

ACTIVATION OF PASSIVE IRON AS A MODEL FOR THE EXCITATION OF NERVE* †

By K. F. BONHOEFFER

(From the Physical Chemistry Institute of the University, Berlin)

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I. INTRODUCTION

If a piece of passive iron in concentrated nitric acid is touched momentarily with a zinc rod, the iron may become active and the activation may spread from the point of contact over the whole piece of iron. Whether the iron will become active, and if it becomes active, whether it will return to its former passive state depends on the concentration of the acid. There is an intermediate interval of acid concentration in which repassivation will take place. Working with an iron wire at this concentration of acid one may observe a spreading wave front of activation followed by a spreading wave front of repassivation, the whole giving the appearance of a moving spot of activity. Wilhelm Ostwald was the first to note the resemblance of this phenomenon to the transmission of an excitation running along a nerve. In 1900 he suggested to Heathcote, one of his students, that he should investigate this analogy more thoroughly. The papers of Heathcote (1) did not receive the attention they deserve. They contain many interesting facts; *e.g.*, the observation that a wire cannot be reactivated if one touches it with a zinc rod immediately after repassivation. Activation is possible only after the lapse of a certain length of time, in full analogy to the refractory period of a nerve after excitation. The problem was not pursued any further until it was taken up by Lillie (2). Between 1920 and 1935 Lillie published a series of papers in this *Journal* demonstrating a correspondence in the most unexpected details between the excitation of nerve and the activation of passive iron. By analyzing the dependence of the velocity of propagation on the thickness of the surrounding layer of electrolyte his experiments provided definite proof of the rôle of local currents.

It is indeed most astonishing that iron wire and nerve, which from the chemical point of view differ so enormously, function in such a similar way. It does not seem credible that the various functional properties in which the

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two systems resemble each other could be independent and accidental similarities. There is here a most interesting problem from the point of view of reaction kinetics. The existence of a threshold of activation, of a refractory state, of a transmission of activation, of a tendency to give rhythmic reactions, and a suggestion that even the so called accommodation effects are not missing in the model, indicated that all these properties, so uncommon in ordinary chemistry, are in some way related to each other. To get a clearer insight into these relations it seemed necessary to investigate the model more thoroughly from a physicochemical point of view, and such studies are presented in the present paper. The work of previous authors had concerned itself primarily with the *propagation* of activity. The process of *activation* seemed

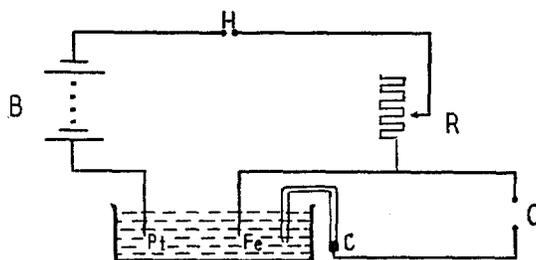


FIG. 1. Arrangement for registering the time course of potential change during a cathodic current pulse on an iron wire in nitric acid. *B* battery, about 60 v.; *H* Helmholtz pendulum (in some experiments with thyatron); *R* resistance, variable from $10^2 \Omega$ to $10^5 \Omega$; *Fe* iron wire, moving with a known speed on a circle of about 2 cm. diameter; *Pt* anode; *C* calomel electrode; *O* direct voltage amplifier and cathode ray oscillograph.

in need of closer study, and for such studies one would prefer to use an electric current of known intensity and duration rather than activation by touching with a zinc rod. It was essential to follow the changes of potential during the reactions as closely as possible and to extend the research to different samples of iron wire, since wires of different composition behave differently. These experiments have led to a better understanding of the remarkable kinetic phenomena mentioned above, perhaps not only for the model, but also for the living cell itself.

II. SHORT ELECTRIC PULSES

Threshold

A schematic diagram of the apparatus used for short electric pulses is shown in Fig. 1. A wire a few centimeters long is dipped into nitric acid. In most of the experiments the concentration of acid was 67 per cent, at which con-

centration the acid has a strong passivating influence on every kind of iron wire we investigated. If intensity and duration of a cathodic electric current pulse are sufficiently great, activation occurs. One then notices a rapid development of gas bubbles at the iron wire, which stops after repassivation. The duration of activity is almost independent of the intensity and duration of the activating pulse and ranges from a tenth of a second to a few seconds. The period of activity is longer, the lower the concentration of acid and, in general, the lower the content of carbon in the iron wire. It may become infinitely long if wires of pure iron in sufficiently dilute acid are used. If intensity and duration of the current are too low for activation, the pulse seems to have no effect at all. Activation, therefore, follows an all-or-none law. For pulses of about 1 msec.

TABLE I
Some Characteristic Data Concerning the Cathodic Behavior of Different Passive Iron Wires in $HNO_3(d = 1.4)$
(Duration of pulse 2 msec.)

Wire No.....	1	2	3	4	5	6	7	8	9	10	11
C, per cent.....	0.09	0.25	0.34	0.39	0.41	0.45	0.54	0.61	0.70	0.85	0.92
Threshold, 10^{-6} coulomb/ cm ²	140	100	103	145	153	158	215	228	150	210	200
Rheobase, } ma./cm ² . }	7 (19)	1.0 (2.5)	3.5 (5.4)	2 (5.6)	2.5 (5.9)	4.5 (7.5)	5.6 (8.5)	9.5 (18)	10 (9.5)	9.5 (18)	12 (29)
Threshold/rheobase, msec...	20	100	29	73	62	35	38	24	15	22	17
Refractory time, sec.....	<10	95	173	168	138	130	125	85	95	70	70
Accommodation r_{ha}/r_{ho} ($a = 500$ msec.).....	20	1.5	1.5	3.5	2.5	3.3	2	6	3.8	7.8	11
Period (60 ma./cm ²), sec....	15	35	46	52	67	—	—	—	—	—	—
Resting potential, volts.....	0.99	0.94	0.93	0.95	0.98	0.98	0.98	0.99	0.94	0.98	0.99

duration the effect depends only on the product of intensity and duration (3). We call the quantity of electricity which is necessary to activate 1 sq. cm. of the surface of iron by a short pulse the *threshold of activation* (3).

In Table I a number of such *thresholds* for different samples of wire are summarized.

These values are reproducible with an accuracy of about 10 per cent. For wires 1 to 11 it was found that the threshold is about 20 per cent lower when the wires are moving. We investigated the dependence on acid concentration and found that the threshold in HNO_3 of 56 per cent is about 40 per cent lower than that in acid of 65 per cent. There is an important influence of nitrous acid on the threshold. We have not made quantitative experiments on this influence, but have found that the addition of a small amount of sodium nitrite results in a manifold increase of the threshold. For threshold measure-

ments it is necessary to be certain of the absence of nitrous acid. This is easily accomplished by blowing air through the acid or still simpler by adding urea to the acid, a procedure which exerts no other disturbing effects. The threshold is lowered by the addition of chloride ions, 10^{-3} N Cl^- giving about one-half of the original value and 10^{-5} N Cl^- giving a barely noticeable effect.

Refractory State

Since nitrous acid is formed during activity an increase of threshold is to be expected immediately after repassivation, before the nitrous acid is removed by urea or by aeration. At first sight it seems plausible that the refractory period of the wire could be explained by the presence of nitrous acid developed during activity. As an example we give experiments performed with a steel wire with a C content of 0.91 per cent (Table II).

The expected increase of threshold as well as its gradual decline will be

TABLE II
Dependence of the Threshold on the Recovery Time after Repassivation (Music Steel Wire, 0.91 per cent C) HNO_3 ($d = 1.4$), Saturated with Urea, 22.5°C.

Time, sec.....	15	20	25	30	50	60	90	100	135	150	240
Threshold, wire not moved, 10^{-6} coulomb/cm ²						1500		1000	800		550
Threshold, wire moving, speed 75 cm./sec., 10^{-6} coulomb/cm ²	1500	1200	1000	925	725		525			350	

noticed. The decline is more rapid if the wire is moving, a fact which also could be expected. However, the great length of recovery time as well as the difference in the behavior of different wires is quite unexpected. If nitrous acid were the sole cause of the refractory behavior the decay of refractoriness should be far more rapid. It should depend on the amount of nitrous acid which had been formed during the period of activity, rising therefore with the duration of the activity. The sixth line of Table I gives the time after which the wire has recovered to a threshold 150 per cent of its ultimate value. There are considerable differences in this refractory time, but no increase of the refractory time with increasing length of the active period is to be noticed. Wire 1, for instance, which has the longest activation period also has the shortest refractory period. One has to look for another, or for an additional cause of the refractory behavior. It may be observed that after repassivation the iron surface is often not as bright as before activation, especially when dealing with wires of high carbon content and long refractory periods. The wires are covered with a visible oxide layer of varying thickness, which disappears gradually during the period of recovery. Once the layer is dissolved, the wire

ceases to be refractory. We believe that the oxide layer constitutes a second cause of refractoriness.

The effect of nitrous acid on refractoriness is easily understood. It can be related to the well known fact that the oxidizing power of nitric acid—or if we put it in another way its reducibility—depends on the presence of nitrous acid. Nitrous acid is the compound which oxidizes and is reduced primarily, nitric acid is reduced only secondarily by the reaction with nitric oxide obtained by reduction of nitrous acid. In the absence of nitrous acid therefore, nitric acid cannot easily be reduced by cathodic treatment and the current then reduces the passivating invisible surface oxide (3, 4). In contrast, in the presence of nitrous acid the current will reduce nitric acid and therefore will be less effective in activating the passive wire.

The thick oxide layer formed during activity may be expected to influence the course of events in two directions. First, the layer may occlude some nitrous acid and protect it against the attack of urea. Second, the layer may use up a part of the electric current for its reduction. Both effects tend to prolong the recovery time. Which of the two effects is the more important has not yet been settled. The decay of the refractory state indicates that there is a superposition of at least two effects. We will return to this question in a later section of this paper.

The refractory period apparently increases if the duration of the testing pulses is increased. This is due to "accommodation" effects which are very pronounced with wires in the refractory state.

Summation and Gildemeister Effect

If we first give a subthreshold pulse and investigate the quantity of electricity necessary to get activation with a second pulse, we find an interesting dependence on the time interval between the two pulses.

Naturally, with a very short interval we find that a lesser quantity of electricity is needed for the second pulse. However, for longer time intervals between the two pulses the sign of the effect becomes reversed, the needed quantity of electricity exceeding that which ordinarily would be necessary for the activation of the wire under investigation. Thus, a subthreshold pulse also engenders some kind of refractoriness. There is here complete analogy to the behavior of nerve, the first effect being the ordinary summation effect, the second effect being one first observed by Gildemeister (4) and later thoroughly investigated by Erlanger and Blair (5). The data in Table III were obtained with wire 2 a. This is a portion of wire 2 (Table I) having a higher threshold than the remainder. As we learned later, it is not very suited for these experiments. Almost any other wire would have given a more pronounced effect, easier to investigate. We believe that this is so because this wire shows very poor accommodation, and, in our opinion, the Gildemeister effect is related to the accommodation effect.

Analogy with Ignition

To explain the existence of a threshold for activation it is useful to compare it with the inflammation point of an explosive mixture of gases. If such a

TABLE III

Summation and Gildemeister Effect. Wire 2 a. $HNO_3(d = 1.4)$, Saturated with Urea. Normal Threshold $150 \cdot 10^{-6}$ Coulomb/Cm.² First Pulse $60 \cdot 10^{-6}$ Coulomb/Cm.²

Time interval	Second pulse	Difference
sec.	10^{-6} coulomb/cm. ²	10^{-6} coulomb/cm. ²
0.03	130	-20
0.05	140	-10
0.1	145	-5
0.2	150	0
0.5	160	+10
1.0	165	+15
∞	150	0

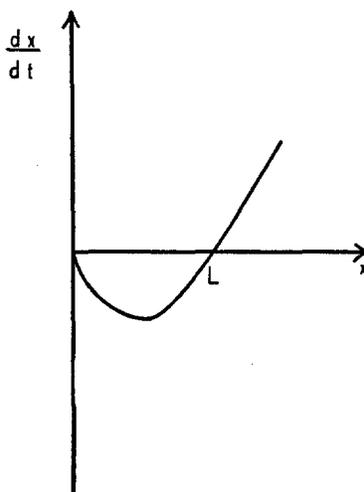


FIG. 2. Diagram showing the analogy between the inflammation point of an explosive mixture (L) and the threshold of activation. x is the difference between the temperature of the mixture and the environment. $t =$ time.

mixture is heated to a temperature just below the inflammation point, and the heat source is then removed, the temperature of the mixture will decrease until room temperature is reached. However, if the mixture is heated to a temperature just above the inflammation point, then the temperature will rise spontaneously, even if the external heat source is removed. In Fig. 2, which illustrates the essential feature of the phenomenon, x means the difference

between the temperature of the mixture and room temperature. The diagram refers to a mixture not exposed to an external source of heat. L is the inflammation point, which is labile.

Assuming similar relations for the threshold of activation we will let the temperature difference x correspond to the degree of activation. There must be a process which is opposed to the activating influence of the electric current pulse. This process corresponds to the cooling of the mixture if left alone. In addition there must be a second process which works in the same direction as the current and which corresponds to the spontaneous heating of the explosive mixture above the inflammation point. The first of the two postulated processes may be attributed to the passivating influence of nitric acid, the second one to the effect of local electric currents which, flowing through the solution from the points already reduced to the points not yet reduced, assist the external current in its activating effect. The existence of these local currents is proved by the fact that activity is transmitted longitudinally, as has been shown elsewhere (15).

Whatever the nature of these reactions, they will take time. If, and only if, the duration of the current pulse is short compared to the time constants of these reactions, should one expect that the effect of the pulse is a function only of the product of intensity and duration of the current.

Oscillograms

Up to this point we have taken the development of gas bubbles as an indication of activity. However, the possibility of observing the changes of potential by an oscillograph gives us another means of detecting activation and this method has the advantage of giving us a clearer insight into what really happens during that process (6). With short electric pulses we get oscillograms like Fig. 3 *a, b, c*, where the course of potential following a short pulse is given schematically. The drop of potential during the electric pulse is so fast, that an almost vertical line is obtained. If the quantity of electricity in the pulse is smaller than threshold, the potential after the pulse rises to the resting potential of $E_H \sim 0.96$ v. For pulses close to the threshold, *i.e.* if a potential of about $E_H = 0.5$ v. (Fig. 3 *a*) is reached, the rise of the potential after the pulse is slower and shows points of inflection. In the immediate vicinity of the threshold, the potential may remain nearly constant for about 50 msec., and then rise rather abruptly. When the threshold is exceeded, the potential, after remaining constant for a while at 0.5 v., drops further to a value of about 0.15 v. indicating that the wire is active (Fig. 3 *b*). The time interval between the application of the pulse and the spontaneous drop of potential depends on the material to be activated and on the intensity of the pulse. Just above threshold this "latency period" has its maximum value. It may be as high as about 100 msec. with wires of very low C content. Fig.

ACTIVATION OF PASSIVE IRON

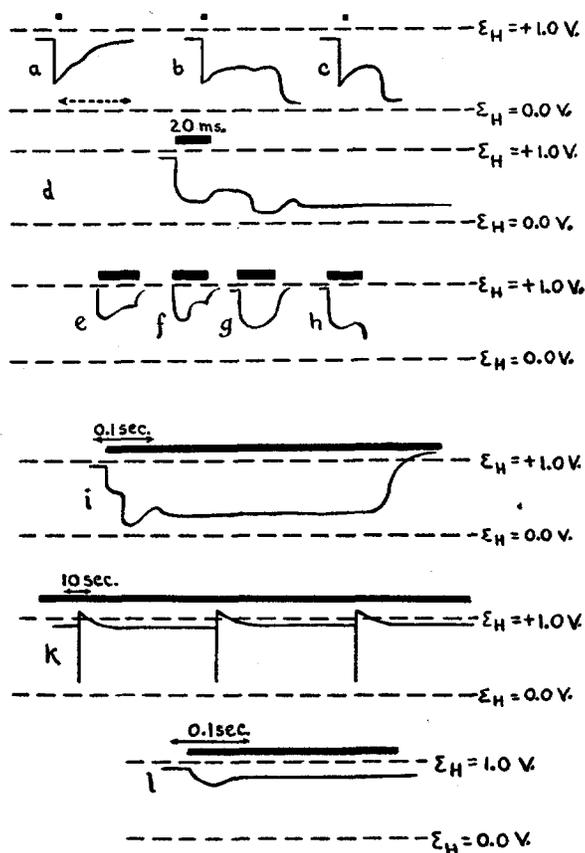


FIG. 3. Time course of the potential E_H of the iron cathode in HNO_3 ($d = 1.4$). The time interval during which the current is flowing is shown by a thick black line above the dotted line $E_H = 1.0$ v.

(a), (b), (c) Duration of pulse 2 msec. (a) Pulse below threshold; (b) pulse barely above threshold; (c) pulse twice threshold.

(d) Activating pulse, duration 20 msec.

(e), (f), (g), (h) Refractory wires, stimulated at various intervals after the conditioning pulse. Duration of second pulse 20 msec. (e) Interval between pulse 15 sec., second pulse does not activate; (f) Interval between pulses 60 sec., second pulse does not activate; (g) Interval between pulses 97 sec., second pulse does not activate; (h) Interval between pulses 105 sec., second pulse does activate.

(i) Activation and repassivation during the flow of a current above rheobase.

(k) Rhythmic activations.

(l) Permanent current below rheobase.

3 c shows the decrease of the latency period if the pulse is doubled. The drop or rise of potential depending on whether or not threshold is reached shows the

existence of the two reactions which we have inferred from the existence of a threshold, one increasing, the other opposing the influence of the electric pulse.

III. ELECTRIC PULSES OF LONGER DURATION

Intensity-Duration Relation

The process which opposes the activating influence of current causes an increase of the quantity of electricity necessary for activation if the duration of the pulse is increased. Fig. 4 shows the logarithm of current density plotted against the logarithm of duration t . A slope of 45° signifies that $i t = \text{constant}$. At about 10 msec. the deviation from 45° becomes noticeable. That means

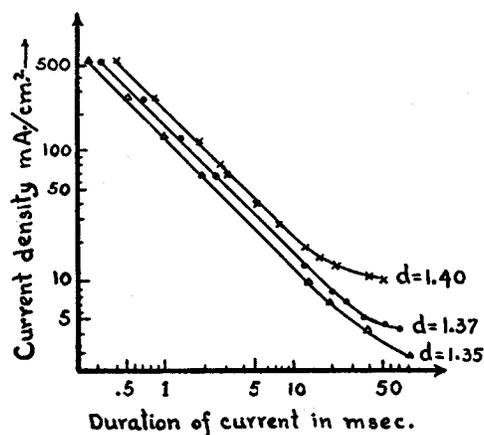


FIG. 4. The current density needed for the activation of an iron wire in its dependence on the duration of the current (three different HNO_3 concentrations).

that the time of 10 msec. is not short compared with the time constant of the passivating counterprocess.

There is a certain current density below which activation becomes impossible. This current density may be called "rheobase" in analogy to the similar behavior of nerve excitation. For HNO_3 ($d = 1.4$) in Fig. 4 rheobase is approximately given by the point with the abscissa $t = 50$ msec. The curves have no asymptotic horizontal for higher values of t , but break off at finite values of t . Rheobases have been measured for different wires and the results are shown in the fourth line of Table I. One of the two figures given for each wire is in parentheses, and refers to measurements obtained with wires which are not yet fully recovered. Accurate measurements of the rheobase of a fully recovered wire are somewhat tedious. The time of rest between two activations has to be at least 20 minutes if the solution is stirred. The figures in parentheses were obtained with waiting times of only 12 minutes during which time the solution was not stirred.

It is of some interest to compare the measurements of rheobase (*i.e.* the lowest activating current density) with those of the threshold (*i.e.* the lowest activating quantity of electricity). A rough parallelism is quite obvious, but there is no exact proportionality. The ratio threshold/rheobase, as shown in the fifth line of Table I, is not constant, it varies between 22 msec. and 185 msec. It is of the order of magnitude of the "chronaxie," the time constant of the counterprocess, but modified by accommodation.

Accommodation

It has been mentioned that the time which corresponds to rheobase in the intensity-duration relation is not infinitely long, but has a finite value analogous to the behavior of nerve. It is the so called maximum utilization time of Gildemeister and is of the order of a tenth of a second. It is possible, therefore, to measure rheobases by means of current pulses of a length of some tenths of a second. The finite value of the maximum utilization time is due to *accommodation*. This effect was revealed by experiments with currents of gradually rising intensity. The dependence of the current density on the time t was given by the equation

$$i = i_0(1 - e^{-t/a})$$

The constant a was varied in the course of different experiments from about 10 msec. to 2 seconds. It was found possible to give i_0 values considerably higher than rheobase without activating the iron. Generally speaking the larger a , *i.e.* the slower the increase of current, the more effective the "creeping-in" of high currents. If we denote the value of i_0 which is just sufficient for activation by rh_a and the rheobase by rh_0 , then the ratio rh_a/rh_0 may become as high as about 20. Undoubtedly even higher values would have been found if our apparatus had been suited for such measurements. With regard to Hill's theory (7) of the accommodation of nerve it is interesting to note that the increase of rh_a/rh_0 with a is not linear, but slows down for higher values of a , and with some wires apparently decreases again. Values of rh_a/rh_0 for $a = 500$ msec. are collected in the eighth line of Table I. The accommodation effects will be discussed in section V.

Oscillograms

It may be inferred from the above that during current pulses of longer duration several secondary reactions take place, some which are connected with the existence of a threshold and others cause accommodation. Both types are revealed by oscillograms. Fig. 3 *d* shows the course of potential during and after an activating pulse of 20 msec. It will be noticed that during the flow of current the potential drop slows down in the vicinity of $E_H = + 0.5$ v. and runs almost horizontally at about $E_H = + 0.4$ v., showing

that a marked counterprocess is balancing the effect of the current. The secondary effect observed after a short pulse, which is shown in Fig. 3 *a*, is now found superimposed on the primary current effect.

There is one incompatibility not yet fully explained. The counterprocess as revealed by the course of the potential begins within a few milliseconds as shown by the turning of the potential curve. On the other hand for pulses of so short a duration the $i t = \text{constant}$ relation is valid for activation. This indicates that no appreciable counterprocess occurs during the first milliseconds. The only explanation that may be offered is that the potential and the degree of activation may not be connected very closely. Specifically, an increase in the potential may not indicate a repassivation to the same extent as the potential has changed. This assumption does not seem unsound, because the polarization potential could hardly be attributed solely to the reduction of the surface.

Fig. 3 *d* shows the course of potential after the pulse for a period of about 150 msec. The continuation of the oscillograms for such a long time in Fig. 3 *b* and *c* would have led to the same shape of curves. This shape is a rather complicated one, but very well reproducible. After activation, where a potential of about + 0.15 v. is reached, there is (in HNO_3 , $d = 1.4$) an increase of potential. After passing a maximum the stationary potential of active iron is reached at about + 0.3 v. A reliable explanation of this behavior cannot yet be given. It is probably connected with the development of large amounts of nitrous acid at the first moment of activation. The shape becomes simpler in more dilute nitric acid.

Since the refractory state is probably in part caused by the presence of nitrous acid it is not without interest to compare oscillograms taken in solutions containing nitrous acid with others taken with wires in the refractory state. Oscillograms in nitrous acid have been published previously (6). In most cases the resting potential is raised somewhat compared with the potential found in solutions free of nitrous acid. The amount by which the potential is raised depends on the nature of the iron. The beginning of the cathodic potential drop does not differ very much from the potential drop in pure nitric acid. Very soon however, the drop slows down and for sufficiently high concentrations of nitrous acid it may even rise during the flow of current, thus showing an apparently "negative" polarization. The higher the concentration the earlier the rise of potential, the minimum passing from right to left on the oscillogram. In the case of very high concentrations the minimum disappears at the left side while the potential remains high, even at high current densities. The explanation of this peculiar behavior of nitrous acid is simple. As mentioned above nitrous acid enables the current to reduce nitric acid thus diminishing the polarizability of the electrode and slowing down the fall of potential. Through the reduction of nitric acid new quantities of nitrous

acid are formed leading to an autocatalytic increase of nitrous acid which is responsible for the reversal of potential change. There remains only the minor difficulty of deciding why at first the presence of nitrous acid does not affect the oscillogram noticeably. This will not be attempted here.

Comparing now the behavior of refractory wires with this influence of nitrous acid, the resting potential will be considered first. In general, the resting potential of these wires is higher than the potential of the normal ones. During the recovery period of the refractor wire this "after-potential" gradually disappears, the wires with a long refractory period giving a long after-potential. The time of decay varies from several minutes to a few seconds depending on the material of the wire and on whether or not the solution is stirred. The amount of the after-potential also depends on the nature of the material, the highest values observed lying around 0.2 v. This fits in very well with the behavior of wires in solutions containing nitrous acid. Fig. 3 *e* to *h* shows oscillograms of refractory wires. They are taken with the same sample of wire at different intervals after activation and show the progressive recovery until activation again occurs. It is interesting to see that there is complete agreement with the shape of the curves taken with nitrous acid, indicating that nitrous acid has something to do with the refractory state. An appreciable amount of nitrous acid must be present on the surface of the wire even 90 seconds after repassivation.

IV. SINGLE AND PERIODIC ACTIVATIONS BY STEADY CURRENTS

To complete the survey we must now discuss the behavior of wires under the influence of steady currents. In this regard the most remarkable fact is that the wires after activation by current generally later again become passive, almost independently of whether or not the current is flowing. The course of potential which is typical for the effect of steady currents is shown in the oscillogram Fig. 3 *i*. Only wires of a very low content of C, which on the whole are more difficult to passivate, sometimes did not return to the former passive state during the flow of current. While repassivation is almost general, the wires show considerable differences in the further behavior during the flow of a current with an intensity greater than rheobase. Every wire investigated by us remained passive if it had become passive during the flow of a current just above rheobase, but at higher current densities and with stirring some wires (*e.g.* wire 1 to 5) again became active followed by a new repassivation. Activation and passivation alternated rhythmically (8). Thus some types of wires (*e.g.* Nos. 6 to 11) may be considered as models of medullated nerve which under the influence of a constant current becomes active only once. The other types of wire are models of non-medullated nerve, *e.g.* of invertebrates, which react rhythmically. In each case, however, a certain limit of current density was found below which no rhythmic activations could be observed. Some-

times, in the transition region between rhythmically repeated and single activation we succeeded in producing an intermediate reaction consisting of a finite number of repeated activations analogous to the observations which Arvanitaki (9) made in her examinations of non-medullated nerve. The range of current density between the first single activation and the region of rhythmic activations is very different with different wires. For wire 2 it is about 0.25 ma./cm.² (rheobase at about 1 ma./cm.²), while for wire 5 it runs up to 40 ma./cm.² (rheobase at about 2.5 ma./cm.²). There is also an upper limit for the rhythmic behavior, at about 300 ma./cm.² for wire 2, and at about 60 ma./cm.² for wire 5. Thus the interval for rhythmic reactions is much smaller for wire 5 than for No. 2. Wires of a higher content of carbon than that of No. 5 showed periodical behavior only at temperatures above room temperature and with concentrated nitric acid ($d = 1.4$). The length of the time during which the wire is passive and recovering is given for different wires in Table I. It effectively determines the length of the period, since the duration of the active state is only a fraction of a second. The oscillogram Fig. 3 *k* may serve as an example of a rhythmic reaction, each peak corresponding to the oscillogram Fig. 3 *i*.

V. CORRELATION BETWEEN THRESHOLD, ACCOMMODATION, REFRACTORINESS, AND RHYTHMS (10)

The Kinetic Equations

We have now gathered the material which will enable us to discuss the interrelations between threshold, accommodation, refractoriness, and rhythmic behavior. Beginning with the last mentioned phenomenon we recall how undamped electric oscillations are generated. There must be an influence which compensates for the natural damping of the oscillations. This self-exciting effect is caused by a so called "negative resistance" in the system, which means that in a part of the system an increase in voltage goes parallel with a decrease of current intensity I . In a system containing in series a condenser C , a self inductance L , and a resistance R with a voltage $E_R(I)$, we have the differential equations

$$\begin{aligned} dE/dt &= -I/C \\ dI/dt &= E/L - E_R(I)/L \end{aligned}$$

where E is the voltage across the condenser. This system has the required properties if at least one region shows a rise of $E_R(I)$ for decreasing I . Simplifying our chemical problem we may assume that its kinetics, too, is determined a set of two similar simultaneous differential equations of two variables x and y , which define the state of the system. We will write them in the form

$$\begin{aligned} dx/dt &= f(x, y) \\ dy/dt &= g(x, y) \end{aligned} \quad (1)$$

In order to obtain solutions of the oscillatory type from a differential equation of the first order there are required at least two variables defining the state of the reacting system at each moment, as, *e.g.* position and momentum in mechanical oscillations, or voltage and current in electrical oscillations. In our system choose the "degree of activation" as one of these variables, for which we may take the electrochemical potential as a rough measure. If we look at Fig. 2 which applies to conditions where no current is flowing we find that above the threshold dx/dt is positive and rises with rising x . This is due to the spontaneous increase of active areas by local currents, and is responsible for the existence of a threshold. We can put this auto-catalytic increase of x into analogy to the increase of dI/dt with rising I in the equation of electrical oscillation. Thus an autocatalytic reaction corresponds to the "negative resistance" and the lability caused by it is the reason for the existence of a threshold and it is also a necessary, though not a sufficient condition for the occurrence of rhythmic reactions.

We must now seek to determine the second independent variable, y , by which the state of the wire is to be described. We will choose the refractoriness of the wire as measured roughly by its threshold (in the inactive state). Since refractoriness is generated in a wire which is becoming active, dy/dt is positive when x is positive; on the other hand the rate of increase of activity, dx/dt , produced by the current, is diminished by the refractoriness y . In a qualitative way the interrelations between the two differential equations are thus given. From this point of view we have to extend the scheme of Fig. 2. First we must realize that x cannot rise indefinitely. Therefore the curve must turn and after passing a maximum must reach the abscissa as shown in curve *a*, Fig. 5. The physical meaning of this decrease is that local currents lose their activating power when the whole surface is active. The S-shaped character of the curve is due to the counteraction of the passivating nitric acid, a counteraction which at low activities outbalances the activating influence of local currents. In Fig. 5 the curve *a* does not begin at the origin of the coordinate system, but at a point very close to it. This is to account for the fact that even passive wires, represented by the point P_0 , show a little dissolution of metal and therefore a small amount of activity.

If an external current is applied the curve is raised and is shaped like curve *b*. Neglecting the influence of x on y one should expect that rheobase is defined by a curve, the minimum of which is touching the abscissa.

Below this current density the curve will cross the abscissa in a stable point which is approached asymptotically from $x = 0$, representing a low degree of activation; after cessation of the current, the system will return to the point P_0 . On the other hand full activation would be obtained above this critical current density and if the current is interrupted after the system has passed the abscissa of L , given by the dotted line, spontaneous activation will occur

along curve a . If the current density and the corresponding lift of the curve are so high that the values of dx/dt for x between O and L may be considered as constant, we have the region where $it = \text{constant}$ may be applied to the intensity-duration relation.

However, to account for accommodation, refractoriness, and rhythms we have to consider the influence of x on y and how y modifies the position of the

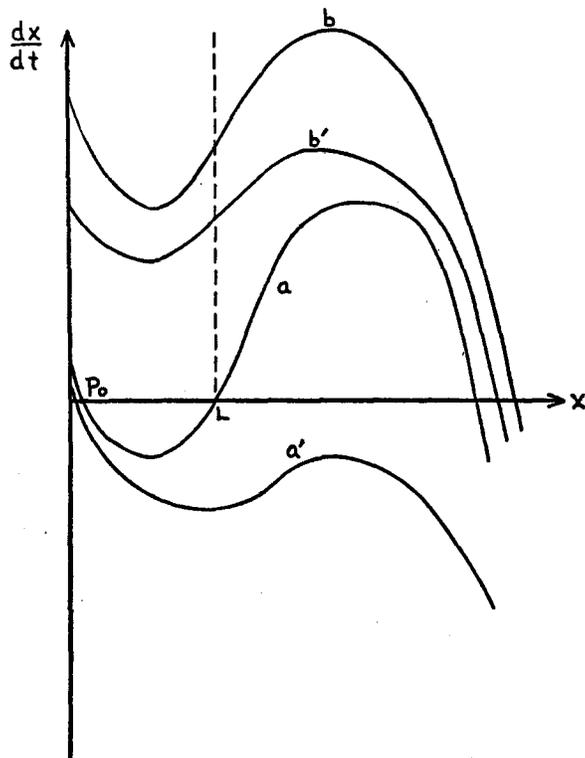


FIG. 5. The rate of change in activity in its dependence on the activity. Curves a and a' , no current, a , no refractoriness, a' , refractory. Curves b and b' the corresponding curves for current densities above rheobase.

point for which $dx/dt = 0$. We assume that nitrous acid and oxide layer are formed not only on the fully active surface of the iron—a factor which causes refractoriness after repassivation—but also on parts of the surface which are only partially reduced, thus causing accommodation.

The curves a and b in Fig. 5 refer to the non-refractory state with $y = 0$. Higher values of y will lower the curves, the new positions being shown by the curves a' and b' . The change of shape of the curves is due to the fact that the activating effect of local currents is also reduced. Thus during the process of

activation by a current of constant intensity the point which is indicating the state of the system is shifting continuously from a higher curve to a lower one corresponding to the increase of the refractoriness y .

The x y Diagram

For a survey of the whole variety of changes of state under the influence of direct currents, it is advisable to use a diagram with the coordinates x and y , and to insert at each point the direction dy/dx of the change, obtained by dividing the two differential equations (1). Qualitatively $f(x, y)$ can be read from Fig. 5. For the construction of the curves dy/dx , however, $g(x, y)$ must first be obtained. From the decay of refractoriness after repassivation we know that dy/dt is negative for very small values of x and tends to zero if y itself is very small. We know, furthermore, that the decay of refractoriness is very slow compared to the development of refractoriness during the short period of activity. Thus the absolute values of dy/dt are generally very much higher if positive than if negative. The change from small negative values of dy/dt to large positive values takes place within a small interval of x values in the vicinity of the threshold. Finally we know that in case of high values of refractoriness the tendency to removal of nitrous acid and of oxide layers will always be stronger than in case of lower values. These data furnish a sufficient basis for a qualitative picture of $g(x, y)$ and therefore also for the construction of a diagram in x, y coordinates for different current densities.

Let x_0 signify the maximum value which is attainable for x (full activity, *i.e.* completely reduced iron surface) and y_0 the maximum value of y ; *i.e.*, the highest grade of refractoriness. Neither dx/dt can be positive if $x = x_0$, nor dy/dt if $y = y_0$, and we obtain the following diagrams (Figs. 6 to 9). In these diagrams the curves $dx/dt = 0$ (Fig. 6, curves HF_1 and LF_2 , Figs. 7 to 9, curves HF) and $dy/dt = 0$ (curves EG) have been inserted. According to our assumptions the curve $dx/dt = 0$ hits the border lines of the square between D and C and between A and B , whereas $dy/dt = 0$ hits between A and D and between B and C . The curve $dx/dt = 0$ may hit the same border line several times because of its S-type shape (Fig. 6). We will first discuss the case when there is only one point of intersection on each side of the diagram (Figs. 7 to 9). We denote these points respectively by H, F, E, G . There must be at least one point of intersection of the curve $dx/dt = 0$ with the curve $dy/dt = 0$. We will assume throughout that there is only one such point and denote it by P (P_0 in Fig. 6). The two curves divide the diagram into four sectors. In going from one sector to an adjacent one dx/dt or dy/dt will change signs. The signs of these derivatives are such that in the lower left sector $A F P E$ the point which represents the state of the system moves upwards from left to right. Correspondingly, in sector $B F P G$ the point moves upwards from right to left, in sector $C G P H$ downwards from right to left, and in sectors

$D H P E$ downwards from left to right. The curve $dx/dt = 0$ is crossed by the path of the point in a vertical direction, the curve $dy/dt = 0$ in a horizontal direction, as indicated by short arrows. Since the changes of y are generally slow compared with the changes of x in the same time, the paths for the most part run almost horizontally. This applies particularly to the left side of the curve $dy/dt = 0$, where dy/dt is negative. Only in the neighborhood of the curve $dx/dt = 0$ does dy/dt become comparable in magnitude to dx/dt , and the path show a considerable deviation from the horizontal direction.

Threshold.—We will now discuss the conditions for different current densities. When there is no current we get a diagram like Fig. 6. It differs from the

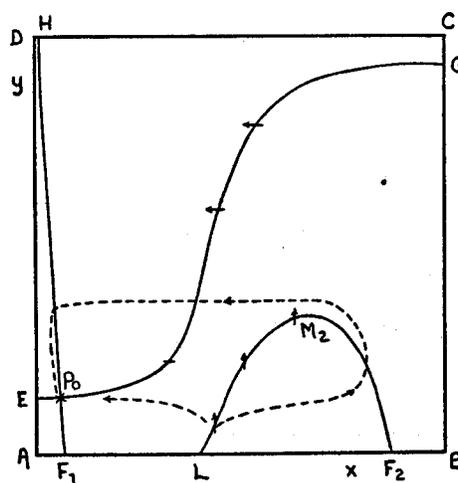


FIG. 6. xy diagram. x activity, y refractoriness. No current. Along HF_1 and LM_2F_2 $dx/dt = 0$, along EG $dy/dt = 0$. The arrows and the dotted lines show how the system changes when no current is flowing.

scheme just discussed by the fact that the curve $dx/dt = 0$ hits the border line AB three times, in F_1 , L , and F_2 . Thereby a new area is formed below the curve LM_2F_2 , in which the direction of path behaves like the direction in the area AF_1P_0E ; *i.e.*, in that region activation is increasing even when no current is flowing. It is the region of spontaneous activation. If after interruption of a current the state of the wire is given by a point lying in the region LM_2F_2 activation takes place. The curve LM_2 indicates the condition of threshold, P_0 the stable resting point of low activity and low refractoriness. For sufficiently low current densities we obtain conditions which are qualitatively illustrated by Fig. 6. We will assume that the only influence of the current is the lifting of the curve $dx/dt = 0$, the curve $dy/dt = 0$ remaining unaffected; this is certainly a crude simplification the value of which may be

doubted. The environment of P_0 is given in Fig. 7 on a bigger scale. The density of the current is below rheobase, and starting from P_0 no activation is possible because the sector $L M_2 F_2$ cannot be reached. The path is marked by a dotted line. We obtain an increase of activity and later a small decrease asymptotically approaching the point P . This result is fully verified by oscillograms with currents below rheobase where the potential is found to go through a minimum (Fig. 3 *l*). The retrogression of the potential is caused by the formation of nitrous acid.

Accommodation.—The rise of the dotted line in Fig. 7 near P shows the increase of refractoriness; *i.e.*, accommodation of the wire for current densities below rheobase. It also shows that the observed rheobase must be larger than

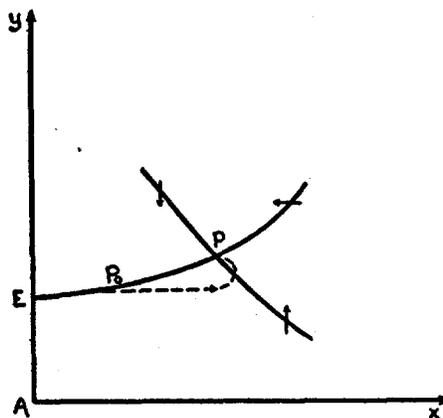


FIG. 7. Part of an xy diagram for current densities below rheobase. P_0 is the resting point of the system when no current is flowing. P the intersection point of the curves $dx/dt = 0$ and $dy/dt = 0$.

the theoretical value without accommodation; *i.e.*, without the rising of the dotted line. The parallelism between rheobase and the ability for accommodation, which our experiments had indicated, suggests that the value of the rheobase is determined at least partially by accommodation. It may be read from the figure that the duration of a rheobasic current needed for activation is finite, because for this current the time to reach the sector $L M_2 F_2$ is finite. Since these diagrams apply to constant currents only they are not appropriate for treating accommodation effects observed with slowly increasing currents.

It turns out that the underlying idea is not so very different from Hill's assumptions in his formal theory of accommodation (7). In both cases the state is described by two variables and the change of state by two simultaneous differential equations. In Hill's theory, as in the one here described, the rise of threshold during activity is assumed to correspond to the increase of refrac-

activations would cease, thus explaining the upper limit of current density giving rhythmic activations, which, in fact, was always observed. It may also happen that two new intersection points appear, one of which may lie between M_2 and F . This would have a similar effect with regard to rhythmic activations.

The method developed here for the discussion of cathodic activation of passive iron is similar to that used by Friedländer (11) and by Kirschstein (12) for the discussion of relaxation oscillations. The idea that rhythmic activations in biological systems should be considered as relaxation oscillations is not a new one. Bethe (13) stressed this idea long ago and a more precise development has been undertaken by van der Pol and van der Mark (14). The aim of our discussion is merely to determine how the differential equations of chemical kinetics can lead to relaxation oscillations. The result is that the assumptions which we must make in order to understand periodic reactions also lead to an understanding of the existence of a threshold, of accommodation, and of refractoriness. We have not here discussed one very characteristic phenomenon of our system, the propagation of activity along a surface. In an earlier communication (15) it has been shown that the lability which gives rise to the existence of a threshold and to rhythmic reactions also provides the necessary condition for the propagation of activity without decrement along the surface. There is the same relation between the inflammation point and flame propagation as between the threshold of activation and the transmission of activity. It could be shown that the velocity of stationary propagation of activity is in good agreement with the value calculated from the observed magnitude of the threshold. However, the more general non-stationary case, the origination of the excitation wave, for example, or its disappearance, or the propagation of activity with decrement, are not equally well understood. Experiments with iron wires in chromic acid have shown that in certain cases the intensity of response (decrease of potential) is not independent of the stimulus (current pulse), in other words, the all-or-none law is not valid here. On the other hand, in these cases the spreading activity generally showed a decrement. A correlation between the two facts, therefore, has to be assumed.

The existence of *spontaneous* rhythmic activations seems to be connected with the possibility of propagation. For this reason spontaneous activations have also not been discussed here. We do not wish to imply that all spontaneous activities are due to waves emitted from an active center and that an inhomogeneous surface is essential for their origination, but certainly that is usually the case and also ought to be expected theoretically.

VI

SUMMARY

The activation by cathodic polarization of passive iron in concentrated nitric acid ($d = 1.4$) has been investigated.

1. For short current pulses (1 msec. or less) a transient activation occurs when the product of current density and time exceeds a certain value. This limiting value is here designated as the "threshold." It is of the order of magnitude of 200×10^{-6} coulomb/cm.².

2. After activation and repassivation the threshold is temporarily several times higher than before. This "refractory state" is due to the presence of nitrous acid and of oxide layers. The return of the threshold to normal values occurs in seconds or minutes, depending on the variety of iron wire.

3. Immediately after a subthreshold current pulse the threshold is reduced (summation). However, if the second pulse occurs a certain interval of time after the first the wire exhibits a certain degree of refractoriness (Gildemeister effect).

4. Oscillographic measurements reveal the existence of a latent period between the application of the stimulating pulse and the establishment of the active state. The duration of this latent period depends on the strength of the current pulse.

5. There exists a minimum current density (rheobase) below which no activation occurs however long the current is applied. Depending on the variety of iron used this current density varies between about 1 and 10 ma./cm.². To produce activation a current of rheobasic strength does not have to be applied for an infinite time but only for about 100 msec. (maximum utilization time). Activation becomes manifest some time after termination of the activating pulse.

6. With currents of slowly increasing strength it is possible to reach current strengths several times higher than rheobase without obtaining activation (accommodation). Accommodation to a large extent depends on the variety of iron used. Details are given for currents increasing with a time constant of 0.5 second.

7. Potential measurements on wires in the refractory state show the existence of after potentials. Wires in the refractory state which are cathodically polarized show peculiar oscillograms. Both types of experiments point to the formation of nitrous acid as an essential element in the course of events.

8. With current densities only slightly above rheobase all wires exhibit simple activations only. With higher current densities certain types of wires exhibit periodic activations. The range of current densities in which such periodic activations occur varies with the type of wire. The lower limit is sometimes quite close to the rheobase.

9. A theory of periodic activations is presented which is modelled on the theory of self-excitatory electrical oscillations. As variables describing the state of the wire, the "degree of activation" and the "degree of refractoriness" are introduced. In the physicochemical system an autocatalytic process corresponds to the "falling characteristic" of electrical oscillations. The theory

leads to a rational view of the interrelations between threshold, rheobase, accommodation, refractoriness, and rhythm. The phenomena of conduction are not discussed here but their relation to the theory is briefly touched upon.

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