THE MERCURY–HYDROGEN PEROXIDE SYSTEM AS AN ANALOGUE OF NERVOUS TRANSMISSION

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(Received for publication, March 8, 1954)

INTRODUCTION

The nerve model to be described in this paper was devised as part of a study of nerve type propagation, the results of which will be set forth in a separate communication. The present paper is concerned only with the construction and behavior of a new nerve model composed of mercury and hydrogen peroxide, a system which shows both similarities and significant differences compared to the well known iron–nitric acid model of Lillie (1). No attempt has been made to determine in detail the electrochemical mechanism of propagation as has been done by Bonhoeffer et al. (2–6) for the Lillie model.

The present device stems from the observation that mercury intermittently catalyzes the decomposition of suitably buffered hydrogen peroxide (7–9). The connection between periodic activity and nerve-like propagation will be discussed in the later paper; it suffices to say here that nerve-like propagation can be obtained on an extended interface between mercury and hydrogen peroxide.

Propagation in the mercury–hydrogen peroxide system can be observed both visually and electrically. The mercury surface spends most of the time in the passive state in which the mercury surface has a golden color due to a thin oxide layer. There is little or no chemical activity in this condition. If a small portion of the mercury surface is reduced cathodically (i.e. by current passing from the solution to the mercury) the silvery color of the mercury is restored and this area is immediately covered by oxygen bubbles produced by the vigorous decomposition of hydrogen peroxide. This decomposition is the fundamental reaction of the system; the mercury is not consumed. Once an active region is established it grows at the expense of the surrounding passive area. At the same time the portion which was previously active returns to the passive state and thus a band of activity passes along the mercury surface. Electrical observation shows that the active region acts as an anode supplying current through the solution to the adjacent passive areas. In a typical case

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the velocity of propagation is 10 cm. per second and the width of the active region is about 3 cm.

EXPERIMENTAL

Materials

Essentially the apparatus consists of a filament of mercury in contact with a buffered solution of hydrogen peroxide. The mercury is introduced as a coating completely covering a noble metal rod or wire, which is laid on the bottom of (or supported within) a trough containing the solution. Smooth platinum electrodes are dipped into the solution to measure changes in the electric potential. Similar electrodes are used to apply stimulating current to the mercury surface.

1. To get all parts of the mercury surface uniformly exposed to the solution the mercury is supported on a metal rod or wire. (If the mercury is simply poured into a groove in the bottom of the trough it will be spontaneously and chaotically active due to the lack of symmetry in the conditions of the upper and lower surfaces.) The material of choice for supporting the mercury is silver. Gold is fairly satisfactory and platinum would be so except for the difficulty of coating it with mercury. All metals less noble than mercury which were tried (Cu, Pb, Sn, Zn, Al, Mg) were useless. In every case the mercury surface remained a bright silvery color and there was no evolution of oxygen.

The mercury surface need not be cylindrical though this shape was used almost exclusively. The dimensions are not critical. The cylinders of silver used in this work were 20 cm. in length with diameters ranging from 0.05 cm. to 0.25 cm. Silver wire was sometimes straightened by annealing and stretching. After straightening the wire or rod was washed and then meticulously polished with fine emery cloth with a view to obtaining the most uniform possible surface prior to the final mercury coating. The silver should not be touched with the fingers during or after the polishing operation. After polishing the silver wire or rod is dipped in mercury. It is then ready for use. This procedure must be repeated daily in most instances.

2. The solution is made by diluting 30 per cent hydrogen peroxide (Merck-reagent grade) to 12 per cent. To 100 cc. of this solution is added 3 cc. of buffer made by mixing 2 volumes of 5 M potassium acetate with 1 volume of 0.1 M acetic acid. None of these proportions is critical; the peroxide concentration may vary from 10 to 13 per cent and the pH from 5.9-6.1. Only ordinary precautions as to cleanliness are necessary but halides must be excluded. Potassium chloride is harmful at concentrations of \( \text{M} / 1,000,000 \). The solution was usually held at 20°C although propagation takes place at least over the range 18–24°C.

3. The trough used to contain the peroxide solution and coated wire was made of lucite in hemicylindrical form 27 cm. long by 3.1 cm. in diameter. It was provided with a jacket through which water was circulated at a temperature controllable to 0.1°C, although such close control is not essential.

4. Auxiliary troughs of glass, also hemicylindrical, 30 cm. × 2.5 cm. were provided to hold distilled water and 2 per cent nitric acid. Their use will be explained below under Methods.

5. The electrodes used in the peroxide solution were of platinum sealed into glass
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tubes of 3 mm. outside diameter. The active part of each electrode was a smooth platinum sphere approximately 1 mm. in diameter. No polarization effects were detectable with these electrodes when used for potential measurement provided the device to which they were connected had an input resistance greater than 50,000 ohms. The oscilloscope and recording potentiometer used had at least 500,000 ohms input resistance.

When it was desired to connect directly to the mercury-covered wire this was done by using another suitably shaped silver wire which was coated with mercury and treated like the main wire though with less care.

6. Potential changes accompanying propagation were observed with a DuMont 304-H oscilloscope and recorded with two Sanborn twin-viso recording potentiometers whose band width is more than adequate for this work.

7. Single pulses of stimulating current were generated by an electronic stimulator and applied to the system through a variable resistance of 30,000 ohms or more. This resistance is high enough to make the current essentially independent of polarization within the system. Simpler current sources are, of course, usable.

Methods

When the mercury-covered wire has been in contact with the peroxide solution for some time (10 to 30 minutes ordinarily) the initially golden color of the film becomes darker presumably due to gradual thickening of the oxide film. When this occurs the surface must be renewed by transferring the wire to a trough containing 2 per cent nitric acid. The bright silvery color is restored in about 0.1 second but soaking for 2 to 5 minutes is beneficial since the higher surface tension of the mercury in acid solution is conducive to smoothing and levelling. After treatment with 2 per cent nitric acid the wire is dipped briefly in two successive troughs containing distilled water after which it may be returned to the trough containing peroxide solution. The several troughs should be arranged so that the transfers can be made quickly enough to prevent drying of the mercury surface. When the renewed wire is returned to the peroxide solution the golden film will form in less than 1 second provided the surface has been kept wet. If the surface has been allowed to dry since the last contact with peroxide the formation of a film will be delayed up to 3 minutes.

The wire is conveniently handled with a two-tined glass fork, the ends of the tines being bent into hooks which support the wire in a horizontal position as it is carried between troughs. Wires are best stored overnight in a horizontal position under water in a covered vessel.

For all the electrical measurements to be described below the wire or rod was supported on two thin glass cross-bars just below the surface of the peroxide solution so that it lay nearly on the axis of a hemicylindrical volume of liquid. This cylindrical geometry simplifies the subsequent analysis.

Stimulation has been produced by scratching the mercury surface with a glass rod and by local application of heat or alkali, but the most convenient means is electric current. Bipolar stimulation is possible but more frequently used was the monopolar arrangement in which one lead from the current source was connected directly to the wire, the other lead going to a small platinum electrode near the wire (usually
at one end). In either case direct current was used, activation occurring where (positive) current passes from the solution to the mercury. Current of 0.001 ampere for 0.1 second was sufficient. The various arrangements of “pick-up” electrodes will be described below in the section on results of measurement.

To the right of Figs. 1, 2, 3, and 5 are diagrams showing the mercury-covered wire (heavy vertical line) along which the propagated impulse travels, the pick-up electrodes (open circles), and the leads connecting the electrodes to the voltage recorder. Each pair of leads is drawn so that when the upper lead of a pair becomes more positive (or less negative) with respect to the lower the corresponding graph shows an upward displacement. In each diagram the propagated impulse travels downward. The stimulating electrodes are not shown.

FIG. 1. Two simultaneous monopolar recordings during the passage of a propagated impulse. The electrodes are 0.6 cm. from the wire and 2.5 cm. apart.

RESULTS

Perhaps the simplest electrical measurement is made with the “ground” lead of the oscilloscope or recorder connected to the mercury-covered wire and the other lead connected to a single platinum electrode placed in the solution near the wire. (The wire used in all experiments described here is 1 mm. diameter.) The recording (Fig. 1) shows a typical “spike” produced when the
platinum electrode goes positive as the active region passes it. Two such recordings from electrodes spaced a known distance apart longitudinally and equally distant from the wire permit the velocity to be measured. In Fig. 1 the velocity is 12.5 cm./second. In Fig. 2 is shown another example of a monophasic spike together with a diphasic wave obtained from the bipolar electrode arrangement in which both recorder leads are connected to electrodes in the solution located at equal distances from the wire but spaced 2.5 cm. apart.

![Chart showing two simultaneous recordings](chart.png)

**Fig. 2.** Two simultaneous recordings with one channel monopolar and the other bipolar during the passage of a propagated impulse. The electrodes are 0.6 cm. from the wire and 2.5 cm. apart.

longitudinally. The instantaneous magnitude of the diphasic wave obtained in this way approximates the slope of the monophasic spike at the same instant.

To get a map of potential throughout the cylindrical volume of liquid three electrodes were placed in a plane perpendicular to the wire and spaced at different distances radially. The simplest way to record would be to connect these three electrodes in monopolar fashion. However greater accuracy is obtained by connecting only the inner electrode monopolarly and using the two remaining channels to record the potential difference between the inner electrode and the middle one and the potential difference between the middle
electrode and the outer electrode as in Fig. 3. The monophasic spikes can then be constructed by point-by-point addition. The result of this construction is shown in Fig. 4 A. If the velocity of propagation (assumed constant) is known Fig. 4 A can be regarded as a plot of potential difference against longitudinal distance with radial distance as parameter. This information can then be replotted with radial distance as the ordinate and potential as parameter. The result (Fig. 4 B) is an instantaneous picture of the equipotentials where
the active region is moving to the left. Of course, the lines of Fig. 4 B must be rotated about the axis of the wire to generate the surfaces which are the actual equipotentials in the cylindrical system.

A family of lines drawn so that they intersect the equipotentials perpendicularly gives the direction of current flow throughout the liquid. Such a family of lines is shown in Fig. 4 C. (Little effort has been made to space these lines to indicate current density.) It can be seen that current enters the solution from the active region on the wire, part of it flowing backward into the refractory region in the wake of the active spot and part of it flowing forward. From a knowledge of the potential differences given in Fig. 4 B together with the dimensions and conductivity of the liquid it can be calculated that the total current flowing backward into the refractory region is 1.7 milliamperes and that flowing forward is 0.9 milliampere.

The current per unit length entering or leaving the wire can be obtained by applying Ohm's law to the known potential field. The result is shown in Fig. 4 D.

In Fig. 4 E current density of Fig. 4 D is plotted against the corresponding values of change in potential difference given in the tallest curve of Fig. 4 A. The resulting complex curve shows the current crossing a thin annular space surrounding the wire as a function of change in potential difference across this annular space throughout the course of the propagating activity. The curve begins and ends at the origin and it is only in the vicinity of the origin that the curve resembles at all that of a passive resistance.

The electrical impedance of the passive film may be determined by applying an alternating current from a very high resistance source and measuring the amplitude and phase shift of the voltage appearing at a second monopolar electrode placed near the wire. (See the diagram accompanying Fig. 5.) For the study of the passive film a mercury-covered wire only 1.3 cm. long was used and the current-supplying electrode placed far enough from it to give essentially uniform current density over the whole mercury surface. The current density used (0.23 ma. r.m.s./cm.²) was small enough so that at frequencies greater than about 40 c.p.s. there was no sign of activation of the mercury surface. At lower frequencies the voltage curve was somewhat peaked indicating that there was some slight response to stimulation on each half cycle of current. In the frequency range from 80 to 5000 c.p.s. the vector impedance had the familiar semicircular locus showing that the impedance of the passive film can be represented by a resistance in parallel with a capacitance. Typical values are 150 ohms and 10 microfarads for 1 sq. cm.

The change in surface impedance during propagated activity can be observed with a similar electrode arrangement but with one in which a full length wire is used in the usual way. Fig. 5 shows the recording obtained when a 60 c.p.s. current from a high impedance source is applied to a portion of the
Fig. 4
curve and the wire is then stimulated by a d.c. pulse at one end. At first the
record shows only the sinusoidal voltage produced by the impedance of the
passive film but as the active region passes under the recording electrode the
usual "spike" is seen with alternating voltage superimposed. In Fig. 5 the

![Fig. 5. Simultaneous monopolar recordings made with a constant alternating current applied to the region near one of the electrodes.](image)

apparent impedance of the mercury surface decreases during the active phase
to about one-third of the resting value. The true impedance change is greater
than this since there is some channeling of the alternating current into the
active region. Better measurements show the active impedance to be approxi-
mately one-tenth of the passive value.

**Fig. 4.** A construction from the data of Fig. 3. Fig. 4 A shows three "spike potentials" at different distances from the wire. Fig. 4 B shows a map of the equipotentials over one-half of the cylindrical volume of solution surrounding the wire. Fig. 4 C shows the direction and approximate density of the current flow during propagation. Fig. 4 D shows the current density at the surface of the wire. The common abscissa of Figs. 4 A, B, C, D is either time or distance along the wire since each figure refers to a disturbance travelling at constant velocity but otherwise unchanging. Fig. 4 E shows the current density at the wire surface vs. voltage change across a thin annular region surrounding the wire.
The mercury–peroxide system has several modes of behavior other than the simple one described above. Some of these alternate activities are undesirable in a nerve model but others may be appropriate.

Perhaps the smallest deviation from “normal” behavior is that in which a spot on the wire becomes spontaneously active and sends out a propagated disturbance in each direction with the whole wire thereafter becoming passive. In this case the propagated waves are entirely similar to those elicited by external stimulation except that usually the spike voltage, the velocity, and the length of the active region (determined visually) are all greater than normal.

A still greater deviation from “orthodox” behavior occurs when the spontaneous activity is prolonged and chaotic. In this case there are as many as four or five active regions in existence at once—some moving toward one end of the wire, some toward the other. They are annihilated when they collide or when they reach the end of the wire but new ones spring up to maintain the activity which may continue in this fashion for several minutes. Electrical recordings during this activity are approximately periodic. Such chaotic activity may subside spontaneously (or be quenched by reverse stimulation) or it may become more intense to the point where each region of the wire is active nearly all the time; i.e., the reaction “runs away.”

The cases of “misbehavior” described above can occur because the system is excessively biased toward the active state due to high temperature, high concentration of hydrogen peroxide, or high pH (i.e., any of these quantities being at the high end of the permissible range). However, excessive activity is most often traceable to lack of sufficient uniformity in the mercury surface. Any appreciable dissymmetry acts as a built-in stimulator and produces spontaneous activity in a system which would otherwise show only the stimulus-response type of behavior. An experimenter working with the mercury–peroxide system must pay more attention to the question of surface uniformity than he does to the composition and temperature of the solution since the latter are easier to control.

Still greater deviations from normal behavior are the cases in which the oxide film never forms on the mercury surface and the case in which the film is excessively thick and permanently refractory. In the first instance the mercury surface remains silver-colored and there is a steady evolution of oxygen from all parts of the surface. This behavior is brought about by a pH much above 6.1 or by peroxide concentration below 8 per cent. In the second case the film is black as soon as it is formed and, while a region of the surface can be brought into the active state by stimulation (cathodic reduction), this region will immediately revert to the passive state when stimulus is removed and no propagation occurs. Such behavior is indicative of excessively low pH. There is usually a very slow evolution of oxygen in this permanently refractory state.

In the case just described the film is black from the moment it is formed.
In the normal case the film is initially golden but it gradually becomes darker colored until after a period of 10 minutes to 1 hour or more the film has become black and permanently refractory. When this point is reached the wire must be rejuvenated with dilute nitric acid. It is, of course, desirable to postpone the refractory state as long as possible and, while the composition and temperature of the solution play a part, the most important factor in determining the duration of the golden phase is again the uniformity of the mercury surface.

The two extreme cases described above (i.e. no film formation and refractory black film) will never be seen if reasonable care is taken to establish proper conditions. It is more difficult to reproduce a given type of behavior in the normal range of activities; for instance the stimulus-response behavior in preference to spontaneous activity. Better control of surface uniformity is needed and perhaps electrodeposition of either or both silver and mercury would be helpful.

Even when the model is producing only stimulus-response behavior there is appreciable variability in the details of the activity such as propagation velocity, length of the active region, maximum spike voltage, minimum adequate stimulus (threshold), etc. These details depend upon three time intervals, the most important of which is the time elapsed since the system was last in the active state. This interval is of the order of seconds and is entirely analogous to the refractory period in nerves. The second significant interval is the time elapsed since the “fresh” wire was put in contact with the peroxide solution. This interval is of the order of minutes and corresponds to the gradual darkening of the golden film. It is perhaps analogous to the fatigue of a nerve preparation in vitro. The third interval which affects the performance of the model is the time elapsed since the wire was last dipped in mercury. This interval is of the order of hours and probably corresponds to diffusion of silver and mercury. It is because of this slow deterioration of the system that the wire must be treated with mercury every day. The measurements presented in Figs. 1 to 5 were made after an adequate recovery period (10 to 30 seconds) when the wire had been in contact with the solution no more than 5 minutes since the last treatment with nitric acid and no more than 4 hours had elapsed since the last treatment with mercury.

DISCUSSION

The value of an analogue lies in its resemblance to the system of primary interest. However knowledge of differences in structure and function is also valuable since it helps to avoid the mistake of pursuing the analogy too far. Accordingly it is of interest to compare the mercury–hydrogen peroxide system with both the iron–nitric acid system and the nerve fiber, noting similarities and differences from several points of view.

1. Physical Structure.—Each of the three systems is composed of two bulk phases separated by a third phase in the form of a thin membrane or film. In
the two nerve models one of the bulk phases is a metal and the other is a solution of a substance capable of oxidizing it, while the third phase is a layer composed of metallic oxides. In the nerve fiber the bulk phases are the axoplasm and the surrounding solution and these are separated by the third phase, the neuromembrane. While there is a vast difference between the properties of the three phases in the nerve fiber and the corresponding phases of either model, all systems are junctions with a barrier layer.

2. Chemical Activity.—In all three systems the barrier film is labile. When the film is intact the system is quiescent; when the film is obliterated, or at least profoundly modified, the two bulk phases interact producing the basic action of the system. In the iron-nitric acid model this basic action is the dissolution of iron by the acid. In the mercury-hydrogen peroxide system the basic action is the decomposition of hydrogen peroxide catalyzed by metallic mercury. Thus in one model each bulk phase is a reagent while in the other model one phase provides all reagents and the second phase acts only as a catalyst. In the case of the nerve fiber the basic activity involves both bulk phases and appears to be simply the counterdiffusion of sodium and potassium ions (11).

3. Electrical Activity.—In all three systems electric current can be detected and the circuits followed by the current in each case cross the barrier region twice, lying partly in one bulk phase and partly in the other. In the case of the two models the current in the solution diverges from the active region entering the metal at remote points and returning through the metal to the active region (cf. Fig. 4 C). In the nerve fiber this polarity is reversed and the current in the external solution converges on the active region returning through the axoplasm to distant parts of the fiber. Thus, while the spike potential of the nerve fiber is negative, it is positive in the models.

In the mercury-hydrogen peroxide system the spike potential falls more rapidly than it rises. From this it can be deduced that, as the current emerging from the active region divides, less than half of this current flows forward where it stimulates the quiescent region ahead of the pulse. In Fig. 4 only about one-third of the total current is available for stimulation and only a fraction of this is actually needed. Moreover, part of the energy released by the decomposition of hydrogen peroxide is dissipated as heat so that the total energy released is considerably greater than that required for stimulation. In contrast to the mercury-hydrogen peroxide system, the spike potential of the nerve fiber rises more rapidly than it falls so that the distribution of current is more efficient. However, it is still true that much more current is produced than is needed for stimulation (Tasaki (10) gives the ratio as 5:1 in myelinated fibers of the toad) and it is not certain that the all energy released appears as electrical energy. Thus it seems that the “stimulating efficiency” is also low in the case of nerve fibers.
Another comparison between the nerve and the mercury-hydrogen peroxide system is in the minimum current density for stimulation. The magnitude of this quantity for the mercury-hydrogen peroxide system varies somewhat according to the composition, temperature, and history of the mercury-covered surface, but is of the order of 0.001 amp./cm$^2$. Measurements given by Tasaki (10) lead to a value of 0.003 amp./cm$^2$ (based on nodal area of myelinated fiber). Data on the rheobase of non-myelinated fiber are rather scarce but for giant squid axon the value is about 0.0001 amp./cm$^2$. Thus the rheobase of the mercury-hydrogen peroxide model is smaller than that of myelinated fiber but larger than that of non-myelinated fiber. Doubtless similar ratios obtain for total current densities in the three systems.

4. Energetics.—We have seen that the current densities in the nerve and in the mercury-hydrogen peroxide system are roughly comparable and that the potential changes during activity in the two cases are practically equal in magnitude though of opposite polarity. It follows that the energy required for stimulation in the two cases is also comparable. By contrast the energy released by the chemical reactions of the two models is considerably greater than that available from the concentration gradients in the nerve. If these gradients are indeed the chief source of energy in the nerve we reach the not surprising conclusion that the models are much less efficient than the nerve. Apparently the delicacy of nerve structure is paralleled by subtlety of function.

SUMMARY

The construction and behavior of a system exhibiting all-or-nothing propagation of an electrochemical disturbance are described. Detailed measurements of the distribution of electric current and potential are given and the device is compared with nerve and with the Lillie model in respect to structure, electrical and chemical activity, and energy relationships.

REFERENCES