noticed in the former class is that, when two stimuli follow each other with definite frequency their effects become added together, and consequently instead of two equal contractions, either separate contractions are produced gradually increasing in height up to a maximal pitch, or a complete fusion takes place of the individual contractions into a single curve higher than the corresponding simple maximal contractions; in the second class, spontaneous changes occur in the line of general tonus over which the fundamental rhythmical contractions are inscribed, under the shape of undulations of various width, height, and regularity, made up of a positive, systolic, or "*contraction*" phase, and a negative, diastolic, or "*expansion*" phase.

It would be useless to mention all the hypotheses put forward to explain the several facts. But for those belonging to the first category, Grützner's hypothesis may be quoted. It was doubtless suggested by the results of v. Kries and v. Frey as to a muscle being "supported" during its work. Grützner considered that in tetanus and in some similar phenomena a kind of "intrinsic support" must take place ("innere Unterstützung"), since it appeared that in complete tetanus, the muscle undergoes so forcible a contraction because it is able in some way or other to support itself; hence the analogy, which particularly refers to the height of the maximal contractions, between the phenomenon noticed by v. Kries and v. Frey during the artificial support of the muscle, brought about by means of rhythmical, isochronic stimuli, and the tetanus. However the cause of such an "intrinsic support" had to be sought for, and for this purpose Grützner availed himself of the recently acquired notions on the structure of striated muscles, viz., the fact of there being present in every muscle amongst the many pale and clear fibres a certain more or less considerable number of dim or red fibres. The latter, he supposed, during their contraction have the former to support them. But it is obvious that Grützner's hypothesis, though resting on a sound histological and functional base, is only of value so far as concerns the striated muscles. The same interpretation cannot be applied to the many other similar facts noticed in cardiac muscle and in unstriated muscular tissue.

With regard to the contractions and the oscillations of tonus shown by the auricles in *Emys europæa,* Fano was of opinion that the two kinds of movement in view of their independence, must have their origin in different kinds of elements. He thought, further, that the muscular fibres of the auricles are composed of two kinds of elements which differ in their nature and which are to a certain extent independent of each other. Grützner's hypothesis is supported by an anatomical fact, whilst Fano's depends upon physiological results, but no histological observation exists which gives us the right of admitting essential differences in the structure of the myocardiac cells of the auricles. It is true that lately certain spots have been found in the sino-auricular segment, where the myocardiac cells show a nearly embryonic structure; but these are grouped in distinct regions, and are not found in all parts of the auricular tissue; whereas Fano's studies lead us to the conclusion that both kinds of muscular rhythm pertain even to the smallest piece of the auricular wall.

It thus happens that no minute and precise explanation is given either of the "oscillations of auricular tonus" or of the other phenomena I have already alluded to.

The observations I have made during this year on the unstriated muscular cells of both adult animals and chick embryos, together with other studies on the "oscillations of auricular tonus" in the hearts of amphibia, and a careful inspection of the many tracings of auricular movements either published or possessed by Fano form the foundation of the new hypothesis which I shall set forth here.

The studies on the unstriated muscular cells are part of a paper, about to be published elsewhere. I propose in this account to deal with my experiments upon the "oscillations of tonus" in the amphibian heart, and to discuss various facts in the light of the hypothesis suggested by these experiments.

II.

The object with which these researches were undertaken, was to see whether the phenomenon which Fano noticed in the tortoise's auricles, and which he named "oscillations of tonus," are to be found in the auricles of other animals also. My method of research only differs from Fano's in one point, viz., that I have always left the stump in normal connection with the sinus and the great vessels of the base instead of doing this only occasionally. Having fastened the animal (*Rana esculenta, Bufo viridis, Bufo vulgaris, Lacerta viridis, Tropidonotus natrix, Anguilla vulgaris,* etc.), I exposed the heart, taking good care that no blood should be lost; I then tied a silk thread around the auriculo-ventricular groove, after which by means of a delicate glass hook I attached the auricles *in situ* to the writing lever. The auricle by this means retained all its blood and there could be no question of the phenomenon observed being due to exhaustion of the auricular muscle. Yet the thread round the auriculo-ventricular groove still remained, acting on the auricle like a continuous stimulus, as did the metallic fork used by Fano to fix the excised tortoise's heart out of the body. Fano himself however saw the appearance of the oscillations of tonus even when the fork was thrust into an extremely small fraction of the auricle, and therefore attributed to these oscillations a myogenous origin. It is also to be mentioned that he obtained a series of tonus-oscillations from hearts left *in situ*—having no injury except that caused by a ligature at the extreme tip of the auricle, made for the purpose of putting the latter into connection with the writing apparatus. It is clear, then, that the oscillations of tonus cannot be a consequence of a stimulation of the vagus. However, with this method the increase of the intra-auricular pressure caused by the blood being unable to flow on account of the ligature, might become a matter of some importance. But, as will be shown later, the double rhythmical function of the auricles suffers no change in its course by their being emptied. This reason together with many others (to be set forth by Fano and myself, in a work shortly to be published) lead to the obvious conclusion that the "tonus oscillations" can appear independently of any abnormal stimulus, and probably exist normally in the heart of normal, living animals. One last difficult point is that these oscillations very often make their appearance some time after the auricles have been fixed to the apparatus. This however is probably nothing but the effect of the mechanical stimulus which cannot be avoided, and is, as everybody knows, most active on the muscular cell tissues, its first effect being either a contracture or an inhibition of movement. As soon as this effect is over the oscillations of tonus begin.

In amphibia the tonus-oscillations begin a short time after the auricles have been hooked up and last for a long time. They show striking dissimilarities even in animals of the same class of amphibia, and also differ from those Fano described in the tortoise.

1. As a rule they are less evident in amphibia, though visible enough, as can be seen in the following tracings (Figs. 1—9).

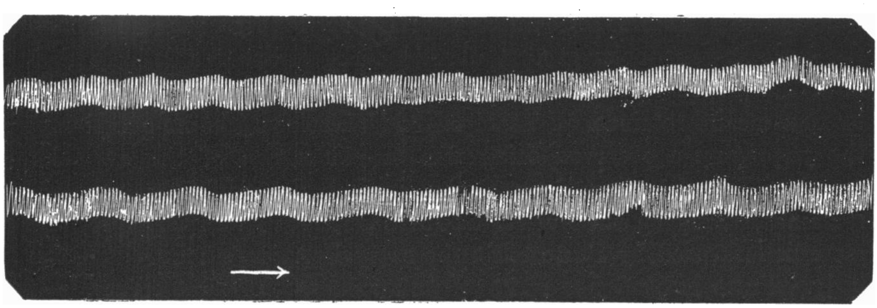


FIG. 1. Auricles of *Bufo viridis*, suspended *in situ*, and full of blood. Oscillations of tonus less frequent in the upper tracing, more in the lower one, where also the height of the fundamental contractions is smaller.

2. They show a great regularity and a constant rhythm, on which appears the more frequent rhythm of the fundamental contractions.

3. In *Bufo vulgaris* (Figs. 2, 3), their frequency is rather slight, notwithstanding the height of the fundamental contraction caused by largeness of the auricles. This perhaps may explain their apparent irregularity. Besides concerning the frequency it is to be mentioned

that in the tortoise all the intermediate grades can be found between the very frequent oscillations in Fig. 6, and the very rare ones, which are

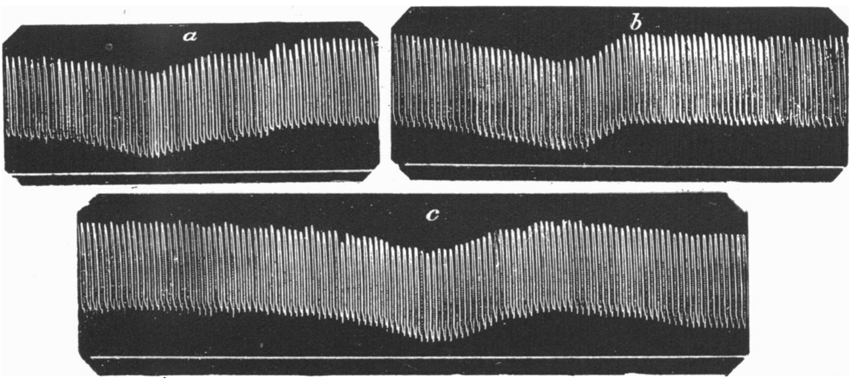


Fig. 2, *a*, *b*, *c*. Three oscillations of the auricular tonus in the heart of *Bufo vulgaris*, with the expansion phase predominating. The oscillations are very slow.

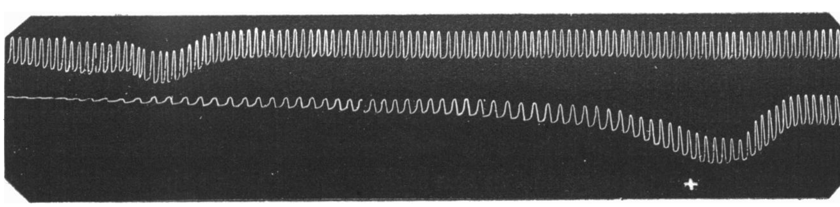


Fig. 3. Contractions of the *sinus venosus* in the heart of *Bufo vulgaris*. Rare oscillations of tonus with the expansion phase predominating. In the point + the vapour of chloroform is made to act. (To be read from right to left.)

like those seen in *Bufo vulgaris* in Fig. 2 *c* and Fig. 3. Compared with these and the tortoise's, the auricular oscillations are very frequent in *Rana esculenta* and *Bufo viridis* (Figs. 4, 5). The difference in the

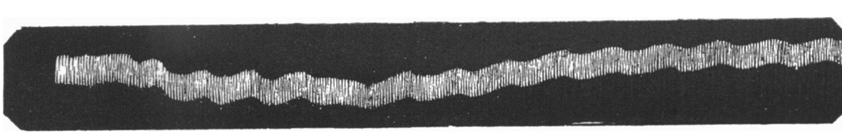
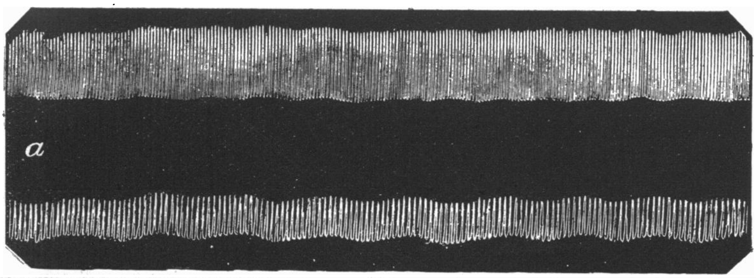


Fig. 4. Normal course of the auricular movements in the heart of *Rana esculenta*. The oscillations of tonus are very regular and very frequent. The tracing shows wide oscillations of the general tonus of the auricular preparation, whose nature is not surely known.

frequency of the fundamental rhythm which is not as great in the tortoise and *Bufo vulgaris* as in the two other amphibia, does not exactly correspond to the difference existing between the oscillations of the tonus.



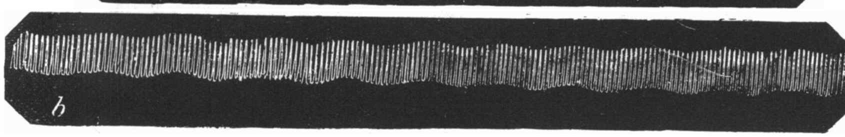


FIG. 5 *a*. Oscillations of auricular tonus in the heart of *Bufo viridis*. The upper tracing was taken immediately after the preparation was suspended, and shows hardly visible oscillations. The lower tracing was taken about half-an-hour later.

FIG. 5 *b*. The preceding tracing continued, after having pierced a vein at the base of the heart and drawn the blood out. No change is produced by such an extraction of the blood.

4. What most attracts our attention however is the fact that, if a single oscillation of tonus be considered, the fundamental rhythmical movement appears to behave in a different way in different cases, for instance in the tortoise and in the toad. As a rule, in the tortoise the fundamental contractions are seen in the tracing to become gradually less extensive during the rise of tonus, and consequently to become sometimes nearly invisible, whilst they become more extensive, *i.e.* have a greater range during the fall of tonus (Fig. 6).

Nothing of the kind can be seen in the auricles of amphibia. In these the extent of the fundamental contractions suffers no change during the two phases of the oscillations of tonus, and certainly this is what makes the corresponding tracing look more regular. This fact Fano observed and ascribed to the lessened margin of contractility of the auricles during the motor phase. The oscillations of tonus being thus weaker in amphibia the constancy in the height of the fundamental

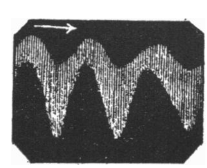


FIG. 6. Oscillations of auricular tonus in *Emys europæa*[1]. Normal course of the movements. Temp. 14° C.

[1] This figure and the others concerning the auricular function in *Emys* Prof. Fano kindly allowed to be reproduced from tracings recently obtained by us in a research not yet published.

contractions during both the phases of every single oscillation is easily explained.

5. Yet not infrequently in the tortoise also, oscillations of tonus may be shown completely similar to those seen in amphibia, so far as concerns the range of the fundamental contractions during the phases of an oscillation (Fig. 7). It cannot therefore be said that the form shown in Fig. 6, though it be more frequently met with, is a characteristic and special feature of the oscillations of tonus in the tortoise. I may mention also that in Fano's tracings, the greatest variety occurs in the form of the oscillations, though these always retain some peculiar features common to all of them. Further on we shall see what causes the important phenomenon discovered by Fano to be so variable.

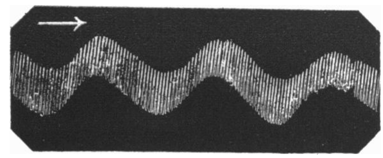


FIG. 7. Oscillations of auricular tonus in the heart of *Emys*. Normal course of the movements. Temp. 14° C.

By the experiments I undertook other facts were brought to light, which may be briefly stated as follows.

6. If, after we have registered the auricular movements of a heart, for instance, of *Bufo viridis*, the auricles still being full of blood, we manage to pierce one of the great veins connected with the auricles, so as to drive gradually all the blood out of the latter, the double rhythmical movement persists, retaining its form, and does not suffer any change, either within a short time or afterwards (cp. Fig. 5 *b*).

7. If the ligature has been tied between the sinus venosus and the auricles, and if the excision of the latter has been performed at the same time as that of the ventricle, the remaining great vessels and sinus show oscillations of tonus (Fig. 3) similar to the auricular ones (of *Bufo vulgaris*).

8. Letting some drops of an isosmotic solution of a potash salt fall gently on the auricular preparation, as its double rhythmical movement is being registered, the fundamental contractions gradually become smaller until they nearly disappear, whilst the oscillations of tonus are kept up for a longer time. Meanwhile the general tonus of the preparation goes on becoming as depressed as its power of distension allows it.

9. Pouring a few drops of chloroform into the moist chamber containing the preparation, and allowing time for the vapour to mix with the air, the fundamental contractions are seen to become smaller and less frequent, and finally disappear, the oscillations of tonus vanishing

at the same time. When the action of the chloroform has ceased for a long time the auricles begin beating rhythmically again. The oscilla-

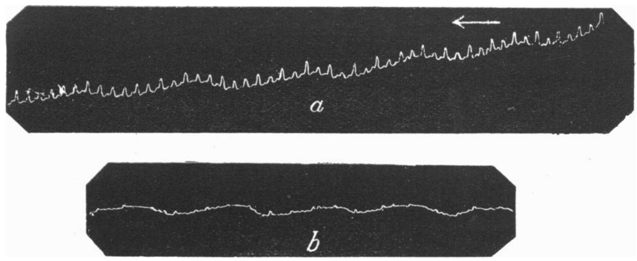


FIG. 8. Auricular preparation of *Bufo viridis*. Tracing *a* shows the auricular contractions almost immediately after the action of an isosmotic solution of KCl; tracing *b* shows the same a few minutes later. Temp. 14° C.

tions of tonus however will be waited for in vain; they do not appear any more, and are suppressed for ever. The same phenomenon can be noticed in the sinus venosus (Fig. 3).

In this way we have found in the salts of potash and in chloroform a new means of separating the two rhythmical auricular movements, besides those Fano found earlier. All the substances however which the latter experimented with, were alkaloids and are to be ranked amongst the so-called nervous poisons of the heart; whilst the two poisons I tried act as well, and principally, upon the chemical composition of the myocardiac cells. This proves that the difference between the two kinds of movement and their respective independence are actually caused by the structure of the myocardiac cells.

In the auricles of *Lacerta viridis*, of *Tropidonotus natrix*, of *Anguilla vulgaris*, and of chick embryos I could not succeed in making any oscillations evident, similar to those seen in amphibia. From the auricles of *Tropidonotus natrix* (Fig. 9) I obtained a very peculiar

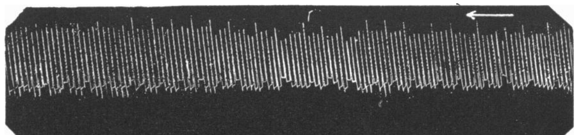


FIG. 9. Auricular function of the heart of *Tropidonotus natrix*. Temp. 16° C.

tracing showing groups of 3 or 4 contractions, and between these a contraction which appears to be higher if compared with the line of the systolic apices, or not as low as the others if compared with the diastolic line, which accordingly is interrupted in this point. The tracings of the auricles of chick embryos, too, show something of this kind. I could not tell whether any distant likeness between this last form of tracing and the normal oscillations of tonus might be considered to exist. I am far from intending to deny the existence of oscillations of tonus in these animals' auricles. Nevertheless, it does not seem to me possible—and I shall give reasons for this later—that the phenomenon should be able to produce itself in animals higher in the zoological scale as clearly as in the lower ones.

III.

As I studied the embryonic evolution of the motor power in unstriated muscular tissue, I found phenomena like those seen in the auricles of *Emys* and of amphibia, even in a small piece cut off from the œsophagus of a full-grown frog or from a chick embryo of the 16th day of incubation and upwards. I noticed that the œsophageal muscular cells, especially the ones belonging to the longitudinal layer, also have a double rhythmical movement. The tracing shows fundamental rhythmical contractions registered over a waving line always bearing an evident likeness to the oscillations of tonus already spoken of. Hence I was led to conclude that the tonus-oscillations present a general phenomenon especially to be met with in tissues composed of unstriated muscle or of myocardiac cells. And as I was convinced from the beginning of their being automatic and exclusively myogenous, I consequently went to work in order to trace their origin and causation. Without doubt the tonus-oscillations have nothing to do with periodical changes in the elastic properties of the muscular tissue, but are related to its contractility: a fact which Fano was the first to point out. In my opinion it is in the sarcoplasma of the muscular cells that such a contractility has to be sought for.

There are many facts which support this hypothesis. In the first place there is the very slow rhythm of the contractions, reminding one of the periodical contractions and expansions of a pseudopodium of an Amœba. Secondly, each oscillation of tonus is composed of two opposite movements following one another; that is to say, one of contraction and another of expansion, the former ascending higher than the abscissa, the latter falling below it. This kind of periodical movement appearing in the tracings in the form of more or less regular waves, particularly belongs to the cytoplasm of the inferior unicellular organisms. The more differentiated muscular substance, that is to say, the anisotropic substance of the muscular tissues is deprived of real expansive movements, for a striated muscle cannot be said to be expanding as it goes back to its former state of equilibrium after the phase of contraction.

We have seen that the double movement of contraction and expansion can only be found in the muscular elements containing a great amount of sarcoplasm, namely, in unstriated muscular cells and in the myocardiac cells of certain parts of the cardiac tube; and we find that another rhythmical movement may be developed independently of the above, exhibiting only a mechanical relationship to it. This, I think, affords reason for believing that the former movement belongs to the undifferentiated part of the muscular cell, to the sarcoplasm, whilst the latter seems to belong to the differentiated portion of it, namely, to the doubly-refractive substance. The absolute independence of the oscillations of tonus and the fundamental contractions,—a fact so clearly brought to light by Fano,—leads of itself to the conclusion that the two actions originate in different parts of the cells.

Lastly, the phenomenon of the oscillations of tonus is observed to depend always upon the quantity of sarcoplasm. The greatest range is attained by these oscillations in the tissue of unstriated muscular cells of either the fully developed or embryonic œsophagus; they are also very evident in the auricles the elements of which are in a lower stage of evolution than are the elements of the ventricles, and in *Emys europœa*, the cardiac fibres of which, as Ranvier stated, contain a much larger amount of sarcoplasm than is to be found in other animals.

It is doubtful whether any such oscillations exist in the higher vertebrates; it is doubtful even whether they exist in Ophidia. I at least did not succeed in bringing them into evidence. They are absolutely wanting in striated muscular tissue. For this reason I think I have sufficient ground for asserting that the oscillations of tonus are simply independent contractions and expansions of the sarcoplasmatic part of tissues composed of muscular cells.

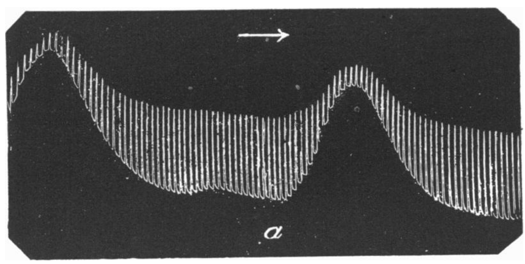
Some confirmation of this view is afforded by the variations occurring in the form of the curve of tonus oscillation, which suggest a survival of the irregular movement which can be seen in the protoplasm of Amœba. It is known that the contracting and expanding movements of the pseudopodium of an Amœba which are both to be considered as active movements, are independent of one another (Verworn). In an exactly similar way the two phases in the oscillations of tonus which I termed positive and negative, and which better still should be called contraction and expansion phases, are independent of one another. In some tracings the regularity and the similarity of the two phases are striking (Figs. 1, 7); sometimes the contraction is predominant (Figs. 10, 11), sometimes the expansion (Figs. 2, 3). We shall probably find out how to act separately on each of them by either chemical or physical means; all that can be said at present is that the potash salts used in small quantity not only favour the expansion phase in every single oscillation, but bring on a lowering of the general tonus, this last fact being of the same nature as the former.

IV.

I have said that in the muscular cells which have reached the highest grade of evolution, and the sarcoplasmatic substance of which is reduced to a *minimum*, the phenomenon called "oscillations of tonus" can no longer be observed. Without entering into the question whether our still rough graphic methods are able to reveal the minimal movement carried out by this infinitesimal quantity of sarcoplasm, we may endeavour to explain the want of oscillations as due to a want of automaticity. Very likely in fact the sarcoplasm of the most differentiated kinds of muscular tissue has lost its automaticity in the same way as the anisotropic substance, which represents a special histological differentiation inside the muscular cell, and which carries out the fundamental rhythmical contractions, has become deprived of automaticity.

The properties of the sarcoplasm however appear to be somewhat different in the most differentiated muscular tissues (ventricles of the heart, striated muscles), although this remains substantially of the same nature. In these properties can be found, I think, the explanation of all the phenomena I alluded to at the beginning of the paper, namely, the phenomenon of the "staircase," etc. It is the contraction of the sarcoplasm, with its special features of greater duration and tonus, that forms the "intrinsic support" for the independent contraction of the anisotropic substance, and has a similar action to that of the "extrinsic support" in v. Frey's and v. Kries's experiments.

What should most attract our attention is the fact of this "intrinsic support" being equally afforded by the sarcoplasm both when the muscle is contracting of its own accord and when the contraction is brought about by means of external stimuli of definite frequency and strength. The truth of this statement will be further shown by inspecting the following figures and comparing them with the Figs. 1 and 2 in v. Frey's work published in the *Beiträge zur Physiologie* dedicated to C. Ludwig.



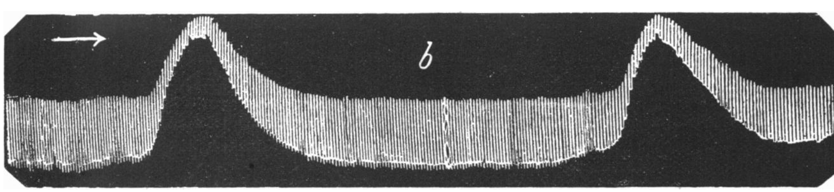


FIG. 10 *a*. Oscillations of auricular tonus in the tortoise's heart, the contraction phase being made to prevail by elevating the temperature (23° C.).

FIG. 10 *b*. (See explanation of preceding Fig.) Temp. artificially raised 22·5° C. The contractions of the sarcoplasm become considerably wider, and the fundamental rhythmical contractions go up to an unusual height.

It is striking how nearly identical these and v. Frey's tracings are. And yet his tracings were taken from a frog's striated muscle which was "supported" during contractions brought on by rhythmical electrical stimuli; whilst our tracings were obtained from the automatically acting auricle of *Emys europœa.* In the former case it was the "extrinsic support" which caused the contractions to rise so high as to reach the line of tetanus, here it is the contraction of the sarcoplasma, viz. the contraction phase of the corresponding oscillation of tonus, which "supports" the auricular muscle and makes the line of the systolic apices of the fundamental contractions become so much higher.

The stimulus always acts either first on the sarcoplasm and so by transference on the anisotropic substance, or on the muscular fibrillæ and on the sarcoplasm at the same time. In the sarcoplasm however the excitation and the respective contraction last for a longer time and are more tonic; hence it happens that in the sarcoplasm not only the summation of consecutive excitations, even when these do not so closely follow each other, but also Grützner's phenomenon of the "intrinsic support" are made possible, the muscle receiving the following stimulus while the sarcoplasm is still in the phase of excitation or contraction. This I believe to be the reason why the more sarcoplasm there is contained in the elements of the preparation which is being experimented on, the less the frequency of stimuli which is required to produce the summation of single contractions or of states of excitation. And thus the reason of different muscular tissues answering the external stimuli in a dissimilar way, can be explained on the view that the sarcoplasm—provided with an irritability and a contractility similar to those of the cytoplasm of the lowest unicellular organisms—is present in a different quantity in the various muscular elements, and that in the same sarcoplasm only such excitations are summed up which are individually unable to produce a single contraction of the muscle, or such excitations as are sufficient to cause the phenomena of superposition and fusion of the single contractions.

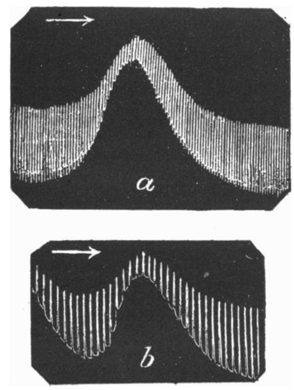


FIG. 11 *a* and 11 *b*. (See explanation of fig. 10 *a*.) The reader is requested to observe the likeness of the phenomenon, notwithstanding the difference in the frequency of the fundamental contractions.

If however we admit that the sarcoplasm receives the external stimuli, and that it accumulates and sums up the insufficient stimuli; if we admit, in short, that all the chemical and physical processes producing secondarily the mechanical fact of the contraction in the anisotropic substance of a striated muscle, resides in the sarcoplasm, in it we must also acknowledge that the similar processes take place primitively, which are the real cause of movement in automatically acting organs. Such movements we call automatic only because the special kind of inner stimuli producing them escapes our powers of perception. In other words, we must acknowledge the automatism to reside in the sarcoplasm.

On the one hand we see how muscular organs provided with automatic movements always contain a greater amount of sarcoplasm, whilst on the other hand the most differentiated form of muscular tissue shows no automatism at all, and possesses but a scanty residue of sarcoplasm surrounding the anisotropic substance.

We have besides reason to believe that the metabolism of the muscular elements is principally carried out in the sarcoplasm; but its opposite phases do not probably quite correspond to the two opposite phases of the movement; firstly, because such a slow chemical rhythm of nutrition is not at all likely to exist; secondly, because we must consider the expansion phase, too, as an active movement thereby accompanied by disassimilatory processes; and lastly, because of the production, during this phase, of contractions of the doubly-refractive substance, which, though somewhat weaker, are equal to those of the contraction phase as far as the frequency is concerned. We can therefore recognise a difference in the anabolic and katabolic phenomena during each phase of the movement, and we can believe also that the anabolic ones are prevailing in the expansion phase, whilst the katabolic prevail in the contraction.

Since also the original cause of the automatic movements is to be sought for in oscillatory trophic changes of the living substance, we think this affords a further proof of our hypothesis that the automatism resides in the sarcoplasm.

Every automatic movement however assumes the rhythmical, periodical form; nor could we even in our case think of a different form of movement. The sarcoplasm therefore supplies the rhythm of the movements in muscular organs provided with it. But here a question arises which is worth some discussion. If, as a consequence of our preceding remarks, we suppose the doubly-refractive substance of the muscular elements to have undergone further differentiation during the phylogenetic development for the purpose of a more rapid contraction, and if we represent it as destitute of automaticity and rhythmical power, we are obliged to admit that whenever in the same organ two rhythmical movements simultaneously show themselves, and are wholly independent of each other in their frequency, nature and seat; the one of them, which we said to be due to the doubly-refractive substance, necessarily can be but an effect of stimuli coming from the sarcoplasm, which carries out the other movement, in the same manner as rhythmical movement may be produced in a muscle possessing no automaticity by means of electrical stimuli properly applied to it. The following question may then be asked: whence does the different frequency of the rhythm between the two simultaneous movements arise?

As the quickest rhythmical movement of an automatic muscular organ is, in its frequency, very nearly equal to that which external stimuli can produce, and as the rhythm of the stimulus is independent of the actual movement in both cases, we are left no other way of explaining the matter than by admitting that the doubly-refractive substance of muscular automatic organs possesses the property of answering to both internal and external stimuli with a special rhythm, the frequency of which, constant in single organs and special animals, is the result of an hereditary adaptation to the special rhythm of the inner trophic stimulus innate in the sarcoplasmatic part of the element. We may add that any other stimulus, of whatever kind it may be, can only produce the usual rhythm of the organ or have no effect at all[1].

We therefore make a decided distinction between the rhythmical property of the automatic movements of the sarcoplasm, and the property the anisotropic substance has of answering with rhythmical contractions either internal or external stimuli. The first is strictly connected with the automatic movement itself and always accompanies this wherever it appears; the second is the consequence of a special physiological differentiation of the anisotropic substance, it is not automatic, it may be found more or less even in muscles completely deprived of automatism, and, the frequency of the special rhythm in each single case being constant, is to be considered as the effect of a particular adaptation to the rhythm of the physiological stimulus, which depends upon the kind, intensity and nature of the local metabolism.

A somewhat interesting question is whether in muscular tissues the wave of excitation, and therefore also the electrical and contraction waves are transmitted through the doubly-refractive substance, or through the sarcoplasm, or through both.

Starting from the fact of the variations in velocity with which the wave of excitation is transmitted in different muscular tissues,

[1] The rhythmical movements produced by Ranvier and Biedermann by means of electrical and chemical stimuli in skeletal muscles utterly destitute of automaticity, are but the remains of the rhythmical property, which is developed to the highest degree in automatic muscular organs.

Biedermann believes that the sarcoplasma transmits the slow waves, whilst the quick waves go through the fibrillæ.

I think it unlikely that the two fundamental substances of the muscular element take part in the transmission of the excitation at the same time. It is undoubted that the slow waves can be transmitted through the sarcoplasm; this may happen in smooth muscular tissue and in the cardiac tissue of cold-blooded animals. The idea of the doubly-refractive substance having a part in the transmission of the rapid waves might be opposed by saying that the wave of excitation would have in any case to go through the sarcoplasm at some points, as for instance at the junctions of the cells and the fibres, and therefore would have also necessarily to suffer changes of form, length and velocity. Had we only to give explanation of the difference existing in the rate of transmission in the various tissues and organs, we might be quite free to think in the different cases of special local chemico-physiological evolution of the sarcoplasm, and of special forms of adaptation.

But, how can we account for the fact that the same muscle is able to transmit long and short, slow and rapid waves? This can only be the effect of the general conditions in which the transmission is effected. And is not for instance the difference in the power of transmission, between a tired, exhausted heart, and a normal one, equal to the difference existing between the power of transmission of a smooth muscle and that of a striated muscle? And why cannot the various conditions of the metabolism of the sarcoplasm, the different irritability, the force or nature of the stimulus, the different innervation of the organ, the temperature, etc. sufficiently account for the various powers of transmission of one and the same substance? All the more, as the transmission of the excitation is but the spreading from one molecule to another of a chemical disintegrative process, which is of course dependent upon all the above referred conditions, and is apt by reason of them to suffer radical changes. I therefore do not find it necessary to accept Biedermann's view, and I think nothing for the moment prevents us from considering that the power of transmission of the excitation in muscular organs resides only in the sarcoplasm.

V.

We have not however yet tried to explain each of the above-mentioned phenomena according to our theory. This we shall briefly now endeavour to do.

When two contractions are added together, and this is the fundamental fact in nearly all the phenomena we have been speaking about, it is sarcoplasm, which being in its phase of contraction when the second stimulus comes into action, "supports" the doubly-refractive substance during the second contraction, which accordingly rises higher.

The residual shortening is caused by a residual contraction of the sarcoplasm.

All the phenomena of contracture, together with the pseudo-tetanus of the ventricular muscle are nothing but tonic contractions of the sarcoplasm, which cannot be kept long in such a state unless the extrinsic stimulus has attained a certain strength.

The same can be said of Ranvier's "tetanus of tonus," and of the other similar phenomena; the same of the "rhythmical tetanus" of Richet, and of the similar form that can be produced in the ventricle of the heart (Ranvier, etc.) and in the bulbus aorticus (Engelmann). In these cases the rhythmical contractions of the anisotropic substance, which show a definite frequency, are executed on a more or less elevated line of tonus, determined by the permanent state of contraction or contracture of the sarcoplasm.

We can easily pass from these facts to the incomplete and to the complete tetanus of striated muscles: since on account of the action of the sarcoplasm the muscle is put into a state of tonic shortening, the single contractions of the doubly-refractive substance cannot be shown any more: they only appear in the ascendant phase of the tetanus, in which the sarcoplasm has not yet reached its highest pitch of contraction.

The idiomuscular contraction both on account of its duration and because it can be more easily produced during exhaustion of the muscle, etc. appears to be a tonic contraction of the sarcoplasm: this less developed form of contractile substance, in fact, though it be less irritable, nevertheless maintains its irritability for a longer time than the doubly-refractive substance.

We have discussed the phenomena seen during the "oscillations of tonus" in the auricles of *Emys* (p. 6, 7). We have asserted them to be nothing but consecutive contractions and expansions of the sarcoplasm of the myocardiac cells, and we have said that the gradual increase in the height of the contractions of the anisotropic substance during the contraction phase of the oscillation is caused by an "intrinsic support" which is supplied by the contraction of the sarcoplasm similar to that observed by v. Kries and v. Frey[1]. The phenomenon is far more evident in the auricles of *Emys*, the amount of sarcoplasm contained in the morphological elements of the cardiac muscle being in this animal, according to Ranvier's studies, most remarkable. If, as seems certain, the oscillations of tonus are nothing but movements of the sarcoplasm, and as they are so evident and so easy to be registered in the smooth muscular tissue of the œsophagus and in the cardiac auricles, these organs afford us the best means of minutely studying the movements of the sarcoplasm and the influence many physical and chemical agents have on it. But even now we are able to say that the strongest effect on muscular organs composed of elements richly provided with sarcoplasm is produced by mechanical[2] and thermal stimuli, which fact is consonant with the ideas we hold at present about the special features of the irritability of the cytoplasm in the monocellular organisms, to which cytoplasm we must imagine the sarcoplasm of the muscular elements in a certain way to be similar..

We are however obliged to admit that the sarcoplasm in various muscular tissues has suffered special differentiations in its fundamental properties: its irritability and its contractility, and that the effect of the stimuli is not dependent on the quantity of the sarcoplasm alone. A striking difference must also be acknowledged to exist in the irritability, the quickness of contraction, and the property of transmitting the stimulus, which are much less prominent in the sarcoplasm of a muscular cell than in a striated fibre. This remark seems to us to be so necessary and logical and so likely to be true, that we do not think it needful to insist further upon it.

In some phenomena, however, as for instance, in Bowditch's "Treppe" phenomenon and in other similar ones, it is impossible to speak of a contraction of the sarcoplasm, in the real and mechanical meaning of the word, as helping the contraction of the doubly-refractive substance. But we should not forget that in such cases we make use of compara-

[1] Frank also observed in the heart a phenomenon like that described by v. Frey and v. Kries, and that shown by the tortoise's auricles; namely that "...der Gipfel der Ueberlastungszuckung bei steigender Unterstützung, d. h. geringerer Anfangsspannung sich erhöht." It should be remembered that in Frank's experiments the intracardial pressure was used as a stimulus.

[2] One of the highest mechanical stimuli is the tension of the muscular preparation: it gives rise to the expansion of the sarcoplasm, that is to say produces in the sarcoplasm a chemical disintegrative process.

tively weak stimuli, that the sarcoplasm, like all irritable and contractile substances, has the property of adding together the stimuli, and that the irritability of the anisotropic substance is greater than that of the sarcoplasm. We may well imagine the disintegration of the molecules of the irritable substance, (which at its beginning give rise to the state of excitation, and at its end or in the stage of explosion, give rise to the contraction) to be more or less intense as the force of the stimulus producing it is greater or smaller. We are also right in believing that a weak stimulus may start the disintegration, which afterwards goes on increasing with the following weak stimuli, until it reaches the liminal value which is required for producing a contraction of the doubly-refractive substance; the phenomenon being the consequence either of the chemical process itself, or of the thermal effect of this (Engelmann). In a similar way equally weak but sufficient consecutive stimuli are the cause of contractions of increasing force, because the chemical disintegration which takes place in the sarcoplasm has been gradually becoming more intense as the stimuli followed each other. This will appear to be all the more probable if it be allowed that in the sarcoplasm the opposite katabolic and anabolic phases of its metabolism last longer than in the anisotropic substance, as it is the case with the duration of the excitation and the contraction, and have a more or less slow course in the various muscular tissues and in different species of animals. Therefore, in Bowditch's "Treppe" phenomenon the gradual heightening of the contractions appears to depend upon a corresponding increase of the katabolic processes, caused by the fact that the disintegrative effects of the external stimuli are added together inside the sarcoplasm. In this case the external stimulus is not strong enough to produce a contraction of the sarcoplasm, but has given the disintegrative chemical process intensity enough to bring on the contractions of the anisotropic substance. In fact, simply by increasing the force and frequency of the stimuli, the tonic contractions of the sarcoplasm will appear.

Recapitulating, we believe that irritability and contractility of the sarcoplasm afford the explanation of all the phenomena of muscular physiology in which the addition of several excitations and the superposition of single contractions occur.

The sarcoplasm in its tonic contraction supports the anisotropic substance in its quicker contractions.

The movement of the sarcoplasm is shown in automatic muscular organs in its simplest and also most evident form of alternate contractions and expansions wholly independent of the movement of the anisotropic substance. We can thus make experiments with great ease on this less developed form of contractile substance which can be found in the comparatively highly developed tissues of higher organisms.

In the muscular organs that possess no automatism, the movement of the sarcoplasm is not quite so evident, but it aids and sustains the movement of the doubly-refractive substance, which in this case is predominant.

I am fully aware that this theory is in opposition to the opinion generally accepted that in the metabolism of muscular tissues the sarcoplasm only acts as a connection between the intercellular nutritive materials and the anisotropic substance, and that this alone is contractile.

This opinion, though nearly universal is not so entirely; for Biedermann relying chiefly upon the different forms of contraction which occur in ciliate infusoria, considers that the possibility of contraction of the sarcoplasma cannot be entirely disregarded, and Kühne has gone so far in the contrary direction as to consider the sarcoplasm the only contractile substance, the fibrillæ being elastic.

Oct. 19 1896.

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