

THE SENSITIVITY OF MUSCLE SPINDLE AFFERENTS TO SMALL SINUSOIDAL CHANGES OF LENGTH

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SUMMARY

1. Nerve impulses were recorded from spindle afferents of the soleus muscle during sinusoidal changes in muscle length at frequencies from 0.03 to 300 c/s. This was done in the decerebrate cat with intact motor outflow and 'spontaneous' fusimotor activity. Computer averaging over a number of cycles was used to measure the response, in impulses/sec, at different phases of the cycle.

2. A linear range was described in which the discharges of the endings were approximately sinusoidally modulated, and in which increasing the amplitude of the stretching produced a proportional increase in the response. At 1 c/s the linear range extended up to only about 0.1 mm for primary endings, but was greater than 1 mm for secondary endings.

3. The sensitivity of an ending in its linear range was defined as the amplitude of its response divided by the amplitude of the length change. The sensitivity of both primary and secondary endings increased progressively on increasing the frequency of stretching above 1 c/s. The experimental observations relating the sensitivity to the sinusoidal frequency were fitted over much of the range by a curve given by the vector sum of components proportional to the length and to the velocity of stretching. This curve has two parameters, a sensitivity at low frequencies (S), and a corner frequency (F) at which the length and velocity contributions are equal. The value of F was about 1.5 c/s for both primary and secondary muscle spindle endings. The value of S was very much greater for primary endings (median value 95 impulses/sec/mm) than for secondary endings (median value 7 impulses/sec/mm). The increasing sensitivity of the endings at higher frequencies caused a progressive reduction in the linear range when it was expressed as an amplitude of stretching, but it remained approximately constant when it was expressed as a modulation of the frequency of discharge.

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4. The primary endings were also extremely sensitive to maintained changes in length provided they were of sufficiently small amplitude.

5. In the presence of fusimotor activity a high sensitivity of small changes was found over a wide range of muscle lengths. De-efferented endings had a comparable high sensitivity when the muscle was at or beyond physiological full extension, but not when the muscle was shorter.

6. The results are contrasted with those obtained previously using stretches of large amplitude, and the physiological significance of the high sensitivity of primary endings to small stretches is discussed in relation to the reflex control of movement.

INTRODUCTION

The importance of muscle spindles for the reflex regulation of muscular contraction has long been recognized. More recently, analogies have been drawn between the reflex pathways, and automatic control systems developed by engineers. The response of control systems to sinusoidal inputs of various frequencies is often studied, for in a linear system the response to any other input can then be conveniently predicted. A linear system is one in which increasing the input causes a proportional increase in output. Attracted by this approach, and because approximately sinusoidal movements may occur in muscular tremors, a number of workers have studied the response of muscle spindle endings to sinusoidal muscle stretches (Lippold, Redfearn & Vučo, 1958; Crowe & Matthews, 1964*b*; Stuart, Ott, Ishikawa & Eldred, 1965; Grüsser & Thiele, 1968; Jansen, Poppele & Terzuolo, 1967; Poppele & Terzuolo, 1968). Unfortunately, with the exception of the last two rather brief articles, the stretches applied to primary muscle spindle afferents have usually far exceeded their rather small linear range for this kind of input. There is then no unique frequency-response curve, so that sinusoidal analysis loses some of its attractiveness.

In the present experiments we have studied a wide range of sinusoidal frequencies and have been careful to reduce the amplitude of stretching until the endings were responding linearly and firing at all phases of the cycle. Decerebrate cats showing substantial 'spontaneous' fusimotor activity were used throughout. The behaviour of the endings is then presumably closer to that in the intact animal than when they are de-efferented. Two main results emerged. First, the primary ending is relatively much more sensitive to small stretches than it is to large stretches (preliminary note, Matthews & Stein, 1968); secondly, the frequency-response curves of primary and secondary endings over the range 0.03–20 c/s are similar in form though they differ by a constant multiplying factor. Neither of these results was expected from previous work.

METHODS

Twenty-five primary endings and nineteen secondary endings were studied in eleven decerebrate cats. The preparation and apparatus were the same as that described in more detail in another paper (Matthews & Stein, 1969), and, indeed, many of the endings were used for both studies. Nerve impulses from muscle spindle afferent endings in the soleus muscle were recorded from thin dorsal root filaments. Spindle afferent fibres were assumed to supply primary endings if they conducted at above 80 m/sec, and to supply secondary endings if they conducted at below 60 m/sec. Afferents conducting at intermediate velocities were not studied. The appropriate dorsal roots were cut so that the responses were not influenced by reflex effects of stretching the muscle. The ventral roots were intact so that the endings were being influenced by the 'spontaneous' fusimotor activity which occurs in the decerebrate preparation. All endings studied showed the characteristic irregularity in their discharge (Eldred, Granit & Merton, 1953; Matthews & Stein, 1969). In addition, for most of the endings, we confirmed that their frequency of discharge fell by 10–30 impulses/sec on cutting the ventral roots.

The muscle was stretched sinusoidally by an electromagnet controlled by feed-back to form a positional servo-mechanism. The amplitude of stretching (half its peak-to-peak value as in engineering literature) was varied from below a micron to 3 mm, and the frequency of stretching from 0.03 to 300 c/s. The noise level of the system, expressed as spontaneous movements of the stretcher, was generally below 1μ . The length of the muscle was usually set a few mm below the maximum possible length in the body where it had a tension of 30–100 g. The endings studied fired at between 20 and 80 impulses/sec at that length.

The responses of up to five afferent fibres were recorded simultaneously on a multi-channel tape recorder. The discharges were recorded for periods of 15–25 sec for sinusoidal frequencies of 1 c/s or greater. The recording time was progressively increased for lower frequencies so as to include at the very least 3 complete cycles. Three primary endings and two secondary endings were usually studied together so that their responses could be compared the more reliably in spite of the different amounts of fusimotor activity which may occur in different decerebrate cats or in the same cat at different times. One channel of the tape recorder was used for reference signals from the sine wave generator (Servo-mex TWG 100 or Advance JIB). The phase of the applied sinusoids could then be determined after compensation for the lags produced by the stretcher. Phase comparisons were only made for frequencies below 40 c/s.

Techniques of analysis

Average frequency method. For sinusoidal frequencies up to about 3 c/s the response was averaged as follows. The cycle of the sine wave was divided into approximately 72 bins (i.e. each bin covered about 5° of the cycle). The average interspike interval of all the spikes occurring in each bin was then calculated over a number of cycles. The inverse of the mean interval is the average frequency. The lower part of Fig. 1 shows the average frequency computed from a discharge of which a part is shown above. The response is more definitely sinusoidal and the scatter is reduced, though less markedly for the low spike frequencies, which are inevitably based on averaging fewer intervals.

The curve in Fig. 1 gives the best-fitting response obtained by the method of least mean squares using the equation

$$y = a \sin(2\pi t/T) + b \cos(2\pi t/T) + c,$$

where y is the response in impulses/sec at a time t after the start of a cycle of duration T . The computer calculated T from the timing of reference marks occurring at a particular phase of each cycle of stretching. They were punched on to paper tape as well as the times of nerve impulses using an automatic device (Stein, 1965). The remaining three coefficients

were determined so as to minimize the sum of squares of the deviations of the experimental points from the curve (Sokolnikoff & Redheffer, 1966, sect. 10, 11). In doing this, each bin was weighted according to the number of spikes in it, so that the lower frequencies which were relatively less accurately determined got less weight. The constant c corresponds to the mean level of the response. The modulation of the frequency about its mean level represents the amplitude of the response and is given by $\sqrt{(a^2 + b^2)}$. The phase advance of the response is given by $\tan^{-1}(b/a)$. These quantities are shown diagrammatically on Fig. 1. The residual deviations from the best curve provide a measure of its goodness of fit, and the standard errors of the coefficients can also be calculated. One can show that the amplitude $\sqrt{(a^2 + b^2)}$ will tend to have a smaller coefficient of variation than either a or b alone. The quotient b/a will tend to be more variable than either b or a so that measurement of phase advance is less accurate than either b or a . Thus, measurement of phase advance is inherently less accurate than measurement of response amplitude.

Probability density method. As the sinusoidal frequency is increased, the method of averaging just described becomes increasingly unsatisfactory (see below). Instead the response was determined by simply dividing the number of spikes in each bin by the number of cycles and by the duration of the bin. This gives a probability density function for the occurrence of spikes at a given time after the start of a cycle and is related to a post-stimulus time histogram or a 'cycle histogram' (Talbot, Darian-Smith, Kornhuber & Mountcastle, 1968). The best-fitting sine curve was computed as before, except that all points were given equal weight, irrespective of the number of spikes contributing to them. This second method was applicable over the entire range of frequencies studied, and the measured values again have the units of impulses/sec. Figure 2 shows the response of an ending which was firing briskly at nearly 75 impulses/sec. A 100 c/s sinusoid was applied with an amplitude just over 1μ and this produced an appreciable modulation of the spike probability density without altering the mean level.

Comparison of the two methods. The spike probability density retains information about the exact timing of spikes relative to the cycle, but discards any information contained in the value of the interspike interval. Theoretical considerations show that as the frequency of stretching is reduced the results from the two methods must converge to the same values, but that on any limited sample the average frequency points will have appreciably less scatter. Both these things were also found experimentally. For a typical secondary ending studied at 1 c/s or below, the standard deviation from the fitted curve of the points determined by the average frequency method was about an order of magnitude less than that of the points determined by the probability density method. The difference was less for the primary endings because they discharged less regularly. However, the average frequency method becomes less useful at higher cyclic frequencies. This is partly because the interspike interval was placed in a bin corresponding to the end of the interval. If equal sensory inputs applied at different times within an interspike interval had equal effects, then it would be appropriate to place the interval in a bin occurring at the middle of the interval. However, sensory inputs occurring shortly after the previous spike, when the fibre is refractory, will have relatively little effect, so the optimum position is not known. Placing the data in a bin at the end of the interval, as we have done, can produce spurious phase lags of uncertain amount. These become increasingly serious when the cyclic frequency is high enough to allow an interspike interval to cover a large fraction of the cycle, and the amplitude measurements then also become unreliable. This is because the duration of the interval is then influenced by events occurring over an appreciable fraction of the cycle, so tending to blur the effects of changes in the sensory input within the cycle.

The second method involves a computation of the probability density of spikes over the short period of one bin. Provided that spikes occur fairly frequently in all parts of the cycle, the variations in this probability more nearly represent the effect of the stretching at a point in time, irrespective of the timing of the last spike. This argument is no longer valid when

the amplitude is large enough for spikes to tend to occur at only one or more specific points in the cycle (phase-locking). Interpretation is then more difficult, and involves considering the conditional probabilities of firing (Cray, 1967). In short, the probability density method may give information about the magnitude and phase of processes generating nerve impulses at frequencies where the interspike intervals are too long to follow these changes faithfully. The probability density method may also be more meaningful physiologically, since it is the

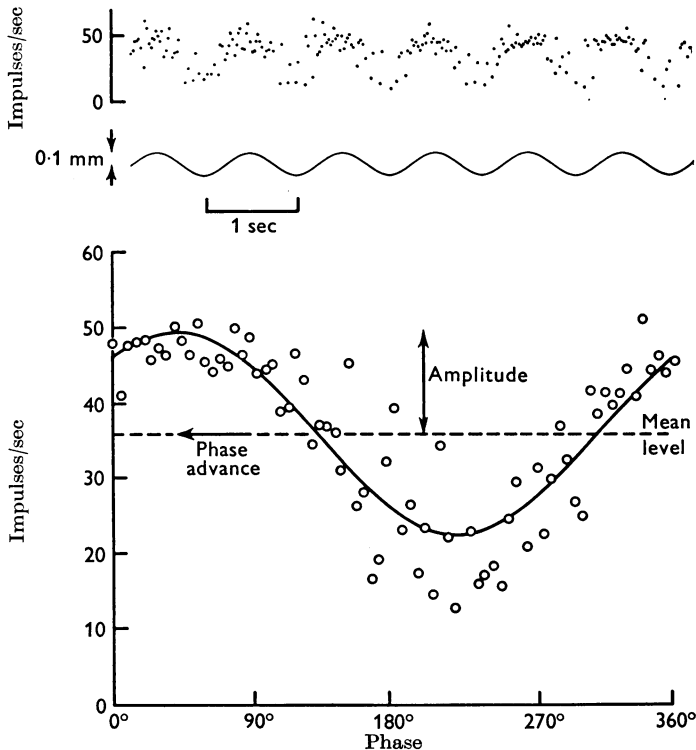


Fig. 1. The response of a primary ending to sinusoidal changes of length of 0.1 mm amplitude at 1 c/s. Above, reciprocal pulse interval display giving the instantaneous frequency of each spike (the instantaneous frequency is the reciprocal of the time since the preceding spike). Below, the average frequency for each 5° of the cycle of stretching determined by computer averaging over 10 cycles. The continuous line is the best-fitting sinusoid. The peak extension of the muscle occurred at 90° on the scale. The arrow labelled 'phase advance' shows the angle by which the sinusoid fitted to the points led the sinusoidal stretching.

impulse probability which determines the average amount of transmitter that will be released synaptically. If a form for the resulting synaptic potentials is assumed, the average post-synaptic wave form can be simulated.

Our computer programme applied both methods of analysis to the data so that any deviations between them were apparent. The frequency-response curve up to about 10 c/s was very similar for the two methods. In compiling results from a range of cyclic frequencies, the average frequency method was preferred for amplitude measurements at frequencies of stretching below 3 c/s and for phase measurements at frequencies below 1 c/s. The probability density method was used otherwise.

Other errors. Phase measurements were not made above 40 c/s for a number of reasons. Uncertainties in the measurement of conduction time from the point of spike initiation to the point of recording became appreciable above this cyclic frequency. Also, correction for the phase lags in the apparatus became somewhat more difficult. In fact, the phase angles given in the present paper have been corrected for lags in the apparatus, but not for the conduction time of the afferent fibre. An extra difficulty in measuring phase occurred near

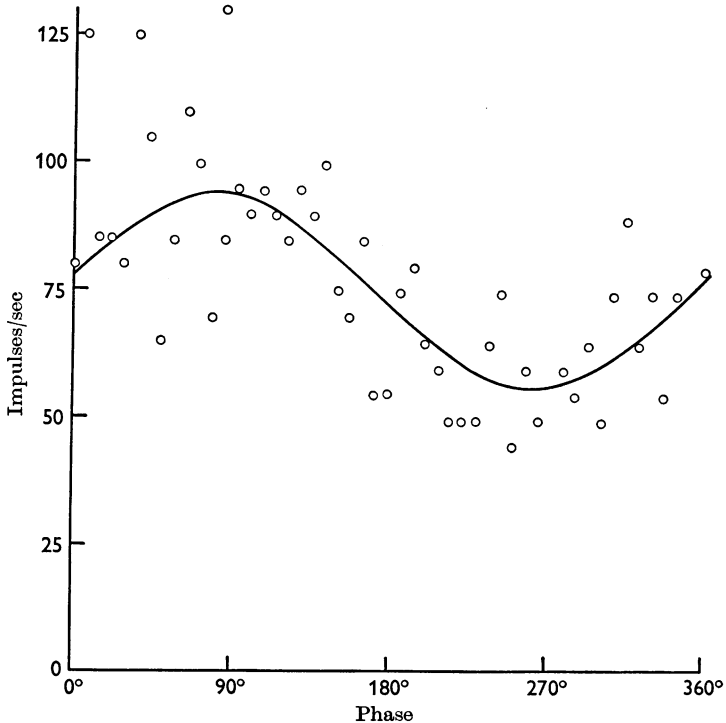


Fig. 2. The response of a primary ending to stretching of 1.2μ amplitude at 100 c/s determined by the probability density method. The average frequency measured from interspike intervals of the ending was little affected, although the density of spikes was appreciably modulated. The continuous line is again the best-fitting sine curve. The relation between the phase of the response and the phase of the movement is unknown.

the spontaneous frequency of the endings which was often around 40 c/s. Phase-locking, in which the ending discharged a single spike at a relatively fixed part of the cycle, was then common. An absence of spikes in a part of the cycle was associated with, and partly the cause of, non-linear behaviour. An unexpected advantage of the irregularity induced by the 'spontaneous' fusimotor activity in the decerebrate cat was a reduction in the tendency to phase-locking. Where it did occur, we attempted to overcome it by further reducing the amplitude of the stimulus to distribute the spikes throughout the cycle. Measurement of the response was then not as accurate, and, particularly with the more regular secondary endings, satisfactory measurements became virtually impossible very close to the 'spontaneous' frequency. Slight tendencies to phase-locking produced more serious errors in phase measurements than in amplitude measurements. At cyclic frequencies somewhat below its

spontaneous frequency, the ending will be ready to fire early in the cycle and so substantial phase advances result. Similarly, just beyond the spontaneous frequency, the ending will not be ready to fire until later in the cycle and so tendencies towards phase lags result. The same effects, though less marked, tend to occur at the nearest harmonics and subharmonics of the spontaneous frequency of nerve impulses.

Spontaneous and sometimes cyclic changes in fusimotor activity occur in decerebrate cats (Eldred *et al.* 1953). Cyclic changes, when present in our experiments, often had frequency components around half a cycle per second or lower, and these made it difficult to measure the responses to low frequency sinusoidal stretching. This difficulty became increasingly serious at the lowest frequencies used (down to 0.03 c/s), because three cycles then took $1\frac{1}{2}$ min and spontaneous changes in one of them could seriously affect both measurements of the phase and the amplitude of the response. However, these changes were fairly obvious during the experiment, and could be examined later by playing back from the magnetic tapes periods in which the muscle was held at a constant length. Comparing the results from cats which showed large fluctuations and those which did not suggests that there were no systematic errors introduced in the former, but just an increase in the scatter of our measurements.

RESULTS

Sinusoidal length changes of small amplitude caused the frequency of nerve impulses in a spindle ending to vary in a rhythmic manner as already shown in the top part of Fig. 1. The characteristic irregularity of the discharge of an ending being excited by fusimotor fibres makes it difficult to fit a sine wave to the response by eye. In addition, the finite number of spikes in a single cycle make the manual fitting of a sine curve comparatively inaccurate. To overcome these difficulties, we have averaged the response of the ending over a number of cycles and fitted a sine curve to it by the method of least squares as described in the Methods section.

Determination of the linear range. The effect of different amplitudes of stretching was investigated initially to determine whether the spindle endings behaved linearly over any part of their range. Figure 3 shows the non-linearities in the response of a primary ending to quite limited amplitudes of sinusoidal stretching at 1 c/s. The points give the average frequency of nerve impulses for an ending during each 5° of the cycle, determined by summing the interspike intervals (average frequency method, see Methods). The fitted curve gives the best estimate of the response of the ending, assuming it is sinusoidal. In Fig. 3*a* a 0.1 mm amplitude of stretching (half the peak-to-peak extent as throughout this paper) modulated the discharge of the ending by ± 13.5 impulses/sec. This figure represents the amplitude of the primary ending's response, so it was quite sensitive to this small stretch. Increasing the amplitude of stretching a factor of five in Fig. 3*b* produced less than a doubling of the response, so the response did not increase linearly with the stimulus. The non-linearity presents certain puzzling features, for the response is still reasonably sinusoidal with little sign of harmonic distortion or change in the phase

angle. In both Fig. 3*a* and *b* the mean level corresponded, within the limits of error, to that found without sinusoidal stretching.

In Fig. 3*c* the amplitude of stretching was increased a further factor of four to 2 mm and the ending ceased firing during about a quarter of the cycle. The line again shows the result of fitting a sine curve to the points, but it is no longer such a good fit, even though the curve is allowed to project into regions below zero frequency. The response of the ending to 2 mm

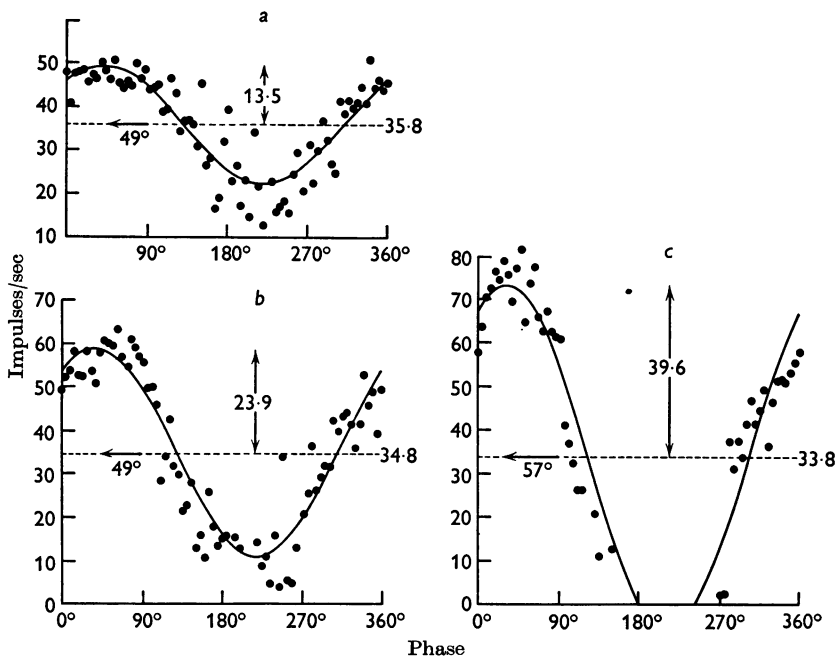


Fig. 3. The response of a primary ending to stretching at 1 c/s of three different amplitudes (*a*, 0.1 mm; *b*, 0.5 mm; *c*, 2 mm) determined by the average frequency method. The figures give the mean level, the amplitude, and the phase advance, with respect to the stretching, of the best fitting sinusoids.

length changes is 40 impulses/sec, which is again a less than proportional increase. The phase advance is increased, which is a further sign of non-linearity. This increase in phase with increasing amplitudes at low frequencies was typical on moving into grossly non-linear regions.

Figure 4 shows the amplitude of the response of the primary ending in Fig. 3 and of a secondary ending which was studied simultaneously, using a range of amplitudes of stretching. For amplitudes of stretching up to 0.1 mm the response of the primary ending increased proportionally with the stimulus, showing that the ending did have a linear region, provided that the input was sufficiently restricted in magnitude. In contrast, the

response of the secondary ending was well fitted by a straight line over a wide range of inputs.

The straight line fitted to the secondary ending in Fig. 4 does not quite pass through the origin. This was allowed because the computational procedure fits a sine curve of small amplitude to the spontaneous variations in the discharge of the ending which occurred with no input. In some endings, the slope of the line relating stimulus and response for secondary endings appeared to be somewhat greater for the smallest inputs, but we could not be certain of this because of the noise level.

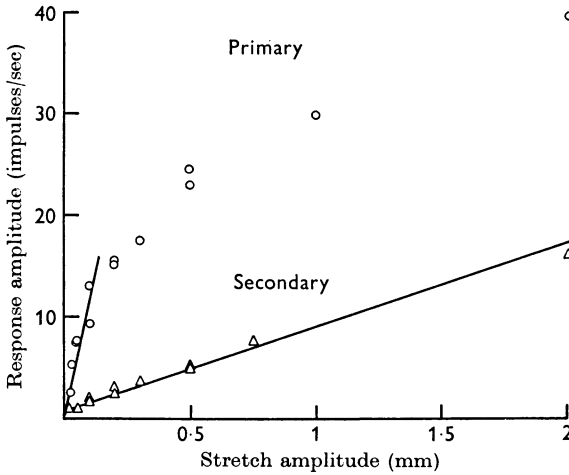


Fig. 4. The responses of a primary and a secondary ending as function of the amplitude of stretching at 1 c/s (determined by the average frequency method).

The modulation of the discharge of the primary ending at the end of its linear range was approximately the same as the modulation of the secondary ending for the length changes of largest amplitude. This suggests that the linear range of an ending is limited by the magnitude of its response rather than by the magnitude of the input. When both primary and secondary endings were studied with a range of sinusoidal frequencies, the linear range corresponded approximately to a certain amount of modulation of the response in impulses/sec, rather than to a certain amplitude of input. For both kinds of ending, therefore, in studying the effect of increasing frequencies, the amplitude of the input was progressively reduced so that the modulation was typically 30% or less of the resting discharge. Linearity checking was not done as systematically at high frequencies as at low frequencies. However, two or three amplitudes were applied and it was usually possible to demonstrate that the response increased proportionally over the particular range of amplitudes studied.

For sinusoidal frequencies up to 3 c/s an amplitude of 0.05 mm was usually appropriate to keep primary endings within their linear range and

an amplitude of 0.5 mm was appropriate for secondary endings. For sinusoidal frequencies of 100–300 c/s the appropriate amplitude for primary endings was about $1\ \mu$ or less, and about $10\ \mu$ for secondary endings. Such small amplitudes of stretching at high frequencies produced little alteration in conventional records of spikes. An impulse would only occur after several complete cycles without one (for example, on every fourth cycle for 200 c/s stretching of an ending discharging at 50 impulses/sec). The stretching merely increased or decreased the probability of the impulses occurring at some phases of the sinusoidal cycle (see Fig. 2), and did not change the average frequency. These probabilities of firing were calculated in each of a number of bins, and then were divided by the bin width to give a probability density measured in impulses/sec (see Methods). The results could then be directly compared with the values of average frequency calculated at lower cyclic frequencies; the two procedures were compared in the Methods. They gave very similar results for frequencies of stretching up to about 10 c/s.

Relation between frequency and response

We were able to study the response of some endings to sinusoidal stretching varied over the four decades from 0.03 to 300 c/s. The sensitivity of an ending to a particular frequency of stretching applied within the linear range may be defined as the amplitude of the response in impulses/sec, divided by the amplitude of stretching in mm. The sensitivity is analogous to the dimensionless gain used by Poppele & Terzuolo (1968) in that it gives the ratio of the output of the ending to its input, but it has the additional advantage of being expressed in the actual units of measurement. For example, the modulation of the response of the primary ending in Fig. 3*a* was 13.5 impulses/sec for an amplitude of stretching of 0.1 mm, giving a sensitivity of 135 impulses/sec/mm at 1 c/s. On increasing or decreasing the length of the muscle by several mm a similar high sensitivity to small amplitude changes was found again at each of the new lengths. For most of the endings studied in this respect the sensitivity to 1 c/s stretching remained within 50% of its initial value on varying the length of the muscle over a range of 6–8 mm. The precise length of the muscle at which the effect of varying the frequency of stretching was studied therefore appeared to be unimportant. The results to be described were obtained at a single length, and with the muscle stretched a few mm below the maximum length which it could take up in the body.

Figure 5 shows on a log-log scale the typical way in which the sensitivity varied with the frequency of stretching for a primary and a secondary ending which were studied at the same time. At any given frequency of stretching, the sensitivity of the primary endings was appreciably greater

than that of the secondary ending. At frequencies below 1 c/s the sensitivity of both endings changed little, although variations in fusimotor activity over a period of low frequency stretching made the measurements rather variable (see Methods). At frequencies above 1 c/s the sensitivity of both kinds of endings increased dramatically. At the highest cyclic frequency the sensitivity of the primary ending reached the remarkable

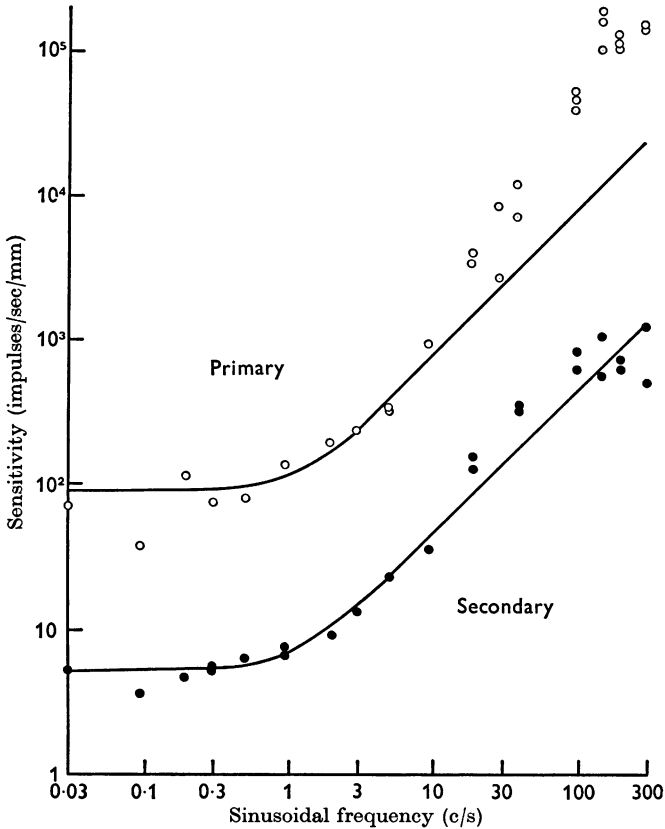


Fig. 5. Comparison of the sensitivity to sinusoidal stretching within the linear range of a primary and a secondary ending studied over a wide range of frequencies. The continuous lines represent the vector sums of a length component (horizontal portion at low frequencies) and a velocity component (diagonal portion at high frequencies) of the stretching for each ending. The same curve transposed vertically fits both endings, showing that they differ only in their absolute sensitivities.

value of 100,000 impulses/sec/mm. At the higher frequencies of stretching the endings were, of course, responding essentially to the velocity and/or acceleration components of the stretching, rather than to the length component. However, following engineering usage, it has still seemed appropriate to express the response as a sensitivity measured in impulses/sec/mm.

The high value for the primary ending does not mean that it fired at extraordinary rates. It discharged on average only at 30 impulses/sec. However, the timing of its spikes was affected by very small stretches indeed, and a sinusoidal change in length of a tenth of a micron at 100 c/s increased the probability density of spikes 10 impulses/sec over part of the cycle and decreased it 10 impulses/sec in the opposite part of the cycle (see Methods). The linearity of such changes was tested by varying the amplitude of stretching, and the multiple points in Fig. 5 for a single frequency result from computations for different amplitudes.

Such high values of sensitivity also result from the rather different data of Brown, Engberg & Matthews (1967). They found that during fusimotor stimulation the majority of primary endings could be driven to discharge a spike for each cycle of sinusoidal stretching at 300 c/s when the amplitude of stretching was only 5μ (their Fig. 13 in which amplitude was expressed as peak-to-peak extent). Their responses were clearly not linear, but are useful for comparison with the present data. As the spikes all occurred at about the same phase of the cyclic stretching, the discharge of the endings was modulated at least 300 impulses/sec, for no spikes occurred over more than 180° of the cycle (see below). This would give a sensitivity of more than 60,000 impulses/sec/mm. Thus, the present values of sensitivity are in line with previous work, and further define the extreme sensitivity of primary endings to vibratory stimuli applied longitudinally to the muscle.

When the response is phase-locked, the modulation is not uniquely defined. However, the same curve-fitting procedures may be applied. In the extreme example where all the spikes occur in a single bin of width δt , the impulse probability density would be $1/\delta t$ in that bin and 0 in all the others. Calculating the sums for least mean squares shows that for a cyclic frequency f , the mean level is f , the amplitude of modulation is $2f$, and the phase advance is given by the position of the bin containing all the spikes relative to the peak of the applied sinusoid. If all the spikes do not occur in one bin, but are restricted to less than 180° , one can show that the amplitude of modulation will be greater than f but less than $2f$.

The curves in Fig. 5, which fit the majority of the points reasonably, are simply those expected for an ending which responded to the vector sum of the length and the velocity components of the sinusoidal stretching. The response to a sinusoidal frequency f is then given by $S(1 + jf/F)$ where S is the sensitivity at low frequencies, F is the 'corner' frequency at which the length and velocity contributions are equal, and j is $\sqrt{-1}$. The sensitivity of an ending is then $S\sqrt{(1 + f^2/F^2)}$. The curves of Fig. 5 are drawn according to this expression with the same corner frequency, but different values of S . The phase advance of the response is given by $\tan^{-1}(f/F)$.

Within the range 0.3–20 c/s the curves fit the experimental points quite well, but outside the region the fit is less good, as was usual. At frequencies below about 0.3 c/s both kinds of ending generally showed a gradual decrease in sensitivity on reducing the cyclic frequency, but the amount and degree of this was variable (cf. Jansen *et al.* 1967). At frequencies above 30 c/s the sensitivity of the primary endings invariably increased more rapidly than the curve, and at frequencies of 100–300 c/s was 3–8 times above that given by the curve for all the ten endings studied. Secondary endings were much better fitted by the high frequency part of the curve, as in the example of Fig. 5, but three out of the six endings studied had sensitivities at 100–300 c/s nearly twice that given by the curve. The

effect on the sensitivity of the endings of increasing the frequency from 100 to 300 c/s was not well established with the limited number of endings studied at these frequencies: sometimes the sensitivity increased throughout, and sometimes it became approximately constant. The difference between these modes of behaviour could be important in formulating models of the endings.

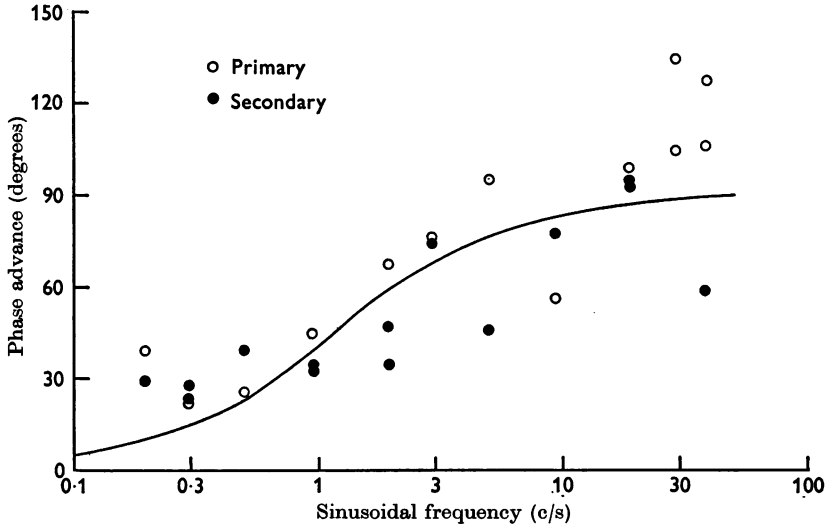


Fig. 6. The relation between the phase of the response and the cyclic frequency for the primary and secondary endings of Fig. 5. The continuous line is the relation expected from the curves of Fig. 5.

Phase advance. Variations in the phase angle of the responses with the frequency of stretching suggest that the deviations in the measurements of sensitivity from the simple curve are probably significant. Figure 6 shows the measurements of phase as a function of the frequency of stretching for the endings of Fig. 5. The continuous line is that expected for both endings on the basis of the curves of Fig. 5. At low frequencies the response of both kinds of ending shows more phase advance than that given by the curve. This would be expected if the sensitivity continues to fall at frequencies appreciably below the corner frequency (both effects could be described by an equation with a further term giving some differentiation at low frequencies). At frequencies around 30 c/s the phase advance observed for the primary ending is greater than the 90° which is the maximum an element responding to length and velocity alone can give. This, together with the deviation in the frequency-response curve, suggests that the response of the ending might be better described by including an additional term related to the acceleration of stretching. Whether the

response of the endings to large amplitude stretches is usefully described by including an acceleration term is at present controversial (Jansen & Matthews, 1962*a*; Grüsser & Thiele, 1968; Schäfer, 1968; Lennerstrand & Thoden, 1968*a*). Some of the observed effects can equally well be described by postulating an effect analogous to static friction. As discussed in the Methods, our measurements of phase, particularly in this frequency range, are not sufficiently reliable to conclude with certainty that an acceleration response exists in the linear range.

Comparison of endings. Curves such as those in Fig. 5 provide a basis for systematically comparing the behaviour of primary and secondary endings in the range 0.3–20 c/s. This range is of great physiological interest for the reflex control of muscle. Curves of the form already described were fitted by eye. The corner frequency F regularly proved to be similar for the two kinds of endings, as it is in Fig. 5. The median value of the corner frequency for twenty-five primary endings was 1.6 c/s (range 0.9–2.3) and that for seventeen secondary endings was 1.4 c/s (range 0.7–2.5). This similarity is surprising, for the primary ending is much more sensitive to the velocity of large amplitude stretches than is the secondary, and so a lower corner frequency might have been expected. The sensitivity at low frequencies (S) differed systematically between the two kinds of endings. The median value for the twenty-five primary endings was 95 impulses/sec/mm (range 25–210), while that for nineteen secondary endings was 7.1 impulses/sec/mm (range 1.8–13). The range of sensitivities presumably partly reflected differences in the fusimotor activity in the different preparations, for the values obtained in a single experiment were more constant. Because of this, the median value of S appeared of more interest than the mean. All the preparations probably had appreciable 'spontaneous' activity of static fusimotor fibres, as the discharge of the secondary endings decreased on cutting the ventral roots (Matthews & Stein, 1969). In addition, at least half of the preparations also had 'spontaneous' activity of dynamic fusimotor fibres, as the dynamic indices of their primary endings decreased considerably on cutting the ventral roots (Jansen & Matthews, 1962*a*).

The difference between the two kinds of ending in their sensitivity to low frequencies is surprising, for previous studies with large amplitude stretches found similar static sensitivities for the two kinds of ending in the decerebrate cat (Jansen & Matthews, 1962*b*). We confirmed this result for most of the present endings by stretching the muscle in steps of 2–3 mm over a range of 9 mm, and plotting the average frequency of nerve impulses against the extension. The points were approximately fitted by a straight line, the slope of which may be defined as the static sensitivity for large stretches. Measurements were made 30 sec after reaching each new length,

and the muscle was then released for a similar period before the next stretch. The median value of the static sensitivity of eighteen primary endings was 2.5 impulses/sec/mm (range 1.9–4.9) and that of fourteen secondary endings was 2.2 impulses/sec/mm (range 0.5–9.4). These values are slightly lower than those given before (Jansen & Matthews, 1962*b*; Granit, 1958), probably because the measurements were made rather longer after the muscle had been stretched up to each new length, thus allowing more adaptation of the endings. For secondary endings, the values of S (median 7.1) are of the same order of magnitude as the static slopes (median 2.2), and the differences are not particularly surprising. For the primary endings, the differences between S (median 95) and the static slope (median 2.5) are so great that they cannot be measuring the same thing. One reason is that the measurement of the responses 30 sec after the onset of stretch will be influenced by frequency components much lower than the frequencies used to determine S . However, when the slopes of the frequency–extension relation of some of the endings were measured 0.5 sec after the onset of stretch, they were not very much greater. More significantly, S was measured with stretches of about 0.1 mm whereas the static sensitivity was obtained using stretches of several mm. Moreover, the small sinusoidal stretches tested the response of the ending to alternate stretching and releasing, while the large maintained stretches tested its response only to progressive increases in the degree of stretch.

Small sudden stretches. The result of measuring the static sensitivity of an ending with a small stretch is shown in Fig. 7. Alternate sudden stretches and releases of 0.5 mm were applied to the muscle at intervals of 2.5 sec. The resulting change in the frequency of a primary ending was approximately 25 impulses/sec, giving a sensitivity of 50 impulses/sec/mm. Although the response had probably not adapted to a steady level, it was well maintained throughout the 2.5 sec at each length and was thus close to a true static response. Similar observations were made using computer averaging over a range of amplitudes of stretching, when, as with sinusoidal stretching, the linear range of primary endings was only 0.1–0.2 mm total displacement. The response of Fig. 7 actually fell outside the linear range, and a slightly higher sensitivity was found when smaller amplitudes were applied in the same preparation. In conclusion, the sensitivity of the primary ending to stretches of small amplitude, whether sinusoidal or maintained, is very much greater than its sensitivity to stretches of large amplitude.

De-efferented endings. Subsidiary observations were made on a number of the same endings after cutting the ventral roots and thus eliminating the constant fusimotor stimulation they had been receiving. The chief finding was that the de-efferented primary ending could still have a very

high sensitivity to small sinusoidal stretches, provided the muscle was extended close to or slightly beyond the maximum length it could take up in the body. Above the linear range, the response of the ending increased only very slowly with increasing amplitude and was no longer approximately sinusoidal, showing a fairly obvious saturation rather like that illustrated by Poppele & Terzuolo (1968; it is not clear whether their endings were under appreciable fusimotor drive). Because of the much

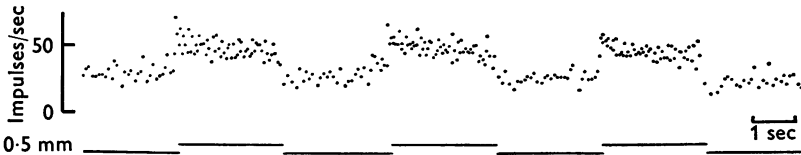


Fig. 7. The responses of an innervated primary ending to sudden stretches and releases applied at intervals of 2.5 sec. The points show the frequency of discharge of the ending with a reciprocal pulse interval display. To eliminate part of the variability of the discharge the circuit was supplied with every second spike and the sensitivity scale adjusted so as to give the frequency of the original spike train.

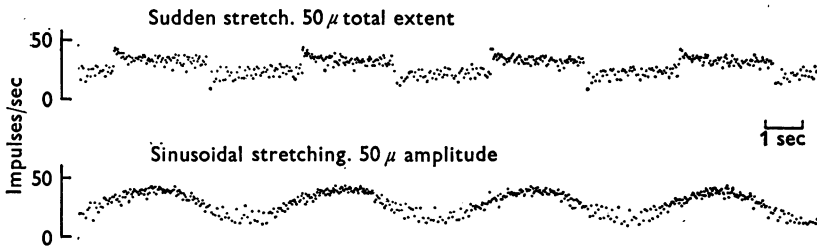


Fig. 8. A high sensitivity to small stretches shown by a de-efferented primary ending. The length of the muscle was approximately the maximum possible in the body. The stretch and release were applied either sinusoidally (5 sec period), or suddenly and then maintained for 2.5 sec (transit time about 20 msec). Records taken with a reciprocal pulse interval display as in Fig. 1.

greater regularity of the de-efferented primary ending, its high sensitivity could be readily appreciated from a reciprocal pulse interval display without the need for computer averaging. Figure 8 illustrates this by showing the response of an ending to 0.2 c/s sinusoidal stretching of 50 μ amplitude, and to alternate sudden stretches and releases of 50 μ every 2.5 sec. In both cases the sensitivity of the ending was about 250 impulses/sec/mm.

The sensitivity of the de-efferented ending, unlike that of the innervated ending, depended markedly on the mean length of the muscle. For example, the sensitivity of one ending increased tenfold when the muscle was stretched by 6 mm while it was de-efferented. The sensitivity of the same

ending was only slightly affected by the same stretch when it was under fusimotor drive. The sensitivity of the de-efferented endings relative to their sensitivity when innervated thus depended on the mean length of the muscle, and both increases and decreases could be found for the same ending. Quite surprisingly, this result applied equally to the secondary endings, which could show quite considerable sensitivities to small amplitude 1 c/s stretching when they were de-efferented.

DISCUSSION

The response of a completely linear system to small stretches can be predicted from its response to large stretches. In fact the linear range of the primary ending proved to be only a fraction of a mm. This may appear paradoxical, as it is well known that its frequency-extension relation on stretching a muscle over many mm is approximately a straight line, both when the stretch is maintained (Eldred *et al.* 1953) and during the course of stretching at constant velocity (Crowe & Matthews, 1964*a*). The response of the primary ending to the length component of a large stretch can therefore certainly be usefully described as linear. But its response to the velocity component of a large stretch is not easily described in linear terms (Matthews, 1963; Lennerstrand & Thoden, 1968*a*), especially during shortening of the muscle when there is the additional complication that the ending often stops firing. The response to large stretches is not, therefore, linear in the strict engineering sense, which requires that the linearity applies to dynamic as well as to static behaviour.

Our findings with a range of sinusoidal frequencies differed in two respects from those we expected on the basis of previous work. With large stretches, the static behaviour of the two kinds of ending is broadly similar, while the dynamic sensitivity of the primary ending is much greater than that of the secondary ending (Matthews, 1964). In response to small amplitude sinusoidal stretching at 0.3–20 c/s both kinds of ending behaved as if they were sensitive to the vector sum of the length and the velocity components of the stretching. The 'corner' frequency at which the length and velocity components contributed equally was around 1.5 c/s for both kinds of ending, though a much lower corner frequency might have been expected for the primary. The sensitivity to low frequency stretching (S), an approximate measure of the static sensitivity, was very much greater for the primary ending than for the secondary ending, though similar values might have been expected. The response of the primary ending to maintained stretches of small amplitude was also much greater than expected. The reason for the discrepancies is that the behaviour of primary endings is quite different outside and inside their linear range, whereas the linear range of the secondary endings covers

stretches of the sizes used before. All these responses were found in the presence of fusimotor activity, which increases their physiological significance.

The present results suggest the attractive idea that for small amplitudes of stretching over the range 0.3–20 c/s, a unique frequency–response curve fits the behaviour of all endings, whether primary or secondary, and whether in the presence or absence of intrafusal contraction. Further, the difference between different conditions might reside solely in differences in the low frequency sensitivity S rather than in differences in the corner frequency. This, however, has yet to be fully established. There is no difficulty in principle in explaining the form of the frequency–response curves. Many physical systems could produce such a curve, including a mechanical system with an appropriate arrangement of elastic and viscous elements (Matthews, 1964). In order to develop an exact model, the precise behaviour at the extremes of frequencies would also be important.

The internal mechanisms within the spindle which lead to its complex behaviour remain to be investigated. However, the high sensitivity of the primary ending in the decerebrate cat, and its persistence over a range of muscle lengths, seems likely to result from ‘spontaneous’ activity in dynamic fusimotor fibres. Crowe & Matthews (1964*b*) found that the sensitivity of primary endings to sinusoidal stretching is markedly greater during stimulation of dynamic fusimotor fibres than it is during stimulation of static fusimotor fibres. Their Fig. 7 illustrates this on stretching at 2 c/s with an amplitude of 0.05 mm. This gave an approximately sinusoidal variation in the frequency of discharge of the ending, which thus may be presumed to have been in its linear range. The sensitivity during the dynamic fusimotor stimulation was then about 500 impulses/sec/mm. The present findings, showing a high sensitivity of the primary ending over a range of lengths where it would otherwise have been low, are entirely compatible with the idea that the main function of the dynamic fusimotor fibres is to control the sensitivity of the primary endings, rather than to alter their mean frequency of firing (Jansen & Matthews, 1962*a*; Crowe & Matthews, 1964*a*; Brown & Matthews, 1966; Schäfer & Henatsch, 1968; Lennerstrand & Thoden, 1968*b*).

Functional significance

The fact that the primary ending responds non-linearly to large stretches does not mean such responses are physiologically unimportant. Large movements of the muscle occur normally in life, and the spindle primary alters its discharge in a systematic way with the extent and velocity of large stretches (Matthews, 1963). It would be remarkable indeed if it did not play a role in reflexly regulating such movements.

It might be suggested that the rather small high-sensitivity region of the primary ending is physiologically unimportant, especially as we used computer averaging to measure the responses. For frequencies above 20 c/s this objection seems likely to be true, and though the results may throw light on the internal working of the spindle (Brown *et al.* 1967) they are unlikely to be relevant to its normal functioning in the body. Frequencies up to about 20 c/s, however, occur in tremors, and are probably also a component of many movements. The high-sensitivity linear range of ± 0.1 mm in a muscle about 50 mm long is small when expressed as a movement, but it is not small when expressed as a $\pm 30\%$ modulation of the pre-existing discharge of the ending. In the body, the averaging that we performed over many cycles of stretch could be performed over a single cycle by summing the responses of a number of endings at the relevant synapses. Moreover, after a stretch of large amplitude, the ending could 'reset' itself so that the high sensitivity applied again at the new length, thus compensating for the saturation which might have been expected in a highly sensitive system. In conclusion, the present unexpected finding of a high sensitivity for small amplitude stretches shows that the primary ending is an even more complex measuring instrument than had previously been realized.

Control of position. The present results are of particular interest in relation to the reflex control of muscle. As Merton (1953) originally pointed out, the stretch reflex mediated by the Ia fibres from the spindle primaries on to the α motoneurons of the same muscle provides a 'servo-mechanism' for controlling muscle length. More recently, the efficiency of such a control mechanism was questioned (Matthews, 1966, 1967) as the gain around the stretch reflex loop appears to be comparatively low. The present finding of a high sensitivity of spindle primary endings to small movements, even at low frequencies, indicates that the stretch reflex should be relatively much more effective in resisting small perturbations of the muscle length than could otherwise have been supposed. Previous measurements (Matthews, 1966), in conjunction with the present finding of sensitivities of the primary ending up to 200 impulses/sec/mm, suggest that the soleus muscle of the cat could reflexly resist a change in length of only 0.1 mm by developing 60 g tension. Thus, the primary endings do seem likely to play an important part in reflexly stabilizing the length of a muscle at a constant value, particularly in adjusting for small disturbances.

Control of movement. Merton (1953) further suggested that some movements might be initiated by activity occurring first in the fusimotor fibres. This would excite the primary endings of the spindle and so reflexly cause contraction of the muscle. The fusimotor discharge would then serve as a control signal, and the whole stretch reflex loop would function as a

'follow-up length servo' (Hammond, Merton & Sutton, 1956). There are now, however, certain difficulties with this attractive idea in its simplest form. Among these are that fusimotor neurones are usually excited in parallel with α motoneurones by reflex activity or central stimulation (Matthews, 1964; Koeze, Phillips & Sheridan, 1968), and that large modulations of fusimotor activity produce relatively modest modulations of the spindle afferent discharge (Andersson, Lennerstrand & Thoden, 1968). Alternatively, movements might be produced by matching the discharge in the alpha and fusimotor neurones so that the muscle spindle discharge remained approximately the same throughout the course of a movement; any deviation from the progress of the movement as planned by the c.n.s. would then be corrected by servo action (Matthews, 1964; Euler, 1966; Koeze *et al.* 1968). The primary ending could obviously mediate such an action more effectively if the high sensitivity it shows for small displacements from a fixed length also applied for deviations from the 'desired' time course of length changes during the course of a movement. If, as a result of fusimotor activity, the discharge of the primary ending were to remain approximately constant during a movement, then its sensory fibres and the region of intrafusal fibre on which they lie would also be in the same state throughout, and so it might well still show a high sensitivity. Whether this is actually so can only be determined by further experiment.

REFERENCES

- ANDERSSON, B. F., LENNERSTRAND, G. & THODEN, U. (1968). Response characteristics of muscle spindle endings at constant length to variations in fusimotor activation. *Acta physiol. scand.* **74**, 301-318.
- BROWN, M. C., ENGBERG, I. & MATTHEWS, P. B. C. (1967). The relative sensitivity to vibration of muscle receptors of the cat. *J. Physiol.* **192**, 773-800.
- BROWN, M. C. & MATTHEWS, P. B. C. (1966). On the subdivision of the efferent fibres to muscle spindles into static and dynamic fusimotor fibres. In *Control and Innervation of Skeletal Muscle*, ed. ANDREW, B. L. Dundee: Thomson and Co.
- CROWE, A. & MATTHEWS, P. B. C. (1964*a*). 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.
- CROWE, A. & MATTHEWS, P. B. C. (1964*b*). Further studies of static and dynamic fusimotor fibres. *J. Physiol.* **174**, 132-151.
- ELDRED, E., GRANIT, R. & MERTON, P. A. (1953). Supraspinal control of the muscle spindles and its significance. *J. Physiol.* **122**, 498-523.
- EULER, C. V. (1966). The control of respiratory movements. In *Breathlessness*, ed. HOWELL, J. B. L. & CAMPBELL, E. J. M. Oxford: Blackwell.
- GRANIT, R. (1958). Neuromuscular interaction in postural tone of the cat's isometric soleus muscle. *J. Physiol.* **143**, 387-402.
- GRAY, P. R. (1967). Conditional probability analyses of the spike activity of single neurones. *Biophys. J.* **8**, 759-777.
- GRÜSSER, O. J. & THIELE, B. (1968). Reaktionen primärer und sekundärer Muskelspindelafferenzen auf sinusförmige mechanische Reizung. I. Variation der Sinusfrequenz. *Pflügers Arch. ges. Physiol.* **300**, 161-184.
- HAMMOND, P. H., MERTON, P. A. & SUTTON, G. G. (1956). Nervous gradation of muscular contraction. *Br. med. Bull.* **12**, 214-218.

- JANSEN, J. K. S. & MATTHEWS, P. B. C. (1962*a*). The central control of the dynamic response of muscle spindle receptors. *J. Physiol.* **161**, 357–378.
- JANSEN, J. K. S. & MATTHEWS, P. B. C. (1962*b*). The effects of fusimotor activity on the static responsiveness of primary and secondary endings of muscle spindles in the decerebrate cat. *Acta physiol. scand.* **55**, 376–386.
- JANSEN, J. K. S., POPPELE, R. E. & TERZUOLO, C. A. (1967). Transmission of proprioceptive information via the dorsal spinocerebellar tract. *Brain Res.* **7**, 382–384.
- KOEZE, T. H., PHILLIPS, C. G. & SHERIDAN, J. D. (1968). Threshold of cortical activation of muscle spindles and α motoneurons of the baboon's hand. *J. Physiol.* **195**, 419–449.
- LENNERSTRAND, G. & THODEN, U. (1968*a*). Dynamic analysis of muscle spindle endings in the cat using length changes of different length–time relations. *Acta physiol. scand.* **73**, 234–250.
- LENNERSTRAND, G. & THODEN, U. (1968*b*). Muscle spindle responses to concomitant variations in length and in fusimotor activation. *Acta physiol. scand.* **74**, 153–165.
- LIPPOLD, O. C. J., REDFEARN, J. W. T. & VUČO, J. (1958). The effect of sinusoidal stretching upon the activity of stretch receptors in voluntary muscle and their reflex responses. *J. Physiol.* **144**, 373–386.
- MATTHEWS, P. B. C. (1963). The response of de-efferented muscle spindle receptors to stretching at different velocities. *J. Physiol.* **168**, 660–678.
- MATTHEWS, P. B. C. (1964). Muscle spindles and their motor control. *Physiol. Rev.* **44**, 319–288.
- MATTHEWS, P. B. C. (1966). The reflex excitation of the soleus muscle of the decerebrate cat caused by vibration applied to its tendon. *J. Physiol.* **184**, 450–472.
- MATTHEWS, P. B. C. (1967). Vibration and the stretch reflex. In *Myotatic, Kinesthetic and Vestibular Mechanisms*, ed. DE REUCK, A. V. S. & KNIGHT, J. London: Churchill.
- MATTHEWS, P. B. C. & STEIN, R. B. (1968). The sensitivity of muscle spindle afferents to sinusoidal stretching. *J. Physiol.* **198**, 43–44*P*.
- MATTHEWS, P. B. C. & STEIN, R. B. (1969). The regularity of primary and secondary muscle spindle afferent discharges. *J. Physiol.* (In the Press.)
- MERTON, P. A. (1953). Speculations on the servo-control of movement. In *The Spinal Cord*, ed. WOLSTENHOLME, G. E. W. London: Churchill.
- POPPELE, R. E. & TERZUOLO, C. A. (1968). Myotatic reflex: its input-output relation. *Science, N. Y.* **159**, 743–745.
- SCHÄFER, S. S. (1968). The acceleration response of a primary muscle-spindle ending to ramp stretch of the extrafusal muscle. *Experientia* **23**, 1026–1027.
- SCHÄFER, S. S. & HENATSCH, A. D. (1968). Dehnungs antworten der primärer Muskel-spindel-Afferenz bei elektrischer Reizung und natürlicher Innervation der beider fusi-motorischen Fuser typen. *Expl Brain Res.* **4**, 275–291.
- SOKOLNIKOFF, I. S. & REDHEFFER, R. M. (1966). *Mathematics of Physics and Modern Engineering*, 2nd edn. New York: McGraw-Hill.
- STEIN, R. B. (1965). A high-speed timer and recorder for computer analysis of physiological data. *J. Physiol.* **181**, 5–6*P*.
- STUART, D., OTT, K., ISHIKAWA, K. & ELDRED, E. (1965). Muscle receptor responses to sinusoidal stretch. *Expl Neurol.* **13**, 82–95.
- TALBOT, W. H., DARIAN-SMITH, I., KORHUBER, H. H. & MOUNTCASTLE, V. B. (1968). The sense of flutter-vibration: comparisons of the human capacity with response patterns of mechanoreceptive afferents from the monkey hand. *J. Neurophysiol.* **31**, 301–334.