J. Physiol. (1950) 111, 399–407 612.178.1

AFFERENT NERVES FROM THE HEART REGION

By C. J. DICKINSON

From the Physiological Laboratory, University of Oxford

(*Received* 28 *January* 1950)

In recent years considerable work has been done to investigate the behaviour of the different pressoreceptors found in the walls of blood vessels. Endings of this sort were suggested by Bainbridge (1915) to be the receptors responsible for the reflex which bears his name. Sassa & Miyazaki (1920) extended the original observations, but later workers cast doubt on the regularity with which the effect could be observed. Tiitso (1937) claimed that the cardioacceleration following a rise of venous pressure was a local reaction of the heart; and Ballin & Katz (1941) suggested that pressoreceptors in the great veins and right atrium could not be solely responsible for the Bainbridge reflex. Nonidez (1937, 1941) has shown that subendothelial endings exist in the venous system on both sides of the heart, but their precise function has yet to be elucidated. Amann & Schaefer (1943), Walsh & Whitteridge (1944), Walsh (1947), Whitteridge (1948) and Jarisch & Zotterman (1948) have all recorded impulses derived unmistakably from venous pressoreceptors; but it has so far proved impossible to study the behaviour of these endings accurately, mainly because of the difficulties of accurate recording of effective venous pressure. The first object of these experiments was observation of the activity of these fibres with the chest open and with an improved venous manometer. The types of fibre (other than the venous) which pass to the vagus via its cardiac branches have also been investigated.

METHODS

Satisfactory results have been obtained from fourteen cats, which were in every case deeply anaesthetized with 'Dial', given intraperitoneally half an hour before operation. The chest was opened along the mid-line, under artificial ventilation, and ribs 1–7 inclusive on the right side were ligated close to the vertebral column, using a curved needle from inside the chest. The length of the seventh rib was separated from the eighth, and the first seven ribs were then cut distal to the ligatures. This allowed the upper part of the right chest wall to be reflected as a flap, giving a good exposure of the right vagus and its cardiac branches. A specially shaped glass cannula, 11 cm. long, and 1·2 mm. internal diameter, was inserted by the right external jugular vein, and passed down until its tip could be felt in the right atrium.

After the preparation had been placed in a steam chamber, the cardiac branches of the right vagus were dissected out, using fine cataract knives, and also knives fashioned from small splinters of safety razor blades. Fine dissection was carried out with the aid of a binocular loupe. For recording, a small slip of nerve was cut centrally, laid across the two silver electrodes, and covered with liquid paraffin to prevent drying. Action potentials, amplified by a conventional five-stage resistance/capacitance coupled amplifier, were displayed on a multichannel system. By this means the electrocardiogram (lead III), right atrial pressure, intratracheal pressure, and a time marker could be simultaneously recorded.

Intratracheal pressure was recorded by a mirror membrane manometer and an optical system, and venous pressure was recorded by a specially designed electrical capacitor manometer (Baxter, 1950). Early trials with optical manometers showed that an adequate sensitivity, combined with a high natural period, could not be obtained. For this reason the venous pressure changes were transmitted by heparin saline in lead tubing to a circular brass diaphragm, $\frac{1}{8}$ in. diameter, and $\frac{20}{1000}$ in. thick—turned from the solid. This diaphragm formed the moving plate of an air capacitor, whose other electrode was a fixed plate, $\frac{1}{1000}$ in. away. The whole capacitor 'head' was designed to be insensitive to changes of temperature and external strains. The capacitance of the head, together with that of the coaxial connecting cable and a variable tuning capacitor, formed part of a tuned circuit, which was driven at approximately 500 kcyc./sec. by a master crystal oscillator. Changes in head capacitance caused by movement of the diaphragm produced changes in resonant frequency; and the phase difference between the resonant frequency and the fixed crystal oscillator frequency was compared with a new type of phase discriminator, which produced a steady output voltage proportional to the phase angle. This output was directly coupled to one deflector plate of the cathode-ray tube display system.

The electrical system, with the cannula and liquid system described, was adequate for the accurate recording of venous pressure. Maximum sensitivity was 6 mm. deflexion on the record for a change of pressure of 10 cm. of water, and the natural period of vibration was 200 cyc./sec. The latter is adequate to reproduce the highest significant frequency components of the venous pulse.

In all cases the frequency of a single unit discharge has been estimated by the reciprocals of the time intervals between impulses, and frequency has been plotted against the mid-points of the time intervals. The resulting histograms have been plotted alongside the electrically recorded pressure changes, to determine the relation between the frequency of discharge of a receptor and the pressure over any given period of time—usually one heart-beat. Since there is no parallax between the cathode-ray tube traces, this method is legitimate.

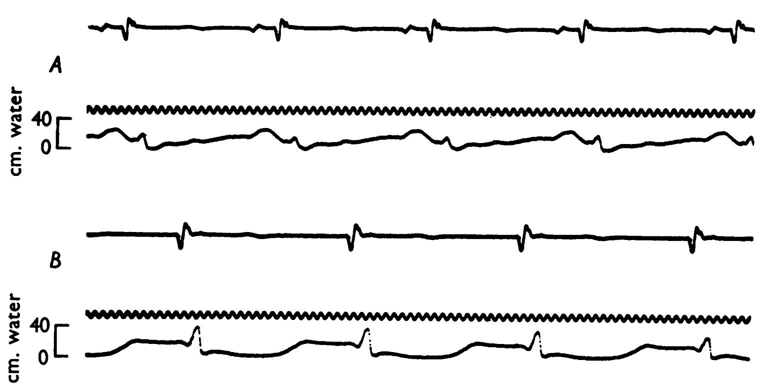

Fig. 1. Two records of right atrial pressure in the cat, made with the electrical capacitor manometer. From above downwards, the e.c.g.; time in 50 cyc./sec.; right atrial pressure. *A*, normal rhythm; *B*, nodal rhythm.

RESULTS

Performance of the venous manometer. A typical record of right atrial pressure, obtained with the liquid system described, is shown in Fig. 1. The chest is open, and artificial ventilation (not shown) is being maintained. Fig. 1*A* shows the heart in normal rhythm, with the *a*, *c*, and *v* waves clearly visible. Fig. 1*B* shows the same heart 2 min. later, after nodal rhythm had developed. The very large *a* wave, caused by the atrium contracting against closed atrio-ventricular valves, is the most conspicuous feature of this record.

Types of receptor discovered in the cardiac branches of the right vagus

The most conspicuous feature of a typical multifibre record obtained from a large slip of the main cardiac branch of the right vagus is shown in Fig. 2. It consists of the discharge from many venous pressoreceptors in the great veins and right atrium. The discharge can be seen to be approximately related to the venous pressure. In addition to these venous fibres, there are several other types. Since the cardiac branch of the vagus usually receives a small

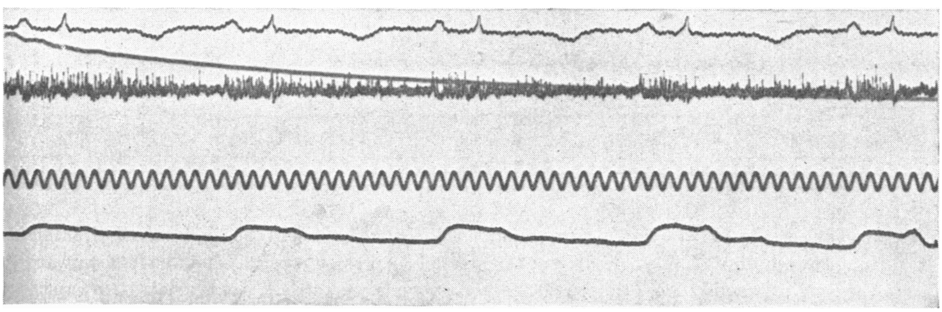

Fig. 2. Multifibre record from a large slip of the cardiac branch of the right vagus, showing conspicuous venous fibre discharge. From above downwards, the e.c.g.; intratracheal pressure; nerve impulses; time in 50 cyc./sec.; right atrial pressure.

contribution from the right lung, typical lung stretch fibres have often been seen, and this has been confirmed by Dawes & Whitteridge (1948). The activity of a single fibre dissected from the nerve examined is shown in Fig. 3*A*. The frequency of discharge is evidently related to the intratracheal pressure. Fig. 3*B* shows a record obtained from a receptor which lies almost certainly in the wall of a vessel of the arterial system, since the position of its discharge in the cardiac cycle is that generally considered typical of an aortic 'depressor' fibre. In Fig. 4 the activity of two fibres identified in another record has been plotted, to show the respective time relations. The fibre whose discharge occurs comparatively late in the cardiac cycle (starting from the *QRS* wave of the e.c.g.) is that from another arterial pressure receptor; but the other fibre, whose discharge is of high frequency and occurs early in the cycle, is clearly of an entirely different type. It may possibly be a 'ventricular' fibre, since its discharge pattern exactly parallels that described by Whitteridge (1948) and presumed to result from the activity of a pressure receptor in the ventricular wall itself.

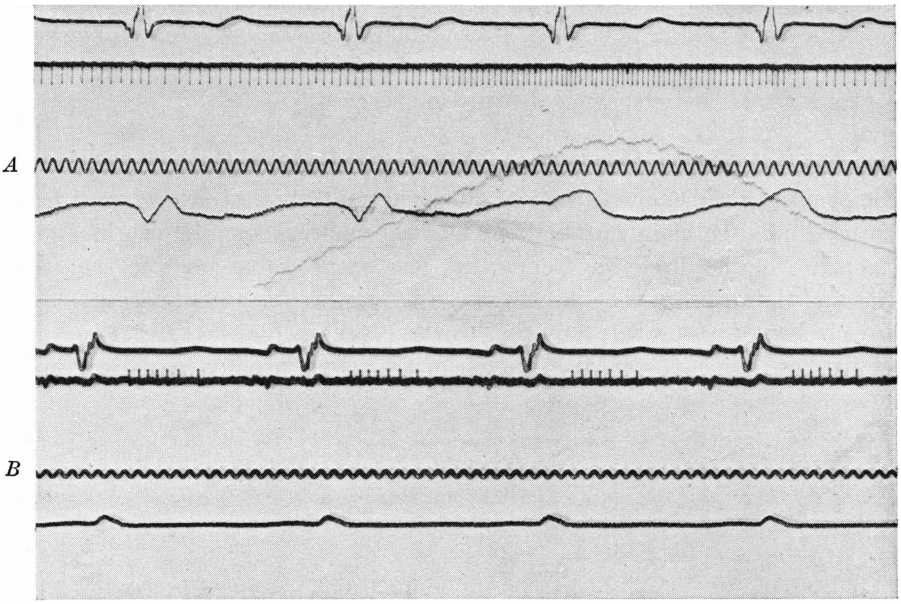

Fig. 3. The activity of two types of fibre found in the cardiac branch of the right vagus. *A*, a single lung stretch fibre; *B*, a single fibre of the arterial 'depressor' type. From above downwards, the e.c.g.; fibre discharge; time in 50 cyc./sec.; venous pressure (*A*, right atrial; *B*, in superior vena cava); intratracheal pressure (in *A* only).

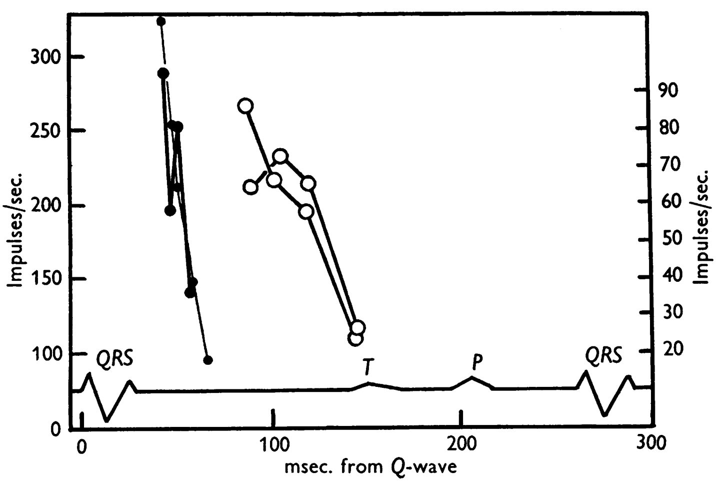

Fig. 4. Record of activity in two fibres recorded simultaneously, in relation to the cardiac cycle. The reciprocal of the interval between successive impulses is plotted as the frequency in impulses per sec. Time is measured from the *Q* wave of the e.c.g., simultaneously recorded. The ordinate scales at the left refer to the fibre discharge shown at the left (black circles); those at the right refer to the other discharge (hollow circles).

The pattern of discharge from pressure receptors in the great veins and right atrium

Fig. 5 shows a record from a small nerve slip containing an 'arterial' fibre of the type already indicated, and a 'venous' fibre. The venous fibre can be seen to discharge twice only, between the *P* and *QRS* waves of the e.c.g., corresponding to the *a* wave of the venous pulse. In this experiment the cannula was in the superior vena cava, and the venous pressure was very low indeed.

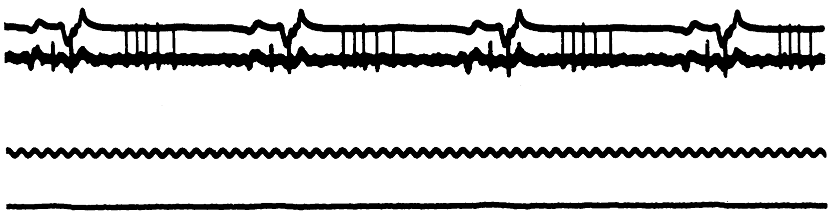

Fig. 5. Record of activity of two different fibres made simultaneously from the same slip of nerve. The pre-systolic discharge (two impulses) comes from a pressoreceptor in the superior vena cava; and the late systolic discharge (five impulses) is from an arterial pressoreceptor. From above downwards, the e.c.g.; nerve impulses; time in 50 cyc./sec.; pressure in the superior vena cava (very low). (The arterial fibre impulses have been retouched to make their position clear when reproduced.)

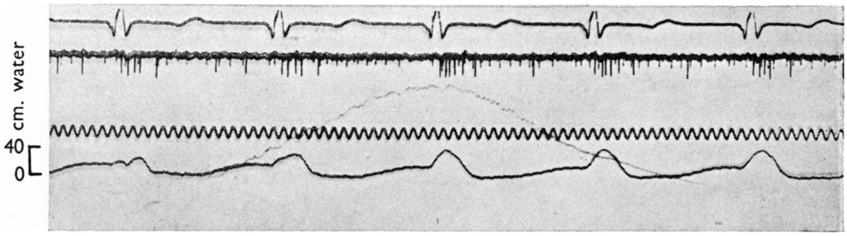

Fig. 6. Record of the activity of a single pressoreceptor in the wall of the right atrium. The heart is in nodal rhythm. From above downwards, the e.c.g.; fibre discharge; time in 50 cyc./sec.; right atrial pressure; intratracheal pressure. (The venous fibre impulses have been retouched to make their position clear when reproduced.)

Even the *a* waves of the venous pulse are scarcely visible, although the manometer sensitivity is the same as that used in Fig. 1 for atrial pressure recording. At higher pressures the pattern of discharge becomes more complex, corresponding to the shape of the venous pulse. Fig. 6 shows the discharge of a pressoreceptor which probably lies in the wall of the right atrium, together with a record of right atrial pressure. (Since the chest was open, this recorded venous pressure represents the actual pressure inside the system, and no correction is necessary for intrapleural pressure changes.) The heart is in nodal rhythm, and the large *a* wave comes after the *QRS* wave of the e.c.g. Fig. 7

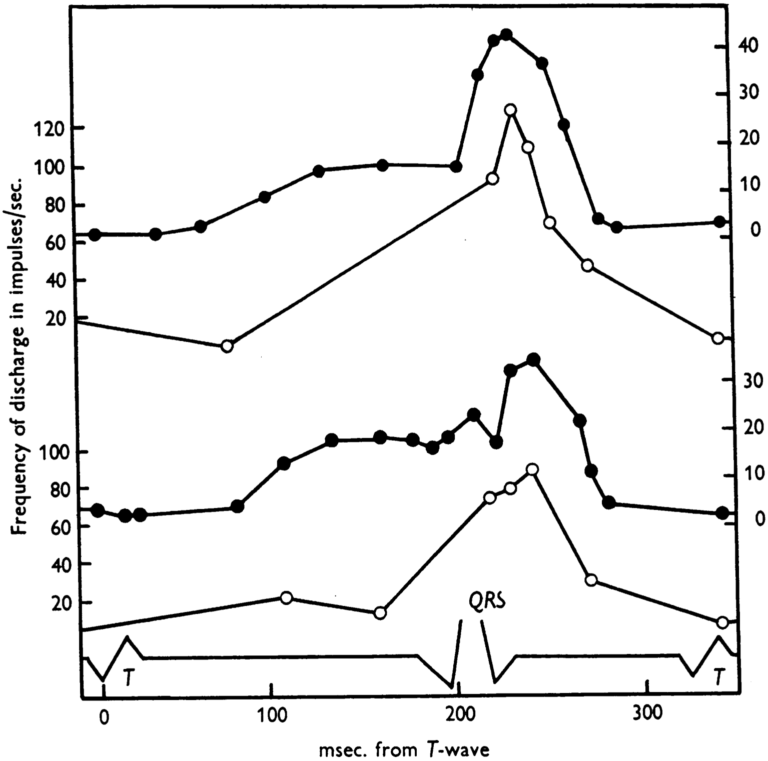

Fig. 7. Relation between fibre discharge and right atrial pressure, for the same fibre, for two heart-beats (upper and lower graphs). The time relations with the e.c.g. are shown below. Black circles: right atrial pressure (scales on right); hollow circles: frequency of discharge of the receptor (scales on left).

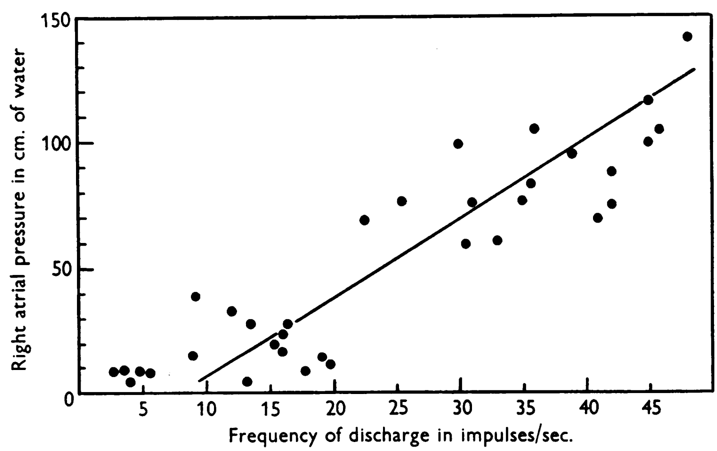

Fig. 8. The relation between pressure and discharge frequency for a pressoreceptor in the right atrium, during six successive heart-beats. The line has been drawn by eye, ignoring the five points at the lower left corner. These represent the intervals between each group of impulses, when the fibre was not discharging, and do not thus indicate any real relation between pressure and frequency of discharge.

shows the discharge frequency of this receptor plotted on a time scale together with pressure, for two complete heart-beats. When the pressure is changing rapidly, the impulse discharge frequency follows the pressure fairly accurately. However, at the beginning of the diastolic *v* wave, Fig. 6 shows that the receptor responds by a single or double discharge, but does not exhibit any further activity while this slight pressure is maintained. There is therefore some evidence for adaptation of the ending. Fig. 8 shows a graph, covering the six heart-beats in Fig. 6, relating frequency of discharge to pressure. It was observed that for the most part the points lying above the straight line were recorded when the pressure was rising, and those below when the pressure was falling—which appears to be further evidence for adaptation. More experiments are evidently required to elucidate this behaviour completely, and it is possible that a perfusion method (similar to that used by Bronk & Stella (1935) for the carotid sinus) may ultimately be necessary.

DISCUSSION

The existence of afferent fibres in the cardiac branches of the right vagus other than those from typical venous pressoreceptors is of some interest. They have not been reported by Jarisch & Zotterman (1948), but these authors comment that Nonidez (1935) discovered typical pressoreceptors in the wall of the descending aorta, giving rise to the 'rami aortici vagi'. These nerves presumably contribute to the cardiac nerves examined; and it seems much more likely that the typical arterial pressoreceptor discharge recorded from fibres in this region represents the activity of receptors in the descending aorta, rather than that of receptors at the arch of the aorta. The presence of these fibres, whatever their derivation, makes it necessary to regard the afferent fibres contained in the main cardiac branch of the right vagus as of more than one type. This is one possible reason why the experiments of Jarisch & Zotterman (1948) on stimulating the cut central end of the nerve were so inconclusive. (Another is, of course, that since the main efferent side of the Bainbridge reflex is represented by a decrease in 'tonic' cardio-inhibitory discharge, cutting off this discharge on one side—by cutting the cardiac branch of the vagus before stimulating it—will greatly reduce the efficiency of the efferent side of the reflex.)

Ballin & Katz (1941) have cast considerable doubt upon the possible functions of the venous pressoreceptors. They were unable to produce a reflex cardio-acceleration in dogs by distending the great veins and right atrium with specially designed balloons; although they were consistently able to produce an increase of heart rate by saline infusion. They therefore suggested that venous pressoreceptors on the right side were not the most important receptors for the Bainbridge reflex. If it is true that the endings adapt to some extent, it might be possible that the stimulus of a sustained distension (such as would be provided by any kind of inflating cannula) is inadequate to produce a significant increase in discharge of the receptors. However, Megibow, Katz & Feinstein (1943) found that they could consistently produce an increase in rate and depth of breathing, but no change in heart rate, by distending the region where the superior vena cava joins the right atrium. Thus unless other endings (e.g. pain endings) were stimulated, which seems improbable, the distension was probably an adequate stimulus to the venous pressoreceptors. If the conclusions suggested by these experiments are correct, it may be necessary to reconsider completely not only the role of venous pressoreceptors, but the Bainbridge reflex itself. If, however, the stimulus of steady distension is not adequate for the venous pressoreceptors, they may still be concerned in the Bainbridge reflex. It is certainly probable that the normal function of the endings is a response to increased venous return resulting from muscular exercise. Both cardio-acceleration and hyperpnoea would seem to be useful physiological responses.

It is fairly certain, however, that the venous pressoreceptors studied take no part in a 'venopressor reflex' (McDowall, 1924). The type of fibre required by McDowall's hypothesis should have a discharge whose frequency is increased by a fall of pressure. In the course of this investigation, and of many others conducted by different investigators, no fibre of the type required has ever been seen. Recently, Coleridge, Kenney & Neil (1949) have confirmed that the removal of tonic discharge from chemoreceptors (by cutting the vagi) is quite sufficient to produce the conditions of the 'venopressor reflex'; and it does not at present seem necessary to postulate the existence of any new ending.

SUMMARY

1. The afferent activity of the cardiac branches of the right vagus of the cat has been examined by direct electrical recording with the chest open.

2. In addition to typical venous pressoreceptors, lung stretch fibres and arterial pressoreceptors have been found to contribute fibres to these nerves.

3. A linear relation has been found between venous pressure and frequency of discharge in fibres from the right atrium.

4. Some evidence of adaptation of venous pressoreceptor discharge has been found.

The author wishes to thank Dr D. Whitteridge and Mr I. G. Baxter for much help, and Mr W. T. S. Austin for technical assistance.

REFERENCES

Amann, A. & Schaefer, H. (1943). *Pflüg. Arch. ges Physiol.* **246**, 757.
Bainbridge, A. (1915). *J. Physiol.* **50**, 65.
Ballin, I. R. & Katz, L. N. (1941). *Amer. J. Physiol.* **135**, 202.
Baxter, I. G. (1950). To be published.
Bronk, D. W. & Stella, G. (1935). *Amer. J. Physiol.* **110**, 708.
Coleridge, J. C. G., Kenney, R. A. & Neil, E. (1949). *J. Physiol.* **110**, 27*P*.

Dawes, G. S. & Whitteridge, D. (1948). Unpublished observations.
Jarisch, A. & Zotterman, Y. (1948). *Acta physiol. Scand.* **16**, 31.
McDowall, R. J. S. (1924). *J. Physiol.* **59**, 41.
Megibow, R. S., Katz, L. N. & Feinstein, M. (1943). *Arch. intern. Med.* **71**, 536.
Nonidez, J. F. (1935). *Amer. J. Anat.* **57**, 259.
Nonidez, J. F. (1937). *Amer. J. Anat.* **61**, 203.
Nonidez, J. F. (1941). *Amer. J. Anat.* **68**, 151.
Sassa, K. & Miyazaki, H. (1920). *J. Physiol.* **54**, 203.
Tiitso, M. (1937). *Pflüg. Arch. ges Physiol.* **238**, 738.
Walsh, E. G. (1947). *J. Physiol.* **106**, 466.
Walsh, E. G. & Whitteridge, D. (1944). *J. Physiol.* **103**, 37 *P*.
Whitteridge, D. (1948). *J. Physiol.* **107**, 496.