ANALYSIS OF REFLEX VARIABILITY IN TERMS OF PARTIALLY CORRELATED EXCITABILITY FLUCTUATION IN A POPULATION OF MOTONEURONS

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Nerve cells characteristically exhibit fluctuation in excitability. In the case of neurons lying within the central nervous system it is reasonable to suppose that multiple influences contribute to excitability fluctuation. Certain of these influences might depend upon factors intrinsic to individual nerve cells while others might be due to extrinsic factors. It may be assumed that, among a group of neurons, coincidence of excitability swings due to intrinsic sources of fluctuation would be determined purely by chance. On the other hand, extrinsic factors might be expected to influence members of a population to some degree in unison; *i.e.*, in a correlated manner. These considerations suggest that members of a functionally homogeneous population of nerve cells might be subject to excitability fluctuations that are in part independent and in part correlated. Such appears to occur in spinal motoneurons (3). For a fuller understanding of the reflex behavior of populations of neurons it would be desirable to determine the role of independent and correlated excitability fluctuations.

Monosynaptic reflex response of a motoneuron population varies in magnitude on successive application of standard test volleys, indicating that the number of motoneurons responding varies on successive trials. A corollary of this variation in population response is that certain of its members discharge on some but not all of a series of trials. By analysis of individual motoneuron response Lloyd and McIntyre have shown that in response to a series of standard monosynaptic excitatory volleys some members of a motoneuron population never respond, others invariably respond, and a certain number respond on an intermediate number of trials (5). They employed firing index as a measure of individual motoneuron response, this index being defined as the per cent of monosynaptic reflex responses in a given number of trials. It was found that units with firing indices at the upper and lower extremes of the intermediate range (between zero and 100) occurred more frequently than those in the middle part of this range; that is, the distribution of units with respect to firing indices was U-shaped. This was considered to result from a uniform distribution of

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motoneurons with respect to differences in transmitter potentiality and an assumed normal distribution of fluctuating excitability levels. This working hypothesis of a normal distribution of excitability fluctuation in the individual motoneuron receives experimental support from the present study.

Unit response, as measured by firing index, depends upon the relation between the fluctuating excitability levels of a motoneuron and the level of excitability which is critical for discharge; independence or correlation of excitability fluctuation among several units would not be expected to affect their individual firing indices. However, the variation in population response will be greatly influenced by the degree to which excitability fluctuation is correlated among its members.

A previous investigation (3) has indicated that excitability fluctuations affect members of a motoneuron pool in a partially correlated manner. This evidence is, in brief, that the variation in pool response amplitude is less than would be expected if the excitability changes affecting motoneurons in the intermediate firing zone were completely correlated, but greater than that anticipated were there no correlation.

The present study aims to define, in quantitative terms, the extent to which excitability fluctuations of a motoneuron pool are correlated and the precise manner in which the response of the individual motoneuron is linked to the response of the population of which it is a member. The approach to this problem has been made in two ways: (1) to record the simultaneous responses of two fractions of a motoneuron pool, or in some cases different pools, to successive applications of monosynaptic excitatory volleys and to determine the extent to which variations in response amplitude are correlated; (2) to record simultaneously the response of a population and of one of its members to successive test volleys and to determine the relation between response of the individual and of the pool. All experiments have been performed on acutely decapitate cats. Response of motoneurons has been recorded in distally severed ventral root, or filaments thereof, following application of single stimuli at a uniform rate of 30/minute to the appropriate, distally cut muscle nerves.

Correlation between Response of Two Fractions of a Homogeneous Population.— The degree to which fluctuations in excitability are correlated among members of a homogeneous population of motoneurons may be qualitatively estimated from successive monosynaptic reflex responses recorded simultaneously from two fractions of such a population. This has been achieved by separate recording of monosynaptic reflex response in two distally severed ventral roots (L7 and S1) following maximal group I stimulation of triceps surae nerve. Alternatively, response has been separately recorded in the nerves to medial gastrocnemius and to lateral gastrocnemius-soleus following maximal group I stimulation of the dorsal roots containing the monosynaptic excitatory fibers that are afferent for this reflex. An experiment of the latter type is illustrated in

Fig. 1 which is a plot of successive monosynaptic reflex response amplitudes of medial gastrocnemius (GM) and lateral gastrocnemius (GLS) motoneurons recorded in the respective muscle nerves. Inspection of Fig. 1 gives the impression that the fluctuations in response amplitudes in the two pools are more often in like direction than in opposite direction. This impression is confirmed by a more precise comparison of the simultaneous fluctuations in amplitude of the two responses, namely by determination of the correlation coefficient. For the 100 paired responses shown in Fig. 1 the correlation coefficient is +0.74.

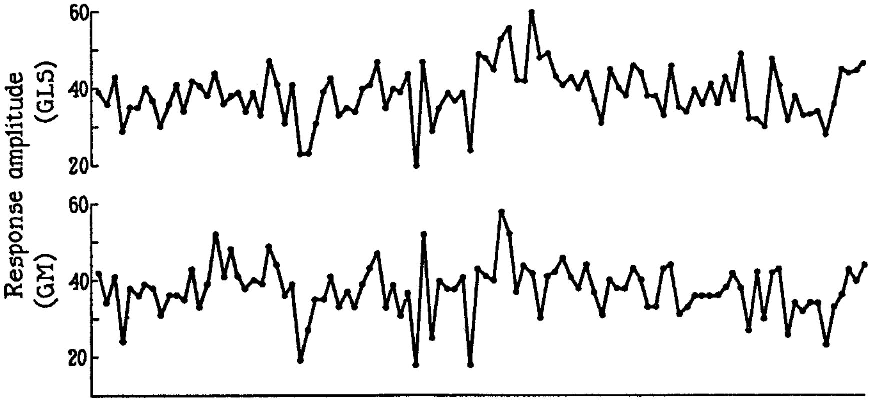


FIG. 1. Monosynaptic reflex responses recorded simultaneously in the nerves to lateral gastrocnemius-soleus and to medial gastrocnemius following stimulation of dorsal roots L7 and S1. Amplitudes of successive paired responses appear as points; connecting lines are a guide to direction of change between points and do not represent a continuous function.

In another experiment 100 paired responses, similarly recorded in the medial gastrocnemius and lateral gastrocnemius-soleus nerves, showed a correlation coefficient of +0.73. Analysis of 100 monosynaptic reflex responses to triceps surae volleys in ventral roots L7 and S1 in a third preparation also led to a correlation coefficient of +0.73.

The response amplitudes of two portions of a population depend upon the number of motoneurons (units) that respond in each case. On successive trials certain units in both portions may or may not respond to the test volley, depending upon the instantaneous level of fluctuating excitability in each unit: such units are in the intermediate firing index category of response (5). If the units in the intermediate firing zone were completely independent of each other in their excitability swings, the variations in response amplitude of two portions of a population would be expected to show a correlation coefficient not significantly greater than zero. On the other hand, if excitability fluctuations of members of the population were due, in part at least, to some common influence, the variations in response amplitude of two portions of the population would be expected to exhibit a positive correlation coefficient; a maximum value (*i.e.* correlation coefficient = 1.0) would be expected only if the excitability fluctuations of the various intermediate firing units were always in the same relative proportions to each other (*i.e.* complete correlation of unit excitability fluctuations).

The experimentally obtained correlation coefficients (cited above) have large positive values, which, however, are significantly smaller than 1.0. It may be concluded that the excitability fluctuations of the various units have a common (proportional) component of significant magnitude, but there is also a significant component with respect to which the various units are independent of each other. From this evidence alone, it is not possible to deduce the relative magnitudes of these component fluctuations, or the degree of difference that might exist between the various units in respect to this relative magnitude. To describe more adequately the degree of independence and correlation in individual motoneuron responses, studies have been made of the relation between individual unit responses and the response of a population to which it belongs.

Relation between Unit and Population Response.—In order to determine the relation between monosynaptic reflex response of a population and one of its members, the discharge of individual triceps surae motoneurons was recorded in a filament of ventral root (usually from L7), while the response of a population of triceps surae motoneurons was determined by simultaneous recording from a whole ventral root (usually S1). Stimulation of the muscle nerve was maximal for group I fibers. The two responses were displayed after suitable amplification on a dual beam oscilloscope. The beam displaying the population response was s stationary spot, that was intensified during the response and deflected by the amplified signal from the whole root. The beam recording the unit response was caused to sweep in the same direction as the deflection recording the population response, the unit response deflecting its beam at right angles to the sweep. By employing slowly and continuously moving film the successive paired unit and population responses to muscle nerve volleys, repeated at a rate of 30 per minute, were recorded as illustrated by the strip reproduced in Fig. 2. The deflections of variable height represent population response, the occurrence of unit response associated with each of these is signalled by a diphasic deflection which intersects the population deflection. For each series, population response amplitudes were measured by projection and for every such response amplitude the fact of discharge or no discharge of the unit was noted. Population response amplitudes were then collected in appropriate class intervals and for each class interval the numbers of responses and no responses of the unit were collated. Fig. 3 displays 1000 population responses as a frequency distribution with respect to response amplitude. The shaded portion of this histogram indicates the population responses associated with unit discharge. Immediately below each class interval of population response the ratio of number of unit discharges to total number of trials is plotted as a filled circle. This experimental ratio provides an estimate of the firing probability of the unit at that class interval of population response. The vertical bars accompanying each filled circle indicate the standard error expected for the observed probability value, taking into account the number of trials in that class interval (1, 4). The unit of Fig. 3 gave a monosynaptic reflex response on 923 of the 1000 trials, the over-all firing index (F.I.) being 92.3. It is apparent that the unit response is not completely independent of the population response for, were this so, the unit would be expected to have the same probability of firing, about 0.92, at all class intervals of population response. Nor is the unit response completely correlated with population response, for then its firing probability would be expected to rise abruptly from zero to 1.0 within a single class interval. Clearly the situation is intermediate; the unit response shows correlation with pool response as well as some independence of response. The relation between unit firing probability and population response indicated by the solid line in Fig. 3 is a normal sigmoid curve which represents a good fit to the experimental firing probability estimates (see later).

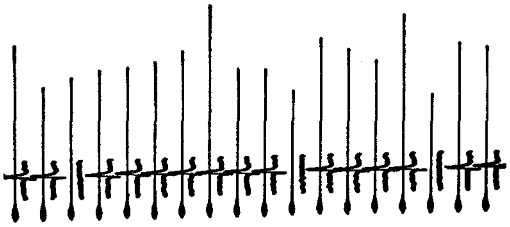


FIG. 2. Portion of record showing simultaneous responses of a triceps surae motoneuron and of the population to which it belongs. See text.

Fig. 4 illustrates another experiment in which unit and population responses of triceps surae motoneurons were compared. This unit responded in 697 of the 1000 trials (F.I. = 69.7). It will be noted that the experimental unit firing probability estimates agree well with a normal sigmoid relation between firing probability and population response amplitude. The normal sigmoid curve in Fig. 4 has its midpoint ($p = 0.5$) associated with a population response amplitude which is nearer the mean population response than is the midpoint of the corresponding sigmoid curve in Fig. 3.

Fig. 5 displays the response of another triceps surae motoneuron together with the associated population response. This unit had a low intermediate firing index of 13.6. The array of firing probability estimated again shows good agree-

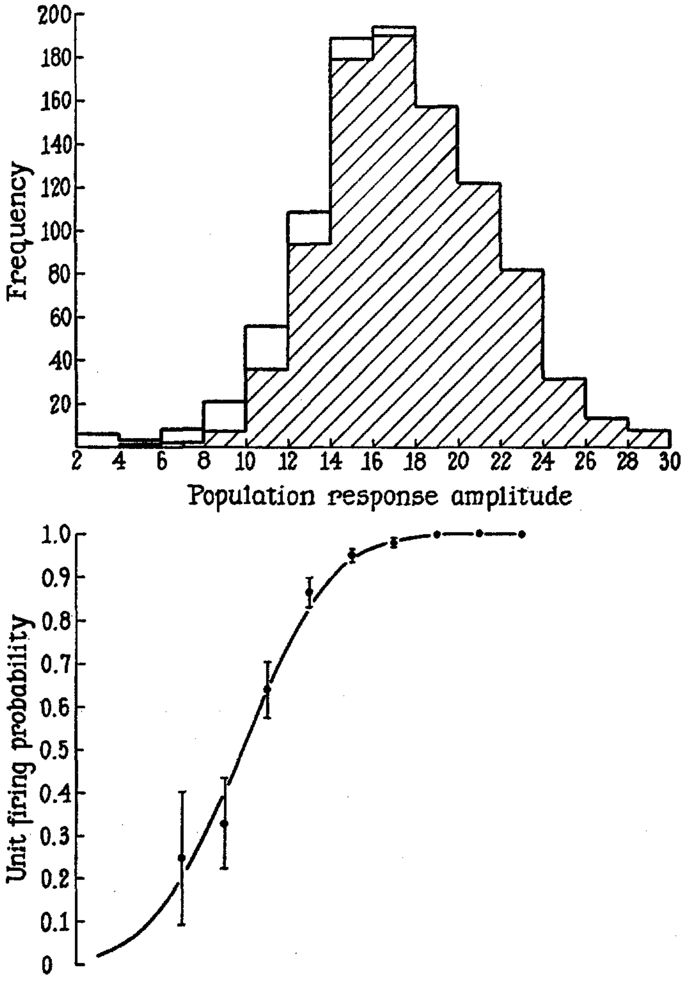


Fig. 3. Distribution of unit and population responses. Upper, histogram of population response amplitude (measured on arbitrary scale). Lower, unit firing probability estimates for each class interval of population response amplitude indicated by circles. Normal sigmoid curve of unit firing probability indicated by solid line. Shaded area of histogram indicates population responses associated with unit discharge. Unit firing index = 92.3.

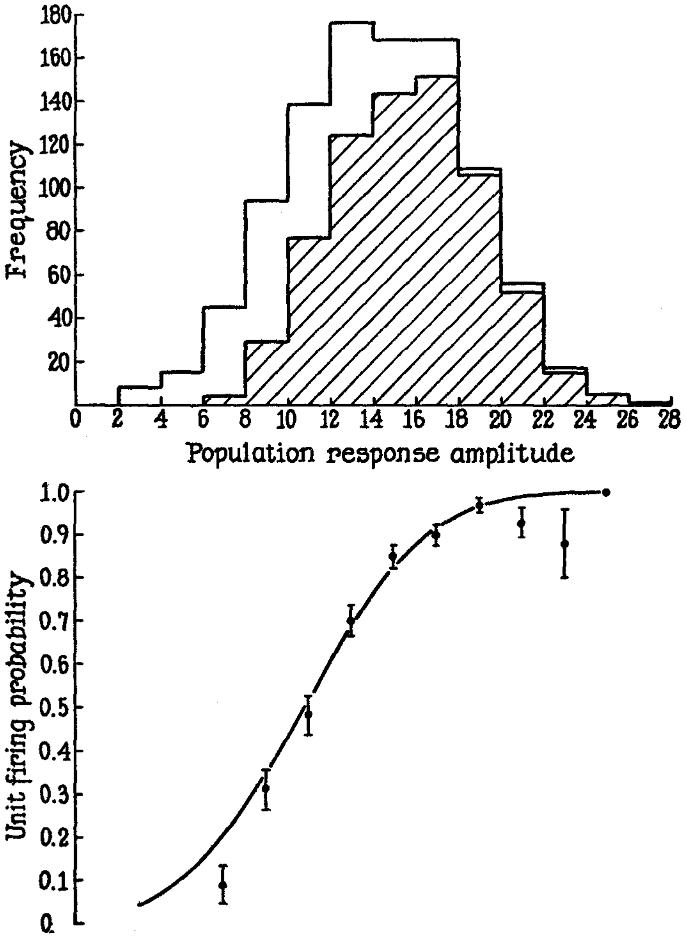


FIG. 4. Distribution of unit and population responses. Upper, histogram of population response amplitude (measured on arbitrary scale). Lower, unit firing probability estimates for each class interval of population response amplitude indicated by circles. Normal sigmoid curve of unit firing probability indicated by solid line. Shaded area of histogram indicates population responses associated with unit discharge. Unit firing index = 69.7.

ment with a normal sigmoid curve for the relation between unit firing probability and population response amplitude. Comparison of this relation in Figs. 3, 4, and 5 indicates that the normal sigmoid curves are successively displaced to the right, relative to mean population response, as unit firing indices decrease from 92.3 to 69.7 to 13.6.

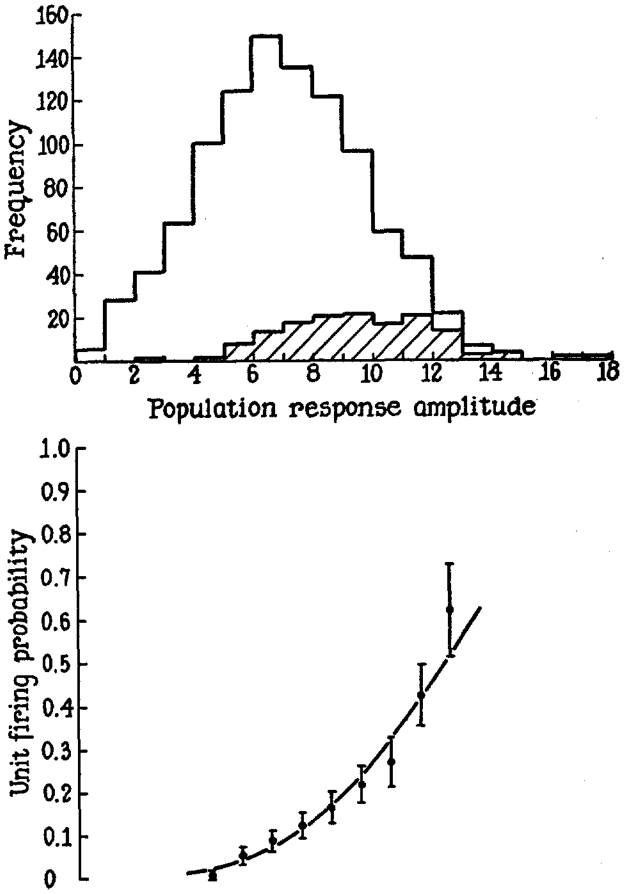


FIG. 5. Distribution of unit and population responses. Upper, histogram of population response amplitude (measured on arbitrary scale). Lower, unit firing probability estimates for each class interval of population response amplitude indicated by circles. Normal sigmoid curve of unit firing probability indicated by solid line. Shaded area of histogram indicates population responses associated with unit discharge. Unit firing index = 13.6.

These normal sigmoid curves have been fitted to the experimental unit firing probability estimates on the working assumption that the independent unit excitability fluctuation has a normal distribution. In practice the experimental points were placed on normal probability paper and the best line through them was estimated visually; the use of standard error for each point assisted in the proper weighting of points. Application of the χ^2 test indicated that in each case the normal sigmoid curve fell within the usual limits for goodness of fit; in most cases the agreement was excellent. It appears justifiable therefore to regard the true unit firing probability as having a normal sigmoid relationship to population response amplitude.

The observed unit firing probability curves indicate that unit excitability fluctuation contains a component with respect to which units are independent of population response. The normal sigmoid form of the unit firing probability curves signifies that this independent component is normally distributed. The magnitude of the independent component of unit excitability fluctuation may be measured relative to the scale of population response by the standard deviation, σ_i, of the normal sigmoid unit firing probability curve. From considerations already discussed, it may be stated that the larger the standard deviation, σ_i, of the unit firing probability curve relative to the standard deviation, σ_v, of population response variation, the more the unit will approach the condition of complete independence in its excitability fluctuation. Conversely, the smaller σ_i is in relation to σ_v, the greater will be the relative magnitude of the correlated component of unit excitability fluctuation. The relative proportions of the independent and correlated components of unit excitability fluctuation will be proportional to the ratio σ_i/σ_v. It may be seen, by reference to Figs. 3 to 8, that the average slope of the unit firing probability curve, relative to the scale of population response amplitude, is related to the ratio σ_i/σ_v.

The firing index of an individual motoneuron may be considered to depend upon the unit firing probabilities at each class interval of population response and the frequency of trials at each interval. The array of firing probabilities of a given unit for the various class intervals of population response will depend upon the ratio σ_i/σ_v, and upon the displacement of the unit firing probability midpoint ($p = 0.5$) relative to the average population response amplitude.

If it were possible to alter the mean responsivity of an individual motoneuron without changing the population response, one might expect the unit firing probability curve to be shifted relative to the population with a consequent change in firing index. This can be done by stimulating the ventral root filament used for unit recording and comparing the unit and population responses when the unit is at different stages of recovery from conduction of an antidromic impulse. Antidromic stimulation thus confined to a single unit cannot be supposed to have an appreciable effect on the response of the remainder of the population.

In the experiment of Figs. 6, 7, and 8, responses of an individual and a popu-

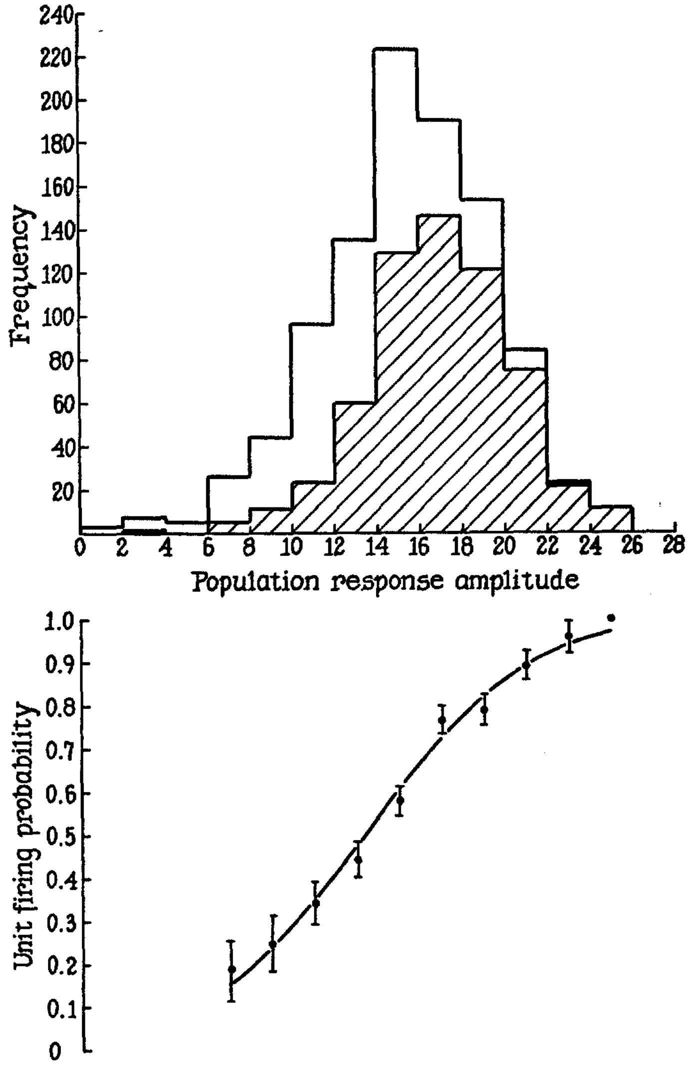


FIG. 6

FIGS. 6, 7, and 8. Distribution of responses of a population and of a unit tested at three intervals following conduction of an antidromic impulse. Firing index, Fig. 6 = 61.4, Fig. 7 = 47.7, Fig. 8 = 25.1. Note that unit firing probability curves are the same in the three figures except for lateral translation along the abscissa.

lation of triceps surae motoneurons were recorded with the unit at three stages of recovery from conduction of an antidromic impulse. Antidromic stimulation was confined to the filament used for unit recording, different intervals between the antidromic unit stimulus and the test stimulus to the muscle nerve being selected for each series. In the series of Fig. 6 the unit responded to 614 of the 1000 trials (F.I. = 61.4). The normal sigmoid curve shown provides a good fit to the set of experimental firing probability estimates. The midpoint (p = 0.5) of the unit firing probability curve is to the left of the mean population response by an amount 0.56 σ_v. In Fig. 7, at a different interval between antidromic and test volleys, the unit discharged on 477 of the 1000 trials (F.I. = 47.7), the unit firing probability curve being shifted to the right as compared with Fig. 6; the midpoint (p = 0.5) in Fig. 7 is 0.12 σ_v to the right of the

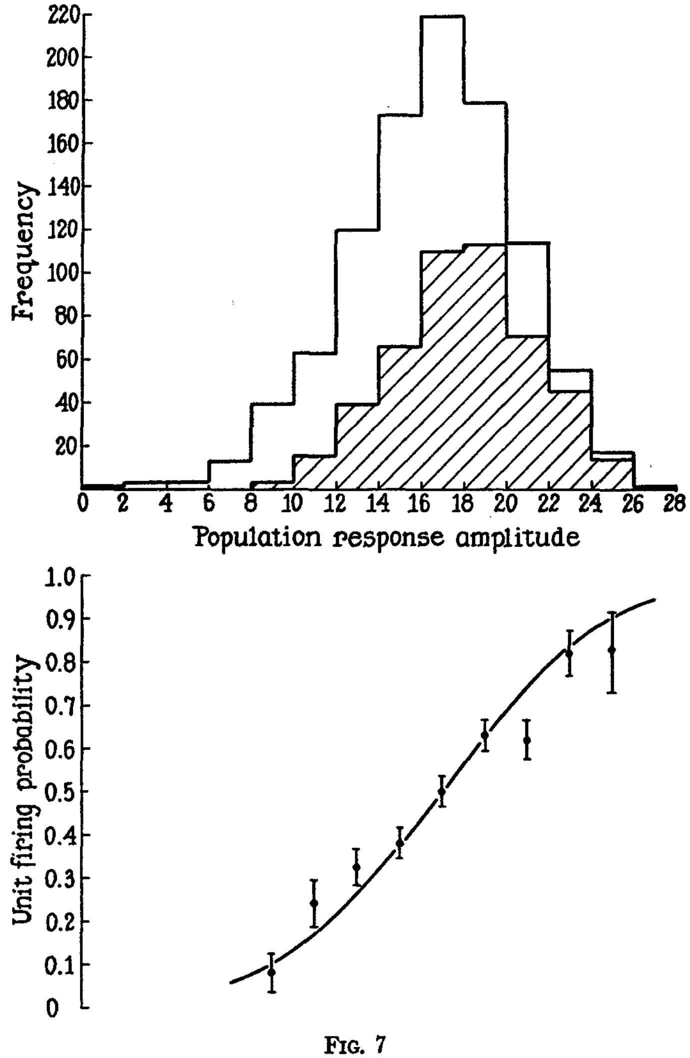


FIG. 7

population mean. A third antidromic interval was used to obtain the results in Fig. 8 and the unit response was further reduced, discharge occurring on 251 of the 1000 trials (F.I. = 25.1). The unit firing probability curve in Fig. 8 shows a further shift to the right; its midpoint is *1.11* σ, to the right of the population mean.

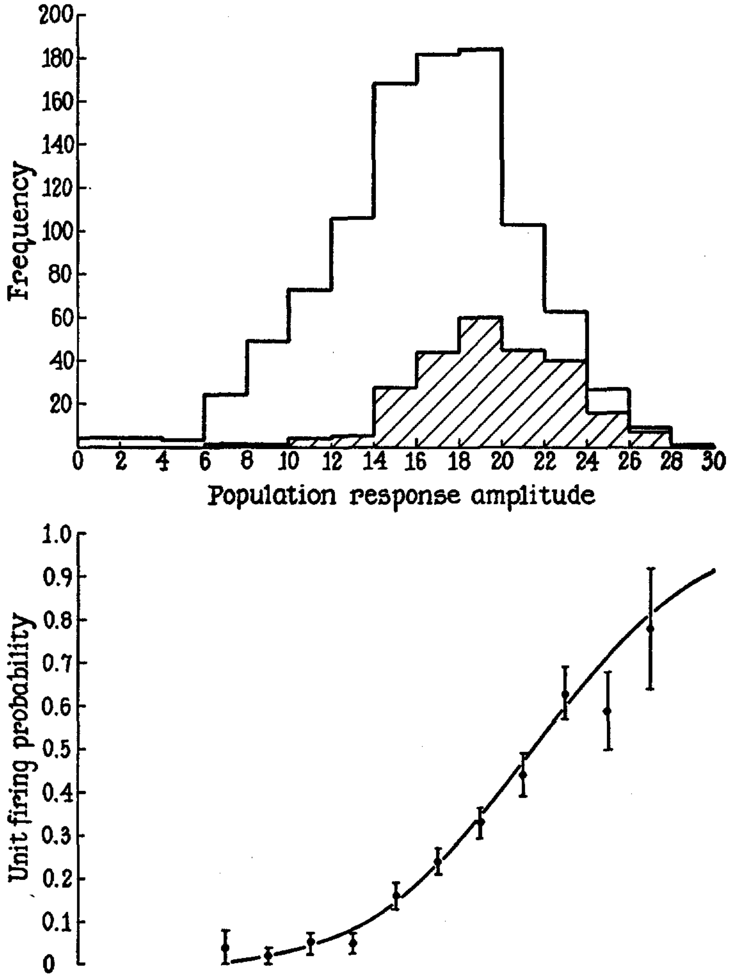


FIG. 8

The effect of varying the antidromic interval in Figs. 6, 7, and 8 was to shift the unit firing probability curve in relation to the population response distribution, the latter remaining essentially constant. The standard deviation,

σ_i, of the unit firing probability curve remained substantially the same in the three series; in fact, the normal sigmoid curves, displayed in Figs. 6, 7, and 8, were drawn with identical standard deviations, and differ only in the lateral displacement of their midpoints ($p = 0.5$) from the population response mean. From the fact that the standard deviation, σ_i, of the unit firing probability curve remained the same in the three series, it may be concluded that the proportions of correlated and independent fluctuations of the unit remained essentially the same. The differences among the three firing index values obtained with this unit may be attributed almost entirely to the differences in the displacement of its firing probability curve relative to the population response distribution.

TABLE I

Summary of Unit-Population Responses

Units 1, 2, and 3 are illustrated in Figs. 3, 4, and 5 respectively. Unit 4 (*a*, *b*, and *c*) is shown in Figs. 6, 7, and 8.

Unit	F.I.	$\bar{v}$	σ_v	$\frac{\text{Displacement}}{\sigma_v}$	$\frac{\sigma_i}{\sigma_v}$	$\frac{\text{Displacement}}{\sqrt{\sigma_v^2 + \sigma_i^2}}$
1	92.3	17.25	4.26	−1.75	0.78	−1.38
2	69.7	14.23	4.13	−0.83	1.09	−0.56
3	13.6	7.0	2.71	+1.95	1.48	+1.09
4 *a*	61.4	15.5	3.92	−0.56	1.57	−0.30
4 *b*	47.7	16.53	3.91	+0.12	1.58	+0.064
4 *c*	25.1	16.5	4.42	+1.11	1.39	+0.65
5 *a*	90.8	17.17	2.47	−1.98	1.15	−1.30
5 *b*	83.6	17.02	2.45	−1.31	1.16	−0.86
5 *c*	37.3	15.02	2.31	+0.55	1.22	+0.35
5 *d*	6.3	14.11	2.25	+2.4	1.26	+1.49
5 *e*	87.8	13.12	2.42	−1.78	1.17	−1.16
6 *a*	76.5	81.3	3.7	−1.89	2.44	−0.72
6 *b*	40.4	87.8	3.65	+0.51	1.84	+0.24
6 *c*	25.9	89.3	3.71	+1.22	1.83	+0.58
7	83.8	10.5	3.78	−1.43	1.03	−1.00

Comparison of Different Units on a Common Quantitative Basis.—Table I presents a summary of the results obtained by simultaneous recording of unit and population responses in fifteen experimental series. The results were obtained with seven different units, some studied in the resting state and some in the period of recovery from conduction of an antidromic impulse. The mean, $\bar{v}$, and standard deviation σ_v, of the population responses in each series are expressed relative to an arbitrary scale of measurement. The standard deviation, σ_i, of the normal sigmoid unit firing probability curve is expressed relative to σ_v as the ratio σ_i/σ_v. It may be seen that in all but two of the seven units the value of the ratio σ_i/σ_v falls between 1.0 and 1.6, with a value of 1.3 as average. Since this ratio is determined by the relative magnitude of the independent and correlated components of unit excitability fluctuation, it may be concluded that the various units differ somewhat in this relative magnitude.

Also shown in Table I are the experimental values found for the displacement of the unit firing probability midpoint ($p = 0.5$) from the mean of population response amplitude; this displacement is expressed, for each experiment, both relative to σ_v, and relative to the compound standard deviation, $\sqrt{\sigma_v^2 + \sigma_i^2}$ As will become clearer below, the displacement, when expressed relative to this compound standard deviation, provides a fundamental parameter of unit excitability fluctuation. This parameter provides a means of comparing the displacements of different units on a common quantitative basis, regardless of their differences in the σ_i/σ_v ratio. In fact, a definite relation can be shown to exist between firing index values and the corresponding values of this fundamental parameter. The fifteen points plotted in Fig. 9 represent paired values of these two parameters as given by the fifteen sets of experimental results listed in Table I. It may be seen that these points are in excellent agreement with the standard ($\sigma = 1.0$) normal sigmoid curve also shown in Fig. 9.

The relation demonstrated in Fig. 9 provides a precise quantitative statement of a qualitative generalization noted earlier; as the unit firing probability midpoint is displaced in the positive direction, smaller firing indices are observed. The existence of this precise empirical relation invites explanation.

Each motoneuron is subject to excitability fluctuations which may be treated as separable into two components, designated as the independent component and the correlated component. The independent component fluctuations are represented by the sigmoid unit firing probability relation; they are normally distributed, with a standard deviation, σ_i. It is asserted (on the basis of theoretical results derived in the following section of this paper), that the essentially normal distribution of population response amplitudes, with its standard deviation, σ_v, represents, with negligible error, the distribution of correlated excitability fluctuation component values, when expressed on the same arbitrary scale as σ_i. Since these two components fluctuate independently of each other, it follows, from statistical theory, that when the component fluctuations are combined, the resulting compound fluctuations have a variance equal to the sum of the two component variances; hence, the compound standard deviation is given by $\sqrt{\sigma_v^2 + \sigma_i^2}$. Further, since the distributions of the component fluctuations are both normal, as well as independent, the distribution of the compound fluctuations must also be normal. Thus, the frequency distribution of compound unit excitability fluctuations, although not directly observable, is obtained indirectly from experimental measurements of the component distributions.

The significance of this compound distribution is that it permits a calculation of the proportion of trials on which the unit may be expected to undergo an excitability fluctuation greater or less than any specified value. Each motoneuron may be expected to have a critical level of excitability such that, whenever its excitability fluctuates above this critical level, the response to an invariant test volley would always be unit reflex discharge, and whenever its excitability fluctuates below this critical level, the response to the same invariant test volley would never be unit reflex discharge. Once the position of this critical level is known, relative to the frequency distribution of fluctuating excitability levels, the expected firing index can be predicted from the proportion of the normal frequency distribution containing excitability levels above the critical level. As is illustrated in Fig. 10, the displacement of the unit firing

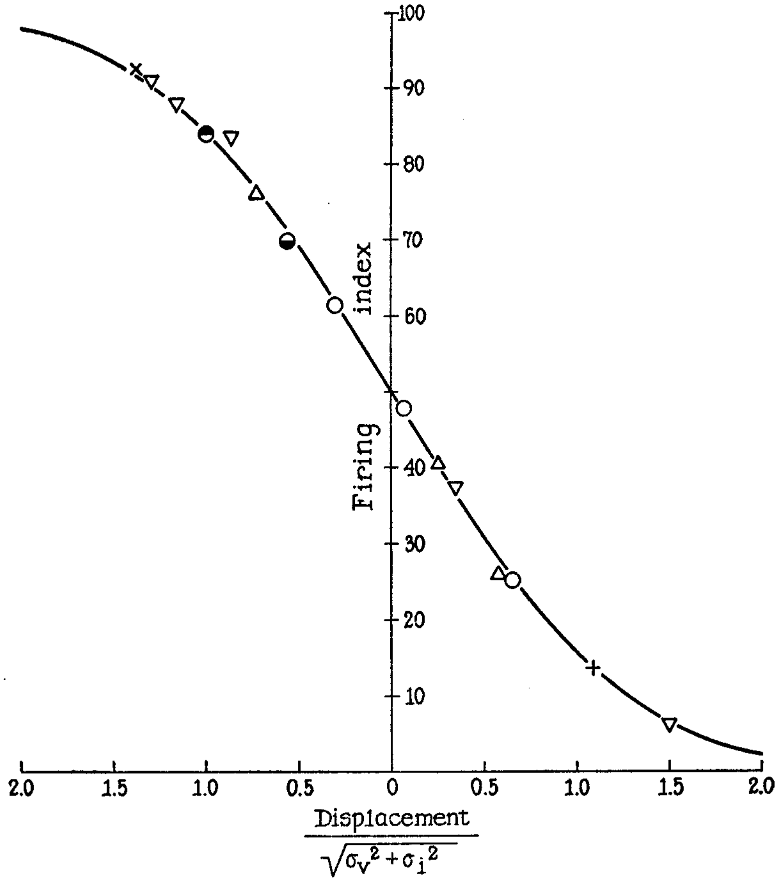


FIG. 9. Relation between firing index and unit displacement.

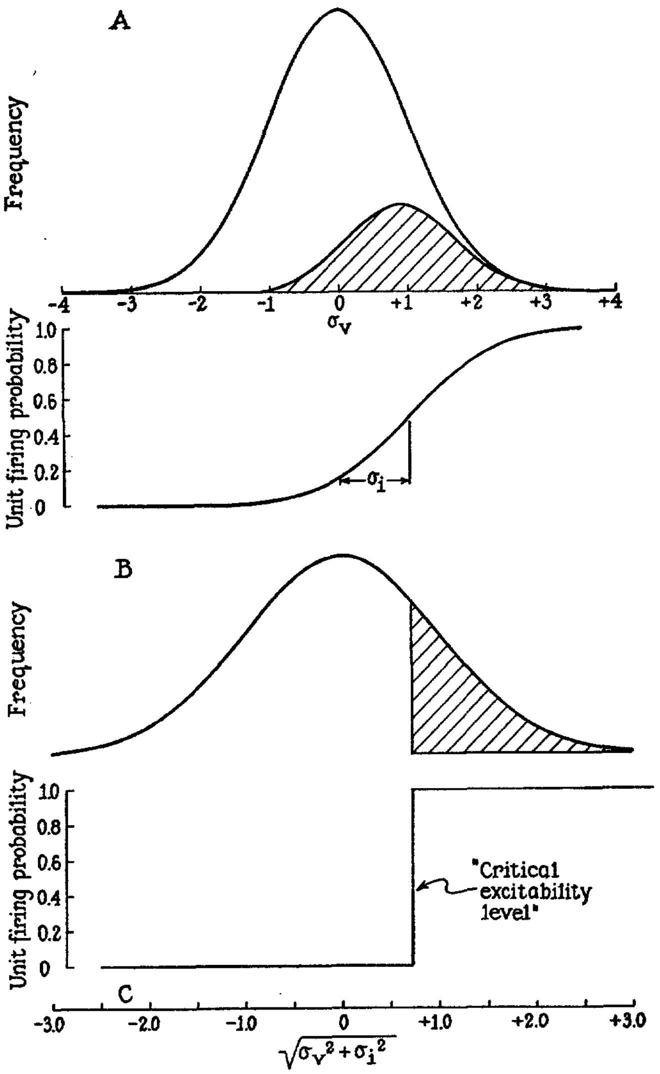


FIG. 10. Schematic representation of the manner in which the independent and correlated components of unit excitability fluctuation have been added to derive the distribution of over-all fluctuation. A, representative relation between population response and a unit firing probability curve. Shaded area indicates portion of population response associated with unit discharge. Standard deviation, σ_i, of unit firing probability curve equal to standard deviation σ_v of population response (the latter is assumed equal to σ_c). B, distribution of combined unit excitability fluctuation. The variances of unit fluctuation have been added to give the variance of the normally distributed compound fluctuation. By this maneuver a distribution of excitability levels is obtained as well as a "critical" level above which the unit would always discharge to test volleys (shaded area) and below which it would never respond. C, scale based on combined variance. See text.

probability midpoint ($p = 0.5$) from the population response mean, defines the position of the critical excitability level relative to the mean of the excitability fluctuations. When this displacement is expressed in terms of the compound standard deviation of the excitability fluctuation distribution, it becomes reduced to a displacement from the mean of the standard ($\sigma = 1.0$) normal curve. The resulting dependence of firing index upon displacement, when displacement is expressed in this way, is shown by the standard normal curve in Fig. 9.

Fig. 10 illustrates the manner in which the frequency distribution of the compound excitability fluctuations, and the position of the critical excitability level, may be determined. In A, a typical relation between unit firing probability and population response amplitude is shown; for convenience, σ_i has been shown equal to σ_v, and the unit midpoint ($p = 0.5$) displacement has also been shown equal to σ_v. It is assumed that the population response standard deviation, σ_v, is equivalent to the standard deviation of the correlated excitability fluctuation component, when expressed on the same scale as σ_i. Thus, the normal curve in A may be taken to represent the distribution of the correlated component values. In contrast, the normal curve in B represents the distribution of the compound excitability fluctuation values; it has been drawn with the standard deviation, $\sqrt{\sigma_v^2 + \sigma_i^2}$, which results from combining the two component variances. Since σ_v and σ_i are equal in this example, the compound standard deviation is greater than σ_v by a factor of 1.4, or, more precisely, the square root of 2; the resulting standard scale is shown (C) at the bottom of Fig. 10. In B, the independent excitability fluctuations are included in the compound normal distribution; consequently, the range of intermediate firing probabilities has been reduced to zero on this scale; thus, the unit firing probability relation rises abruptly from zero to 1.0 at the critical excitability level. Since this firing probability relation corresponds to a normal sigmoid curve with zero standard deviation, it is clear that its position must be the same as the midpoint ($p = 0.5$) of the firing probability curve in A. In both A and B the shaded area represents the proportion of tests in which the compound excitability level fluctuates above the critical excitability level. In B the area under the normal curve to the right of the critical excitability level is found to comprise 24 per cent of the total area; hence a firing index of 24 is implied by the midpoint displacement in the example of Fig. 10.

The theoretical relation between firing index values and midpoint displacement values is shown as a standard normal sigmoid curve in Fig. 9. The agreement with the experimental results suggests that no serious error is introduced by the assumptions made. Also it may be noted that the U-shaped relation found for the distribution of intermediate firing index values (5) is what would be predicted from the normal sigmoid relation of Fig. 9, on the assumption that all displacement values in the intermediate range are equally probable.

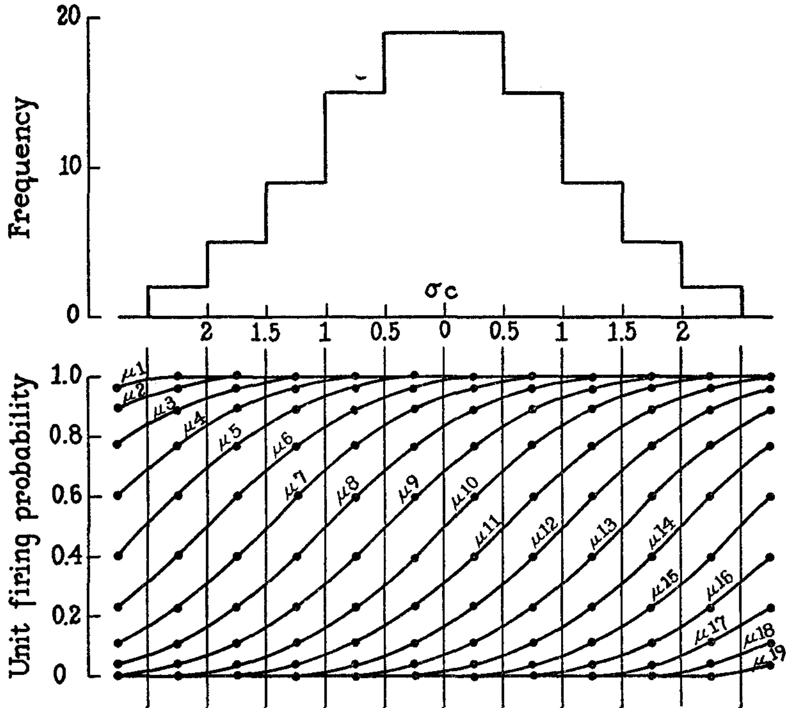
Theoretical Model of a Population of Motoneurons Subject to Partially Correlated Excitability Fluctuations

The experimental results already presented indicate that excitability fluctuations of spinal motoneurons may be considered as separable into two components; in respect to one, the units of a population are independent, and in respect to the other, they are correlated. It is clear that the population response is the composite of response in a number of units. Variation in population response is therefore determined by excitability fluctuation in the participating units. In order to define the contriubtion of the independent and correlated components of unit excitability fluctuation to population response variation it has proven necessary to construct a theoretical model of a population of motoneurons. This model comprises an array of units each subject to partially correlated excitability fluctuation. Before defining the theoretical model in a more general form, it will be illustrated by a specific example involving a small number of units.

The frequency histogram in the upper part of Fig. 11 represents the correlated component of unit excitability fluctuation; immediately below this are shown the firing probability curves representing the independent component of excitability fluctuation in 19 different units. The frequency histogram is essentially normal, and consists of 10 class intervals, in steps equal to one-half of σ_c, in which σ_c is defined as the standard deviation of the correlated unit excitability fluctuation. The 19 unit firing probability curves all imply the same standard deviation, σ_i, for the independent unit excitability fluctuation of these units. The value σ_i has been made equal to σ_c, for simplicity of illustration; also, the spacing of the unit firing probability curves has been made uniform, with intervals equal to half this standard deviation.

Altogether, this frequency histogram and these 19 unit firing probability curves specify the array of unit firing probabilities which corresponds to each class interval of correlated unit excitability fluctuation. This is made explicit in the table of Fig. 11, where, for each of the 10 class intervals, the midvalue of firing probability of each of the 19 units is specified; (negligible error results from the simplification of considering probability values less than 0.02 as equal to zero, and values greater than 0.98 as equal to one). By means of simple calculations with the various rows and columns of this table, it is possible to predict the expected firing index of each unit, and to predict the relative contributions of the correlated and independent components of unit excitability fluctuation to the expected population response variability of this population.

Inspection of the table shows that unit 1 is certain to fire on each trial, unit 19 never fires, and the remaining 17 units exhibit uncertainty on some of the trials; (for convenience, uncertainty here refers to firing probabilities greater than 0.02 and less than 0.98). The expected firing index of each unit is obtained by considering its horizontal row of firing probabilities, multiplying each of



Unit firing probability

F→	2	5	9	15	19	19	15	9	5	2	F.I. ±	std. error
μ1	1	1	1	1	1	1	1	1	1	1	100 ±	0
μ2	0.96	1	1	1	1	1	1	1	1	1	99.9 ±	0
μ3	0.89	0.96	1	1	1	1	1	1	1	1	99.6 ±	0.2
μ4	0.77	0.89	0.96	1	1	1	1	1	1	1	98.6 ±	1.1
μ5	0.60	0.77	0.89	0.96	1	1	1	1	1	1	96.5 ±	1.7
μ6	0.40	0.60	0.77	0.89	0.96	1	1	1	1	1	92.3 ±	2.3
μ7	0.23	0.40	0.60	0.77	0.89	0.96	1	1	1	1	85.6 ±	3.0
μ8	0.11	0.23	0.40	0.60	0.77	0.89	0.96	1	1	1	75.9 ±	3.6
μ9	0.04	0.11	0.23	0.40	0.60	0.77	0.89	0.96	1	1	63.7 ±	3.9
μ10	0	0.04	0.11	0.23	0.40	0.60	0.77	0.89	0.96	1	50.0 ±	4.1
μ11	0	0	0.04	0.11	0.23	0.40	0.60	0.77	0.89	0.96	36.3 ±	3.9
μ12	0	0	0	0.04	0.11	0.23	0.40	0.60	0.77	0.89	24.1 ±	3.6
μ13	0	0	0	0	0.04	0.11	0.23	0.40	0.60	0.77	14.7 ±	3.0
μ14	0	0	0	0	0	0.04	0.11	0.23	0.40	0.60	7.7 ±	2.3
μ15	0	0	0	0	0	0	0.04	0.11	0.23	0.40	3.5 ±	1.7
μ16	0	0	0	0	0	0	0	0.04	0.11	0.23	1.4 ±	1.1
μ17	0	0	0	0	0	0	0	0	0.04	0.11	0.4 ±	0.2
μ18	0	0	0	0	0	0	0	0	0	0.04	0.1 ±	0
μ19	0	0	0	0	0	0	0	0	0	0	0.0 ±	0
Σp	5	6	7	8	9	10	11	12	13	14		

FIG. 11. Theoretical model of a motoneuron population subject to partially correlated excitability fluctuation. See text.

these firing probabilities by the frequency of trials in the class interval to which it belongs, and then adding the 10 product terms so obtained. The resulting expected firing index values are collected in the right-hand column of the table, together with plus or minus the calculated standard error of the firing index for 100 trials. It may be seen that 11 of the 19 units have expected firing indices which are greater than 2 and less than 98; these units correspond to those usually designated experimentally as having intermediate firing indices (5).

If attention is focussed upon the (vertical) columns of this table, it may be seen that the number of units possessing uncertainty on any trial is only 8. Although different groups of 8 units are involved in the 10 different columns of this table, the same array of intermediate firing probabilities applies to every trial. This array is symmetrical about $p = 0.5$; consequently, for a large number of trials of such an array, the average number of uncertain units to fire per trial would be 4 units.

The contribution of correlated unit excitability fluctuations to population response variations may be seen by noting the differences between successive (vertical) columns in the table. Progressing from left to right, it may be seen that each step involves both the gain of one unit which is certain to fire, and the loss of one unit which is certain not to fire. The average population response for each column is equal to 4 units plus the number of units certain to fire; this response value is given at the foot of each column in the table. Each of these response values may also be obtained directly as the sum (Σp) of the probability array in its column. When these response values are considered together with the frequencies given at the heads of the columns, one obtains a frequency histogram of the population response variations which result from the correlated component of unit excitability fluctuation. This frequency histogram has a mean value of 9.5 units firing per trial; its standard deviation, σ_{vc}, is appropriately expressed in number of units. It is apparent that this number depends upon the density of unit spacing, relative to σ_c. In the example shown, σ_{vc} equals 2 units as a consequence of the fact that the units have been spaced in class intervals corresponding to one-half σ_c.

The contribution of the independent component of unit excitability fluctuation to variation in population response may be determined for each class interval of the table from the sum of the pq products in that interval (p being the firing probability of each unit and q its probability of not firing). It is known from statistical theory that, given a group of independent probabilities, the group response on repeated trials has a variance equal to the sum of the individual pq products (*cf.* references 1 and 4). For each class interval it may be seen that eleven of the units have a pq product equal to zero (either p or q being zero) and hence these units are certain to discharge or not to discharge; they do not contribute to the variation of responses belonging to any given class interval. The array of pq products that are not zero is the same for each class interval and hence the sum of the pq products is the same. This sum is approximately 1.1 for each class interval and represents the variance, σ_{vi}^2, of population response due to the independent component of unit excitability fluctuation. Since σ_{vi}^2 is the same for all class intervals this represents the variance of the over-all population response due to the independent component of unit excitability fluctuation.

The total variability of population response is due to both of the sources discussed; that portion which corresponds to the frequency distribution of correlated unit excitability fluctuations has a variance, σ_{vc}^2; that portion which results from the independent excitability fluctuations of the 8 uncertain units per trial has a variance, σ_{vi}^2. Since these two variances represent two sets of additive variations in population response, and are independent of each other in their occurrence, it follows (from statistical theory) that the resultant variance, σ_v^2, of population response is equal to the sum of the two separate variances. Thus, we may write,

$$\sigma_v^2 = \sigma_{vi}^2 + \sigma_{vc}^2$$

In the present illustration this combined variance equals approximately 5.1 (the sum of 1.1 and 4) in terms of units, implying a standard deviation of 2.26 units, about average response of 9.5 units per trial.

It is interesting to note that, although equal variance has been assumed for the independent and correlated components of unit excitability fluctuations, the portion of population response variance, σ_{vc}^2, which results from correlated unit excitability fluctuations, is approximately four times as great as the portion of population response variance, σ_{vi}^2, which results from independent unit excitability fluctuations. This variance ratio $(\sigma_{vc}^2/\sigma_{vi}^2)$ applies to the present illustration, in which the number, N, of units having firing indices between 2 and 98, is equal to only 11. A larger value of N would result in a larger value of this variance ratio. In fact, this ratio can be shown (see below) to have a value of very nearly $N/3$ for the case in which σ_c and σ_i are assumed equal to each other, for all units. The significance of this result is that, with large values of N, the major portion of population response variance results from the correlated component of unit excitability fluctuations.

In the example of Fig. 11 the ratio of the independent to correlated component of unit excitability fluctuation was assumed to be one. Further, the hypothetical population considered contained a number of units in the intermediate firing range, N, equal to only 11. It is useful to consider a more general formulation in which the ratio σ_i/σ_c need not be one and in which different values of the number N may be considered. As in the simpler model of Fig. 11 all units are considered to have the same ratio σ_i/σ_c (henceforth called α) and to be equally spaced on the scale of σ_c. As before, it is assumed that both components of unit excitability fluctuation are normally distributed.

Since the excitability fluctuations of each unit are treated as separable into two components, one with a variance, σ_c^2, and the other with a variance, σ_i^2, and since these two components are independent of each other, it follows (from statistical theory), that the variance σ_u^2, of the total excitability fluctuations of each unit, must be equal to the sum of the two component variances. Making use of the definition of α, according to which $\sigma_i = \alpha\sigma_c$, the combined variance may be written,

$$\sigma_u^2 = \sigma_c^2 (\alpha^2 + 1) \tag{1}$$

Since a normal distribution of excitability fluctuations is assumed, use may be made of the fact that 2 per cent of the area under a normal curve lies beyond a deviation of $+2.05\sigma$ from the mean, and another 2 per cent lies beyond a deviation of -2.05σ from the mean. In view of the relation between the firing index of a unit and the displacement of its midpoint (*cf.* Fig. 10), it may be expected that the range of midpoint displacement for units having firing indices between 2 and 98, is equal to twice 2.05 σ_u; making use of equation (1), this range may be expressed in terms of σ_c, as 4.1 $\sigma_c \sqrt{\alpha^2 + 1}$. When σ_{vc} is substituted for σ_c in this expression, this range becomes equivalent to the number, N, of units having firing indices between 2 and 98; this result follows from the fact that σ_{vc} is related to σ_c by a proportionality factor which expresses the density of unit spacing in the model. The resulting relation between N and σ_{vc} may be written,

$$N = 4.1\, \sigma_{vc} \sqrt{\alpha^2 + 1} \tag{2}$$

Rearranging this equation, the population response variance resulting from the correlated component of unit excitability fluctuations may be expressed,

$$\sigma_{vc}^2 = \frac{(N/4.1)^2}{\alpha^2 + 1} \tag{3}$$

It may be seen that this variance is proportional to N^2; its dependence upon the value of α is illustrated in row A of Table II.

To obtain an expression for the portion of population response variance which results from the independent component of unit excitability fluctuations, it is necessary to obtain, first, the number, N_t, of units per trial, whose response is uncertain. As defined in the earlier illustration, these are the units having firing probabilities between 0.02 and 0.98, for any class interval of the correlated fluctuation component. If attention is focussed on any one class interval, it may be seen that a unit, whose firing probability is 0.98, will have a sigmoid firing probability curve whose midpoint ($p = 0.5$) lies 2.05 σ_i to the left of the middle of this class interval. Similarly, a unit, whose firing probability is 0.02, will have a sigmoid firing probability curve whose midpoint ($p = 0.5$) lies 2.05 σ_i to the right of the middle of this class interval. It may be seen that all units, with firing probabilities between 0.02 and 0.98 for this class interval, will have sigmoid firing probability curves whose midpoints lie within the range defined by plus and minus 2.05 σ_i, relative to the middle of this class interval. This range, 4.1 σ_i, may also be written 4.1 $\alpha\sigma_c$. The number of units, with firing probability midpoints ($p = 0.5$) lying in this range, is the required number, N_t, of uncertain units per trial. When σ_{vc} is substituted for σ_c this range becomes expressed relative to the density of unit spacing, and thus becomes equivalent to the number, N_t. This result may be written,

$$N_t = 4.1\ \alpha\ \sigma_{vc} \tag{4}$$

TABLE II

Relations between Parameters Concerned with Population Response Variation

	$\alpha = 0$	$\alpha = 1$	$\alpha = 1.5$	$\alpha = 2$	$\alpha = \infty$
A. σ_{vc}^2 ($N = 60$)	$N^2/17$ (214)	$N^2/34$ (107)	$N^2/55$ (66)	$N^2/84$ (43)	0 0
B. Nt ($N = 60$)	0 (0)	0.71 N (43)	0.83 N (50)	0.89 N (53)	N (60)
C. σ_{vi}^2 ($N = 60$)	0 (0)	0.093 N (5.6)	0.103N (6.5)	0.117 N (7.0)	0.131 N (7.9)
D. σ_v^2 ($N = 60$)	(214)	(113)	(72)	(50)	(8)
E. σ_v ($N = 60$)	(14.6)	(10.6)	(8.5)	(7.1)	(2.8)
F. $\sigma_{vc}^2/\sigma_{vi}^2$ ($N = 60$)	∞ (∞)	$N/3$ (20)	$N/6$ (10)	$N/10$ (6)	0 (0)
G. σ_{vc}^2/σ_v^2 ($N = 60$)	1 (1)	$N/N + 3$ (0.95)	$N/N + 6$ (0.91)	$N/N + 10$ (0.86)	0 (0)

The ratio of this number, to the number, N, may be obtained simply from the ratio of equation (2) to equation (4); this ratio may be written,

$$N_t/N = \frac{\alpha}{\sqrt{\alpha^2 + 1}} \tag{5}$$

The dependence of N_t upon different values of α is illustrated in row B of Table II.

The portion of population response variance, σ_{vi}^2, resulting from the independent component of unit excitability fluctuation is equal to the sum of the

pq values of the uncertain units per trial. This variance may therefore be obtained as the product of the number of uncertain units per trial, and the average pq value for such units. An average pq value of 0.131 per uncertain unit is found, by calculation, to correspond to the range of p values between 0.02 and 0.98, on the assumption that the midpoints ($p = 0.5$) of the units are uniformly spaced. Using this average pq value, the resulting expression for the variance σ_{vi}^2, may be written,

$$\sigma_{vi}^2 = \frac{0.131\,\alpha N}{\sqrt{\alpha^2 + 1}} \tag{6}$$

It may be seen that this variance is proportional to N; its values for different values of α are given in row C of Table II.

The over-all population response variance, σ_v^2, is equal to the sum of the two variances given by equations (3) and (6). The differences in the values of α, may be seen by comparing rows A and C in Table II; row D of this table gives the total variance in each case, when $N = 60$; row E gives the corresponding standard deviations. It is clear that the major contribution to population response variance, is provided by the correlated component of unit excitability fluctuation.

The relative magnitude of these two variances may be conveniently expressed by the ratio,

$$\frac{\sigma_{vc}^2}{\sigma_{vi}^2} = \frac{N}{2.2\alpha\sqrt{\alpha^2 + 1}} \tag{7}$$

obtained from equations (3) and (6). It may be seen that the value of this ratio is proportional to N. Row F of Table II gives this value for different values of α. Row G gives the corresponding values of the variance ratio, σ_{vc}^2/σ_v^2. It is of interest to note that this variance ratio represents the maximum correlation coefficient to be expected between the responses of two halves of a motoneuron population, each half containing N units with intermediate firing indices. A correlation coefficient smaller than this maximum value would be expected if the component of unit excitability fluctuation responsible for σ_{vc}^2 in one-half of the population were not completely correlated with that responsible for σ_{vc}^2 in the other half.

The value, $N = 60$ units, has been used for illustrative purposes because it corresponds approximately to the number of medial gastrocnemius motoneurons in a total population of about 300 that are in the intermediate range of firing indices (5). The standard deviation σ_v of population response variation, recorded in the medial gastrocnemius nerve, was found to represent about 2.6 per cent (range 1.9 to 3.4) of the total population (3). The total population in this case being about 300 units, it follows that σ_v equals 7.8 units (range 5.7 to 10.2). Reference to Table II reveals that this experimental value of σ_v is in close agreement with the value σ_v predicted by the theoretical model in which $N = 60$ and $\alpha = 1.5$.

COMMENT

The present study has shown that motoneurons are subject to normally distributed excitability fluctuation that may be separated into two components. With respect to one component units are independent of each other; with respect to the other they are completely correlated in their excitability fluctuations. The relative proportions of the independent and correlated components in individual motoneurons have been determined. It should be emphasized that only the relative magnitudes of the two components are measurable. Thus, although the ratio of the independent to correlated component of unit excitability fluctuation differs to some degree among the several units examined, it is not possible to say whether these units differ in their compound excitability fluctuation.

The separation of unit excitability fluctuation into two components, although useful, is arbitrary in the sense that the same influence may contribute to both components. Any influence affecting a motoneuron, to the degree that it influences other members of the population in a like manner, contributes to the correlated component of unit excitability fluctuation. To the degree that the same influence differs among the various units, it also contributes to the independent component.

A number of sources of excitability fluctuation may be considered intrinsic to the motoneuron and its synaptic connections. Among these, inherent instability in motoneuron responsivity, synaptic "noise" similar to that found at the nerve-muscle junction (2), and lability of individual knob action might contribute to variability of response to standard excitatory volleys. With respect to these sources of excitability fluctuation the individual motoneurons may be considered to be independent of each other.

Two major sources of excitability fluctuation may be considered extrinsic to the motoneurons. Specific synaptic influences, resulting from internuncial activity, as well as non-specific current flows, might contribute to both the independent and correlated components of unit excitability fluctuation.

The independent component of unit excitability fluctuation may therefore be ascribed to factors both intrinsic and extrinsic to the motoneurons. No estimate can be given of the relative contributions of intrinsic and extrinsic sources of excitability fluctuation to the independent component, although it is likely that the extrinsic factors play a considerable role. The magnitude of the independent component of unit excitability fluctuation was found to be as great as or slightly greater than the magnitude of the correlated component. It is possible that preparations other than the acutely spinal animal might have a smaller ratio of independent to correlated unit excitability fluctuation. If, for example, internuncial activity were more completely integrated in organized patterns, that fraction of independent unit excitability fluctuation which is due to internuncial activity might be reduced.

Consideration of a motoneuron population as an array of units, each subject to independent and correlated components of excitability fluctuation has indicated the manner in which the two components contribute to variation in population response. It is clear that correlated fluctuations in excitability of units comprising a population will be much more effective in causing variation in population response than will independent fluctuations, providing the number of units is reasonably large.

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