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A METHOD FOR STUDYING THE EFFECTS OF IONS AND DRUGS ON THE RESTING AND ACTION POTENTIALS IN SMOOTH MUSCLE WITH EXTERNAL ELECTRODES

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A number of papers have dealt with the effects of drugs on the rate and height of action potentials in smooth muscle (cf. Bozler, 1948; Bülbring, 1956), but there are relatively few descriptions of changes in the resting potential. This is probably because an external electrode technique has not been available and resting potential measurements with internal electrodes are difficult to make, owing to the small size and spontaneous motility of the smooth muscle fibres (Bülbring, 1955).

A few years ago Stämpfli (1954) described a relatively simple method for measuring the full value of the resting potential with external electrodes. His method is based on the theoretical calculation that the full value of the membrane potential can be measured with external electrodes on a core conductor, when the short-circuiting is negligible (Hodgkin & Rushton, 1946). Stämpfli obtained this condition by increasing the outside resistance of the preparation in the interpolar region by replacing most of the ions in the interstitial fluid with a nearly ion-free sucrose solution. This method has so far been applied to bundles of myelinated nerve fibres (Stämpfli & Straub, 1954), and to non-medullated fibres (Ritchie & Straub, 1956, 1957), where action potentials were also recorded. The present paper deals with the application of this technique to smooth muscle.

METHODS

Most experiments were done on smooth muscle strips taken from the taenia coli of the guinea-pig. They were 10–15 mm long and 0·5 mm in diameter. The strips contracted strongly on removal from the gut but were stretched to their '*in situ*' length when mounted in the apparatus. At this size the taenia coli exhibits little tension (Bülbring, 1955). In addition, a number of preparations

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were obtained from the longitudinal muscle coat of the small intestine of the pike, frog, rabbit, rat, guinea-pig and cat and of the rectum of the trout. These preparations were dissected according to the method described by Evans & Schild (1953). All strips used were teased off from larger pieces and never cut to size. Not more than 10 min were required to dissect and mount the preparations in the apparatus. The results obtained with preparations from different animals were so similar that they have not been dealt with separately.

The strips were mounted in the apparatus described by Stämpfli (1954), and in more detail by Straub (1956*a*) so that they lay in a horizontal insulating tube containing isotonic sucrose solution, while each end was suspended in a vertical tube through which Locke's solution flowed. A pair of Ag–AgCl electrodes, connected over a KCl–Agar bridge to the Locke's solution, recorded the potential difference between the two sucrose–Locke junctions. The electrodes were connected to a pair of cathode followers and the potential difference, amplified by a direct-coupled amplifier, was displayed on a cathode-ray tube, and recorded on a moving film.

The Locke's solution used for the mammalian preparations contained (mM) NaCl, 154; KCl, 5·6; $CaCl_2$, 2·2; $NaHCO_3$, 1·9; dextrose, 5. The Ringer's solution used for preparations taken from cold-blooded animals contained (mM) NaCl, 119; KCl, 1·9; $CaCl_2$, 1·1; $NaHCO_3$, 2·2; dextrose, 5. Solutions with higher potassium concentration were obtained by replacing an equivalent amount of sodium chloride by potassium chloride. In addition, a 'sulphate-Locke's solution' was used, in which the chloride ions had been replaced by sulphate ions and the calcium increased to 10 mM. It was necessary to add an excess amount of calcium to the sulphate-Locke's solution so that in the final solutions, made up by mixing Locke's with sulphate-Locke's solution, the amount of free calcium ions calculated from the solubility product $6{\cdot}1 \times 10^{-5}$ (Landolt & Börnstein, 1923) varied by not more than 0·5 mM, except in solutions with less than 80 mM chloride. Throughout the whole course of the experiment all solutions were equilibrated with 95% O_2 and 5% CO_2. The pH of the Locke's and the sulphate-Locke's solution was 6·5, that of the Ringer's solution 7·0. The isotonic sucrose solutions flowing through the horizontal insulating tube of the apparatus contained sucrose (A.R.), 10% (w/v) for mammalian preparations and 7·3% for cold blooded preparations, in distilled water which had been passed over ion-exchange resin. Both had a specific resistance of more than 10^5 Ωcm. The fluid in the vertical tube on one side of the chamber was kept at room temperature (17–20° C.) so that the muscle remained inactive, thus maintaining a stable potential against which the test solution in the other vertical tube, kept at body temperature, could be compared.

RESULTS

Assuming that the smooth-muscle preparation acts as a core conductor when mounted between two recording electrodes, an increase of the outside resistance produced by the flow of the sucrose solution would be reflected by the increase in the amount of depolarization produced by a standard potassium chloride solution applied to one side of the preparation. This supposition was tested in four experiments where it was found that the depolarization increased during the first 25 min, and during the next 4 hr it declined slowly to about two-thirds of its peak value. This implied that the penetration of the sucrose solution was near completion after the first 25 min, while the decline which followed was probably due to a progressive deterioration of the preparation. For this reason no records were taken from muscle strips exposed for more than 4 hr.

When the preparations were placed in the apparatus at 37° C they usually showed bursts of uneven spike activity as shown in Fig. 1. In some experiments, however, the spikes became larger and more regular. The shape of the

spikes was similar to that described by Bülbring (1957) and Holman (1957*a*) showing an initial slow phase of depolarization and a rapid repolarization with after-hyperpolarization.

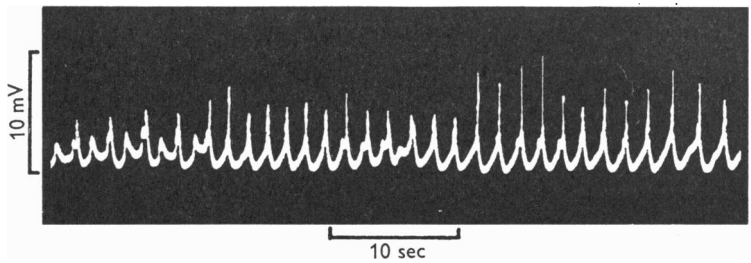

Fig. 1. Spontaneous irregular spike activity recorded from a strip of guinea-pig taenia coli by the sucrose-gap method. Temperature 35° C.

Effects of changes in ion concentration

Potassium ions. Solutions with a high potassium concentration produced a depolarization which was almost complete within 10–20 sec. On returning to Locke's solution an initial rapid repolarization was followed by a slow rise in potential which lasted about 60 sec until the original level was reached. A characteristic trace of such an experiment is shown in Fig. 2.

Preparations were bathed in a series of solutions containing different potassium concentrations. The relation between the depolarization produced and the logarithm of the potassium concentration is shown in Fig. 3, where the values obtained from a rabbit taenia coli and a trout rectum are plotted. The measurements were taken after the preparation had been bathed in the new solution for about 3 min. Table 1 summarizes results from eight experiments on various preparations showing depolarization by isotonic potassium chloride. The depolarization produced by isotonic potassium chloride was not more than 30 mV, and the steepest part of the curve in Fig. 3 gives a slope of 26 mV per tenfold change in potassium concentration.

When, instead of isotonic potassium chloride, potassium sulphate was used, a much greater depolarization was obtained (Table 1). The value of 51·6–60·6 mV which we found is close to the resting potential of 60 mV, measured with internal electrodes for *in situ* length taenia coli (Bülbring, 1954).

Apart from the changes in resting potential produced by increase in potassium concentration, fast regular spike activity developed gradually, decreasing in amplitude as the depolarization proceeded. After a potential fall of about 12 mV no further spike activity was observed and on recovery in Locke's solution the spikes reappeared as illustrated in Fig. 4.

Chloride ions. When the effect of decreasing the chloride concentration was investigated, chloride was substituted by sulphate, since it is known for

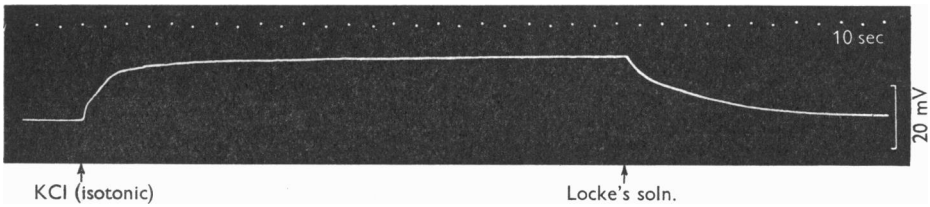

Fig. 2. Influence of isotonic potassium chloride on the resting potential recorded from a longitudinal muscle strip from the pike intestine. Upward deflexion represents depolarization. Temp. 18° C.

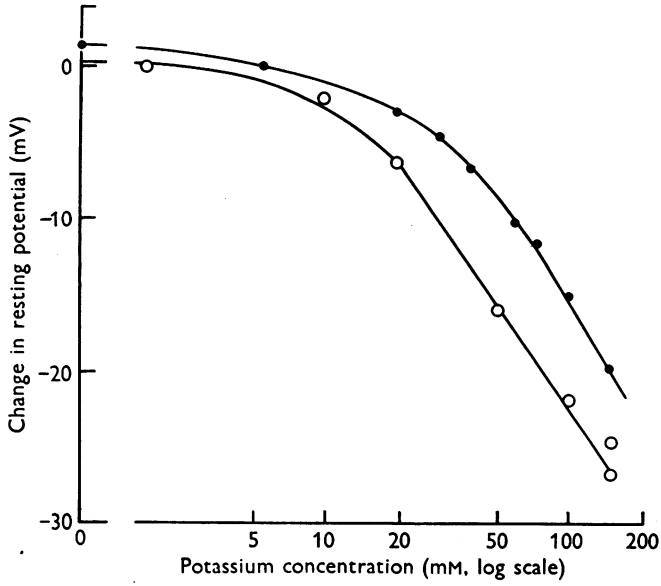

Fig. 3. The relationship between the logarithm of the potassium concentration and the depolarization produced in (*a*) rabbit taenia coli (●), and (*b*) longitudinal muscle strips from the trout rectum (○). Slope per tenfold change = 26 mV. Temp. 18° C.

TABLE 1. Depolarization produced by isotonic potassium chloride and sulphate.

Preparation	Temp. (°C)	Depolarization (mV) in isotonic KCl solution	Depolarization (mV) in isotonic K_2SO_4 solution
Trout rectum	16	23·6 (17·2–32·5)	—
Trout rectum	18	26·2	—
Pike intestine	16	19·3 (13·1–23·6)	—
Rabbit taenia coli	22	23·9 (20·0–30·5)	55·2 (51·7–58·7)
Guinea-pig taenia coli	25	21·3 (16·5–24·8)	56·1 (51·6–60·6)
Guinea-pig taenia coli	35	22·0	54·0
Guinea-pig taenia coli	35	20·0	—

striated muscle that this larger anion does not diffuse through the membrane (Boyle & Conway, 1941; Hodgkin & Horowicz, 1957). The solutions we used were made up by mixing different proportions of Locke's solution with one in which all the chloride ions were replaced by sulphate ions.

Solutions with a decreased chloride concentration caused a rapid depolarization which was complete in 1 min. The relation between the chloride concentration and the change in the resting potential is shown in Fig. 5. A tenfold decrease in the chloride concentration caused a 41 mV fall in potential. In addition to the change in resting potential, chloride concentrations of 100 and 75 mM produced bursts of regular spike activity.

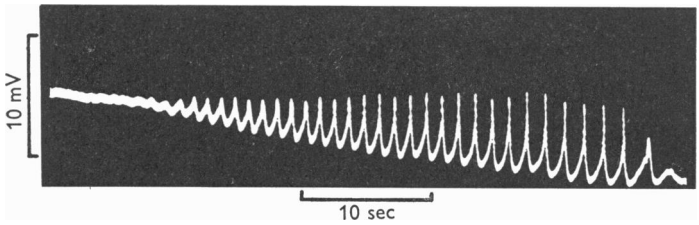

Fig. 4. Regular recovery spikes produced after depolarization by KCl solution (80 mM). Taenia coli preparation. Temp. 35° C.

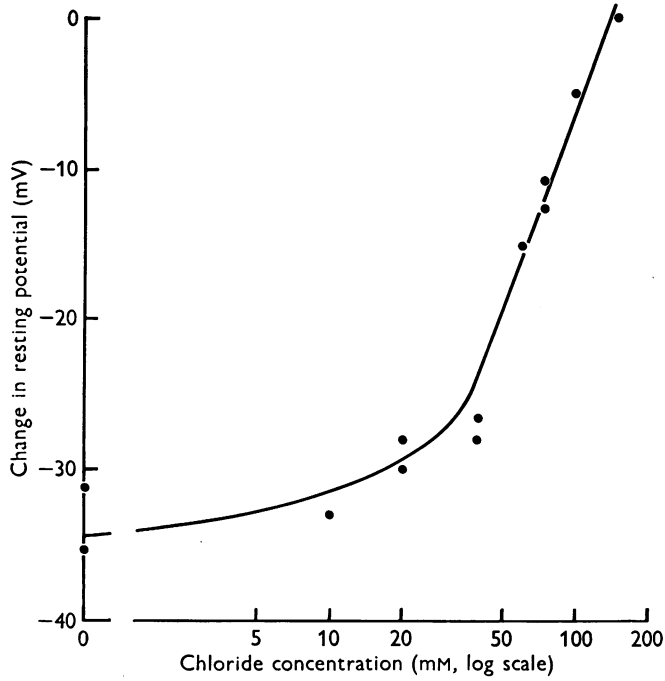

Fig. 5. The relationship between the logarithm of the chloride concentration and the depolarization produced in guinea-pig taenia coli. Slope per tenfold change = 41 mV. Temp. 18° C.

Lack of calcium ions. The effect of calcium-free Locke's solution was a depolarization amounting to about 13 mV. A typical experiment is illustrated in Fig. 6. This figure shows that the time for complete depolarization was about 1 min, whereas the recovery in Locke's solution took only about 30 sec. The resting potential recovered to a value 5 mV higher than the initial level in Locke's solution. The changes in polarization seen in Fig. 6 are similar to those observed for nerve fibres by Stämpfli & Nishie (1956) and by Straub (1956*b*).

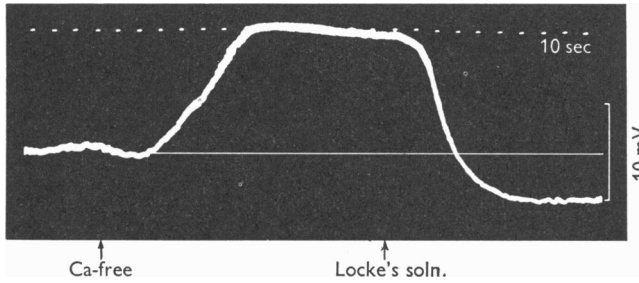

Fig. 6. The effect of calcium-free Locke's solution on the resting potential recorded from guinea-pig taenia coli. Temp. 18° C. The inserted base line signifies the position of the mean resting potential before the application of the calcium-free solution; deflexion upwards, depolarization.

Effects of drugs

Acetylcholine. Concentrations of 10^{-6}–10^{-7} g/ml. acetylcholine were used. When the acetylcholine solution reached the preparation there was an initial slight fall of the resting potential, followed after some seconds by the sudden appearance of large regular spikes of about 12 mV at a frequency of 1·6/sec. This spike activity lasted for about 20 sec, after which the spikes gradually decreased in amplitude. During this time the resting potential showed a slow fall to a new level, where it remained. A typical record is shown in Fig. 7, taken from an experiment in which there was no spike activity before the application of the acetylcholine.

When some spike activity was already present before the application of the drug, the main effect of actylcholine consisted of an increase of spike frequency from 0·9 to 1·6/sec, together with depolarization (Fig. 8). This is the effect which has been described by Bülbring (1957) with intracellular electrodes.

In five experiments a depolarization ranging from 4 to 8 mV was produced by acetylcholine (10^{-6}). When the preparation was then washed in Locke's solution, the potential slowly returned to its original level or to a somewhat higher value.

Choline. In one experiment (Fig. 9) a solution was used in which all the sodium chloride was replaced by an equivalent amount of choline chloride. This solution produced an initial depolarization of 10 mV, followed after 1 min

by a burst of regular spikes lasting 40 sec. During this burst of activity the resting potential was still low but afterwards it increased gradually. It is rather surprising that spikes occur in a sodium-free solution. This finding suggests that smooth-muscle fibres may produce action potentials in a similar way to that described by Fatt & Katz (1953) for crab muscle, where large spikes were observed in sodium-free 'choline-Ringer'. An obvious question,

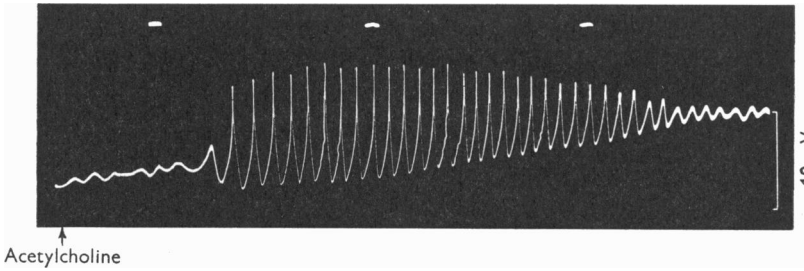

Fig. 7. Resting potential changes and regular action potentials produced by the application of acetylcholine (10^{-6}) on guinea-pig taenia coli. Temp. 34° C; time 10 sec.

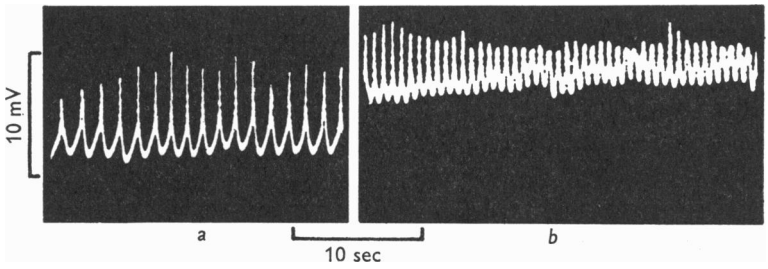

Fig. 8. (*a*) Effect of ACh (10^{-7}) on guinea-pig taenia coli, showing spontaneous activity. (*b*) Result after 3 min where there was a depolarization of 6·5 mV and a marked increase in spike rate. Temp. 36° C.

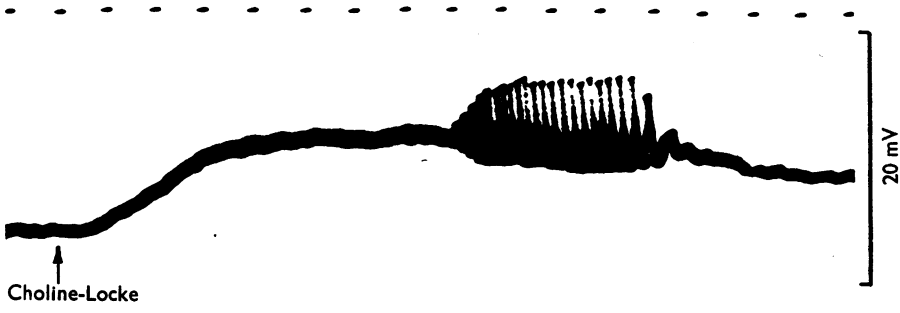

Fig. 9. Change in resting potential and regular spikes produced by the application of a sodium-free 'choline-Locke's' solution to guinea-pig taenia coli. Temp. 35° C, time 10 sec.

as already pointed out by Fatt & Katz, is whether there may not have been retention of sodium ions in the space immediately surrounding the fibre membrane. This question cannot yet be definitely answered. In the same experiment, however, the effect of other solutions was complete in 30 sec. Similar results with low sodium were recently obtained on smooth muscle by Holman (1957*a*). She found that the spikes disappeared only after a prolonged soaking in sodium-free solutions, and that normal spikes still occurred in a solution containing only 17 mM-Na.

DISCUSSION

Our results show that the method for measuring resting potentials described by Stämpfli (1954) is applicable to smooth muscle. It was possible to measure the changes in the resting potential produced by ions and drugs. The values found were similar to those measured by the micro-electrode technique (Bülbring, 1954, 1956; Holman, 1957*a*). In addition, we recorded spike activity, the frequency and height of which was altered by drugs and ions. Our technique allows a quick change of the bathing solution, since the solutions are continuously flowing. Therefore the whole sequence of changes in resting potential and spike activity caused by the test solutions could be continuously recorded.

The question naturally arises, how can one record from smooth muscle with external electrodes 7 mm apart, when the muscle between the electrodes is bathed in a high-resistance sucrose solution. As the length of a single muscle fibre is only from about 50 to 100 μ (E. Bülbring, personal communication) the recording electrodes are separated by a large number of muscle fibres bathed in the sucrose solution. One possibility is that the sucrose solution fails to replace all the ions lying in the inter-fibre spaces, so that a low-resistance bridge exists between them. Another possibility is that there is some kind of electrical connexion between the individual fibres, since it is known that smooth-muscle fibres do not behave as single independent units. For instance, Engelmann (1870) showed that there is a correlation between the contraction of different fibres. This is also seen by the propagation of action potentials along smooth muscle which, according to Bozler (1948), cannot be explained by a nervous mechanism. This hypothesis has recently been confirmed on nerve-free preparations by Evans & Schild (1953, 1956). Finally, Prosser, Sperelakis & Bergmann (1955) suggested that smooth-muscle fibres are linked by regions of low impedance. It may be on account of this property of smooth muscle that we were able to record potential changes with the sucrose-gap method.

One may argue that artifacts due to junction potentials complicate the interpretation of results obtained with this technique when measuring changes in resting potential produced by different ion concentrations. At the interface between the sucrose solution and the Locke's solution there is a junction

potential of about 35 mV, as calculated from the formula given by Henderson (1907, 1908), and the ion-mobilities given in Landolt-Bönstein's tables (1936). Further, when isotonic potassium chloride is applied this junction potential drops to 3·5 mV, the potassium-treated side being negative. However, only a small fraction of the difference between these two junction potentials will be recorded if there is little short-circuiting by the external medium. The exact value of this fraction cannot be estimated as we lack detailed information about the value of the short-circuiting factor. For most of the effects we observed the junction-potential artifacts can almost certainly be excluded because: (1) concentrations of drugs, too small to alter the junction-potential, produced changes in the potential between the electrodes as high as 10 mV; (2) replacement of the Locke's solution by a calcium-free Locke's solution was followed by a 13 mV change of potential, although this does not appreciably alter the value of the junction potential; (3) replacement by 'choline-Locke's solution' resulted in a lowering of the recorded potential, whereas the junction potential is increased; (4) although replacement by sulphate solutions and solutions with increased potassium concentrations caused depolarization and the calculated change in the junction potential would be in the same direction, the depolarization in potassium chloride could not be to any great extent due to the junction potential, since the depolarization was found to show the steepest increase in the high potassium concentrations, whereas the calculated junction potential changed only very slightly at these concentrations.

The depolarization which we found with isotonic potassium chloride was relatively low but of the same order as the depolarization obtained by previous workers in corresponding experiments on smooth muscle. We found that the depolarization was not more than 30 mV, both for cold- and warm-blooded animals, and that the steepest part of the curve relating depolarization to the potassium concentration (Fig. 3) showed a 26 mV depolarization for a tenfold increase in the potassium concentration. Holman (1957*b*) observed a 32 mV fall per tenfold change in K concentration for taenia coli muscle using the micro-electrode technique. In frog striated muscle, however, Ling & Gerard (1950) found that isotonic potassium chloride produced an 80 mV depolarization and that a tenfold change of potassium resulted in a potential fall of 44 mV. Burgen & Terroux (1953) working on heart muscle recorded a 50 mV depolarization with isotonic potassium chloride and a 38 mV slope per tenfold change. If the resting potential were only governed by the distribution of potassium ions on either side of the membrane, a tenfold change in the outside potassium concentration should give a 58 mV potential change. The deviation of the measured membrane potential change from this theoretical value is known to be due to the permeability of the membrane to other ions than potassium, such as sodium or chloride (Hodgkin & Katz, 1949; Adrian, 1956). Recently Hodgkin & Horowicz (1957) found that the part played by chloride

ions can become important when the potassium concentration is suddenly changed and the chloride left unaltered. In this condition the chloride may temporarily dominate the membrane potential, until the chloride concentration inside the fibre has changed in accordance with the potassium potential. This may explain why we found a relatively small fall in potential when only the potassium concentration was changed and the chloride remained at high constant level. The importance of chloride ions in maintaining the resting potential in smooth muscle explains also why a depolarization of the order of the resting potential could be recorded when the muscle was treated by isotonic potassium sulphate. We found under these conditions a depolarization of 54–58 mV, which is very close to the resting potential of 60 mV measured by Bülbring (1954) with intracellular electrodes.

Apart from the changes in the resting potential, we have observed both regular and irregular spikes. Although it is difficult to estimate the number of muscle cells from which action potentials are recorded, the irregular spike activity observed in Locke's solution suggests that records were being obtained from a number of cells firing off fairly independently. The finding that on the application of acetylcholine or potassium chloride the action potentials became large and regular suggests that the cells in contact with the electrodes were firing fairly synchronously. The largest spikes we recorded were about 14 mV, which is less than the height of the spikes recorded from a single fibre with intracellular electrodes (Holman, 1957*b*). This is not surprising, since we record from a large number of muscle fibres and even if they seem to fire synchronously, temporal dispersion of individual spikes and the occurrence of inactive fibres would reduce the height of the recorded spike. In spite of the fact that the recorded spikes are smaller than those obtained from single fibres the method we used is suitable for studying the effects of drugs and ions on the frequency and form of spike activity. It is clear that resting potential and spike activity are related, spikes disappearing as a depolarization develops beyond a certain critical level. Drug effects can be studied at different 'preset' resting potential values by a previous application of potassium, or the change in resting potential caused by a drug can be investigated by testing this drug in a solution with various amounts of ions. In this way more information may be obtained about the mode of action of drugs on smooth muscle.

SUMMARY

1. The application of the 'sucrose-gap' technique for recording resting and action potentials of strips of smooth muscle from the gut has been described.

2. Isotonic potassium chloride (150 mM) produced a depolarization of up to 30 mV. A 26 mV depolarization per tenfold change in the potassium concentration was observed. Isotonic potassium sulphate produced a depolarization of 55 mV.

3. Substituting sulphate for chloride decreased the resting potential by 35 mV and there was a depolarization of 41 mV per tenfold change in the chloride concentration.

4. Calcium-free Locke's solution produced a potential fall of 13 mV.

5. Irregular spike activity was observed in spontaneously active preparations, while regular spikes were obtained by application of potassium and acetylcholine.

6. Acetylcholine produced a depolarization of 4–8 mV.

7. Regular spike activity occurred also in sodium-free 'choline-Locke's solution'.

The greater part of the experiments were carried out at the National Institute for Medical Research, but they were concluded at the University Laboratory of Pharmacology, Oxford, and we wish to thank Sir Charles Harington and Professor J. H. Burn for hospitality, and Dr Edith Bülbring and Dr W. Feldberg for encouragement and advice.

REFERENCES

ADRIAN, R. H. (1956). The effect of internal and external potassium on the membrane potential of frog muscle. *J. Physiol.* **133**, 631–658.

BOYLE, P. J. & CONWAY, E. J. (1941). Potassium accumulation in muscle and associated changes. *J. Physiol.* **100**, 1–63.

BOZLER, E. (1948). Conduction, automaticity and tonus of visceral muscle. *Experientia*, **4**, 213–218.

BÜLBRING, E. (1954). Membrane potential of smooth muscle fibres of the taenia coli of the guinea-pig. *J. Physiol.* **125**, 302–305.

BÜLBRING, E. (1955). Correlation between membrane potential, spike discharge and tension in smooth muscle. *J. Physiol.* **128**, 200–221.

BÜLBRING, E. (1956). Electrophysiology of smooth muscle with autorhythmicity. *Abstr. Rev. XX int. physiol. Congr.* pp. 230–238.

BÜLBRING, E. (1957). Changes in configuration of spontaneously discharged spike potentials from smooth muscle of the guinea-pig's taenia coli. The effect of electrotonic currents and of adrenaline, acetylcholine and histamine. *J. Physiol.* **135**, 412–425.

BURGEN, A. V. S. & TERROUX, K. G. (1953). The membrane action and resting potential of the cat auricle. *J. Physiol.* **119**, 139–152.

ENGELMANN, T. W. (1870). Beiträge zur allgemeinen Muskel- und Nervenphysiologie. *Pflüg. Arch. ges. Physiol.* **3**, 247–326.

EVANS, D. H. L. & SCHILD, H. O. (1953). The reactions of plexus-free circular muscle of cat jejunum to drugs. *J. Physiol.* **119**, 376–399.

EVANS, D. H. L. & SCHILD, H. O. (1956). Reactions of chick amnion to stretch and electrical stimulation. *J. Physiol.* **132**, 31*P*.

FATT, P. & KATZ, B. (1953). The electrical properties of crustacean muscle fibres. *J. Physiol.* **120**, 171–204.

HENDERSON, P. (1907). Zur Thermodynamik der Flüssigkeitsketten. *Z. phys. Chem.* **59**, 118–127.

HENDERSON, P. (1908). Zur Thermodynamik der Flüssigkeitsketten. *Z. phys. Chem.* **63**, 325–345.

HODGKIN, A. L. & HOROWICZ, P. (1957). Effects of K and Cl on the membrane potential of isolated muscle fibres. *J. Physiol.* **137**, 30–31*P*.

HODGKIN, A. L. & KATZ, B. (1949). The effect of sodium ions on the electrical activity of the giant axon of the squid. *J. Physiol.* **108**, 37–77.

HODGKIN, A. L. & RUSHTON, W. A. H. (1946). The electrical constants of a crustacean nerve fibre. *Proc. Roy. Soc.* B, **133**, 444–479.

HOLMAN, M. E. (1957*a*). The effect of changes in the sodium chloride concentration on the smooth muscle of the guinea-pig's taenia coli. *J. Physiol.* **136**, 569–584.

HOLMAN, M. E. (1957*b*). The effect of changes in potassium chloride concentration on the membrane potential, electrical activity and tension of intestinal smooth muscle. *J. Physiol.* **137**, 77–78*P*.

LANDOLT, H. & BÖRNSTEIN, R. (1923). *Landolt-Börnstein physikalisch-chemische Tabellen*, 5th ed., Ed. ROTH, W. A. & SCHEEL, K., Hauptwerk 2, p. 1183. Berlin: Springer.

LANDOLT, H. & BÖRNSTEIN, R. (1936). *Landolt-Börnstein physikalisch-chemische Tabellen*, 5th ed., Ed. ROTH W. A. & SCHEEL, K. Ergänzungsband 3, pp. 2059–2060. Berlin: Springer.

LING, G. & GERARD, R. W. (1950). External potassium and the membrane potential of single muscle fibres. *Nature, Lond.*, **165**, 113–114.

PROSSER, C. L., SPERELAKIS, N. & BERGMANN, R. A. (1955). Conduction in intestinal circular muscle. *Amer. J. Physiol.* **183**, 652.

RITCHIE, J. M. & STRAUB, R. W. (1956). The effect of cooling on the size of the action potential of mammalian non-medullated fibres. *J. Physiol.* **134**, 712–717.

RITCHIE, J. M. & STRAUB, R. W. (1957). The hyperpolarization which follows activity in mammalian non-medullated fibres. *J. Physiol.* **135**, 80–97.

STÄMPFLI, R. (1954). A new method for measuring membrane potentials with external electrodes. *Experientia*, **10**, 508–509.

STÄMPFLI, R. & NISHIE, K. (1956). Effects of calcium-free solutions on membrane-potential of myelinated nerve fibres of the Brazilian frog Leptodactylus ocellatus. *Helv. physiol. acta*, **14**, 93–104.

STÄMPFLI, R. & STRAUB, R. (1954). Demonstration der Membranpotentialmessung von markhaltigen Nervenfasern mit Hilfe von Aussenelektroden. *Helv. physiol. acta*, **12**, C 6–8.

STRAUB, R. (1956*a*). Die Wirkungen von Veratridin und Ionen auf das Ruhepotential markhaltiger Nervenfasern des Frosches. *Helv. physiol. acta*, **14**, 1–28.

STRAUB, R. (1956*b*). Der Einfluss von Lokalanaesthetika auf ionenbedingte Ruhepotentialänderungen von markhaltigen Nervenfasern des Frosches. *Arch. int. Pharmacodyn.* **57**, 414–430.