A MODEL FOR THE SYNAPSE

(LILLIE'S NERVE MODEL MODIFIED)

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INTRODUCTION

It is a well known fact that the conduction at the ganglionic synapse is irreciprocal at least at higher animals. This made us think of a sort of discontinuity there, of a functional unit to exist in each neurone, which made us establish finally the neurone theory in the physiological sense. As to the precise mechanism, however, nothing is clear yet although there are various hypotheses proposed, and the question is left for the future, together with that of the finest histological structure there, to be answered. On the other hand, it is also widely accepted since Bethe(1) that in lower animals the excitation is transmitted in both directions as well, that, therefore, there must be something continuous through the ganglioni cell so that the whole nervous system makes a large complicated net as a whole (Bethe's theory of neuro-fibrils). These two ideas cannot be harmonized at present, and we have simply to take the facts of reciprocal and irreciprocal conductions as facts due to the difference of animals. Now, the author, who has been engaged in the studies on Lillie's model during past few years, has succeeded in having a model for the synapse, which is something like the actual synapse in structure and can be of various grades of irreciprocity according to the conditions given. It can, therefore, bridge over the disharmony between the neurone theory and the fibril-theory to a certain extent and, moreover, it affords a possibility of explaining the synaptic delay in general.

EXPERIMENTS PERFORMED

A long steel wire and a few short wires were prepared to be used as the cores. One ends of the short cores were attached together to a point somewhere at the middle of the long core by soldering, and the soldered part was covered with paraffin along a few millimetres or centimetres according to necessity (Fig. 1, P). The

Fig. 1

paraffin plays two roles, namely 1) to protect the solder from the attack of the nitric acid, and 2) to make the activation current flow necessarily over the P-part from one side to the other when the wave is being transmitted beyond that part. Of these two roles, the essential one is of course the second one. As will be described later, the soldering and paraffinizing is not always necessary, but instead of that the cores can

be bent upwards at that part to be drawn out into the air and connected together by means of mercury (see Fig. 3). Anyway, the length of the P-part, paraffinized or exposed to the air, is controlling the intensity of the local activation current.

The model thus composed is then immersed in strong nitric acid to be stimulated at various immersion times. Observations were made on whether the activation wave evoked by stimulations R_1 or R_2 (Fig. 1) could be conducted beyond the P-part or not. They were performed 1) on one and the same model, or 2) on two models similarly made and set parallel in opposite direction (Fig. 2). In the former case, the

Fig. 2

effect of the stimulation R_1 was first examined, and after the minimum immersion time necessary for the passage of the wave from left to right (Fig. 1) was determined, the stimulation R_2 was tried to determine the minimum immersion time necessary for the transmission from right to left. The benefit of this method is that the observations are made on one and the same model, but it has a drawback that a fairly long time is needed for a couple of determinations, during which the surface character of the core may more or less alter. In the latter case, the stimulation R_1 is given to one of the models at a certain immersion time, and directly after the effect was observed, the stimulation R_2 is given to the other model. This method saves the time very much but is not good in having two different models. In fact, however, both methods gave the same results.

The stimulation was always done by means of touching the core with a piece of zinc metal.

THE FACTS OBSERVED

1) The irreciprocal conduction:

Let us take the model represented by Fig. 1. An important fact observed is that the activation wave can be transmitted over the P-part from left to right, but not in the opposite direction. This statement is, however, a little rough, because it is not that the transmission from right to left does not take place absolutely. It does so, if the P-part is made a little shorter. But then the conduction gets again irreciprocal, if only the immersion time is made correspondingly shorter. This is what is really meant in the above statement.

Whether the conduction is reciprocal or irreciprocal depends thus on the length of the P-part on one side, and on the duration of the immersion time on the other. It can be made irreciprocal by enlarging the P-part or by limiting the immersion time in

proper magnitude, and if the P-part is made larger than a certain limit, we have an absolute irreciprocal conduction without regard to the length of the immersion time. It is out of question that if the P-part is made too large, even the conduction from left to right is also interrupted.

Two simple examples of observations will be given here:

Example 1. The vessel for the model: 49 cm, 2.5 cm and 1.3 cm in length, breadth and depth respectively.

The nitric acid: Specific gravity=1.39.

The long core: 16 cm long and 0.5 mm thick.

The short core: 7 in number, each being ca 5 cm long and ca 0.5 mm thick.

The P-part: 4 cm in length.

The stimulation: Zinc metal touching.

The moment of immersion: 10^h 30'.

Moment of stimulation	Stimulation	Conduction to the other half	Remarks
10 ^h 40'	R ₁	—	R ₁ is effective at a 20' immersion, while R ₂ is ineffective even at a 50' immersion.
50'	"	—	
11 ^h 5'	"	—	
25'	"	+	
45'	R ₂	—	
12 ^h 5'	R ₁	+	
25'	R ₂	—	
Pause			
13 ^h 15'	R ₂	—	
35'	R ₁	+	

Example 2. Another model similarly constructed. The conditions are the same, except that the P-part is a little shorter.

The moment of immersion: 4^h 30'.

Moment of stimulation	Stimulation	Conduction to the other half	Remarks
4 ^h 40'	R ₁	+	The conduction beyond the P-part occurs in 5' to 10' in the case of R ₁ but not even after 20' in the case of R ₂ .
50'	"	+	
55'	"	—	
5 ^h 5'	"	+	
15'	R ₂	—	
35'	"	—	
45'	R ₁	+	

2) The decrease of the velocity in the region of multiple core:

The activation wave evoked by the stimulation R₁ comes along the single core M (see Fig. 1) with a certain velocity. Now, when the wave gets in the region of multiple core, the component cores are all activated simultaneously and the waves go along together with one and the same velocity, which is much smaller than the previous one. The details of this phenomenon were described in a previous paper (Yamagiwa(2)) together with other phenomena of interaction. Here it will be just mentioned that

the velocity fell down, for example, to 1/2.2, 1/3 and 1/3.5 when the component cores were 3, 5 and 7 in number respectively.

QUANTITATIVE EXAMINATIONS

Whether the wave proceeds on beyond the P-part or not, depends, as mention above, on 1) the immersion time (t), and 2) the length of the P-part (l), provided that the quantity of the acid is kept constant. Now, there is another important factor, that is, 3) the number of the component cores (n) in the part of multiple core. For a certain combination of l and n , there is a certain minimum t , at which the wave can first pass over the P-part. To examine the relation quantitatively, it was planned to measure t systematically for various combinations of l and n . The method adopted is shown schematically in Fig. 3.

Fig. 3

The container for the model was the same as in Example 1). The acid was of a specific gravity 1.36 and was 65 cc in quantity. The length of the core was each ca 20 cm in both halves. As seen in the figure, the multiple (left) and the single (right) cores are connected in the air by means of mercury. For simplicity, just two component cores are shown in the figure, but actually the cases of 3, 5 and 7 components were examined, each component being set ca 2 mm apart from each other. The distance, l , which corresponds to the P-part in Fig. 1, is controlled simply by moving the single core to the right or to the left. Some parts of each core, above and below the liquid surface, were covered with paraffin (Fig. 3, T), which was useful for preventing from chance activations and also for making the distance l distinct. One more thing to be remarked here is that the stimulation R_1 , which is given to any of the component cores, evokes activation in all others simultaneously, but if the connection by Hg is broken, the activation occurs in the stimulated core only, to show the so-called isolated conduction.

We will give here a couple of measurements as examples:

a) The conduction from single to multiple core (Table 1 and Fig. 4)

Table 1.

	$l \backslash n$	7	5	3	1
t_1 (Minimum immersion time measured)	3 mm	5' 55''	5' 5''	5' 10''	4' 40''
	20 mm	13'	10' 45''	10' 15''	8' 15''
	30 mm	>180'	>60'	17' 30''	8' 30''

Fig. 4

b) The conduction from multiple to single core (Table 2 and Fig. 5)

Table 2.

	n	7	5	3	1
t_2 (Min. immersion time measured)	l				
	3 mm	4'	4' 15''	4' 45''	5'
	20 mm	7' 45''	8'	8' 45''	10' 15''
	30 mm	8'	8' 45''	9' 15''	11'

Fig. 5

From these two sets of measurements, the ratio of t_1 to t_2 , that is, the ratio of the minimum immersion time necessary for the transmission from single to multiple core to that from multiple to single core, was made, which is shown in Table 3.

Why the value of t_1/t_2 for the case $n=1$ deviates from unity, is perhaps due to

Table 3.

$l \backslash n$	7	5	3	1
3 mm	1.5	1.2	1.1	0.9
20 mm	1.7	1.3	1.2	0.8
30 mm	>22.5	>6.9	1.9	0.8

the difference in the nature of the cores on both halves of the model. Anyway, it was smaller than unity. If, therefore, correction were made so as to make it unity, all other values of t_1/t_2 will get correspondingly larger. Let it be aside for the moment. Still we can see quite clearly from Table 3 that the ratio t_1/t_2 is always larger than unity, and that it gets larger and larger with larger n and l , even to infinity in extreme cases. Notice, for example, the cases $n=7$ or 5 and $l=30$ mm. These extreme cases are nothing but those of complete irreciprocity. The irreciprocity of the conduction gets thus surer with larger length of the P-part (Fig. 1) and with larger number of the short cores attached. Here we can say perhaps that we have a model for the synapse of various grades of irreciprocity.

We should like to add another type of the model examined (Fig. 6), which looks more like the actual synapse in structure.

Fig. 6, a

Fig. 6, b

Schematic illustration of Fig. 6, a.

- L (2 mm long): The part soldered and paraffinized.
 P (15 mm long): A paraffin block enclosing the free ends of the short cores.
 B (5 cm long): The part of multiple core.

The material for the new model is different from that of the old, so the results obtained do not coincide numerically with the previous ones, but qualitatively they are just the same, namely: the minimum immersion time necessary for the conduction from A to C due to the stimulation R_A was 7' (that of from B to C due to the stimulation R_B was 4'), while that of from C to A due to the stimulation R_C was larger than 40' (exact determination was not carried out). In other words, the conduction from C to B cannot take place even after 40', while the conduction from A to C take place in 7', that from B to C even in 4'. (The difference between the cases R_A and R_B is

certainly due to the existence of the soldered part L, over which the wave has to jump from A, a single core, to B, a multiple core. This part could not be made shorter than 2mm. If it were made zero, the above difference would probably disappear.)

CONSIDERATIONS

The reason why the conduction gets irreciprocal in the model is very simple. When the wave is being transmitted from one half to the other, the activation current flows out of the core on one side of the P-part into the core on the other side. The strength of this current should of course be the same on both sides, but as the core is single on one side and multiple on the other, the current flowing in and out of the single core is n -times as strong as that of each component of the multiple core. Here we find the general reason, why the conduction is sometimes completely and sometimes incompletely irreciprocal, and why the grade of irreciprocity depends on the number of the component cores. We can also see why it depends on the length of the P-part as well, because the P-part is acting as a resistance in the circuit, so, if it is increased, the strength of the current in each component core can become subthreshold much sooner than that in the single core does so.

What on earth will be the state of affairs at the actual ganglion? It is a difficult problem in physiology still now, and we ought to behave ourselves in granting any hasty conclusion about that, but still it is tempting, from the experiences in the model, to imagine a similar structure at the synapse (Fig. 7).

Fig. 7

In Fig. 7, G represents a ganglion cell, N and D the belonging axon and dendrons respectively, and N' the axon of another neurone. In a), N and N' are supposed to be continuous through G like the neuro-fibril in Bethe's theory, and D to be amalgamated at a point, S, of N, while in b), N, D, G and N' are supposed to make a protoplasmic body as a whole. If assumed now that the surface membrane of G is of a very high electric resistance like the sheath of medulated nerve fibres (Tasaki (3)), then G in Fig. 7 will just correspond to the P-part in Fig. 1, and we can naturally expect the irreciprocal conduction to occur without any serious difficulty. The question may be, whether the activity of N' coming down towards G is really capable of exciting every D or not, because the inner resistance of the fibre must be fairly high. It seems, however,

to be quite possible and probable as long as Tasaki's confirmation that the impulses in freshly excised nerve fibres can jump over at least two Ranvier's nodes (Tasaki(4)), is right. Even if his confirmation be wrong, still the activation of D_s can be the case at the moment when the impulse in N' reaches very near the surface of G , if only the uniting point S is situated very near the inner surface of the cell membrane (Fig. 7, a), and much more easily if N' and the cell make a protoplasmic body as a whole (Fig. 7, b). In those cases, the excitation waves in D_s will go in cellulifugal way. It does not matter, because what is needed is the simultaneous excitation of all D_s , but not the direction.

If the exon ends by a terminal arborisation to the cell body, the general configuration will be schematically something like Fig. 8, a) or Fig. 8, b), according to

Fig. 8

whether the protoplasmic union exists or not between the fibres and the cell. In those cases the matter becomes very much easier, because there is no doubt that the impulse coming down along N' will spread into all D_s . It was confirmed experimentally, too, in one of the possible cases represented in Fig. 8, a) (see Fig. 6).

Man can further imagine various configurations of D in relation to N and N' , among which a special couple seem to be worth while to be noted here (Fig. 9). In Fig. 9, a), all the dendrons are situated concentratedly near a pole of the cell, while in Fig. 9, b) distributed along the cell surface. In the former case, the con-

Fig. 9

duction will be irreciprocal, as described before, because of the large distance, l , between N and D , while in the latter case, the conduction can be reciprocal, because,

the distances l_{1-4} being small, the wave can be transmitted from N to N' as well as from N' to N through the successive activations of the Ds in between. In those cases, the spacial distribution of D in relation to N (N') is the unique cause of reciprocity or irreciprocity of the conduction.

That which was described above as to the actual synapse is nothing but imaginations lacking of a number of anatomical as well as physiological examinations to be done. But still it is very suggestive and also interesting that they make us understand quite easily the most peculiar facts at the synapse, that is, the irreciprocal conduction and the delay of the propagation there, fairly well, and that, moreover, they can harmonize the neurone theory and the fibril theory by pointing out the possibility of irreciprocal conduction even in a continuous structure.

SUMMARY

Modifying Lillie's nerve model a little bit, a model for the synapse, which is something like the actual synapse in structure, was devised. The points are as follows:

- 1) Some middle part of a long core was made multiple by attaching a few short cores there. The connection was done metallicly, and a certain portion near the connection was covered with paraffin (to be immersed in nitric acid) or exposed to the air. This is the general condition necessary for obtaining the irreciprocal conduction.
- 2) The grade of irreciprocity gets larger with larger length of the paraffinized or the air-exposed part of the core, on one side, and with larger number of the component cores at the part of multiple core, on the other.
- 3) The conduction velocity in the multiple core is much smaller than that in the single core.
- 4) It was discussed that the ventril-mechanism of the synapse and the large conduction time there might be due to the structure similar to that of the model.

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The expenses for this work were defrayed by the grant of the Notional Research Council of Japan.