Principles Underlying New Methods for Chronic Neural Recording


SUMMARY: Chronic recording is possible from nerve fibers which have grown through holes in an insulating medium (regeneration electrodes) or which are enclosed by an insulating sheath (cuff electrodes). Use of three electrodes in a balanced configuration permits good rejection of electromyographic (EMG) signals and other sources of electrical interference (fluorescent lights, 60 Hz signals from the mains, etc.). Equations are derived and tested for predicting the amplitude and form of the signals expected for a given cuff length and diameter. These equations can be used to design electrode units optimally for a given application. Finally, the use of transformers permits the neural signals to be carefully matched to the recording apparatus and further optimizes the neural signal-to-noise and signal-to-EMG ratios. Use of these methods in several physiological and clinical applications, as well as potential abuses, are discussed.

RESUME: En enregistrement continu est possible à partir des fibres nerveuses qui se sont développées à travers les trous d’un médium isolé (electrodes de régénération) ou qui sont recouvertes d’une gaine isolée. L’utilisation de trois électrodes dans une configuration balancée permet un bon filtrage des signaux électro-myographiques (EMG) et d’autres sources d’interférence électrique (lumières fluorescentes, signaux 60 Hz, etc.). Des équations sont émises et vérifiées afin de prédire l’amplitude et la forme des signaux escomptés pour une longueur donnée de gaine ainsi que pour son diamètre. Ces équations peuvent être utilisées pour désigner optimalement des unités d’électrodes pour une application donnée. Finalement, l’utilisation de transformeurs permet aux signaux neuraux d’être soigneusement reliés à l’appareil d’enregistrement et de plus optimise les relations signal — bruit et signal — EMG. L’utilisation de ces méthodes dans plusieurs applications physiologiques et cliniques est discutée, ainsi que certains abus possibles.

INTRODUCTION
Advances in understanding the function of the nervous system have resulted from the application of microelectrode techniques to the brains of unanaesthetized, behaving animals (Evarts, 1966) and the peripheral nerves of man (Vallbo & Hagbarth, 1968; Vallbo, 1971). These advances have been particularly striking in understanding motor systems because of the obvious link between motor output and behaviour. However, microelectrodes are limited to use in acute experiments by two factors: their sensitivity to movement and their need to be carefully positioned by external devices. Both these limitations arise from the necessity that the tip of the microelectrode be very close to the nerve fiber being studied in order to ensure high signal-to-noise ratio. The noise level is determined mainly by the impedance of the microelectrode tip which must be quite high due to the small electrode size. Because the fluid surrounding the fiber represents a three-dimensional volume conductor, the signal amplitude will fall off steeply with distance from the nerve fiber. The amplitude will only exceed the noise level if the electrode diameter is comparable in size to the diameter of the fiber and within a distance equal to a few diameters from the fiber (Frank & Becker, 1964).

The problem of movement is more severe in recording from peripheral nerves than from neurons in the brain because the skull represents a point of fixation for a micro-drive. In either location long-term use is precluded by the need for positioning the electrode with external devices.
which means that there is a pathway for infection to enter the body.

Methods for chronic recording would permit 1.) the same fibers to be studied over a wider variety of conditions during development, conditioning, etc., and 2.) offer the possibility of prosthetic applications such as the control of artificial limbs by amputees, the control of the lower limbs in a paraplegic, etc. Recently, several reports (e.g., Wise et al., 1970; Sonn & Feist, 1974) have suggested using microelectronic techniques to fabricate arrays of microelectrodes which might be implanted. The use of multiple electrodes would permit simultaneous recording from several nerve cells, which has many advantages. Furthermore, if many electrodes are used, the probability is increased that some of the leads are close enough to nerve cells to obtain a reasonable signal-to-noise ratio. Nonetheless, the records shown in these reports are all from acute experiments and, to our knowledge, the possibility that connective tissue will grow around such an array and prevent good recordings chronically has not been eliminated. Finally, prosthetic applications of such electrode arrays may be limited since the high impedance of the electrodes will make the device sensitive to various sorts of electrical interference (fluorescent lights, motors, etc.) in environments other than carefully shielded rooms.

An alternative approach is to isolate a nerve fiber or fibers from the general body fluids by surrounding part of the fiber or fibers in an insulating medium. This technique, which will be referred to as placing the nerve in a restricted extracellular space, is well known to neurophysiologists who have for years recorded from nerve filaments in paraffin oil or other non-conductors. The challenge is to do this chronically without damaging nerve fibers and to choose the geometry of the recording arrangement so that the nerve signal is recorded above the noise while rejecting other sources of interference (e.g., EMG, movement artefacts, electrical interference). This article describes recent progress towards this goal and the principles underlying the methods being developed. A short account of some of these results has appeared elsewhere (Stein et al., 1975).

**Regeneration electrodes**

Our group succeeded in obtaining chronic recordings a couple of years ago (Mannard et al., 1974) from amphibian nerves using regeneration electrode units*. These consist of a series of holes through a non-conductor, each of which has an electrode ending near the center of the hole. Regeneration electrode units were placed in the path of a partially transected sciatic nerve in an amphibian, *Xenopus laevis*. After a few months, recordings were made from sensory and motor fibers which had grown through the various holes. Unfortunately, we have not yet been able to reproduce these results in mammalian preparations because of 1.) the higher conduction velocity and hence lower spatial gradients in warm-blooded animals (see Amplitude of neural signals), 2.) the small size of the regenerated fibers, and 3.) the greater proliferation of connective tissue in mammals. The growth of connective tissue may block the holes before nerve ingrowth can take place.

Nonetheless, we have shown histologically (Fig. 1), as have others (Holz, 1974) that mammalian nerve

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*U.S. patent pending
fibers do grow through such holes, although they tend to be small, unmyelinated fibers, or weakly myelinated fibers. The small size, together with the relatively higher conduction velocity at body temperature (see Amplitude of neural signals) makes it extremely difficult to record from such fibers. We are still attempting to optimize conditions for regeneration and recording so that the regeneration electrode units can be used in mammalian preparations.

Cuff electrodes

In the meantime, Hoffer et al. (1974) have demonstrated that it is possible to record chronically from mammalian nerve fibers if a length of nerve filament is dissected and placed in an insulating cuff. We have used cuffs of medical grade silastic, which are opened to insert the nerve and then sealed with silastic. The cuff contains one or more silver or platinum-iridium electrodes, so that recording can begin immediately from histologically normal fibers. The teflon-coated wires from one or more cuffs are further coated with silastic and led out to a twelve-pin integrated circuit socket. The socket is fixed with epoxy in the center of a vitreous carbon Biosnap (Bentley Laboratories Inc., Irvine, Calif.) which is sutured into the skin overlying the hip. The vitreous carbon is a very hard, smooth material which is not rejected by the body and can be placed in the skin, even of human subjects, for years without infection (Stanitski & Mooney, 1973). The entire implanted unit can be sterilized in an autoclave and contains only components which have been thoroughly tested for chronic use in animals and man.

Hoffer et al. (see also Brindley, 1972) indicate that chronic recording requires that the dissected filaments contain an undamaged blood supply. We have found (Stein et al., 1975) that with proper precautions recordings can be made from whole nerves as large as the sciatic nerve in the cat (3-4 mm in diameter), as shown in Fig. 2, which was recorded from a cat walking on a treadmill over a month after implantation. No special precautions were taken to shield either the motor driving the treadmill or other sources of interference.

Rejection of EMG

If a whole nerve such as the sciatic nerve in the cat is stimulated, and recordings are made between an electrode in the limb and one in another part of the body, a large compound action potential (about 10 mV) is recorded (Fig. 3A). This is almost entirely due to the electrical activity of muscle (EMG) because of the much greater size and number of muscle fibers, compared to nerve fibers. If, however, a segment of nerve is enclosed in a nonconducting medium (paraffin oil or a cuff), the nerve signal recorded at the center of the length of nerve in the non-conducting medium can be detected (early wave in Fig. 3A). At the same time the indifferent electrode can be placed in the fluid nearby so that distant EMG sources will be picked up by both electrodes (Fig. 3B) and can be rejected by a differential amplifier (common-mode rejection). The EMG is, however,
Figure 4—Method for recording using an insulating cuff with three electrodes around a nerve. The reasons for the recording configuration shown and the use of a transformer are described in the text.

Figure 5—The effect of increasing the length of a nerve in a restricted extracellular space on the amplitude and waveform of recorded extracellular potentials from a single A β fiber (conduction velocity = 64 m/sec). In this experiment varying lengths of the sural nerve in the cat were lifted from saline into paraffin oil. The lengths used were A) 0.4 cm, B) 1 cm, C) 1.8 cm, and D) 4.9 cm. The vertical bar in each case represents 5 µV. The time scale is identical for each part of this Fig. Each part of the Fig. was obtained by averaging the responses to 512 stimuli applied to a dorsal root filament.

still large enough to swamp the neural component. Much better common-mode rejection can be obtained if two electrodes are built into the ends of the cuff (Fig. 4), and recording is carried out between the center of the cuff and the two ends which are shorted together (Fig. 3C).

The principle underlying this procedure is that once the two ends of the cuff are shorted together, there can be no potential gradient across the cuff. Hence, EMG currents will tend to flow around rather than through the cuff (the flow of current across the longitudinal resistance of the cuff requires a potential gradient according to Ohm's Law). Even though an electrode is placed around the nerve, this does not preclude some potential gradients in the radial direction and hence there is still some residual EMG. We have found that this residual EMG is minimized if the recording configuration is symmetrical. Asymmetric placement of the internal electrode reduces the neural signal, which is generated by the current flow along the length of the nerve within the cuff, while increasing the EMG. The ratio of the neural signal to the EMG can be enhanced still further by carefully matching the input impedance of the recording apparatus to that of the electrodes being used. In Fig. 3D a Hammond audio transformer (Model 585D) has been placed between the recording electrodes and the preamp. This transformer amplifies the signals over ten times and has other desirable filtering properties which will be described later (Amplification and filtering of neural signals). Finally, the EMG is much slower in time course and hence contains lower frequency components than the neural signal. Fig. 3E shows the effect of applying a first-order high-pass filter with a half-power point of 300 Hz. There is now quite good rejection of EMG, and the neural signal stands out clearly. Thus, the large EMG components in Fig. 3A have been systematically reduced while the neural components have been enhanced until they stand out clearly in Fig. 3E. The same principles which are demonstrated for compound action potentials in Fig. 3 apply to data from single nerve fibers and now will be discussed in more detail in successive sections.

Form of the neural signals
Whether neural signals are recorded by means of regeneration electrodes, cuff electrodes, or simply by picking the nerve out of saline and into a non-conductor such as paraffin, the form of the action potential will be triphasic. Mathematically, what is recorded is the second difference between the voltage at the center electrode and the two ends of the restricted extracellular space. In most cases the restriction will be cylindrical in form and the electrode will be placed in the center of the cylinder, as shown in Fig. 4. Then the voltage recorded will be (Stein & Pearson, 1971)

\[ V(t) = c \left[ \frac{1}{2} V_n(t + \Delta t) - V_n(t) + \frac{1}{2} V_n(t - \Delta t) \right] \]

where \( V_n \) represents the intracellular potential in a nerve fiber, \( \Delta t = l/2v \), \( l \) is the length of the restriction in extracellular space, and \( v \) is the conduction velocity of the nerve fiber. The form of the intracellular action potential and the constant \( c \) can be determined by classical monophasic recording methods.

To do this, cats were prepared for recording acutely from peripheral
nerves and a laminectomy was performed to expose sacral and lumbar roots. Nerves varying in diameter from the sural (0.5-1 mm) to the sciatic (3-4 mm) were either placed in a silastic cuff containing electrodes or lifted into a non-conducting medium (paraffin oil). Either dorsal or ventral roots were dissected until a filament was obtained which produced a single all-or-none action potential (paraffin). Recording between the filament and end of the fast rising phase. The third phase will be much smaller (Fig. 5), due to the much more gradual change of slope at the end of the action potential.

**Amplitude of the neural signals**

As the length $l$ is increased the voltage increases as the square of the length, but the approximation in equation 2.) becomes less good (Fig. 5B). The third phase becomes more prominent and the action potential lengthens out (Fig. 5C). Eventually, equation 1.) predicts that the first and third phase will be equal and the second phase will be twice as great (Fig. 5D). Each will be a replica of the monophasic action potential and the peak-to-peak amplitude of the triphasic waveform will be 1.5 times that of the monophasic amplitude (Stein & Pearson, 1971).

The monophasic action potential ($V_1$) recorded classically as described in the previous section is a scaled-down version of the intracellular action potential ($V_m$) and affected by the same constants as the triphasic potentials, i.e.,

$$V_1 = c V_m.$$ 

Monophasic action potentials were recorded at the end of each experiment for all units studied. These potentials were then used to reconstruct the expected triphasic waveforms according to equation 1.) using a short computer program.
at different velocities when long lengths are used, but the small difference when the length of restriction is small. This is because the parameter \( c \) in equations 1 and 2 depends on the square of the ratio of the fiber diameter \( a \) to the diameter \( d \) of the restricted extracellular space (see Fig. 4 and Stein & Pearson, 1971).

If \( a \ll d \), Stein & Pearson (1971) showed that equation 1 becomes

\[
V = \frac{a}{d} \Delta V
\]

The actual constant of proportionality will depend on the ratio of extracellular to intracellular conductivities, the percentage of the extracellular space within the restriction occupied by myelin and other factors. The difference notation (\( \Delta \)) has also been introduced to shorten the expression 5.). To the extent that the conduction velocity \( v \) is proportional to fiber diameter \( a \) (Hursch, 1939; see Coppin & Jack, 1972, for conflicting evidence), simple expressions can be written from 5.) for the peak-to-peak amplitude \( V_P \) of the waveforms in the limit of short and of long lengths \( l \) in the restricted extracellular space

6.) \[
V_P = k_1 \frac{l}{d^2}
\]

for \( l \ll 1 \text{ cm} \) and

7.) \[
V_P = k_2 \frac{a}{d}
\]

for \( l \ll 1 \text{ cm} \). The values of the constants \( k_1 \) and \( k_2 \) can be determined empirically from data such as shown in Fig. 6. Typical values for nerves in cats were in the range \( k_1 = 0.05-0.1 \mu \text{V} \) and \( k_2 = 0.1-0.2 \text{V} \). If the single fiber has approximately the same longitudinal resistivity as the other material in the restricted extracellular space, the value of \( k_2 \) will be about equal to 1.5 times the intracellular action potential. The measured values of \( k_2 \) agree with this suggestion.

The values of \( k_i \) are much smaller in warm-blooded animals such as cats than in cold-blooded animals such as amphibians because of the marked effect of conduction velocity on temperature. The higher \( v \) at body temperature in mammals means that for a given \( l \) the value of \( \Delta t \) in equation 1.) will be smaller and hence \( V(t) \) which depends on the second difference \( (\Delta t)^2 \) will be correspondingly reduced. Even within a species \( k_1 \) and \( k_2 \) will not be rigorously constant because the duration of the action potential is well known to depend on conduction velocity or fibers diameter (see Fig. 7 and Paintal, 1966, 1967) and the assumption of linearity between conduction velocity and diameter may not be valid. We have not examined these factors in detail, but have been satisfied to obtain approximate values of \( k_1 \) and \( k_2 \) to use in the design of suitable electrodes. For example, if we construct a regeneration electrode with holes of diameter \( d = 50 \mu \text{m} \) and length \( l = 1 \text{ mm} \), we would expect signal levels of 20 \( \mu \text{V} \) or more from equation 6.). (There may, however, be significant differences in the
Amplification and filtering of neural signals

The large background EMG signals and other sources of noise ( mains current, fluorescent lights, etc.) can be reduced by using the circuit shown in Fig. 4. Balancing takes place at three stages: 1) in the electrode array, by recording from the center electrode with respect to the two end electrodes, 2) by use of a transformer (Hammond 585D or 585F), 3) by use of a differential input to a standard low-noise physiological preamp (e.g. Grass Instruments Co., P15B).

The importance of a balanced electrode configuration in the rejection of EMG has already been demonstrated in Fig. 3. The use of the transformer has several functions. Most physiological preamplifiers have high input impedance \((\geq 10 \, \text{M} \, \Omega)\) and approach the minimum noise level theoretically possible (the so-called Johnson or thermal noise) with a high impedance source. However, these preamps are not optimized for low impedance sources. By using a transformer with a low impedance primary and a high impedance secondary the impedance can be matched to that which the preamplifier handles best. Secondly, in "stepping up" the impedance, the voltages recorded can also be amplified. The Johnson noise level increases only as the square root of the source impedance, so an increase in signal-to-noise ratio equal to the square root of the amplification ratio is possible. For this reason transformers have long been advocated for human sensory nerve action potential studies (Buchthal & Rosenfalck, 1966).

Finally, the transformer provides useful filtering, as illustrated in Figs. 8 and 9. This statement requires some explanation, since normally preamplifiers are designed to operate with a wide range of frequency cuts and high input impedance, so as to distort the biological signal as little as possible. The input stage is often directly coupled to the preparation, since capacitative coupling could be detrimental to the common-mode rejection of the preamp and may increase the noise level. Filtering is done at a later, less sensitive point in the circuit. However, with direct coupling, transients can cause blocking of the preamp for some time and low-frequency movement artefacts are also troublesome. However, these low-frequency artefacts and low-frequency components in the EMG are reduced by the filtering characteristics of the transformer.

Fig. 8 shows the impedances of typical cuff electrodes one month after implantation. There is a fairly constant resistance at high frequencies which is mainly due to the resistance of the fluid filling the cuffs and their fibers. The resistance of a cylinder of saline of resistivity \(\rho\), length \(l\) and diameter \(d\) is (Mannard et al., 1974)

\[
R = \frac{\rho l}{\pi d^2}
\]

The sciatic and lateral gastrocnemius-soleus nerve cuffs shown in Fig. 8 had lengths \(l = 2.0\) cm and 1.2 cm, and diameters \(d = 0.34\) cm and 0.15 cm respectively. If the effective resistivity were \(\rho = 200 \, \Omega \cdot \text{cm}\) (Ruch & Patton, 1966), one would expect resistances of about \(R = 11000\) and \(3500\), in reasonable agreement with the observed values. Note, however, that the effective resistivity depends on the space occupied by the extracellular fluid (which has a relatively low resistivity), axoplasm and poorly-conducting materials such as myelin. The resistivity of the cuffs tends to increase with time, presumably due to the proliferation of connective tissue in the extra-cellular space.

In addition, the impedance varies inversely with frequency at the lower frequencies. This is presumably due to the capacitance of the electrode-saline interface (Robin- son, 1968; Pollak, 1974). The capacitance of such an interface is actually quite complex in that the impedance varies as a fractional power of the frequency (Pollak, 1974). The capacitance also tends to increase with time after implantation.
transformers as a function of frequency. Note that the impedances are highest at frequencies just above 1 KHz, whereas at low frequencies the impedances are much lower than that of the electrodes. Since the capacitance of the electrode and the transformer are effectively in series, only a small fraction of the nerve voltage will be dropped across the transformer at low frequencies. This will not be true at frequencies where the impedance is higher, so the transformer serves as a band-pass filter. This is shown quantitatively in Fig. 9 by plotting total amplification of the electrodes plus transformer as a function of the frequency. The response is best at frequencies near 1 KHz and low-frequency signals such as 60 Hz interference, movement artefacts, and EMG are strongly rejected.

The frequency response was determined by stimulating through one cuff (e.g., lateral gastrocnemius-soleus) and recording the potential evoked in a second cuff (e.g., sciatic). The responses were averaged and the fast Fourier transform was used to determine the magnitude of the components at each frequency 1) when the electrode was connected directly to the preamplifier, and 2) when the electrode was connected indirectly as shown in Fig. 4. The ratio of the magnitude of the components recorded with and without various transformers as a function of frequency was determined and is shown in Fig. 9. This ratio measures the extent to which a given frequency of signal will be amplified (ratio > 1) or attenuated (ratio < 1).

Note also in Fig. 9 that the two transformers behave differently with the two nerves. For a nerve with an impedance as high as that of the lateral gastrocnemius-soleus, there is little difference in the amplification of the signal, but the noise level is substantially greater with transformer D. Thus, transformer D provides a greater amplification of the neural components and better rejection of lower frequency signals such as the EMG. Therefore, transformer D is preferable for use with the sciatic nerve. These brief comments should indicate how one can begin to match the recording apparatus to a given nerve so as to optimize the transmission of desired signals and reject unwanted frequency components.

Further filtering can, of course, be included in the preamplifiers to reject low-frequency signals. Fig. 10 shows the spectrum of the signals recorded from a cuff electrode on the sciatic nerve of a cat while it was walking. Two peaks are seen, one at 200-300 Hz corresponding to the EMG, and a second one near 2000 Hz due to the neural component. Even with the transformer and some filtering, the EMG component in this example is still dominant. The frequency at which the minimum occurs between the two peaks is near 1000 Hz. A high-pass filter with a suitable frequency cut could further reduce the EMG component in Fig. 10.

The peak frequency of the neural component will depend on the length of the cuff. For a neural waveform with a peak-to-peak duration \( t_p \) msec, one might expect the peak frequency component \( f_p \) in kHz to be

\[ f_p = \frac{1}{2t_p} \]

since the peak-to-peak measurement represents only half a cycle. This characteristic frequency is shown on the right of Fig. 7. The peak is relatively independent of cuff length until lengths are reached (approximately 1 cm) at which the waveform lengthens out markedly. The neural signals will then have lower frequency components and be relatively harder to distinguish from the EMG.

Physiological and clinical applications

At this stage of their development, we have been forced to consider mainly the technical aspects of these methods, so that reliable recordings can be obtained from freely-moving chronic animals. We have now had cuff electrodes implanted in cats and functioning for over six months, and have implanted up to four cuff electrodes in one animal. Once the method is developed and tested adequately, there are several immediate applications. Firstly, a rectified and filtered signal such as shown in Fig. 2 can be used to measure the relative activity of different nerves under different behavioural conditions. While techniques for single unit recording have added greatly to our knowledge of physiological mechanisms, there is also a need for methods of estimating the total amount of activity during normal function. The only available method has been to use gross surface electrodes. These electrodes record attenuated and distorted signals from a variety of sources which often cannot be clearly defined.

There are also recently developed methods of analysis using recordings from more than one electrode which are based on cross-correlation (Mann, 1973; Heetderks & Williams, 1975) and optimal filtering techniques (Roberts & Hartline, 1975). These techniques permit different groups of fibers to be distinguished on the basis of conduction velocity, waveform, etc. Thus, in addition to measuring the total nerve activity, this activity can be partitioned into one or more afferent and efferent components so that the function of different fiber groups can be studied in normal behaviour. This should be particularly useful in motor systems where the functions during posture and locomotion of various, clearly defined afferent and efferent groups of fibers are still controversial (Stein et al., 1973; Stein, 1974).

The methods also have obvious clinical applications, for example in prosthetics. An amputee may have stumps of some muscles which can provide signals to control a powered artificial limb. However, there will be no remnants of other, more distal muscles, even though the nerve fibers are still present. Cuff electrodes could provide a means of recording chronically from these nerve fibers and the signals would serve as a source for controlling other degrees of freedom in an artificial limb. Since

242 - AUGUST 1975

Chronic Neural Recording
the nerves are ligated, there would be no sensory information and the signals from the smaller γ-motorneurons are too small to be recorded in the larger human nerves. Thus, a good measure of α-motorneuronal activity should be provided by the cuff electrodes. However, it remains to be shown that the signals from a ligated nerve are maintained more or less indefinitely at useful levels. Cuff electrodes may also be useful as a stimulating electrode on sensory nerves to provide feedback from the artificial limb, and thereby improve its effectiveness. These applications in basic physiological research and in clinical areas are being pursued vigorously by our group in Edmonton and others in various centers.

Finally, we wish to point out that we are aware of potential misuse developing in the future from refinements to this system. The degree of specificity and discreteness of stimulus site and recording site implied in the use of small nerve bundles will inevitably lead to increased interaction between the information flow within the human body and information systems outside the body. Neural signals which until now have been private information flowing within the individual are becoming accessible to outside monitoring and modification. We feel that such a powerful method for the control and modification of individual thought and behaviour will not go unnoticed by those who believe in the desirability of controlling the thought and behaviour of others. We openly welcome discussion on this matter, and encourage you to make suggestions both verbally and in print. We hope that other workers in this field will have the courage to mention this important potential abuse of their work. Hopefully a policy will be developed concurrently with the technological development which states that direct neural connections should be used for prosthetic aids only, and not for conditioning (including aversion therapy) or information retrieval not directly related to a prosthetic application (e.g., lie detection for governmental or employment purposes). In no case shall the privacy, dignity, freedom or individuality of the subject be compromised.

**DISCUSSION**

Jasper (Montreal) commented on the distortion of the action potential which occurred with cuff electrodes. Stein replied that the actual form of the action potential was not important for his particular purposes. He was interested mainly in a signal of maximal amplitude which could be related to either the total level of voluntary contraction or the level of sensory feedback, depending on the nerve which was being used. Diamond (Hamilton) questioned whether the placement of a chronic cuff around a nerve might interfere with axoplasmic transport. Stein thought this unlikely because the nerves continued to function in apparently normal fashion for prolonged periods of time while the cuff was on, and also because ultrastructural studies had not shown any significant differences between nerves with and without cuff.

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