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AN ANALYSIS OF RECEPTOR POTENTIAL AND TENSION OF ISOLATED CAT MUSCLE SPINDLES IN RESPONSE TO SINUSOIDAL STRETCH

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SUMMARY

In isolated cat muscle spindles the receptor potential responses of primary and secondary endings as well as tension responses to sinusoidal length changes in the steady state have been analysed.

1. At a given stimulus frequency, receptor potential per unit length change (receptor potential gain) in both primary and secondary endings is constant when displacement is less than about 10 μm. With larger stretches, receptor potential gain decreases approximately as a power function of displacement, the gain of primary endings decreasing more rapidly with increasing displacement than that of secondary endings. Tension per unit length change (tension gain) shows a similar constant range above which it also decreases as a power function of displacement.

2. In spite of the large reduction in gain at high displacement amplitudes, response wave forms remained essentially sinusoidal. The gain reduction results principally from a displacement-dependent non-linearity which has a rapid onset and slow decay.

3. Receptor potential and tension responses to small amplitude sinusoidal stretch depend, in a parallel manner, on the initial length of the preparation.

4. Both receptor potential and tension responses are highly dependent on frequency of sinusoidal stretch. In primary endings receptor potential gain increased as a power function of frequency over the range 0·01 to about 40 Hz, above which frequency the gain decreased; phase advance remained relatively constant up to 10 Hz then decreased to become a phase lag at higher frequency. In secondary endings receptor potential gain remained fairly constant between 0·01 and 1 Hz then rose as a power function of frequency but less steeply than in primary endings.

5. The possible mechanisms underlying these findings are discussed.

INTRODUCTION

Since the pioneering investigations by B. H. C. Matthews (1935), stretch receptors in muscle have been studied by applying length changes at a constant velocity, holding the muscle at the new length and then returning to the initial length. Such ramp-and-hold stretches give useful information about dynamic and static responses of the receptors. In the mammalian spindle ramp-and-hold stretch shows clearly

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that primary and secondary endings typically differ in their dynamic responses and that the modification of the response of primary endings by dynamic or static fusimotor activity is also characteristically different (see Matthews, 1972).

More recently, several groups of investigators have used sinusoidal stretch for the study of mammalian muscle spindles. While non-linearities in response have prevented the full application of linear systems analysis, much new information has been gained about the response to small amplitude displacements and to a wide range of sinusoidal frequency. Beginning with the studies of Matthews & Stein (1969) and Poppele & Bowman (1970) modulation of impulse activity has been used to analyse the effects of sinusoidal stretch (see also, Hasan & Houk, 1975*a*, *b*; Goodwin, Hullinger & Matthews, 1975; Cussons, Hullinger & Matthews, 1977; Hullinger, Matthews & Noth, 1977*a*, *b*; and Chen & Poppele, 1978). Impulse activity in response to sinusoidal stretch has also been studied in frog spindles (Kirkwood, 1972; McReynolds & Ottoson, 1974) and in invertebrate muscle receptors (Chapman & Smith, 1963).

In the present study both receptor potential and tension responses to sinusoidal stretch have been analysed in isolated cat spindles. The receptor potential response to sinusoidal stretch has been described in both primary and secondary endings of mammalian spindles (Hunt & Ottoson, 1977) but that study was done without the availability of computating facilities to allow detailed analysis. Use of the receptor potential permits the analysis of a continuously varying response, rather than the fitting of a sinusoidal waveform to impulse data. It also eliminates contribution of the impulse initiating site to the response, providing a closer approach to transduction mechanisms. It will be shown that the range over which response is linearly related to amplitude is similar in the receptor potentials of both primary and secondary endings and in tension developed by the isolated spindle. Beyond this range responses show a compressive nonlinearity. Further, analysis of the effect of frequency of sinusoidal stretch indicates that receptor potential responses in primary endings are not determined simply by addition of a static positional sensitivity and a velocity sensitivity.

METHODS

Adult cats were anaesthesized with pentobarbitone, 35–40 mg/kg, I.P. Spindles were visualized in the thin muscles in the dorsolateral region of the tail and isolated with the axons of primary or secondary endings as previously described (Hunt & Ottoson, 1975). Occasionally, primary and secondary axons reach the sensory region in separate nerve branches, permitting isolation of both a primary and a secondary ending in the same sensory region.

The isolated spindle with its sensory axons was placed in an experimental chamber containing a modified Locke's solution at room temperature. The ionic composition (mM) of the bathing fluid was: NaCl 124, KCl 4·8, $CaCl_2$ 1·3, $MgSO_4$ 2·4, KH_2PO_4 1·2, HEPES (N-2-hydroxyethyl piperazine-N′-ethane-sulfonic acid) buffer 5·0. The pH was adjusted to 7·4. Tetrodotoxin (TTX, Sigma Chem. Co., 10^{-7} wt./vol.) was added to the solution to block impulse activity. One end of the spindle was tied to a nylon rod which was coupled to a tension transducer. The other end was tied to a stiff boron rod connected to a stretching device. Characteristics of the stretcher and force transducer are given below. The resting length of the preparation when slack had just been taken up (l_0) was measured with a calibrated reticle. One axon was raised on a pipette containing agar-Locke's solution into mineral oil. (In some early experiments, the axon was instead drawn down into a well containing heavy fluorocarbon oil (Fluorolube S-30, Hooker Corp., Niagara Falls, N.Y.). The pipette was connected via a sintered Ag-AgCl junction to the non-inverting input of a DC differential amplifier (Princeton Applied Research, model 113)

and an identical junction connected the inverting amplifier input to the bath. Low capacitance (32 pF/m) coaxial cable was used.

The stretcher was a servo-activated recorder pen motor (Brush, Gould Inc., Cleveland, Ohio) modified to reduce noise output and to increase stiffness and resonant frequency. Signals from the motor's internal feedback transducers were combined in an electronic network to provide a voltage proportional to the displacement of the stretching rod. Phase shift in the displacement signal, with respect to an independent measurement of stretching rod movement using a microscope and silicon photodetector, was less than 1° from DC to 100 Hz. Noise (1 kHz band width) was the equivalent of approximately 0·1 μm peak-to-peak displacement.

The tension transducer was an integrated semiconductor strain gauge beam (AE802, Akers Electronics, Horton, Norway) to which a 5 mm wooden extension was attached. Resonant frequency of the assembly was 800 Hz. The transducer was excited by a DC bridge and was connected to an amplifier identical to that used for recording the receptor potential. Tension and receptor potential signals were bandwidth limited by single pole adjustable lowpass filters contained within their respective amplifiers. Corner frequency of the filters was maintained approximately two decades above the fundamental measurement frequency. Displacement, tension and receptor potential amplitudes are expressed as peak values.

A minicomputer (980B, Texas Instruments, Dallas, Texas) was used both to deliver sinusoidal waveforms to the command input of the stretch amplifier and to digitize responses of the displacement transducer, tension transducer, and the receptor potential. Resolution of the digital-to-analogue (D/A) converter used to generate stretch waveforms was 1 part in 1024, independent of stretch amplitude. Two analogue-to-digital (A/D) converters sampled receptor potential and either tension or displacement, respectively. Maximum simultaneous sampling rate was approximately 15,000/sec, with a resolution of 1 part in 4096.

The measurement protocol depended on whether the desired frequency, f, was below or above 1 Hz. In either case, several periods of sinusoidal stretch (from 1 cycle at 0·01 Hz to 80 at 80 Hz) were delivered to the preparation before collecting data so that a steady state was reached. Next, for $f \leqslant 1$ Hz, the stretch continued for 8 periods, each period consisting of 1024 discrete increments from the D/A converter. Receptor potential, R, was sampled after each increment; at the same time displacement, D, and tension, T, were sampled alternately. Data sampled at corresponding times during each cycle of stretch were summed, so that at the conclusion of stretch 1024 points for R, 512 points for T, and 512 points for D resided in computer memory, representing one cycle of data averaged from 8 cycles of stretch. For $f > 1$ Hz, 64 periods of sinusoidal stretch were delivered, each period consisting of 128 discrete increments from the D/A converter. The method of averaging remained the same, so that the retained data points represented 8 periods of data average from 64 periods of stretch. Data sets from each stretch sequence were stored on a magnetic disk for subsequent analysis. Some parameters were computed immediately to provide an indication of the stability of the preparation and to allow selection of appropriate stimuli.

Analysis consisted of determining the in-phase and quadrature components of the averaged periodic wave forms D, T and R with respect to the computer-generated sinusoid and its harmonics. Each wave form was analysed independently by computing the coefficients of a discrete Fourier series expansion. Results were expressed as the peak amplitudes D_0, T_0, and R_0 and the phases (with respect to the computer stretch sinusoid) θ_D, θ_T, and θ_R of the fundamental (first harmonic) components of D, T, and R, respectively, plus similar amplitudes and phases for higher harmonics. Initially, the first to fifth harmonics were computed. However, upon comparing results of harmonic analysis with original digitized data, it was found that the fourth and fifth harmonics were seldom present to a significant extent unless they were associated with noise or other artifacts. For this reason, only the first to third harmonics were routinely computed. Second and third harmonic distortion in the displacement signal, D, were typically less than 0·1 % of D_0, rising as stretch amplitude was reduced to approximately 2 % at 1 μm peak stretch (the smallest used), and was probably due to noise in the displacement transducer and its electronics. The measured amplitude D_0 simply verified the programmed stretch amplitude. The phase θ_D, however was frequency-dependent and indicated the delay between the stretch command and the actual motion of the stretching rod. Phases of the fundamental components of T and R relative to the actual stretch sinusoid were therefore defined as ϕ_T and ϕ_R,

respectively, given by

$$\phi_T = \theta_T - \theta_D, \quad (1)$$

$$\phi_R = \theta_R - \theta_D. \quad (2)$$

Amplification ratios or gains A_T and A_R were defined as

$$A_T = T_0/D_0, \quad (3)$$

$$A_R = R_0/D_0, \quad (4)$$

for the fundamental component. Similar ratios and phases with respect to D_0 and θ_0 were computed for harmonics in an analogous manner. These ratios are subsequently referred to as harmonic 'gains' even though the displacement waveform consisted only of the fundamental component.

A control sinusoidal stretch (usually $D_0 = 5\ \mu m, f = 10$ Hz) was delivered frequently during each experiment; data sets were rejected unless response to controls remained stable.

RESULTS

Data from thirty-one primary and fourteen secondary endings were obtained. Endings were identified during dissection as primary or secondary by the criteria described previously (Hunt & Ottoson, 1975). Impulse and receptor potential responses to ramp-and-hold stretch were used to confirm the identification. Primary endings showed an initial burst, a prominent initial dynamic component of the receptor potential and, generally, a greater dynamic sensitivity than secondary endings. Measurements of receptor potential and tension were made after one or more 'warm up' cycles so as to approach a steady-state condition.

Dependence of response on amplitude of stretch.

The amplitude of the receptor potential in both primary and secondary endings increased linearly with the magnitude of sinusoidal displacement over a limited range. Beyond that range the receptor potential amplitude per unit displacement, or gain, decreased progressively as stretch was increased. Tension developed by the isolated spindle showed a similar linear range, beyond which tension gain also exhibited a progressive decrease as stretch amplitude was increased.

While the receptor potential responses to small displacements were nearly sinusoidal in form, the responses to large amplitude stretches, especially in primary endings, showed distortion, manifest mainly in the second and third harmonic components. However, the amount of distortion was small and, it will be seen, not sufficient to account for the fall in gain of the fundamental component as displacement was increased beyond the linear range. Indeed, the receptor potential response generally retained an essentially sinusoidal form well beyond the linear range. The fall in receptor potential gain with increasing displacement appears to result from a compressive nonlinearity. Its onset occurs rapidly after the beginning of stretch and it persists through continuing cycles of sinusoidal displacement.

Representative responses to sinusoidal stretch may be seen in Figs. 1 and 2. In the spindle of Fig. 1 both a primary and secondary ending were isolated. Their receptor potentials increased approximately in proportion to displacement when stretch amplitude was increased from 6 to 15 μm and remained nearly sinusoidal in form. At 60 μm displacement the receptor potential responses were considerably

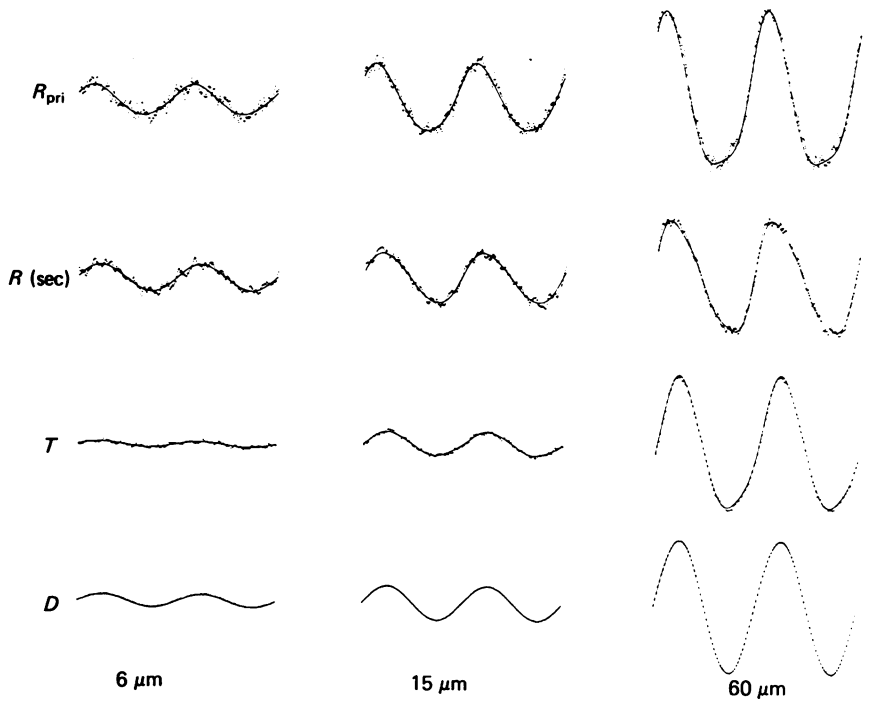

Fig. 1. Receptor potentials of a primary (R_{pri}) and a secondary (R_{sec}) ending from the same spindle, together with displacement (D) in response to 10 Hz sinusoidal stretch of 6, 15 and 60 μm. In this, as well as Figs. 2 and 7, averaged digitized data points are shown as dots while the solid lines represent the waveform resynthesized by adding the fundamental, second and third harmonic components; traces begin at zero crossing of D.

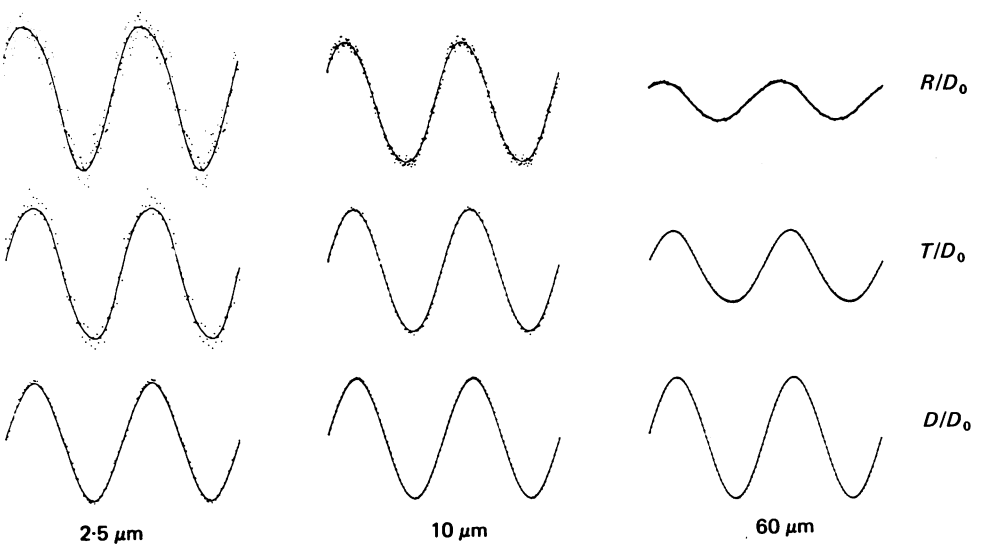

Fig. 2. Primary ending receptor potential, tension, and displacement to 1 Hz sinusoidal stretch at amplitudes of 2·5, 10 and 60 μm, normalized with respect to displacement (receptor potential, R/D_0; tension, T/D_0; and displacement, D/D_0). In this figure peak values of R/D_0 and T/D_0 correspond to gains A_R and A_T. Each record displays one averaged period, shown repeated.

less than 10 times those to 6 μm in both the primary and secondary ending. Further, the responses at 60 μm showed evident distortion, particularly in the primary ending.

The response of another primary ending is illustrated in Fig. 2. In this case the responses have been scaled vertically so as to be normalized with respect to stretch amplitude. Non-linearity is evident in both the receptor potential and tension responses. Responses of both receptor potential and tension relative to displacement

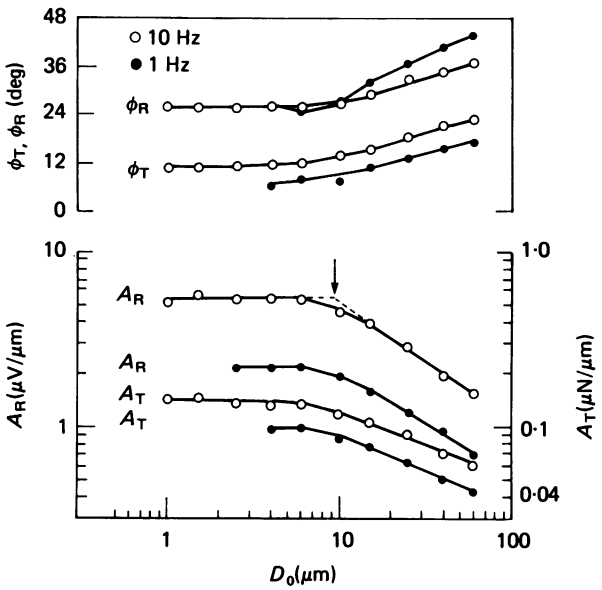

Fig. 3. Dependence of fundamental components of response on amplitude of sinusoidal stretch at 1 and 10 Hz. Primary ending. A_R, receptor potential gain; A_T, tension gain; ϕ_R, receptor potential phase; ϕ_T, tension phase. Open circles, 10 Hz; filled circles, 1 Hz. Arrow indicates corner, $D_{C,R}$.

were slightly less at 10 μm than at 2·5 μm. At 60 μm there was a more marked reduction, especially in receptor potential. In spite of the large decrease in the amplitude of the normalized receptor potential at 60 μm compared to 2·5 μm, the response in this ending showed little distortion. There was a greater phase advance in the receptor potential responses of primary than of secondary endings, while tension responses showed less phase advance than either (Figs. 1 and 2).

Receptor potential and tension responses were examined over a wide range of displacements. We have defined the gain of the receptor potential (A_R) and tension (A_T) responses as the peak amplitudes of the fundamental components per unit displacement (R_0/D_0 and T_0/D_0). The relation between fundamental receptor potential gain (A_R) and peak stretch amplitude (D_0) of a representative primary ending examined at 1 Hz and 10 Hz is shown in Fig. 3. Gain remains essentially constant at both frequencies until stretch amplitude reaches about 10 μm. Beyond this 'linear range', A_R decreases as an approximate power function of D_0, as evidenced by the straight line fit to the data at higher stretch amplitudes. (Linear range refers to the constancy of gain of the fundamental component without taking into consideration

harmonic distortion.) The extrapolation of this straight line together with a horizontal line through the data in the linear range (dashed lines) defines a corner. The value of D_0 at this corner ($D_{C,R}$) was taken as the approximate upper limit of the linear range. A_R and D_0 are plotted on identical logarithmic axes such that the geometric slope α_R (expressed in dimensionless units) of the straight line fitting the data for $D_0 > D_{C,R}$ appears in the exponent relating R_0 and D_0:

$$R_0 \sim D_0^{\alpha_R+1}, \tag{5}$$

where $\alpha_R = \Delta \log A_R / \Delta \log D_0$. Parameters for tension responses, $D_{C,T}$ and α_T, were determined in an analogous manner.

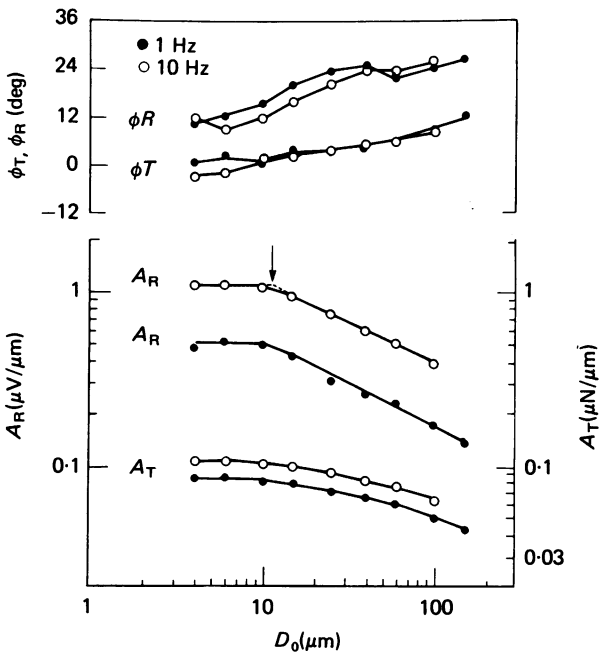

Fig. 4. Dependence of fundamental components of response on amplitude of sinusoidal stretch at 1 and 10 Hz. Secondary ending. Symbols as in Fig. 3.

Although the gain at 1 Hz is considerably less than at 10 Hz, the linear amplitude range and α_R are similar (Fig. 3). There was no systematic dependence of $D_{C,R}$ or α_R on frequency over the range from 0·1 to 50 Hz.

Receptor potential phase lead (ϕ_R) remained essentially constant over the linear range and then increased as stretch amplitude was increased (Fig. 3).

Tension gain (A_T) at 1 Hz as well as tension phase (ϕ_T) are also shown in Fig. 3. A_T appeared to be constant within the linear range of A_R. With higher stretch amplitudes A_T also fell as an approximate power function of D_0, but the slope (α_T) was less steep than α_R. Tension gain was higher at 10 Hz than at 1 Hz; however the difference was less than that of A_R at the two frequencies. Tension phase (ϕ_T) was less advanced than ϕ_R, was nearly constant below 10 μm and advanced with increases of D_0 beyond the linear range.

Fig. 4 shows a similar plot of the response of a secondary ending to sinusoidal

stretch at 1 and at 10 Hz. Receptor potential gain is greater at 10 than at 1 Hz but, at both frequencies, remains constant until D_0 reaches about 10 μm. Above the corner, the data fit a straight line with a lesser slope (α_R) than the primary ending of Fig. 3. Receptor potential phase lead is less than in the primary ending of Fig. 3 but again shows some increase as D_0 is increased.

In all the spindles examined, A_R, ϕ_R, A_T, ϕ_T, $D_{C,R}$ and $D_{C,T}$ showed a similar dependence on D_0 as the examples shown in Figs. 3 and 4. These data are presented in Table 1. The linear ranges of receptor potential gain in primary and in secondary endings and of tension gain, as indicated by $D_{C,R}$ and $D_{C,T}$ were not significantly different. There was a significant difference between the average values of α_R in primary and secondary endings ($P < 0{\cdot}01$, see Table 1).

The effect of changes in initial length

It is known that sensitivity of the primary ending to small amplitude sinusoidal stretch increases markedly when the initial length of muscle is increased. Matthews & Stein (1969) found the sensitivity of an ending of a de-efferented preparation increased tenfold when the initial length of the soleus muscle was increased by 6 mm. In the isolated spindle the effect of changing initial length has been examined on the amplitude of receptor potential and tension responses to sinusoidal stretch (Fig. 5). Both the receptor potential (R_0) of the primary ending and tension (T_0) increased in a parallel and nearly linear manner with increase in initial length. The increase in spindle length of about 2·3 percent augmented both R_0 and T_0 by approximately 50 %.

The linear relation between T_0 and l (where $l = l_0 + \Delta l$) is consistent with an effective elastic modulus K_{eff}, which increases approximately linearly with increasing length Δl beyond some reference length l_0;

$$K(l)_{eff} = \lim_{D_0 \to 0} (T_0/D_0) = k_1 + k_2 \Delta l \qquad (6)$$

An effective elastic modulus, as given in eq. (6), predicts second harmonic distortion in response to larger amplitude sinusoidal stretch (see below).

Distortion

One might anticipate that, while receptor potential responses to small amplitude sinusoidal stretch may be nearly sinusoidal in form and show little distortion, larger stretches might produce distortion for a variety of reasons. (1) If instantaneous gain were nonlinear, being greater near cross-over than near the peaks of displacement, the waveform would deviate from a sinusoidal form. (2) With large stretches the preparation might become slack during the relaxation half cycle, causing the response to flatten out. (3) With large depolarizations significant nonlinearity could result from approach of the receptor potential to the equilibrium potential for the receptor conductance change. (4) Mechanical factors might introduce several types of distortion.

On inspection, the most evident type of distortion in primary endings was flattening during the relaxation phase of the response to large stretches; with higher amplitudes there was also a tendency for the rising phase to be steeper than the falling

TABLE 1. Amplitude-response data

Frequency	Parameter	Primaries	Secondaries	All	Units
10 Hz	α_R*	$-0{\cdot}50 \pm 0{\cdot}10$ (25)	$-0{\cdot}33 \pm 0{\cdot}12$ (14)	—	—
	α_T*	—	—	$-0{\cdot}2 \pm 0{\cdot}02$ (28)	—
	$D_{C,R}$*	$7{\cdot}8 \pm 4{\cdot}7$ (23)	$9{\cdot}1 \pm 5{\cdot}5$ (11)	—	μm, peak
	$D_{C,T}$*	—	—	$9{\cdot}5 \pm 2{\cdot}9$ (25)	μm, peak
	$2HD_T$ (D_o = 30 μm)	—	—	$4{\cdot}7 \pm 2{\cdot}3$ (24)	% fund
	$2HD_R$ (D_o = 30 μm)	$15{\cdot}9 \pm 4{\cdot}0$ (19)	$6{\cdot}8 \pm 2{\cdot}9$ (11)	—	% fund
	$3HD_T$ (D_o = 30 μm)	—	—	$1{\cdot}1 \pm 0{\cdot}8$ (24)	% fund
	$3HD_R$ (D_o = 30 μm)	$5{\cdot}6 \pm 3{\cdot}8$ (19)	$3{\cdot}1 \pm 1{\cdot}6$ (11)	—	% fund
1 Hz	α_R	$-0{\cdot}45 \pm 0{\cdot}16$ (9)	$-0{\cdot}36 \pm 0{\cdot}12$ (8)	—	—
	α_T	—	—	$-0{\cdot}24 \pm 0{\cdot}11$ (12)	—
	$D_{C,R}$	$8{\cdot}3 \pm 3{\cdot}7$ (12)	$10{\cdot}3 \pm 5{\cdot}6$ (9)	—	μm, peak
	$D_{C,T}$	—	—	$12{\cdot}5 \pm 8{\cdot}0$ (12)	μm, peak
	$2HD_T$ (D_o = 60 μm)	—	—	$6{\cdot}9 \pm 2{\cdot}7$ (12)	% fund
	$2HD_R$ (D_o = 60 μm)	$11{\cdot}6 \pm 6{\cdot}8$ (8)	$4{\cdot}4 \pm 1{\cdot}8$ (7)	—	% fund
	$3HD_T$ (D_o = 60 μm)	—	—	$1{\cdot}9 \pm 1{\cdot}4$ (12)	% fund
	$3HD_R$ (D_o = 60 μm)	$3{\cdot}7 \pm 1{\cdot}2$ (8)	$2{\cdot}6 \pm 1{\cdot}2$ (7)	—	% fund

Values shown are mean $\pm$ S.D., followed by number of spindles in parentheses

* Among individual spindles there appeared to be no correlation between particular values of $D_{C,R}$ and $D_{C,T}$ and only a slight correlation between α_R and α_T. The average value of α_R for primary endings was the same for twelve decapsulated spindles ($-0{\cdot}49 \pm 0{\cdot}11$ S.D.) as for nine whose capsule remained intact ($-0{\cdot}52 \pm 0{\cdot}09$ S.D.).

phase. Secondary endings showed less distortion and its form was more variable. Table 1 compares second and third harmonic distortion in primary and secondary endings at amplitudes of 30 μm (10 Hz) and 60 μm (1 Hz). At 10 Hz second harmonic distortion averaged 15·9 % of the fundamental in primary endings and 6·8 % in secondary endings, while third harmonic distortion was less, averaging 5·6 % in primary and 3·1 in secondary endings. At 1 Hz both second and third harmonic distortion were less.

The changes in the amplitudes of the fundamental, second harmonic and third harmonic components of the tension and receptor potential responses to varying amplitudes of sinusoidal stretch have been compared. Such a comparison might indicate the mechanisms underlying distortion. For example, the effective elastic modulus defined in eqn. (6) predicts distortion of the tension response which is purely second harmonic and which increases as the square of displacement amplitude (D_0). Thus, gain of the second harmonic component should increase as the first power of D_0.

A representative example is shown in Fig. 6. Tension fundamental component gain remained essentially constant until D_0 reached about 10 μm and then fell with increasing D_0 (Fig. 6*A*). Below 3 μm most of the second harmonic component was due to noise; above 5 μm 2*HD* gain increased approximately as the first power of D_0. This is consistent with the prediction noted above. Third harmonic distortion appeared to be mainly due to artifactual noise, 3*HD* gain decreasing with a slope of about 1.

The gains of the fundamental components of both the primary and secondary endings' receptor potentials (Fig. 6*B*) showed a linear range of < 10 μm; they then fell as a power law function of D_0 (see above). Gain of the second harmonic component of the primary increased within the linear range of the fundamental; beyond the linear range it fell but less steeply than did the fundamental. Thus, although 2*HD* gain was falling its fraction in the total waveform increased.

In the secondary ending the second harmonic component gain changed little with increasing D_0. Again since the gain of the fundamental in this secondary ending was falling, the percent of 2*HD* in the response was increasing. The third harmonic component gain was very small and appeared to fall with increasing D_0, suggesting it was due largely to noise.

The two types of amplitude nonlinearity observed in the receptor potential, reduction in fundamental component gain at stretch amplitudes beyond the linear range and generation of harmonic distortion, have been described separately. Quantitatively, the former was dominant by approximately one order of magnitude. In Fig. 6*B*, for example, as D_0 increased from 10 to 100 μm the primary receptor potential underwent a decrease in fundamental component gain of approximately 3 μV/μm while its harmonic component gains remained well below 1 μV/μm. Generally, distortion was sufficiently low so that behaviour ascribed to the fundamental was representative of the receptor potential waveform as a whole. In Fig. 6, square symbols denote gains determined by dividing measured peak-to-peak tension or receptor potential amplitude by peak-to-peak displacement. Dependence of gain determined in this manner on D_0 was nearly identical to that of the fundamental component alone in both primary (open symbols) and secondary (filled symbols)

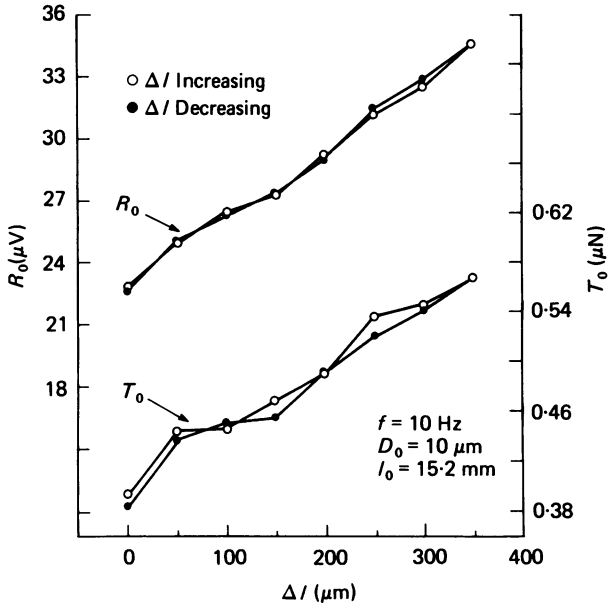

Fig. 5. Effect of initial length on fundamental components of receptor potential, R_0 and tension, T_0. Primary ending: sinusoidal stretch of 10 μm at 10 Hz. Responses recorded with increasing (open circles) then decreasing (filled circles) step changes in length, Δl, of 50 μm beginning at initial length, l_0, of 15·2 mm. After each change of initial length, a period of 0·5 min was allowed before testing the response to sinusoidal stretch. Note absence of hysteresis.

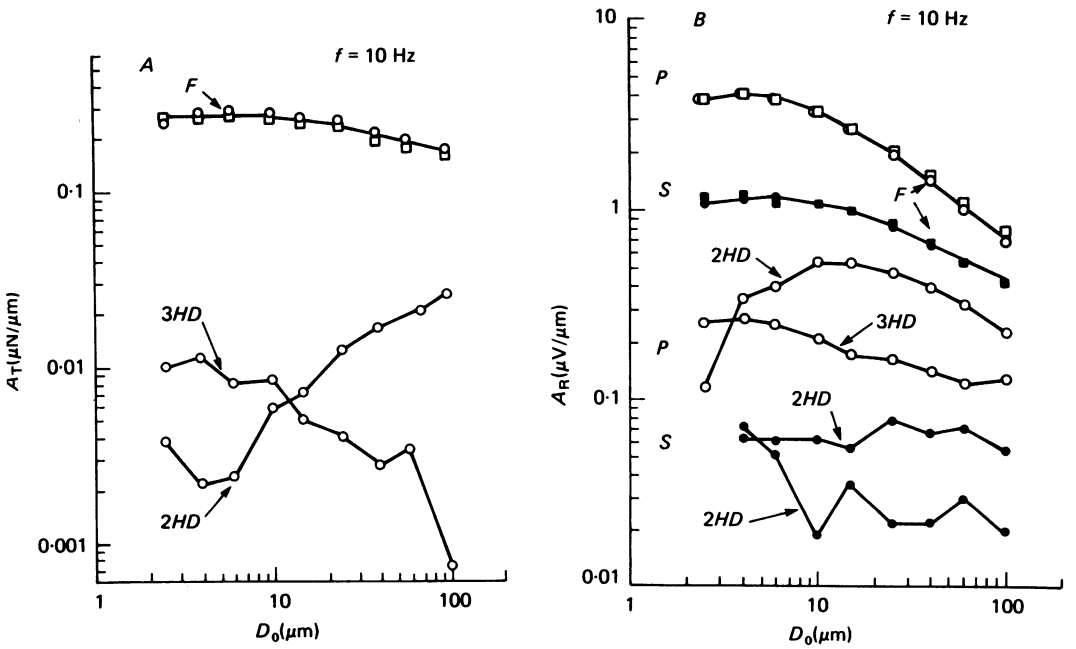

Fig. 6. Relations of the fundamental, second, and third harmonic components of response to amplitude of sinusoidal stretch at 10 Hz. A, tension gain; B· receptor potential gain of primary (P) and secondary (S) ending of same spindle. F, fundamental; $2HD$, second harmonic; $3HD$, third harmonic. Circles indicate values of F, $2HD$ and $3HD$. Squares are peak-to-peak values of tension and receptor potential response divided by peak-to-peak values of displacement.

endings. Root-mean-square gains (see Hullinger *et al.* 1977*a*) were also computed and found to exhibit the same amplitude dependence as the fundamental component.

Frequency response

Responses to constant amplitude sinusoidal stretch were examined over the frequency range 0·01–100 Hz. Stretch amplitudes used were generally at the upper end of the linear range, although higher stretch amplitudes gave similar results. Receptor potential and tension responses showed a marked frequency dependence.

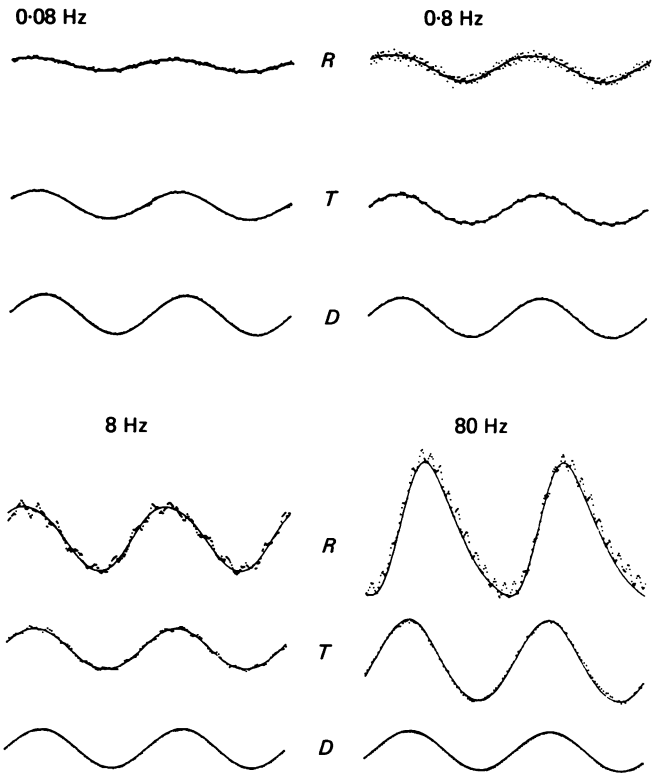

Fig. 7. Tension, T, and receptor potential, R, in response to sinusoidal stretch, D, delivered at four frequencies. Peak stretch amplitude, 7·5 μm. Only one averaged period of responses was obtained at 0·08 and at 0·8 Hz (shown repeated).

Receptor potential amplitude in primary endings showed a progressive increase as frequency was raised up to about 50 Hz and declined slightly at still higher frequencies. Secondary ending receptor potentials showed little change in amplitude until frequency reached 1 Hz; from 1 to 50 Hz the increase in amplitude was less than in primary endings.

An example of the response of a primary ending is illustrated in Fig. 7. Receptor potential response increased progressively wth increasing frequency; tension response also increased but to a lesser extent. At the 3 lower frequencies receptor potential phase was advanced relative to displacement; at 80 Hz it was retarded. At 80 Hz the receptor potential response showed obvious distortion. Similar

distortion at high frequencies was observed in most endings examined, even at extremely low stretch amplitudes.

The changes in gain and phase of the receptor potential response of a primary ending and of the tension response, as frequency of sinusoidal stretch was varied from 0·01 to 80 Hz, are shown in Fig. 8. The gain of the fundamental component of the receptor potential (A_R) was highly dependent on the frequency, rising about twenty-fold between 0·01 and 20 Hz. There was some drop in A_R at 40 Hz and above, a fall more marked in this unit than was typical (see Fig. 10). Tension gain (A_T) increased

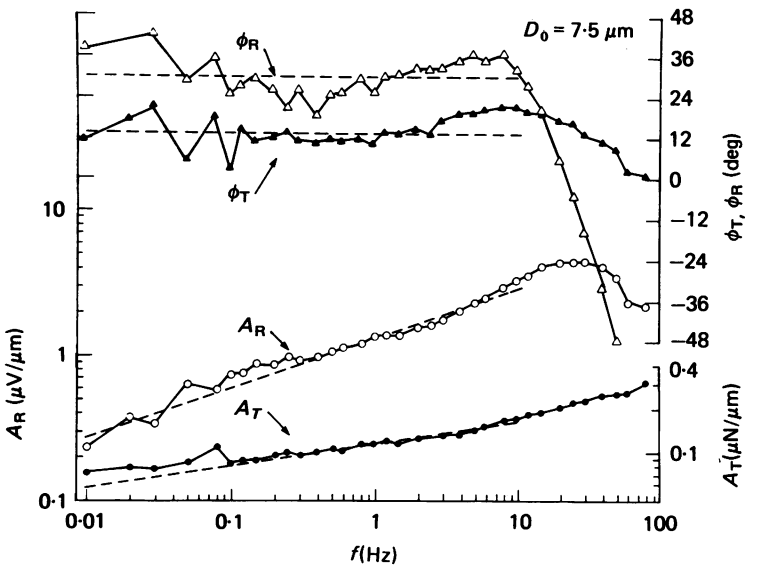

Fig. 8. Frequency response of primary ending. Peak stretch amplitude, 7·5 μm. Receptor potential (fundamental component) gain, A_R, and phase, ϕ_R, open symbols. Tension (fundamental component) gain, A_T, and phase, ϕ_T, filled symbols. Dashed lines are predictions of minimum phase power-law model (see Discussion).

about fourfold as frequency was raised from 0·01 to 80 Hz. The phase of the fundamental of the receptor potential response (ϕ_R) was advanced by about 30° relative to displacement over the frequency range 0·01–10 Hz; at higher frequencies ϕ_R fell, becoming negative above 20 Hz. Tension phase, ϕ_T, also was advanced relative to displacement between 0·01 and 10 Hz but to a lesser extent than ϕ_R. Above 10 Hz ϕ_T fell, but much less steeply than ϕ_R, reaching zero at 80 Hz.

Comparable data from a secondary ending are shown in Fig. 9. Gain, A_R, changed little as frequency was raised from 0·05 to 1·0 Hz, but approximately doubled when frequency was raised from 1·0 Hz to 30 Hz. Above 30 Hz A_R fell. Receptor potential phase, ϕ_R, led displacement by about 12° over the frequency range 0·05–8 Hz. As frequency was increased above 8 Hz ϕ_R fell, becoming negative above 10 Hz. In this spindle ϕ_T began to fall at a lower frequency than in the spindle of Fig. 8 and became negative above 20 Hz.

The responses of three pairs of primary and secondary endings, each pair from an individual spindle, are shown in Fig. 10. Frequency of sinusoidal stretch was varied

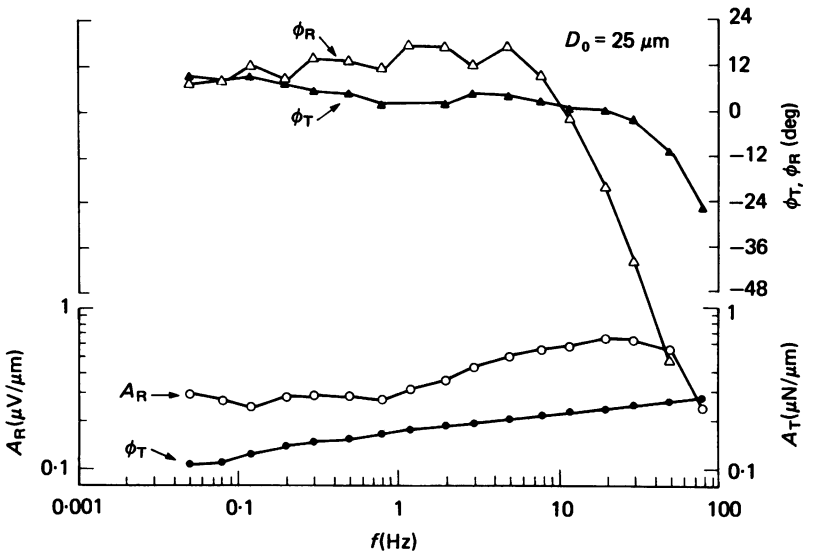

Fig. 9. Frequency response of secondary ending. Peak stretch amplitude, 25 μm. Symbols as in Fig. 8.

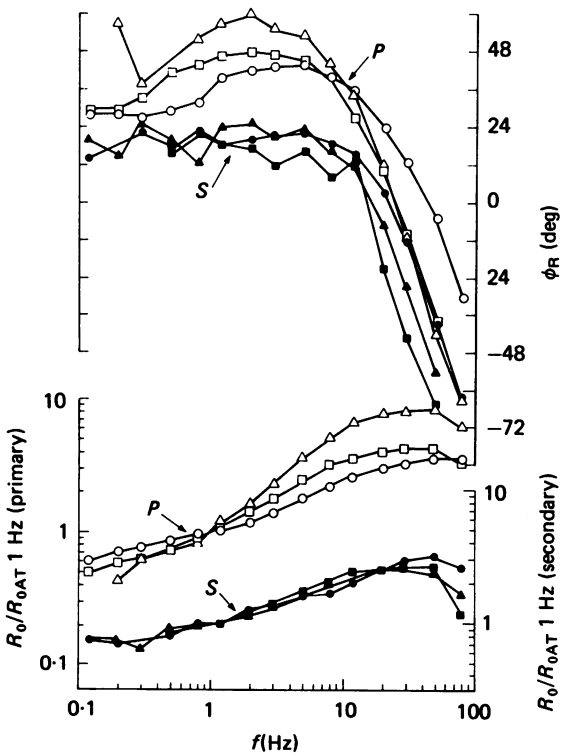

Fig. 10. Frequency–response of three pairs of endings, each pair from the same spindle. Open symbols, primary endings. Filled symbols, secondary endings. Peak stretch amplitudes 12·5 μm, circles; 15 μm, squares; 10 μm, triangles. Phase of fundamental components, ϕ_R. Normalized fundamental receptor potential component, R_o/R_o at 1 Hz.

from 0·12 to 80 Hz. The receptor potential gains have been normalized with respect to gains at 1 Hz. Over the frequency range 0·12–20 Hz the gains of primary endings increased, on average, about 3 times more than the secondary endings. Phase advance of primary endings over the range 0·12–10 Hz was consistently greater than that of secondary endings. There was also a greater tendency for phase advance in primary endings to increase as frequency was raised from 0·5 to 5 Hz.

Maximal phase advance observed in tension ($\phi_{T,\,max}$) and receptor potential ($\phi_{R,\,max}$) was recorded for each ending; mean values are given in Table 2. In the frequency

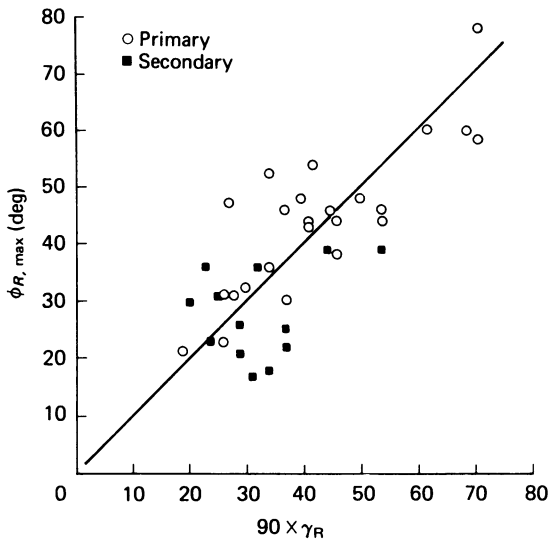

Fig. 11. Plot of maximum phase advance, $\phi_{R,\,max}$, *v.* power law slope, γ_R, for all endings examined. Open circles, primary endings. Filled squares, secondary endings. Abscissa calibrated in units of $90 \times \gamma_R$. Line passing through data has unity slope (equ- (6b); see Discussion).

TABLE 2. Frequency–response data

Parameter	Primaries	Secondaries	All	Units
γ_R	0·46 ± 0·16 (21)	0·36 ± 0·1 (12)	—	—
$\phi_{R,\,max}$	43·8 ± 12·4 (21)	28·0 ± 7·5 (12)	—	deg
γ_T	—	—	0·14 ± 0·06 (19)	—
$\phi_{T,\,max}$	—	—	11·8 ± 3·8 (19)	deg
$\gamma_R'(f < 1$ Hz)	0·37 ± 0·17 (19)	0·1 ± 0·18 (12)	—	—

Values shown are mean ± S.D. followed by number of spindles in parentheses.

range from 1 to 10 Hz, gains A_T and A_R increased as approximate power functions of frequency for all endings examined. Power law slopes $\gamma_R = \Delta \log A_R / \Delta \log f$ and $\gamma_T = \Delta \log A_T / \Delta \log f$, were determined graphically by fitting straight lines to data in this range. Analogous slopes, γ_R', were also determined in the lower frequency range 0·1–1 Hz. Tension and receptor potential from primary endings showed little change in slope down to the lowest measurement frequency; in contrast, receptor potential from secondary endings usually showed a discernable corner at approximately 1·0 Hz

(compare γ_R and γ_R' in Table 2). Fig. 11 is a plot comparing $\phi_{R,max}$ to power law slope γ_R for all endings from which frequency response data were obtained. Those endings with higher phase advance tended to have steeper slopes. There was considerable overlap between the populations of primary and secondary endings, although average phases and slopes differed significantly ($P < 0.05$, Table 2).

DISCUSSION

The present results show that the gains of the receptor potential response of both primary and secondary endings to sinusoidal length change have a similar linear range. In isolated spindles this range extends to about 10–15 μm. There are difficulties in comparing these values of the linear range with those obtained from impulse activity, for the measurements are different and the receptor potential data permit a more accurate determination of gain. Nevertheless, impulse data of Matthews and Stein (1969), Hasan & Houk (1975*b*) and Hullinger *et al.* (1977) all suggest that the primary ending shows a response that increases proportionately with stretch up to about 0·1 mm in the soleus muscle. If one assumes a spindle is about one fifth the length of the muscle and that the displacement is equally distributed along this length, this would correspond to a displacement of about 20 μm of the spindle. This, at least, approximates the linear range observed in the receptor potential of the isolated spindle. The data on the linear range of impulse response of secondary endings are less clear. Several investigators have suggested that secondary endings respond linearly over a wide range, up to several mm of stretch amplitudes (Matthews & Stein, Chen & Poppele, 1978). However, Cussons *et al.* (1977) showed responses of secondary endings to sinusoidal stretch which increased steeply with the amplitude up to about 60 μm and then increased more gradually. This again is roughly comparable to our measurements of the linear range.

Estimates of the range over which spindle endings respond linearly are difficult to determine from impulse data, particularly for secondary endings. The present study indicates that, beyond the linear range, the power law exponent of the relation between receptor potential gain and displacement (α_R) averages -0.33 in secondary and -0.50 in primary endings. This may result in a less prominent corner in plots relating impulse response to displacement in secondary endings than in primary endings. It seems likely that the very large estimates of the linear range, up to several mm in soleus, were based on an inability to resolve the smaller range of linear response. An earlier study of receptor potential of primary and secondary endings also failed to detect the small linear range of the secondary ending (Hunt & Ottoson, 1977). The fact that a linear model gives a better prediction of the response to large stretches in a secondary than in a primary ending (Hasan & Houk, 1975*b*) may also depend on the value of α_R being less in secondary endings.

The linear range of receptor response appears, from the present studies, to depend on amplitude of displacement and to be the same at all frequencies studied. The close similarity of the linear range of gain in both primary and secondary receptor potentials, as well as in tension, strongly suggests a common basis, most likely in the mechanical properties of the intrafusal muscle fibres. A possible mechanism is the short range elastic component which probably results from cross bridges between thick and

thin filaments present in resting muscle fibres. There is indirect evidence from impulse responses to stretch (Brown, Goodwin & Matthews, 1969), as well as more direct evidence from tension responses of isolated spindles (Hunt & Ottoson, 1976), indicating that such a short range elasticity in intrafusal fibres underlies the initial burst response of primary endings to ramp stretch. The short range elasticity would cause the intrafusal fibres to be relatively stiff for small stretches, transmitting a high proportion of the length change to the sensory region. With larger stretch, exceeding the limits of the short range elasticity, the intrafusal fibres would become more compliant and transmit proportionately less of the length change to the sensory region.

Since the sensory region of the intrafusal muscle fibres is probably more compliant and more purely elastic in its properties than are the more polar regions of the intrafusal fibres, tension may be considered as an indication of displacement within the combined sensory regions of the intrafusal fibres. This displacement may, of course, differ among the individual fibers, particularly between bag and chain fibres. Furthermore the tension responses may depend to some extent on other elements parallel to the intrafusal fibres such as collagen, elastic fibres and other cellular elements. Nevertheless, at first approximation tension may be taken to indicate the average displacement of the sensory region. Certain aspects of the response to sinusoidal stretch are similar in both tension and receptor potential. The extent of the linear range in the receptor potential gain of primary and secondary endings is similar to the linear range of tension. Beyond the linear range α_T is $-0{\cdot}2$ whereas α_R for primary endings averages $-0{\cdot}5$ and for secondary endings $-0{\cdot}33$. The difference between these slopes might depend upon the contribution of other than mechanical factors to the receptor potential response, for example the conductance changes in the terminals. Alternately α_R of the primary ending might reflect the mechanical contribution of both nuclear bag and chain fibers, α_R of the secondary that of chain fibres, while α_T might be less than either because of other mechanical components. Second harmonic distortion also differs in the receptor potential and tension responses, increasing in tension with the square of displacement amplitude but showing a more complex dependence of receptor potential on displacement. At this point it is difficult to assign the role of mechanical factors to the production of distortion in the neural response.

Beyond the linear range the response per unit increment of length decreases but the response does not simply suffer a progressive instantaneous attenuation as stretch amplitude increases. That would result in a highly distorted response to sinusoidal length change. As noted by Matthews & Stein (1969), the response beyond the linear range 'is still reasonably sinusoidal with little sign of harmonic distortion or change in phase angle.' The gain becomes compressed so that with a large sinusoidal stretch the receptor gain appears to have been changed to a lesser value, operative over the entire sine period. This includes the periods near zero crossings when displacement is momentarily within the linear range. Hasan & Houk (1975) referred to this type phenomenon as 'resetting'. Gain compression allows the receptor to give a relatively undistorted sinusoidal response to stretch beyond the linear range. Gain or sensitivity appears to vary as a continuous power function of peak displacement amplitude beyond the linear range. As has been noted, the slope α_R, which deter-

mines the degree of compression, is significantly different in primary and secondary endings.

Tension gain also shows compression beginning at approximately the same amplitude of displacement as receptor potential compression. The slope of the relation between log tension gain and log displacement, α_T, however, is less steep than α_R of either primary or secondary endings.

The time courses of the onset and decay compression have not yet been studied in detail, but preliminary experiments (R. S. Wilkinson & C. C. Hunt, unpublished results) indicate that the onset is very rapid and the decay much slower. The recovery of maximal gain in response to sinusoidal stretch within the linear range following a large brief rectangular pulse (400 μm, 20 msec, for example) requires several seconds. The onset of compression induced by the pulse is extremely rapid. It may occur nearly instantaneously when stretch exceeds the linear range, as in Hasan & Houk's (1975*b*) experiments on ramp-and-hold stretch. If compression occurs when the short range elasticity of the intrafusal fibres has been exceeded, this may occur as soon as cross bridges between thick and thin filaments have been broken. Decay of compression may depend on the time taken for cross bridges to reform. Lack of distortion in receptor potential response to 1 Hz large amplitude stretch (Fig. 2) also indicates a compression decay time on the order of 1 sec or longer. Time course of compression in tension gain has not been examined.

The observed characteristics of gain compression appear well suited to the role of the spindle as a mechanoreceptor operating over a wide dynamic range. The rapid onset of compression permits spindle receptors to respond to large and sudden length changes without saturation, as occurs with large amplitude ramp stretch delivered at high velocity (Hasan & Houk, 1975*b*). The slow decay of compression allows the response to a repeated large stretch to follow a particular wave form such as a sinusoid with negligible distortion. A number of sensory systems exhibit some form of compressive nonlinearity which allows them to function over a wide range of signal amplitudes. This occurs most notably in the visual and auditory systems.

The effect of varying frequency on receptor potential gain and phase of primary and secondary endings may also be compared with its effect on the gain and phase of impulse responses to sinusoidal stretch. In the present study impulse initiation was blocked by TTX. Thus the recorded receptor potential response to applied stretch depends upon the electrotonic spread from the nerve terminals to the recording site. Attenuation by spread through the branched ending might decrease the response, particularly at higher frequencies of sinusoidal stretch. Similar attenuation may occur in the spread of receptor current to the impulse initiation site. Since the site, or sites, of impulse initiation in primary and secondary endings is not known, it is not possible to compare the extent of attenuation in the two cases. However, particularly in decapsulated spindles, it is our opinion that the recording site is probably as close to the terminals as the impulse initiating site, so that the attenuation is probably similar.

It has been suggested (Matthews & Stein, 1969) that while sensitivity or gain of primary endings is greater than secondary endings, they both have a similar dependence on frequency. Gain was found to increase little as frequency was raised up to about 2 Hz. Above this 'corner frequency' gain was considered to increase with

frequency in an approximately parallel manner in both primary and secondary endings. Poppele & Bowman (1970) also considered the relationship between gain and frequency to be similar in primary and secondary endings except for a scaling factor.

The present results show that gain of receptor potential increases with frequency of sinusoidal stretch in both primary and secondary endings in a roughly similar manner. However, the rate of increase of gain in primary endings appears to exceed that of secondary endings especially in the range 0·01–1 Hz. Also, a distinct corner frequency was not observed in primary endings. There was a tendency for the secondary endings to show a relatively constant gain over the lower frequency range (0·01–1 Hz). At the higher frequencies, above 40–50 Hz, the gain in both primary and secondary endings fell, in contrast to gain observed in impulse responses of spindles *in situ* (Matthews & Stein, 1969; Cussons *et al.* 1977) where sensitivity or gain appears to increase with frequency up to 100 Hz and then remain fairly constant up to several hundred Hz.

The difference could well depend on the experimental conditions. The isolated spindle has been studied at room temperature; the *in situ* spindle, at body temperature and supplied by blood, may be able to maintain response amplitude at higher frequency because of increased capacity of recovery processes. The tendency for the gain of impulse responses to be maintained at higher frequencies than the gain of receptor potential could also result from some accommodation in the impulse initiating process. The isolated spindle may also be subject to slightly different mechanical interactions than the *in situ* spindle and these could contribute to the differences in frequency response. Wave propagation and viscous interaction with the surrounding fluid (Ford, Huxley & Simmons, 1977) might be more prominent in the isolated preparation. Another possibility, which we consider less likely, is that the recorded receptor potential suffers more high frequency attenuation than does receptor current at the impulse initiating site (see Hunt & Ottoson, 1975).

Tension gain (A_T) increased as an approximate power-law function of frequency, as did primary ending receptor potential gain (A_R). There was no apparent tendency for gain to flatten below 1 Hz, as occurs in receptor potential gain of secondary endings. The phase advance of receptor potential response in primary endings was characteristically greater than in secondary endings and in tension. All showed little change over the frequency range 0·1–10 Hz, except for a gradual peaking around 10 Hz. Above 10 Hz phase fell in receptor potential gain of both primary and secondary endings, becoming negative above about 20 Hz. Tension phase fell above 10–20 Hz but to a lesser extent than receptor potential phase in either primary or secondary endings.

As Goodwin *et al.* (1975) have pointed out, there are several difficulties in the measurement of phase from cycle histograms of impulse activity at higher frequencies. When recording from dorsal root axons, uncertainties in the values af conduction times could appreciably affect estimates of phase at high frequencies. Wave propagation of movement in muscle could also introduce delay contributing to phase measurement. Carrier dependence (Poppele & Bowman, 1970) can further complicate the measurement. For these various reasons, phase information from impulse responses to sinusoidal stretch is not available above about 30 Hz from studies using dorsal

root recording. Matthews & Stein (1969) show phase advance increasing with frequency to about 90° for primary endings and somewhat less for secondary endings at 30 Hz. Poppele & Bowman's (1970) data show phase advancing with frequency up to about 135° at 10–20 Hz while Chen & Poppele (1978) found phase advances of about 135° for primary endings and 90° for secondary endings at about 20 Hz. The maximal phase advance in receptor potential response in the present study was considerably less, about 36–48° for primary endings and 12–24° for secondary endings at 5–10 Hz. One possible explanation for the greater phase advance in cycle histograms of impulse data may be a contribution of accommodation at the impulse initiating site. Above 10 Hz we observed a progressive decrease in phase reaching 0° at about 20 Hz and becoming negative at still higher frequencies. This is consistent with the decrease in gain at higher frequencies as noted above. Our results on the effect of frequency on phase are more similar to Kirkwood's (1972) results on impulse activity in the frog spindle than to data from mammalian spindles. Kirkwood found a qualitatively similar effect of frequency in that phase lead increased only slightly up to 1 Hz, fell to 0° at 10 Hz and phase became negative at higher frequencies.

The dominant effect of frequency on gain and phase of the receptor potential of the primary ending can be described by the model used to describe the behaviour of the cockroach stretch receptor (Chapman & Smith, 1963) and frog muscle spindle (Kirkwood, 1972) to varying frequency of sinusoidal stretch. In this distributed-parameter model gain is a power function of frequency,

$$A = f^{\gamma}, \tag{7a}$$

where A is normalized gain and γ is a dimensionless parameter. For minimum phase shift the phase, ϕ, is frequency-independent and related to γ by

$$\phi = 90° \times \gamma. \tag{7b}$$

The parameter γ in (7a) is equivalent to the experimentally determined parameters γ_R and γ_T; its relevant range is from 0 to 1.

This model provides a reasonable fit to the observed gain and phase of primary ending receptor potential and of tension over the frequency range between 0·01 and 20 Hz. In Fig. 11, the theoretical relation (7b) between ϕ and γ is included to allow comparison with measured values of these parameters (continuous line). Primaries show fair agreement with the model, while secondaries do not. The dashed lines in Fig. 8 are the empirically determined slopes γ_T and γ_R and the corresponding frequency-independent phases ϕ_T and ϕ_R predicted by (7b). In contrast to the power law slope predicted by the model (eqn. 7), secondary endings show a relatively constant gain below 1 Hz. Also, phases of receptor potentials in primary and secondary endings as well as of tension tended to peak gradually at about 10 Hz and fall with increasing frequency, rather than remaining constant as predicted by the model. The addition of a single low pass filter to the model is required to account for this decline in phase and gain of receptor potential at higher frequency. The physical basis of this low pass element probably lies in the properties of the receptor membrane, as discussed above.

The minimum phase power law model may be represented physically by a continuous distribution of viscoelastic elements, or their electrical analogues, although

it is not possible to identify the actual elements involved. However, some of the implications of this model may be considered. Using a constant amplitude sinusoidal stretch, peak stretch velocity, V_0, is proportional to frequency. Therefore, rewriting eqn. (7*a*), receptor potential amplitude (R_0) for frequencies below about 20 Hz may be expressed as

$$R_0 \sim (V_0)^{\gamma_R}. \tag{8}$$

This is analogous to the empirical expression relating receptor potential amplitude to displacement (eqn. (5)) and implies an analogous compressive velocity nonlinearity. The primary endings may, thereby, signal dynamic stretch information over a wide range of velocities without saturation and with minimal build-up of phase advance.

The relationship between receptor potential gain and frequency in a primary ending (see Fig. 8, eqn. (7)) is not consistent with a response depending on a simple superposition of a static (displacement sensitive) and a dynamic (velocity sensitive) component. Were this the case, the response at very low frequencies should be dominated by displacement sensitivity with consequent low phase lead, while at high frequencies velocity sensitivity should dominate with phase advance approaching 90°. Instead, the ratio of velocity to displacement sensitivity is independent of frequency over a wide range in which γ_R and ϕ_R remain constant. This suggests that the effective stimulus for the primary ending is intermediate (the 'fractional' or logarithmic time derivative of displacement) between pure displacement and its first derivative, pure velocity.

It should be emphasized that the present results have been obtained from spindles in which the intrafusal fibres are passive. It is clear from the studies of Goodwin *et al.* (1975), Cussons *et al.* (1977), Hullinger *et al.* (1977) and Chen & Poppele (1978) that the responses of primary and secondary endings of mammalian spindles to sinusoidal stretch are strikingly modified by static and dynamic fusimotor activity.

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