FURTHER STUDY OF SOMA, DENDRITE, AND AXON EXCITATION IN SINGLE NEURONS*

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INTRODUCTION

In the preceding study some of the physiological mechanisms of excitation between the dendrites, the cell body, and the axons of single sensory cells were investigated. It was found that by controlling events in the dendrites, the membrane potential and excitability of the nearby cell soma could be regulated over a considerable range. Thus, graded amounts of stretch deformation create within the dendrites the generator potential, a depolarization of varying intensity, which spreads electrotonically to the more central portions of the cell. At a critical membrane potential level, conducted impulses are started, spreading centrally (orthodromically) into the sensory axon. The frequency of rhythmic activity is determined and regulated by the generator mechanism. It is clear that for a better understanding of processes of excitation in these cells one should know more about the differences between nerve impulses in axons, in the cell body, and in the dendrites. The first two structures could be studied directly by recording their action potentials through intracellular leads. By comparing and analyzing soma and axon impulses the approach to the dendrite problem is narrowed down but still remains indirect. The principal tool in following excitation beyond the cell body is by detection of the generator potential which, originating in the dendrites, reflects the state of dendritic activity.

Furthermore some of the steps in the transmission of antidromic impulses between axon and the cell soma were analyzed, together with excitation spread across the soma itself. The relationship between the "afterpositivity" and "afternegativity" and the membrane potential of nerve cells was studied. It will be shown that a "relaxed" or "resting" cell, with full membrane potential, does not show an appreciable "positive" swing after the impulse but only a postspike negativity. After its resting potential has been reduced, however, a positive component appears. Evidence will be presented that apart

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from the generator mechanism in the distal dendrite portions, giving rise to rhythmic activity, there exists a second mechanism which can produce repetitive discharges. Relatively short bursts of "grouped" high frequency activity apparently can be caused by delays in conduction which take place around the soma-dendrite junctions.

The experimental set-up has already been described in the preceding paper. *Procambarus alleni* (Faxon) and *Orconectes virilis* (Hagen) were used exclusively.

<div align="center">RESULTS</div>

<div align="center">*1. The Antidromic Impulse in the Soma-Dendrite Complex*</div>

Relationship to Resting Potential.—If a receptor muscle strand is not stretched its sensory neuron does not discharge and generally shows membrane potentials between 70 and 80 mv. Such potentials will be called full resting or relaxed cell potentials, referring to the state of the cells in the absence of depolarization by deformation. An antidromic impulse, set up centrally in the axon, then causes in the cell soma an action potential which rises to its peak in about 0.5 to 0.7 msec. The recovery consists of a rapid falling phase of the impulse proper, followed by a slower gradually decaying component. The slow repolarization component will be called afternegativity since at present it is uncertain to what extent it can be related to other well defined afterpotentials (see *e.g.* Gasser's designation (13, 14); Grundfest (15)). It generally lasted 10 to 20 msec. at 20–24°C., although afternegativities of 30 msec. or longer have been seen (see below). An example is shown in Fig. 1 A recorded from a slowly adapting cell. The resting potential of that cell was 70 mv. and the action potential peak was 90 mv. A hyperpolarization component, even with high amplification, was absent. In some cells, however, although completely relaxed, the afternegativity was followed by a small positive swing. In many of these instances this was due to microelectrode pull, pressure, or some other kind of cell deformation, since after slight movement of the microelectrode by raising, lowering, or sideways adjustment, or after reinsertion, the positivity or hyperpolarization disappeared. It is therefore concluded from many measurements that cells which are not stretched and are in a "normal" state, do not have a positive potential exceeding 0.5 mv. while giving impulses of 70 to 90 mv. The situation is always different if a cell is stretched and its membrane potential is reduced to a new level. An antidromic soma–dendrite impulse then acquires a positive phase; *i.e.*, after the spike the cell interior becomes transiently more negative in relation to the outside. An example, taken from a slow cell is shown in Fig. 1 B, where the resting membrane potential has been reduced by about 10 mv. to a new steady level prior to stimulation. The afterpositivity is near 6 mv.

In Fig. 2 A intracellular records were taken from the soma of a fast cell while gradual stretch was applied. At the same time the general behavior of the cell was tested by antidromic impulses at 1.25/sec. Initially the potentials resembled those of Fig. 1 A but as stretch increased an obvious positive recovery phase component appeared with increasing stretch depolarization. The impulse peaks remained practically unaltered. During the plateau of
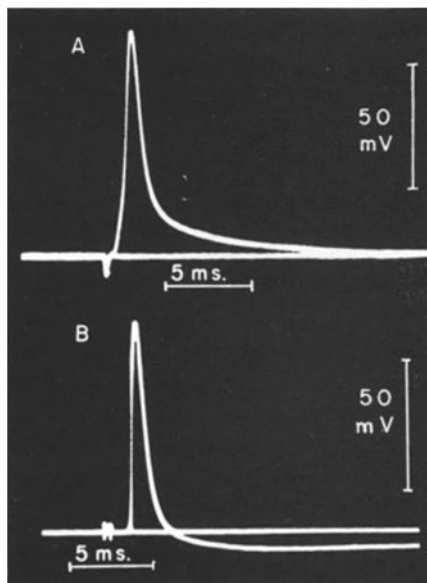

FIG. 1. A, antidromic impulse recorded with an intracellular lead from the soma of a slowly adapting receptor cell in the lateral receptor of the eighth thoracic segment. Cell was relaxed, with a resting potential of 70 mv., spike peak 90 mv., the afternegativity disappearing within about 13 msec. No afterpositivity seen. Short axon-soma delay responsible for slight inflection on rising phase (see later, Figs. 5 and 6). B, slow cell under light stretch, resting potential reduced by about 10 mv. Antidromic impulse followed by afterpositivity of 6 mv.

the initial stretch, when the firing level around 20 mv. was reached, several orthodromic discharges were added to the regular antidromic impulses. A light additional stretch (arrow 2) then caused a strong afferent burst. Relaxation showed the converse picture to increasing stretch, the positive potential phase disappearing when relaxation was complete. From the highly amplified record of Fig. 2 B, taken from the same cell, more details can be seen. Thus an appreciable positive potential is detected only after the resting-potential has been reduced by about 3 mv. Provisionally the term afterpositivity will be adopted for that part of the impulse which represents a hyperpolarization *relative* to the point at which the impulse arises (*cf.* also Fig. 9).

The results were essentially similar in slowly adapting cells except that the afterpositivity tended to appear as soon as stretch was started. While this may have been a genuine finding one could not be certain that stretch was actually started at the highest possible resting potential found in a "truly"
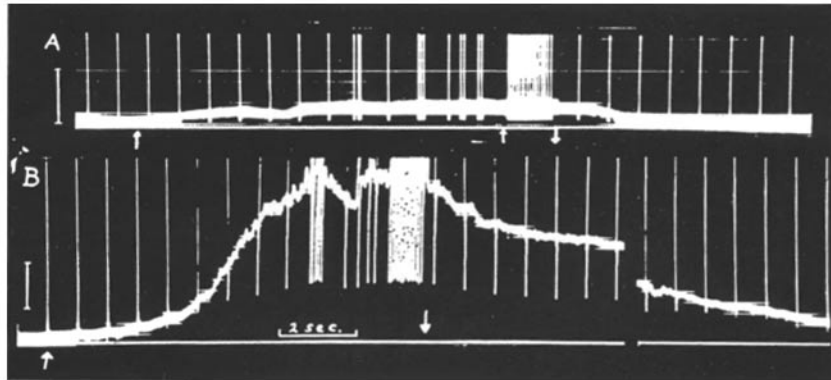

FIG. 2. Afterpositivity and membrane potential. Intracellular records from the fast cell in the median receptor, eighth thoracic segment. Membrane potential approximately 75 mv. at rest. Antidromic stimuli at 1.25/sec. given during stretch depolarization. A, stretch started at arrow and gradually increased. Spike peaks of 90 mv. not appreciably changed. During plateau of stretch a depolarization level of around 20 mv. causes several orthodromic discharges between the regular antidromic spikes. Slight additional stretch (arrow 2) sets up burst of afferent activity, cut short by start of relaxation (arrow 3). As stretch increases afterpositivity appears. B, same cell during stretch and relaxation at high amplification; impulse peaks off screen. First sign of afterpositivity appears when resting potential reduced by about 3 mv. Afterpositivity increases to 10 mv. as the depolarization level reaches 15 mv. Two orthodromic bursts appear at peak of stretch. During gradual relaxation the afterpositivity disappears again. At gap several seconds of record cut out. The irregularities represent membrane potential fluctuations set up by vibration of the stretcher. Between the two orthodromic bursts, accidental partial relaxation was accompanied by appropriate change in afterpositivity. Calibration, 50 mv. in A and 5 mv. in B.

relaxed state; i.e., some initial depolarization may have been present. The relationship between reduction of membrane potential and afterpositivity for the fast cell shown in Fig. 2 is plotted in Fig. 3. The straight line relationship for relatively weak stretches was the rule for rapidly and slowly adapting neurons. The actual amount of afterpositivity was measured between the potential level at which the antidromic impulse arises and the peak value of the repolarization potential. A further analysis of the time courses of the afterpotentials will be given in section 5.

2. Axon-Soma Transmission Processes

Under some conditions impulses may be blocked at the axon-soma boundary region, or antidromic invasion may be incomplete, or it may be merely delayed. These conditions are described because they show that the safety margin of conduction is not uniform in all parts of the cell.

If two successive antidromic impulses (a_1 and a_2) are sent into a lightly stretched slowly adapting cell, at an interval of 5 to 10 msec. apart, they differ
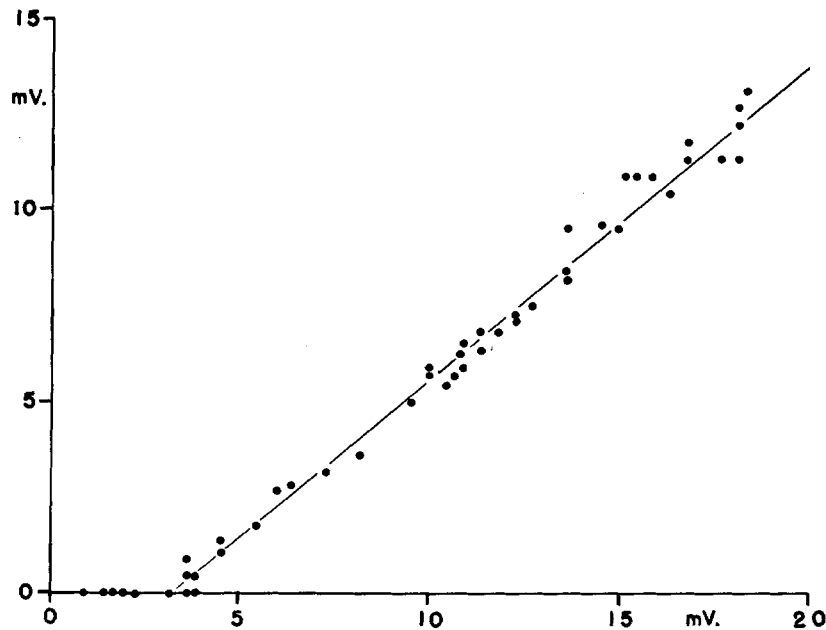

FIG. 3. Relationship between reduction of membrane potential (abscissa) and afterpositivity (ordinate) during stretch in a fast cell. The slope of the line is 0.82. Measurements taken from Fig. 2 B.

very little except for a frequent tendency of the second impulse to show an inflection in its rising phase. At still shorter intervals of 2.0 and 3.0 msec. a_2 may add only a relatively small potential on top of the falling phase of a_1. Two examples of double stimulation are seen at intervals of 6 and 3 msec. in Fig. 4 A and B. In C the two stimuli were fixed near the critical interval range of 2.0 msec. and stimulation was continued for 1 to 2 sec. at a repetition rate of 10/sec. a_2 added on occasions only a small simple component and was apparently unable to invade the cell soma. In some exposures, however, a second faster component appeared which was abortive, or after some delay flared up into a fully grown impulse. All transitional phases were seen. In analogy with many similar events in axons (below, Fig. 15), motoneurons

(5), or in other conducting structures, *e.g.* in the sciatic nerve (17) or single muscle fibers (20), one may assume that the smallest a_2 additions are made by axon impulses which become blocked and spread electrotonically into the cell soma. The fluctuating second rapid component of the a_2 potential apparently indicates a graded or partial invasion of the cell. If a local impulse survives long enough into the recovery phase it will presumably involve a greater area and also become larger.
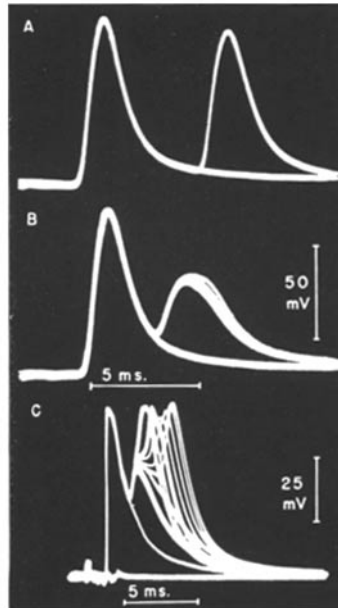

FIG. 4. Axon-soma transmission: Fast adapting cells, intracellular lead. A and B, first antidromic soma impulse (a_1) 90 mv.; a_2 at an interval of 6 msec. and 3 msec. is reduced. C, a_1a_2 interval fixed at 2 msec., repetitive stimulation, records superimposed. a_2 is either completely blocked or after a varying delay fully invades the cell soma. Transitional intermediary steps are also seen.

A second type of reversible block has been mentioned in the preceding study during "overstretch." During stretch of the dendrites the whole soma-dendrite region and a portion of the axon become depolarized to a variable extent, depending on the amount of extension. The orthodromic impulses become gradually smaller and eventually are blocked when the soma depolarization exceeds a critical level which may be between 35 and 40 mv. in slow cells. Under such conditions also antidromic impulses fail to invade the cell soma. It is assumed that both antidromic and orthodromic impulses become eventually blocked a short distance centrally from the cell body along the axon (see Fig. 9 (11)).

3. Interaction between Antidromic Impulses and Dendrite Potentials

Some information about factors which enhance or counteract invasion of the soma-dendrite system is presented in Fig. 5. When this slow receptor cell was completely relaxed and showed a resting potential of 70 mv., antidromic
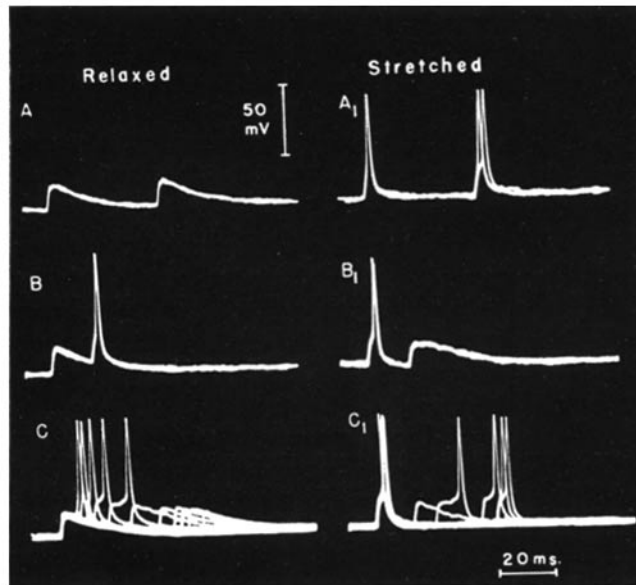

Fig. 5. Axon-soma invasion and membrane potential in a slowly adapting cell. Left portion, relaxed cell has resting potential of 70 mv. A, two axon impulses at 40 msec. interval fail to invade cell soma. B, at 13 msec. interval a_2 invades. C, a_2 is moved closer to a_1 during exposure and at 20 msec. it propagates into cell soma. The axon-soma delay becomes progressively shorter at small intervals. Right portion, cell lightly stretched, resting potential reduced by several millivolts. A_1, both axon impulses invade cell soma. B_1, second antidromic now blocked at 16 msec. interval. C_1, a_2 is moved closer to a_1 and is blocked during afterpositivity. Axon-soma delay becomes progressively longer at shorter intervals. Afterpositivity not well seen at this amplification and stretch (see Fig. 9).

impulses failed to invade the cell fully. The blocked axon impulse did, however, set up small 'local' potentials of about 20 mv. (Fig. 5 A). If a second axon impulse (a_2) was close enough, it added its own potential to the first one and at a critical level of about 25 mv. a full soma impulse of 80 mv. peak voltage arose (Fig. 5 B). This facilitation of invasion had a similar time course as the local potential set up by the blocked a_1. The whole sequence of events is better seen in Fig. 5 C where during repetitive sweeps a_2 was moved closer to a_1. The first invading a_2 impulse again arises at a membrane potential

level of about 25 mv., but after a considerable delay. The delay becomes progressively shorter at briefer intervals as the facilitating action of a_1 becomes stronger. The converse picture was obtained in the same cell if its dendrites were depolarized by a small steady stretch, reducing the resting potential by several millivolts. In Fig. 5 A_1, two antidromic impulses at 40 msec. intervals now invaded the soma and showed a small afterpositivity (not easily seen at this amplification), characteristic of a lightly depolarized cell. The safety margin for conduction fluctuated slightly in a_2 as seen from the variable axon-soma delays (see also below) with superimposed repeated sweeps. In B_1, at an interval of 13 msec., a_2 failed to propagate fully into the cell body, giving the opposite picture from the events when the cell was completely relaxed. In the stretched cell the delay or block of a_2 was clearly related to the afterpositivity (see higher amplification, Fig. 9) left behind by the first impulse. Fig. 5 C_1, illustrates more fully the different stages of axon-soma invasion in a lightly stretched slow receptor neuron. The converse result from the relaxed cell was obtained, with a_2 invading at long intervals and the axon-soma delay increasing as the interval became progressively more critical during the afterpositivity of a_1.

Fig. 5 has shown that the safety factor of axon-soma transmission can be greatly influenced by changing the membrane potential. The axon-soma delays are longest when the safety factor is near the critical range. In some cells no detectable delay or inflection was seen on the impulse rising phase even in a relaxed cell. Whenever such a delay occurred, however, it could be reduced or made to disappear by stretch. Some of the delay times, as measured from the first inflection of the potential to the spike peak, were surprisingly long. They were apparently related to the ability of cells to give abortive impulses. Examples are shown in Fig. 6 A where a_2 at a stimulus interval of 17 msec. set up three different responses in an unstretched cell, only one ending up in soma invasion after a delay of nearly 15 msec. During the delay period the potential remained critically poised in an equilibrium, neither rising nor decaying. In Fig. 6 B the stimulus interval was 14 msec., the cell lightly depolarized by stretch, and in three superimposed sweeps all a_2 impulses invaded the cell soma, but after varying delays. The records of Fig. 6 C at twice the amplification are similar. In all these instances one can assume that the soma of a cell can be invaded partially and that local impulses are able to survive for remarkably long periods, the cell being in an unstable in between state. The local impulses are obvious when large and distinct "humps" appear. But even the potentials in Fig. 5 A which at first sight may be regarded as merely a passive electrotonic spread from a source beyond the axon hillock, presumably are largely made up of "local" impulses, since their duration far exceeds that of the axon impulse which sets them up. Examples of a relatively brief electrotonically conducted axon

component are seen in Fig. 4, detected in the soma, and in Fig. 15, recorded in an axon when block occurred near the electrode tip. Therefore it seems that
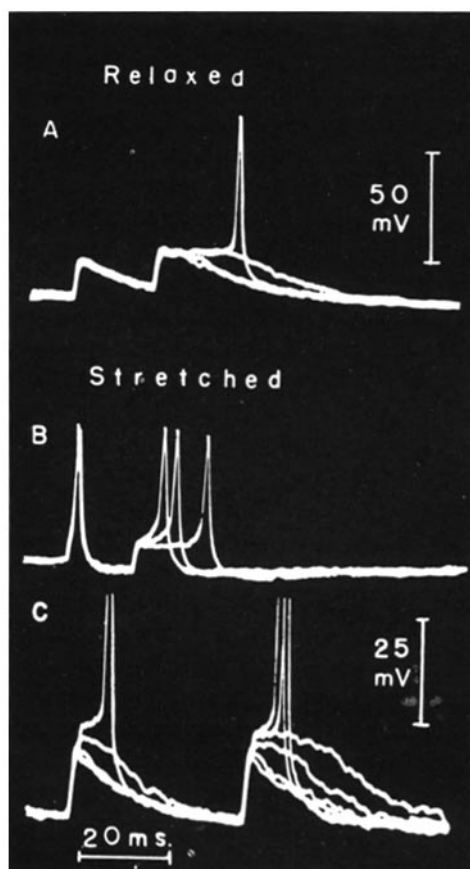

FIG. 6. Axon-soma delays in slow cell under varying degrees of stretch. Superimposed repeated sweeps. A, second axon impulse at 17 msec. interval sets up in soma local activity which may flare up into full soma impulse after delay of 15 msec., or may gradually die out. B, a_2 during afterpositivity has long axon-soma delays (2 to 12 msec.). C, higher amplification, impulses off screen. All cells show tendency to local abortive impulses when safety margin for axon-soma transmission is low.

the cells which are blocked in their relaxed state have a great tendency to give local partially conducted impulses.

The varying stages of transmission (Figs. 5 and 6) were obtained for hours in the same cells and could be produced predictably by altering the resting potentials of the soma-dendrite region. The phenomena are, therefore, not

merely signs of rapidly deteriorating cells, a state which is also unlikely in view of the large maintained resting and action potentials.

The preceding results apply to slow and fast cells and it seems that the following general interpretation can be made: As an axon impulse approaches the cell body there occurs a decrease in the safety margin of propagation into the expanded surface of the soma-dendrite region. It is not known whether our sample was adequate or to what extent the varying configuration of the different cells influences the safety margin for antidromic invasion. It is our impression, however, that normally the safety margin for an antidromic axon impulse is adequate to invade the soma-dendrite complex. Once, however, due to any reason, including fatigue, "subnormality," or refractoriness, conduction becomes critical, the creation of potential gradients becomes important (see also inhibition). Thus when the cell is relaxed one may assume that it has a resting potential similar to that of the axon. When the dendrites become depolarized, current flow between the approaching axon impulse and the cell body will be reinforced. In fact, the soma region can be brought quite near to its firing range by light stretch and therefore can be triggered readily by a weak stimulus. The subthreshold excitatory depolarization of the soma should sum with the advancing front of the axon impulse which should be speeded up. This actually is shown in Fig. 5, expressed in shortened axon-soma delay times.

The failure of invasion by a second axon impulse in Fig. 5 B_1 when the cell was stretched cannot have been due to "refractoriness" of the cell itself because at intervals of 13 msec. the "firing level" of the soma was not increased. That is the case at much shorter intervals only (Fig. 4 B, C). In Fig. 5 the threshold for full invasion was around 25 mv., related to the *relaxed* membrane potential and measured at the inflection point of the rising phase. The experiments rather seem to show that during the positive repolarization phase of a_1 the membrane potential transiently returns toward its relaxed equilibrium state (see section 5). During that period, therefore, the cell is virtually relaxed (the generator effect is decreased) and the axon impulse may not produce the adequate depolarization which normally constitutes the discharge threshold for antidromic excitation of the cell soma.

The experiments of Figs. 5 and 6 are also relevant to the problem of the site of origin of orthodromic impulses. In the previous study (11) a firing level of 8 to 12 mv. has been seen in slow cells while in fast cells it was near 20 mv., all the measurements being made in the cell body. It is thought that during block of an antidromic impulse the genuine firing level of the cell body can be established, because the transition between local and fully conducting impulses is sharp, and especially because the recording electrode must be quite near to the site of the events. Furthermore, as tested by blocked invasion experiments, the threshold for setting up conducted impulses in the cell body

was similar in slow and fast cells. Therefore it was concluded that the ortho-dromic impulses set up by stretch in slow cells start in the dendrites, while in fast cells they may arise in the cell body or quite near to it. This conclusion may also be relevant to spinal motoneurons in which a discrepancy was seen between thresholds for conducted impulses set up by synaptic and antidromic excitation (5).
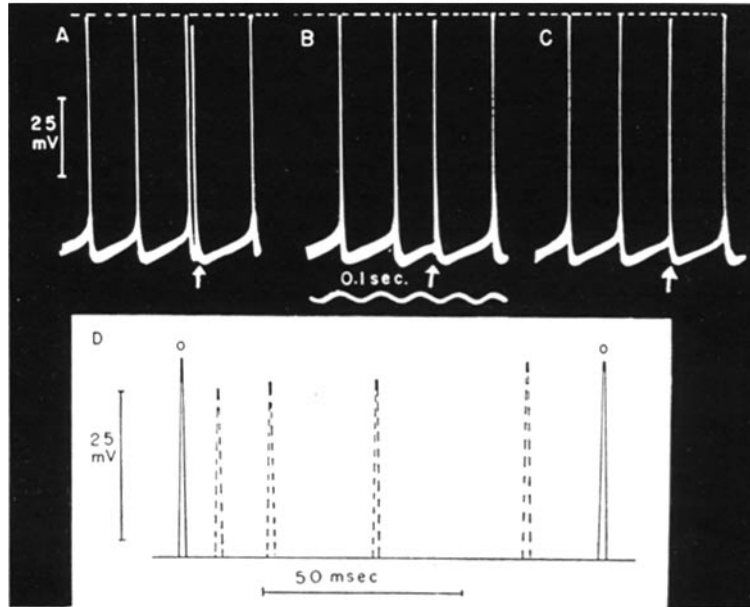

FIG. 7. Height of antidromic impulses (arrows) during prepotentials. Slow cell of second abdominal receptor discharging at 8/sec. A, antidromic impulse is reduced in height by 3 mv. if it arrives early after an orthodromic discharge (*o*), but well outside the cell's refractory period. In B, less impulse diminution. In C antidromic invasion of the cell soma occurs when it is about to discharge orthodromically. Broken line connects peaks of regular orthodromic spikes. D, higher amplification shows progressive diminution of *a* (dotted lines) as it is moved closer to preceding (*o*) discharge.

4. Interaction between Orthodromic and Antidromic Soma Impulses

Height of Impulses.—Orthodromic impulses (*o*) do not arise until the relaxed resting potential of the soma is reduced by about 8 to 12 mv. in slowly adapting cells and by up to almost 25 mv. in fast adapting neurons. Once a stretched cell discharges, one can interpose antidromic impulses (*a*) and these can be compared with *o* impulses. Such experiments are easily done with the slow cell which has a highly regular discharge. It is consistently found that the *a* impulse peak was reduced as compared with *o*. In Fig. 7 three records

are shown with an *a* interposed (arrows) at different intervals between two orthodromic discharges. *a* is reduced most if it arrives soon after *o* before the prepotential leading to the next discharge, develops.

When *a* invades the cell soma just before the expected orthodromic impulse (Fig. 7 C) it is several millivolts larger than *a* in Fig. 7 A. The tracings of Fig. 7 D illustrate more graphically the relationship between the *o* and *a* impulse peaks, which are apparently related to the prepotential height, which in turn seems to indicate the graded soma-dendrite depolarization level. Naturally, below the orthodromic firing range such comparisons cannot be made. It is expected, however, that gradual stretch at the "subthreshold" level will also increase the impulse peaks of antidromic test impulses. This addition, however, is presumably small, since it can be only a portion of the impressed depolarization, and it is not readily detected in tests shown in Fig. 2 at low amplification. It is therefore thought that the generator action at the near threshold range superimposes a small potential on the soma impulses. This seems significant in view of the occasional opposite effect of the depolarizing phase of inhibitory action (21).

5. Analysis of Generator Action and Dendrite Invasion

It was shown in the preceding study that the generator potential is set up within the dendrite terminals by stretch deformation. After it has caused the discharge of the first impulse the generator gives rise to the prepotential which precedes and in turn initiates each new impulse in a series. In fact, it is the main function of the dendrites (and of the generator) to transmit their own potential to the cell soma and beyond, by electrotonic spread. For instance, if a cell is stretched and depolarized by 10 mv., an antidromic impulse will transiently wipe out a large portion of that impressed potential, thus creating the afterpositivity (Figs. 1 B, 2, and 3). The recovery phase from that afterpositivity during subthreshold stretch (Fig. 9) will be an expression of generator action and will be controlled by the generator in the same manner as the prepotentials during rhythmic activity. Both events are absent without stretch and depend on the same processes within the dendrites. Therefore, the best available tool for studying activity in the dendrites is by an analysis of the different manifestations of the generator potential. In the absence of intracellular recording from the fine dendritic terminals (not the larger dendritic trunks which can be penetrated), a solution of the following question has been attempted. Does an orthodromic or antidromic impulse actually wipe out for a short period not only the secondary manifestation of dendrite terminal activity, but also the generator action itself? If the latter remains, even partially, one probably will have to conclude that excitation spread in the dendrites differs from the axon type conduction.

Effect of Antidromic Impulses on Discharge Frequency.—A close reexamination of Fig. 7 reveals that if an *a* impulse arrives at the cell soma when an *o* impulse is just about to fire orthodromically, it will have little effect on the timing of the subsequent response and the rhythm of discharge is not appreciably disrupted; *a* virtually substitutes for the *o* impulse (Fig. 7 C). If, however, *a* arrives during the afterpositivity of *o* (Fig. 7 A) it delays the next *o* impulse and at the same time the prepotential rise after *a* is slowed. It is
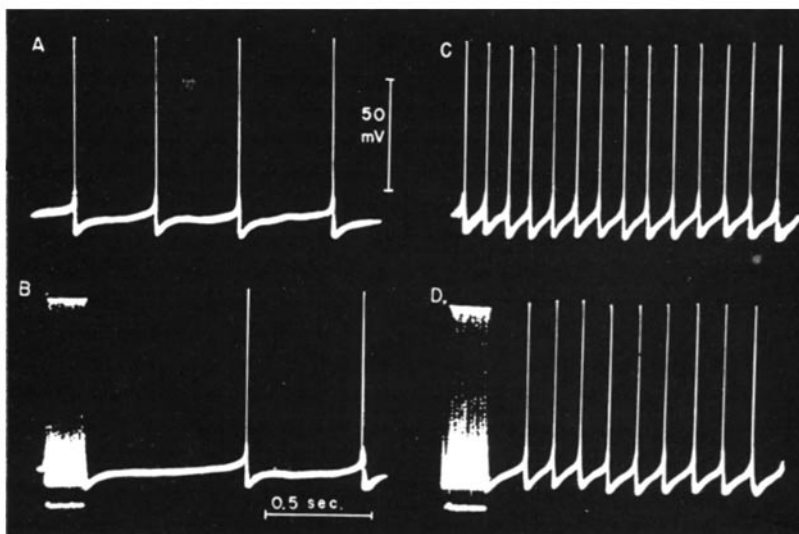

FIG. 8. Effect of antidromic impulses on discharge frequency of slow cell. A, low tension sets up discharge at 3/sec. B, burst of 20 antidromic impulses at 100/sec. causes a pause of 0.75 second and increases the subsequent orthodromic discharge interval. C, higher tension, resting discharge of 9/sec. Same antidromic burst is less effective in causing pause and in changing frequency in D.

assumed that *a*, by having spread into the dendrites, delays reexcitation by interfering with the generator action. The depressant action of antidromic stimuli as measured by the reduction of afferent activity, is best seen during low frequency discharges under weak stretch. Thus a train of *a*'s may stop a discharge of 3 to 4/sec. for a second or more, while its effect on high frequency rhythmic acitivity may be relatively small. An example is shown in Fig. 8. A train of 20 *a*'s at 100/sec. caused in the weakly stretched cell a pause of 750 msec., measured between the last *a* and the resumption of *o* activity, while the corresponding effect was 175 msec. in the discharge at higher frequency. Furthermore, the discharge frequency returned only gradually to its control level. These differential results during weak and strong stretch may be expected if the antidromic impulses either depress the generator itself or

attenuate the electrotonic spread from dendrites to the cell soma. At near threshold stretch a diminution of the barely adequate generator potential would therefore be more readily detected.

Time Course of Antidromic Impulses at Different Resting Potentials.—If a receptor cell is completely relaxed the entire soma-dendrite potential change always lasts about 10 to 20 msec., varying in different cells (Fig. 1 A). It may be assumed that the entire cell soma becomes involved by the time the impulse peak is reached. The large diameter dendrite trunks, even if they did conduct at a very slow rate, such as 0.1 to 1 m./sec., would be largely invaded within 1 to 2 msec. after the spike peak. The long afternegativity may well be a special property of the soma region itself but part of it at least may also be contributed by the finer portions of the dendrites. This is made more likely because many axon impulses had a brief time course (see below, Fig. 10). The following observation also seems to relate to this problem: If a second antidromic impulse (a_2) invades the cell soma at an interval of 3 to 4 msec. after the first (a_1), it does not add a large afternegativity of its own. The repolarization phase of a_2 is speeded up. One may interpret this result to mean that a_2 did not penetrate the more distal finer regions of the dendrites which are expected to have a longer refractory period than the cell soma and the large dendrite portions. Therefore the afternegativity which survives such a short interval double invasion should be due mainly to activity in the dendrites remaining after a_1. In contrast, when one recorded from axons with a relatively long afternegativity (as Fig. 15), a second impulse at a 3 to 4 msec. interval added its own negative afterpotential to that remaining after the first one. The above experiments suggest that excitation processes in the dendrites are relatively slow and contribute to the afternegativity of impulses recorded from the cell soma.

The generator action as an indicator of dendrite processes can be used only during stretch. It can be seen from Fig. 2 A at a relatively low amplification that during weak stretch the impulse peaks remain practically unchanged. This makes it possible to analyze in some detail the recovery phase of impulses and to compare their time course. In trace a of Fig. 9 a slow cell gave a long afternegativity of a total duration of nearly 30 msec. when completely relaxed. A light stretch reduced the resting potential by 3 mv. and, as expected, the recovery phase showed an afterpositivity (trace b). Additional stretch further reduced the membrane potential and increased the afterpositivity (trace c). In the stretched cells the spike recovery phase became progressively shorter and the end of the repolarization peaks is marked by arrows. They indicate the turning point when the generator action takes over, working in the opposite direction to the recovery phase, again depolarizing the cell soma to the level determined by the extent of stretch. In addition, during stretch the levels of repolarization as referred to the relaxed resting potential become less complete (see Figs. 2 B and 3).

Interpretation.—The afterpositivity as seen in these experiments is merely a byproduct of a reduced resting potential, its time course and duration determined by the amount of stretch. It is a hyperpolarization not in relation to the relaxed equilibrium level, but relative to the reduced resting potential caused by stretch. This reduced potential is maintained by the persisting
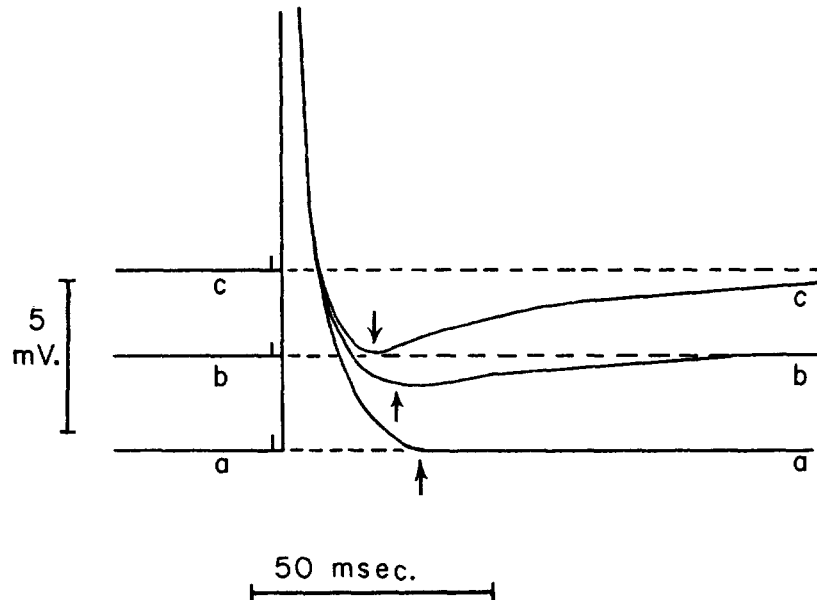

FIG. 9. Slow receptor cell from second abdominal segment. Tracings of three anti-dromic impulses at high amplification, superimposed to compare changes in time course of repolarization phase at three levels of stretch. Spike peaks (not seen in these tracings) remain unchanged during stretch, but impulses start from different displaced (depolarized) resting levels (see Fig. 2). Repolarization phase of impulses in stretched cells overshoots the new resting level (dotted lines), creating the after-positivity. End of repolarization marked by arrows, showing progressive shortening of that portion of the cycle by stretch (see text).

generator action in the absence of impulses (Fig. 3 (11)). During the soma impulse falling phase the large dendrites become invaded and their conductance is bound to increase greatly (10). This will interpose a shunt between the generator regions in the dendrite terminals and the soma. Therefore, for the period of conduction over the relatively long distances toward the dendrite terminals, the generator action should be effectively removed or reduced. Accordingly the cell will repolarize towards its resting (relaxed) equilibrium level, as if no or little generator action were present. The above interpretation tends to explain the observed afterpositivity in terms of "shunting out" of a

persisting generator potential. Actually, the generator may have in addition been temporarily abolished or decreased during the soma recovery phase by dendrite impulses propagating through the site of its origin. A "wiping out" of the generator action, however, does not occur even during weak stretch depolarization since the recovery phase does not return to the full resting potential level. Therefore, one may assume that axon type impulses do not propagate through the distal dendrite portions. Further, the increasing lack of impulse repolarization toward the relaxed equilibrium level (Figs. 9 b, c, and 2 B) during progressive stretch suggests a combination of the following events: (a) the impulses penetrate less and less distally as the dendrites become more depolarized, and (b) the "shunt" between terminals and soma becomes less effective as the generator potential becomes greater. Progressive impulse blockage should be a significant factor, since it has been shown in the soma-axon boundary region that impulse peaks become reduced as stretch progresses (Fig. 5 (11)) and when a steady depolarization level of about 35 mv. is reached (Fig. 9 (11)), conduction ceases. Similarly, increasing depolarization of the terminals should result in reduction and eventual blockage of impulses, especially if the safety margin for conduction in the fine filaments is lower than in the large portions. The actual amount of stretch depolarization in the distal dendrite regions is not known, but due to spatial decrement it should be appreciably greater than the change recorded at a distance in the soma. The blocking range for conduction should therefore be reached well before that of the axon-soma region. These considerations indicate that stretch not only increases the generator potential but also, when it exceeds a certain range, reduces the distance of "active" propagation toward the dendrite terminals. More direct evidence of a persisting generator action during antidromic invasion of the dendrites by all-or-none impulses will be shown in Fig. 10 of the succeeding paper (21). Inhibitory impulses during the peak of the antidromic afterpositivity may further repolarize the cell, thus showing that during that period a generator potential persisted.

The shortening of the repolarization cycle (arrows, Fig. 9) with increasing stretch may be partly due to a facilitation of dendrite invasion, analogous to the phenomena between axon and soma (Fig. 5) and in part due to the increasing action of the augmented generator potential which is able to overcome and cut short the late recovery phase.

6. The Axon Impulse

With suitable microelectrodes it was usually possible to impale repeatedly a number of nerve fibers in each preparation. By the use of the enzymes chymotrypsin and trypsin this procedure was made still easier. No significant effect of these agents (0.2 to 1.0 mg. per cc. physiological solution) on action or resting potentials was found. Axons of varying diameters (10 to 20 μ),

innervating the abdominal musculature were used in addition to the sensory axons of the fast receptors which are most conspicuous and can be followed centrally under the microscope for a long distance. It may be stated at the outset that numerous variations in axon potential time course were seen, but the reasons for the variability were not explored. Therefore no accurate description of a typical axon impulse can be given. The experiments were limited to those aspects which were thought to be helpful in the analysis of
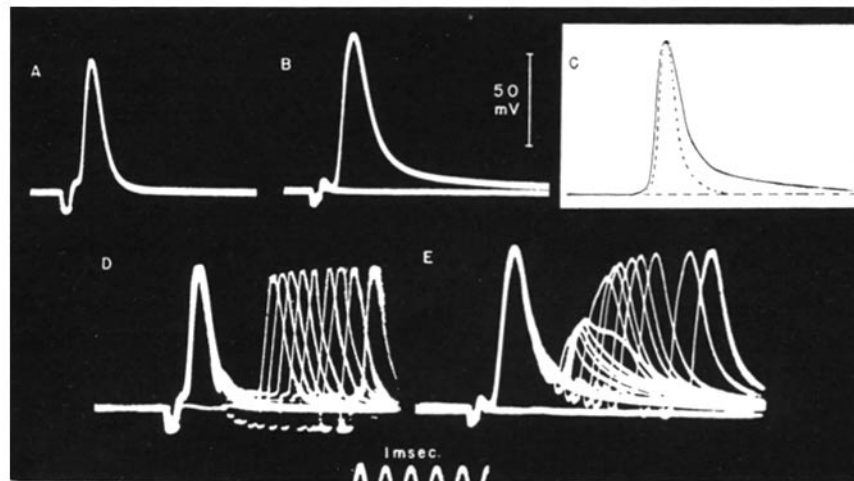

FIG. 10. Comparison of axon and some impulses in a fast neuron in the eighth thoracic segment at 20°C. A, impulse recorded from axon (peak 77 mv.). B, recording from relaxed cell soma (peak 88 mv.). C, both impulses superimposed after scaling them to the same height. The rising and falling phase of the axon impulse is appreciably shorter. D, axon impulses superimposed as interval was shortened. Stimulating electrodes about 10 mm. from the intracellular lead. Even if intervals are further reduced, the second impulse height decreases only little. E, same procedure while recording from the soma. Second axon impulse 3 msec. after the first invades cell body only partially. All transitions are seen (see also Fig. 4).

soma-dendrite problems. The axon impulses of Fig. 10 are presented because they were obtained from the same neuron whose cell soma impulse was also studied and found to be normal. The impulses are hoped to be typical according to present criteria. The records from axon and soma were obtained in succession from a chymotrypsin-treated relaxed preparation. The axon impulse of Fig. 10 A rose to its peak of 77 mv. in 0.4 msec., had a duration at half-height of 0.8 msec., and decayed completely within 4 to 5 msec. without a sign of an afterpositivity. The resting potential was 60 mv. The soma potential of that cell (Fig. 10 B) also had a resting potential of 60 mv. in the relaxed state, a slower rise time (0.7 msec.), and spike duration at half-height

of 1.3 msec., while its afternegativity was longer than 10 msec. The differences are illustrated in Fig. 10 C with both traces superimposed, scaled to the same size. Another finding which is typical, contrasts the axon and soma-dendrite responses at short intervals of excitation. In Fig. 10 E, leading from the soma of the same fast cell, sweeps were superimposed at a repetition rate of 10/sec. while a second stimulus was moved closer to the first one. At short intervals soma invasion was incomplete, as already described earlier (Fig. 4). No similar graded activity was seen in *normally* conducting axons. The axon impulse could be slowed or reduced, as it travelled in the relatively refractory trail of its predecessor, but below that critical range it disappeared in an all-or-none fashion as illustrated in Fig. 10 D. Only when the axon conduction was impaired or delayed near the recording lead, was graded activity seen (below, Fig. 15).

As stated above, axon impulses varied in time course, although the fast "spike" component was consistently shorter than the soma spike. Small (1 to 2 mv.) positive afterpotentials were also seen occasionally but a correlation with axon membrane potentials could not be made. The following values give the observed outside ranges for axon impulses: Rise time 0.4 to 0.9 msec.; spike duration at 50 per cent height 0.5 to 1.2 msec. The corresponding parameters for soma impulses are 0.5 to 0.9 and 1.0 to 1.5 msec. Negative afterpotential values for axons are omitted since they were conditioned by too many uncontrolled factors. For instance, afternegativities of 15 to 20 msec. (Fig. 15) are suspected to be due to some processes of deterioration which slow repolarization. The short rise time values are presumably distorted somewhat by the recording system, particularly when high resistance (over 50 megohm) electrodes were used.

7. Grouped Discharges

Some slow cells gave "spontaneous" grouped discharges when completely relaxed or lightly stretched. They consisted of short high frequency bursts, followed by a pause. This discharge type differs in important aspects from the high frequency impulses during strong stretch. An analysis of the phenomenon became possible when it was found that such bursts could be initiated by antidromic stimulation. Thus, a single antidromic impulse elicited an orthodromic train from the receptor cell, containing a similar number of impulses as the spontaneous orthodromic burst. Generally two recording and stimulating electrodes were placed on the sensory axon and an intracellular lead in the cell soma. Thereby all the discharges going in, as well as those leaving the soma-dendrite region, could be monitored and correlated.

The first consistent observation was a decrease in the number of impulses within each high frequency burst as the tension was increased. This is illustrated at three different tensions recorded with external leads from the axon

(Fig. 11). The first potential following the artefact is larger since it contains besides the slow axon impulse another one from a neighboring fiber excited at the same time. The slow cell, however, received only one antidromic impulse (see below). The number of the afferent impulses decreased from six in the relaxed cell of Fig. 11 A, to two in B during more stretch, while in C the antidromic alone was seen. At that stretch the receptor discharged single impulses in the usual rhythmic fashion, one seen just preceding the antidromic stimulus. At the tension of Fig. 11 B the orthodromic activity in the absence of antidromic excitation alternated between bursts of two to three, while in the relaxed state the cell was silent unless excited antidromically. Fig. 12 A gives an intracellular record of an orthodromic grouped discharge in a
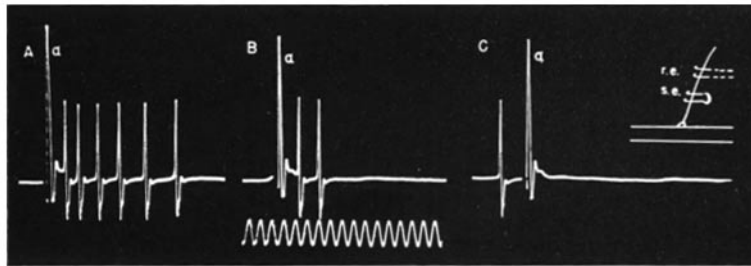

Fig. 11. Grouped discharges from a slow cell at different tensions. A, antidromic impulse (a) sets up six afferent discharges when the receptor is relaxed. B, at greater stretch only two sensory discharges follow. C, at still higher tension (a) does not cause afferent impulses. There was no resting discharge during relaxation (A), while in B under light stretch low frequency orthodromic double or triple discharges were seen and in C the stretch discharge was single. An impulse unrelated to antidromic stimulation precedes (a). Insert, arrangement of extracellular recording and stimulating electrodes. Time 500 c.p.s.

slow cell which was lightly stretched. The first impulse (o) shows part of the usual prepotential which is absent in the subsequent smaller components. Simultaneous records (not shown) from the axon gave three separate conducted impulses. Essentially the same picture is presented in Fig. 12 B in the same cell, photographed at a faster sweep speed. The only difference seems to be the absence of the prepotential in the first impulse a, with a peak voltage of 80 mv. which was set up antidromically. The peak of the smaller deflection 1 follows in 3.5 msec., in turn followed by 2 within 2.5 msec. The simultaneous lower sweep reveals that there were afferent impulses associated with deflections 1 and 2, showing the same polarity as all other orthodromic discharges. A correlation of afferent impulses with the small deflections seen in the cell was based on the following observations. Thus, in Fig. 13 A, for instance, deflections 1 and 2 were regularly accompanied by an axon impulse, and the records could be superimposed at repetition rates of

10/sec. In this slow cell the external stimulating and recording electrodes were in the reverse location from that indicated in the insert of Fig. 11 and
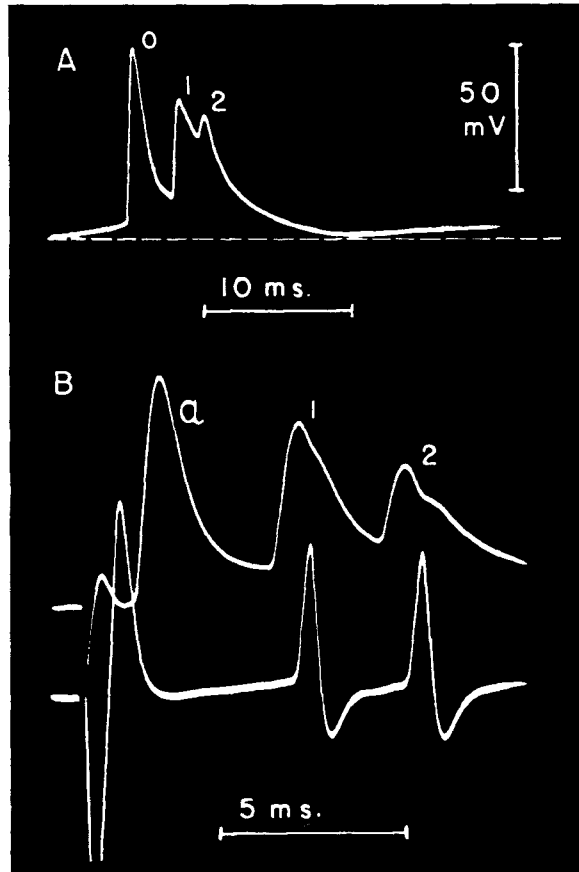

FIG. 12. Grouped discharges from a slow cell (thoracic receptor). A, intracellular lead from cell soma of a lightly extended cell. No antidromic stimulation. The complex potential was accompanied by three sensory axon impulses (not shown). A prepotential precedes the first large deflection (o). B, same cell with simultaneous extracellular axon impulses on the lower beam. First deflection set up by antidromic stimulus (a). Components 1 and 2 were always associated with afferent impulses recorded in the axon.

further, the sensory neuron was excited exclusively by the stimulus. The first impulse on the lower sweep of Fig. 13 A was set up antidromically, while the subsequent two were of opposite polarity and therefore conducted orthodromically in the other direction. A closer examination of such intracellular records at higher amplification and speed (single trace) in Fig. 13 B,

reveals additional deflections, one between 1 and 2, another after 2 on the falling phase, marked by arrows. These were clearly not associated with affer-
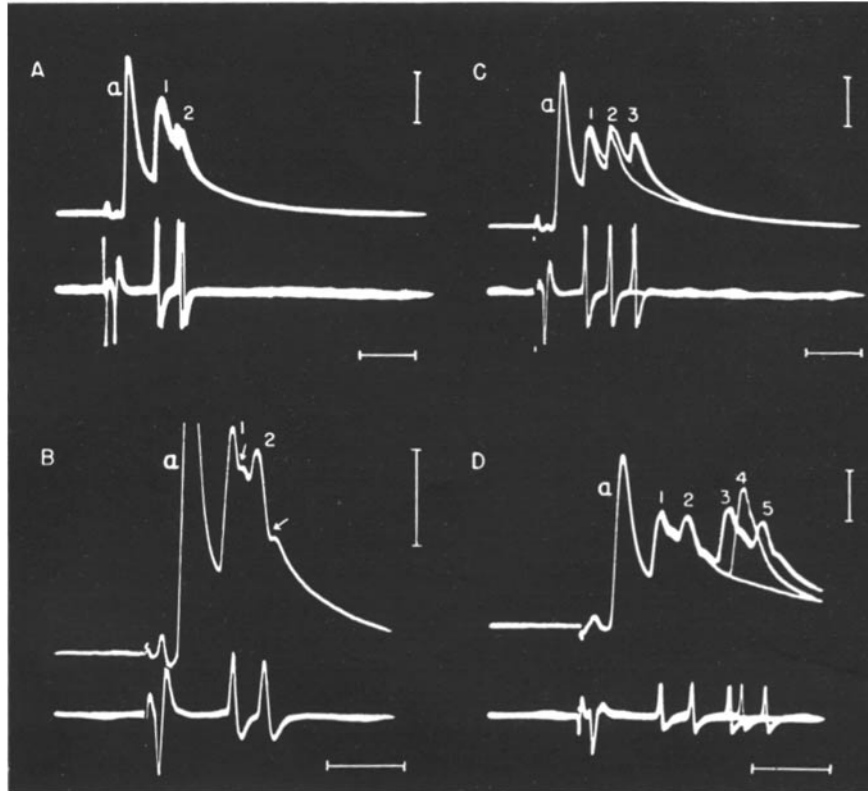

FIG. 13. Simultaneous intra- and extracellular records of grouped discharges in a slow cell. A, intracellular soma record (upper trace) shows superimposed at a 10/sec. stimulation rate components 1 and 2 following the large antidromic spike (a). The lower trace shows consistently two afferent axon impulses. B, higher amplification, single sweep, shows that in addition to components 1 and 2 there occurs abortive soma activity (arrows), not associated with axon impulses which are only 2 msec. apart. C, superimposed repeated exposures. Component 3 and its associated axon impulse drop out in several sweeps. D, components 1 and 2 are always present while 3 and 5 do not appear on some traces. Component 4 (fainter trace) is seen once or twice in the absence of 3 and 5. Note that small soma potential components (not numbered) may be only 0.5 to 2 msec. apart. Potential calibration, 25 mv. Time, 5 msec.

ent impulses and must represent abortive activity which did not survive into the axon recovery phase. In fact, the two conducted impulse peaks (lower sweeps) are only 2 msec. apart, so close to the refractory period of the axon

that no third impulse could have been interposed. The recovery cycle for full soma impulses is appreciably longer (Figs. 4 and 10 E). Further evidence associating each larger soma deflection with a conducted axon impulse is given in Fig. 13 C and D. At this particular stretch of the receptor, with antidromic excitation at 10/sec., axon impulses occasionally dropped out and at the same time a component in the soma disappeared. Components 1 and 2 in C were present in each sweep, while 3 was intermittent, similar to the axon impulse below. (Note the base line going through the last axon impulse on occasions.) In Fig. 13 D antidromic impulse a (88 mv. peak) and smaller components 1 and 2 again superimpose accurately and the same is the case with the corresponding axon spikes below. Components 3 and 5 appear and disappear together on several occasions, while component 4 is present only in one or two sweeps (fainter trace).

The absence of prepotentials preceding each member in such grouped discharges, and the high frequencies (up to 500/sec.), clearly distinguish this type of activity from the usual stretch-evoked impulses. Further, the fact that stretch actually reduces the repetitiveness or abolishes it, indicates that the impulses are not set up by the generator mechanism. The following interpretation seems to fit the observations: The first fully grown impulse in the cell soma, resulting from antidromic invasion or from orthodromic excitation, invades one or more dendrites with some delay. During that delay period the soma recovery phase sets in and when the dendrite impulse occurs it does not propagate merely toward the terminal region, but also adds to the falling phase of the soma impulse. Since the latter is still refractory, for instance 0.5 to 2.0 msec. after the spike peak, only a local response can be added. The local response may be too small and may die out like the soma deflections not correlated with afferent impulses (as in Fig. 13 B), or it may spread into the axon which not only has a briefer refractory period but by that time has more fully recovered. In this manner, if several dendrites are invaded at different times, each dendrite impulse can add its distinct effect to the partially recovered soma and thereby excite the more fully recovered axon. The quantal nature in which the soma components come in or drop out implicates a distinct structure or portion of the cell, most likely individual dendrites. Stronger supporting evidence for this type of mechanism comes from the effect of stretch. The latter depolarizes the dendrites, creates a more favorable gradient, and thereby facilitates the dendritic invasion which will become more synchronous through reduction of the soma-dendrite delays. The likelihood of a dendrite impulse firing centrally into the axon thereby becomes reduced. Stronger stretch may be expected to restore the usual almost simultaneous impulse spread into dendrites. The stretch facilitation mechanism postulated here between soma and dendrite has already been demonstrated between axon and soma.

Another finding favoring the present explanation of grouped activity and fractional activation of the cell soma is the change in the complex soma potential during excitation at short intervals. In Fig. 14 a stimulus 4 msec. after the first sets up an impulse in which the second component is appreciably altered and appears delayed on the falling phase of the potential. At an interval above 6 msec. both potentials are similar once more.

Finally, the possibility of delays within the cells, ranging from a fraction of a millisecond up to 10 to 15 msec., has been demonstrated between axon and soma and therefore may also occur between soma and dendrite. In addition graded excitation spread in conjunction with delays has been obtained
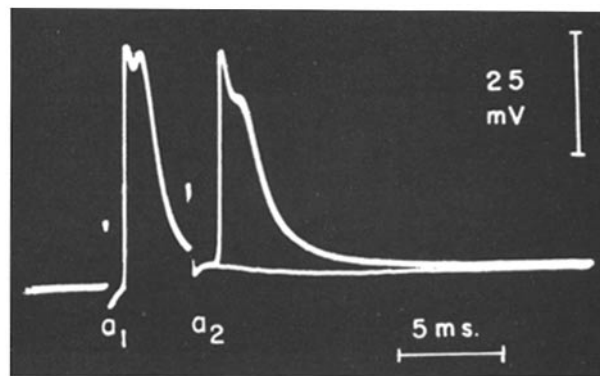

FIG. 14. Slow cell, abdominal receptor, recorded in the soma. The double peak of a_1 is modified during a second impulse (a_2) at a 4 msec. interval, the second component appearing on the falling phase of a_2.

in axons in which the safety margin for propagation was found to be reduced near the recording electrode. The impulses of Fig. 15 were either large, and propagated fully through the axon, or they stopped at various distances from the intracellular lead and therefore were smaller. Thus in Fig. 15 C double stimuli were applied at 5/sec. at a distance of about 10 to 15 mm. from the recording electrode, the first stimulus setting up a fully conducted impulse with a somewhat prolonged afternegativity of 15 to 20 msec. The second impulse started to decrease by several millivolts at an interval near 4 msec. and at 2msec. it added a potential of only 15 mv. In Fig. 15 D the interval was fixed at 2.8 msec., with the second occasionally giving a smaller dual response. An essentially similar picture is seen in B, but there neither of the axon impulses fully reached the recording lead. They were small, each lasting about 15 to 20 msec. Fig. 15 A differs from the other records, having been set up by a *single* stimulus at a repetition rate of 10/sec. There are clearly two components, the second not appearing each time but coming in on occasions after a delay of 2 msec.

The events in Fig. 15 are analogous to excitation spread experiments through blocked regions in frog nerves (17, 29, p. 277) or to the delays and blocks at the axon-soma boundary. There must have been several obstacles to conduction, otherwise a single impulse (Fig. 15 A) could not appear in two distinct steps. The first component presumably is the electrotonic potential transmitted by an impulse which was blocked at a certain spot only occasionally, while at times it managed to proceed further after a definite delay
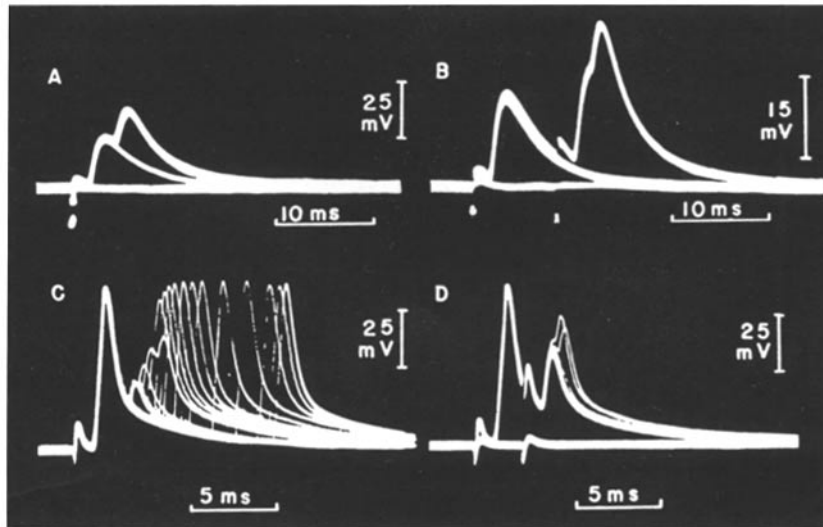

FIG. 15. Delays and local potentials near the recording electrode in an impaled axon. A, axon stimulated at 10/sec. Impulse block at two different locations some distance from the intracellular lead. B, two impulses at 8 msec. interval. C, double stimulation at repetition rate of 5/sec., second stimulus moved closer during exposure. First impulse conducts fully, second impulse blocked at short intervals. D, interval fixed at 2.8 msec. (see text).

(2 msec.), only to be blocked, however, at another point nearer to the recording electrode. Although graded conduction with varying delays is undoubtedly abnormal in the axon, the mechanisms are of some interest in connection with the postulated delays at soma-dendrite regions.

A hypothetical scheme in Fig. 16 illustrates one of the possibilities by which grouped discharges could be started and then maintained for varying periods. In A an antidromic inpulse fully invades the soma and encounters a delay when entering the left dendrite. During the delay, lasting one to several milliseconds, the potential change as recorded in the soma declines. Thus, when the impulse in the large portion of the left dendrite proceeds, as shown in Fig. 16 B, it will be able to spread not only in the peripheral direction,

but also back into the partially recovered cell body. There it will set up a local potential of variable size, dependent on the length of the preceding recovery period. The local impulse may persist in the cell body for a short period and die out (Fig. 13 B, arrows), or it may survive and set up an axon impulse. It will also tend to spread into those dendrites (Nos. 2 and/or 3) which were originally invaded without an appreciable delay and therefore can conduct once more. This second dendrite invasion may in turn start
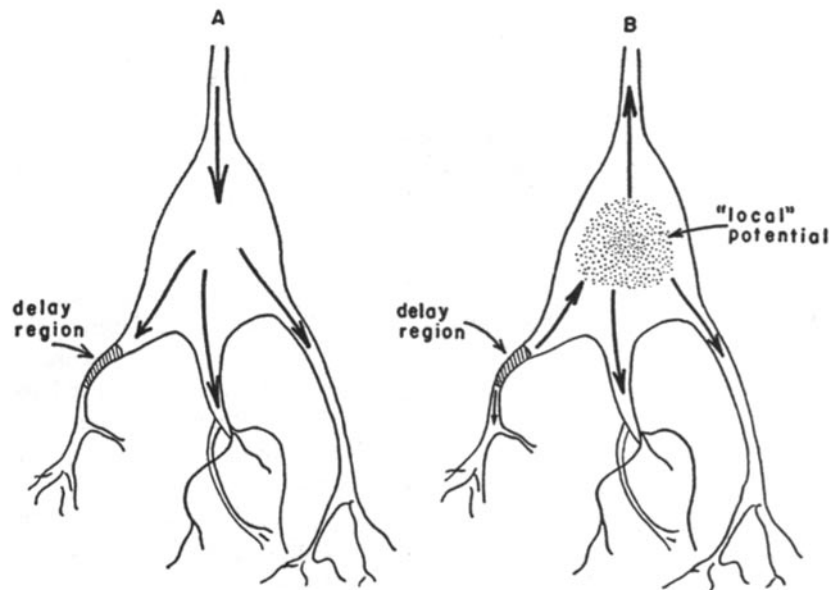

Fig. 16. Scheme for initiation of grouped discharges by soma-dendrite delays. Only one of a number of variants is given. A, antidromic impulse delayed when entering one of the dendrites. B, delayed impulse spreads distally and also reexcites soma (local impulses) and secondarily the axon and dendrites (see text).

another local excitatory process in the soma (not drawn) and thereby the cycle can be repeated. Reexcitation of the soma could go on as long as the differential recovery rates in dendrites are long enough to survive the refractory period. Only one of a number of variants is given here in a hypothetical cell with only three main dendrites. For instance, the delays in several dendrites of one cell may vary sufficiently to produce in sequence several axon discharges, approximately corresponding in interval to the delays. Any asynchrony in dendrite excitation would tend to add to the number of impulses in a burst. It should be pointed out here that conducted "explosive" all-or-none impulses in the large dendrite portions adjoining the soma have to be postulated. A "standing (persisting) negativity," as postulated by

some authors, could not excite a cell in such rapid sequence (Fig. 13). The persisting generator action, even if strong, would cause lower frequency bursts, *each* preceded by a prepotential.

Some alternatives in respect to the site of origin of grouped discharges are as follows: The soma itself may, after the first impulse, start to oscillate at a rate seen here, thus dispensing with a mechanism acting from outside the cell body. However, oscillations as observed, for instance, in Ca-deficient tissue (4) would not be expected to show an irregular quantal progression which is seen frequently. Another possible site of origin is the axon-soma boundary region. The occurrence of abortive local responses in the soma (arrows, Fig. 13 B) after an antidromic impulse contraindicates this. Since the axon recovers more rapidly than the soma, it is unlikely that a local response should be able to spread back into the latter without firing an afferent impulse. Further, the behavior during the subnormal phase (Fig. 14) rather implicates more than one distinct component in the cell.

Grouped discharges, when they appeared, were regarded as a sign of some abnormality since they were absent in most preparations, including the undissected ones. The underlying mechanism, however, is of interest since it may be a normal feature of some other cells with peculiar configuration, perhaps predisposing them to asynchrony in dendrite invasion. Similar bursts at high frequency have been observed recently by Rose and Mountcastle (32) who have made a careful and exhaustive study of analogous repetitive firing of single thalamic cells under well controlled conditions, almost certainly excluding an abnormal state. Similarly Tasaki, Polley, and Orrego (33) reported in single cells multiple responses of very similar character to those described here, following orthodromic or antidromic stimuli (see Discussion).

DISCUSSION

A relationship between the results in the present preparation and between those obtained in other tissues may exist in specific instances in which corresponding experiments were done, for instance on single motoneurons (see below). References will, however, be made freely to a wide field although no assurance of a valid analogy exists. In the present study all the recording was done from the center of the soma region. In several instances the electrode was successively inserted into different portions of the cell, including the axon, within 100 μ of the admittedly ill-defined axon-soma boundary region. Further, the dendrite base region was also explored in some suitable preparations. Such recording did not contribute significant features. There were no "essential" differences when the cell configuration obviously varied in the same type of neuron (2, 12), nor was a difference detected between fast and slow cells when antidromic excitation was studied. All this indicates that

the one-lead internal recording technique has a limited resolution for fine intracellular detail. It appears adequate, however, to resolve certain differences among axon, soma, and dendrite contributions.

The variability of the soma-dendrite potentials with change in resting potentials, clearly within the physiological range, makes it difficult to speak of "fixed" properties of these cells. Thus the "afterpotentials" have to be defined for the varying membrane potential levels. An afterpositivity in reference to the relaxed equilibrium level has not been found but can be related to a reduced membrane potential. By the same standard a postspike negativity can be properly identified in a cell at full resting potential only. Therefore, the conventional well defined terms of negative and positive afterpotential have been avoided. It is questionable whether such labile behavior is shared by other cells in different species. It is, however, known from careful and extensive studies, that the negative and positive afterpotentials vary a great deal in different peripheral nerves (for references (15)) and are very sensitive to changing experimental procedures, for instance to temperature, repetition rate, or pH changes (14, 29). It is likely then, that membrane potential fluctuations are just one factor. Experimental conditions certainly become exceedingly important if a great lability of afterpotentials exists even within the range of physiological activity and if excitability cycles are to be explained in those terms. Within the present framework, with practically isolated cells in a relatively large volume of fluid, the experiments were consistent and seem to explain in terms of potential changes many features of transmission processes.

First of all, the occurrence of a lowered safety margin at axon-soma boundaries (5, 24, 31) has been confirmed and demonstrated under two essentially differing conditions. (1) A second antidromic nerve impulse, arriving 2 to 3 msec. after the first, was either delayed or blocked near the soma. (2) Occasionally, for some reason transmission between axon and soma may be impeded or blocked if the soma is within several millivolts of its resting or relaxed state. If stretch is applied and the membrane potential depolarizes beyond this critical range, transmission will be restored (Fig. 5 A_1). Soma impulses in such a stretched cell may show an afterpositivity which brings the membrane potential temporarily into the critical range of block. During that phase of the potential a second impulse will be blocked (Fig. 5 B_1, C_1). The block, or delay, then is more properly referred to the resting potential than to the "positive afterpotential." The latter merely creates a transient "quasi-relaxed" state and has no relationship to the subnormality of refractoriness. Whether this block may be compared to the well known block of motoneuron invasion during the positive afterpotentials in the cord is open to speculation (for references (5)). The opposite situation applies if the first impulse is blocked and only partially invades the soma by its electrotonic

front, usually setting up local impulses which slow down the potential decay (Fig. 5 A). This may bring the soma potential temporarily out of the critical range into a "quasi-stretched" state and a second impulse will fully invade the soma (Fig. 5 B, C). Again, in both instances, the changes can be reproduced by stretch or relaxation, acting on the membrane potential. Provided that analogous situations in the central nervous system exist one can well see how synaptic background bombardment will change the excitability cycle. For instance, the antidromic soma-dendrite invasion could be enhanced by concurrent orthodromic stimulation in the spinal cord (6, 24, 31). Such a synaptic-antidromic synergistic interaction has actually been demonstrated in single motoneurons (5).

Assuming that changes in the environment of cells produced by variation of temperature, oxygen supply, or by drug action influence different components of the axon–soma–dendrite system in a selective or progressive fashion, one could expect profound and even partly predictable changes. As an an example may be quoted Lloyd's (27) detailed analysis of the effect of anoxia on motoneurons. Asphyxia leads to a depolarization or cathodal block (*cf.* also reference 16) but not before the motoneuron undergoes a succession of stages of facilitated soma invasion and enhanced dendrite conduction. Some analogies to such a sequence may perhaps exist in the present preparation during various stages of stretch, eventually leading up to block by over-stretch. There exist numerous examples in the receptor cells which show how large effects can be produced wherever conduction with a critical safety margin is concerned. The critical loci seem to be the axon-soma region and the dendrites. In the latter it appears that especially the depth of invasion is variable (see below). There is no evidence which would attribute to the large dendrite branches specific properties which differ from those of the soma from which they arise (28). This area has been implicated indirectly only in the case of the grouped discharges. The postulated delay around the region of the soma-dendrite base may well be due to geometrical configuration.

The mode of conduction in the dendrites has been approached by pursuing the time course of the generator activity which is located in the peripheral dendrite region and is transmitted to the cell soma. The question is not whether the dendrites are invaded, but whether dendritic conduction differs from axonal propagation. The fine terminals certainly have some special attributes shown by their deformation sensitivity and also by their presumably extensive synaptic relationship with inhibitory fibers (21). They may perhaps be compared in their specialized properties with synapses elsewhere. The end-plate, for instance, does not conduct in the same manner as the rest of the muscle fiber. It does, however, serve, perhaps in analogy with the generator site, as a focus from which the surrounding muscle fiber becomes electrotonically depolarized. The present conclusion that dendrite

terminals, once they are invaded in the relaxed state, contribute relatively slow changes, agrees with findings on sensory terminals by Katz (19) and by Tasaki, Polley, and Orrego (33) on dendrite potentials in the geniculate body and the striate centers. Also in other parts of the central nervous system of mammals the dendrites appear to produce slow potentials (8, 23, 26, 30). The evidence that the generator action is not wiped out during stretch indicates that axon type all-or-none conduction is at least modified in the terminal dendrite portions. This should not be interpreted that dendritic invasion does not affect the generator site. For instance, a train of antidromic stimuli has a long lasting effect on the recovery period of the generator action (section 5) which can hardly be attributed to changes in properties of the soma and large dendrite portions. The long lasting changes ascribed to terminals by Larrabee and Bronk (22) in ganglia and by Lloyd (25) in the cord, should be recalled here. It is thought that conduction as seen in the axon or soma becomes progressively attenuated, at least in a partially depolarized dendrite. Thus, while moderate dendrite depolarization (below the level of overstretch) facilitates conduction into the soma, it seems to act in the opposite direction within the dendritic terminals, by progressively barring invasion of this seat of the generator action by "proper" conducted impulses. A direct comparison between fine dendrite action and other cell portions such as can now be made between axon and cell soma is desirable but technically not possible at present. Local graded activity in cortical dendrites has recently been shown by Clare and Bishop (9) and modified dendritic conduction was postulated. Also Chang's (8) local paradendritic activation may be recalled here.

The results on repetitive firing tend to explain the occasional complexity of the soma potentials by the contribution of dendrites which accordingly give all-or-none types of reactions, at least in their portions near the soma. The postulated system may also be relevant to the well known burst type activity, so frequently seen in the central nervous system (for surveys see 1, 3, 18, 32). If certain short delays in the soma-dendrite base can be assumed, a mechanism may be available which could keep going for longer periods by spread from dendrites to soma and back again. Being marginal, such activity is expected to be strongly influenced by changes in the soma-dendrite system, once more pointing out the effect of small shifts in the resting potential. This grouped discharge differs essentially from the system of orthodromic activation which puts a more or less permanent "drive" into the dendrites, capable of regular maintained control of rhythmic activity. Such high frequency bursts could not be caused by the relatively slow events in terminals of dendrites. Foci for activation, based on differential recovery rates within cells, have recently been proposed (7, 9, 33).

In conclulion it may be worthwhile to point out some of the almost detailed

similarities between the performance of the present sensory cells and the motoneurons in cat, activated antidromically (5). In both, axon-soma delays and cell invasion are similarly affected by refractoriness and by afterpotentials. The destruction of a preexisting synaptic potential in motoneurons during an impulse seems analogous to our "collapse" of soma potentials impressed from the dendrites.

SUMMARY

The present investigation continues a previous study in which the soma-dendrite system of sensory neurons was excited by stretch deformation of the peripheral dendrite portions. Recording was done with intracellular leads which were inserted into the cell soma while the neuron was activated orthodromically or antidromically. The analysis was also extended to axon conduction. Crayfish, *Procambarus alleni* (Faxon) and *Orconectes virilis* (Hagen), were used.

1. The size and time course of action potentials recorded from the soma-dendrite complex vary greatly with the level of the cell's membrane potential. The latter can be changed over a wide range by stretch deformation which sets up a "generator potential" in the distal portions of the dendrites. If a cell is at its resting unstretched equilibrium potential, antidromic stimulation through the axon causes an impulse which normally overshoots the resting potential and decays into an afternegativity of 15 to 20 msec. duration. The postspike negativity is not followed by an appreciable hyperpolarization (positive) phase. If the membrane potential is reduced to a new steady level a postspike positivity appears and increases linearly over a depolarization range of 12 to 20 mv. in various cells. At those levels the firing threshold of the cell for orthodromic discharges is generally reached.

2. The safety factor for conduction between axon and cell soma is reduced under three unrelated conditions. (*a*) During the recovery period (2 to 3 msec.) immediately following an impulse which has conducted fully over the cell soma, a second impulse may be delayed, may invade the soma partially, or may be blocked completely. (*b*) If progressive depolarization is produced by stretch, it leads to a reduction of impulse height and eventually to complete block of antidromic soma invasion, resembling cathodal block. (*c*) In some cells, when the normal membrane potential is within several millivolts of the relaxed resting state, an antidromic impulse may be blocked and may set up within the soma a local potential only. The local potential can sum with a second one or it may sum with potential changes set up in the dendrites, leading to complete invasion of the soma. Such antidromic invasion block can always be relieved by appropriate stretch which shifts the membrane potential out of the "blocking range" nearer to the soma firing level. During the afterpositivity of an impulse in a stretched cell the membrane potential may

fall below or near the blocking range. During that period another impulse may be delayed or blocked.

3. Information regarding activity and conduction in dendrites has been obtained indirectly, mainly by analyzing the generator action under various conditions of stretch. The following conclusions have been reached: The large dendrite branches have similar properties to the cell body from which they arise and carry the same kind of impulses. In the finer distal filaments of even lightly depolarized dendrites, however, no axon type all-or-none conduction occurs since the generator potential persists to a varying degree during antidromic invasion of the cell. With the membrane potential at its resting level the dendrite terminals contribute to the prolonged impulse afternegativity of the soma.

4. Action potentials in impaled axons and in cell bodies have been compared. It is thought that normally the over-all duration of axon impulses is shorter. Local activity during reduction of the safety margin for conduction was studied.

5. An analysis was made of high frequency grouped discharges which occasionally arise in cells. They differ in many essential aspects from the regular discharges set up by the generator action. It is proposed that grouped discharges occur only when invasion of dendrites is not synchronous, due to a delay in excitation spread between soma and dendrites. Each impulse in a group is assumed to be caused by an impulse in at least one of the large dendrite branches. Depolarization of dendrites abolishes the grouped activity by facilitating invasion of the large dendrite branches.

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