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The Genesis of Tetanus and Characteristic Features of a Single Muscular Contraction

Clarence S. Livingood

"THE GENESIS OF TETANUS AND CHARACTERISTIC FEATURES OF A SINGLE MUSCULAR CONTRACTION"

A Thesis

Submitted in Partial Fulfillment of
the Requirements for Department Honors.

BY Clarence S. Livingood
Ursinus College,
Collegeville, Pa.

Approved by J. H. Brownback,
Department of Biology

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In introduction, it is imperative to define a number of terms and outline in a very brief way just what was done in an experimental way in preparing this paper. It willbe necessary from time to time to say something about the apparatus which was used and also to describe exactly every detail of the necessary labarotory work.

I worked with a distinct type of animal tissue known histologically as muscular tissue but popularily known as flesh. It is thus necessary to describe histological features.

Muscular tissue is peculiar in that it possesses the power of contraction and is thus in higher animals the tissue by which their movements are executed. Histologically as well as physiologically, the muscles are divided into two great classes-voluntary and involuntary. The histological difference is that the voluntary muscles are striated and the involuntary muscles are non-striated. The former are under the control of the will and the involuntary muscles are, as the name implies, not under the control of the will. They are however controlled by the nervous system but by a different part. Since my work has been confined to the study of voluntary muscle let it suffice to simply note histological differences of the two types of muscle.

All muscular tissue is made up of muscular fibers which are small elongated thread-like structures bound together by connective tissue. In addition the muscular fibers of voluntary muscles are marked by alternate light and dark striations-the involuntary muscles present no such striations with the exception of the muscular tissue in the heart. This striated involuntary muscle is desiginated cardiac muscle andis found only in the heart. It presents other histological features which are characteristic of cardiac muscle. It is understood that these histological features are apparent only when the the tissue is subjected to microscopic examination. This could be dwelt upon at great length but I shall not do it in this work because I am concerned with only the physiological aspect of voluntary muscle-the phenomenon of voluntary muscular contractility and irritability.

(Research workers in the field of physiology have been devoting their attention to muscular contraction in every aspect. The results of their work have been published in book form as well as in periodicals. I have consulted freely the work of the outstanding scientists in the field and will refer to their findings from time to time. I consulted the most recent work that has been done by refering to "Biological Abstracts" and "The Journal of Physiology".)

Now we define irritability as the power which certain tissues possess of responding by some change (transformation of energy) to the action of an external agent which is called the stimulus. Contractility is the power that certain tissues possess of responding to a stimulus by a change of form. It is well to note that contractility and irratilibility do not necessarily go together, for it will be found that both muscle and nerve are irritable but of the two, only muscle is contractile.

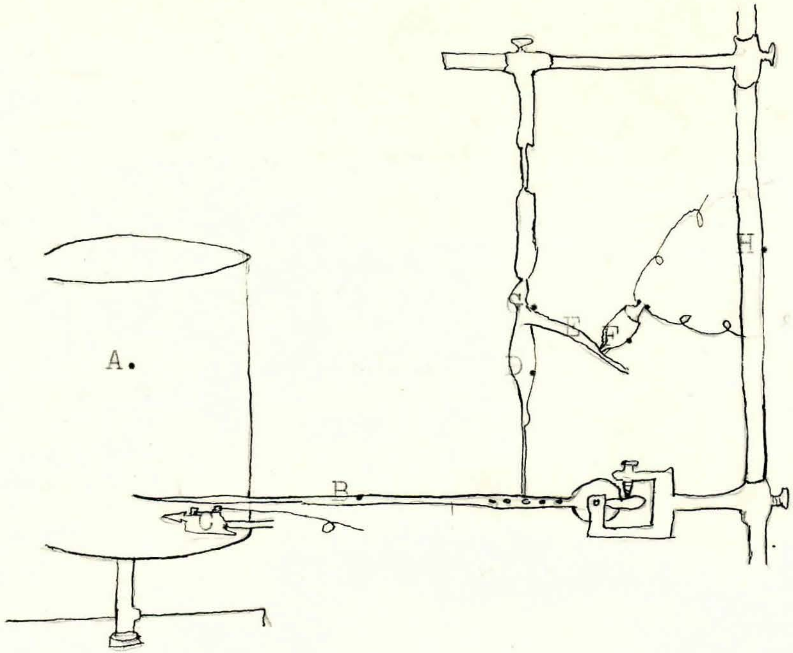
To elaborate on the contractile process, according to Mitchell, the nature of the process, as it appears in the light of our present knowledge, is that the excitation causes the sudden liberation of lactic acid and probably phosphoric acid from some very unstable chemical compound in muscular substance. This compound is probably hexose diphosphate. Changes of hydrogen ion concentration at some definitely localized parts of the cellare caused by this reaction. According to this theory, this change causes the development of tension in the muscle fibrallae. It is not definitely known just why this tension develops but it is probably due the change in the location of water, because of the increased attraction by muscle colloids. It may also be the result of sudden change in osmotic pressure. According to Bayliss, "the hydrogen ions from the dissociation of lactic acid polarize the cell membrane and in the separation of inorganic salts from absorption by colloids, these electrolytes set free, increase osmotic pressure of contents and cause shortening by attracting water from one part of the fiber to another." It may also be the result of a sudden change in surface tension. Also, perhaps each of these forces is in part responsible for the development of tension. As soon as acid is produced in the muscle, the process of restoration begins. This includes oxidation in part (10%) of the lactic acid and restoration of the remainder (90%) to its original state. Some of the glycogen store in the muscle is used up in this restoration process. Tension decreases and the muscle relaxes with the disappearance of the acid.

The normal stimulus that leads to muscular contraction is a nervous impulse and this in turn is converted into a muscular impulse which is visible as a contraction only at the end-plates. In the living animal,this nerve impulse starts at the nerve center,either brain or spinal cord,and travels down the nerve to the muscle. In a reflex action,the nervous impulse in the nerve center is started by a sensory impulse from the periphery. Instead of studyingthe details of muscular contraction in the living animal,I have studied the gastrocnemius muscle of the frog,which in all my work, was removed from the body and made to contract by artificial stimuli. The artificial stimulation may be mechanical,electrical,or chemical. I used electrical stimulation in all my work,using induced current. This method of control is of course more under control and the strength and duration of the stimulus can be regulated easily.

It is not necessary to describe in detail the electrical apparatus used,but let it suffice to say that a dry cell hooked up with an induction coil was used to produced the stimulus. Platinum electrodes from the secondary coil of the inductorium were used to conduct the stimuli to the nerve. From time to time as they are needed,drawings of the apparatus will be made in a simple manner in order to show the nature of the apparatus that was used.

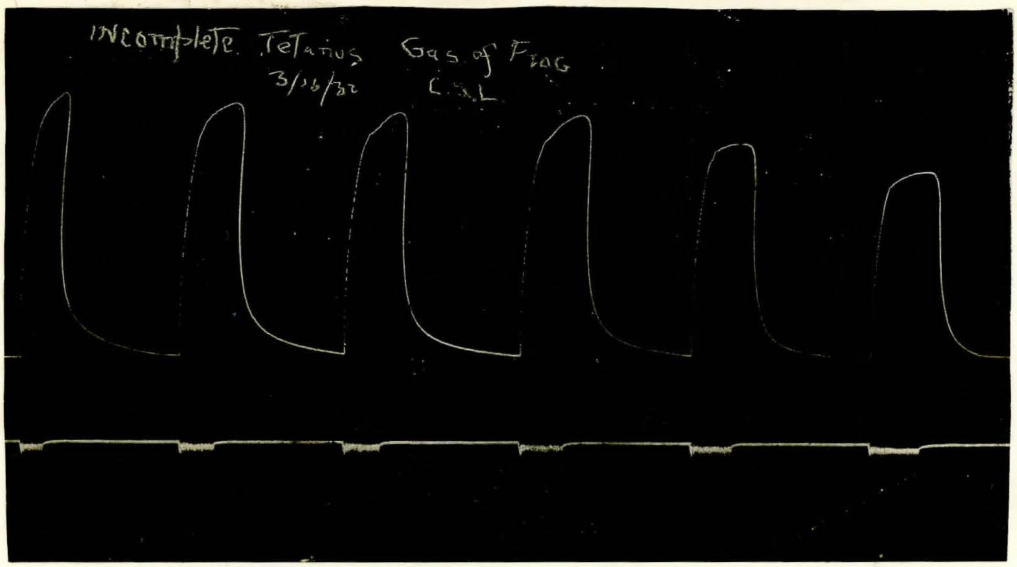
It is necessary to describe the muscle-nerve preparation which I used. First of all, the nerve connections between the brain and spinal cord were severed by pithing the frog. The sciatic nerve which comes from the sciatic plexus between the muscles of the thigh to supply the muscles of the fore-leg,is then carefully dissected out and the gastrocnemius is removed along with the sciatic nerve, preserving as much of the tendon of Achilles as possible. A small portion of the femur is preserved to be used as a means of clamping the muscle, the tendon of Achilles being used as an attachment to the writing lever.

A diagram of the apparatus which was used is shown below:



A. Kymograph drum
B. Writing lever
C. Signal magnet
D. Muscle
E. Nerve
F. Electrodes
G. Muscle clamp
H. Stand.

Now to pass on to the results. Before going ahead with the genesis of tetanus and the effect of temperature I shall present first the result of a single instantaneous stimulus upon an exised gastrocnemius muscle of a medium sized frog. This causes a simple muscular contraction or twitch. The graphic KYMOGRAPH record of such a contraction is shown below. It is called the simple muscle curve. I shall analyze this record and discuss in detail the significance of such a record.



1

This is a KYMOGRAPH record showing what is known as incomplete tetanus. It consists of six individual muscle contractions caused by the same number of faradiac stimulations. "Broadly speaking however, theetwitch is a physiological abstraction, for single responses such as are shown here, seldom occur in the intact animal."-Fulton. Nevertheless, the single muscular contractions such as are shown here, do serve as a means of studying the basic principles of muscular contraction.

The muscle which was used in making this record was an excised gastrocnemius muscle of the frog and it differs from the twitch of an intact gastrocnemius muscle of the frog in that the sharp angle is obscured.

As stated above, electrical stimulation was used. One dry cell was connected in series with an inductorium and the stimulation was conducted to the sciatic nerve of the muscle-nerve preparation by platinum electrodes. A simple key in the circuit served as a means of making and breaking the current. A single magnet included in the primary circuit indicated on the lower line at what time th e stimulation was applied and also its duration. This record was made with the writing lever and thus the muscle unweighed. The temperature of the room in which the work was carried on, was 23 Centigrade.

It is seen that the ascending curve begins abruptly and is wholly convex in outline. At the culmination of each twitch is a relatively flat plateau which terminates abruptly to form a somewhat obscured angle. This corner, according to Fulton may be appropriately termed 'the subsidence angle' but it may be simply refered to as the "angle". The abrupt and convex ascent, the plateau, and the sudden terminatio n of the plateau may be taken as fundamental characteristics of a single isometric contraction curve. It can be seen that the longer the duration of stimulus as shown by the signal magnet the more clearly defined and longer is the plateau. The duration of electrica l response is thus seen to be directly proportional to the duration of electrical stimulation.

Each curve is seen to reveal the duration of three periods-the contraction period (phase of muscle shortening), the latent period and the relaxation period or phase of muscle restoration. According to Mitchell, in the frog, the first of these three periods or the latent period lasts about .01 second, the second phase lasts about .04 sec. and the phase of muscle restoration about .05 second.

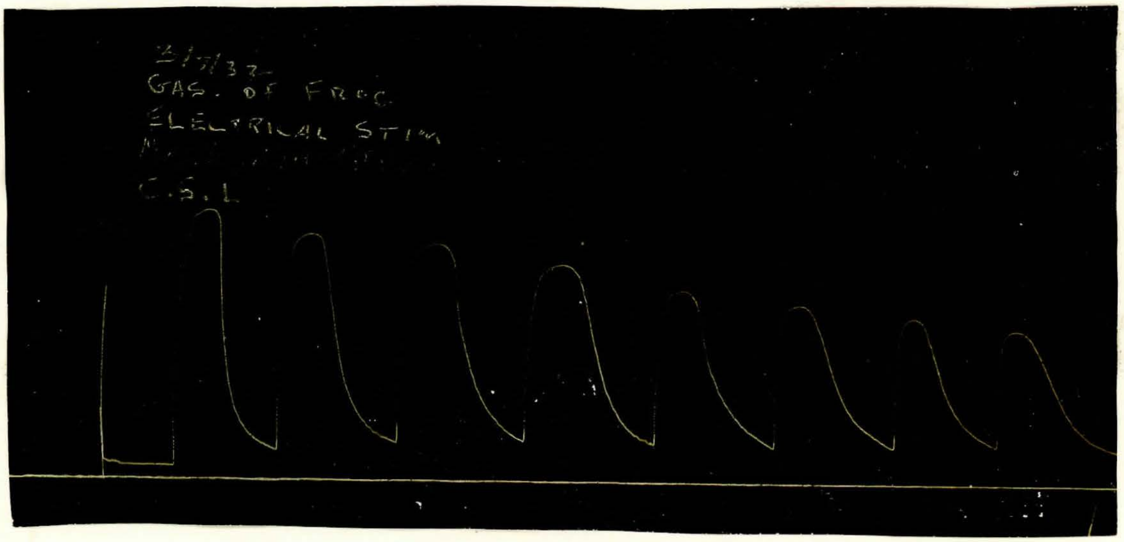
The latent period may be defined as the interval between the instant of stimulation and the commencement of mechanical shortening of the muscle. As mechanical recording instruments have been improved, the latent period of skeletal muscle has become progressively smaller until it would have seemed to have been reduced to nothing. deJongh who published his investigations in the field in 1923 expresses the beleife that the moment of stimulation and the beginning of the mechanical response of heart muscle are simultaneous. Fulton divides the latent period of skeletal muscle into four phases-the conduction time of the motor nerve,the delay at the motor end-plate, a period following the beginning of the muscle action current during which mechanical properties of the muscle remain apparently unaffected by the stimuli,(this has been termed the true latent period) and a period of rigidityduring which the muscle,altho affected by the excitation does not shorten appreciately. The latent period marks the spread of the wave of excitation over the muscle cells. The process of excitation,in my work, the application of electrical stimulation,results in the development of tension in the normal muscle. This tension ,once it has been developed in muscle is bound to be followed by contraction unless it is attached to a weight greater than it can move.

According to Mitchell,"when the tension developed becomes sufficient to overcome the inertia of the muscle and the attached weights, the latent periods ends and the contraction or shortening period begins. It is generally conced that in this process the dark bands of the fibrillae are increased in volume while the muscle contracts. The minute details of this process of shortening are exceedingly difficult to make out but it is almost a certainity that movement of water is involved."

In this kymograph record shown above the lever is raised by the shortening of the muscle. The relationship can be clearly established by refering to the diagram of the apparatus. The lever, of course writes upon the smoked paper and thus the movement is recorded, more or less magnified according to the leverage which is used. The recording surface was in movement by virtue of the movement of the kymograph drum, and thus the record above is in the form of a curve. The recording surface moved with uniform velocity at a comparatively low speed of drum.

The process of relaxation as pictured by the descending curve is not a pulling out of the muscle to its resting shape by external forces but it is a reversal of the process of contraction and it thus depends upon definite chemical or physio-chemical changes within the muscle cells. It is noted that the time for the contraction period in this record is slightly shorter than the time required for the relaxation period. The relative variations of time between these two processes differs under certain conditions. For example, cold prolongs the relaxation of frog muscle much more than it does the contraction period. Also, during the onset of fatigue in a frog musclethe relaxation phase is so prolonged in proportion to the contraction phase that the muscle does not completely relax between the separate when they are given at the rate of only one per second. This failure to relax completely is called contracture and it may be caused either by cold or fatigue. I stated above that, according to Mitchell (and Howell holds the same theory) some of the material in the light bands is imbibed into the darker bands. The process is evidently a reversible one because during the process or phase of relaxation the imbibed material passes back to the light band. Refering to certain external conditions causing changes in the time of the phases of contraction and relaxation, it is noteworthy that the phase of relaxation is more easily prolonged or shorte-ened by varying conditions than the phase of contraction.

The kymograph smoked-paper record below shows the effect of fatigue on the phase of relaxation.



II

A comparatively slow drum was used in making this record. The temperature of the muscle was about 23 degrees Centigrade. It is seen that as the muscle becomes fatigued, the phase of relaxation is noticeably prolonged while the phase of contraction remains about the same.

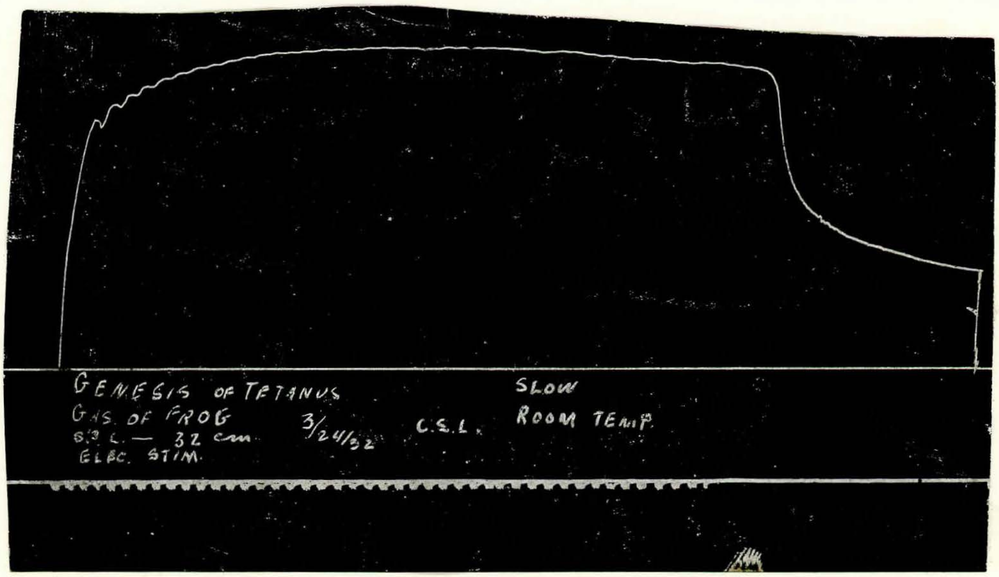
Now I shall discuss tetanus and present the experimental work which I have done on the genesis of tetanus. As stated above muscular contractions as used for motion and locomotion are not mere twitches as were shown and described above but are muscular contractions sustained for an indefinite period.

This sustained contraction is called tetanus. It is the result of a nuscle receiving a series of rapidly repeated stimuli which results in its contraction as long as the stimuli are sent in or until its irritability from the effect of fatigue. Bayliss states a very comprehensive definition in his "Principles of Physiology"- "When a second stimulus is applied to a skeletal muscle before the first contraction has disappeared,the contraction due to the second stimulation starts at the level at which the first contraction is at the time,and so on for consequent stimuli. A summation is thus produced by which the strength of contraction is much greater than brought about by a single stimulus. After a certain number have been applied no farther increase in height of contraction results and the constant level thus maintained is tetanic contraction."

Before taking up the genesis of tetanus,it is necessary to the note the facts of summation,because compound or tetanic contractions are possible because of the tendency of the contractions of individual muscle fibers to fuse,that is,their effects are added together and this addition may be demonstrated by the process called summation of muscular contraction. This process occurs when two stimuli are given in rapid succession to a muscle nerve preparation. The second stimulus falls into the muscle at the apex of the contraction caused by the first stimulus and even if the first contraction is maximal, the muscle will shorten still farther. This is because the effects of a second stimulus are added on to those of the first one,so that a summating effect occurs. According to Mitchell"Some of the fibers that are not thrown into contraction by the first stimulus are effectively excited by the second one. This must be the effect to be in accord with the "all or nothing"principle to the contraction of muscle fibers."

To explain breifly the"all or nothing"principle in muscular contraction, Fulton states that Gotch made the important observation early in the present century, that when one of the lumbar roots supplying the gastrocnemius muscle of the frog, a certain portion of the muscle fibers remained unstimulated and could be called into action by the stimulation of the other root. In view of this and other evidence, Gotch suggested that muscular response was brought about byvariation in the number of contractile units in activity at any one time rather than thru variation in size of the nerve impulse.

The extent of the summations in cases such as are described above varies with a number of conditions-the interval between the stimuli, the relative strengths of the stimuli, the load carried by the muscle, etc. If we take the simplest condition of two maximal stimuli and a moderately loaded muscle, it is found that the greatest summation occurswhen the stimuli are so placed that the second contraction begins at the apex of the first. If the stimuli are closer together, so that the second contraction falls shortly after the first has begun, the total shortening is less and the same is true as the second contraction falls later and later in the period of relaxation after the first contraction. If instead of two successive stimuli, we use three stimuli, falling into the muscle at proper intervals, a still farther summation occurs. If a number of stimuli are given to a muscle in rapid succession a partial fusion of all the resulting contractions occurs. The more rapidly the stimuli of such a series are repeated, the more nearly do the resulting contractions tend to fuse until at a certain definite rate which varies with different muscles, contraction is steadily maintained with no sign of relaxation between the seperate stimuli. Also the number of stimuli required to produce tetanus varies with the condition of the muscle. The number of stimuli required to produce tetanus in the gastrocnemius muscle of the frog or in other words the genesis of tetanus, was carefully worked out in my experimental work. But before presenting that part of this report, there is shown below a kymograph record of voluntary frog muscle which will aid in illustrating summation.



III

This is a kymograph record of a tetanic contraction of an excised gastrocnemius muscle of a medium sized frog. The temperature of the muscle was about 23 degrees Centigrade and a slow speed of drum was used in recording the contraction. The summation effect can be seen. It will be noted that the first four stimuli are summated and thus a greater shortening of the muscle is obtained than that of the first stimulation. The shortening reaches a maximum and after that a flat tetanic contraction curve results.

The work that has been done on the genesis of tetanus by physiologists who worked in this particular field of physiology,was conducted with intact muscle. All the experimental work that I did,was done with the excised gastrocnemius muscle of the frog. The frogs which I used were medium sized winter frogs. Before presenting the records which I obtained,I shall summerize the results of the work done in this field as described in Fulton,Mitchell,Howell,and Roaf.

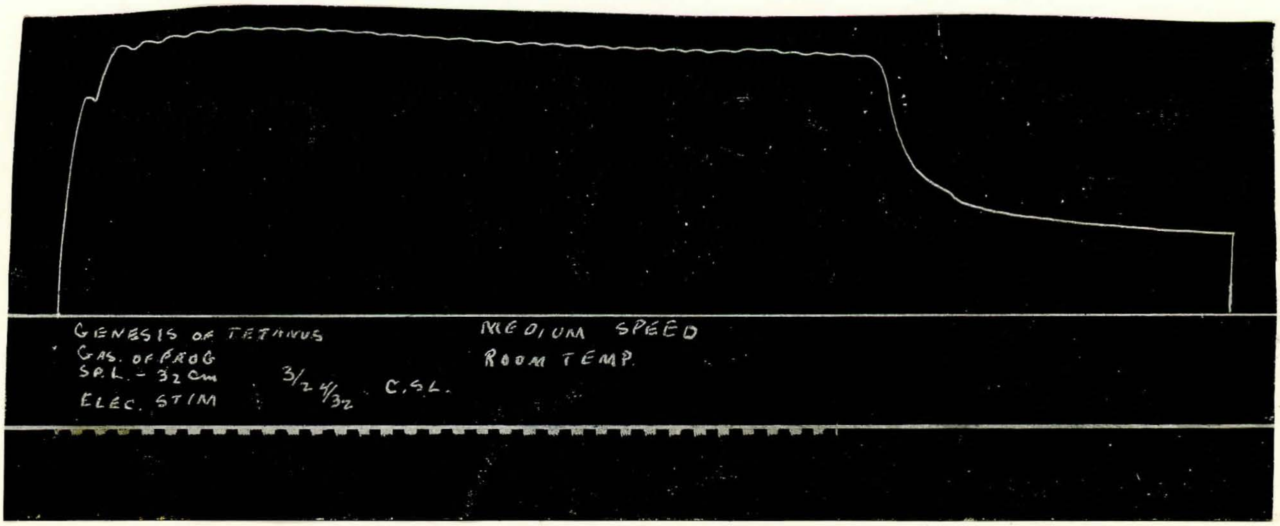
Fulton's work is perhaps the most recent. He states that a rate of stimulation of 25 per second gives rise to a tetanic contraction. He notes that by increasing the rate of stimulation the rate of the tetanus ascent is increased but the total tension developed is not greatly increased. His work,in a large number of observations showed that as between a rate of 25 per second which would cause fusion of individual responses and one of 100 per second the increase of total tension developed is usually not more than 5 to 10 per cent. The duration of the ascent,however,might be two or three times as rapid at the higher rate of stimulation.

Mitchell states that at the rate of about twenty stimuli per second for the gastrocnemius muscle of the frog,contraction is steadily maintained with no sign of relaxation between the seperate stimuli. I stated above that most of the work that has been done refers to intact muscle,but it seems that Mitchell refers to excised muscle. In other words,the same muscle-nerve preparation that I used. These results should therefore compare with the results which I obtained. He also states that the rate of stimulation required to produce tetanus varies with differnt muscles andwith its condition.

Howell and Roaf both state that the frog's muscle goes into complete tetanus with a rate of stimulation of from 20 to 30 per second. Halliburton states that the rate of stimulation necessary to produce complete tetanus in the gastrocnemius muscle of the frog averages 15 to 20 per second. It is not stated whether the muscle is excised or intact,but probably Halliburton is refering to excised muscle.

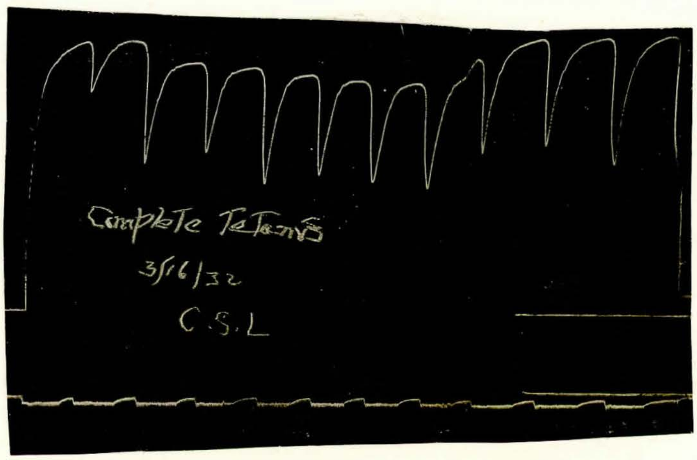
That sums up,in breif,a large amount of work that has been done and more or less compiled by eminent physiologists in the field and it is appropiate at this time to present my kymograph records together with a brief analysis and comparison of each record.

The first of these is one which records the tetanic contraction produced by five electrical stimulations per second.

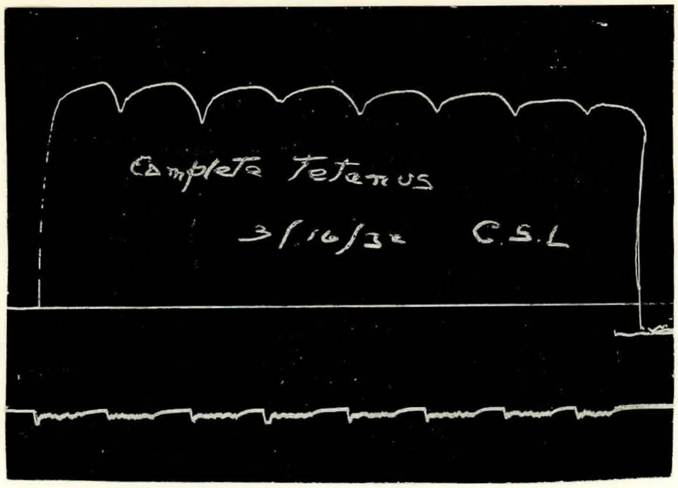


IV

The temperature of the muscle was about 23 degrees Centigrade. A medium speed of drum was used. It can be seen that the phase of relaxation of each contraction is apparent,so that there is not complete tetanic contraction. For stimulations of say,three per second,two per second or one per second, the state of contraction will not be as complete, that is, the contractions will not tend to fuse to the same extent as shown here. The three records below illustrate this very well.

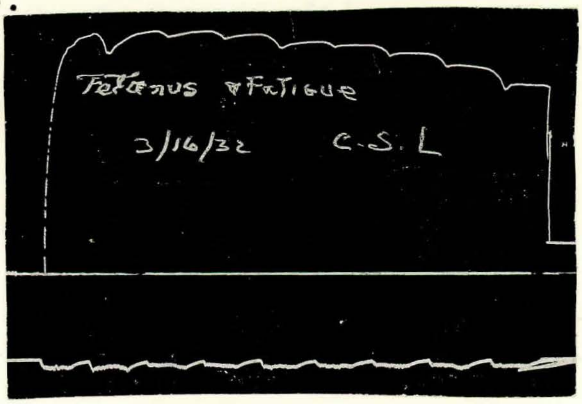


This record is labeled complete tetanus but this is an error because it is incomplete tetanus. The temperature is the same as above but the speed of the drum is relatively faster than thatt of the first record involving the genesis of tetanus. About one stimulation per second was sent into the muscle in making this contraction. The lower line is the signal magnet.



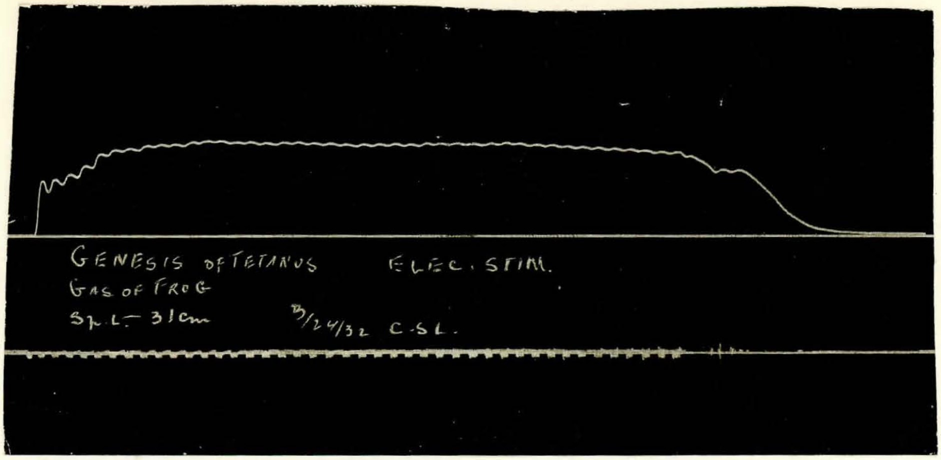
VI

This kymograph record of muscular contraction is also erroneously labeled complte tetanus. It is complete tetanus. About two stimulations per second were sent into the muscle and it can be seen that the individual contractions are more fused that of the records immediately preceding. The temperature and speed of the drum are the same as that of the record above.



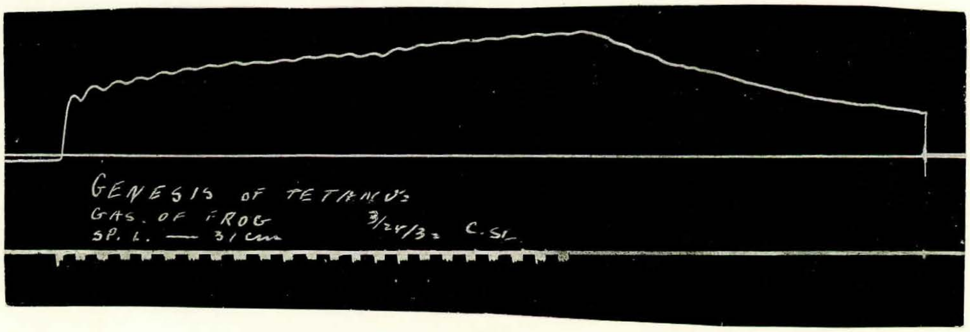
VII

This kymograph record was made under the same conditions as the records above with the exception that three stimulations per second were used in producing the incomplete tetanus. It is also erroneously labeled complete tetanus. It is noticed that the contractions tend to be more fused.



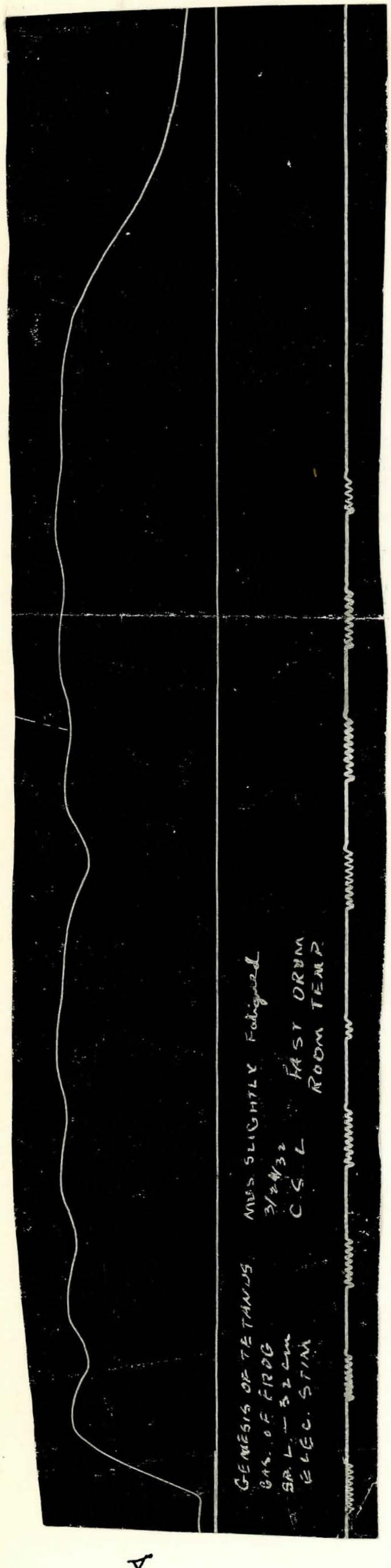
VIII

The number of stimulaitons used in this contraction was five per second. However the strength of the electrical stimulation was not as strong as that used in the contractions recorded above. This is shown by the decreased heigth of contraction. Other conditions were the same as above.



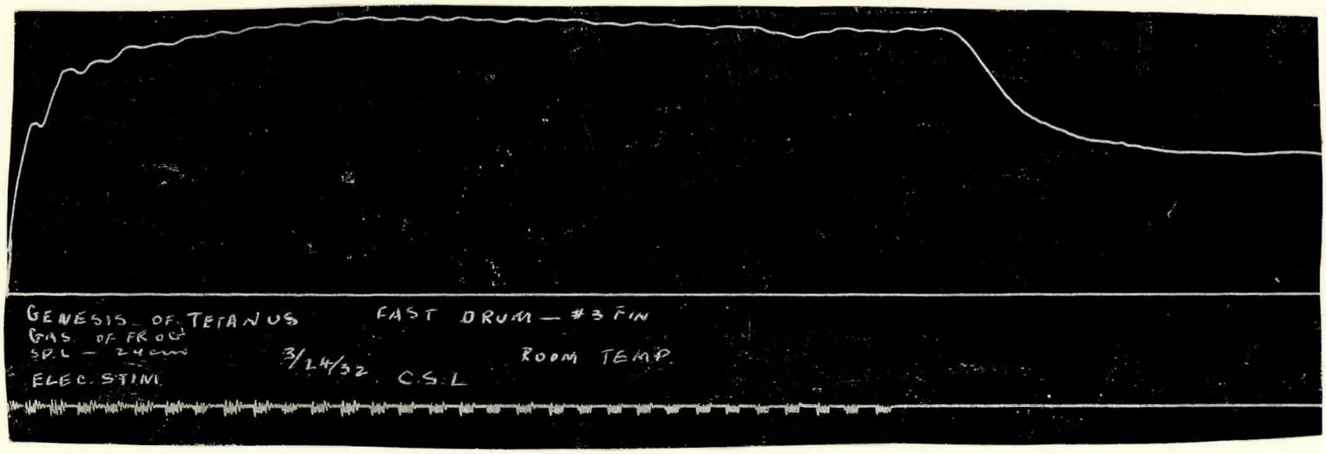
IX

The rate of stimulation was five per second. Otherwise, same conditions as in record immediately preceding. It is seen that the muscle becomes fatigued as this happens the muscle shows less external sign of relaxation between successive stimuli. Fatigue is a factor which definitely affects the rate of stimulations per second necessary to produce complete tetanus. The gastrocnemius muscle of a frog, if it is fatigued may go into a state of complete tetanus with a rate of stimulation of ten per second.



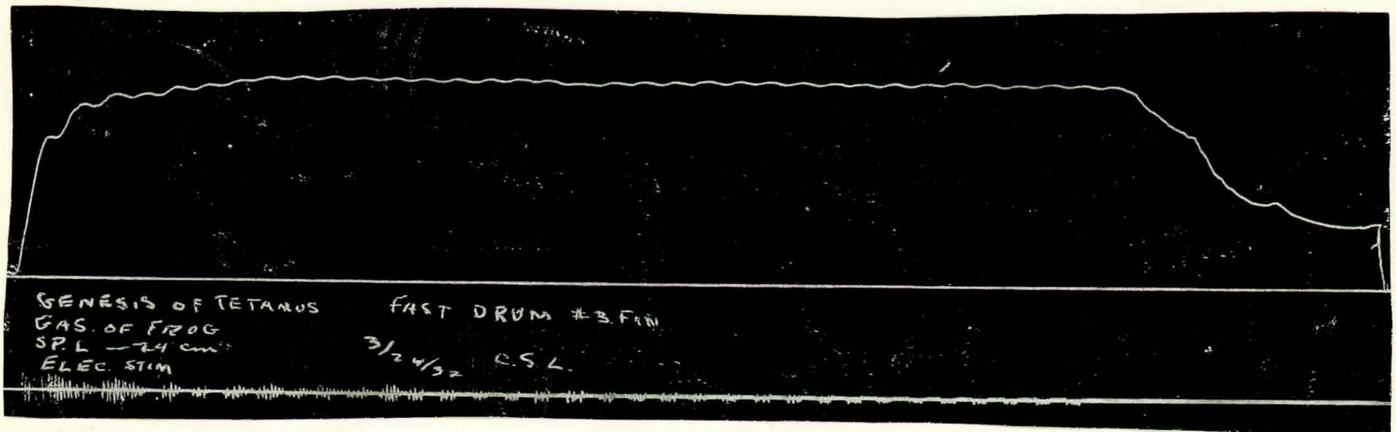
X

The rate of stimulation used in the muscular contraction recorded in this kymograph record was five per second. Other conditions were the same as above with the exception that a very fast speed of drum was used. It is seen that as the muscle fatigues slightly, the contractions tend to fuse to a greater extent. The line below is that of the signal magnet. Note the duration of stimulation.



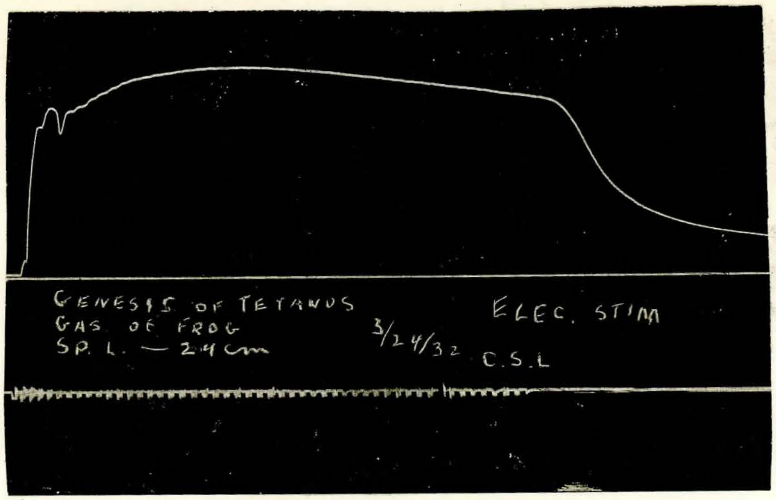
XI

Temperature the same as above, a moderately fast drum was used but the rate of stimulation was increased from five per second to ten per second. Note that altho there is about the same heigth of contraction the contractions tend to be more fused and the muscle is in a more complete condition of tetanus.

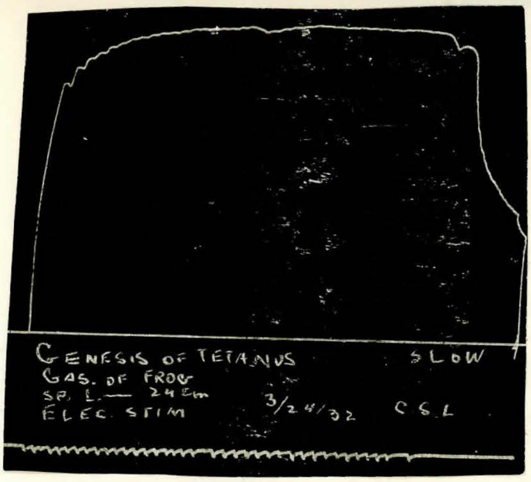


XII

This record was made under exactly the same conditions as the one immediately preceding with the exception that the strength of electrical stimulus used is not as great. The same features noted in the preceding muscular contractions are present in this record.



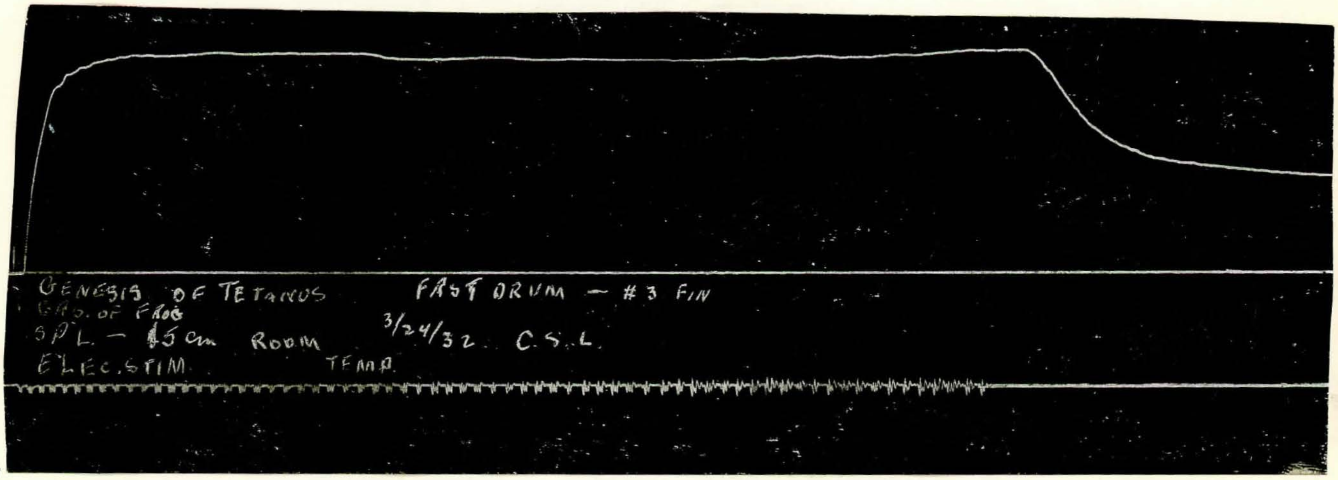
The rate of stimulation in this muscular contaraction was ten per second. The temperture of the muscle was about 23 degrees Centigrade and a medium speed of drum was used in recording the contraction. Before stimulating the muscle I fatigued it in order to find out the difference in the number of stimuli per second required to produce complete tetanus as compared with the rate of stimulation required to produce tetanus in the normal muscle. It is seen that the contractions tend to fuse as soon as the maximum heigth is attained and as the plateau slopes toward the base line the contractions are entirely fused. In connection with this, Howell states "that ten stimulations per second applied to a frog muscle will after a time cause complete tetanus altho at first the contractions are not fused to any markes degree. The reason for this is that the phase of relaxation is slower as the muscle becomes fatigued."



XIV

The muscle used in preparing this kymograph was stimulated under exactly the same conditions as in the record immediately preceding, with the exception that the muscle was not in a fatigued condition. It is noted that the individual contractions are distinctly not fused altho the rate of stimulation is ten per second.

All the kymograph records shown above with the exception of XIII show incomplete tetanus-there is not a complete fusion of individual contractions.



XV

The rate of stimulation was sixteen per second. The temperature was about 23 degrees Centigrade and a fast drum was used in recording the contraction. It is senn that the individual contractions are completely fused-tetanus is complete. Compare this record with VIII and XI and note that only in XV is tetanus complete. As stated above the rates of stimulation in VIII, and XI were five and ten per second respectively. I found then that a rate of stimulation of sixteen per second will give rise to a complete tetanic contraction, or in other words will cause fusion of individual responses.

CONCLUSIONS

The data above were results of my own experimental work and the conclusions and results of work done by prominent physiologists as they are recorded in the text-books I refered to. They are listed in the bibliography.

From the results obtained in my own experimental work, it seems that a rate of stimulation of 16 per second gives rise to a complete tetanus, under normal conditions. This is true only of fresh muscle and at a temperature of about 23 degrees Centigrade. My results also indicate that a rate of stimulation of ten per second in a muscle which has been fatigued results in the same fusion of individual responses as a rate of stimulation of sixteen per second provokes in a fresh muscle. It was also evident that the strength of the stimuli had no effect on the rate of stimulation necessary to cause complete tetanus. This can be seen by comparing kymograph records XI and XII.

As stated before all my work was done with an excised muscle and it was noted above that the rate of stimulation necessary to produce complete tetanus is different with an intact muscle. The rate of stimulation necessary to produce complete tetanus as determined by my experimental work compares favorably with that stated by Howell in that he states a rate of fifteen-twenty is necessary. Also Michell, Hoaf, and Halliburton state that a rate of twenty stimulations per second is necessary, and in addition all of them state that it is dependent within a certain range, upon the size and age of the frog so a rate of stimulation of sixteen per second closely approxmiates the results stated by the sources of information to which I refered.

This experimantal work was done under the direction of Professor Brownbach, He also refered me to all the references sources available on the subject. This included the latest work done as recorded in "Biological Abstracts" and "The Journal of Physiology".

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