SPREAD OF EXCITATION IN AN INHOMOGENEOUS MEDIUM (STATE SIMILAR TO CARDIAC FIBRILLATION)*

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THIS paper considers an excitable medium with properties similar to the excitable tissue of the heart or the nerve fibres. It will be shown that as well as the normal resting state (or conduction of pulses supplied from without) a state of activity resembling fibrillation is possible.

1. INTRODUCTION

In certain pathological changes of the heart, the heart may pass from a normal state of contraction to fibrillation. The contractions of individual zones of the heart during fibrillation occur chaotically and the record of electrical activity displays rapid fluctuations of irregular form and duration. In experiments the healthy heart can be made to fibrillate by stimulating it for a certain period with a high frequency from an electrical stimulator. Short-lived fibrillation can usually be removed by a powerful electrical discharge after which the heart passes to a normal state of contraction. Until recently, there was no hypothesis on fibrillation compatible with the facts. Views were expressed that the noise character and high frequencies in the electrocardiogram during fibrillation might be caused either by a large number of non-interacting generators in the heart (as with spontaneously active cells) or by complex transformation of the rhythm of one source of activity ("ectopic focus" or a pulse circulating around an aperture) appearing as a result of the inhomogeneity of the heart in terms of refractoriness. Quite recently [1] it was argued that thanks to the difference in the refractoriness of adjacent portions of tissue closed irregular pathways of conduction may appear leading to self-sustained arhythmia. The consistency of this point of view was confirmed by means of modelling on a digital computer [2].

Theoretical examination of the spread of a pulse over a homogeneous excitable tissue was made by Wiener [3]. The main concepts as a result of this work are now widely used. Gel'fand and Tsetlin described an interesting model of an excitable medium with spontaneously active elements [4]; they showed, in particular, that the spontaneously acting elements are synchronized and operate at a frequency equal to the frequency of the fastest of them. Balakhovskii [5] demonstrated the possibility of circulation of a pulse in a medium without apertures and obstacles.

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In the present work we shall follow up the phenomena which occur in an excitable medium inhomogeneous in terms of refractoriness.

2. EXCITABLE MEDIUM

We shall consider and excitable medium without spontaneously active elements in which the duration of the excited state is finite and the phase of relative refractoriness absent. The properties of the medium will be such that it will facilitate its investigation to the maximum but preserve the basic phenomena known for excitable media (section III). We shall consider that the excitable medium consists of points each of which may be in one of three states: resting, excited or refractory. The point may continue to be in the resting state for as long as desired until the exciting signal is received. After receiving a signal the point passes into the excited state in which it remains during time ϑ, then passes to the refractory state in which it is present for time r after which it again returns to the resting state. Throughout the time ϑ in which the point is in the excited state it sends an exciting signal to the points next to it. The points in the refractory state do not respond to this input signal and do not conduct it further. The points in the excited state also do not respond to the "foreign" signal. Over the region of resting points excitation spreads at a constant speed v.

We shall consider the inhomogeneous medium to be made up of homogeneous regions. The refractoriness changes abruptly from region to region and the other parameters (ϑ and v) will for simplicity be taken as constant.

We shall call the value $R=r+\vartheta$ the refractoriness. It will be seen that no point x can be excited at a frequency exceeding $1/R(x)$. The frequency $f_0=\dfrac{\min}{x}[1/R(x)]$ will be called critical for the given medium. The time of spread of the excitation wave from one point to another will depend on how long ago the medium was last excited: running into the refractory zones the wave may "wait" but not longer than ϑ.

3. CONDUCTION OF PULSES

For the subsequent discussion we must define the following facts relating to excitable media.

A. If a certain point of the medium is excited, then the excitation wave will spread from it to all sides. Since the wave of refractoriness spreads after the excitation wave, then the two waves encountering each other will die away. For this reason there are no reflected waves [3].

B. If to a medium inhomogeneous in terms of refractoriness we apply excitation with sufficiently high frequency, then transformation of the rhythm occurs—periodic fall-out of certain pulses [6–8]. Let the fibre (one dimensional medium) be made up of two pieces with the refractoriness R_M and R_b ($R_M<R_b$) similar in magnitude: $R_b-R_M<\vartheta$. If piece 1 is excited rhythmically with a period T such that $R_M<T<R_b$, then the zone with refractoriness R_b cannot allow through all the pulses. Already the second wave approaches it earlier than it emerges from the state of refractoriness. If $\vartheta=0$ then this

wave would be extinguished at the boundary. However, according to the properties the medium the point on being excited is in the excited state for the time $\vartheta > 0$; if in th period the second zone has time to come out of refractoriness, then the wave will mo further. At the boundary the delay $\Delta = R_b - T$ appears. The zone with refractoriness may be excited at moments $0, R_b, 2R_b, 3R_b, \ldots$ and so on and excitation will approac it at times $0, T, 2T, 3T, \ldots$ etc. As follows from this, with spread of the second wave the boundary of two zones the delay $\Delta = R_b - T$ appears, for the third wave the delay equal to 2Δ for the next one 3Δ and so on. The approaching wave will have time t excite the zone with refractoriness R_b only as long as this delay is less than ϑ. If for a certain wave the delay exceeds ϑ, then this wave dies at the boundary and the next one afte it can again pass through.

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[illegible] where θ is derived from delay (conduction)

If $\vartheta < \frac{1}{2}R_b$, then from each $(n+1)$ pulses only n will pass through (periodic $(n+1):n$). The number n is determined from the conditions $n\Delta > \vartheta$, $(n-1)\Delta < \vartheta$ so tha

$$n = \left(\frac{\vartheta}{R_b - T}\right) + 1$$

reformulate in terms of conduction delay

where $|x|$ is the whole part of x (if $\vartheta > \frac{1}{2}R_b$, then the delay of the wave following afte the omitted one differs from zero, which may lead to complication of the picture) As can be seen from (1) the closer the period T of stimulation to the refractoriness R_b the longer the period $(n+1)$ of transformation of rhythm.

Assume, fixed conduction velocity [illegible] R_b — but also true for variable Vf fixed R_b

C. Circulation of the excitation wave over a circle or in a two-dimensional mediu about an aperture (Fig. 1*a*) is possible. The points of the medium are rhythmically excited with the period T equal to the time of circulation of the wave about the apertur (1). The ring movement is possible only if each point has time to come out of refractoriness. This imposes limitations on the minimum length of the ring which for $\vartheta = 0$ must be equal to the wavelength of refractoriness Rv.

4. REVERBERATOR

In papers [1, 2, 9] hypotheses were put forward to the effect that circulation of a pulse is possible not only about an aperture. It was assumed that thanks to the difference in the refractoriness of adjacent portions of tissue [10] reverberation may appear—enveloping incompletely rested regions by a wave and returning to the initial point. The possibility of circulation of a pulse in a one-link region was considered in detail by Balakhovskii [5]. He showed that if in a homogeneous one-link region a regime of circulation of a pulse is produced, then the pulse will move over the same closed path as long as desired and this case in substance does not differ from the propagation of a pulse about a very narrow aperture.

We shall see what happens on instantaneously "sewing together" the margins of the aperture around which the wave moves (Fig. 1*a* and *b*). For a certain period it will move as before, i.e. only to the right of the line *AN* since to the left of *AN* the points are in the state of refractoriness. This will continue until the leading and trailing edges of the wave are in the positions shown in Fig. 1*c*, now the leading edge of the wave may "jump" through the line AN. The point of jump is denoted by M. Then the excitation wave will constantly move about the line MN in precisely the same way as if a section were drawn along the line MN. We shall describe MN as the line of rupture of the phases and a generator of such a type as a reverberator (as distinct from propagation of a wave about the aperture). The apperance of reverberators is examined in section 6.

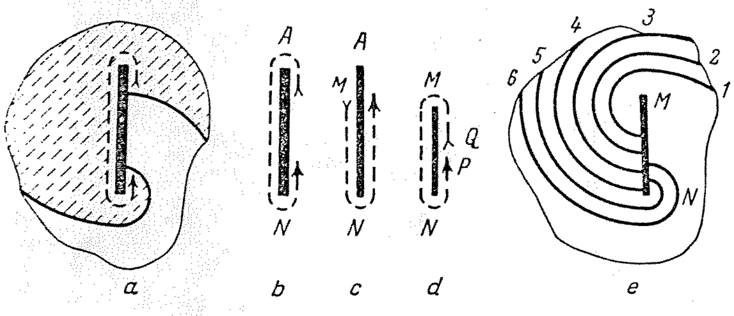
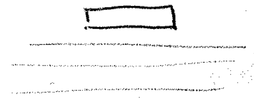


FIG. 1. Movement of excitation wave about aperture (*a*) and its diagrammatic representation (*b*). Formation of reverberators (*c*) and (*d*) and succesive positions of the front of the wave of reverberator (*e*).



thickness vs θ_{udary}
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$\frac{7}{2}$ v → slower
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5. PROPERTIES OF REVERBERATORS

Property 1. The period of work of a reverberator lying within a homogeneous region is equal to R (refractoriness of the piont of the medium).

In fact, the clearance between the leading and trailing edges of the wave (PQ, Fig.1d) in the work of the reverberator is equal to zero [11]. If it differed from zero, then on jumping through the line of rupture of the phases (at point N or M — Fig. 1c) it would be shortened to zero but the clearance in a homogeneous region cannot increase. Therefore each point close to the line of rupture of the phases is excited immediately as soon as it passes from refractoriness. From this follows both property 1 and the statement that no excitation waves spreading over the medium can change the moment operation of the points of the reverberator. If the reverberator is located in an arbitrary inhomogeneous region, then we may say only that some of the pionts will be excited in the maximum possible rhythm. However, this suffices to show that for reverberators, as distinct from spontaneously active cells this is true.

Property 2. Reverberators are not synchronized. By virtue of this property on interaction of reverberators a complex picture of activity may appear.

6. APPEARANCE OF REVERBERATORS

If some points of the medium inhomogeneous in refractoriness (section 2) are excited at frequency (less than f_0) then over the medium will spread waves which in the simplest case have the form of diverging circles. Reaching the boundaries of the medium the waves die away. If the frequency is high, then at ceratin points transformation of the rhythm will be observed. The regions with raised refractoriness cannot pass all the waves through and at their boundary the front of the wave will be disrupted. We shall show that in this case reverberators may appear. We shall consider an excitable medium consisting of two different semi-planes with different refractoriness R_M and $R_b (R_M < R_b)$ and let R_M and R_b differ not greatly: $R_M - R_b < \vartheta$. Figure 2*a* shows the wave a_{n+1} spreading only in the left semi-plane (where refractoriness is less). On the right the front of this wave abuts against a longer refractory tail of the preceding wave a_n and therefore, does not spread to the right semi-plane. Let wave *b* move towards these waves (Fig. 2*b*). The waves a_n and *b* on colliding die out. At their site will remain the narrowing refractory islet (Fig. 2*c*). When it disappears the wave a_{n+1} will no longer be prevented from spreading to

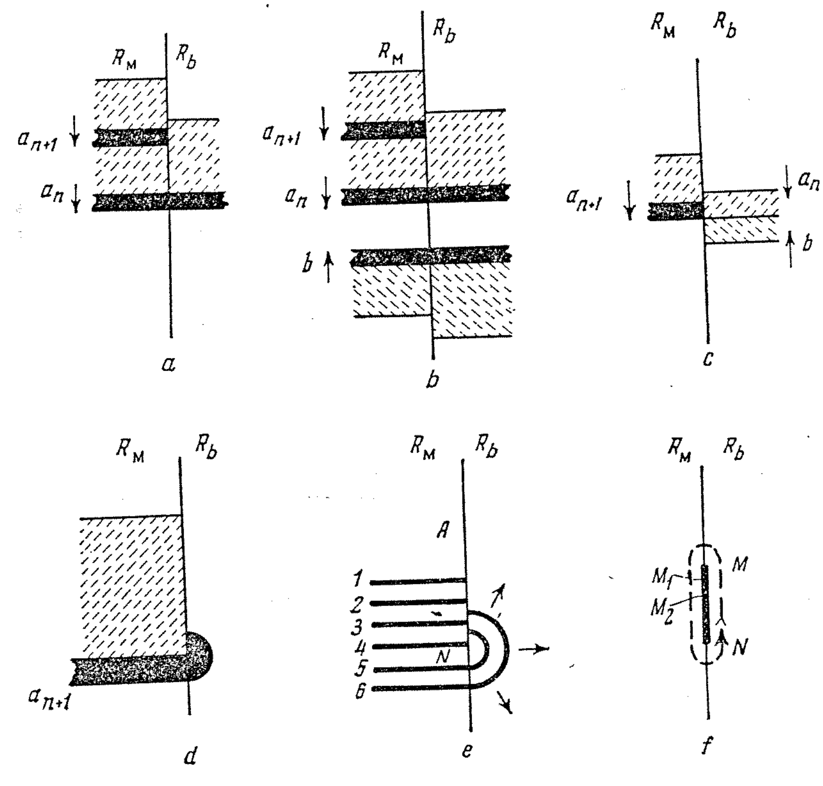

FIG. 2. Origin of reverberator in an inhomogeneous medium. Refractoriness in right semi-plane R_b greater than in left R_M. The points in an excited state are blackened and the refractory zones are hatched. *a*—wave a_{n+1} does not embrace the right semi-plane and spreads only over left (on the right the wave a_{n+1} runs into the refractory tail of the preceding wave a_n); *b*—wave *b* moves towards waves a_n and a_{n+1}; *c*—waves a_n and *b* on colliding die out and their place remains a narrowed refractory islet; *d*-*e* and *f*—scale enlarged; *d*—wave a_{n+1} penetrates into right semi-plane; part of it spreading upwards does not embrace the left semi-plane as long as the refractory tail does not pass by; *e*—diagram of the succesive positions of the front of wave a_{n+1}. At point *N* the wave begins to penetrate the right semi-plane. In the portion *AN* the wave at first passes on the left downwards (positions *1*, *2*, *3*, *4*) and then on the right upwards; *f*—reverberator.

the right semi-plane. In the right semi-plane this wave will have the form of a semi-circle expanding to all sides. In the zone *AN* the wave now moves upwards (Fig. 2*e* and *f*) and when it bypasses at point *M* the refractory tail of the wave moving downwards, it can likewise pass into the left semi-plane and close the path. A reverberator is formed.

For the production of reverberators according to the mechanism described here it is necessary in a medium inhomogeneous in refractoriness to have several non-synchronized sources of activity operating at sufficiently high frequency. The role of such sources of activity may be performed by the reverberators themselves. Therefore, in certain conditions the number of reverberators in the medium may increase in avelanche form.

7. LIFETIME OF REVERBERATOR

In an ideally homogeneous medium a reverberator may exist for an unlimited time. We have seen that reverberators appear in inhomogeneous parts of the medium where breaks in the fronts may form. Let a reverberator appear at the boundary of two homogeneous regions. We will show that the lifetime of such a reverberator is finite. As we shall see later, close to the point of "jump" of *N* (Fig. 2*e*) the points with less refractoriness (R_M) operate with the maximum frequency possible for them. Therefore, here transformation of rhythm is observed. When excitation cannot pass from the left semi-plane (where refractoriness is less) into the right the reverberator "dies".

We shall consider this in greater detail. We shall follow the excitation wave only in the small neighbourhood of the line of rupture of the phases *MN*. Let the initial length *MN* be $\frac{1}{2}vR_\mathrm{b}$. It is not difficult to see that excitation moving from *N* to *M* over the right semi-plane performs a jump through line *MN* not extending to *M* at point M_1 the distance of which from point *N* is such that the time of travel from M_1 to *N* and back is equal to R_M. As a result, excitation will reach *N* of the time R_M after its preceding operation and the right semi-plane of the point *N* will pass from refractoriness and may be excited only after time R_b; therefore, here the delay $\Delta = R_\mathrm{b} - R_\mathrm{M}$ appears. Excitation performs the nex jump at point M_2 located even closer to *N*: the time of travel from M_2 to *N* and back plus the time of delay Δ must be equal to R_M. Now time of delay at point *N* will be equal to 2Δ and so on. When it exceeds ϑ the right semi neighbourhood of point *N* will pass from refractoriness as soon as the excitation wave comes from *N*. The jump has not occurred. The wave travelling in the left semi-plane will spread further along it.

We shall show that in the direct proximity of *N* it cannot pass into the right semi-plane. We would note that during the work of the reverberator the directions of spread of the waves in the right and left semi-planes are opposite only in the portion between the points of jump (*N* and *M*); beyond the line of rupture of the phases these directions coincide: the higher the points *M* of the wave move upwards, the lower the points *N* move downwards (Fig. 2*e*). The jump occurs when the excitation wave bypasses the refractory tail of the wave moving towards it. Outside the segment *MN* the wave and the refractory tail of the preceding wave changing its jump spread to the same side and the jump is impossible (see Fig. 1*e*).

The lifetime of the reverberator measured by the number of turns n of the excitation wave about the line of rupture of the phases is approximately equal to (section 3*b*)

$$n=\left[\frac{\vartheta}{\Delta}\right]+1=\left[\frac{\vartheta}{R_b-R_M}\right]+1\,,$$

i.e. smaller the greater the inhomogeneity (the greater the difference R_b-R_M).

The wave with ruptured front remaining after disappearance of the reverberator may either reach boundaries of the medium and die away or a new reverberator may form from it in suitable conditions (for example, as in section 6).

8. "CRITICAL MASS"

If the reverberators did not die away it would be enough for one reverberator to appear for continuous activity to be recorded in the medium. However, taking into account the finiteness of the lifetime of the reverberators the problem arises of elucidating those critical conditions (size of medium, distribution of refractoriness, number and position of reverberators) in which the activity in the medium may be supported for an indefinitely long time, i.e. conditions in which the number of "dying" reverberators per unit time does not exceed the number of those "being born".

If thanks to a certain influence the number of reverberators in a given medium exceeds the critical N_{crit} then activity in the medium also persists after removal of this influence. If the number of reverberators is less than the critical, then the activity dies away.

It is possible by means of a specially chosen stimulation to keep the number N of reverberators in the medium at a level less than N_{crit}. If N is sufficiently great, then as long as the stimulator operates, in the medium a complex picture of activity may be observed (fibrillation). But after cutting out the stimulator the activity dies aways.

9. DIMENSIONS OF REVERBERATOR

We shall at first consider the spread of the pulse over a homogeneous ring. If the activity of the excited state $\vartheta=0$, then the minimum length of the ring along which a pulse may move is equal to $\lambda=Rv$ [3].

We shall show that if $\vartheta>0$ then the pulse may circulate also over a ring with length $l<Rv$. Let $Rv>l>(R-\vartheta)v$ and all the points of the ring be in the resting (relaxed) state. Let a pulse be released at a certain point A of the ring spreading only to one side. This pulse moving at the speed v makes a complete revolution in the time $t'=l/v<R$ and approaches the initial point A before it passes out of the refractory state. If $\vartheta=0$ the excitation wave would die away. But since $t'>R-\vartheta$, then the point A comes out of the refractory state before excitation dies away and the ware performs a second revolution, This picture will then periodically be repeated: the pulse will travel around the ring at a speed v and at point A the delay $\Delta=R-l/v<\vartheta$ will be observed. This delay, unlike the transformation of rhythm remains constant and does not depend on the revolution number.

However, the length $l_1 = (R - \vartheta)v$ is not critical. The pulse may move for an indefinitely long time also over the ring with length $l < l_1$. If the initial conditions (distribution of the states of the points) are such that in the ring there are two points (A and B) at which delay of the pulse is observed, then the length of the ring must be not less than $l_2 = (R - 2\vartheta)v$. If in the ring the initial conditions release K points in which a delay is possible, then the minimal length of the ring is equal to $l_K = (R - K\vartheta)v$ (at no point can the delay exceed ϑ). Thus, for finite duration of the excited state in the ring of length as small as desired it is possible to ensure circulation of the pulse. The period of excitation of the points for $l < \lambda$ does not depend on the length of the ring and is equal to the refractoriness R.

If $l > l_1$ then it is possible to ensure circulation by releasing it into the rested ring; if the length of the ring $l < l_1 = (R - \vartheta)v$ then it is necessary to choose specially the initial conditions. Thus, if $l < l_1$ and all points of the ring are in the rested state, then the pulse cannot circulate: it passes through all the ring at the speed v in time $t' = l/v < R - \vartheta$ and excitation dies away before the initial point comes out of the refractory state.

Similar assertions may be made regarding the perimeter of the reverberator. This value is necessary for determining the minimum dimensions of the strip of tissue in which fibrillation is still possible. However, the important thing is not the minimum possible dimensions but the dimensions of the reverberators appearing in the medium. We have seen (section 7) that a reverberator located at the boundary of two regions with different refractoriness contracts in dimensions: delay appears on passage to the region with higher refractoriness. Through "lack of space" reverberators may form with two delays: the second delay appears on passage to a region with lower refractoriness, i.e. point M in Fig. 2*f*. The minimum perimeter of the reverberator with two delays is $l_2 = (1 - 2\vartheta)R_b v$. It will be seen that this dimension closely depends on the duration ϑ of the excited state and for ϑ close to $\frac{1}{2} R_b$ may be considerably less than the wavelength of refractoriness $\lambda = Rv$.

10. COMPARISON WITH THE HEART

We would note the facts concerning fibrillation which are interpreted within the framework of the model considered. Fibrillation may be removed by a powerful electrical discharge: the current must be sufficient to excite simultaneously the whole surface of the heart including the refractory zones. The appearance of fibrillation is facilitated by many influences increasing the inhomogeneity of the heart in relation to refractoriness. It has been possible to demonstrate the existence of a "critical mass" of the strip of the atrium [12] on which it is still possible to elicit fibrillation. Apparently, there also occurs the phenomenon described at the end of section 8. In the dog, fibrillation of the atrium caused by local application of aconitine is interrupted if the aconitinic focus is isolated [13]. If the vagus is stimulated (with reduction in refractoriness and increase in the inhomogeneity of the heart) then the insulation of the aconitinic focus does not influence fibrillation [10].

One of the weak points of the various theories of fibrillation associated with "circular rhythm" is the difficulty of explaining the small dimensions of the strip of tissue in which fibrillation is possible—approximately λ. It has been noted that this is too small to accommodate a sufficient number of circular pathways. In addition, as shown by cinefilm [13] on fibrillation of the atrium of a dog, the size of the independently contracting segments does not exceed 0·8 mm and for the dog $\lambda \approx 3$ cm [3] and for the rabbit $\lambda \approx 5$ cm [12]. It would be interesting to establish whether in the heart reverberators can exist with a length less than λ through delays in conduction similar to those presented in section 9. For this purpose it is necessary to evaluate the equivalent value ϑ for different tissues of the heart. It is known that the response to a stimulator pulse appears with a latent period which in the dog may reach several tens of milliseconds. The value of the latent period on interaction of the action potential and refractory tissue is of interest.

SUMMARY

We have considered the propagation of excitation in a plane medium inhomogeneous in refractoriness. It has been shown that a state of activity resembling fibrillation is possible. This state appears if the medium is supplied with several pulses following at high frequencies. Closed pathways of conduction are formed—reverberators, which for the medium are foci of automatic activity. Reverberators operating at different frequencies are not synchronized. The high frequency of impulsation appearing on their interaction in a medium may lead to the appearance of new reverberators.

Each reverberator lives only a finite time—longer the more homogeneous the adjacent areas of the medium. In a medium of sufficient dimensions "dying" of some reverberators and the appearance of others constantly occurs.

If excitation is not instantaneous, then the perimeter of the reverberator may be less than the Wiener wavelength—product of the refractoriness and the velocity. The requirements fall for the dimensions of the medium in which "fibrillation" is possible.

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