ON THE RELATION OF THE STRENGTH-FREQUENCY CURVE IN EXCITATION BY ALTERNATING CURRENT TO THE STRENGTH-DURATION AND LATENT ADDITION CURVES OF THE NERVE FIBER

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In 1908, as is well known, Nernst derived from his theory of nerve excitation that the threshold strength of alternating currents should increase in proportion to the square root of the frequency of the applied currents. A considerable divergence, however, of the actual data from Nernst's law has been pointed out by a number of investigators (see Coppée, 1934).

Later, Blair (1932), Hill (1936), and Rashevsky (1940) deduced the relation $v \propto \sqrt{k^2 + (2\pi f)^2}$ for high frequency alternating currents, where v represents the threshold strength, f the frequency of current, and k the constant which characterizes the state of the nerve. But, careful experiments done by Hill, Katz, and Solandt (1936) and by Katz (1939) disclosed an unmistakable discrepancy of the observed strength-frequency curve from the calculated one.

The present investigation was undertaken with a view to securing rigid experimental data on the strength-frequency relation with single nerve fibers. To obtain detailed information as to the state of the nerve fiber under investigation, the strength-capacity curve and the time course of the threshold changes by a brief subthreshold shock were mapped out on the same preparation.

The results of our investigation indicated very clearly that, in excitation of single nerve fibers by alternating currents, the threshold strength increases more markedly than what has been predicted by Blair, Hill, and others. In the range of frequency from 500 up to 1500 cycles per second, the theory of nerve excitation advocated by one of us (Tasaki (1942)) proved to yield results which agree well with the observed values, while the previous theory assuming simple exponential decay of the local excitatory state in the absence of imposed current was found to give values far greater than the observed ones. For frequencies higher than 3000 cycles per second, however, alternating currents of near the threshold strength were found to modify the state of the nerve fiber and,

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in consequence, it was not feasible to derive the threshold strength for a steady response from the data obtained in the normal resting state of the nerve fiber.

Method

The alternating current stimuli were obtained from the arrangement shown diagrammatically in Fig. 1. Alternating current from an oscillator circuit was led to the first grid of a heptode (6L7G). To the third grid of this vacuum tube was applied an exponentially rising voltage started by closing the contact K in the figure; the contact was operated automatically by means of a thyratron connected to the sweep circuit for the Braun tube. The output of the heptode was amplified with a power tube (amp. 1 in the figure) and was then led to the Braun tube. The voltage applied to the Braun tube was tapped so as to apply to the nerve fiber. The strength of the alternating
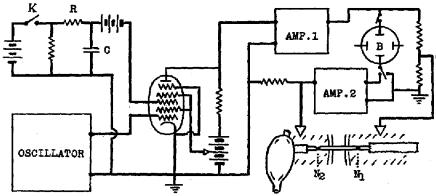

Fig. 1. Experimental arrangements used for excitation of a single nerve fiber by exponentially increasing A.C. The RC product of the condenser circuit determined the rate of rise in the amplitude of the A.C. Amp. 1 in the figure served to amplify the stimulating currents and amp. 2 to amplify the action currents from the fiber. B, Braun tube. K, contact to start stimuli.

currents acting upon the fiber was read off from the amplitude of the figure on the screen of the Braun tube and from the potential divider leading to one of the nonpolarizable electrodes (Zn-$ZnSO_4$-Ringer type).

The stimulating currents were applied, as a rule, to the single fiber preparation mounted on the "bridge-insulator" (Tasaki, 1939). The length of the myelinated region of the preparation suspended in the air was generally between 0.7 and 1.0 mm. On several occasions, however, the central intact portion of the single fiber preparation was mounted on the bridge-insulator having a gap of about 3 mm. and threshold determinations were made taking muscular contractions as index of nerve excitation. In most cases, large motor nerve fibers innervating the gastrocnemius muscle of the toad were used for the experiments.

Condenser shocks were obtained by the technique described in a previous paper (Tasaki, 1942). The interval between two brief condenser shocks was controlled by means of a Helmholtz pendulum.

With the nerve fiber preparation mounted on a bridge-insulator, it is in general easy to record action currents at the site of stimulation (Tasaki and Takeuchi, 1941). In the diagram of Fig. 1, the electrode on the left-hand side in the figure serves to lead the action currents from the fiber, together with stimulating currents sent through the fiber, to the amplifier (amp. 2). Between this lead electrode and the earth, a resistance of about 0.1 megohm was connected (cf. Tasaki and Takeuchi, 1941).

When the frequency of the alternating current was increased up to 3000 cycles per second or more, the threshold became so high that observation of the action currents at the site of stimulation was quite difficult. For such high frequencies, threshold determinations were made taking muscle action potentials as an index of nerve excitation. In doing so, the shallow pool of Ringer's fluid in which the muscle was placed was grounded by the use of an auxilliary electrode and the grid electrode (leading to amp. 2) was brought in contact with a part of the muscle.

When the effects of the alternating currents upon the configuration of the action current were investigated, the alternating current Wheatstone bridge was adopted to suppress the deflection of the electron beam by the applied currents.

RESULTS

1. Action Currents Recorded at the Site of Stimulation by A.C. and the Effects of A.C. upon the Nerve Fiber.—The temporal configurations of the stimulating currents obtainable by the arrangements of Fig. 1 are shown by several examples of oscillograph records furnished in Fig. 2. In most cases, the amplitude of the sinusoidal currents (50 to 40,000 cycles per second) was increased exponentially at a time constant between 0.02 and 0.2 second. By a series of preliminary experiments, it was shown that the change in the rate of increase of the alternating current amplitude does not affect the threshold strength for a steady response of the nerve fiber to alternating currents of below 4000 cycles per second. With currents of above 5000 cycles per second, it was found difficult to obtain a steady response, due apparently to a progressive change in the state of the nerve fiber during passage of the currents.

Records of action currents from single nerve fibers were taken at the site of stimulation by the use of the experimental arrangements illustrated in Fig. 1. Records furnished in Fig. 3 were obtained with alternating currents of 50 (left column) and 500 cycles per second (right column). As the upper deflection plate of the Braun tube in the figure has been disconnected from the stimulating circuit in this case, the irregularity in the form of the observed sinusoidal currents is evidently attributable to the distortion of the currents by the nerve amplifier (amp. 2) with small coupling condensers.

It is seen in the figure that, in threshold excitation of a nerve fiber by low frequency alternating currents (Fig. 3 B), action currents are released at the moments when the stimulating current attains the maxima. When the intensity of the alternating current was increased, either single or repetitive responses in every half cycle of the stimulating current were generally observed (Fig. 3 C).
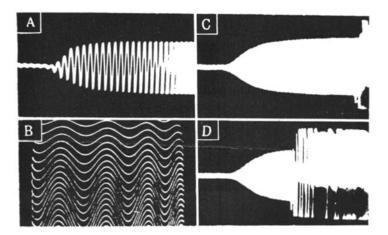
FIG. 2. A, record of A.C. of 50 cycles per second obtained with the circuit shown in Fig. 1; the amplitude rose with time constant of 0.08 second; amp. 2 in the preceding figure was switched off. B, A.C. of 1000 cycles per second increasing its amplitude exponentially with a time constant of 0.08 second; the electron beam of the Braun tube was repetitively sweeping in the horizontal direction at a frequency of 250 times per second, and the figure on the screen of the tube was slowly moved in the vertical direction. C, superimposition of muscle action potentials upon the stimulating current of 30,000 cycles per second increasing exponentially with time constant of 0.16 second; the pool of Ringer in which the node $N_?$ in the preceding figure was immersed was grounded by means of another non-polarizable electrode and the grid electrode was placed on the muscle; the final value of the amplitude of the A.C. was 1.2 volt; temperature was 13°C. D, same as C, but with stimulating current 1.3 times as strong as in C.
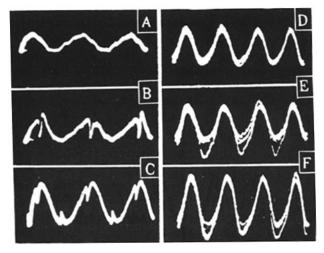

FIG. 3. Action currents of a single nerve fiber led from the site of stimulation by A.C., recorded by the use of the arrangement shown in Fig. 1 (with the stimulating circuit disconnected from the deflection plate of the Braun tube). A, frequency 50 cycles per second, amplitude 42 mv., the time of exposure of the camera (Leica) to the figure on the Braun tube face about 0.08 second. B, same as A, but at 49 mv. C, at 118 mv., time of exposure approximately 0.18 second. D, E, and F, stimulation by A.C. of 500 cycles per second at three different strengths; time of exposure of the camera approximately 0.03 second; a large afferent fiber arising in the toad gastrocnemius muscle at 13°C.

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With much higher stimulus frequencies, however, nerve impulses were found to be released at several alternating current cycles, owing doubtlessly to intervention of refractoriness following initiation of every impulse.

It is interesting to compare the records of Fig. 3 with those obtained by Galambos and Davis (1943, Figs. 12 and 13) showing the relation of the aural microphonic cycle to the response of a single auditory unit. The resemblance
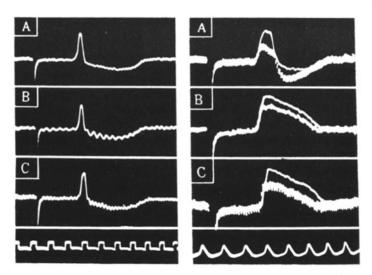

FIG. 4. Effects of high frequency A.C. upon the configuration of the action current from a nerve fiber. The A.C. was applied to the fiber by means of a Wheatstone bridge balanced for the resistance of the fiber at rest. Left column, records taken from a large motor fiber of the toad at 11°C.; the resistance between the electrodes, including the fiber, was 25 megohms; A, normal binodal action current; B, action current induced during passage of an A.C. of 2300 cycles per second in frequency and 0.02 volt in amplitude; C, 4500 cycles per second and 0.02 volt. Right column: Records of two successive sweeps on the Braun tube face, one during passage of strong A.C. of 9000 cycles per second and the other at rest; A, A.C. strength 0.9 volt; B and C, after introduction of a 0.2 per cent cocaine-Ringer solution into the distal pool, A.C. strength 0.7 and 0.9 volt respectively. Time marker, 1000 cycles per second.

between their records and ours would be more than superficial, if the aural microphonic effect is responsible, as is generally assumed, for initiation of impulses in the auditory nerve fibers. It will be noted that the variability in the spot on the stimulus cycle, at which the nerve impulse arose, was much smaller in the present experiments than in those of Galambos and Davis.

With stimulating currents of above 3000 cycles per second, it was not feasible to record action currents at the site of stimulation by the technique just mentioned due (1) to augmentation of the amplitude of the stimulating cur-

rent resulting from the rise of threshold at high frequencies and (2) to reduction in the strength of the action current by the effect of a strong alternating current (Rosenblueth, Reboul, and Grass, 1940). Records furnished in Fig. 4 were obtained after suppression of the observed alternating current amplitude, using the Wheatstone bridge. As it was not possible to elicit a steady response with such high frequency alternating currents, action currents of the fiber were evoked in these cases by applying induction shocks to the proximal nerve trunk of the single fiber preparations. By this technique, the loss of impedance of the nerve fiber during passage of a nerve impulse (cf. Tasaki and Mizuguchi, 1949) could easily be demonstrated in the frequency range from 2000 to 5000 cycles per second. Records B and C in Fig. 4 (left column) were obtained by balancing the bridge for an alternating current of far below threshold. The slight increase in the amplitude of the alternating current during the negative phase of the "binodal" (Tasaki and Takeuchi, 1941) action currents attests undoubtedly to a decrease in the resistance of the nerve fiber during the period in which the two nodes (N_1 and N_2 in Fig. 1) on both sides of the bridge-insulator are in action simultaneously.

With frequencies higher than 7000 cycles per second, impedance change during activity could not be demonstrated (see Tasaki and Mizuguchi, 1949, discussion). But, when the strength of alternating current was increased and was approached to threshold, it was observed, confirming the observation by Rosenblueth and others, that the size of action current was suppressed to a considerable extent. Record A in Fig. 4 (right column) shows the effect of an alternating current of 9000 cycles per second in frequency and about 0.9 volt in amplitude. It is seen that the normal "binodal" action current has become markedly diphasic, indicating prolongation of the transmission time by the action of the alternating current. Records B and C in Fig. 4 (right column) were obtained after introduction of a 0.2 per cent cocaine-Ringer solution into the pool on the distal side of the bridge-insulator.

2. Determination of the Strength-Frequency, Strength-Duration, and Latent Addition Curves on One Single Fiber Preparation.—In an attempt to figure out the relationship among different types of strength-time curves, it is very desirable to determine all those curves on one and the same preparation under identical experimental conditions. With single nerve fiber preparations mounted on the bridge-insulator, excitability of the fiber shows amazing stability for many hours (Tasaki, 1939). We could easily determine the strength-frequency and strength-duration curves repeatedly on one and the same preparation, with satisfactory agreement between the data obtained at the beginning and at the end of a series of threshold determinations.

Threshold measurements were started about 15 minutes after introduction of a 0.2 per cent cocaine-Ringer solution into the pool on the proximal side of the bridge-insulator. We generally determined the strength-duration curve for

condenser discharge stimuli first, then the "latent addition curve," next the strength-frequency relation for alternating current stimuli, and finally the strength-duration curve again. By the term "latent addition curve," we mean the curve showing the time course of threshold variation brought about by a brief subthreshold (or conditioning) shock, traced by means of another brief (testing) shock applied at various intervals *before* and *after* delivery of the conditioning shock. The strength of the conditioning shock was chosen to be ±40 (sometimes ±50) per cent threshold. Both conditioning and testing stimuli were of the duration (time constant) of about 10 microseconds. As can
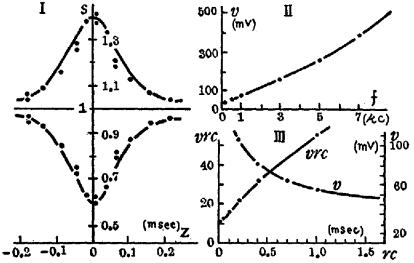

Fig. 5. Latent addition curve (I), strength-frequency curve (II), and strength-duration curve (III) determined on one and the same single nerve fiber. Large motor fiber innervating the gastrocnemius muscle of the toad. 12°C.

be seen in the example of the experiments shown in Fig. 5, threshold for the testing shock is temporarily reduced by a conditioning shock of the positive sign (namely, by a shock causing a current flowing in the same direction as the testing current) and is heightened by a conditioning shock of the negative sign. In the diagram of Fig. 5, I, threshold for the testing shock is plotted against the time interval from the delivery of the conditioning shock to the moment at which the testing shock is applied. The measurements were carried out with an accuracy of about 3 per cent, taking an electrical (sometimes mechanical) response of the muscle as index of nerve excitation.

In excitation by alternating currents of below 2000 cycles per second, threshold determinations could be done with high degree of reproducibility. The threshold strength determined by taking a train of muscle action potentials

as index agreed with the value obtained by taking a single response as index within the limit of about 3 to 4 per cent. For currents of above 5000 cycles per second, however, it was found that a repetitive response is induced at voltages considerably (10 to 20 per cent) above the single response threshold. Even at a strength well above threshold, the response in the muscle died out fairly rapidly. Furthermore, the rate of increase in the amplitude of alternating current seemed to affect the threshold value to some extent. Action currents of the nerve fiber set up by such high frequency alternating currents are, as we have seen in the experiment of Fig. 4 (right column), far smaller than those induced by low frequency currents; and, for a complete recovery in the response size after removal of the alternating current, about 20 seconds or more were required. It seemed therefore evident that the state of the nerve fiber is changed appreciably by high frequency alternating currents of threshold strengths.

3. Treatment of the Data by the Blair-Monnier-Hill-Rashevsky Theory.— According to the theory developed by Blair (1932), Monnier (1934), Hill (1936), and Rashevsky (1940), the development of the local excitatory state set up by a relatively short stimulating voltage is described by the differential equation

$$\frac{dp(t)}{dt} = KV(t) - kp(t), \tag{1}$$

in which $p(t)$ is the local excitatory state, $V(t)$ the stimulating voltage, and K and k are constants. For condenser discharge stimuli

$$V(t) = v\, e^{-t/rc},$$

the solution of this equation expressing the relation between the threshold strength v and the duration rc is given by

$$v\, rc = Q\, (k\, rc)^{krc/(krc-1)}, \tag{2}$$

in which Q represents the minimum quantity required for excitation (see Blair, 1932, and note that the rheobase R is equal to the product Qk).

For alternating current stimuli

$$V(t) = v\sin(2\pi ft),$$

the threshold condition becomes

$$v = Q\sqrt{(2\pi f)^2 + k^2}, \tag{3}$$

in which v in this case is the crest voltage of the alternating current of the threshold strength and f the alternating current frequency (see Hill, 1936).

The value of Q in these equations is best determined by extrapolation of the quantity-duration ($v\, rc$-rc) relation, and k from the latent addition curve stated

above. Equation (1) tells us that, following termination of a brief subthreshold shock, the excitatory state should decay exponentially with time constant $1/k$, and, as the equation is linear, the time course of this decaying excitatory state should be traced by the shock test method.

TABLE I

The Quantity-Duration, Strength-Frequency, and Latent Addition Relations Determined on One Single Fiber Preparation

The column "cal. (1)" shows the values calculated according to the Blair-Monnier-Hill-Rashevsky theory, and "cal. (2)" the values calculated by the method advocated by the present authors. 11°C. The quantity is given by the product of the threshold voltage v and the duration rc.

Quantity-duration relation				Latent addition	
rc	vrc (observed)	vrc cal. (1)	vrc cal. (2)	z	$f(z)$
msec.	*mv.·msec.*	*mv.·msec.*	*mv.·msec.*	*msec.*	
0	(16.6)	(16.6)	(16.6)	−0.24	0.09
0.008	17.0	18.4	17.0	−0.21	0.17
0.012	17.6	19.6	17.4	−0.18	0.28
0.02	18.2	21.0	17.8	−0.15	0.42
0.04	19.7	25.5	19.0	−0.12	0.56
0.10	23.5	37	22.5	−0.09	0.71
0.20	29.5	46	29	−0.06	0.86
0.40	40	69	41	−0.03	0.97
1.00	68	137	78	0	1.00
2.00	108	230	130	0.03	0.94
				0.06	0.82
Strength-frequency relation				0.09	0.63
Frequency	Strength observed	Strength cal. (1)	Strength cal. (2)	0.12	0.54
				0.15	0.43
kc.	*mv.*			0.18	0.34
0.1	42	94	58	0.21	0.27
0.5	62	106	61	0.24	0.21
1.0	88	138	82	0.27	0.16
1.5	127	170	128	0.30	0.11
3.0	231	326	Above 400	0.33	0.08
5.0	455	509	—		
7.0	770	728	—		

In the column labelled "cal. (1)" in Table I are given the values calculated according to equations (2) and (3) stated above, together with the experimental data from which the values of Q and k adopted for the calculation are derived. By extrapolation of the observed quantity-duration relation, the value of Q for this preparation was found to be 16.6 mv.·millisecond. The value of k was determined from the observed latent addition data presented in the right-hand

column of the table. The letter z in this column represents the time interval from the conditioning shock to the test shock, and $f(z)$ the degree of the threshold change divided into the strength of the conditioning shock employed. The data in the lower half of this column indicate that the local excitatory state in the sense of Blair, Monnier, Hill, and Rashevsky decays in this preparation with a time constant which is approximately equal to 0.18 millisecond and we adopted this value for the calculation. One finds in this table a considerable divergence of the calculated values from the data obtained by direct observation.

4. Calculation by the Method of Integrating the Whole Latent Addition Curve.— In 1936, Blair and Erlanger pointed out that the latent addition phenomena can adequately be interpreted in terms of the summation of the excitatory processes which arise and then fall, instead of falling exponentially, after withdrawal of the applied brief current pulse (see also Blair, 1938). Later on, one of us showed that it is possible to derive the strength-duration relation from the latent addition curve through integration (1942).

Diagram A in Fig. 6 illustrates how the excitatory state $E(t)$ develops when two brief subthreshold current pulses are applied to a nerve fiber at a short interval. The symbols q and s signify the quantities of the conditioning and testing shocks respectively, and z the time from the conditioning shock to the testing. The time course of the excitatory state caused by the conditioning shock is supposed to be given by

$$E(t) = \frac{q}{Q} F(t),$$

where $F(t)$ is a function of time which takes a maximum at $t = a$ regardless of the strength of the shock. When two shocks are applied to the fiber at interval z, the excitatory state is given by the sum of the two terms expressing the effects of the individual shocks, namely, by

$$E(t) = \frac{q}{Q} F(t) + \frac{s}{Q} F(t - z).$$

When the strength of the conditioning shock is far below threshold, this function attains maximum at approximately $t = a + z$, the maximum value being given by $\frac{q}{Q} F(a + z) + \frac{s}{Q} F(a)$. If the strength of the testing shock is so adjusted that the nerve fiber is just excited by the concurrent action of these two shocks, this maximum value must be equal to a certain critical level h required for evoking an impulse:

$$\frac{q}{Q} F(a + z) + \frac{s}{Q} F(a) = h.$$

If one introduces, by the formula

$$\frac{F(a + z)}{h} = f(z),$$

a function of time interval $f(z)$, this equation reduces to

$$\frac{q}{Q}f(z) + \frac{s}{Q}f(0) = 1.$$

From the last equation, it is found that the form of the function $f(z)$ can be determined directly from the latent addition data (note that $f(0) = 1$). We have already shown the numerical values of this function for a preparation in the last column of Table I.
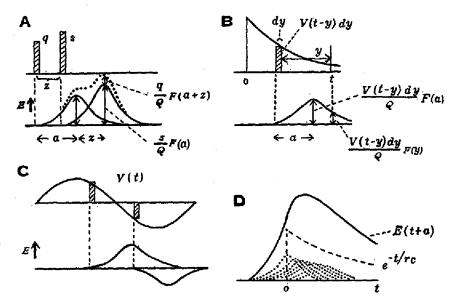

FIG. 6. Diagrams showing development of the excitatory state in stimulation of the nerve fiber by various types of electric stimuli. For further detail, see text.

Now, turning to the effect of a continuous stimulating voltage, we may regard $V(t)$ as a rapid succession of brief subthreshold shocks, each having a strength $V(t)\,dt$. Hence, the excitatory state set up by all these voltage pulses is given by

$$E(t) = \int_0^t \frac{V(t - y)}{Q} F(y)\,dy,$$

in which y is a parameter illustrated in Fig. 6 B. From this equation, it follows that

$$\frac{1}{h} E(t + a) = \frac{1}{h} \int_0^{t+a} \frac{V(t + a - y)}{Q} F(y) \, dy$$

$$= \frac{1}{h} \int_{-a}^{t} \frac{V(t - z)}{Q} F(a + z) \, dz$$

$$= \int_{-a}^{t} \frac{V(t - z)}{Q} f(z) \, dz.$$

Since the term on the right-hand side of the last equation consists only of known functions, it is possible to calculate the time course of $\frac{1}{h} E(t + a)$ numerically for any given stimulating voltage pulse. If the stimulus is to barely excite the fiber, the maximum value of $\frac{1}{h} E(t + a)$ must be equal to unity. From this condition, we can determine, for any given configuration of stimulus, the threshold strength for the fiber.

Unfortunately, it was found impossible to give the function $f(z)$ a simple analytical form. In the present investigation, we have conducted numerical calculation by the method of dividing the interval from $-a$ to t into a large number of subintervals, each having a duration of about 25 microseconds, and replacing the integral calculus with summation of a finite number of terms (see diagram D in Fig. 6).

In the fourth column of Table I are given the results of our calculation for this preparation. Confirming what has been stated in a previous paper (Tasaki, 1942), the quantity-duration relation obtained by calculation agreed perfectly with the observed one in the range of duration shorter than about 0.4 milli-second. The discrepancy between the observed and calculated data in the range of duration above 1 millisecond has been attributed in the previous paper to the presence of some unknown independent variable required for description of the excitatory processes.

For the strength-frequency data, our calculation yielded good results only in the frequency range between 0.5 and 1.5 kilocycles per second. The disagreement in the high frequency range is undoubtedly to be ascribed to the change in the state of the nerve fiber by strong alternating currents. The discrepancy in the low frequency range is to be attributed to the same cause as that in the long duration range for the strength-duration data.

5. *The Effects of Direct Currents and the Surrounding Inactive Tissues upon the Strength-Frequency Curve.*—To clarify the effect of electrotonus upon the strength-frequency relation, we applied a constant voltage to the nerve fiber by connecting the distal (left) electrode in Fig. 1 to a source of direct currents. The proximal (right) electrode was led to the alternating current source as before, and another electrode which was brought in contact with the muscle was led to the amplifier. The fluid on the proximal side of the bridge-insulator

was a 0.2 per cent cocaine-Ringer solution as usual. Determination of the strength-frequency curve was conducted during the passage of the direct current.

It is easy to demonstrate with single fiber preparations that anelectrotonus heightens the threshold for brief shocks and accelerates the progress of the excitatory process and that catelectrotonus affects the fiber in the opposite manner. Qualitatively, the observed effects of the electrotonus upon the
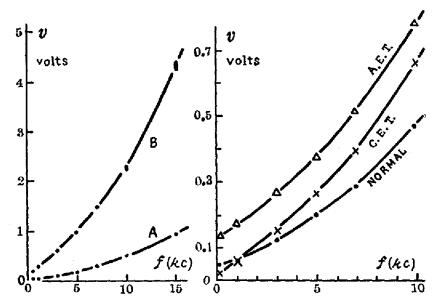

FIG. 7. Left, strength-frequency curve determined on a single nerve fiber mounted on the bridge-insulator (A) and the result obtained with the proximal nerve trunk of the same preparation placed on the bridge-insulator (B), 13°C. Right, effect of electrotonus upon the strength-frequency curve; a large motor nerve fiber of the toad at 12°C.; the polarizing voltage, 50 mv.

strength-frequency curve can be fully interpreted in terms of the effects just mentioned upon the excitatory process. We did not make simultaneous observations of the latent addition and the strength-frequency curves on single fiber preparations under electrotonus.

Next, to make it easier to compare our data with those obtained with whole nerve trunks, we have determined the strength-frequency curves with the stimulating electrodes placed on the proximal nerve trunk of a single nerve fiber preparation. In Fig. 7, left, curve A was obtained with the isolated region of the preparation placed on the bridge-insulator as usual. After this curve had been mapped out, the proximal nerve trunk of the same preparation was

mounted on the bridge-insulator, now about 3 mm. wide, and the experiment of exciting the fiber by alternating currents was conducted taking muscular contractions as index. It was found by this method that, at every frequency of alternating current, the threshold strength for the nerve trunk was 6 to 10 times as high as that obtained at the isolated region. This indicates that the general character of the curve is not affected appreciably by the shunting effect of the inactive tissues surrounding the fiber under observation.

6. *Excitation of a Single Nerve Fiber by Two-Way Condenser Discharges.*— From the theoretical point of view, it is much easier to calculate the excitatory state set up by a series of alternating brief shocks, following one after another at a given regular interval, than the excitatory state caused by an

TABLE II

Threshold Strengths for Two-Way Condenser Shocks and the Latent Addition Relation Determined on a Motor Nerve Fiber at 13°C.

Two-way condenser shock		Latent addition	
Frequency	Threshold	Interval	Threshold change
kc.	*mv.·msec.*	*msec.*	
0.1	21	−0.25	0.10
0.3	20	−0.20	0.15
0.5	20	−0.166	0.20
0.7	19.5	−0.10	0.45
1.0	19.5	0	1.00
2.0	20	0.10	0.56
3.0	25	0.166	0.29
4.0	32	0.20	0.23
5.0	41	0.25	0.16

alternating current. Hill, Katz, and Solandt (1936) employed two-way brief condenser discharges, namely, a series of brief shocks of the same strength alternating their direction one after another, and pointed out that the minimum strength needed to cause a steady response remained practically unaltered when the frequency was varied in the range between 200 and 2000 per second. We could readily confirm their findings with single fiber preparations.

The data furnished in Table II represent an example of the results we obtained with two-way condenser stimuli. The term "frequency" in this table signifies the number of shocks in one direction, and the threshold is given in terms of the quantity of electricity carried by each shock. The two columns on the right-hand side of this table give the latent addition data for this preparation.

It is expected from the consideration stated above that, unless the interval of the shocks is reduced to such a point that the excitatory state left by the preceding shock affects the effect of the next shock, the threshold strength of

the two-way condenser shocks should remain unaltered by a change in the frequency. In fact, the threshold was found to be constant for a wide range of frequency. But, with higher frequencies at which a considerable rise of threshold is expected from the above stated consideration, we found that the observed change in the threshold is decidedly smaller than what is predicted by theory.

DISCUSSION

The experimental data shown in Table I bring out very clearly the failure of the Blair-Monnier-Hill-Rashevsky theory to account for the parallel observations made with three different types of stimuli, namely, alternating currents, condenser discharges, and two brief shocks. The discrepancy between the observed and the calculated data is such that it can be described by saying that Blair's constant k (the reciprocal of Hill's time constant k) derived from the strength-duration data is too small as compared with that derived from the latent addition data. This undoubtedly arises from the neglect of the ascending phase of the excitatory state in the previous theory.

The effects of a strong high frequency alternating current upon the fiber are evidently such that the action current of the fiber is thereby reduced and the threshold is lowered. These apparently resemble the effects brought about by catelectrotonus. In the light of the findings reported by Cole and Curtis (1941), it seems probable that an electric current flows outwards through the plasma membrane at the node of Ranvier more readily than in the opposite direction and further that such a rectifying action is less marked in the myelin-covered portion than at the node of Ranvier; and, if so, a catelectrotonic change in the state of the node by a strong alternating current would not be very surprising.

As to the effect of low frequency alternating currents, it is well known that there is a gradual rise in the threshold voltage with decreasing frequency (see Coppée, 1934). This we can readily demonstrate with single fiber preparations (cf. Tasaki, 1950). We shall reserve a description of this phenomenon for a subsequent paper.

SUMMARY

1. Determinations were done of the strength-duration, the strength-frequency, and the latent addition curves with single fiber preparations.

2. Calculation of the strength-duration and strength-frequency curves from the latent addition data by the Blair-Monnier-Hill-Rashevsky theory yielded results which showed a considerable divergence from the actual data. Calculation by the method of integrating the whole latent addition curve yielded satisfactory results.

3. The effects of electrotonus and the inactive tissues around the nerve fiber upon the strength-frequency relation were investigated.

4. It was suggested that, for alternating current stimuli and two-way con-

denser discharge stimuli of very high frequencies, threshold was lowered by the rectifying action of the plasma membrane.

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Note added to Proof.—After the manuscript of this paper was submitted, one of us wrote a paper concerning the nature of the excitatory process and showed that the delayed rise of the excitatory effect is due to electrotonic spread of the membrane potential along the myelin-covered portion of the nerve fiber (Tasaki, I., *Japan. J. Physiol.*, 1950, **1**, 75).