# STEPS IN THE PRODUCTION OF MOTONEURON SPIKES

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The first report on action potentials recorded with intracellular electrodes from motoneurons (Brock, Coombs, and Eccles, 1951) described orthodromic and antidromic spikes as identical except for presence of a synaptic potential at the foot of the spike evoked by orthodromic stimulation. It was later recognized (Brock et al., 1952 a and b) that a difference exists in the rising phase of spikes evoked by orthodromic or antidromic stimulation, and it was stated that antidromic spikes show an initial fast rise of about 35 mv., an inflection, and a further fast rise to peak, while the orthodromic spikes present an initial slow rise of about 10 mv. (the synaptic potential) an inflection there, and a further fast and smooth rise to peak. It was then suggested that ". . . the spike response of the neurone began at the inflection on the rising phase. . . . In the former [antidromic] the inflection indicates origin of the neuronal spike from the spike of the non-medullated axon, in the latter [orthodromic] its origin from the synaptic potential" (Brock et al., 1952 a, p. 440). This view was further developed in a later article (Brock et al., 1953) in which an attempt was also made to justify the difference of depolarization level required for initiation of soma firing following orthodromic or antidromic stimulation.

Araki, Otani, and Furukawa (1953) working with toads noted that an inflection is often present also in the rising phase of orthodromically evoked spikes, and Araki and Otani (1955) recorded a similar inflection also in spikes evoked by direct stimulation of toad's motoneurons. They interpreted these findings by assuming that ". . . the non-myelinated segment is more excitable than the soma, so that the local current due to synaptic potential may excite it primarily, as suggested by Gesell" (Araki and Otani, 1955, p. 475). Frank and Fuortes (1955 b) confirmed the presence of an inflection in the rising phase of orthodromic spikes and showed in addition that orthodromically evoked spikes may be made to fall from the point of inflection just as occurs for antidromic

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spikes. These results were interpreted at the time by assuming that orthodromic impulses normally originate in dendrites and are conducted from there to the soma. The inflection was therefore tentatively ascribed to delay of conduction between dendrites and soma similar to the delay of conduction between axon and soma previously postulated.
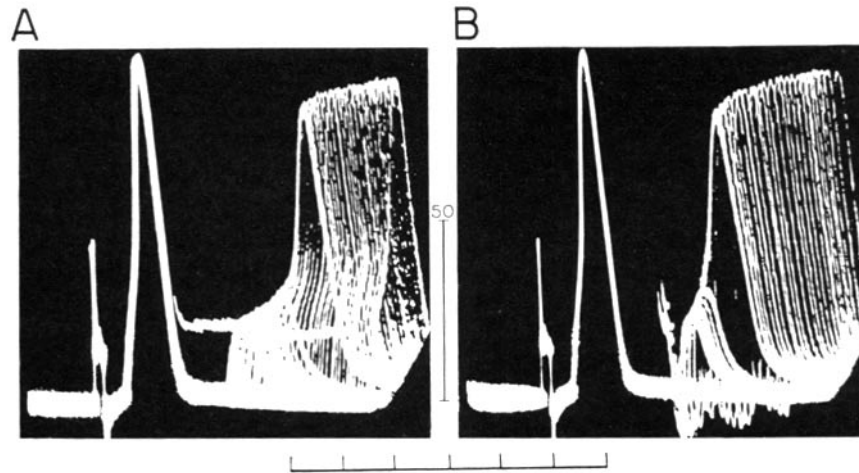


FIG. 1. Spikes evoked in the aftermath of an antidromic spike. Superimposed sweeps. Calibration, 50 mv. Time, 1 msec.

A. Antidromic stimulus followed at different intervals by a second antidromic stimulus. The second stimulus evokes only a small spike at stimulus intervals less than 2.6 msec. and no spike at all when stimulus interval is less than 1.8 msec.

B. Antidromic stimulus followed at different intervals by a brief direct stimulus. Strength of direct stimuli constant throughout. The direct stimulus evokes a small spike only at (corrected) stimulus intervals less than 2.3 msec. and no spike at all at less than 1.8 msec.

The present study is an attempt to analyze the experimental conditions controlling the described features of motoneuron spikes with the aim of understanding their mode of production. The analysis has been performed systematically for spikes originated by antidromic or direct stimulation but the study of synaptically evoked spikes has been limited to few incidental observations.

## Methods

This research was performed on cats anesthetized with pentobarbital sodium (nembutal). KCl-filled micropipettes were inserted in spinal cord motoneurons and used both for leading off potential changes and for applying electrical stimuli directly to the penetrated cells. Reference is made to two previous papers (Frank and Fuortes, 1955 a and 1956) for details of the methods used for preparing the animal and for stimulating and recording.

RESULTS

*Spikes Evoked in the Aftermath of a Preceding Spike.* Motoneuron spikes evoked by antidromic excitation or direct stimulation through the microelec-
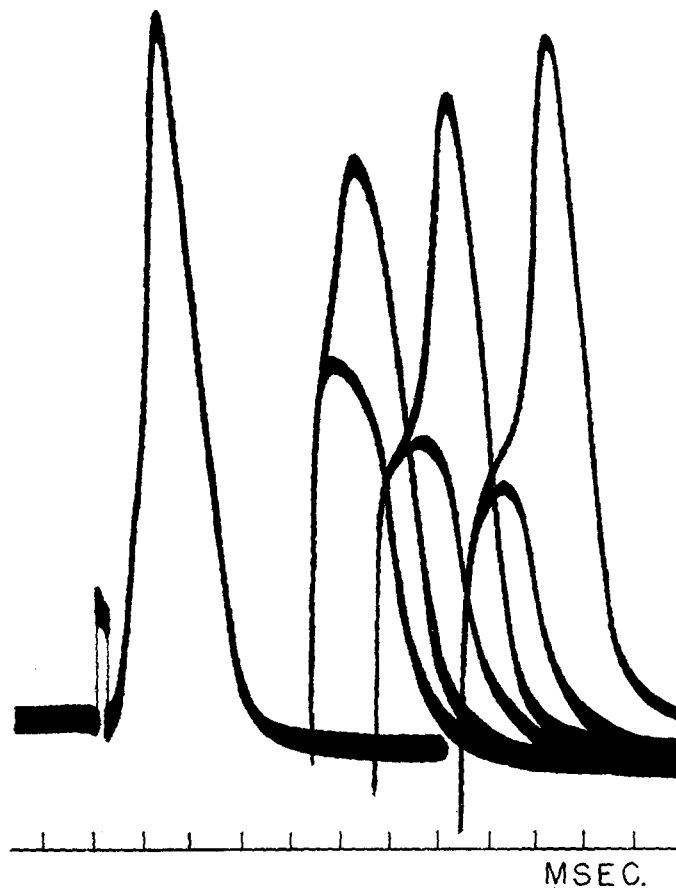


MSEC.

FIG. 2. Tracing of spikes evoked by direct stimuli in aftermath of an antidromic spike. As stimulus interval was decreased, strength of direct stimulus was increased to the intensity which would elicit either a small or a large spike. Level of transition between small and large spike is raised as stimulus interval is decreased. Time, 1 msec.

trode change their features if they are evoked within a short time after a preceding spike. The changes occurring in antidromic spikes have already been described (Brock *et al.*, 1953; Frank and Fuortes, 1955 *a*) and are again illustrated in Fig. 1 A. Fig. 1 B shows that similar changes occur when a spike is evoked by brief direct electrical stimuli of constant strength applied at different

times after a spike of antidromic origin. In either case the height of the second spike decreases gradually and the inflection becomes more prominent as the second stimulus approaches the first. At an interval previously referred to as "critical stimulus interval" (Frank and Fuortes, 1955 a) the second spike fails to develop fully and falls instead from the point of inflection, thus leaving a small spike only. This small spike further decreases in size and duration as
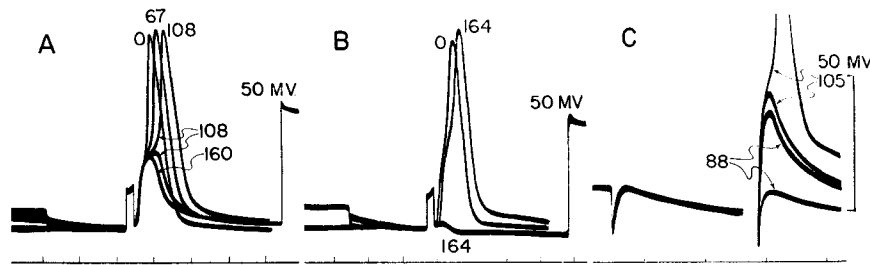


FIG. 3. Tracings of spikes evoked during hyperpolarization. Calibration, 50 mv Time, 1 msec.

A. Antidromic spikes evoked during flow of hyperpolarizing currents of different intensities (indicated in arbitrary units). At current intensity 108 antidromic stimuli may elicit either a full spike with a prominent inflection or a small spike only. Both peak height and area of small spike decrease with current of higher intensity (160). Note that since polarizing currents are applied through a bridge circuit (cf. Frank and Fuortes, 1956) baseline positions have no relation to actual membrane potential, but are adjusted to superimpose at the time of antidromic stimulation. Square wave at end of sweep is the 50 mv. calibration.

B. Experiment as in Fig. 3 A, but on another unit. In this experiment, when intensity of hyperpolarizing current is 164 the antidromic stimulus may evoke a full spike or no spike at all.

C. Direct spikes evoked during hyperpolarization. Strength of hyperpolarizing current pulse constant throughout. The numbers indicate strength of direct stimuli in arbitrary units. Stimulus strength 105 may evoke either a (larger) small spike or a full spike.

stimulus interval is shortened, until no spike at all can be elicited by the stimulus used. The tracings of Fig. 2 illustrate the results of an experiment in which not only the timing relative to a preceding spike but also the strength of the direct testing stimulus to a motoneuron was changed. Critical stimulus interval was about 7 msec. for the weakest stimulus used. For stronger stimuli, the critical interval was shortened while transition from small to full spikes was shifted to higher potential levels.

*Spikes Evoked during Hyperpolarization of the Motoneuron Membrane.* Some of the changes occurring in antidromic spikes when the motoneuron membrane is hyperpolarized have been mentioned in a previous article (Frank and Fuortes, 1956). These changes are illustrated in Fig. 3 A which shows that, with in-

creasing polarization, the notch in the rising phase becomes more prominent and "partial block" may occur. The same results are obtained if a spike is evoked by brief direct stimuli while the motoneuron is hyperpolarized. When direct stimulation is used, stimulus strength can be changed at will. It is seen then that on the background of a constant hyperpolarization a weak stimulus may give rise to a small spike only, while a full size spike may be obtained
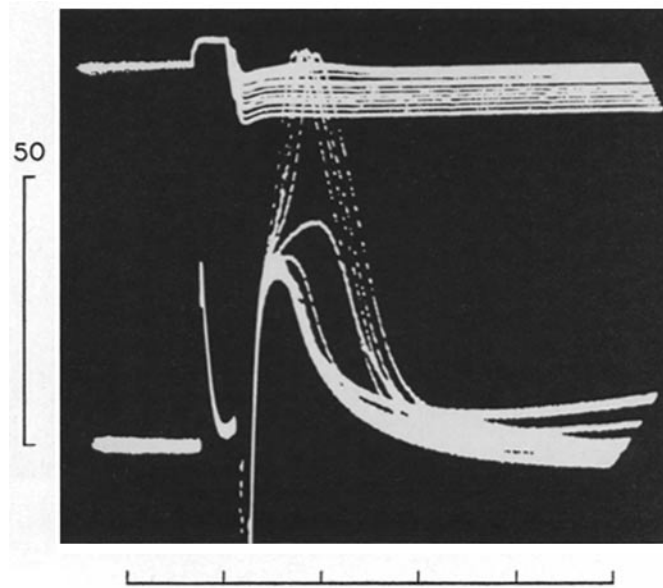


FIG. 4. Spikes evoked by diphasic direct stimuli. Stimulating current, indicated by upper beam, consists of a brief depolarizing pulse of constant intensity, followed by a longer hyperpolarizing pulse of different intensity in the individual sweeps. As hyperpolarizing current is increased, inflection in rising phase of spike is made more prominent until a small spike only is evoked. Calibration, 50 mv. Time, 1 msec.

with stronger stimulation (Fig. 3 C). Whereas partial block can always be obtained in the aftermath of a spike (Fig. 1), in some units it is not obtained with continuous hyperpolarization. The effect of hyperpolarization on units of this type is illustrated in Fig. 3 B in which it is seen that, at a critical level of hyperpolarization, antidromic stimuli evoke either a full spike or no spike at all.[1] This result indicates that the region of the motoneuron responsible for

[1] A similar "total block" has been evoked by Brock *et al.* (1953) with high frequency repetitive stimulation. They recorded then a small (1 mv.) deflection (their "M" spike) which they ascribed to activity of the myelinated axon. In the present study, small potential changes were often contributed by activity of elements surrounding the penetrated unit, and no attempt was made to distinguish these from similarly small changes due to activity of the impaled cell.

generation of the small spike is close enough to the microelectrode tip to be readily affected by currents applied through it. However, partial block of a spike can always be obtained with hyperpolarization if the hyperpolarizing current is applied after the spike has been initiated, as illustrated in Fig. 4.

*Spikes Evoked in the Aftermath of a Small Spike.*—The results mentioned so far appeared to be compatible with the assumption that the two components of motoneuron spikes result from activity of different portions of the moto- neuron and other experiments were designed with the aim of testing this as-
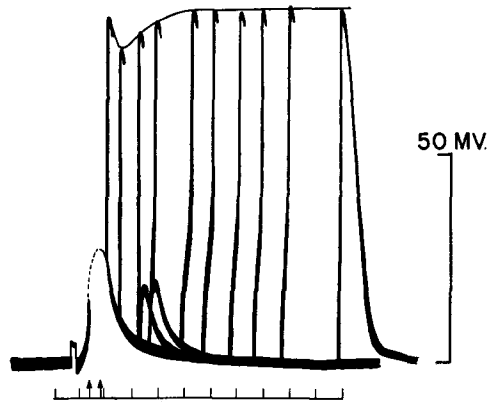


FIG. 5. Spikes evoked by direct stimuli in the aftermath of a small spike. The first small spike is evoked by the combination of an antidromic stimulus (indicated by the artifact) and a brief hyperpolarizing pulse (indicated by the arrows). Strength of direct stimuli applied at different intervals after small spike was adjusted to be just threshold for firing (*cf.* Fig. 9). At stimulus intervals between 2 and 3 msec. weak stimuli elicited small spikes only and stronger stimuli elicited full spikes. Calibration, 50 mv. Time, 1 msec.

sumption and perhaps of establishing how different areas of a motoneuron participate in the processes of excitation and conduction.

It will be convenient to call the region of the motoneuron responsible for production of the small spike "A," and the region responsible for production of the later phase of the spike "B."

If the small spike is followed by a period of absolute refractoriness of the area responsible for its generation ("A"), it might be possible to elicit in isola- tion the spike due to the firing of other portions of the motoneuron ("B").

If the small spike is the result of activity of one area of the motoneuron, then, with simple assumptions, it might be expected that activity of the remaining area in isolation would also give rise to a spike of reduced height. Therefore, the experiments described in this section and illustrated in Figs. 5 to 7 were designed to analyze the features of spikes elicited in the aftermath of a small

spike. In the experiment of Fig. 5 the conditioning small spike was elicited by blocking an antidromic spike with a brief hyperpolarizing pulse while in the experiment of Fig. 6 the small spike was elicited by the second of two antidromic stimuli within the critical stimulus interval. In both cases a direct testing stimulus of constant strength was delivered at different times relative to the small spike. For the longer stimulus intervals, the responses to the test shocks are similar to those occurring following a full spike shown in Fig. 1 B; as stimulus interval is decreased, the spike evoked by the direct test stimulus
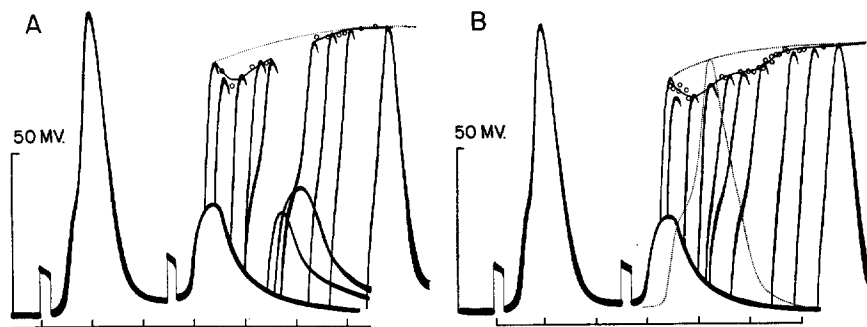


Fig. 6. Spikes evoked by direct stimuli in the aftermath of a small spike. The small spike is evoked by the second of two antidromic stimuli, indicated by the artifacts. The following spikes are evoked in A by weak and in B by stronger direct stimuli applied at various intervals after the second antidromic stimulus. Strength of direct "test" stimuli is kept constant throughout each experiment. Note increased prominence of rising phase inflection with block possible at a critical stimulus interval (A) and absence of visible inflection at shorter intervals. Broken tracing in B shows one response to test shock when second antidromic conditioning shock is omitted. The upper broken line plots the peaks of such responses (see Fig. 1). Calibration, 50 mv. Time, 1 msec.

presents a more and more pronounced inflection and may critically change into a small spike (Figs. 5 and 6 A). (As seen in Fig. 6 B, using slightly stronger test shocks this partial block does not occur.) At very short stimulus intervals the test stimulus again evokes a larger spike and this does not present any visible inflection. The solid lines in Figs. 5 and 6 indicate peak height of the potentials generated by the combination of stimuli used, and the dotted lines the height of the potentials evoked by the direct test stimulus in the absence of the small conditioning spike.

The responses which do not present a rising phase inflection and which occur when the "A" area is presumably refractory can be ascribed to activity of the non-refractory "B" area of the motoneuron. "B" spikes evoked in this way cannot be recorded in isolation because they can be elicited only during the falling phase of the "conditioning" "A" spike.

Fig. 7 illustrates the results of an experiment in which an antidromic shock was used as a test stimulus. In this case, partial block occurred at a critical interval and, for shorter intervals, the small spike further decreased in size, until no spike at all could be elicited.

These results show that the non-refractory area of the motoneuron can be reached by stimuli applied through the microelectrode, but not by antidromic stimuli.

*Excitability Following a Full Spike.*—All results quoted so far agree in showing that in a variety of conditions it is easier to elicit a small than a large spike from a motoneuron. According to the working hypothesis mentioned above,
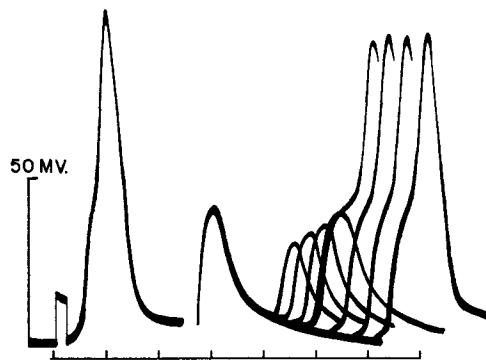


FIG. 7. Spikes evoked by antidromic stimuli in aftermath of a small spike. The conditioning small spike is evoked by a direct stimulus following an antidromic stimulus. The subsequent antidromic test stimuli evoke either a notched spike or a small spike only and no spike at all is elicited by antidromic stimuli applied at less than 1.5 msec. after initiation of the first small spike. Calibration, 50 mv. Time, 1 msec.

this means that firing of the "A" area of a motoneuron may be elicited by stimuli which, in those conditions, are incapable of eliciting firing of the whole motoneuron. Analysis of this phenomenon was approached by means of excitability studies to determine the relative strengths of the stimuli required to evoke partial or total firing of a motoneuron under various circumstances. In normal conditions a short direct stimulus to a motoneuron has an all-or-none effect evoking either a full spike or no response at all, while if a stimulus is applied shortly after firing of an impulse a small spike only may be evoked. Fig. 8 shows the strength of the stimuli required to evoke a small or a full spike at various times after firing of an antidromic spike. It is seen that, when weaker stimuli evoke a small spike only, a full spike can still be evoked if stimulus strength is increased. It will be noted that the late excitability changes illustrated in Fig. 8 appear to correlate with the afterpotentials of the spike. In the majority of the units studied both afterpotentials and excitability changes
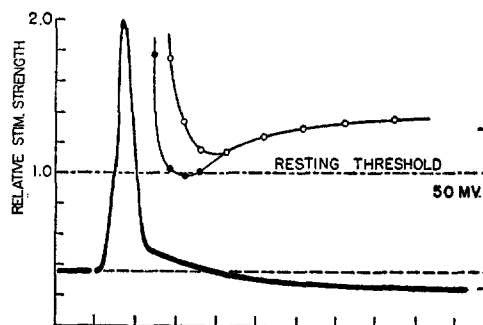
FIG. 8. Excitability following a full spike of antidromic origin. Ordinate, strength of threshold test stimulus expressed as a fraction of resting threshold. Abscissa, time in milliseconds. Filled circles indicate height of stimuli producing a small spike only and open circles indicate height of stimuli on the same time scale evoking a full spike. The conditioning antidromic spike is traced to show time relation of excitability changes to the spike itself and to its afterpotentials. 50 mv. calibration applies to this tracing.
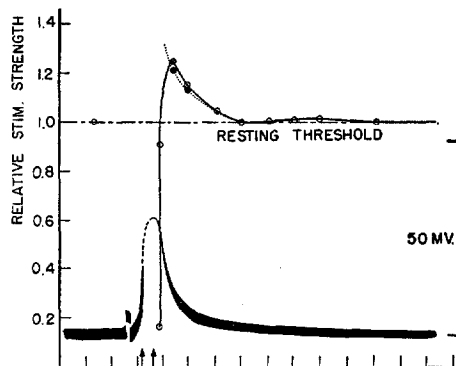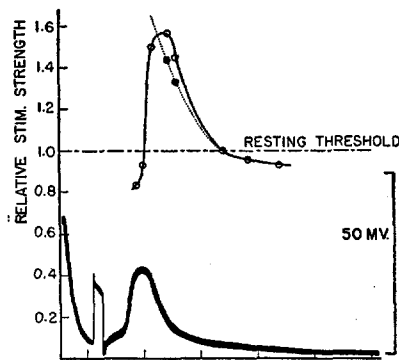


FIG. 9



FIG. 10

FIG. 9. Excitability following a small spike. Small spike was evoked by the combination of an antidromic stimulus and a strong hyperpolarizing pulse (indicated by arrows). The experimental data are plotted as in Fig. 8. 50 mv. calibration refers to spike tracing.

FIG. 10. Excitability following a small spike. Experiment similar to that illustrated in Fig. 9, but small spike was evoked by the second of two antidromic stimuli, as in the experiments illustrated in Fig. 6. 50 mv. calibration refers to tracing.

were the same following an antidromic or a direct spike. In other units both hyperpolarization and excitability changes were larger after antidromic than after direct spikes presumably as a consequence of activation of motoneuron axon collaterals (Renshaw, 1946; Eccles, Fatt, and Koketsu, 1954).

*Excitability Following a Small Spike.*—If an antidromic spike is partially blocked by a brief hyperpolarizing pulse so that a small spike only occurs, then

excitability follows a curve such as that of Fig. 9 showing, for decreasing stimulus intervals, at first a rise, then a conspicuous dip, which is a mirror image of the small spike itself. For stimulus intervals around 2 msec. it is slightly easier to evoke a small than a full spike, but at shorter intervals spike size suddenly increases and no sign of inflection can be seen in the rising phase (Figs. 5 to 7). Essentially the same events occur when a brief direct stimulus is applied after a pair of antidromic stimuli, the second of which elicits a small spike only (Fig. 10). The greater difference observed in this figure between stimuli required to elicit small and large spikes occurs probably because of the relatively refractory period of the "B" area following the large spike.

*Excitability of Ventral Root Fibers Following Small and Large Soma Spikes.*—The proposed assumption that the small spike results from activity which does not spread over the whole motoneuron has no implications concerning its possible propagation along the axon. Information on this question would, however, be expected to provide useful indications of the location of the region involved in production of the small spike. In order to establish whether or not small spikes resulting from direct stimulation propagate to the axon, the strength of ventral root stimuli required to excite the axon of an impaled motoneuron was measured at various times after that motoneuron was made to fire a small or a full spike. Small or large spikes were elicited by the method illustrated in Fig. 4, and it was found that identical changes occur in the axon in the two cases. This shows that the axon undergoes refractoriness of identical time course following discharge of a small or a full spike from the motoneuron soma. Therefore it must be concluded that following discharge of a small spike propagation along the axon occurs.[2]

*Observations on Orthodromic Spikes.*—Spikes evoked by orthodromic stimulation present only a barely appreciable inflection in their rising phase and block at this point is more difficult to evoke than it is for spikes elicited by antidromic or by direct stimuli. Partial block was observed, however, to occur at a critical stage of deterioration as an irreversible event (Frank and Fuortes, 1955 b). In later experiments partial block could be reversibly obtained in the absence of clear signs of damage, for instance by applying a hyperpolarizing pulse shortly after initiation of the spike. However, since very strong hyperpolarizing pulses were required to evoke partial block, in the experiments performed the records obtained were obscured by large artifacts and therefore

[2] Measurements performed after completion of this study show that these conclusions on site of initiation of directly evoked spikes apply also to spikes of orthodromic origin. Small spikes of orthodromic origin were obtained by applying a short hyperpolarizing pulse to the motoneuron just after initiation of the impulse. Analysis of ventral root excitability following discharge of the small spike revealed that this small spike elicits a conducted impulse in the axon. It appears therefore, that orthodromic spikes are also initiated in the region of the axon hillock.

were unsuitable for analysis. The features of orthodromic spikes observed in this study resemble those of spikes generated by direct stimulation with long depolarizing pulses or by antidromic stimulation applied on a background of depolarization, since in these conditions the inflection on the rising phase becomes less apparent and block becomes more difficult to evoke (Frank and Fuortes, 1956). The results obtained are therefore consistent with the assumption that orthodromic spikes are initiated and spread over the motoneuron soma in a way similar to that occurring for antidromic spikes if it is accepted that synaptic impingement exerts on motoneurons a depolarizing action which outlasts spike initiation. The number of experiments performed in this study on orthodromic spikes was, however, insufficient for reaching a reliable conclusion on details of their mode of initiation and production.

## DISCUSSION

Since the results of the various experiments performed did not contradict the basic hypothesis stated above, that the components of motoneuron spikes are the result of activity of different parts of the motoneuron, it is legitimate to attempt an interpretation of the findings on the basis of a more specific statement of the same fundamental hypothesis.

The following assumptions will now be made:

1. Excitation of the motoneuron soma following antidromic or direct stimulation is initiated in a limited region of the cell membrane and spreads from there to other areas by the usual mechanism of conduction, the active region acting as an electrical stimulus for the inactive regions (see Hodgkin, 1937 a and b).

2. The resistance of soma membrane and cytoplasm is such that the interior of the soma is very nearly isopotential both during activity and during application of currents through the microelectrode.[3] Large potential drops may exist instead between the inside of the soma and the inside of its axon or dendrites (see Brock et al., 1952 a).

Some conclusions can be drawn from these assumptions if it is accepted that the electrode is located in the motoneuron soma (see Frank and Fuortes, 1955 a). When only a part of the soma membrane is active, the action potential across that part will be reduced by the inactive area whose depolarization it must support. Local activity of the soma will thus give rise to a spike of reduced height. The spikes recorded by the electrode during such local activity will be only a little smaller than the spike at the active area and very slightly larger than the induced depolarization of the inactive area.

[3] During application of currents through the microelectrode a large potential drop occurs in the cytoplasm immediately surrounding the electrode tip. This drop, however, is limited to a very small volume and therefore does not affect the isopotentiality of the greater part of the soma.

Currents through the microelectrode initiate local firing at a threshold depolarization of about 10 mv. (Coombs, Eccles, and Fatt, 1955; Frank and Fuortes, 1956). This local spike will not spread over the rest of the cell, however, until the cell is depolarized by 30 or 40 mv. Thus it becomes necessary to abandon the view that the properties of the motoneuron membrane are uniform in favor of the view that different regions of the motoneuron have different thresholds.

The size of the spikes resulting from isolated activity of the "A" or "B" regions of the motoneuron indicates that the "A" region, where firing is initiated, is small in comparison with the "B" region. The finding that firing of the "A" region alone produces a normal conducted action potential in the ventral root without producing a full sized spike in the soma suggests that the "A" region is located between the axon and the microelectrode, and therefore presumably in the neighborhood of the axon hillock.

Application of these interpretations to a simplified model in which the motoneuron soma is represented by a sphere permits one to show diagrammatically how an impulse may be initiated by a depolarizing constant current through the microelectrode situated in the center of the sphere. The potential drop generated across the membrane by applied currents will be almost equal in all parts of the soma but will decay exponentially along the axon. If the decay of depolarization occurs in a region peripheral to that where threshold is supposed to decrease, excitation will arise somewhere in the region of the axon hillock (Fig. 11 A).

In the case of antidromic excitation, the potential change ahead of an antidromically conducted impulse will decrement along the axon but will decrement only very little in the soma itself, since large potential drops are not supposed to occur in the cytoplasm. As activity progresses towards the axon hillock, the low resistance and the capacity of the soma will act as a load on the axon spike which consequently will decrease in size. The effect on this reduced impulse on the regions immediately ahead is, however, sufficient to evoke firing of a localized region in the neighborhood of the axon hillock. This region should be approximately the same as that which is first excited by direct stimuli, thus permitting one to explain the similar inflection observed in spikes evoked by direct and antidromic stimulation.

The rapid slope of the initial phase of antidromically evoked spikes would be expected if the axon hillock region is excited by a smooth process of conduction progressing with high safety factor. By contrast, the depolarization responsible for initiation of firing following synaptic impingement develops in many conditions with slow time course. In these cases, the familiar inflection between synaptic potential and spike will be recorded.

Firing of the axon hillock evokes passive depolarization of the inactive ("B") parts of the soma membrane and the depolarization recorded at this time by

an inserted microelectrode will be somewhat smaller than the height of the local spike at the axon hillock and just a little greater than the depolarization of the major portions of the soma membrane. Since the threshold of most of the soma is high, this passive depolarization will not necessarily be sufficient to evoke firing of the rest of the soma at once.

If spread of the local impulse is aided by sustained depolarization of the soma (as happens during applied depolarization and probably following synaptic stimulation), firing of the whole soma will occur without delay and little or no inflection will be seen in the rising phase. In other conditions, however, the local impulse may grow only gradually by evoking firing of immediately neighboring areas which are slightly more depolarized and perhaps also possess lower threshold than the distant regions. While this gradual process occurs, the potential recorded by a microelectrode will change slowly and the slope of the rising phase of the spike will decrease. As the area involved by the impulse grows, the inactive area of the soma will decrease, until a point will be reached at which the stimulus supplied by the local activity will be safely sufficient to excite the whole soma. At this point the rise of the recorded spike will again be rapid, progressing in explosive fashion to its peak.

If the threshold of the soma is increased by refractoriness or by hyperpolarization, the local impulse initiated in the "A" region either by antidromic conduction or by direct stimulation may die out before invading the whole soma membrane. In this case a small spike only will be recorded by the microelectrode. When the local activity is just insufficient to evoke firing of a refractory or hyperpolarized soma, it should still be capable of propagating along the axon because the axon has lower threshold and because conduction towards the periphery is not endangered by the increase of area which presumably lowers the safety factor of conduction towards the soma. If a small spike is initiated by antidromic stimulation it could not be expected to propagate back into the axon, since this would be absolutely refractory. If instead the small spike is elicited by direct stimulation when both soma and axon are only relatively refractory or when hyperpolarizing current is delivered through the microelectrode, propagation along the axon occurs, as seen above (p. 744).

Other results of this study may be justified under the proposed assumption that the transition between high and low threshold areas is not abrupt, but occurs gradually over a finite region of the motoneuron membrane as diagrammatically shown in Fig. 11 A. This assumption implies that strong stimuli will excite areas larger than those excited by weak stimuli. During the refractoriness following a full spike, activity of a large area may still be insufficient to elicit generalized firing. Therefore, strong direct stimuli applied in the aftermath of a spike, may elicit large "local" spikes as illustrated in Fig. 2.

Another consequence of the same assumption is that absolute refractoriness may be difficult to detect after local firing since, even if a part of the "A" area is absolutely refractory a direct stimulus may still evoke firing of its remaining
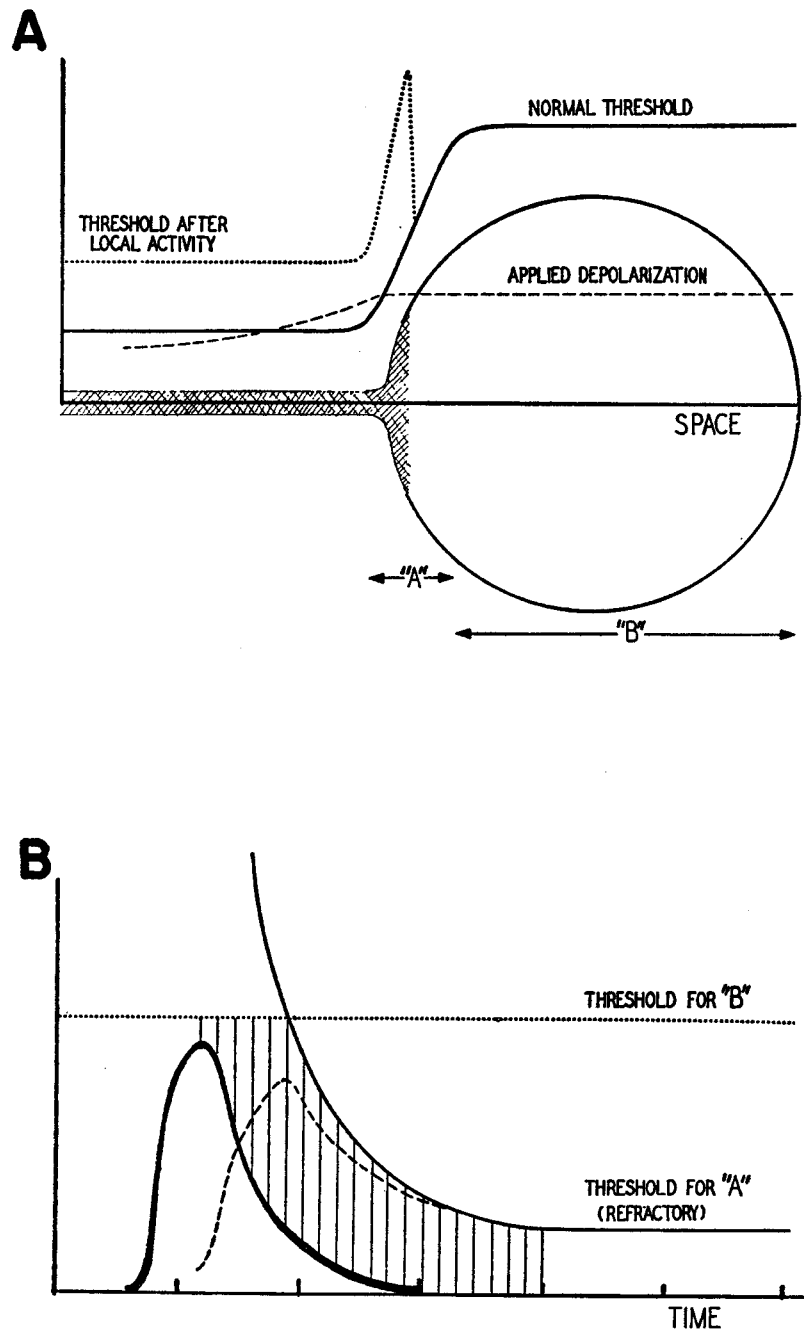
Fig. 11

portions before reaching the strength necessary to elicit generalized firing (Fig. 11 A). Therefore a stimulus applied immediately following local activity may still evoke a local rather than a generalized spike, as seen in Fig. 6 A.

Since local activity may be evoked twice in close succession, isolated firing of the "B" area of the motoneuron could be evoked only during the falling phase of the small spike. Thus the potential at the peak of the "B" spike evoked in this way is determined both by activity of the "B" area and by the decaying potential of the small "A" spike. A lower peak potential might be reached by the spike resulting from activity of the "B" area alone.

The diagram of Fig. 11 B is finally presented to explain the changes in excitability and spike form obtained following stimuli producing a small spike only (cf. Figs. 5 to 7). It is supposed in the diagram that the height of the small spike was just insufficient to elicit generalized firing and that excitability of the "A" area (as determined by current measurement) followed a curve such as illustrated.

According to this diagram, as stimulus interval is decreased, threshold membrane potential of the "A" area will be at first lower (more negative) later higher than threshold for "B." The strength of the direct stimuli required to elicit firing of the "B" area will steadily decrease when these are superimposed on the small spike since the major portions of the soma membrane will be sub-

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FIG. 11. Diagrams to illustrate initiation of impulses in motoneuron soma.

A. A spherical motoneuron soma is indicated and its axis passing through the center of the axon is used as abscissa of the plot. Ordinate, membrane depolarization measured from resting membrane potential. The dashed (– – –) line indicates the distribution of the potential changes evoked in various portions of the motoneuron by currents applied through a microelectrode situated in the center of the sphere. The solid line represents the depolarization level required to evoke firing of different parts of the motoneuron membrane. In normal conditions threshold stimuli applied through the microelectrode will initiate an impulse in a region where the dashed line is above the solid line.

The dotted line (. . . .) is supposed to indicate the depolarization required to elicit firing shortly after activity which has involved only the shaded areas of the motoneuron. A stronger stimulus is required in these conditions to evoke firing, but the soma impulse may still be initiated in the region of threshold transition ("A").

B. In this diagram, ordinate represents soma membrane depolarization as in Fig. 11 A, while abscissa represents time in milliseconds. It is assumed that, following activity of the "A" region of the motoneuron (indicated by the small spike), threshold for excitation of "A" is temporarily increased as shown by the solid line, while threshold for excitation of "B" remains unchanged (dotted line). The vertical lines indicate the height of depolarization required to reach threshold after and during local activity. At short intervals threshold of "B" will be reached before threshold of "A." The dashed curve measures the height of the vertical lines from baseline and resembles the experimental excitability curves illustrated in Figs. 9 and 10.

jected to the depolarization brought about by the sum of the small spike and the directly applied stimuli. The dashed line is a plot of the strength of the stimulus capable of evoking firing as a function of time, constructed on the basis of this diagram. Its resemblance to the excitability curves obtained experimentally is apparent (cf. Figs. 9 and 10).

It will be noted that the present hypothesis is perhaps more specifically stated but not essentially different from the hypotheses previously set forth by Araki and Otani (1955) and by Eccles (1956). Also, the results of the present study do not contradict the view expressed by the same authors that orthodromic excitation originates in a region of the motoneuron membrane adjoining the axon hillock, but no satisfactory test of this assumption has been worked out.[4]

Some difference exists instead between these views and another proposed interpretation. Fatt (1957) found signs of centrifugal conduction along the dendrites when a full spike is recorded from the soma but not otherwise. From this he concluded that the initial portion of the spike is due to soma activity whereas the portion above the inflection is due to firing of dendrites. While his experimental results do not contradict the views expressed in the present paper, Fatt's interpretation cannot be reconciled with the observation (Crain, 1956) that spikes elicited by antidromic or direct stimulation of spinal ganglion cells of frogs in tissue culture present the same inflection described above despite absence of dendrites in these cells.

It should be noted that not all details of the experimental results have been adequately considered in relation to the proposed model. This was advisable for the sake of simplicity, since several of the observed phenomena, although not inconsistent with the proposed hypothesis, could be included only with the addition of further assumptions. Conversely, for the sake of clarity, the proposed model was made more specific than was actually required by the results.

For instance it has been assumed (Fig. 11 A) that the "A" area is a continuous region around the axon hillock. Under this assumption antidromic impulses could propagate to the "A" area through a process of continuous conduction and thus the high safety factor for antidromic excitation of the "A" area could readily be accounted for. It is possible, however, that the "A" area consists instead, of small spots scattered over soma and dendrites as might occur, for instance, if the regions under the synaptic knobs had properties different from those of the other regions of the motoneuron membrane.

Also, it has been assumed throughout the foregoing discussion that the potentials recorded by the microelectrode faithfully reflect the changes occurring at any area (including the "A" area) of the soma membrane. This will be the case if (1) only small potential drops occur within the soma cytoplasm, and (2) the microelectrode tip is located in the cytoplasm. If either of these two

[4] However, see footnote 2.

conditions does not apply, then the recorded potential changes may be different from those occurring at the "A" area of the soma, which have been presumed to be critically involved in initiation of excitation (see Frank and Fuortes, 1956, p. 467). For mixed synaptic impingement, the recorded potential change could differ even in sign from the change occurring at the "A" region.

Finally, whereas it is assumed in the present discussion that changes in the size of the recorded spike are due to changes of area of the firing membrane, it is quite possible that at least some of the observed size variations may have a different origin.

Despite these shortcomings, the simplified model proposed in this discussion appears to provide a not unreasonable explanation of the principal findings of the present study.

### SUMMARY

1. Spikes evoked in spinal motoneurons by antidromic stimulation normally present an inflection in their rising phase. A similar inflection is present in spikes evoked by direct stimulation with short pulses.

2. In either case the inflection becomes less prominent if the motoneuron membrane is depolarized and more prominent when it is hyperpolarized. Both antidromic and direct spikes may fall from the level of the inflection thus evoking a "small spike" only if sufficient hyperpolarization is applied. Similar events occur when antidromic or direct spikes are evoked in the aftermath of a preceding spike.

3. Spikes evoked by direct stimuli applied shortly after firing of a "small spike" may also become partially blocked at a critical stimulus interval. At shorter intervals, however, spike size again increases and no inflection can be detected in the rising phase.

4. When a weak direct stimulus evokes a small spike only, a stronger stimulus may evoke a full spike. Curves of the strength of the stimuli required for eliciting small or full spikes have been constructed in a number of conditions.

5. To explain the results it is assumed that threshold of the major portions of the soma membrane is higher than the threshold of the axon, the transition occurring over a finite area near the axon hillock. Following antidromic or direct stimulation, soma excitation is then initiated in the region of the axon hillock. Spread of activity towards the soma occurs at first slowly and with low safety factor. At this stage block may be easily evoked. Safety factor for propagation increases rapidly as the growing impulse involves larger and larger areas of the soma membrane so that, once the critical areas are excited, activation of the remaining portions of the soma membrane will suddenly occur.

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