J. Physiol. (1974), **240**, *pp.* 33–52
With 7 text-figures
Printed in Great Britain

THE AFFERENT DISCHARGE PATTERN OF ATRIAL MECHANORECEPTORS IN THE CAT DURING SINUSOIDAL STRETCH OF ATRIAL STRIPS *IN SITU*

BY J. O. ARNDT, P. BRAMBRING, K. HINDORF AND M. RÖHNELT

From the Physiologisches Institut der Freien Universität Berlin, and the Abteilung für Experimentelle Anaesthesiologie der Universität Düsseldorf, Düsseldorf 1, Germany

(*Received 29 June 1973*)

SUMMARY

1. The differences in spike discharge from atrial mechanoreceptors *in vivo* suggest the existence of different receptor types. To test this possibility, and to see how atrial receptors compare with other mechanoreceptors, their response was studied under comparable stimulus conditions.

2. Sinusoidal length changes, with frequencies from 1 to 10 Hz and amplitudes of 1·5–5·0 mm at a given static extension, were imposed *in situ* on strips of atrial receptor areas of cats.

3. The receptor response was evaluated from functional single fibres in terms of number of spikes per stimulus period, average discharge rate, instantaneous spike frequency, and phase angle between forcing function and instantaneous frequency.

4. Irrespective of the fibre type, atrial fibres appear to originate from identical mechanoreceptors which sense length at low stimulus frequency and low stimulus amplitudes, but also sense velocity in the high frequency range and with large stimulus amplitudes.

5. The difference in the discharge pattern and in the functional behaviour of the atrial fibres *in vivo* can be explained on the basis of identical receptors.

6. The difference in the temporal occurrence of the atrial burst is still open to debate, but probably is related to the site of the receptor.

INTRODUCTION

The mechanoreceptors of the heart give rise to several types of afferent bursts which, when recorded *in vivo*, can be distinguished from one another by their relative position in the cardiac cycle (Paintal, 1953, 1963*a*, 1972). Two of these bursts, the A and the B-type, originate from the atria

and they differ in (1) their temporal occurrence during the cardiac cycle, (2) their discharge pattern, and (3) their functional behaviour. Specifically (1), the A-burst coincides with the a-wave of the atrial pressure curve, i.e. it occurs during atrial contraction. In contrast the B-burst coincides with the v-wave, i.e. it occurs during atrial relaxation and filling. (2) The A-burst is characterized by its high frequency discharge and more or less constant duration, and the B-burst by its lower frequency discharge and fluctuating duration. (3) The discharge of the A-burst remains constant in spite of massive changes in atrial mechanics and it has been suggested that it might signal heart rate (Arndt, Brambring, Hindorf & Röhnelt, 1971). In contrast, the B-burst discharge changes with atrial stretch (Paintal, 1953, 1963; Henry & Pearce, 1956; Langrehr, 1960*a*) and there is much evidence to show that these afferents play a part in the antidiuretic aspects of blood volume control (Gauer & Henry, 1963; Gauer, Henry & Behn, 1970). These differences suggest the existence of two receptor types in the atria differing either in their adaptation properties (Struppler, 1955) or in their orientation to the atrial musculature (Whitteridge, 1948, see also Paintal, 1963, 1972). However, this was doubted by Langrehr (1960*a*) and also Neil & Joels (1961) because they occasionally observed spontaneous shifts of A to B-type discharge and vice versa which is hard to reconcile with the existence of two different receptor types.

It is virtually impossible to characterize these receptors by studying the discharge with the intact circulation, because the stimulus parameters are extremely difficult to control under these conditions. Accordingly we studied the discharge of the atrial receptors under defined conditions with respect to static stretch, the stimulus amplitude and the stimulus frequency imposed on strips of the atrium containing the receptor. This was done *in situ*. We found that atrial afferent fibres originate from identical mechanoreceptors which resemble closely other mechanoreceptors of different systems and species.

METHODS

Fourteen functional single fibres were dissected from either vagus nerve in the neck of chloralosed (α-chloralose 80 mg/kg body wt. I.P.) cats weighing between 1·8–3·2 kg. The fibres were dissected under paraffin oil (Stämpfli, 1952; Paintal, 1953). The localization of the receptors in the atrial wall, their discharge type, and their survival times are listed in Table 1.

The atrial bursts were identified according to their time of occurrence during the cardiac cycle with respect to the ECG and aortic and right atrial pressures, as well as by their functional behaviour with respect to respiration, blood volume changes or atrial pacing (Paintal, 1953, 1972).

The nerve activity was sampled with bipolar platinum-iridium electrodes and the e.c.g. with needle electrodes. The right atrial and aortic pressures were measured with Statham P 23dB electromanometers via catheters. The resonant frequency of

the catheter-manometer systems was more than 35 Hz, which was achieved by flushing them with gaseous CO_2 and filling them with boiled 0·9% saline solution.

After identification of the atrial nerve activity, thoracotomy was performed by sternotomy. The epicardium was removed. While the recording of nerve activity continued the receptor was localized by determining that point from which a high frequency discharge was most easily elicited when probing the atrial wall from the outside with a fine glass rod (Coleridge, Coleridge & Kidd, 1964).

TABLE 1. Localization and survival time of the receptors

Discharge type	Localization in the atrium	Survival time after arrest of circulation (min)
A	right	30
A	left	23
A	right	19
A	left	20
A	right	14
B	right	38
B	right	35
B	right	23
B	right	21
B	left	28
B	right	17
B	left	27
B	left	—
Intermediate type*	right	17

* Intermediate type discharges with atrial systole (A-type) and also with diastole (B-type).

At this point, the circulation was interrupted by clamping both caval veins and removing both ventricles just above the valvular ring. The part of the atrium containing the receptor was separated by cutting with a pair of scissors from the atrial base towards the posterior wall. This resulted in an atrial strip usually 1·5 cm wide and 2–3 cm long with one free end and with the opposite end of the strip remaining with its natural connexions to the mediastinum via the caval or pulmonary veins, thus preserving the innervation of the strip. The mediastinum posterior to the atrial strip was clamped with a strong haemostat in order to fix the preparation to some extent.

In general the procedure from circulatory arrest to the isolation of the receptor zone lasted not more than 1–2 min. The preparation remained within the thorax and was then bathed with Tyrode solution equilibrated with 95% O_2 and 5% CO_2 at 36–38° C.

Finally, the free end of the atrial strip was connected to a stretch device of special design (designed and fabricated by Mr Dannenberg, Engineering Department of the Department of Physiology, Freie Universität, Berlin; his cooperation is gratefully acknowledged) using the cross-axle principle which furnished, first, static stretches over a range of 5 cm, either continuously or in steps of 100 μm each, and secondly, dynamic stretches, i.e. sinusoidal length changes over a frequency range from 1 to 10 Hz and amplitudes of up to 5 mm.

A linear variable differential transformer was used to measure the change in length imposed on the strips by connecting the magnetic core to the movable parts of the stretch device. The coils were fixed in such a way that a voltage was induced proportional to the relative position of the coils and the core. The relation between core and coils was adjusted in each experiment so as to be optimal for linearity. The system was calibrated with the stretch device which furnished linear displacements in steps of 100 μm as mentioned above.

To test the phase relationship between the dynamic stretches and the tension at the atrial strip, the changes in tension were recorded in addition to the length changes in two experiments using a photoconductive transducer. The output voltage of the transducer was proportional to the position of a relatively stiff steel rod which controlled the light flux to the photo-sensitive material. The transducer was attached to the stretch device and the free end of the atrial strip to the tip of the steel rod in such a manner that the tension transducer and the atrial strip were connected in series.

The frequency responses of both the length and the tension transducers were tested for sinusoidal inputs with the stretch device and were found to be flat for sine wave inputs from 1–10 Hz and amplitudes up to 5 mm.

Data processing

The analysis of the nerve discharge is based on the following parameters:

(1) spikes per stimulus period (period of one sine wave);

(2) average discharge rate (number of spikes/sec);

(3) frequency per burst (N-1 divided by burst duration; where N stands for the number of spikes per burst);

(4) instantaneous frequency (spike interval^{-1});

(5) phase angle: from the time lapse between the maximum of the change in length and the shortest time interval per burst, i.e. maximum instantaneous frequency.

To derive parameters 1, 2, and 4 the nerve discharge was processed automatically with electronic counters and the analog voltages representing the number of spikes per stimulus period and the instantaneous frequency were recorded along with the change in length with slow paper speed (see Figs. 2 and 6).

The more detailed analyses like phase relationship, frequency per burst, and duration of the bursts required evaluation of single stimulus periods using an expanded time base, i.e. slow speed play back of the magnetic tape and high chart speed (see Figs. 1 and 4).

All parameters were recorded on magnetic tape (Ampex 300 SP) and on an Offner type R Dynograph.

Experimental protocol

With one exception, listed in Table 2, the atrial strips were stretched until the receptors fired tonically under static conditions; then dynamic stimuli (sine waves with amplitudes of 1·5, 3·0 and 5·0 mm and frequencies from 1 to 10 Hz) were imposed on them. Usually each run lasted 20–30 sec with pauses of 10–15 sec between successive runs.

RESULTS

The differences between the discharge of type A and type B atrial afferent fibres were mentioned in the introduction. Fig. 1 illustrates these points and clearly shows that these characteristic differences disappear when the receptor activity is studied under comparable conditions. It is obvious (left-hand part of Fig. 1) that the A-type fibre fires during atrial contraction with a short but high frequency burst, whereas the B-type fibre fires during atrial diastole (atrial filling phase) with a burst of longer

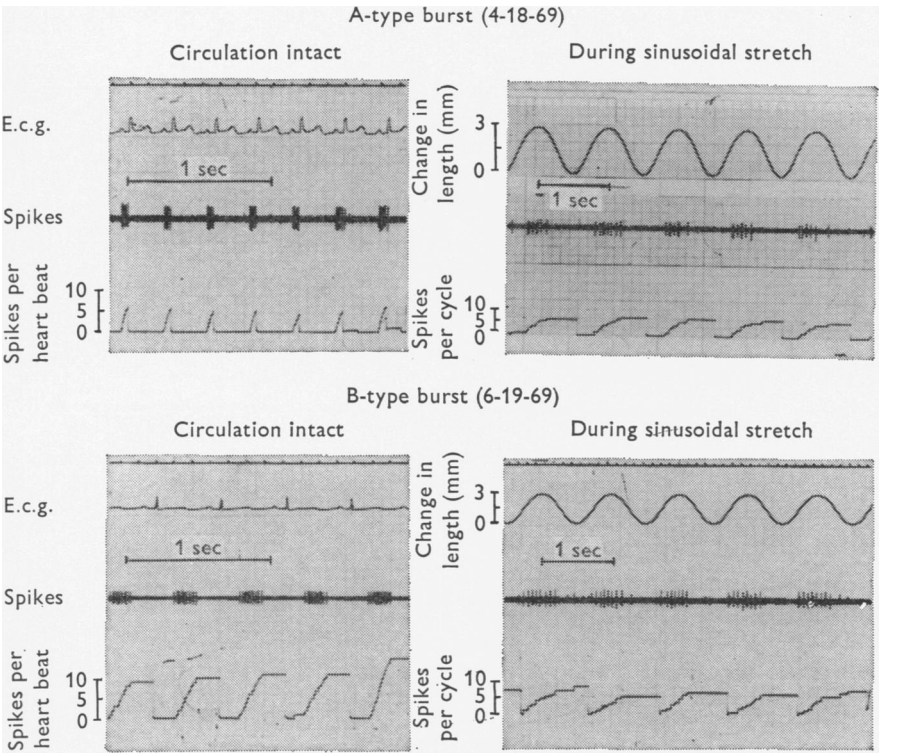

Fig. 1. Comparison of the discharge patterns of A- and B-type fibres with intact circulation and during sinusoidal stimulation of the receptor area *in situ*. Note the similarities in discharge with sinusoidal stimulation (right-hand part of the Figure).

duration and lower frequency. When, however, the respective receptor-zones are stimulated sinusoidally (right-hand side of Fig. 1) the differences vanish, and both receptors are activated with increasing stretch and fire bursts of similar pattern and spike number.

This observation, which was confirmed in every preparation, strongly suggests that both kinds of atrial afferent fibres originate from identical receptors.

Relationship between receptor responses and stimulus parameters

Stimulus frequency

With increasing frequency, i.e. with decreasing stimulus duration, the number of spikes per stimulus period decreases as is shown in Fig. 2. Sinusoidal length changes with an amplitude of 3 mm (uppermost record)

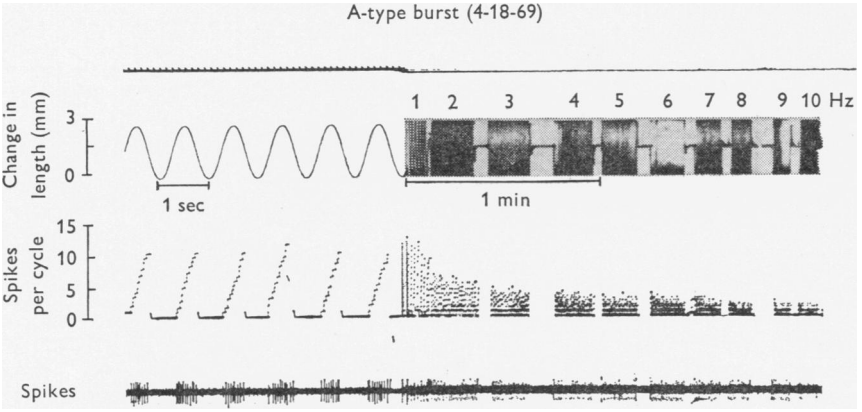

Fig. 2. Relationship between stimulus frequency (initial stretch and stimulus amplitude constant) and number of spikes fired per stimulus period (original recording).

were imposed on an atrial strip with frequencies ranging from 1 to 10 Hz. The number of spikes per stimulus period was counted electronically, the counter being reset by the sine wave generator with the end of the burst. Obviously the number of spikes per stimulus period (centre record) of the A-type fibre decreases with increasing frequency. A closer analysis reveals a hyperbolic relationship between the two parameters.

The evaluation of a representative example is given in the left hand part of Fig. 3. In contrast to Fig. 2, it is an example of a B-type fibre. The following points should be stressed: (1) the relationship is hyperbolic; (2) the discharge fluctuates by only 1 spike per stimulus for a given stimulus frequency; and (3) the receptor fires the same number of spikes when, at the end of the run, the sine wave generator is again driven at 1 Hz (see interrupted line with arrow).

Seven other fibres behaved similarly, as is shown on the right-hand side of Fig. 3. There are no differences between the A-, the B- and the Inter-

mediate-type fibres. Intermediate type refers to those fibres which discharge during atrial systole like A-type, but also during atrial diastole like B-type fibres (Paintal, 1963*b*).

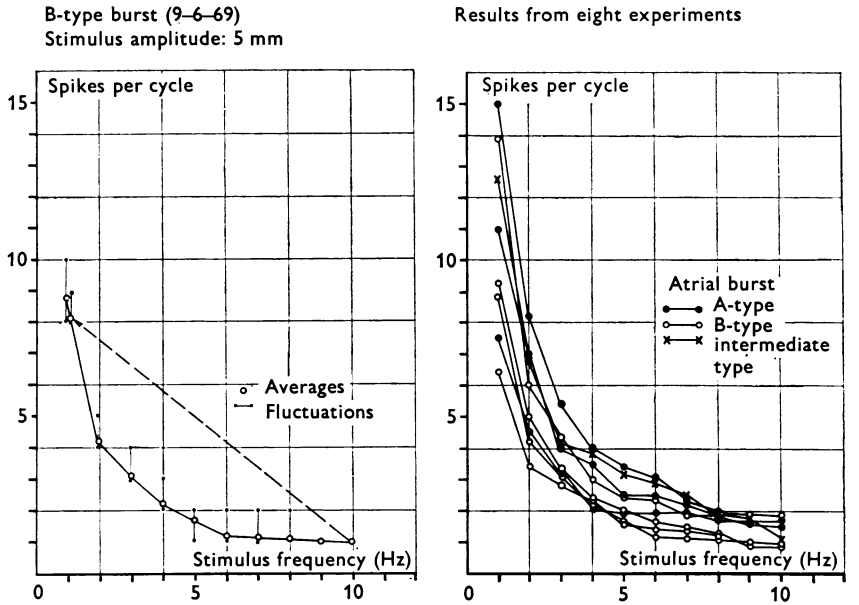

Fig. 3. Quantitative relationship between spikes per stimulus period and stimulus frequency (initial stretch and stimulus amplitude constant for each run). Left-hand part of the diagram shows a representative example. Note the hyperbolic relationship between the two parameters, the small spontaneous fluctuations in receptor discharge by only 1 spike, and the agreement in discharge at 1 cycle for the start and the end of this run. The right-hand part shows results from eight fibres in eight experiments. Note the hyperbolic relationship irrespective of the fibre type.

The difference in the number of spikes per stimulus at 1 c/s is not related to the fibre type but rather to the control conditions, i.e. the degree of initial stretch and the amplitude of stretch. The three fibres with the lowest response in spikes/cycle were stimulated with amplitudes of 3 mm and the others with 5 mm.

Curiously, the average discharge rate (spikes/sec) remained constant over the range of stimulus frequencies tested in these experiments. This can be appreciated from Fig. 3 which shows that the relationship between spikes per stimulus period and stimulus period must be linear according to $f = 1/p$ where f stands for stimulus frequency and p for stimulus period.

The actual values and computations for five additional fibres are listed in Table 2, columns 5 and 6. Note that the average discharge rate remains

constant throughout each experimental run, and also that it agrees closely with the static discharge rate (column 2). For some stimulus frequencies two numbers are listed because the number of spikes fluctuated spontaneously from cycle to cycle.

It is concluded, that the number of spikes per stimulus period decreases with increasing stimulus frequency but that the average discharge rate remains constant irrespective of the fibre type.

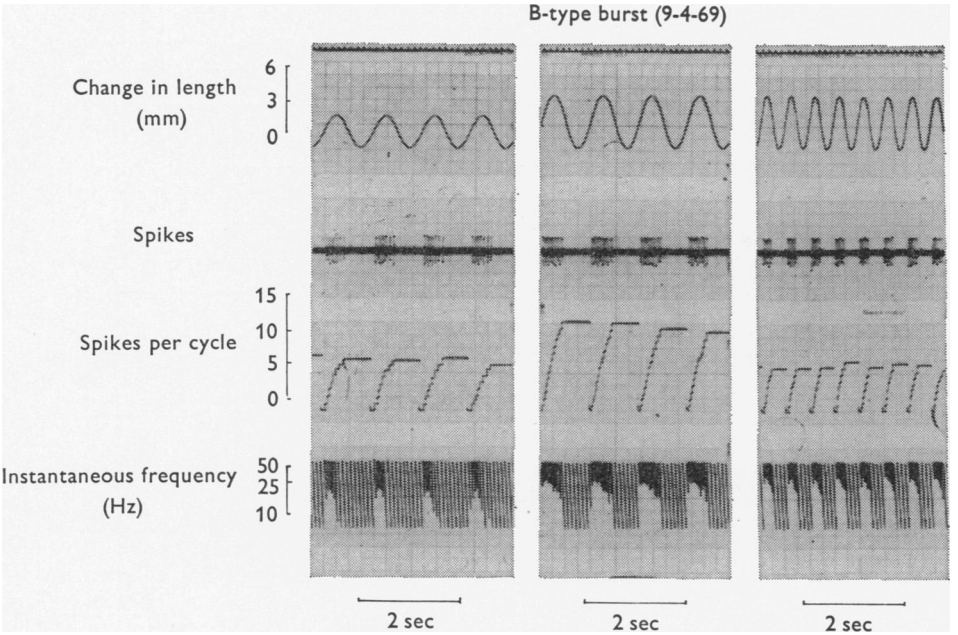

Fig. 4. The effect of changing stimulus frequency and amplitude at constant initial stretch on the number of spikes per stimulus period, the instantaneous frequency, and its phase relationship with the forcing function (for details see text).

Stimulus amplitude

The receptor response to a change in stimulus amplitude could not be systematically pursued in each preparation because of their limited survival time (see Table 1). The conclusions therefore rest on the analysis of representative examples. Fig. 4 shows the response of a B-type fibre which was stimulated with amplitudes of 3 and 5 mm, respectively, at a constant prestretch and stimulus frequency. The number of spikes per burst increased proportionally from 8 to 14 (compare left-hand side with centre recording).

Although two A-type fibres responded to the same amplitude changes

TABLE 2. Data from five fibres not depicted diagrammatically which were studied at different initial stretch and different amplitudes

	Fibre-type	Static discharge (spikes/sec)	Stimulus: Amplitude (mm)	Stimulus: Frequency (Hz)	Spikes per stimulus period	Average discharge rate (spikes/sec)	Burst-duration (msec)	Burst-frequency (Hz)	Maximum instantaneous frequency (Hz)	Phase angle (degrees)
1	B	25	1,5	1	26	26	Continuous discharge		29	0
		26		2	14	28	Continuous discharge		32	0
		28		4	6/7	24/28	Continuous discharge		36	—
		28		8	4	32	Continuous discharge		36	—
		49	1,5	1	48	48	Continuous discharge		68	0
		49		2	22	44	Continuous discharge		68	0
		50		4	11	44	Continuous discharge		83	—
		50		8	5/6	40/48	Continuous discharge		90	—
		47		1	43	41	Continuous discharge		64	0
		35	5,0	1	40	40	Continuous discharge		76	0
		39		2	20	40	Continuous discharge		76	—
		39		4	8/10	32/40	Continuous discharge		76	—
		36		8	4/5	32/40	Continuous discharge			—
		33		1	36	36	Continuous discharge		76	0
2	B	14	3,0	1	15	15	625	25	29	−13
		14		2	7	14	187	31	32	−18
		15		3	5	15	100	40	40	−29
		16		4	4/5	16/20	88	45	45	−36
		15		1	16	16	410	26	29	−13
		19	5,0	1	19	19	510	36	37	−12
		19		2	9	18	200	40	40	−18
		19		3	6/7	18/21	111	50	50	−35
		20		4	4/5	16/20	75	55	55	−54
		20		1	16	16	540	30	33	−12
3	B	29	1,55	1	29	29	Continuous discharge		35	0
		28		2	10	20	310	28	35	−9
				3	5	15	195	20	31	−28
				4	3/5	12/20	100	30	35	—
		18		1	18	18	Continuous discharge		31	0
		22	5,0	1	16	16	730	23	35	0
		21		2	8	16	250	32	38	−18
		22		3	5	15	200	25	38	−28
		18		4	3/4	12/16	75	27	50	—
4	B	Sporadic discharge	3,0	1	13	13	450	26	29	0
		Sporadic discharge		2	7/8	14/16	250	28	32	−18
		Sporadic discharge		4	5	20	110	36	50	—
		Sporadic discharge		8	2	16	75	42	—	—
		Sporadic discharge		1	15	15	500	28	35	0
		Sporadic discharge	5,0	1	20	20	450	42	67	−9
		Sporadic discharge		2	10	20	200	45	67	−24
		Sporadic discharge		4	5/6	20/24	88	50	67	−36
		Sporadic discharge		8	3	24	38	53	75	—
		Sporadic discharge		1	20	20	380	50	55	0
5	A	10	1,5	1	9	9	500	16	36	0
		10		2	5	10	190	27	42	0
		10		4	2/3	8/12	120	30	50	—
		10		1	10	10	550	16	36	0
		10	5,0	1	12	12	410	27	42	−9
		14		2	6	12	150	33	50	−14
		10		4	4	16	75	40	64	—
		9		1	11	11	350	29	42	0
		Sporadic discharge	5,0	1	9	9	400	20	25	0
		Sporadic discharge		2	5	10	175	23	31	0
		Sporadic discharge		4	2/3	8/12	75	31	—	—
		Sporadic discharge		8	1	8	—	—	—	—
		Sporadic discharge		1	9	9	400	20	25	0

with a change in their discharge pattern (increasing spike frequency per burst and maximum instantaneous frequency), the bursts were shorter and the number of spikes per stimulus period remained constant.

This, however, ought not to be interpreted as a general difference between A and B-type fibres. A closer analysis of this point in five additional fibres, summarized in Table 2, shows that the amplitude effect might be masked when the static activity which is a measure of static extension has changed at the same time. Only in the last two preparations of Table 2 did the receptor activity remain relatively constant under static conditions (see static activity column 2) and in both cases the number of spikes per stimulus period increased with stimulus amplitude. In the other three fibres the amplitude effect only becomes recognizable when compared for approximately identical static fibre activities.

It was concluded, therefore, that the number of spikes per stimulus period increases with increasing amplitude irrespective of the fibre type; other parameters like maximum instantaneous frequency, spike frequency per burst, and phase angle (see Table 2) respond clearly to amplitude change, which will be pursued further below.

Static stretch

All fibres discharged continuously when the static stretch was above threshold and the activity increased with increasing static stretch. Because of the limited survival time of the fibres and for methodological reasons (see critiques of method, p. 47) it was impossible to study this relationship quantitatively. However, the qualitative aspects can be seen from the behaviour of an A-type fibre demonstrated in Fig. 5. The lower curve shows the hyperbolic relationship between the number of spikes per stimulus period and the stimulus frequency for low stretch near threshold. With an increase in stretch the hyperbola is clearly shifted upward and to the right, the increase in the number of spikes per stimulus being larger in the low stimulus frequency than in the high frequency range. It is appropriate to note here that such behaviour was to be expected only for the slowly adapting B-type fibres but not for the A-type fibres which have been thought to originate from fast adapting receptors (Struppler, 1955; Langrehr, 1960*a*; Paintal, 1963*b*). The interaction of static and dynamic stimuli is demonstrated in another A-type fibre (Fig. 6). The centre recording of the lower part of the graph shows the instantaneous frequency during dynamic stimulation with a frequency of 1 Hz at an amplitude of 1·5 mm (left-hand side of the record), and static stretch (right-hand side).

The receptor discharge follows the change in length during dynamic stimulation, and the receptor fires continuously during static stretch. With interruption of the dynamic stimulation the stretch was adjusted

manually to its mid-position as indicated by the initial decrease in length. Note that the instantaneous frequency follows exactly the stretch and the receptor fires continuously for as long as 30 sec with constant static stretch, i.e. the A-type fibre does not adapt during this time.

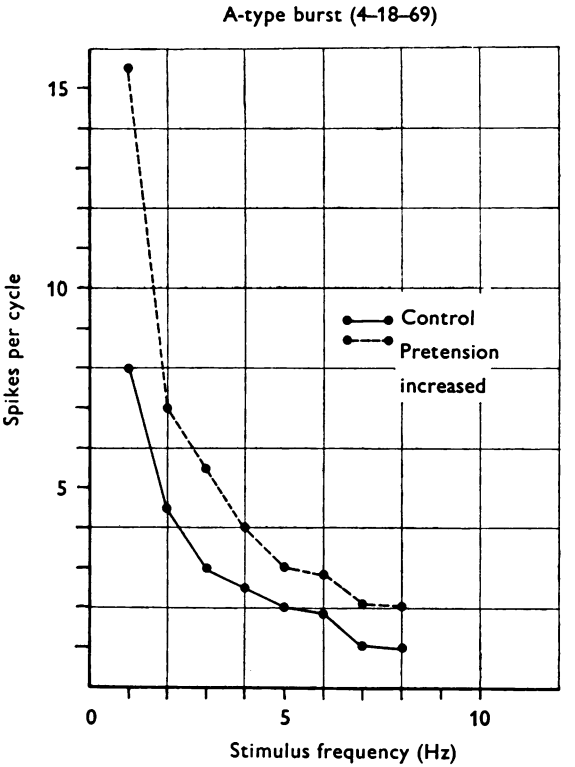

Fig. 5. Fibre discharge and state of stretch: note the increase in the number of spikes per stimulus period for each stimulus frequency with stimulus amplitude held constant.

A closer analysis of the interrelationship between the dynamic stimulus and the instantaneous frequency on an expanded time scale (upper part of the graph) reveals that the instantaneous frequency is modulated by the forcing function without appreciable phase shifts between the two parameters, i.e. the receptor signal length at each instant under these conditions.

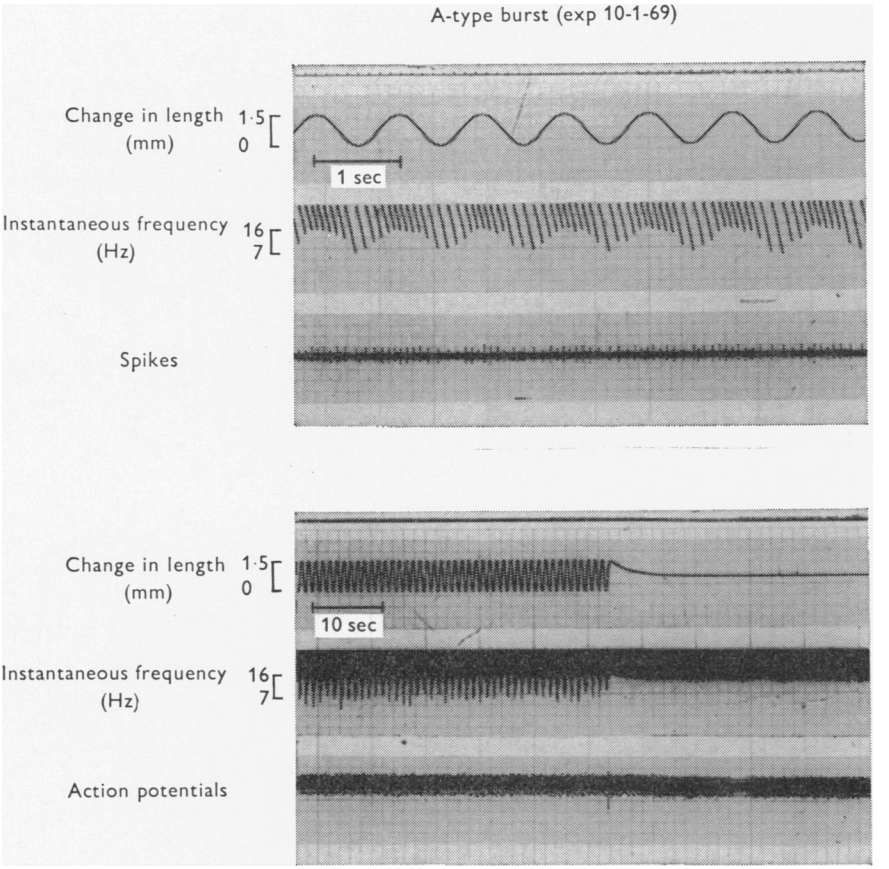

Fig. 6. Phase relationship between stimulus and instantaneous frequency in an A-type fibre. There is no phase shift (upper part of the graph). Consequently this receptor discharges continuously during static stretch (lower part of the graph).

Static/dynamic sensitivity

However, the last statement holds only for low amplitude and low frequency stimulation. A phase shift of $-14°$, the instantaneous frequency leading the forcing function, occurred in the A-type fibre of Fig. 6 when the stimulus amplitude was increased from 1·5 to 5 mm with the stimulus frequency (1 Hz) and the pre-stretch held constant. The time lag due to the conduction velocity in the atrial fibre was neglected. This was calculated from the average conduction velocity in atrial fibres, which is 20 m/sec (Paintal, 1963*b*), and from the distance between the receptor ending and the recording electrode, assumed to be 8 cm. From these data

the time lag amounts to only 4 msec or 1·4°. For a B-type fibre the following phase angles were determined: At 1 Hz – 19°, at 2 Hz – 32° and at 4 Hz – 61°.

The tendency of the phase shift to increase with the frequency and amplitude of the stimulus is also brought out from the fibres listed in Table 2. With the exception of fibre no. 1 the phase angle clearly increases with increasing stimulus frequencies, whereas the amplitude effect is only indicated to a relatively small extent in fibres no. 2, 3, and 5.

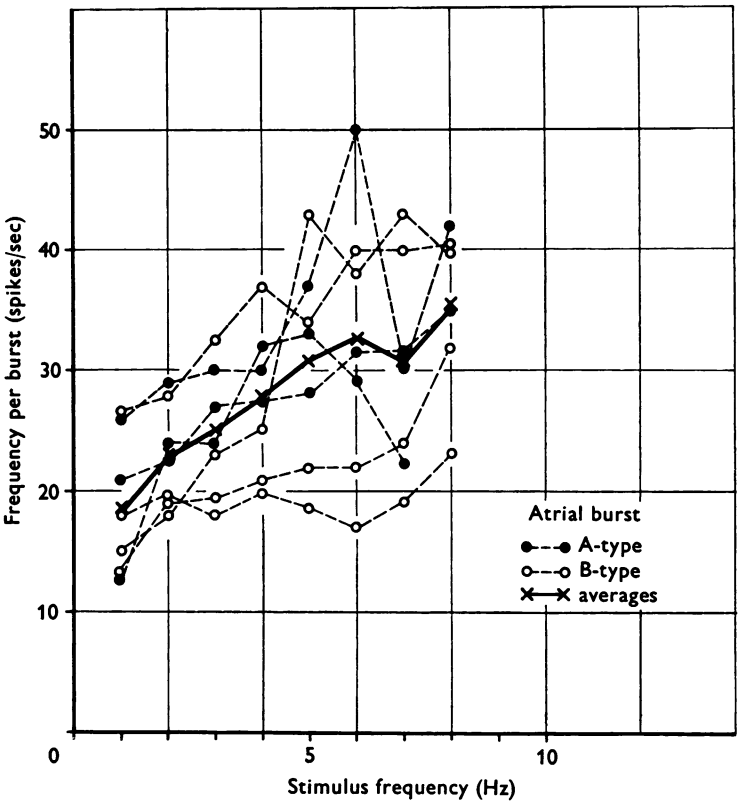

Fig. 7. Frequency per burst and stimulus frequency. On the average this parameter increases proportionally with stimulus frequency. Results from seven experiments.

The velocity sensitivity, although small, seems to be responsible for the relationship between spike frequency per burst and stimulus frequency. Both parameters are related in a linear fashion. This is demonstrated in Fig. 7 and also in Table 2, column 8.

The scatter of the data points in Fig. 7 in the high frequency range is

due to the fact that the calculation of the frequency per burst is open to some error when the burst consist only of 3 to 4 spikes, since spontaneous fluctuations of 1 spike per burst may occur (see Fig. 3). Nevertheless, in the majority of fibres the frequency per burst increases clearly with increasing stimulus frequency.

Clearly atrial receptors sense length as well as velocity, depending on stimulus frequency and amplitude. Again, no difference was seen between the atrial fibre types with respect to the response to dynamic and static stimuli. It should also be stressed that a phase lag of 90° C, indicating pure velocity sensitivity, was never observed.

Critique of the method

In order to decide whether or not atrial afferent fibres all originate from identical mechanoreceptors, their responses to clearly defined mechanical stimuli have been analysed.

Sinusoidal length changes at given static stretches were chosen because both the dynamic receptor response and the linearity of the system can be tested easily by such an approach (Houk & Simon, 1967; Grüsser & Thiele, 1968; Lennerstrand, 1968; Matthews & Stein, 1969; Terzuolo & Knox, 1971). As will be discussed below, the stimulus parameters were approximately within the physiological working range of the atrial receptors, though the static stretch could not be quantitated because of experimental limitations.

Stimulus frequency and amplitude

The changes in atrial circumference and the velocity of its change during the cardiac cycle were studied previously in cats (Arndt, 1966; Arndt & Klauske, 1967). The following observations are relevant to the present study.

(1) Atrial circumference varies, on the average, by 1·05 mm during each cardiac cycle, i.e. by about 1 % of total circumference. The maxima of the circumference coincide with the peak of the v-wave and the beginning of the a-wave of the atrial pressure curve.

(2) The atrial wall moves at a maximum velocity of 0·6 cm/sec during the atrial filling phase (v-wave), and at 8·0 cm/sec during atrial contraction (a-wave).

(3) Variations in heart rate have almost no effect on the wall movement during atrial filling and during atrial contraction.

(4) Atrial circumference varies only by 0·8 mm (about 1 %) for blood volume changes of 28 % (Arndt, 1966).

The atrial strips were stimulated with velocities from 0·42 to 14·4 cm/sec

(calculated for stimulus frequencies of 1 and 10 Hz and amplitudes of 1·5 and 5 mm), a range which is consistent with the above figures.

Static stretch

The atrial nerve activity had to be identified in the intact animal from single fibres in the vagus nerve rather than from nerve strands in the vicinity of the heart because the cardiac innervation is too complex. To preserve the fibres the preparation had to be left partially *in situ* (see Methods). Therefore, neither initial length nor tension were measurable but only the changes of these parameters. Consequently, receptor threshold could not be quantitated.

However, the fibres are comparable in their above-threshold behaviour since all preparations were stretched until the receptors fired continuously. In fact, the relationship between stimulus and threshold is critical for the receptor response, because the average discharge rates during static and dynamic stimulation are only identical if the dynamic stimuli are constantly above threshold and below saturation (Franz, 1969; Angell James, 1971). This condition holds in all experiments except the one in Table 2.

Although receptor thresholds were not ascertained it appears unlikely that receptors differ in their thresholds for the following reasons: On the one hand the atrial receptors do not differ in their above-threshold behaviour according to the data presented. This indicates that they are located in tissues with similar mechanical properties. On the other hand, *in vivo* the receptors are excited at different times even though the atrial circumference prior to atrial systole, i.e. the beginning of the A-burst, is approximately identical with that during the v-wave, i.e. during the occurrence of the B-burst.

Phase angle

The sinusoidal stimulus has two components, the 'active' stretch imposed by the function generator on the atrial strips, and the elastic recoil of the tissue. Sinusoidal deformation of the receptor area can only be assured if both forces are equal. Consequently, only in this case will the instantaneous discharge frequency be modulated sinusoidally (Fig. 6).

The phase angle refers to the relationship between maximum change in length and the maximum instantaneous frequency during the stimulus period. Since, for example, in the muscle spindle the receptor response correlates better with tension than length (Husmark & Ottoson, 1970) it should be noted that in two test experiments no phase shifts between length and tension were observed when atrial strips were stretched at frequencies up to 10 Hz.

Survival time

Atrial receptors are relatively insensitive to O_2-shortage, as are other enteroreceptors, like the stretch receptors of the lung (Adrian, 1933), those of the stomach (Paintal, 1954), and those of the carotid sinus (Bronk & Stella, 1932).

Without any attempts to supply oxygen, atrial nerve fibres remain active for up to 15 min (Langrehr, 1960*a*); bathing the receptor areas with oxygenated Tyrode solution extends survival time to an average of 25 min, and in one example even to 38 min (see Table 1).

The deterioration of the fibres was signalled clearly by the sudden occurrence of irregularly grouped spikes, which no longer responded to dynamic stimulation. When this happened the experiments were discontinued.

Therefore we concluded that the receptors were indeed studied under comparable conditions and that the stimulus parameters were such as to allow extrapolations to their *in vivo* behaviour.

DISCUSSION

The main question which we attempted to answer was whether the type A and type B receptors were identical as far as their basic properties were concerned.

The results obtained here have demonstrated unequivocally that the responses of type A and type B receptors to dynamic stimuli are identical in practically every way examined. They primarily sense length and, depending on stimulus frequency and amplitude, to a small extent also the rate of change of length (i.e. velocity); a pure velocity response with a phase angle of 90° was never observed.

In general, atrial receptors have many features in common with other mechanoreceptors such as wing receptors of insects (Pabst, 1965), stretch receptors of crustacea (Terzuolo & Knox, 1971), muscle spindles of amphibia (Ottoson & Shepherd, 1971) and of mammalia (Crowe & Matthews, 1964; Grüsser & Thiele, 1968; Dabbert & Grüsser, 1968), tendon organs (Houk & Simon, 1967), and baroreceptors of cats (Angell James, 1971). In these receptors, as in atrial receptors, the number of spikes per stimulus period depends on stimulus duration; instantaneous frequency, spike frequency per burst, and their dynamic sensitivity depend on the stimulus frequency and amplitude.

Nevertheless, there are quantitative differences between the various mechanoreceptors. The discharge frequencies are, for example, appreciably higher in muscle spindles of amphibia and mammalia. These mechanoreceptors fire with frequencies from 30 to 150 Hz for stretch velocities from 0·7 to 5 cm/sec (Crowe & Matthews, 1964; Toyama, 1966; Ottoson & Shepherd, 1971; Lennerstrand, 1968). This may be related to their high dynamic sensitivity (Schäfer & Henatsch, 1967; Grüsser & Thiele, 1968; Dabbert & Grüsser, 1968; Matthews & Stein, 1969).

From the identical response of A- and B-type endings to the same stimuli one can conclude that the generator and regenerative mechanisms of the endings are identical, in particular that the type A receptors do not show evidence of greater adaptation than the type B receptors as one would be led to think from the observations of Struppler (1955) and Langrehr (1960*a*) (see also Paintal, 1963*b*). If this is so, why do the type A and type B receptors show such remarkable differences in their responses to the mechanical events occurring naturally in the atrium? In spite of our conclusion that the A- and B-type receptors belong to one group, a view supported by the observation that the discharge of one type can change into that of the other (Langrehr, 1960*a*; Neil & Joels, 1961), the fact remains that in the normally beating heart the type A fibres are not active at a time when the type B fibres are maximally stimulated and vice versa (Fig. 1).

Whitteridge (1948) suggested that the A-type fibres may originate from receptors in series with atrial muscle fibres, thus being excited directly by atrial contraction, whereas the B-type fibres may originate from receptors being in parallel with muscle fibres, thus being silent with atrial contraction. However, an in-parallel orientation of receptor (B-type fibre) and muscle fibre is hard to reconcile with Paintal's observation (1953) that the discharge of a B-type fibre increased with atrial contraction in an isolated atrium under isometric conditions. Consequently, the differences in the temporal occurrence of the burst appear not to be connected with a particular orientation of the receptors with respect to the contractile element. Possibly the difference is related to receptor localization but in the sense that the A-type bursts may originate from receptors located within the atria where they are apt to be excited 'actively' by muscular contraction, whereas the B-bursts may originate from receptors located in the pulmonary or caval veins (Nonidez, 1937; Coleridge, Coleridge & Kidd, 1964) where they may be excited 'passively' through distension of these particular receptor zones. The high degree of activity of the A-type fibres fits well with their 'active' excitation; tendon organs are, for example, about 50 times more sensitive to 'active' than to 'passive' stimuli (Houk & Simon, 1967).

Although the question as to why identical receptors are excited at different times during the cardiac cycle remains a matter of debate, the differences in the discharge pattern and in the functional behaviour of A- and B-type fibres seen *in vivo* can be explained on the basis that they originate from identical receptors.

The high frequency discharge of A-type relative to B-type fibres is understandable bearing in mind: (1) the increase in the dynamic receptor response with increasing stimulus frequency, which we have shown here, and (2) the peculiarity of atrial mechanics in that the velocity of atrial

wall movement is appreciably faster (8 cm/sec) during the contraction phase than during the atrial filling phase (0·6 cm/sec). Accordingly, one might expect the receptors which are excited during the 'fast' contraction phase (A-type fibres) will fire with higher spike frequencies than those (B-type fibres) which are excited during the 'slow' filling phase.

Furthermore, one must also bear in mind the working range of a receptor on the stimulus–response curve in order to understand the differences in discharge pattern and functional behaviour. Generally, the relationship between stimulus strength and receptor response is not linear, but instead the receptor response decreases with increasing stimulus strength until saturation is reached.

This has already been shown in atrial receptors (Langrehr, 1960*b*), in muscle spindles (Toyama, 1966; Crowe & Matthews, 1964; Husmark & Ottoson, 1970), and baroreceptors (Angell James, 1971). In atrial receptors spike frequency increases linearly with atrial pressure from 0 to 10 cm water to spike frequencies of about 100 Hz. Beyond this range the curve flattens out. The A-type fibre discharge therefore is insensitive to changes in atrial mechanics because the receptors involved operate in the saturation range, as indicated by their high spike frequency per burst of about 200 Hz in chloralosed cats with intact circulation, and it was suggested that these fibres signal heart rate (Arndt, Brambring, Hindorf & Röhnelt, 1971). In contrast, the B-type fibres operate in the linear part of the stimulus–response curve. Thus their activity will vary with the state of distension of the atria (Paintal, 1953, 1972; Henry & Pearce, 1956; Langrehr & Kramer, 1960), and there is much evidence that B-fibres play a part in blood volume control (Gauer, Henry & Behn, 1970).

In conclusion, it has been shown that the atrial afferent nerves originate from a single type of mechanoreceptor which is characterized as a slowly adapting stretch receptor. The differences in their discharge pattern and their functional behaviour *in vivo* can plausibly be explained on the basis of identical receptors when the stimulus conditions and the working range on the stimulus–response curve is taken into consideration. The question as to why identical receptors are excited at different times during the cardiac cycle still remains a matter of debate, but is possibly related to their localization.

The support of the Deutsche Forschungsgemeinschaft through the Schwerpunktprogramm 'Receptorphysiologie' (Ar 64/4) and the Sonderforschungsbereich Kardiologie Düsseldorf is gratefully acknowledged.

The results were used to a large extent in M. Röhnelt's doctoral thesis and were reported in part at the 36th Annual Meeting of the Deutsche Physiologische Gesellschaft (*Pflügers Arch. ges. Physiol.* **312**, 23 (1969)).

The authors wish to express their gratitude to Professor J. P. Henry, University of Southern California, Los Angeles, and to Professor A. S. Paintal, Patel Chest Institute, University of Delhi, for their valuable criticism and assistance with the English translation.

REFERENCES

ADRIAN, E. D. (1933). Afferent impulses in the vagus and their effect on respiration. *J. Physiol.* **79**, 332–358.

ANGELL JAMES, J. E. (1971). The effects of altering mean pressure, pulse pressure and pulse frequency on the impulse activity in baroreceptor fibres from the aortic arch and right subclavian artery in the rabbit. *J. Physiol.* **214**, 65–88.

ARNDT, J. O. (1966). Die Beziehung zwischen Umfang der Vorhöfe und Vorhofdrucken bei Volumenänderungen an narkotisierten Katzen. *Pflügers Arch. ges. Physiol.* **292**, 343–355.

ARNDT, J. O., BRAMBRING, P., HINDORF, K. & RÖHNELT, M. (1971). The afferent impulse traffic from atrial A-type receptors in cats. Does the A-type receptor signal heart rate? *Pflügers Arch. ges. Physiol.* **326**, 300–315.

ARNDT, J. O. & KLAUSKE, J. (1967). Umfang der Vorhöfe und Vorhofdruck in den einzelnen Herzphasen. *Pflügers Arch. ges. Physiol.* **294**, 3.

BRONK, D. W. & STELLA, C. (1932). Afferent impulses in the carotid sinus nerve. The relationship of the discharge from single end organs to arterial blood pressure. *J. cell. comp. Physiol.* **1**, 113–130.

COLERIDGE, H. M., COLERIDGE, J. C. G. & KIDD, C. (1964). Cardiac receptors in the dog, with particular reference to two types of afferent ending in the ventricular wall. *J. Physiol.* **174**, 323–339.

CROWE, A. & MATTHEWS, P. B. (1964). The effects of stimulation of static and dynamic fusimotor fibres on the response to stretching of the primary endings of muscle spindles. *J. Physiol.* **174**, 109–131.

DABBERT, H. & GRÜSSER, O.-J. (1968). Reaktionen primärer und sekundärer Muskelspindelafferenzen auf sinusförmige mechanische Reizung. *Pflügers Arch. ges. Physiol.* **304**, 258–270.

FRANZ, G. N. (1969). Nonlinear rate sensitivity of the carotid sinus reflex as a consequence of static and dynamic nonlinearities in baroreceptor behaviour. *Ann. N.Y. Acad. Sci.* **156**, 811–824.

GAUER, O. H. & HENRY, J. P. (1963). Circulatory basis of fluid volume control. *Physiol. Rev.* **43**, 423–481.

GAUER, O. H., HENRY, H. P. & BEHN, G. (1970). The regulation of extracellular fluid volume. *A. Rev. Physiol.* **32**, 547–595.

GRÜSSER, O. J. & THIELE, B. (1968). Reaktionen primärer und sekundärer Muskelspindleafferenzen auf sinusförmige mechanische Reize. *Pflügers Arch. ges. Physiol.* **300**, 161–184.

HENRY, J. P. & PEARCE, J. W. (1956). The possible role of cardiac atrial stretch receptors in the induction of changes in urine flow. *J. Physiol.* **131**, 572–585.

HOUK, J. & SIMON, W. (1967). Responses of Golgi tendon organs to forces applied to muscle tendon. *J. Neurophysiol.* **30**, 1466–1477.

HUSMARK, I. & OTTOSON, D. (1970). Relation between tension and sensory response of the isolated frog muscle spindle during stretch. *Acta physiol. scand.* **79**, 321–334.

LANGREHR, D. (1960*a*). Entladungsmuster und allgemeine Reizbedingungen von Vorhofreceptoren bei Hund und Katze. *Pflügers Arch. ges. Physiol.* **271**, 257–269.

LANGREHR, D. (1960*b*). Beziehung zwischen Vorhofreceptoraktiväten und Herzmechanik von Hund und Katze bei verschiedenen Kreislaufzuständen. *Pflügers Arch. ges. Physiol.* **271**, 270–282.

LANGREHR, D. & KRAMER, K. (1960). Bezeihung der mittleren Impuls-frequenz von Vorhofreceptoren zum thorakalen Blutvolumen. *Pflügers Arch. ges. Physiol.* **271**, 797–807.

LENNERSTRAND, G. (1968). Position and velocity sensitivity of muscle spindles in the cat. I. Primary and secondary endings deprived of fusimotor activation. *Acta physiol. scand.* **73**, 281–299.

MATTHEWS, P. B. C. & STEIN, R. B. (1969). The sensitivity of muscle spindle afferents to small sinusoidal changes of length. *J. Physiol.* **200**, 723–743.

NEIL, E. & JOELS, N. (1961). The impulse activity in cardiac afferent vagal fibres. Naunyn-Schmiedebergs. *Arch. exp. Path. Pharmak.* **240**, 453–460.

NONIDEZ, J. F. (1937). Identification of the receptor areas in the venae cavae and pulmonary veins which initiate reflex cardiac acceleration (Bainbridge's Reflex). *Am. J. Anat.* **61**, 203–231.

OTTOSON, D. & SHEPHERD, G. M. (1971). Transducer properties and integration mechanisms in the frog's muscle spindle. In *Handbook of Sensory Physiology*, vol. 1, ed. LOEWENSTEIN, W. R. Berlin, Heidelberg, New York: Springer-Verlag.

PABST, H. (1965). Elektrophysiologische Untersuchung des Streckreceptors am Flügelgelenk der Wanderheuschrecke Locusta Migratoria. *Z. vergl. Physiol.* **50**, 498–541.

PAINTAL, A. S. (1953). A study of right and left atrial receptors. *J. Physiol.* **120**, 596–610.

PAINTAL, A. S. (1954). A study of gastric stretch receptors. Their role in the peripheral mechanism of hunger and thirst. *J. Physiol.* **126**, 255–270.

PAINTAL, A. S. (1963*a*). Vagal afferent fibres. *Ergebn. Physiol.* **52**, 74–156.

PAINTAL, A. S. (1963*b*). Natural stimulation of type B atrial receptors. *J. Physiol.* **169**, 116–136.

PAINTAL, A. S. (1972). Cardiovascular receptors. In *Handbook of Sensory Physiology*, vol. 2, ed. LOWENSTEIN, W. R. Berlin, Heidelberg, New York: Springer-Verlag.

RÖHNELT, M., BRAMBRING, P., HINDORF, K. & ARNDT, J. O. (1969). Der Impulsstrom von Vorhofafferenzen bei sinusförmiger Dehnung des isolierten Vorhofstreifenpräparates. *Pflügers Arch. ges. Physiol.* **312**, 23.

SCHÄFER, S. S. & HENATSCH, H. D. (1967). Dehnungsantworten der primären Muskelspindelafferenz bei elektrischer Reizung und natürlicher Innervation der beiden fusimotorischen Fasertypen. *Expl Brain Res.* **4**, 275–291.

STÄMPFLI, R. (1952). Bau und Funktion isolierter markhaltiger Nervenfasern. *Ergebn. Physiol.* **47**, 70–165.

STRUPPLER, A. (1955). Afferente vagale Herznervenimpulse und ihre Beziehung zur Hämodynamik. *Z. Biol.* **107**, 416–428.

TERZUOLO, C. A. & KNOX, C. K. (1971). Static and dynamic behaviour of the stretch receptor organ of Crustacea. In *Handbook of Sensory Physiology*, vol. 1, ed. LOEWENSTEIN, W. R., pp. 500–522. Berlin, Heidelberg, New York: Springer-Verlag.

TOYAMA, K. (1966). An analysis of impulse discharge from the spindle receptor. *J. physiol. Soc. Japan* **16**, 113–125.

WHITTERIDGE, D. (1948). Afferent impulses from the heart and lungs in the cervical vagus. *J. Physiol.* **107**, 496–512.