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THE EFFECT OF ELECTROLYTE DEFICIENCY ON THE RATE OF CONDUCTION IN A SINGLE NERVE FIBRE

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It has been shown by Hodgkin (1939) that a change of resistance on the outside of a nerve fibre is followed by a change in conduction velocity. This effect was obtained (i) by altering the volume of saline surrounding the fibre, (ii) by placing a metal shunt in parallel with it. In the present paper, similar changes of conduction velocity are described following the replacement of electrolytes by sucrose.

METHOD

Isolated nerve fibres from the meropodite of the walking limb of *Carcinus maenas* were used. The technique of dissection and of immersing a portion of the fibre in saline or paraffin oil was similar to that described by Hodgkin (1938, 1939). The arrangement of stimulating and recording electrodes is shown in Fig. 1. Brief thyratron discharges were applied through platinum wires, and the action potential was recorded at two places (*CD* and *EF*, Fig. 1) just before it entered, and after it emerged from, the tested portion of the fibre. The solution consisted of a mixture of volumes of sea water and 1·0 molal sucrose (1 g.mol. sucrose to 1000 g. H_2O) which is approximately isotonic with sea water. The loop of fibre between *D* and *E* was held taut at its centre by a fine glass hook. The upper portions of the fibre, surrounded by a film of sea water, remained in paraffin oil throughout the experiment. The fibre was lowered into the required solution until the interface touched the electrodes *D* and *E*. It was then lifted slightly until interface and electrodes *D* and *E* were separated by about 0·5 mm., and the action potential was recorded in this position. The whole fibre was then lifted into paraffin oil and the action potential recorded again. Attention was paid mainly to the comparison of velocities in 'oil' and 'solution', with any given saline/sucrose mixture, as this comparison should be unaffected by membrane changes induced by electrolyte deficiency (see, however, Discussion). As the distances between *C* and *D*, and *E* and *F* were only

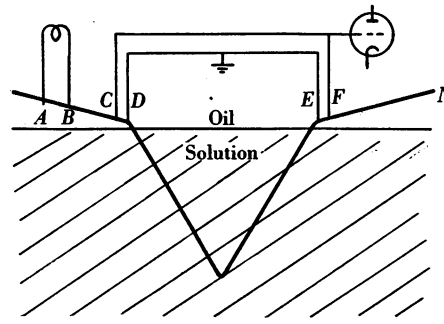

Fig. 1. *N*, *Carcinus* nerve fibre. *A*, *B*, stimulating electrodes. *C*, *D* and *E*, *F*, two pairs of recording electrodes. The fibre was held at the ends by screw-controlled pairs of forceps and was depressed at its centre by a glass hook (not shown).

about 0·5 mm., quick diphasic spikes were recorded which crossed the base-line at a high rate (cf. Schmitt, 1939). The distance between the two points of intersection with the base-line could be measured very accurately, and conduction times could thus be determined to within 10 μsec.

To compare the conduction velocities in 'oil' and 'solution', the time for conduction between the mid-points of *CD* and *EF* respectively and the interface, 0·75 mm. away, must be deducted from the total conduction time. For example, if the total distance between the mid-points of *CD* and *EF* was 15·5 mm., and the conduction time of the 'sea-water axon' 2·52 msec. with the loop in saline, but 4 msec. with the loop in oil, a deduction of 0·4 msec. (conduction in oil over 1·5 mm. of fibre) must be made from both values to obtain an accurate ratio of velocities in oil and saline. When, for example, a 50% sucrose/sea-water mixture is used, the deduction becomes somewhat larger (0·53 msec. in the case of Table 1 below), because the velocity of the impulse between the interface and *D* (or *E*) is rather less. In Table 1, both original and corrected ratios of impulse velocities are shown.

The electric resistance of saline/sucrose mixtures was determined in a conductivity cell with alternating current of 300 and 600 cyc./sec. The relative resistivities of the solutions are shown in the appropriate tables below.

RESULTS

The results are illustrated in Fig. 2 and Tables 1 and 2. In Fig. 2 the following points require attention: (i) If one follows the upper horizontal set of records

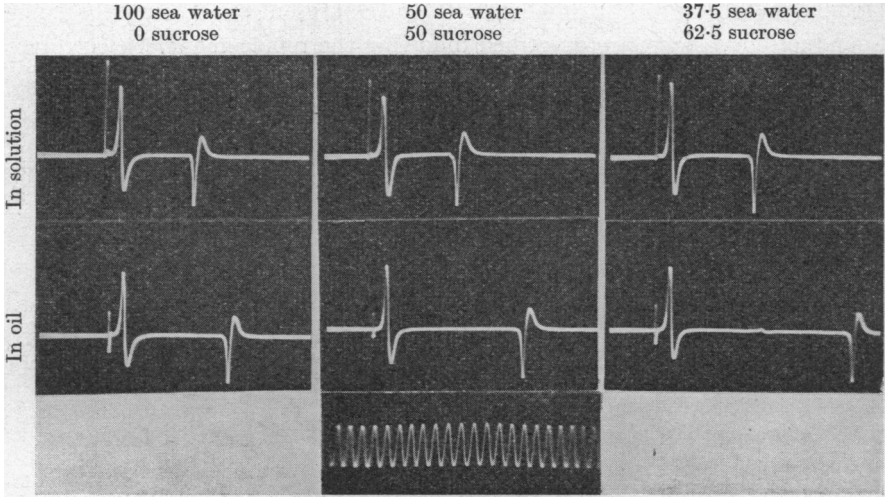

Fig. 2. *Carcinus* nerve fibre at 21° C. 15·5 mm. conduction distance. *Upper* set of records: axon in a large volume of solution. *Lower* set of records: axon in paraffin oil. Time marks: 2000 cyc./sec.

from left to right, it is seen that electrolyte deficiency has only a slight effect on the impulse rate, provided the fibre is kept in a large volume of solution. (ii) There is, however, a very marked reduction of velocity, with increasing sucrose content, if the fibre is surrounded by oil (lower row). Examining each vertical pair of records, we see that a *volume reduction* of the external solution has a much more pronounced effect when the salinity is low. The quantities of the velocity changes are shown in Tables 1 and 2, where they are expressed as

ratios of the conduction times. A summary of several experiments is given in Tables 3 and 5.

TABLE 1. Single *Carcinus* axon. 21° C. Total conduction distance 15·5 mm., corrected for 1·5 mm. conduction 'in oil'. Uncorrected velocity changes are shown in brackets

Sea-water/ sucrose volume ratio	Relative resistivity of solution	Conduction times in msec. Uncorrected 'Solution'	Uncorrected 'Oil'	Corrected 'Solution'	Corrected 'Oil'	Ratio of conduction velocities 'Solution' to 'oil'	Ratio of conduction velocities 'Sea water' to 'solution'
100/0	1	2·92	4·0	2·52	3·6	1·43 (1·37)	—
50/50	2·46	3·15	5·96	2·62	5·43	2·07 (1·90)	1·04 (1·08)
37·5/62·5	3·39	3·65	8·04	2·98	7·37	2·48 (2·20)	1·18 (1·25)
28/72	4·55	4·5	11·6	3·6	10·7	2·97 (2·58)	1·42 (1·54)
100/0	1	2·94	4·1	2·53	3·69	1·46 (1·40)	—

TABLE 2. Single *Carcinus* axon. 21·5° C. Total conduction distance 14·7 mm., corrected for 1 mm. conduction 'in oil'

Sea-water/ sucrose ratio	Relative resistivity of solution	Conduction times in msec. (for 13·7 mm.) 'Solution'	Conduction times in msec. (for 13·7 mm.) 'Oil'	Ratio of conduction velocities 'Solution' to 'oil'	Ratio of conduction velocities 'Sea water' to 'solution'
100/0	1	2·5	3·14	1·255	—
50/50	2·46	2·64	4·19	1·585	1·055
36/64	3·52	2·76	5·08	1·84	1·105
26/74	5	3·2	6·6	2·06	1·28
18/82	7·3	3·83	9·2	2·40	1·53
13/87	10·75	4·88	Blocked	—	1·95
9/91	14·8	Blocked	Blocked	—	—
100/0	1	2·95	3·66	1·24	—

These results are in agreement with Hodgkin's (1939) findings and, in a qualitative way, might have been predicted on the basis of the electrical theory of propagation (e.g. Rushton, 1937). The results seem accurate enough to justify a somewhat more detailed analysis and a quantitative comparison with theory.

Henceforth the following symbols will be used:

v = impulse velocity.

r_i = resistance of axoplasm.

r_w = effective external resistance, with the fibre in a *large volume of normal sea water*.

r_0 = external resistance, with the fibre surrounded by a *film of normal sea-water* and immersed in *paraffin oil*.

According to the local circuit theory (e.g. Rushton, 1937; Offner, Weinberg & Young, 1940), v is inversely proportional to $\sqrt{(r_i+r_0)}$, hence a change of outside resistance should affect the impulse velocity in the manner described by equation (1)

$$\frac{v}{v'}=\sqrt{\frac{r_i+r_0'}{r_i+r_0}}, \qquad (1)$$

where v and v' are the conduction velocities, r_0 and r_0' respectively being the longitudinal resistances on the outside.

Now, one cannot expect this simple relation to apply to the case of electrolyte withdrawal, for it is unlikely that this would leave the properties of the membrane unaffected. On the other hand, with any given chemical composition of the bath, a change of the conducting outside volume (e.g. transfer from 'solution' to 'oil') might be expected to have no other effect than simply to reduce the external conductance, and to this, equation (1) should apply.

Let us consider the results for *seawater* and *½-sucrose* shown in Table 1. First, the conduction rate falls by only 4% when the axon is transferred from a large volume of sea water to a large volume of ½-sucrose. In either case the effective external resistance might be regarded as negligible, compared with that of the axoplasm, and the slight drop of velocity might be wholly due to membrane alteration. Alternately, the external resistance may not be negligible, and the 4% change would then be partly, or perhaps entirely, due to an external conductance change. Both assumptions will be examined.

A. If r_w is negligible, we obtain for *sea water*, comparing the velocities in 'oil' and 'solution'

$$\sqrt{[(r_i+r_0)/r_i]}=1{\cdot}43, \tag{2}$$

hence

$$r_0/r_i=1{\cdot}05.$$

From this, we can calculate the velocity change which should occur on transferring the '*½-sucrose axon*' from 'solution' to 'oil'. With ½-sucrose (external resistivity being 2·46 times that of sea water) we obtain

$$\sqrt{[(r_i+2{\cdot}46r_0)/r_i]}=\sqrt{3{\cdot}58}=1{\cdot}9.$$

Thus the velocity should be reduced to 1/1·9. The observed change was to 1/2·07. In Table 3, the results of seven experiments are shown to which this calculation has been applied. The observed effect is, on the average, slightly greater than the calculated, though the agreement is reasonably good.

TABLE 3. Comparison of observed and calculated velocity changes, from 'solution' to 'oil', with ½-sucrose. r_w is assumed to be negligible

	Ratio of velocities in 'solution' and 'oil'							Mean
Sea water	1·43	1·24	1·28	1·31	1·43	1·255	1·415	1·34
½-Sucrose: Obs.	2·07	1·50	1·585	1·815*	1·94	1·585	1·90	1·77
Calc.	1·90	1·54	1·61	1·70*	1·90	1·55	1·87	1·725

* In this experiment a 20% hypertonic sucrose stock solution was used.

B. The effective external resistance in a large volume may be appreciable, and although it is difficult to estimate its true value, an upper limit can easily be found. If we assume that the 4% velocity change on transfer from sea water

to $\frac{1}{2}$-sucrose is wholly due to an increase of external resistance, we can find the limiting value of r_w/r_i as follows:

$$\sqrt{\frac{r_i+2{\cdot}46r_w}{r_i+r_w}}=1{\cdot}04,$$

hence $$r_w \leqq 0{\cdot}058 r_i.$$

Using this extreme value of r_w and recalculating the velocity change from 'solution' to 'oil' we find

for sea water $$\sqrt{[(r_i+r_0)/(r_i+r_w)]}=\sqrt{[(r_i+r_0)/1{\cdot}06r_i]}=1{\cdot}43,$$

hence $$r_0/r_i=1{\cdot}17;$$

and for $\frac{1}{2}$-sucrose

$$\sqrt{[(r_i+2{\cdot}46r_0)/(r_i+2{\cdot}46r_w)]}=\sqrt{(3{\cdot}88/1{\cdot}148)}=1{\cdot}84,$$

which does not differ much from the ratio (1·9) calculated in § A.

With higher concentrations of sucrose, the calculated results are more seriously affected by the assumed value of r_w. As 6% appears to be an extreme value of r_w/r_i (§ B), the calculations in Tables 4 and 5 were based on two alternative assumptions, (*a*) that r_w is completely negligible, as argued in § A above, and (*b*) that r_w/r_i equals 3%.

TABLE 4. Comparison of observed and calculated effects, using the results of Tables 1 and 2

Relative saline content (sea water = 100)	Relative resistivity	Ratio of velocities in 'solution' and 'oil': Observed	Calculated: (*a*) $r_w/r_i=0$	Calculated: (*b*) $r_w/r_i=0{\cdot}03$
		Experiment of Table 1		
100	1	1·43	—	—
50	2·46	2·07	1·9	1·87
37·5	3·39	2·48	2·14	2·08
28	4·55	2·97	2·41	2·31
		Experiment of Table 2		
100	1	1·255	—	—
50	2·46	1·585	1·55	1·54
36	3·52	1·84	1·74	1·70
26	5	2·06	1·97	1·90
18	7·3	2·40	2·27	2·14

TABLE 5. Mean values of observed and calculated velocity changes

No. of experiments	Relative saline content (sea water = 100)	Relative resistivity	Mean ratio of velocities in 'solution' and 'oil': Observed	Calculated: (*a*) $r_w/r_i=0$	Calculated: (*b*) $r_w/r_i=0{\cdot}03$
7	100	1	1·34	—	—
7	50	2·46	1·77	1·725	1·695
5	37	3·45	2·06	1·94	1·88
4	28	4·55	2·32	2·18	2·09
3	20	6·45	2·42	2·40	2·27

On the whole, the observed slowing of the impulse 'in oil' is somewhat greater than calculated, though, taking the average values in Table 5, the discrepancies are not striking.

DISCUSSION

As the electrolytes are progressively replaced by sucrose, the impulse is slowed, and eventually blocked, even in a large bath of the solution (Tables 1 and 2). These changes, at least with a salt reduction to less than $\frac{1}{3}$, cannot be accounted for by an increase in external resistivity, even if an improbably high value of r_w/r_i is assumed, and they are presumably due to a change in the membrane properties.

When the axon is transferred from 'water' to 'oil', there is a more marked slowing of propagation, most of which seems to be due to an increase of external resistance. But in some experiments, after fairly drastic salt withdrawal, there appears to be a residual effect which is not fully covered by a simple resistance change. A possible explanation of this discrepancy is provided by recent work of Hodgkin & Huxley (1946). During activity a leakage of potassium from the axoplasm occurs, accompanied by a lowering of the membrane resistance. It is possible that withdrawal of electrolytes disturbs the membrane and causes potassium and perhaps other substances to leak from the fibre until a new steady state is established (see e.g. Höber, 1945; Erlanger & Blair, 1938). If such leakage occurred, it would alter the electrical membrane properties (resting potential, transverse resistance and 'threshold') and, therefore, affect the impulse velocity. Moreover, the leaking substances would accumulate when the fibre is immersed in oil and thus have a greater effect than when it is bathed in a large volume of solution.

Such complicating factors should perhaps be expected when working with salt-deficient, or other abnormal, solutions. It is noteworthy, however, that the anomalous effects do not become appreciable until the salt deficiency exceeds some 60%. There is, therefore, no reason to doubt that in Hodgkin's (1939) experiments, where a normal, balanced, medium was used, the change from 'water' to 'oil' was due entirely to an increase of external resistance.

SUMMARY

1. The effects on conduction rate of electrolyte deficiency and of resistance changes on the outside of a non-medullated nerve fibre (*Carcinus maenas*) are studied.

2. Transferring the axon from sea water to sucrose/sea-water mixtures reduces the conduction velocity progressively as the salinity is reduced.

3. This effect is relatively slight if the fibre is surrounded by a large volume of solution, but very pronounced if the axon is immersed in paraffin oil.

4. Attention is paid to the slowing of conduction on transferring the fibre from a bath of solution to paraffin oil, with any *given* salinity of the medium. Assuming that only the external resistance is affected by this transfer, the slowing of the impulse is calculated from the local circuit theory.

5. There is reasonable agreement between observed and calculated velocity changes, though often the observed changes are somewhat larger.

6. If, in electrolyte-deficient media, a leakage of potassium and perhaps other substances were to occur, which accumulated when the fibre was immersed in paraffin oil, this extra slowing would be explained.

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