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Properties of a Mass of Cells Capable of Regenerating Pulses

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PROPERTIES OF A MASS OF CELLS CAPABLE OF REGENERATING PULSES

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CONTENTS

Cells having some properties similar to those of neurons are considered. A mass of such cells, randomly placed together with a uniform volume density, appears capable of supporting various simple forms of activity, including plane waves, spherical and circular waves and vortex effects. The propagation of a plane wave of activity has been considered in some detail.

It is shown that a wave may be initiated in a mass of such cells by a number of individual stimuli. The mass has a very sensitive threshold to such stimulation. This threshold depends on cell properties, and by altering the threshold a mass of cells may be made to act as an on/off switch. The switching of waves may be compared with the shifting of attention in a living organism.

Particularly interesting phenomena emerge if some property of the individual cells, e.g. size, extent of axon or dendrite structure, or threshold, changes with repeated use. The mass of cells may then exhibit an ability to modify its response according to past experience in a manner similar to that of living organisms. Trial and error learning, conditioned responses, and the ability to regenerate internally a sequence of past events may be demonstrated with very little complication of the form of the mass of cells.

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Introduction

A marked feature of certain parts of the cortex is the apparently very large random factor in the distribution of neurons and in the way in which their dendrite and axon fibres spread amongst each other. Do some important properties or forms of behaviour of cortical material arise from this? It is difficult to answer the question unless we first know what forms of activity can exist in a random mass of neurons.

This paper takes the preliminary step in § 2 of examining some forms of activity which may exist in a mass of cells having properties similar to the known properties of neurons. A résumé is given of the nature of propagation of plane waves. The problem has been very much formalized to make a semi-mathematical treatment possible, and it may be found that the structure of the mass of cells considered does not bear a very close relationship to any actual physiological structure. It is hoped, however, that the properties which such a structure appears to have, will be of sufficient interest for the formalized structure to be compared with actual neurological structure.

Variations in cell properties and their effect upon the propagation are considered in § 3. Finally, § 4 is concerned with the interaction between waves and the response of a mass of cells as an integral part of a more complex mechanism.

It will be shown that a mechanism with the minimum of specific organization can, on account of the presence of the mass of cells, exhibit behaviour surprisingly similar to certain behaviour of living organisms.

List of symbols

x, y, z	Cartesian coordinates.
$\xi(x)$	The mean number of connexions, from all the cells in an infinite plane of unit thickness to a single cell at a distance x.
x_1	A specific value of x.
c, a_0	Numerical, and length constants appearing in an empirical formula for the number of fibres intersecting a unit area at a distance a from the perikaryon of a neuron, viz. $c(a_0/a)\,\mathrm{e}^{-a/a_0}$.
a	Radial distance measured from the perikaryon.
b	A constant appearing in the value of $\xi(x)$ estimated from empirical data; b depends on the density of axon and dendrite structures, and on the exact conditions governing the formation of a synapse.
t	Time.
$\chi(t)$	The proportion of the excitation produced by a given primary cell which remains at a time t after it becomes active.
τ	The operating time of a cell—cf. synaptic delay time.
s	Time over which excitation is integrated by cells.
r	Recovery period.
t_1	A specific value of t.
q	Threshold number of integrated excitation impulses.
ρ	Volume density of randomly distributed cells.
$R\rho$	Volume density of sensitive cells.

$(1-R)\rho$	Volume density of used cells.
$F(x, y, z, t), F$	Activity, proportion of cells becoming active per unit time.
$\bar{N}(x, t), \bar{N}$	Mean integrated excitation.
Φ	A function of x and t which gives the probability of a sensitive cell being excited above the threshold level in unit time.
M	Proportion of cells used during passage of a wave.
M_0	The critical value of M.
M_s	Saturation value of M.
β	Propagation constant.
v	Wave velocity.
D	Surface density of active cells.
D_0	The value of D corresponding to the critical amplitude M_0.
G, H, J, T	Designation of various boundaries within a composite mass of cells.
E, E input, F_e	See § 3 *b*.
I, I input, F_i P, Q	See § 3 *c*.
$q_s q_0 \epsilon$ N_1, N_2, W_1, W_2	See § 3 *e*.
A, B, L W_A, W_A', W_B, W_B'	See § 4 *b*.
$R, W_{\text{ext.}}, W_{\text{int.}}$	See § 4 *c*.

1. The cells

1 *a*. *Cells and neurons*

The tree-like dendrite and axon structure of certain neurons has been examined under the microscope by various workers, and some statistical data are available relating to the density of dendritic fibres as a function of distance from the neuron centre (Sholl 1953). A recent paper (Sholl 1955) has also given some statistical information about the distribution, at different cortical levels, of neurons with various forms of axon structure.

The factors causing the formation of a synapse are uncertain. It has been suggested that either the frequency with which impulses pass through the respective neurons, or the occurrence of simultaneous impulses in dendrite and axon might tend to aid the formation of a synapse or affect its conducting properties, but there is little empirical evidence on this point. Nor is it known how the formation of a synapse is affected by the distance apart of a dendrite and axon, though it seems likely that proximity would aid the formation of a synapse. For these reasons a distinction is made between the cells considered below, which will be given precise properties for the purpose of calculation, and actual neurons, many aspects of the behaviour of which are uncertain. The cells are assumed to be randomly distributed with a volume density ρ. They comprise a density $R\rho$ of 'sensitive cells' which have the ability to become active under conditions specified below, and a density $(1-R)\rho$ of 'used cells' which are those which have recently been active. The ratio R is thus a function of position and time. An expression $\xi(x)$ is used to represent the richness of connexions between cells. It is defined as the mean number of connexions from all the cells in an infinite plane of unit thickness to a single cell at a distance x. These connexions are assumed

to have been made by a purely chance process in which the only bias is that represented by $\xi(x)$. A value of $\xi(x)$ estimated from the empirical data about neurons which are available is used for comparative purposes. The term 'connexion' has been used deliberately in place of the word synapse. This is to avoid confusion between the cells and actual neurons. It will, however, be assumed that the probability of connexion between cells, given by $\xi(x)$, decreases with distance in the same manner that the density of connective tissue decreases in actual neurons.

1 *b*. *Cell properties assumed*

Excitation and time decrement

When a sensitive cell (primary cell) becomes active it excites any other sensitive cell (secondary cell) to which it is connected. The initial quantity of excitation received by the secondary cell is proportional to the number of connexions to it from the active primary cell. There is thus an integration of excitation in the cells similar to the summation of post synaptic potential (P.S.P.) in a neuron. In a neuron the time decay or decrement in the summation of P.S.P. is of approximately exponential form, and the effective period over which integration takes place is determined by the exponential time constant. For the purpose of discussion the time decrement on the excitation of the cells will be represented by $\chi(t)$. $\chi(t)$ is the proportion of the excitation produced by a given primary cell which remains at a time, t, after the primary cell becomes active. It will, for simplicity, be taken to be a rectangular function of duration s, i.e. excitation remains effective for a period s after it arrives at a cell. If a secondary cell receives excitation from a number of primary active cells the total excitation is the sum of the increments of excitation received from the individual primary cells, each increment being subject to a corresponding time decrement. It is generally thought that one neuron can only excite another via an axon through a synapse to a dendrite and not in the opposite sense. In the same way it will be assumed here that all individual connexions are 'one way' connexions.

Recovery time

Immediately after activity a cell takes no further part and will be described as a 'used' cell. It is then insensitive and excitation arriving from other cells is assumed to have no effect. Neurons have the property of recovering their sensitivity after a certain time. Cells will also be assumed to have the property of recovering sensitivity after a period r.

Threshold

Each cell is assumed to have an excitation threshold q, and it will be convenient to measure threshold as well as excitation in terms of a unit equal to the initial excitation produced at one secondary cell via one connexion from an active cell. This will be given the name one 'equivalent impulse' or one 'impulse'. If the excitation of a cell rises above threshold the cell becomes active, if it has not recently done so, and in turn excites other cells to which it is connected. The existence of a threshold is another property of actual neurons about which little exact information is available. There is some evidence (Eccles 1953) that the threshold of a neuron is of the order of 10, and while it is known that q varies, and is very high for a period after the neuron has been active, precise data are lacking.

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Operating time

A neuron has a latent period, or operating time, known as the synaptic delay. The cells are taken to have a constant operating time, τ, independent of the excitation. This is the time which elapses between the excitation reaching the threshold level and the cell becoming active. The period τ is also taken as the unit of time in calculations. A given cell is only capable of exciting other cells connected to it at the instant it becomes active, or to put it another way, it has been found convenient to incorporate the length of the period of activity in the form of $\chi(t)$.

1*c*. *Neuron properties for comparison*

Here and there it has been of interest for comparison to insert numerical data corresponding roughly to actual neurons.

The following values have been used:

Synaptic delay time $\tau = \frac{1}{2}$ ms.

Integrating time constant $s = 4$ ms (corresponding to time decrement).

Recovery period, $r = 10$ ms to 100 ms.

It has been difficult to arrive at suitable numerical data for $\xi(x)$ because of the lack of information on the necessary conditions for the formation of a synapse. To obtain any values at all it has been necessary to make several assumptions, i.e.

(1) The axon and dendrite structure is predetermined statistically and entirely by factors within the cell, i.e. there is no tendency for axons and dendrites to grow towards each other.

(2) A synapse is formed automatically between the axon of one neuron and the dendrite of another if the two fibres happen to lie within a given distance (say 1μ) of each other.

(3) The density of the dendrite fibre structure is taken to have the form $c(a_0/a)\,\mathrm{e}^{-a/a_0}$, where a is the distance from the perikaryon, c and a_0 being constants. The expression is derived from results published by Sholl (1953).

(4) The axon structure is relatively compact.

If these assumptions are justified then, using the method described by Uttley (1955), it may be shown that $\xi(x)$ has the form $b\,\mathrm{e}^{-|x|/a_0}$, where b is a constant the magnitude of which depends on the density of the axon and dendrite structures and on the exact conditions (see (2) above) governing the formation of a synapse between neighbouring axons and dendrites. If the axon structure is not compact but is similar to the dendrite structure, the form of $\xi(x)$ is modified slightly, and the number of connexions falls off slightly less rapidly with distance.

In this expression the value of b is rather uncertain, for even if the above assumptions are justified the exact separation of axon and dendrite at which a synapse will form is not known. The constant b is also proportional to the total length of axon fibre which varies considerably between different types of neuron. If the critical separation were equal to 1μ for example, b might vary from 0·6 in units of $1/1\mu$ for average neurons to 4·2 in the same units for neurons with particularly long axons. The constant a_0 derived from Sholl's data is about 50μ.

It may be noted that although a volume density of cells has been mentioned above, the following calculations would apply equally well to a plane density of cells provided a suitably modified form of $\xi(x)$ was employed.

2. Activity in a mass of cells

When we come to consider the activity which may occur in a large mass of cells of the type that has been described, we have a state of affairs that at first appears very complex. Each cell when it becomes active may excite many of its neighbours, and not only immediate neighbours but also some which are separated by a considerable length of connecting fibre. Each cell will be different from any other in the way in which it scatters excitation to other cells. The only common factor is the probability of connexion between any cell and others at a given distance from it which, for convenience in later calculation, has been given in the form of $\xi(x)$. The situation appears to be further complicated by the fact that the excitation arriving from one cell is only effective if the excitation from other cells arrives within a short interval s, before or after, so as to cause the integrated excitation at a sensitive receptor cell to exceed the threshold. The spread of activity is thus essentially of a co-operative nature.

In spite of the apparent complexity which has just been stressed, it is possible by treating the activity statistically to simplify the examination of certain forms of activity. Thus, we shall consider not the activity of any individual cell, but only the proportion of cells becoming active in any region per unit time. This will be denoted $F(x, y, z, t)$, since it is a function of position and time, and will be abbreviated to 'activity' or 'F'. In all the following calculations we shall be considering only the variation of this statistical 'activity' in the x direction, F being invariant in any given y, z plane. This being so, $F(x, y, z, t)$ may be written $F(x, t)$.

$F(x, t)\,\xi(x-X)\,\mathrm{d}X$ will thus be the mean rate of arrival of impulses at single secondary cells in the plane x from cells becoming active at a mean rate F within a plane of thickness $\mathrm{d}X$ at X.

The convolution

$$\int_{-\infty}^{\infty} F(X, t)\,\xi(x-X)\,\mathrm{d}X$$

therefore gives, in terms of x and t, the mean rate of arrival of impulses at cells in the plane x from all other cells.

The convolution

$$\bar{N}(x, t) = \int_{-\infty}^{0}\int_{-\infty}^{\infty} F(X, T)\,\xi(x-X)\,\chi(t-T)\,\mathrm{d}X\,\mathrm{d}T$$

similarly gives the mean value of integrated excitation, $\bar{N}$, for cells in the plane x.

These are the two basic expressions on which the analysis of specific forms of activity will be based. From the mean integrated excitation, $\bar{N}$, given by the second expression, and from a knowledge of the proportion R of cells which are sensitive, we can calculate the proportion of cells which have an integrated excitation of $(q-1)$ and are also sensitive. These are the cells which are ready to be triggered into activity by the arrival of one further impulse. How many of these cells do, in fact, receive this additional impulse during a short period δt will depend on the mean rate of arrival of impulses, given by the first expression above.

Thus we may calculate the proportion of cells which may be expected to become active after an interval equal to the operating time τ. This is the new value of the activity F.

Two specific forms of activity will be analyzed, continuous random activity and the propagation of plane waves of activity.

2*a*. *Continuous random activity*

What would happen if initially, throughout a volume of cells, the activity F was constant and independent of x, and what are the necessary conditions for this activity to be self-maintaining? These questions are here discussed qualitatively, but the same arguments are followed analytically in the Appendix.

As the activity is assumed to be constant throughout, the expressions for mean rate of arrival of impulses and mean integrated excitation are much simplified, as they are independent of x. We are left with a simple, though non-linear, relationship between the activity $F(t)$ at any instant, and the consequent activity $F(t+\tau)$ after an interval τ. Owing to the non-linearity of the relationship (see Appendix, § (*a*)) there is only one value of $F(t)$ for which $F(t+\tau) = F(t)$. If the activity is lower than this critical value, $F(t+\tau)$ will be even lower, and F will go on decreasing during successive intervals of τ until all activity finally ceases. If $F(t)$ is above the critical value, $F(t+\tau)$ will be higher than $F(t)$ and so on, the activity increasing rapidly until it 'burns itself out' by using up all the sensitive cells before any have a chance to recover.

For equilibrium, two conditions must be fulfilled. The first is that the value of F must be equal to the critical value. The second is that there must be a balance between the cells which are excited to activity per unit time, and the cells which are recovering their sensitivity after previous activity. Only for certain values of the parameters $\xi(x)$, q, etc., which represent the primary cell properties, can these two conditions be fulfilled. In particular, the higher the value of q, the greater is the degree of connectivity required to make equilibrium possible. Unfortunately, the empirical data at present available are too inexact for it to be possible to say whether an equilibrium condition of continuous random activity can or cannot exist. One can, however, be certain that there could at most be an unstable equilibrium, because any small local statistical variation in, say, connectivity would initiate a rapid rise or fall of F, away from the equilibrium level of activity. Thus, even if one starts with uniform activity, one may soon find that the activity has died away in some places and has flared up in others. It is for this reason that activity with some form of spatial and temporal organization will always be favoured if q is above unity. Such activity, though it may 'burn itself out' by using too many of the sensitive cells in one region, can then move on to another region where sufficient sensitive cells remain, perhaps to return when the used cells recover. Plane waves are an example of activity with spatial and temporal organization and, as they are of considerable interest, the rest of this section will be devoted to discussing their propagation through a mass of cells.

2*b*. *Plane waves of activity*

The propagation of plane waves through a medium of the type we are considering is different from the propagation of more familiar types of wave, for example, electromagnetic or acoustic waves, through linear media. The properties of the mass of cells are changed

temporarily by the passage of activity, inasmuch as some of the cells are changed from the 'sensitive' state to the 'used' state so that the effective cell density is reduced. The result is that instead of a continuous wave motion we get a transient peak of activity travelling through the medium, followed by a relatively quiescent period. The mechanism of the propagation of such a wave will now be examined in more detail. The discussion will be qualitative but is paralleled by an algebraical analysis in §§ (*b*) and (*c*) of the Appendix.

Activity and density of sensitive cells

Suppose we have a homogeneous mass of cells in which there has been no recent activity. All the cells will be in the sensitive state, and if we plot the density of sensitive cells against distance, x, we shall have a straight line parallel to the axis (curve i, figure 1 *a*). Suppose now

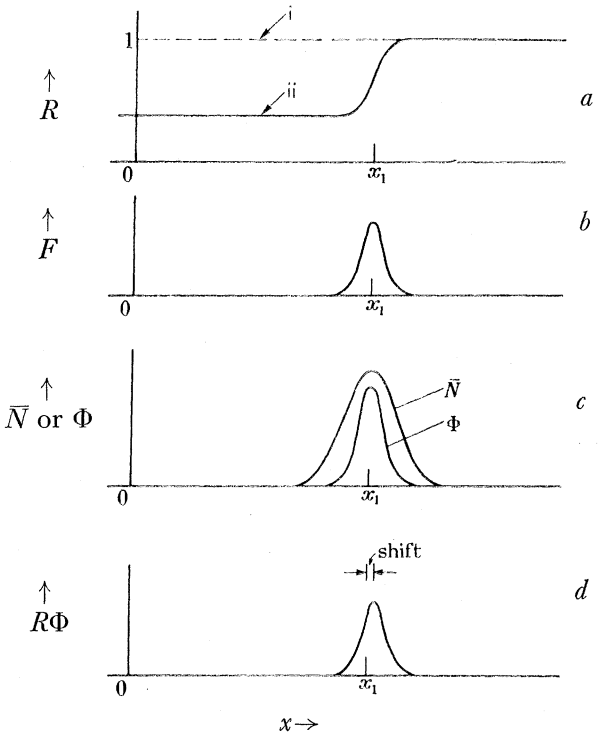

FIGURE 1. Spatial distribution of various parameters associated with a travelling wave of activity. R, proportion of sensitive cells remaining when peak of wave has reached x_1; F, activity; $\bar{N}$, mean integrated excitation; Φ, proportion of sensitive cells which attains threshold per unit time; $R\Phi$, new distribution of activity after a time τ.

that a wave of activity of constant amplitude, such as that shown in figure 1 *b*, is travelling from left to right in the x direction. This travelling wave will have converted some of the sensitive cells, in the region through which it has passed, to the used state. Thus both parameters, F and R, are now variables. When the peak of activity has reached the point designated x_1 in figure 1 *b*, the distribution of sensitive cells as a function of x will be of the form shown in curve ii of figure 1 *a*. There will thus be less sensitive cells in the region through which the wave has passed than in the region through which it has yet to pass. This asymmetry means that the region in front is better able to support further activity, and this, as we shall see, is why the wave continues to propagate in a forward direction.

Activity and excitation

The wave of activity consists of the activation of a large number of individual cells, each of which scatters excitation among its neighbours through the randomly distributed connective structure. Cells in the neighbourhood of the peak of activity will be excited to various levels, the mean level of excitation being highest at the peak. A plot of the mean level of excitation (see curve of $\bar{N}$ figure 1*c*) will be rather broader than the curve representing the distribution of activity, the actual breadth and shape depending on the exact form of $\xi(x)$. Some of these neighbouring cells, especially those near the peak of activity where the mean level of excitation is high, will be excited above the threshold level of excitation q. A plot of the probability of this happening, as a function of x (Φ in figure 1*c*) will thus be narrower than the plot of $\bar{N}$. Only cells which are in the sensitive state will be triggered into activity when their excitation exceeds the threshold. To find the rate at which cells are about to become active at any point we must therefore multiply the distribution Φ of figure 1*c* by the distribution of sensitive cells (R, curve ii in figure 1*a*). The product is yet another peaked curve, but is shifted forward along the x axis by a small distance (figure 1*d*). Thus, although excitation spreads out in all directions from the peak of activity, a greater number of new cells is excited to activity ahead of the peak than in the region through which it has just passed. This is the mechanism by which the advance of the wave is maintained.

2*c*. *Waveforms—dependence on* $\xi(x)$

Little mention has been made so far of the dependence of the waveform on $\xi(x)$ and other cell parameters. If we take a form of $\xi(x)$ based on empirical data at present available, the waveforms are those illustrated in figure 1. The corresponding analytical expressions, if the amplitude of the wave is small (see Appendix, § (*c*)), are:

$$R = 1-\tfrac{1}{2}M-\tfrac{1}{2}M\tanh\beta\{t-(x/v)\},$$

$$F = \frac{M\beta}{2\cosh^2\beta\{t-(x/v)\}},$$

where M is the proportion of cells used during the passage of the wave, for convenience called the 'amplitude' of the wave. The parameter β, which one might call a propagation constant, and the velocity v are, as one might expect, principally dependent on $\xi(x)$ and on the integration time s and the threshold q. The wave shape also depends primarily on the form of $\xi(x)$ (see Appendix, § (*c*)).

If the amplitude of the wave is large, so that the mean integrated excitation $\bar{N}$ at the peak of activity is high, the waveform is modified slightly. These modifications are shown in figure 2.

2*d*. *Attenuation and gain in amplitude*

Owing to the non-linear nature of the threshold effect, there is a critical amplitude of wave which produces just enough excitation to maintain the level of activity in the wave constant. This critical amplitude will be called M_0. If the initial amplitude M of the wave is less than M_0, then the wave will either be attenuated (figure 3, curves *a* and *b*) or will increase in amplitude until it 'saturates', when it uses all the cells in the medium through which it passes, and the amplitude cannot increase further (figure 3, curves *c*, *d* and *e*).

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Saturated and unsaturated waves

As the wave approaches the saturated form it becomes much broader with a slight asymmetrical change in form. There is also a considerable increase in velocity. The saturated waveform is shown in figure 2, for comparison with the other waveforms.

It is important to note that two unsaturated waves may have the same values of M, β and v and yet may not be identical. This is because they may activate different cells as they pass, or may activate the same cells in a different order. If M is small there are a very large number of constitutionally different waves described by the same statistical formula

$$\frac{M\beta}{2\cosh^2\beta\{t-(x/v)\}}.$$

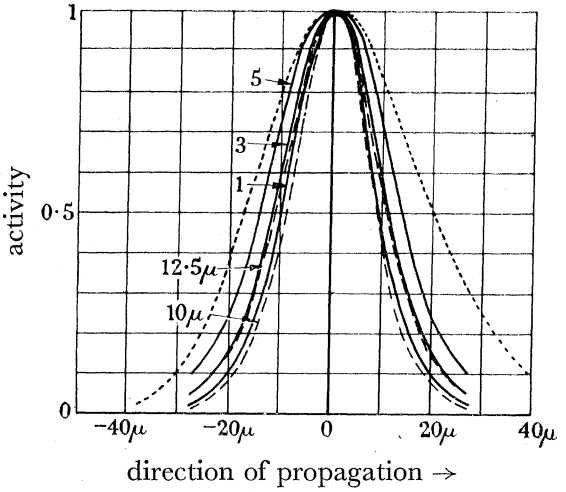

FIGURE 2

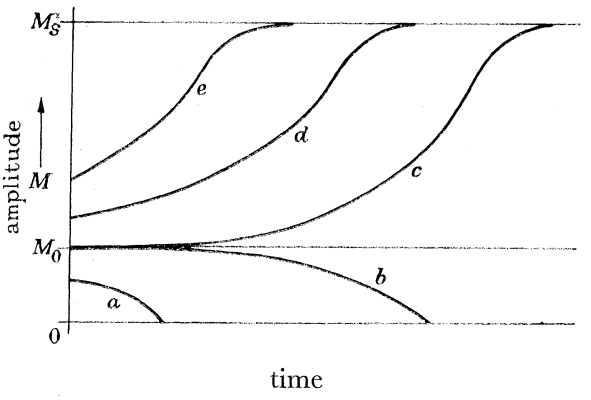

FIGURE 3

FIGURE 2. Waveforms. The full-line curves give waveforms for maximum values of $\bar{N}=5$, 3 and 1. The dotted line gives the saturated waveform. The broken curves give $\cosh^{-2}\frac{\beta}{v}x$ for $\frac{v}{\beta}=10\mu$ and $\beta=12{\cdot}5\mu$. The peaks of all curves have been adjusted to coincide in height on an arbitrary ordinate scale.

FIGURE 3. Dependence of attenuation and gain on amplitude. M_0, critical amplitude; M_s, saturation value = unity.

Unsaturated waves, for which M is less than unity, inherently carry with them more information, in terms of the identity of the individual cells activated, than can saturated waves which activate all cells. They will be of primary interest later in this paper.

2e. *Other forms of activity allied to plane waves*

The above calculations only apply to plane waves of infinite extent in an infinite volume of cells, but similar calculations may be made with regard to the propagation of linear waves in a thin sheet of cells or neurons, provided a suitably modified form of the parameter $\xi(x)$ is used. In practice the calculations may also be applied to any wave which approximates to a plane wave over an area large compared with a_0^2, or which approximates to a linear wave over a range of distance large compared with a_0. Thus the calculations will apply to spherical or circular waves of radius of curvature large compared with a_0, since these waves approximate to plane or linear waves over a limited region.

The same considerations regarding critical amplitude, attenuation or gain, and saturated waves will apply to such waves, but the calculations will not apply strictly at small radii where the distribution of activity will be modified due to the curvature of the wave. The effect of the curvature in a converging wave will be similar to the effect of an increase in amplitude of the wave or an increase in the density of connexions, while in a diverging wave the effect will be reversed. The focus of converging unsaturated spherical or circular waves can in this way become a source of further waves.

Effect of recovery of cells

One property of neurons which has not been considered fully yet is the recovery of sensitivity after a period of time. One reason for avoiding discussion of this point is that neurons appear to regain their sensitivity gradually after activity, and different sources of information give considerably different rates of recovery. However, whatever form the recovery of sensitivity follows, it is evident that it will facilitate the propagation of subsequent waves in a region through which one wave has already passed. In fact, fully saturated waves may follow each other at intervals equal to the period taken by the cells to recover sensitivity completely, and unsaturated waves may follow even closer. This makes it possible for a wave to pass through a region, and return again to the same region some time later when the majority of the cells have recovered. This would allow a relatively local circulation of activity which might be of some importance.

2*f*. *Discussion*

Various physiological investigators have stressed the difficulty of deciding what forms of co-operative activity might exist within the cortex and what the function of such activity might be. It has been commented that there are an almost unlimited number of neuron chains interlinked and superimposed and that activity may pass round all these chains simultaneously, each affecting its neighbours in the process. This leaves one with the impression of a mass of cells the behaviour of which would be almost impossibly complex for analysis. McCulloch & Pitts (1943) consider some forms of activity within circular paths. The subject is treated rather abstractly from the point of view of logical analogy and the circuits themselves are not considered in detail. Other workers (Rapoport 1950, 1951; Shimbel 1950, 1951) have tended to the opposite extreme and have considered only the activity of small sets of two or three, or groups (ganglia) of neurons without considering the effect of their spatial distribution. Their conclusions are therefore not directly applicable to large masses of cells. The aim of this part of the present paper has been to show that large masses of randomly distributed neurons may support certain relatively simple, well-defined forms of activity, in particular plane waves and certain allied types of activity such as spherical or cylindrical waves (in a volume of material), circular waves (in a two-dimensional sheet of neurons), and circulatory effects (the exact form of which depends on the shape of the mass of cells and on their initial state).

Other forms of activity may also exist, but unless the cell threshold is low, the activity must have some form of organization. In any case, activity with some form of organization will be favoured if the threshold is above unity. It is, in fact, the existence of a threshold above unity which is primarily responsible for the forms of activity enumerated above,

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all of which are essentially of a co-operative nature. The non-linear nature of wave propagation consequent on a threshold exceeding unity is an important factor in the behaviour which will be discussed in §§ 3 and 4.

3. Some elementary properties of a mass of cells

In the following paragraphs a number of simple effects are considered: the launching of a wave and the representation by it of the launching stimulus, the switching function of a mass of cells, the stabilization of the amplitude of a wave, etc. Without the possession of properties additional to those outlined in § 1, the cells in the mass would have no ability to store information permanently nor could the mass modify its response on a long-term basis according to past history.

It will be shown in § 3*e* that a mass of cells would have the ability to modify its response if some cell property changed with repeated use. This prepares the way for consideration in § 4 of the response of a mass of cells as an integral part of a more complex mechanism in which it exhibits such behaviour as learning, conditioned response reactions, etc. The mass may thus be shown to produce, in a suitable environment, some forms of behaviour regarded as characteristic of living organisms.

3*a*. *The reaction to activation of a number of individual cells on one surface of the mass*

It will be convenient to consider first the initiation of a wave at a hypothetical boundary where the cell density decreases gradually from one side to the other according to the law $\rho' = \rho\left(1 - \tfrac{1}{2}M_0 - \tfrac{1}{2}M_0 \tanh \frac{\beta}{v}x\right)$ as shown in figure 4 *a* and *b*. This corresponds to the distribution of sensitive cells when a wave is travelling through a continuous mass. Suppose we now stimulate the mass by activating, over a period s, a proportion of cells having a distribution about the boundary given by the expression

$$Fs = \frac{M_0 \beta s}{2\cosh^2 \beta\{t - (x/v)\}} \quad \text{(see figure 4}c\text{)}.$$

We now have a state of affairs exactly corresponding to a wave travelling through a continuous mass and, as we have already seen, it will continue to propagate with a velocity, v, in the x direction.

The critical stimulus which it is necessary to apply in the region of the boundary plane may be expressed as a surface density D_0, in which case

$$D_0 = \rho \int_{-\infty}^{\infty} Fs \, \mathrm{d}x$$
$$= M_0 \rho s v,$$

and since

$$\frac{\beta}{v} = \frac{q}{2a_0}$$
$$D_0 = M_0 \beta \rho \frac{2a_0 s}{q}.$$

If a stimulation less than this is applied, the wave produced will have a value of M less than M_0 and will attenuate. A stimulation greater than D_0 will produce a wave with M greater than M_0 which will rapidly increase in amplitude.

If there is no boundary and the medium is continuous on both sides of the plane $x = 0$, then waves will travel in both directions. These waves will initially reinforce each other, so a rather smaller value of D_0 will be required to initiate waves with $M = M_0$, i.e.

$$D_0 = \text{const.}\, M_0 \beta \rho \frac{2a_0 s}{q}, \quad \text{where} \quad \text{const.} < 1.$$

If instead of a diffuse boundary there is an abrupt boundary with no cells at all available to the left of the plane $x = 0$, then the wave which is launched will lack reinforcement by the activity of these cells but will have extra support from the additional cells to the right so that we may write

$$D_0 = \text{const.}\, M_0 \beta \rho \frac{2a_0 s}{q}, \quad \text{where} \quad \text{const.} \approx 1.$$

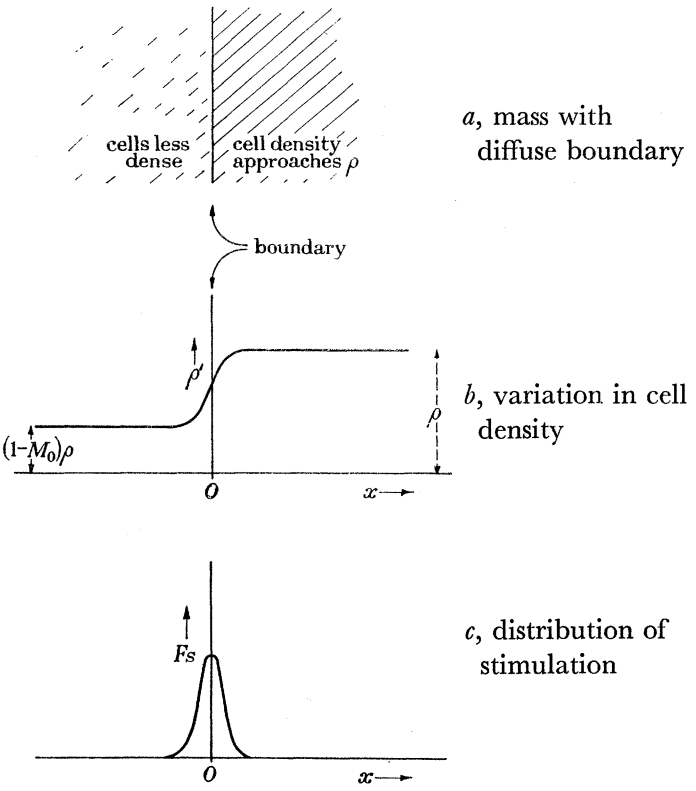

FIGURE 4. Distribution of cell density and stimulation at diffuse boundary. For explanation see text.

Minimum stimulus and switch effect

Whatever the form of the boundary there is a density of stimulation, D_0, which will initiate a wave or waves with the critical value of M which has been called M_0. A stimulation less than D_0 applied to the mass will produce an effect which will die out quickly, but a stimulation greater than D_0 will produce a wave which will quickly rise to saturation.

If we call the plane of stimulation G (figure 5) and consider the activity in a parallel plane H sufficiently far away, we shall find a saturated wave at H for inputs greater than D_0 and zero activity at H for an input less than D_0. Thus a mass of cells acts as an amplitude-sensitive switch with a very sensitive threshold D_0.

Dependence of constitution on spatial and temporal pattern of stimulus

It should be noted that though waves arriving at plane H may all have a similar general form the constitution of each wave will depend on the identity of the individual cells originally activated in plane G. Moreover, if cells are activated not only in plane G but at various points between G and H, the constitution of the resultant wave will depend on the sequence in which these cells are activated as well as on the identity of the cells. The constitution of the wave thus represents the stimulus which initiated it.

Limited area of stimulation

If adequate stimulation ($D \gg D_0$) is applied only over a limited part of the plane G, then a plane wave over the limited area will result. There will be more or less fringing at the edges depending on the actual value of D (figure 5*a*).

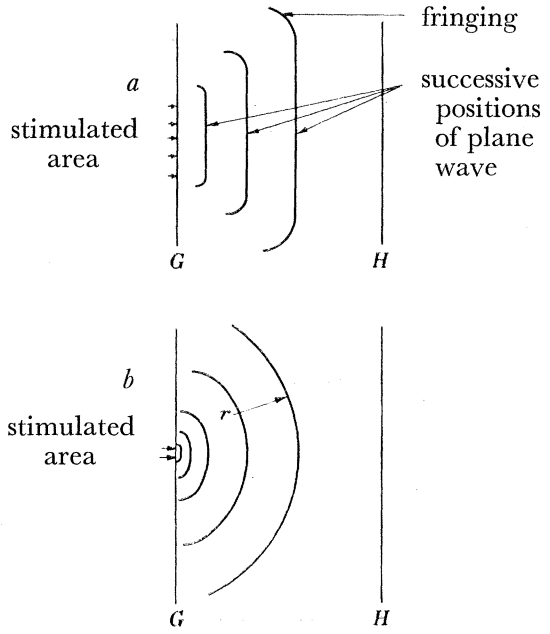

FIGURE 5. Waves arising from a limited area of stimulation.

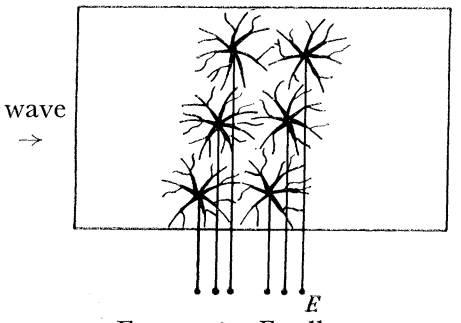

FIGURE 6. *E* cells.

Waves may arise from quite a small area of stimulation. The fringing effects will then be more important and a relatively high value of D will be required to initiate the wave. The result will be a spherical rather than a plane wave (figure 5*b*). It is possible that this form of wave is of more practical importance than the true plane wave. The propagation will be very similar when the radius of curvature is well above a_0 because any small section of the spherical wave will behave like a plane wave.

3*b*. *The effect of slight alterations of threshold either of cells in general or of particular groups of cells*

Consider first a wave having the critical value of M. In general, this will continue to propagate with constant amplitude, although in the end statistical fluctuations may increase its M above or decrease its M below the critical value of M. When this happens the amplitude of the wave will either continue to increase until it reaches saturation or decrease until it ceases to exist.

If, however, the value of threshold, q, is raised even slightly, then the value of M_0 is also raised and the wave having a value of M corresponding to the original M_0 will now attenuate rapidly. If q is reduced to slightly below its original value, then a similar wave will gain rapidly in amplitude until it saturates. Thus if a wave with M equal to M_0 is launched into a mass of cells it may be made to attenuate or gain in amplitude by slightly altering q. For example, alteration of q from 10 to 10·1 or 9·9 would cause a wave to saturate or to disappear within a period of about 10τ.

Sub-threshold excitation

One way of altering the effective value of q without altering the inherent threshold of cells is to supply them with a small amount of excitation from some external source immediately before or during the passage of a wave. Suppose one has, external to the mass, a group of cells whose axons penetrate the mass and ramify randomly within it (E in figure 6).

If these E cells are activated periodically then the cells within the mass will regularly receive excitation from the axons of the E cells. The mean excitation received per cell in this way may be calculated from $\xi(x)$. If F_e is the mean rate of activation of external cells expressed as a proportion of the total number of cells within the region of the mass into which their axons penetrate then the mean rate of excitation will be

$$\bar{N} \text{ per unit time} = F_e \int_{-\infty}^{\infty} \xi(x)\, \mathrm{d}x$$
$$= F_e b a_0,$$

and, if the integrating time constant is s, the mean integrated excitation will be

$$\bar{N} = F_e s b a_0.$$

Now if $\bar{N}$ is small compared with q, say not more than 1, the proportion of cells stimulated above threshold during a period s will be very small (approx. 10^{-7} if $\bar{N}$ is 1). The excitation from these external cells will thus not itself initiate a wave, i.e. it will be 'sub-threshold' stimulation. Nor will it 'use up' sufficient cells in the mass to affect propagation appreciably. It will, however, decrease the effective mean value of q throughout the block from q to $(q-\bar{N})$ which will very radically affect the propagation of any wave across the block.

The external cells postulated above thus give a very sensitive control of the propagation of a wave through the block. They form, in fact, a means whereby a wave entering the block with the critical value of M_0 can be switched on or off by external means. For convenience of reference the external cells will be labelled E in any diagram below and their axons will be called the E input to the block.

Organization

It may be noted that the introduction of the E cells and their axons is the first form of organization which has been postulated in the arrangement of cells in the mass. All the other cells have been taken as randomly distributed and their axon and dendrite structures have been assumed to be independent of their position. The structure of the E cells can be described by fairly simple statistical laws, but these are evidently different from those assumed heretofore for cells within the mass. The same applies to a set of cells with specialized dendrites which will be considered in § 3*c*.

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3c. *The effect of small variations in cell density*

The value of M_0, the critical value of M for a block of cells, depends on the cell density ρ, as well as on the value of q. If ρ is increased then M_0 decreases and vice versa. Thus if there is some means of removing, or 'using up' a small proportion of the cells in the medium before the passage of a wave the propagation of the wave may be affected in the same way as if q had been increased.

Sub-threshold activation

Suppose one has external access to a group of dendrites connected to a proportion of the cells scattered randomly in the mass (I in figure 7). By means of the dendrites these I cells may be excited strongly so as to render them active, after which they will be 'used' cells and will remain in the latter condition taking no further part until the end of the recovery period r. It is essential that the I cells should be excited to activity. If they were merely given a weak excitation an effect similar to that of the E input would be produced.

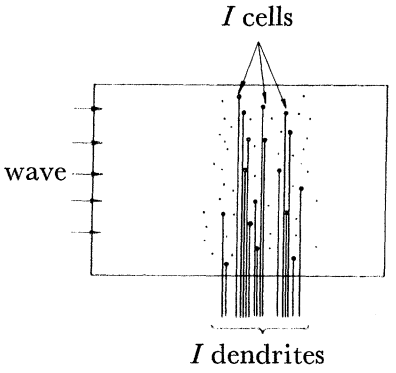

FIGURE 7. I cells.

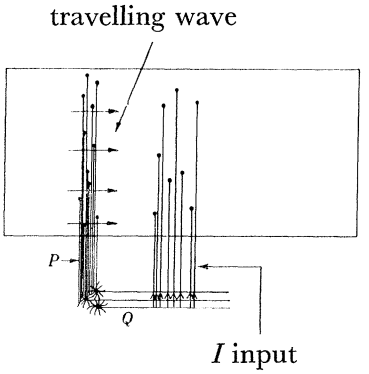

FIGURE 8. Basis of possible servo-mechanism to stabilize M.

The effective reduction in ρ can be calculated as follows.

Let F_i be the rate at which cells are rendered active by means of external dendrites, expressed as a proportion of the total number of cells within the region of the mass concerned.

Then $F_i r$ will be the mean proportion of cells in the 'used but not yet recovered' condition.

Thus $(1-F_i r)$ will be the effective cell density encountered by a wave propagating through the medium.

In calculating the change in M_0, account must be taken of the mean decrease in effective q caused in other cells by excitation received from the I cells rendered active by means of the I dendrites. This will be $F_i s b a_0$ (see § 3 *b*). Provided $F_i s b a_0$ is small compared with q this excitation will be insufficient to initiate a wave (§ 3 *b*), but it will affect the value of M_0.

For small variations M_0 is approximately proportional to $(q/\rho)^{\frac{1}{2}}$. This fraction is increased in the ratio $\dfrac{1-F_i(sba_0/q)}{1-F_i r}$, so that if $r>(sba_0)/q$ there will be an increase in M_0 when both effects are taken into account. If we take the comparative values for actual neurons of § 1, we find that in fact $r>sba_0/q$.

The external dendrites postulated above thus give a very sensitive control of the propagation of a wave through a mass of cells. But stimulation of these dendrites increases the

attenuation of the wave instead of decreasing it as did the stimulation of the E cells considered in § 3 *b*, i.e. the effect is inhibitory rather than excitatory. Apart from this, the effects are rather similar. For convenience of reference these external dendrites will be called the I input to the block.

Timing

It may be noted that the effects described above of E and I cells are dependent on the rate of activation of these cells being constant and continuous. If the cells were activated intermittently both the E and the I input could produce either an excitatory or an inhibitory effect on a wave dependent on the timing of the activation in relation to the passage of the wave. This dependence on timing is made use of in the mechanism discussed in the next paragraph.

Stabilization of the value of M

The parameter M is inherently an unstable factor when it has any value other than zero or M_s. It is in unstable equilibrium when it has the value M_0, and any slight increase or decrease in value due to some statistical fluctuation in density of cells or connexions will start a rapid rise or fall away from M_0.

There are a number of properties of unsaturated waves passing through a mass of cells which only arise if the value M is rendered stable by some means. None of these properties is shown if all cells in the medium are activated by a saturated wave travelling through it. As these properties are in many respects analogous to the behaviour of living organisms, it seems worth considering whether this stability could easily arise. It is possible to conceive a servo-mechanism working somewhat along the lines indicated in figure 8, which might provide the necessary stability.

The axons P arise from the cells scattered at random within the mass. Only those which have just been activated by a wave travelling through are shown. The cells Q are activated if sufficient impulses are received from the P axons and which in turn excite I input fibres a short distance ahead of the wave. Again only those in action at one instant are shown. The P cells thus monitor the activity of the travelling wave, and if this rises high the Q cells, and in turn the I cells, will be activated so that the effective cell density is reduced in the path of the advancing wave, so attenuating it. The activity in the wave is thus controlled by servo action. Because of the threshold effect in the Q cells a small variation in activity would produce a large change in the number of I cells activated.

It is possible that some servo action could occur in other ways without any external cells or connexions by the agency of some inhibitory or depressive effect. On the other hand, it is interesting to note the similarity between the structure of figure 8 and the structure associated with masses of neurons in the cortex as reported by various investigators (Lorente de Nó 1943). The action of any servo-mechanism and its relation to the mass of cells might well be very complex and is a subject which merits detailed study.

Interchangeability of E and I cells

The effects of E and I cells are in a way complementary, in that reduction of the excitation of one set produces a similar effect to an increase of excitation of the other. Thus

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for most purposes they are interchangeable and a group of one type of cell can be replaced by the other type provided a suitable modification is introduced in the manner in which they are excited.

3 *d*. *The reduction of a wave to a single output*

Suppose a wave with M equal to the critical value M_0 reaches a boundary J, at which some property of the cells (e.g. density ρ, a_0, q, etc.) changes in such a way that M_0 is increased. Beyond the boundary, M for the wave will be less than the new value of M_0 and the wave will attenuate. At some point beyond the boundary, the wave will be reduced to the activation of one single cell.

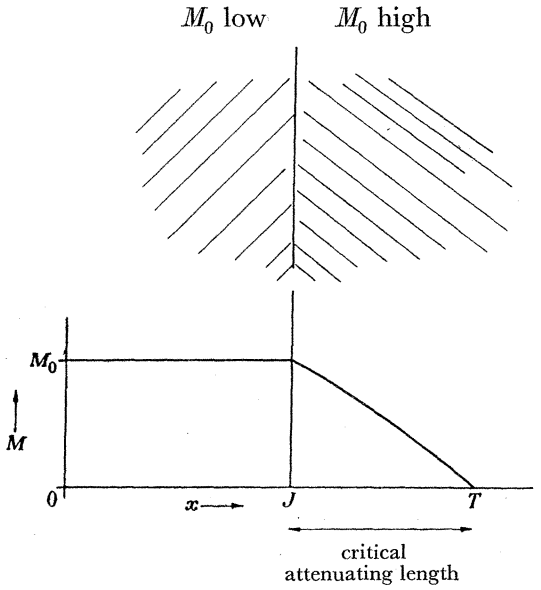

FIGURE 9

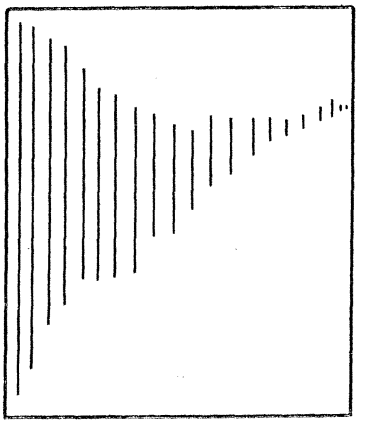

FIGURE 10

FIGURE 9. Plane T is separated from plane J by the critical attenuating length.

FIGURE 10. Successive wavefronts in an attenuating medium eventually dwindle to the activation of a single cell in plane T.

The distance between the boundary J and this point will be subject to a slight statistical variation between waves of different constitution, but the mean value will be described as the critical attenuating length. Let us now terminate the mass of cells at a plane T parallel to plane J and separated from it by the critical attenuating length (figure 9). Then a wave with $M = M_0$ before the boundary T will, on the average, just reach the plane T. If any wave fails to activate even one cell in the neighbourhood of the plane T a very slight increase of M in the wave as it approaches the boundary J will suffice to make it do so. Any further increase in M would produce many active cells in the neighbourhood of T. We could, of course, define a wave as having a value of M above or below M_0 according to whether it activated more or less than one cell in plane T, and for the purpose of discussion this is probably most convenient.

Suppose that in the above manner each wave is made to activate one cell when it reaches T (figure 10). Different waves will in general activate different cells, but a wave of a given

constitution arising from a given set of cells activated in plane G will always activate the same cell in plane T (unless some change has been made in the cells within the mass).

The constitution of the wave and therefore also the identity of the set of cells originally activated in plane G are thus classified in terms of the single cell finally activated in plane T. However, the number of different sets which may be activated in plane G will far exceed the number of cells in plane T so that the classification will either be incomplete or ambiguous. It is also true that living organisms are unable to distinguish completely and unambiguously all possible patterns of stimuli applied to their sensory receptors.

3*e*. *The result of making threshold or growth dependent on activity*

Composite mass

So far, the wave produced by activating a number of individual cells, and the behaviour of the wave at various boundaries designated G, H, J, and T, have been considered. The properties of a composite mass G, H, J, T (figure 11*a*) will now be investigated, the boundaries G, H, J, and T having the same significance as before.

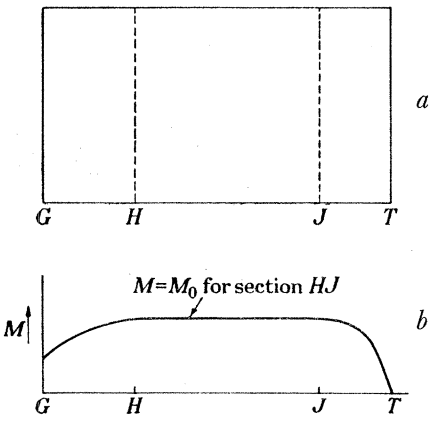

FIGURE 11. *a*, Composite mass of cells; *b*, the variation of M between the boundaries G, H, J and T.

It will be assumed that the value of M of a wave initiated at G is controlled in section GH by servo action. When it enters the section HJ the wave will be assumed to have a value of M equal to M_0 (figure 11*b*). It will then continue without change to J. Between J and T, M will be reduced progressively until finally one cell is activated in the plane T. The identity of the cell activated in plane T will of course depend on the constitution of the wave which reaches J, so that in the plane T there will be a form of classification of the constitution of waves arriving at J.

We shall mainly be concerned with the effect of varying the properties of groups of cells in the central section HJ of the composite region G, H, J, T. It simplifies demonstration of the properties of the mass of cells in this section if we have to deal only with waves with a fixed value of M entering it, and if between J and T the constitution of the wave can be reduced to the activation of a single cell in plane T. The properties which will be discussed are, however, inherent in the nature of the material (i.e. a mass of cells) of which the region is composed, and not due to the division of the material into sections. Various shapes of cell masses and arrangements of them in sections would show similar properties.

Threshold or growth and activity

If the threshold of the individual cells within the section H, J decreases with frequent use, then the mass of cells within this section will have the ability to store information permanently and will modify its behaviour permanently according to past history. It will be shown that there is a very interesting parallel between these phenomena and certain forms of behaviour of living organism. No such phenomena arise unless the cells possess some additional property or properties of this type and $M_0 \ll 1$. This relationship will be assumed from now on. This assumption is in accordance with the histological data available, provided the effective axon length is several hundred microns in length.

The suggestion that the threshold of a neuron might be lowered by frequent use has been put forward as a possible explanation of the simple conditioned response, and is supported by some experimental evidence (Eccles & McIntyre 1951; Eccles 1953). It is appropriate to consider the influence of such an attribute on the propagation of the waves. Similar effects could arise in other ways, for example, if growth of the dendrite and/or axon structure was promoted by activation of a neuron or if the formation of synapses was aided by activation. Growth of either structure would increase the numerical value of the constant, b, in $\xi(x)$ and would thus have the same effect on the value of M_0 as a decrease in q.

Let us assume that initially all cells have a threshold of q_s which is greater than q_0, the value corresponding to M_0. Then the first time the region we are considering is stimulated at G, the resultant wave W_1 will only pass through the section HJ with the help of a mean E excitation of $(q_s - q_0)$. Suppose then that each time a cell between H and J becomes active its threshold q is reduced by a very small amount ϵ away from the value q_s towards q_0. Then the second time the same stimulation is applied to G slightly less excitation, $(q_s - \epsilon - q_0)$, is required from E inputs to enable W_1 to pass. In this way it becomes gradually easier for wave W_1 to pass from plane G to plane T where its arrival is registered by the activation of the corresponding cell. After the wave W_1 has passed N_1 times, the E excitation which will permit it to pass again will be $(q_s - N_1\epsilon - q_0)$.

If a different stimulation (i.e. via a different group of cells selected independently of whether they were activated by W_1) is applied to plane G, the resultant wave W_2 will in general encounter a large proportion, equal to $(1 - M_0)$, of cells with a threshold of q_s and a small proportion, M_0, with a threshold $(q_s - N_1\epsilon)$. The mean value of q will thus be

$$(q_s - N_1\epsilon M_0),$$

which will be hardly less than q_s. For the wave W_2 to pass with this value of q, the E excitation must be raised to

$$(q_s - N_1\epsilon M_0 - q_0).$$

Since $M_0 \ll 1$ this will be considerably higher than the E excitation

$$(q_s - N_1\epsilon - q_0)$$

required for wave W_1. Thus if the E excitation is set at a value just above the latter, W_1 will pass freely while W_2 will not pass. The amount by which the E excitation then has to be raised in order for W_2 to pass freely will be a measure of N_1.

In time, if W_2 is passed frequently with assistance from the E input, the threshold of all the cells activated by it will decrease until, when N_2 equals N_1, it will pass with no more E excitation than W_1. Any other wave W_R initiated by activation of cells chosen randomly (i.e. without reference to past events) will still in general require an E excitation of

$$(q_s - (N_1 + N_2)\,\epsilon M_0)$$

or

$$(q_s - \Sigma(N)\,\epsilon M_0)$$

to assist its passage. Provided again that M_0 is small, this will be considerably more than the excitation required by W_1 or W_2 or any other wave which has passed many times.

Each wave which is permitted to travel through the region thus, in effect, establishes a path for itself along which it can travel more easily (i.e. with less E excitation) in the future. Moreover, the ease with which it passes is a measure of the number of times it has travelled through. The effect has been discussed in relation to a change in threshold, q, but a similar effect would be produced if growth of the cells was promoted by use. It should be emphasized that the reduction in threshold with use need only be a very small one. The passage of one wave need only affect the cells it uses very slightly.

4. Properties of a mass of cells as an integral part of a more complex mechanism

4*a*. *Learning behaviour*

In order to demonstrate fully the significance of the behaviour described in the last few paragraphs it will be necessary to consider the reaction of the composite mass as an integral part of a more complex mechanism. It will be shown that, due to the presence of the mass of cells, this mechanism can exhibit learning behaviour. The mechanism has been kept as simple as possible, since the purpose of this paper is to investigate the properties of a mass of cells and not primarily those of mechanisms of which it may form a part.

The composite region G, H, J, T will be considered as a whole again, as in § 3*e*, complete with E and I inputs within the section H, J (figure 12). The individual cells in the section H, J will be assumed to possess one of the properties discussed in § 3*e*, e.g. either reduction of threshold or growth with use, so that a wave which has traversed the region many times in the past will travel through more easily on a future occasion. The I input has deliberately been shown in a multiple form, each input having a localized effective area.

This whole composite region will be incorporated in a more complex mechanism (figure 13) with the following specific connexions between it and the rest of the mechanism.

(i) It will be assumed that the complete mechanism has a means of discriminating an undesirable situation as shown by the output of certain sensory receptors (e.g. pain in a living organism). The output of this discriminator is connected to the I inputs in such a way that:

- (*a*) A slightly undesirable situation only causes one or a few I inputs picked at random to operate for a period.
- (*b*) A more undesirable situation or a continued undesirable situation operates more I inputs in the same manner.
- (*c*) A highly undesirable situation operates a very large number of I inputs.

(ii) It will be assumed that the complete mechanism has a similar discriminator for satisfactory situations which can operate the E input or cause it to continue in operation. It is not proposed at present to go into the question of the form the discriminators might take, for it is easy to visualize a simple group of cells providing the required action.

(iii) All the sensory receptors of the complete mechanism are connected to the input plane, G, of the complete region G, H, J, T in such a way that any stimulus pattern applied to the receptors causes a corresponding wave to be initiated.

(iv) The cells in the terminal plane T are connected randomly to the various motor responses of the complete mechanism. Thus, when a cell or group of cells in the plane T become active, the corresponding motor action will take place in a deterministic manner.

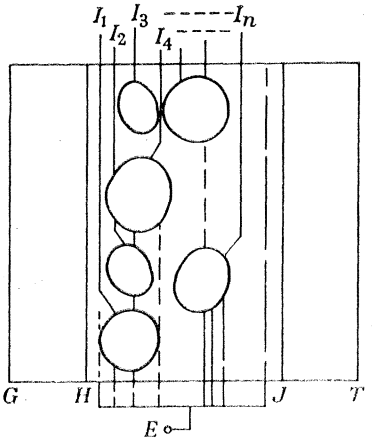

FIGURE 12. Composite mass with E and I input.

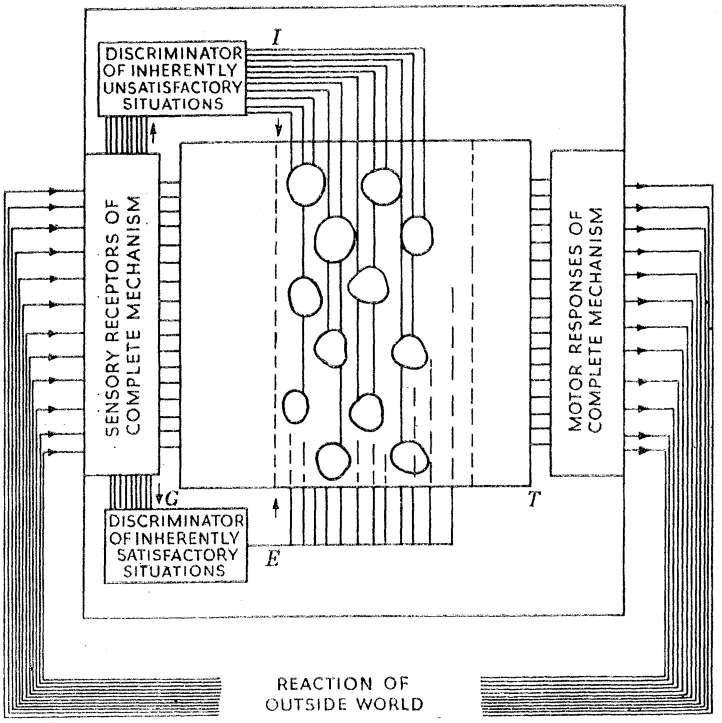

FIGURE 13. Composite mass incorporated in a mechanism complete with sensory receptors and motor responses.

Incorporated in this way into a complete mechanism with sensory receptors and means for providing motor responses, the composite mass of cells is capable of showing learning behaviour. We have already seen (§ 3e) that a wave which has passed through the region unhindered many times will pass through again relatively easily. If, therefore, the complete mechanism of figure 13 is placed in a familiar environment it will respond by motor action (or absence of it) in the same way as it has done previously.

If the complete mechanism is placed in an unfamiliar environment then a wave will be initiated in the mass which does not correspond to any past wave which has travelled through. If there is sufficient E input for the wave to reach the terminal plane, T, then some motor action will be initiated. But except for effects which will be discussed in §§ 4b, 4c and 4d, the point which is stimulated in the plane T is determined by chance. The motor action which results is therefore, with the same exceptions, determined merely by chance.

Two possibilities must therefore be considered.

(i) That the motor action leads to satisfactory results.

(ii) That the motor action leads to an unsatisfactory result.

If (i) is true, then the 'discriminator of satisfactory situations' will cause the motor action to be continued or repeated. The corresponding wave will travel through the composite mass many times and will eventually establish an easy path for itself. The previously unfamiliar environment will thus in time become a familiar environment and the response to it established and automatic.

If (ii) is true, then the 'discriminator of unsatisfactory situations' will operate gradually more and more of the *I* inputs, until the propagation of the wave is affected sufficiently for the wave to be deflected to a different terminal point in the plane *T*. The same process can occur again and again, and only when a satisfactory result is obtained is the corresponding wave allowed to travel unhindered through the mass of cells and establish a path for itself.

The mechanism just described accounts for both learning under deliberate tuition and learning by 'trial and error'. In learning under tuition it is the tutor who deliberately provides the 'satisfactory or unsatisfactory' situations in the form of reward or discouragement. In learning by 'trial and error' the reaction of the environment is classed as satisfactory or otherwise by the corresponding discriminators. In either case the result is to establish a path for the wave through the cell mass to a point in the *T* plane which will produce a motor response leading to a satisfactory result. The complete mechanism thus has the ability to 'guide' a wave through the mass of cells to a suitable output point in the *T* plane and it is on this ability that the whole learning process depends.

Trial and error learning is by its very nature wasteful of time and effort. It will, however, be shown in §§ 4*c* and 4*d* that there are effects which in practice effect considerable economy in both by enabling only 'relatively likely' motor responses to be tried.

A note will probably not be out of place here on the degree of organization which has been postulated in the mechanism shown in figure 13. By making enough assumptions one can 'explain' anything, so it is desirable that a distinction should be made between assumptions made solely in order that the properties of a mass of cells may be demonstrated easily and assumptions which are an addition to the individual cell properties already assumed. It has already been remarked that the subdivision of the composite region into sections *GH*, *HJ* and *JT* serves the former purpose and that other shapes and arrangements would show similar properties. The addition of an input organ consisting of sensory receptors and an output organ with motor responses is essential if there is to be any discussion of the response of the cell mass to its environment. They are, in fact, its only means of communication with the outside world. The assumptions about the discriminators and their manner of connexion to *E* and *I* inputs are the only basic additions to the original assumptions about the nature of the mass. These discriminators are an essential part of the mechanism as far as learning of this sort is concerned. It may be remarked that one could hardly have such a learning process unless something, somewhere within the complete mechanism, specified what had to be learned. For the reasons given in § 3*e* it is possible that one could dispense with either the *E* or the *I* input, replacing it by a modification of the other. In the same way two discriminators may be redundant in view of their complementary functions but have been retained in figure 13 to avoid complexity of connexions.

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Even though the complete mechanism shown in figure 13 has some degree of organization the multiple connexions between the various units are still assumed to be made in a random manner. The whole mechanism can therefore be very simply specified and is thus of the type which one would not be surprised to find in a self-reproductive living organism.

4*b*. *The propagation of successive waves in the mass and the formation of secondary waves*

It has been shown in § 3*c* that the amplitude M of a single wave propagating through a mass of cells can be restored by a simple servo-mechanism to the value M_0, even though, owing to some statistical fluctuation in density of cells or connexions, it departs temporarily from this value. The same servo-mechanism will serve to restore the amplitude if some other influence disturbs it temporarily. It is important to note that if it takes the form postulated in § 3*c* the servo-mechanism will not act immediately. Section *GH* of the composite region discussed earlier consisted of a mass of cells with this form of servo control. The properties of the same kind of medium in the presence of more than one wave will now be considered.

Propagation in a partly used medium with servo control of M

As a wave passes through a mass of cells a proportion M_0 of the cells are used up. It is proposed to consider the properties of the medium through which the wave has passed, during the period before the cells recover. If $M_0 \ll 1$ the reduction in effective cell density will be small and the medium will still be capable of propagating waves. The residual effective cell density will be $\rho(1-M_0)$ and the critical value M_0 for a second wave passing through the medium will be correspondingly increased. M_0 is approximately inversely proportional to $\sqrt{\rho}$, so the increased value of M_0 will be approximately $M_0/\sqrt{(1-M_0)}$ expressed as a proportion of the new effective cell density $\rho(1-M_0)$. Expressed as a proportion of the original cell density ρ, the new value of M_0 will be

$$M_0' = M_0/\sqrt{(1-M_0)}\,(1-M_0) = M_0\sqrt{(1-M_0)}.$$

The number of cells becoming active per unit time in the original wave passing through the medium is given by $M_0\beta\rho$. For the second wave passing in the path of the first the corresponding value is

$$M_0'\beta'\rho' = M_0\beta\rho(1-M)^{-1/q-1}.$$

If q is of the order of 10 and M is small, $M_0'\beta'\rho'$ is only very slightly above the value $M_0\beta\rho$ for the original wave, i.e. the number of cells becoming active per unit time is only slightly affected by the reduction in density. Now, it is the quantity $M_0\beta\rho$ which is monitored and controlled by the servo-mechanism controlling the amplitude of the wave. This mechanism will therefore work equally well on the second wave.

It is of interest to note that further waves may continue to pass through the same region before any of the cells used by the preceding waves have recovered. The second wave encountered a cell density of $\rho(1-M_0)$. The third will encounter a density

$$\rho\{1-M_0-M_0\sqrt{(1-M_0)}\},$$

the fourth, a density

$$\rho[1-M_0-M_0\sqrt{(1-M_0)}-M_0\sqrt{\{1-M_0-M_0\sqrt{(1-M_0)}\}}] \text{ etc..}$$

Neurons have the ability to recover their sensitivity after a period of time, and if cells are also assumed to have this property there will be no need for a continual increase of M

to compensate for the decrease in effective cell density. There will be a temporary decrease in effective density immediately after the passage of a wave, and the exact length of the recovery period does not affect the nature of the encounter between two waves discussed below.

A wave may be initiated in a partly used medium by the same means as the original wave was launched (see § 3 *a*). The initial stimulus D required is slightly increased in proportion to the increased value of $M_0'\beta'\rho'$. Waves in a partly used medium may also arise in other ways which will now be considered.

Two waves meeting

If two waves approach each other from opposite directions, then in the region where they meet the effective value of M will be increased by the interaction of the activity of the two waves. If the servo-mechanism is of the type discussed in § 3 *e* it will not act immediately, and for a very short period the value of M will be more than doubled, because of the

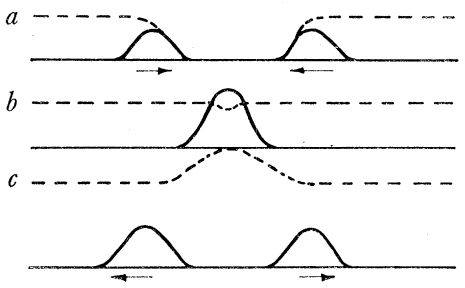

FIGURE 14

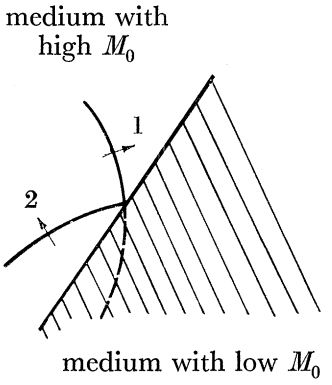

FIGURE 5

FIGURE 14. Sketch to illustrate distribution of activity (full line) and used cells (broken line). *a*, before the encounter (incident waves); *b*, during the encounter; *c*, after the encounter (resultant waves).

FIGURE 15. Interaction with a boundary. 1, initial wave; 2, resultant wave.

non-linear nature of propagation in the medium. This increased value of M will now make it possible for two waves to travel out from the region of the encounter, back along the tracks of the original waves, even though a proportion M_0 of the cells in these tracks has been used already (see figure 14). The initial value of M for these waves may be high but will soon be restored to approximately M_0 by the servo action. It will appear from the form of the waves as though the two had merely passed each other, but in constitution both resultant waves will be a combination of the two incident waves. In a similar manner two waves crossing obliquely may continue in their original direction though the constitution of each will be modified to some extent by the other.

Interaction at a boundary

A resultant wave may also arise in a region through which a single incident wave has travelled as a result of the interaction between the incident wave and a boundary where there is a sudden change in property of the medium. Suppose, for example, that ρ, a_0 or q are altered in some region which the wave encounters so that the critical value M_0 is less than in the region through which the wave has been passing. M will be above the critical value

in the new medium and, again assuming a time lag in the operation of the servo-mechanism, M will be subject to a temporary increase where the wave encounters the boundary. As with the encounter between two incident waves this will produce a resultant wave travelling back along the track of the incident wave. The incident wave may also, of course, continue in a forward direction (figure 15).

The last two subjects which have been considered, the reaction of the medium after encounter of two waves and the formation of a new wave at a boundary in the medium, bear surprising similarities to the behaviour of a wave in a medium obeying the normal linear wave equations. The importance lies in the presence of the high peak of activity in the region of their encounter.

Modification of the medium—Storage of information—Regeneration of waves

If the additional cell property of reduction of threshold with use is postulated, further interesting properties of the medium in the presence of more than one wave arise. This additional cell property, and the complementary one of cell growth being dependent on use, have been considered previously in § 3*e* in relation to a single wave travelling through a

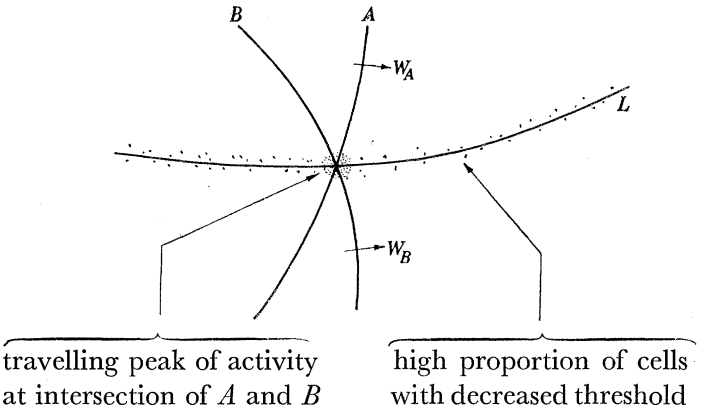

FIGURE 16. Interaction between two waves.

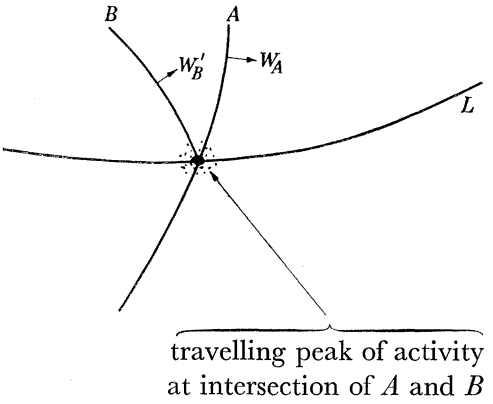

FIGURE 17. Regeneration of a wave.

composite cell mass. It is perhaps easiest to discuss the effect of this property on two waves in relation to two waves crossing each other obliquely. Suppose A and B in figure 16 indicate two wavefronts W_A and W_B which have on many occasions travelled across the region shown in the same time relationship. Then everywhere within the region shown there will be cells which, because they have been used during the passage of the waves, will have correspondingly decreased their threshold. These cells will be uniformly distributed with a density M_0 throughout the region except along the centre line L where, due to the interaction between the waves, a very much greater proportion of cells will have been used and will have decreased their threshold. As a result the critical value M_0 will be lowered all along the centre line L. The passage of one wave alone, e.g. W_A, will then produce a peak of activity where the wave intersects the line L, and if the local value of M_0 has been reduced sufficiently the peak will regenerate a second wave W_B' as it travels along the line L (figure 17).

The regenerated wave, W_B', although of the same form as W_B, will not have exactly the same constitution. The constitution will, however, be similar, since the majority of cells becoming active along the line L will after many simultaneous occurrences of W_A and W_B be the same whether W_A and W_B are both present or W_A only is present.

By the same mechanism the passage of W_B alone may produce a wave W_A' similar in constitution to and the same in form as W_A. There will also be a tendency for other waves to interact with the line L in the same way. The product of this interaction will, however, be unlike W_A and W_B, in that it will not have an established path through the mass of cells. It will therefore be subject to a very high attenuation. This tendency to form spurious waves will, however, be the limiting factor to the amount of information relating pairs of waves which may be stored in the form of lines of decreased threshold in a given volume of cells.

In the above discussion waves W_A and W_B have been shown crossing obliquely because this facilitates demonstration of the regeneration of a wave. Under certain circumstances, however, it is possible for one single wave with two constituent components W_A and W_B to modify the medium through which it travels so that on a later occasion the component W_A occurring alone can regenerate the other component W_B and vice versa.

4*c*. *The mass of cells as a link in conditioned response chains*

We are now in a position to compare the behaviour of the mass of cells with the class of behaviour known as the conditioned response. The essential basis of the conditioned response is that if some stimulus A always produces a response A and a second stimulus B repeatedly occurs in conjunction with A, then eventually the stimulus B occurring alone will tend to elicit the response A.

Now it is easy to see how such behaviour may arise in the manner considered in § 4*b*. Wave W_A is initiated by a stimulus which may conveniently be called stimulus A. Similarly, stimulus B initiates wave W_B. If the two stimuli A and B have repeatedly occurred together then eventually stimulus B may indirectly initiate a wave W_A' which is very similar to W_A. The more frequently W_A has occurred, and W_A and W_B have occurred in conjunction, the greater will be the similarity between W_A' and W_A and the greater will be the probability of W_A' terminating at the same point or points in the terminal plane, T, as W_A does.

Thus the mass of cells will provide a conditioned response. The specific organization of the composite mass of cells within the more complex mechanism, and the use of E and I cells postulated in § 4*a* are not necessary for the occurrence of conditioned responses. Conditioned responses are a form of behaviour inherent in the nature of the medium, i.e. a volume of interconnected cells having the ability to grow or decrease their threshold with use. If, however, this mass of cells is an integral part of some more complex mechanism of the form discussed in § 4*a* the conditioned response will be subject to suppression or reinforcement according to whether it leads to an unsatisfactory or a satisfactory result. The combination of the conditioned response with the mechanism of § 4*a* is thus a means which enables the mass of cells to direct the waves travelling through it to a satisfactory conclusion with less waste of time and effort than is possible if pure trial and error methods are used in choosing tentative responses.

4*d*. *Sequential regeneration of waves—Memory*

A very interesting form of behaviour arises if from cells in the plane J, or somewhere in its neighbourhood, connecting fibres are brought back to the input plane G. These are designated R fibres in figure 18, where for convenience of exposition the plane G is shown in two parts, $G_{\text{int.}}$ where waves are initiated by impulses fed back through these fibres,

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and $G_{ext.}$ where waves due to external stimuli are initiated. The connexions between J and G may be made in a random manner, i.e. the individual connexions need not be specified.

With these R connexions present, the composite mass initially works in much the same way as before. Each wave initiated by external stimuli eventually establishes for itself a path to a point in the plane T which will produce a motor response leading to a satisfactory result. But now each wave as it passes plane J causes a new wave, $W_{int.}$, to be initiated from $G_{int.}$. This will combine with waves, e.g. $W_{ext.}$, initiated from $G_{ext.}$ by later external stimuli to produce a region of reduced threshold along the line L in the manner discussed in § 4 *b*.

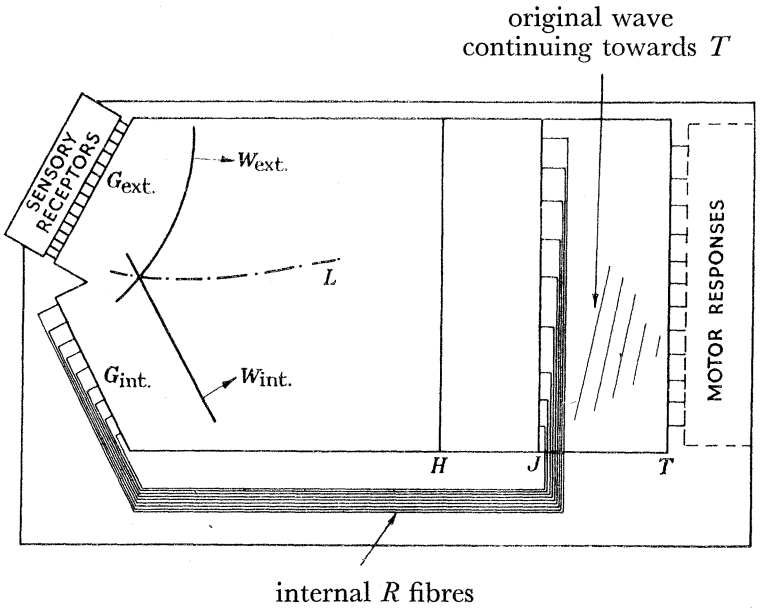

FIGURE 18. Modification of the mechanism of figure 13 by the addition of internal R fibres.

After the cell mass has been in use for some time there will be many regions of reduced threshold similar to L. Each will correspond to the relation between one set of stimuli and a set which has in the past followed it closely. Within these regions of reduced threshold is stored all the information required for the internal regeneration of a long sequence of past events.

To start the composite mass regenerating past events, it is only necessary to initiate a wave of external stimulation at plane G and then remove further external stimuli which would interfere with the process. The wave then travelling through the mass will be carried back by the R fibres to form a corresponding wave $W_{int.}$. If the general threshold is sufficiently low, $W_{int.}$ will then reconstitute a wave, $W'_{ext.}$, corresponding to the stimulus which in the past had followed it. Sometimes different events will in the past have followed a given set of stimuli on different occasions. Then, in general, it will be the wave corresponding to the most probable following event which is regenerated.

The regenerated wave $W'_{ext.}$ will in its turn be returned by the R fibres to form a second wave $W'_{int.}$, which in turn can regenerate a second, most probable, following wave $W''_{ext.}$. In this way a whole series of waves follow each other through the region exactly as they would do if the corresponding sequence of most probable events was actually occurring in

the outside world. This behaviour bears a striking resemblance to the recall of a sequence of memories in the form of a train of thought. The latter can occur without the accompaniment of any muscular action, and it need hardly be pointed out that a temporary increase in threshold throughout the section JT would prevent motor responses accompanying the sequence of waves.

The survival value of this form of behaviour in a living organism is obvious. It allows the organism to explore some way ahead and discover the most probable results of a contemplated action and to decide whether or not to take that action according to the satisfactory or unsatisfactory nature of these anticipated results. It is not difficult to visualize modifications which could be made to the mechanism of figure 13 to allow it to make use of the ability of the composite mass to explore a succession of most probable events. The modified mechanism would then pick a motor action shown by the sequence of most probable events as likely to lead to a satisfactory result. A satisfactory result is of course a result recognized as such by the 'discriminator of satisfactory situations'.

The process which has just been discussed is in effect an extension of the simple conditioned response. It provides an even more powerful means of choosing a likely response to a given situation and thus provides an even greater economy of time and effort as compared with the pure trial and error methods discussed in § 4*a*. Refinements in the simple mechanism would enable the sequential wave regenerating behaviour to be switched in when necessary and would enable it to be stopped when a satisfactory probable result has been found. These are, however, beyond the scope of the present paper.

It is important to note that if the mass of cells is in the shape of an annulus, or forms the surface of a sphere or other closed surface, or if reflexion takes place in the plane J, this sequential memory effect can take place without any additional R fibres.

5. Discussion

The comparisons that have been made in the past between the properties of computing machines and of living organisms are interesting when made in relation to abstract fundamental concepts, but less productive when details are considered. This is because, in the detailed design of most large computing machines, components are connected together exactly according to some specification, and have a precise function in relation to all other components. This specific organization in a computer contrasts with the apparently very large random factor in the interconnexions between neurons in many parts of the cortex.

The aim of this paper has been to show that some of the basic forms of behaviour of living organisms can be simulated by a mass of simple units without the necessity of postulating a large degree of specific organization of these units. Care has been taken to keep the degree of organization to a minimum in discussing the behaviour of a mass of cells in relation to a complete mechanism. It should be emphasized again that the representation of a mass of cells in the form of a composite mass subdivided into several sections was mainly adopted as an aid to demonstration of the properties of the medium. The properties are, however, inherent in the proximity of large numbers of such cells and would be present in various shapes and arrangements of masses of cells. The inputs from sensory receptors and the motor response outputs might be scattered over the surface or within the volume of the mass. Waves

might not be confined to one general direction of propagation but might well travel in all directions. One would therefore not necessarily expect to find anatomical structure closely resembling the composite mass of cells shown diagrammatically in this paper, within an organism making use of the properties which have been discussed. Moreover, there could be considerable variation from point to point in cortical structure without invalidating the comparison between cell and neuron masses. A living organism probably would have a large number of hereditary responses upon which conditioned responses could be built. The connexions from the sensory receptors to the discriminators of § 4*a* are in fact 'built-in' response paths which are assumed to be present initially.

The three effects, trial and error learning, conditioned responses, and the regeneration of past events, have been discussed as if they took place in one mass of cells. This is not essential, and it might very well happen in an organism with a number of well-differentiated types of sensory receptor (e.g. man) that some of the effects were dispersed. Some might be produced in cell masses attached directly to the sensory receptors and some in other masses of cells concerned more with secondary relationships. It might well be that the discriminators of § 4*a*, instead of being the simple mechanisms envisaged there, are themselves masses of cells the outputs of which are connected, not to motor responses, but to groups of E and I cells, and serve the purpose of controlling the distribution of attention between the various senses or between various groups of receptors within one sense.

It is thought that further examination of all three effects would be profitable as only a very simplified, formalized state of affairs has been considered. Mathematical investigation of the properties described above would be desirable and should lead to interesting results. It is hoped to follow this up in due course. It would be particularly interesting to calculate the information storing and handling capacity of a limited mass of cells in terms of the number of cells present, and to make comparisons with living organisms.

The possibilities of continuous random activity, vortex effects and other reverberatory systems within a mass of cells providing, among other things, a short-term memory effect, have been omitted in the above discussion. It is proposed to consider these in detail in a further paper.

It should be noted that there is no particular significance in the exact form of the wave travelling through the medium. The form $\dfrac{M\beta}{2\cosh^2\beta(t-x/v)}$ arises when $\xi(x) = b\,\mathrm{e}^{-|x|/a_0}$. Minor variations in form of $\xi(x)$, which do not materially alter the mean density of connexions, will cause corresponding changes in waveform without affecting anything that has been discussed in this paper. Major changes in waveform might be produced by the presence of certain forms of amplitude controlling servo-mechanism. Under these circumstances the surge of activity could even become reduced to a mere diffuse spread of activity. Even so, the learning, conditioned response and memory effects discussed in this paper might well be unaffected.

The important point about the waves which travel through the medium which has been considered is the non-linear, co-operative nature of propagation. Consequently, even slight changes in almost any cell property, provided they are brought about by use and facilitate activity, will cause a selective action of the medium on waves propagating through

it and result in the types of behaviour which have been dealt with in this paper. The following are examples:

(i) Decrease in threshold with use.
(ii) Increase of strength of activity with use.
(iii) Growth of dendrite structure with use.
(iv) Growth of axon structure with use.
(v) Formation of, or increased effectiveness of, synapses with use.
(vi) Formation of, or increased effectiveness of, synapses when the two cells concerned are activated simultaneously.

If the propagation of waves in the medium were linear, the choice of possibilities would be limited to the last of these, and a much greater change would be required. It would therefore be of interest to know for certain whether any cell property does alter with use and if so how much. Another important question is 'can excitation only pass from axon to dendrite or can it pass in both directions?' In the latter case, regeneration of waves in the manner discussed in § 4 *b* would occur more readily than in the former. In this paper, greater importance has been attached to the propagation of wave motion, in relation to long-term memory, than to continuous random activity. This is because of the supposition that the threshold of neurons may be considerably higher than unity, and continuous random activity is consequently of an unstable nature. If excitation could pass in both directions, or if long-term memory was dependent on the sixth property listed above, then permanent memory storage could come about without the threshold q being greater than unity. There need then be no question of instability, and continuous random activity could be associated with long-term memory. It is thus necessary to know the order of magnitude of the threshold of neurons, and to discover the answers to these allied questions, if we are to progress further with even a qualitative description of the behaviour of a mass of such units.

Relation to other papers

Certain writers (McCulloch & Pitts 1943; Ashby 1950; Cragg & Temperley 1954) have considered the activity of sets or groups of neurons from the rather detached point of view of relation to logic, homeostasis, co-operative phenomena, domain theory, etc. In this paper the aim has been to consider in more detail the forms of activity which could exist in a particular type of cell structure and the behaviour which might be expected to arise as a result of this activity. The treatment is therefore very much less general but allows slightly closer comparison with biological investigations. That the correspondence cannot be closer still is partly due to the lack of data on the properties of neurons and on the structure of the cortex. Perhaps the most important cell property affecting the sort of behaviour which has been discussed is the one about which there is least published information. This is the threshold effect which is primarily responsible for preserving the form of the waves of activity, and is also responsible for the non-linear nature of propagation and may play an important part in the permanent storage of information by individual cells.

Other writers (Rapoport 1950, 1951; Anderson & Rapoport 1951; Shimbel 1950, 1951) appear to have realized the necessity for statistical investigation of the behaviour of neurons, but instead of considering a spatially distributed mass of cells have restricted attention to small sets of two or three, or groups (ganglia) of neurons. As a result their conclusions only

apply to such isolated groups of neurons. This leaves it as a matter of conjecture how a large volume of cells, such as are found in the cortex, would interact. Moreover, there are other disadvantages in only considering the interaction between individual neurons. For instance, in the paper which is of principal interest here, Shimbel (1950) has to assume, without any empirical support, 'that the threshold of a neuron will be lowered if a super-threshold and a sub-threshold stimulus impinge on it in sufficiently close temporal contiguity'. The present paper shows that it is quite sufficient for the threshold simply to decrease with use or for any other equivalent change to take place (see (i) to (vi) above). Then again, Shimbel's treatment over-emphasizes the seriousness of redundant conditioning. In a large, spatially distributed mass of cells a conditioned response is the result of interaction of a large number of neurons over a wide region. A response is only produced if the reaction from every part of this region is confirmatory, i.e. if the response is a true conditioned response; any other response is, relatively speaking, highly attenuated.

The recent work of Sholl (1953, 1955) has drawn attention to the importance of the decrease in connective fibre density with distance from a neuron. It is to exploit these new data that the present paper has been written. In doing this the aim has been to demonstrate the basic properties of a medium comprising a mass of cells having properties as nearly as possible similar to the known properties of actual neurons. By considering the mass as a whole, some of the difficulties encountered by others have been avoided. This method of treatment also shows the importance of the unsaturated form of wave and the necessity for some means of maintaining this form of activity. The comparison of cell masses with actual cortical structure is not invalidated by the fact that the properties of the latter medium vary somewhat from place to place. This variation, particularly in respect of axon structure, is a fact which has yet to be investigated and may prove of considerable importance. By comparison with other papers on the subject the conditioned response is presented in a slightly different light, i.e. as a factor which reduces the waste inherent in trial and error learning.

The earlier methods of treatment failed to bring out clearly the non-linear nature of propagation consequent on a threshold greater than unity, the very selective action of a cortical mass on the activity passing through it, and the fact that a very minute change of some cell property, each time the cell is used, is sufficient to produce a 'memory trace'. The stress, in the foregoing discussion, on waves of activity is interesting in view of recent electroencephalograph investigations with several spatially distributed pick-up probes (Chang 1951; Burns 1951; Walter & Shipton 1951; Walter 1952; Lilly 1954).

The structure considered in this paper bears a particularly interesting relation to the probability machine discussed by Uttley (Sholl & Uttley 1953; Uttley 1956). The machine mentioned in the latter paper stored information about the frequencies of past occurrences in individual units. The inference contained in the present paper is that the practical counterpart of one of these storage units may be a large number of cells each of which serves as a common storage point for information about large numbers of occurrences. The ambiguity which this might cause is avoided by the fact that information about a particular type of occurrence is stored in a very large number of such units in such a way that it may be extracted for use when necessary. There is thus a sort of multiple diversity effect which would readily account for the fact that damage to a limited region of the cortex does not have any marked effect on the operation of the whole storage system.

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Appendix

Additional symbols used in appendix

k	The constant obtained by integrating $\xi(x)$ from $-\infty$ to ∞.
$P_{(q-1)}$	The term $(q-1)$ in the Poisson series.
Z	A correcting factor for $P_{(q-1)}$ so that it applies to the distribution of impulses in sensitive cells.
δt	A very short interval of time.
m	A constant, the ratio of Φ to F in § (b) of Appendix.

This Appendix covers, in analytical form, the same ground as § 2 of the paper. The analysis will be based on the two equations:

$$\text{Mean rate of arrival of impulses} = \int_{-\infty}^{\infty} F(X,t)\,\xi(x-X)\,\mathrm{d}X \tag{1}$$

and

$$\bar{N} = \int_{-\infty}^{0}\int_{-\infty}^{\infty} F(X,T)\,\xi(x-X)\,\chi(t-T)\,\mathrm{d}X\mathrm{d}T. \tag{2}$$

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Continuous random activity will be dealt with first, as it affords a simple illustration of the application of the statistical methods outlined at the beginning of § 2.

(*a*) *Continuous random activity*

We wish to consider what would happen if initially, throughout a volume of cells, the activity F was constant and independent of x, and to find the conditions under which the activity would be self-maintaining.

As the activity is assumed to be constant throughout, the convolution of equation (1), giving the mean rate of arrival of impulses, simplifies to

$$F\int_{-\infty}^{\infty}\xi(x)\,\mathrm{d}x,$$

which will be written Fk. If $\xi(x)$ has the form given in § 1 *c*, then the constant k will be $2ba_0$.

The adoption of a rectangular function of duration s for $\chi(t)$ simplifies equation (2), giving the mean value of the total integrated excitation

$$N = Fks.$$

There will be a Poisson distribution of actual numbers of impulses so that the proportion of cells with a total excitation of $q-1$ will be

$$P_{(q-1)} = \mathrm{e}^{-N}\frac{\bar{N}^{(q-1)}}{(q-1)!} = \mathrm{e}^{-Fks}\frac{(Fks)^{(q-1)}}{(q-1)!}.$$

It may be shown, by a statistical examination of the distribution of numbers of impulses in sensitive cells and used cells, that if s is not much larger than τ, the proportion $P_{(q-1)}$ will be substantially independent of whether the cells are sensitive or used. If $s \gg \tau$, the above expression for $P_{(q-1)}$ must be multiplied by a correcting factor as $\bar{N}$ approaches q, so that it applies to sensitive cells. The proportion of cells which have a total excitation of $(q-1)$ and are also sensitive will then be

$$RP_{(q-1)}.$$

These are the cells which are ready to be triggered into activity by the arrival of one further impulse. The proportion of these cells which actually do receive an impulse during a very small period δt, at a time t, will be

$$F(t)\,k\,\delta t.$$

The proportion of cells receiving more than one impulse will be negligible, provided δt is very small. Thus, the proportion of cells which are sensitive and also fulfil the condition of attaining the threshold q during a period δt, and are therefore triggered off during that period, will be

$$RP_{(q-1)}F(t)\,k\,\delta t.$$

After an interval equal to the cell operating time τ, these cells will become active. The rate at which cells become active will then be

$$F(t+\tau) = RP_{(q-1)}Fk.$$

The factor $P_{(q-1)}$ is proportional to $F^{(q-1)}$, so that if $F(t)$ is large, $F(t+\tau)$ will be greater than $F(t)$, and the activity will thus increase during each successive period of τ. If $F(t)$ is small,

$F(t+\tau)$ will be less than $F(t)$ and the converse will happen. There are two conditions for the activity to be self-maintaining at a constant level. The first is that $F(t+\tau)$ shall be equal to $F(t)$, i.e. that

$$RP_{(q-1)}k = 1.$$

The second condition is that the rate at which used cells recover should equal the rate at which sensitive cells become active, i.e. that

$$\rho - R\rho = Fr\rho,$$

where r is the recovery period. If the cells did not recover after a period they would of course all be used up in a short burst of activity and no continuous random activity could exist.

From these two relationships

$$P_{(q-1)}(1-Fr)\,k = 1.$$

This may be rewritten in terms of Fks

$$e^{-Fks}\frac{(Fks)^{(q-1)}}{(q-1)!}\left(k - Fks\frac{r}{s}\right) = 1.$$

It is of interest to insert approximate values of k and r/s for actual neurons in this equation. The value of k corresponding to Sholl's data is $2ba_0$, and may range in value from 60 for average neurons, to 420 for neurons with long axons, in accordance with the range of possible values of b. If we take $k = 60$, $q = 6$ and $r/s = 25$ as in § 1 *c*, then the left-hand side of the equation is maximum when Fks, the mean integrated excitation, has the value 1·8. The left-hand side is then equal to 0·39 so that the equation cannot be solved. If, however, q is 5 or less, a value of Fks can be found which will satisfy the equation so that uniformly distributed continuous random activity may occur.

Thus it would appear that a block of cells having these properties cannot support uniform continuous random activity if the threshold, q, is above 5. This is because of the non-linear nature of the activity. Below a certain minimum amplitude, activity is incapable of sustaining itself. If q is above 5 this minimum amplitude is so large that the cells become used at a greater rate than they recover. The activity thus rapidly 'burns itself out' by using up all the sensitive cells and thus cannot be continuous. For higher values of q, only activity with some form of 'organization' can continue to exist, activity which, having used a proportion of the cells in one region 'moves on' to another region where sufficient sensitive cells remain, perhaps to return when the used cells recover. The activity will then be a function of position and time.

It should be noted that if q has the value 5 the state of uniform activity will be an unstable state, and any small statistical fluctuation in F will start a rapid rise or fall away from the equilibrium value of F. Thus, though uniform activity may be possible, activity with some form of spatial and temporal 'organization' will always be favoured if q is high.

If instead of $k = 60$, we take the value $k = 420$ corresponding to neurons with long axons, then q can be as great as 10, the value mentioned in § 1 *b*, without making a solution of the equation impossible. The remarks regarding the instability of continuous uniform activity apply with even more force for higher values of q, and activity with some form of spatial and temporal organization is correspondingly favoured. It is proposed to consider one such form of organized activity, the propagation of a plane wave of activity through a volume of cells, as this will serve to illustrate the nature of the behaviour of the medium when q is of the order of 10.

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(*b*) *Plane wave of activity*

We shall consider the possibility of a plane wave propagating in the direction of the x-axis. The parameters F and R are now both functions of position and time. If a wave of activity has reached a given point on the x-axis (figure 1*b*), then the region through which it has just passed will contain a high proportion of 'used' cells. The region on the other side of the peak of activity will, on the contrary, contain a relatively large proportion of 'sensitive' cells (figure 1*a*, curve ii). This asymmetry means that the region in front of the peak of activity is better able to support further activity. Thus, although excitation travels out in all directions from the peak of activity (figure 1*c*), a greater number of new cells is excited to activity ahead of the peak than in the region through which it has passed (figure 1*d*). This is the mechanism by which the advance of the wave is maintained. Propagation is very different from that of the more familiar types of wave motion. One might better describe the disturbance as a 'surge' of activity to emphasize its transient nature. It is possible to construct a model to simulate this type of propagation. This has been done by making use of a high-speed digital computer, but it is more convenient if we can have an analytical representation of the nature of propagation. Owing to the non-linear nature of the medium, which is especially pronounced when q is high, one cannot represent propagation by the differential equations that apply to waves travelling through linear media. For this reason it is difficult to obtain a solution in general terms. What has been done is to obtain a differential equation which may be solved if a certain assumption is made, and to show that this assumption is in accord with the existing data on the connectivity between actual neurons. The differential equation will be based on equations (1) and (2).

In considering the possibility of a plane wave of activity propagating along the x-axis, we may take it that activity is uniform throughout each plane perpendicular to this axis. $F(x, y, z, t)$ may thus be written $F(x, t)$.

The convolution of equation (1)

$$\int_{-\infty}^{\infty} F(X, t)\, \xi(x-X)\, \mathrm{d}X$$

will therefore again give the mean rate of arrival of impulses at cells in any plane, $x = \text{const.}$, and the convolution of equation (2) will give $\bar{N}$. If it were not for a correcting factor allowing for the slight difference in the distribution of impulses according to whether cells are sensitive or used, we should have a Poisson distribution of numbers of impulses among sensitive cells. As it is, we must apply a correcting factor which we may denote by Z, giving

$$P_{(q-1)} = Z\, \mathrm{e}^{-\bar{N}} \frac{\bar{N}^{(q-1)}}{(q-1)!}.$$

The proportion of sensitive cells reaching the threshold q during an interval δt will be

$$P_{(q-1)} \int_{-\infty}^{\infty} F(X, \alpha)\, \xi(x-X)\, \mathrm{d}X\, \delta t.$$

To avoid further consideration of these functions at the moment, the proportion of sensitive cells which reach the threshold in an interval δt will be written

$$\Phi\{F(x, t), \xi(x), \chi(t)\}\, \delta t,$$

or, simply

$$\Phi\, \delta t.$$

It should be noted that, like the activity F, the function Φ is a function of both x and t (see figure 1).

The rate at which cells which are sensitive reach the threshold, expressed as a proportion of the total cell density, is

$$R\Phi.$$

These cells will become active after a time τ, and the rate at which cells become active will then also be

$$R\Phi,$$

i.e.
$$F(x, t+\tau) = R\Phi.$$

Differential equation for plane wave

Now, for a given value of x the change in rate at which cells become active during the operating time τ, i.e. unit time, will be

$$F(x, t+\tau) - F(x, t) = R\Phi - F,$$

i.e.
$$\mathrm{d}F/\mathrm{d}t = R\Phi - F. \tag{3}$$

Each time a cell becomes active the number of sensitive cells is reduced by one so that

$$\frac{\mathrm{d}}{\mathrm{d}t}(R) = -F \tag{4}$$

and
$$\frac{\mathrm{d}^2}{\mathrm{d}t^2}(R) = -\frac{\mathrm{d}F}{\mathrm{d}t}. \tag{5}$$

From (1), (2) and (3)
$$\frac{\mathrm{d}^2}{\mathrm{d}t^2}(R) = \left\{R\frac{\Phi}{F} - 1\right\}\frac{\mathrm{d}}{\mathrm{d}t}(R)$$

and
$$\frac{\mathrm{d}^2}{\mathrm{d}t^2}(R) + \left\{1 - R\frac{\Phi}{F}\right\}\frac{\mathrm{d}}{\mathrm{d}t}(R) = 0. \tag{6}$$

Solution to differential equation for $\Phi = mF$

In equation (6) the distribution of R is expressed in terms of time differentials. The fact that differentials with respect to x do not appear as such in this equation is misleading. In fact, this equation also contains space differentials within the ratio Φ/F. Now, the spatial distribution of F is the spatial distribution of active cells (figure 1*b*). These cells spread excitation among their neighbours and, as a result, some of these neighbours are excited above the threshold q. The spatial distribution of Φ (figure 1*c*) represents the spatial distribution of these latter cells. It is not surprising that there is a particular form of $\xi(x)$ for which the two spatial distributions are the same, i.e. for which Φ/F is a constant. What is perhaps more surprising is the correspondence between this form of $\xi(x)$ and the one which has been derived from Sholl's empirical data (see § 1*c*). This fact leads to interesting results. For this reason, the solution of equation (6) when Φ/F is a constant, m, will be investigated.

If $\Phi = mF$, equation (4) becomes

$$\frac{\mathrm{d}^2}{\mathrm{d}t^2}(R) + \{1 - Rm\}\frac{\mathrm{d}}{\mathrm{d}t}(R) = 0, \tag{7}$$

which has a solution

$$R = \frac{1}{m} - \frac{2\beta}{m}\tanh\beta(t-t_0), \tag{8}$$

and substituting this in (2) gives

$$F = \frac{2\beta^2}{m}\frac{1}{\cosh^2\beta(t-t_0)}. \tag{9}$$

If all cells are in the 'sensitive' condition initially, we have a boundary condition $R = 1$ when $t = -\infty$, and if a proportion M of cells is used during the passage of the wave, $R = (1-M)$ when $t = \infty$. Thus

$$m > 1, \quad \beta = \frac{(m-1)}{2} \quad \text{and} \quad M = \frac{4\beta}{m} = \frac{2(m-1)}{m}.$$

Therefore

$$F = \frac{M\beta}{\cosh^2\beta(t-t_0)}. \tag{10}$$

The parameter M may conveniently be called the amplitude of the disturbance, and the constant β determines the rate of rise and fall of activity.

The purpose of the present calculation is to show whether a plane wave of activity can travel through the medium we are investigating. If $\Phi = mF$, as we have assumed above, then for any particular value of x we have a pulse of activity the form of which is given by equation (10). Is it possible for this pulse of activity to propagate forward through the medium in the x direction? To test this hypothesis we must put $t_0 = t_1 + (x/v)$ in the above expression for x, and then check whether the resultant travelling wave represented by

$$F = \frac{M\beta}{\cosh^2\beta\{t-t_1-(x/v)\}} \tag{11}$$

is consistent with the relation $\Phi = mF$ from which we started. What has in fact been done (see Appendix, § (*c*)) is to find the form of $\xi(x)$ which makes the waveform of equation (11) consistent with $\Phi = mF$. If $\xi(x)$ has the appropriate form, the wave, once launched, should continue to propagate without alteration or increase in amplitude.

We could of course equally well test the hypothesis that the medium can support a backward-travelling wave. To do this we should have to put $t_0 = t_1 - (x/v)$, and check the consistency of the result with $\Phi = mF$. However, as the medium has no directional properties it will be sufficient merely to show that a wave can travel in the forward direction. All that will be said applies equally to a wave travelling in the opposite sense. By suitable choice of time origin t_1 may be omitted, giving

$$F = \frac{M\beta}{2\cosh^2\beta\{t-(x/v)\}}. \tag{12}$$

It should be noted that the basic differential equation, (6), is non-linear. Therefore we cannot put $t_0 = t_1 + (x/v)$ and $t_0 = t_1 - (x/v)$ to give two co-existent solutions. A wave of the form given by equation (10) may either travel from left to right or from right to left, but not both together. If two waves approach each other, then in the region where they meet we cannot expect them to continue to propagate independently. What happens under these circumstances has been considered qualitatively in § 4*b* of this paper.

(c) Requisite form for $\xi(x)$—wave of small amplitude

Because F is now a variable dependent on x as well as t, the evaluation of the function Φ, for any given form of $\xi(x)$, involves numerical integration of the convolution of equation (2):

$$\bar{N} = \int_{-\infty}^{0} \int_{-\infty}^{\infty} F(X, T)\, \xi(x-X)\, \chi(t-T)\, \mathrm{d}X \mathrm{d}T.$$

As this numerical integration is tedious the calculation will not be reproduced here. The details have already been outlined elsewhere (Beurle 1954). The result shows that, provided the amplitude of the wave is small ($M \ll 1$) for 'q' of the order of 10, the form of $\xi(x)$ which satisfies the relationship $\Phi = mF$ is very close to $b\, \mathrm{e}^{-|x|/a_0}$. Thus, if $\xi(x)$ is of this form and the constant b of the right magnitude, the simplified form of the differential equation applies, and its solution, equation (12),

$$F = \frac{M\beta}{2\cosh^2 \beta\{t-(x/v)\}}$$

defines the form of wave that will be propagated through the medium without attenuation or gain.

It will be noted that the expression $b\, \mathrm{e}^{-|x|/a_0}$ coincides with that quoted earlier as an estimate of $\xi(x)$ from empirical data. The requisite magnitude for b may be derived by performing the integration mentioned above. The result is to relate b to the other quantities involved, according to the equation:

$$(0{\cdot}57)^q\, s\, \frac{(m-1)^2}{2}\, (q-1)! = \left\{M\beta s \frac{a_0 b}{q}\right\}^q.$$

The constant, 0·57, arises in the process of integration. It may also be shown that

$$v/\beta = 2a_0/q.$$

The wave velocity may thus be calculated if all the quantities are known accurately. However, as noted in § 1 *c* the value of the empirical constant b depends on several factors which are not known accurately at present. For this reason one can only make a very rough estimate of velocity. If one takes the range of values of b given in § 1 *c* the velocity may range from a few millimetres per second for waves of small amplitude to several hundred for saturated waves.

There is thus a reciprocal relationship between the amplitude of the wave and the constant b. If the density of connexions, represented by b, is increased, then the critical amplitude of wave which will satisfy the relationship $\Phi = mF$ is decreased and vice versa. The width of the wave, given by v/β depends only on a_0 and q. If there is a departure from the above conditions regarding the amplitude of the wave and the value of $\xi(x)$, the nature of propagation is modified.

Waves of large amplitude

If $\Phi = mF$ holds, but the amplitude of the wave is not small, i.e. if M is not very much smaller than unity, then at the peak of the wave the mean integrated excitation $\bar{N}$ will be large. For a given form of $\xi(x)$ this is accompanied by a slight broadening of the waveform.

Examples are shown in figure 2 for various peak values of $\bar{N}$. For comparison, the waveform of equation (12), derived directly from the differential equation for waves of small amplitude, is also given.

Dependence on $\xi(x)$

The form $\xi(x) = b\,e^{-|x|/a_0}$ was an estimate of the statistical distribution of connexions made from rather incomplete empirical data. The form of $\xi(x)$ may differ from this, and any estimate of the value of the constant b must at present be regarded as indicating its order of magnitude only. The exact shape of the $\xi(x)$ characteristic is relatively unimportant in relation to the rest of this paper, as it only affects the waveform of the propagated activity. It is the density of connexions, dependent on the constants a_0 and b, and its relation to the integration time s and the threshold q, which primarily decides whether waves of any given amplitude can propagate through the medium.

(*d*) *Departure from the relationship* $\Phi = mF$

So far, only waves for which the relationship $\Phi = mF$ holds have been discussed. When $\Phi = mF$ the amplitude of the wave is at a critical value such that the excitation it produces just maintains the level of activity constant. This critical value of M will be called M_0. If the wave amplitude is less than the critical value M_0, the excitation produced by the activity is insufficient to maintain that level of activity, and the wave is attenuated progressively more and more rapidly as the amplitude drops away from the critical value (figure 3, curves *a* and *b*). The waveform, however, being largely dependent on the form of $\xi(x)$ is not changed greatly.

If the initial amplitude of the wave is above M_0, then the excitation produced is more than necessary to maintain the activity and there is a consequent progressively more rapid increase in amplitude. Eventually the wave 'saturates' when it uses all the cells in the medium through which it passes and cannot increase further in amplitude (figure 3, curves *c*, *d* and *e*).

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