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IMPLANTABLE ELECTRICAL AND MECHANICAL INTERFACES WITH NERVE AND MUSCLE

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The past ten years have witnessed the introduction of several new methods for chronic recording of electrical activity in peripheral nerves, single nerve fibers and muscles, and for monitoring mechanical events correlated with muscular action. Although these methods were developed as research tools in the study of movements of unrestrained, intact animals, such implantable interfaces with nerve and muscle also promise to be of value in clinical applications; some novel clinical efforts are already being pursued. A review is given of various new techniques that may be clinically applicable and the issues of surgical constraints, quality of signal isolation, and long-term reliability of implantable devices, which ultimately determine the usefulness of each method, are discussed. Experimental devices reviewed include nerve cuff electrodes, floating single-unit electrodes, EMG electrodes, length gauges, and force gauges. General considerations for potential clinical applications are then given.

At least two classes of severely disabling clinical problems may warrant considering the use of implanted devices for the control of prostheses: high-level arm amputations (particularly bilateral) and spinal cord injuries. Experimental ligation of peripheral nerves in cats (1) has shown that the proximal stumps of most severed motor nerve fibers may remain viable indefinitely. Furthermore, motoneurons chronically disconnected from their target muscles continue to be activated in the appropriate patterns characteristic of locomotion in cats (2). Thus, in amputees, the stumps of peripheral nerves that originally projected to the missing limb musculature could be used as sources of output signals to control prosthetic limbs. In addition, sensory information arising from transducers in the prosthesis could be relayed back to sensory nerve fibers in amputated nerves, using electrical stimulation. In spinal cord injury patients the peripheral sensorimotor

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system remains viable but disconnected from the central nervous system, and the challenge is now to reestablish some semblance of the two-way traffic that normally allows motor centers to control movements and to monitor sensory inputs. Thus, potential solutions to these clinical situations hinge on the ability to interface external devices with the neuromuscular system.

DESCRIPTION OF EXPERIMENTAL DEVICES

Nerve Cuff Electrodes

Whereas functional electrical stimulation of nerves has been used clinically for over 100 years (18), the technical challenge of recording electrical activity from intact mammalian nerves using permanently implanted electrodes was met only quite recently. Frank (25) was able to record activity from fine cat dorsal root filaments in continuity for up to two weeks. The first successful chronic preparation focused on recording from fine muscle nerve branches about 200 μm thick (3,5). Similar electrodes have since been used to record from much larger nerves, up to 3 mm thick (1, 20). Longitudinally slit silastic cuffs are implanted around a nerve in continuity, which is freed from surrounding tissue. The long-term success of a cuff implant depends on not disturbing the local blood supply to the nerve, on selecting a site that does not undergo much relative movement, and on avoiding leadout cable routes that might impose torques on the nerve. In general, cuffs implanted around nerves coursing within large body segments fare much better than near joints.

Signal amplitude depends on the internal dimensions of the insulating cuff, the interelectrode separation, and the number and types of active fibers in the nerve (14). Unitary potentials of up to 80 μV have been discriminated from fine, high impedance nerve filaments (3), whereas the aggregate neural activity recorded from larger nerves like the cat's sciatic ranges between 5 and 10 μV during walking (2). A balanced tripolar electrode configuration and a tight cuff seal are required to reject the much larger EMG signals generated by neighboring muscles. Since neural power spectra peak at a higher frequency (2000 Hz) than EMG (200 Hz), filtering can further improve signal isolation. When two adjacent tripolar electrodes are installed in a cuff, afferent and efferent fiber traffic can be segregated by conduction delays (3), allowing the use of temporal cross-correlation techniques to quantify them independently (2). Recording cuff electrodes have been used to monitor long-term changes in nerve fibers following axotomy and regeneration (1) and to study patterns of activation of normal, axotomized, and regenerating nerves during walking (2). Over 100 cat hindlimb nerves were implanted and followed for periods of up to two years. A nerve cuff of similar design recently implanted around the ulnar nerve stump of an arm amputee (21, 22) will be described in a later section.

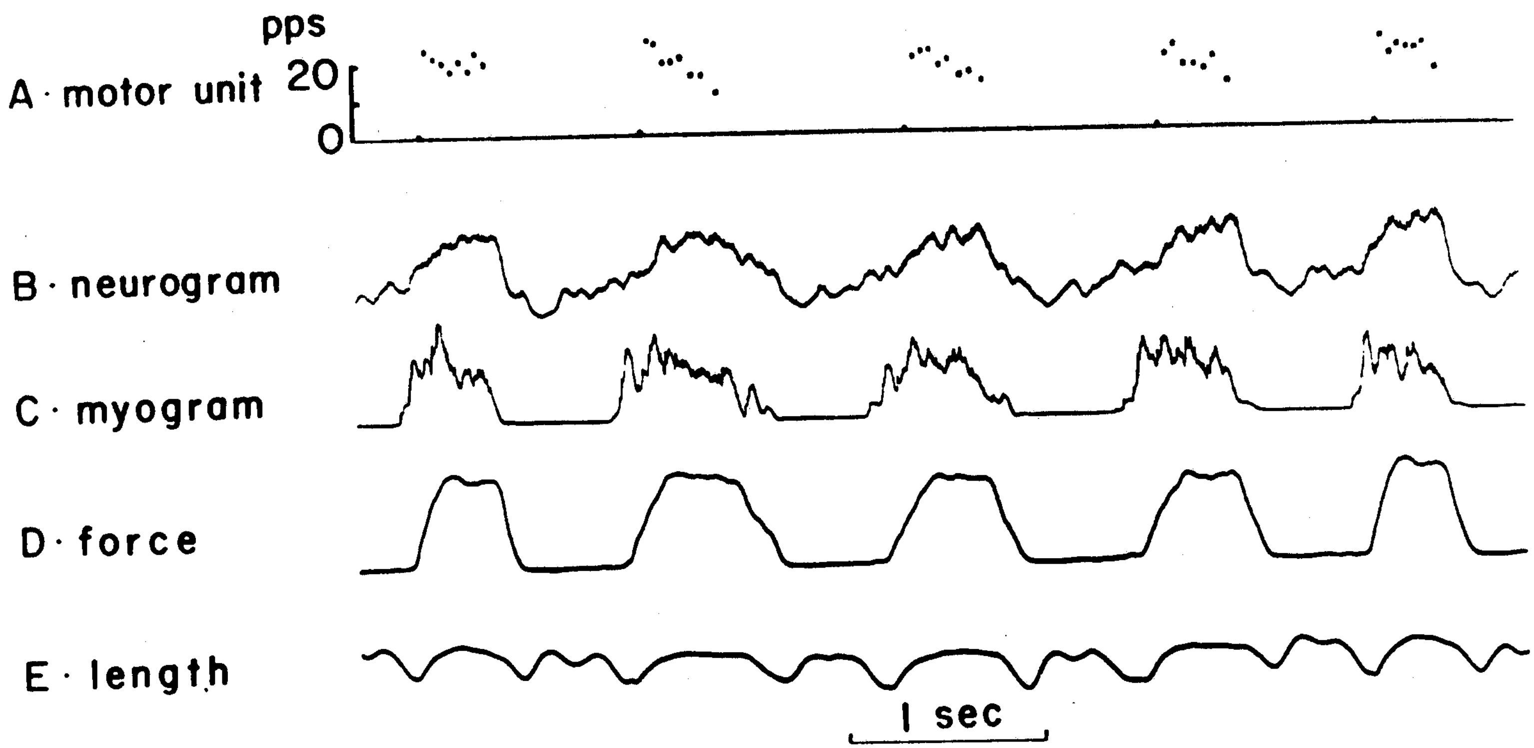

FIGURE 1. Simultaneous records of activity during walking obtained from five different chronically implanted devices in a cat's hindlimb: (A) instantaneous frequencygram of a single motor unit projecting to vastus medialis, recorded from a floating wire microelectrode inserted in the L5 ventral root; (B) rectified, low-pass filtered (3rd order filter, 20 Hz) record of the aggregate neural activity in the intact femoral nerve, obtained from a nerve cuff electrode; (C) rectified, low-pass filtered record of EMG obtained from a spiral bipolar electrode implanted deep in the vastus medialis muscle; (D) direct output of a dc-bridge amplifier connected to an implanted strain gauge monitoring the force developed at the patellar ligament; (E) dc output of an ac-bridge amplifier connected to an implanted length gauge monitoring the length of vastus medialis. All signals have been suitably amplified to operate in the ± 2 V range.

Floating Single-Unit Electrodes

Implanted nerve cuffs can provide a very secure, stable, long-term electrical coupling with a population of nerve fibers, but in general cannot be used to monitor the activity of single fibers because of the large contact area of the electrodes. Single-unit records demand the insertion of small surface area electrodes that monitor the action current flowing in a very restricted volume of tissue. Chronically implanted flexible wire electrodes have been used recently to record from cells in the motor cortex of monkeys (19), cat dorsal root fibers (17), dorsal root ganglion cells (9), and ventral root fibers (6). The most successful electrode designs have been of the "hatpin" version: a fine, very stiff wire (iridium or platinum–iridium, 25–50 μm thick, 1–4 mm long) is welded to a finer, very compliant leadout wire [gold, 25–37 μm;(26)]. The weld is protected with a small ball of epoxy, and the electrode assembly is insulated with Parylene (10). A recording surface is created at the end of the stiff wire by blunt cutting, yielding reasonably low impedance values (100–200 kΩ), or by etching. Such electrodes are easy to insert, even in ganglia which have a thick matrix of connective tissue, and are mechanically quite stable in spite of the substantial movement that these peripheral tissue structures undergo normally. As many as 4 units can be discriminated from individual electrode records from walking cats, with unitary potentials typically 50–100 μV, occasionally as large as 1–2 mV. Electrodes tend to move slowly in the tissue, so that individual units are typically held for 1–2 days, occasionally for up to 3 weeks. Recorded units can sometimes be microstimulated in isolation by passing current through the same electrode, which is particularly valuable for the characterization of single motor units (6,7). Up to a dozen electrodes can be implanted simultaneously in the cat's L5 dorsal root ganglion and/or ventral root. Individual electrodes may sample units for two months or longer. Failures are usually due to leadout wire breakage, local tissue damage, and/or electrode tip encapsulation which separates the electrode tip from the unit and reduces signal amplitude. Practical considerations such as durability and stability of unitary recordings make current versions of single-unit electrodes less desirable for prosthetic applications, although the potential power of methods for coupling to single units, reviewed by Schmidt (this symposium), cannot be denied.

EMG Electrodes

Recordings from single motor units in intact cats have shown that once a unit is recruited, its frequencygram closely resembles the rectified, filtered EMG envelope of the muscle of destination (6,7). In human subjects who were asked to voluntarily control the firing rates of single motor units, the rate of information transfer achieved was about the same as when the whole muscle EMG was the controlled variable (23). Thus, for practical purposes EMG recordings may be just as useful as single motor unit recordings, and the technical approach is considerably easier.

Although the electrical activity of superficial muscles can often be recorded from the surface of the skin, indwelling electrodes have several advantages that may warrant consideration of their use in certain cases: [1] the mechanical and electrical coupling to the source is much more stable, being impervious to changes in skin resistance; [2] impedances are lower reducing noise-related problems; [3] signal amplitudes are larger; [4] cross-talk from other muscles is often much reduced; and [5] stimulus artifact that can be caused by close proximity to sensory feedback stimulators is eliminated or much reduced.

In recording the electrical signals generated by active muscles, a compromise must typically be struck between two conflicting objectives: obtaining large, smoothly graded signals representing a population of motor units, while at the same time keeping cross-talk from neighboring muscles to a minimum. In addition, electrodes must be rugged enough to withstand the continued muscle length changes, and must be attached securely to prevent migration over time.

In order to maximize rejection of unwanted signals from other muscles, differential recording from closely spaced electrode pairs is indicated ("bipolar" electrodes). A pair of teflon-insulated stainless steel wires exposed for several millimeters at the ends, tied together, looped into a muscle with a suture thread tied in place to fascia (11) can be satisfactory for a few weeks, but may migrate out of the muscle. Longer-lasting attachment is obtained by sewing bipolar electrodes to a square of Silastic film which is anchored with sutures to the fascia along the surface of a muscle (3). EMG electrodes of this design were implanted on the surface of four forearm muscles in an amputee, rendering stable, well isolated signals (21, 22). There may be a tendency, however, for connective tissue encapsulation and eventual migration away from the muscle surface. Also, recordings are biased in favor of superficial fibers since surface electrodes sample poorly from deep fibers of the same muscle. Pairs of platinum–iridium stranded wires coiled around a Silastic core with a short segment of each wire exposed at regular intervals can sample a larger volume of muscle when the device is inserted along the longitudinal axis of the muscle, while still retaining adequate common-mode rejection properties for signals from other muscles. This design, however, demands that the coiled wires be subjected to considerable length changes, with reduced durability. Whenever possible, EMG recording should be attempted from the surface of a muscle, preferably near a region where the muscle is attached to bone to insure electrode stability. Surface EMG electrodes attached to the fascia usually cause the least damage to a muscle, are the easiest to install surgically, and are subjected to less severe mechanical demands than deep EMG electrodes, and thus should be favored in clinical applications.

Length Gauges

A simple, convenient way to monitor length changes between two points (e.g., between the origin and insertion of a skeletal muscle) is to implant a mercury- or saline-filled, sealed rubber tube anchored to bone or tendon at its ends (13,16). Since changes in length and cross-section of the constant volume tube cause changes in electrical resistance of the fluid column, the voltage generated by an electrical current injected via electrodes sealed into the ends of the tube will vary accordingly. The saline-filled design is particularly convenient, since it does not carry risks in case of leakage, and can be operated with ac carrier signals at frequencies that do not interfere with nerve and muscle potentials. Typically a 40 kHz signal is used to drive an ac bridge, with the length gauge as one of the arms. Filling the slighty permeable tubing with hypertonic saline (5X isosmolar) causes the gauge to become osmotically pressurized in body fluids. This decreases the possibility of the gauge becoming kinked or flattened by surrounding tissue. Linearity can be a problem, since gauge impedance is not a linear function of its length, and furthermore the path of the tube can be affected by bulging of muscles. However, records are extremely reproducible and can be calibrated as needed from externally measured parameters. A drawback of these devices is their durability. When implanted in cat hindlimbs, length guages typically remain functional for 1–3 months, but they do tend to fail eventually, as can be expected from any device that is subjected to continued mechanical deformation. Further, attachment sutures causing sustained tension in bone or tendon can result in pressure necrosis and can work loose.

Force Gauges

Excellent records of the force developed by a muscle, or group of muscles, on a tendon or ligament can be obtained using deformable spring steel gauges carrying semiconductor strain detectors (13,24). A pair are bonded to opposite sides of the steel substrate which is shaped like a letter "E" and is clipped onto the intact tendon, causing little or no damage. A dc bridge provides a signal which varies proportionally to the amount of deformation impressed on the gauge by tension along the tendon. Signal outputs are quite linear over a wide dynamic range, reaching 40 kg for the patellar ligament of cats during fast walking, while also permitting measurements of single-unit twitch tensions (of the order of 1 g) with the use of averaging techniques. Implanted force gauges have functioned in cats for periods of 2–3 months. Failures have been attributed to leakage through cracks developed in the Parylene coat which protects the sensing elements from the saline environment.

POTENTIAL CLINICAL APPLICATIONS

General Considerations

The use of invasive techniques always entails risk of postoperative infection. In particular, percutaneous passage of connecting wires must be avoided if at all possible. The body can deal reasonably well with biocompatible foreign objects introduced in its midst, but devices that cross through the skin inevitably provide a path for infection. For practical reasons the devices described here, when implanted in experimental animals, have been connected to external equipment through cables crossing the skin, because of the large number of signal channels used (up to 50) and the relatively short duration of experiments (typically 2–3 months). However, any of these devices could be operated in conjunction with appropriate telemetry, avoiding percutaneous invasion. Materials that come in contact with tissue (Silastic, Parylene, platinum–iridium, stainless steel) were chosen for biocompatibility and survival in the body's hostile environment (12).

In arm amputees the severity of the disability is compounded for higher levels of lesion, since the number of functions to be substituted increases while the number of potential EMG control sites at the skin surface decreases. In the extreme case of shoulder disarticulation, a minimum of seven degrees of freedom ought to be provided in a prosthesis (hand opening/closing, wrist flexion/extension, wrist pronation/supination, elbow flexion/extension, shoulder abduction/adduction, shoulder flexion/extension,

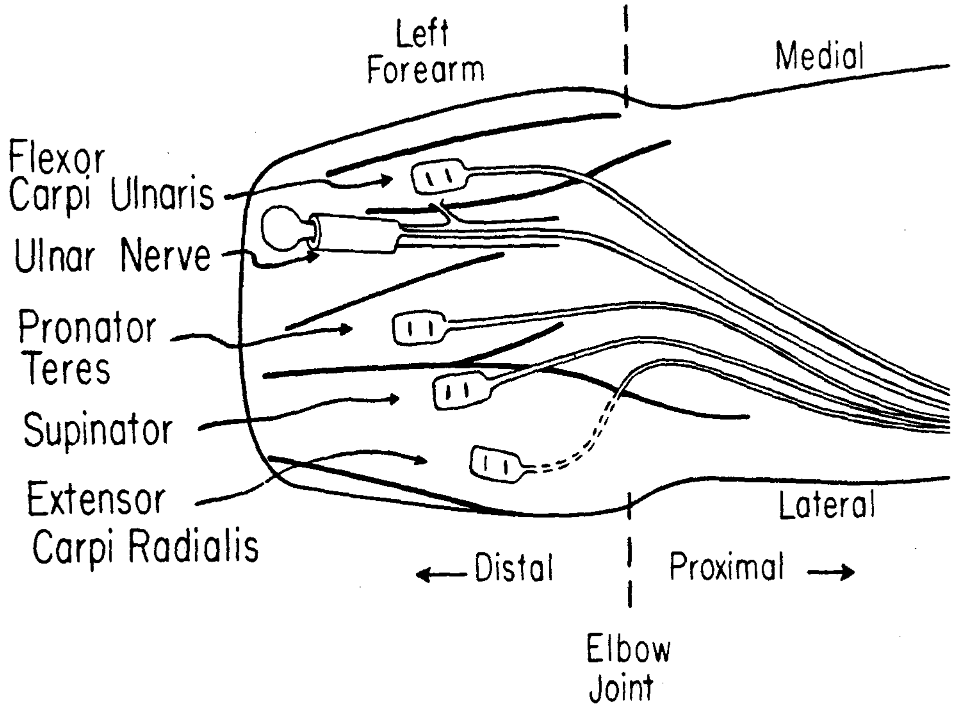

FIGURE 2. Diagram indicating four chronically implanted bipolar EMG electrodes attached to the fascia of four muscles (wrist flexor, wrist extensor, pronator, and supinator) and a nerve cuff implanted around one large fascicle of the ulnar nerve, distal to the last functional motor branch and proximal to the neuroma, in a short below-elbow amputee (21,22). Leadout cables converged onto a 12-pin socket in a vitreous carbon percutaneous connector that emerged through the skin along the side of the upper arm.

shoulder rotation) to match the range of movements of the normal arm. However, only remnants of the shoulder girdle musculature may be available for surface EMG recordings. In addition, the signal source sites are functionally remote from the tasks to be substituted. However, a heretofore untapped source of control signals lies tucked inside the body: the severed brachial plexus nerves, which previously supplied the very muscles that must now be substituted.

Data from cuff electrodes placed around the proximal stumps of severed, ligated peripheral nerves in cats indicate that although the diameters of axotomized nerve fibers are reduced (1), cut motor nerve fibers continue to be activated in the correct pattens during walking (2). Fiber shrinkage following axotomy is more severe in sensory fibers than in motor fibers of the same nerve (8). When nerves are allowed to regenerate and reinnervate muscle or skin, axon diameters and extracellularly recorded potentials increase again; this recovery process takes place in both sensory and motor fibers (4). However, even in an ulnar nerve severed 30 years earlier, and terminating in a neuroma, it has been possible to elicit graded sensations using trains of low current stimuli (10 μsec X 5 mA pulses) delivered through an implanted cuff electrode (21,22). During electrical stimulation the amputee reported tingling sensations referred to the small and ring fingers—the normal innervation field of the ulnar nerve. He was also able to discriminate changes in stimulus rate up to about 20 Hz; for higher frequencies he reported either a fused sensation or no sensation at all.

Since implanted cuff electrodes can be used successfully to render sensory information by stimulating severed nerves, it is conceivable that in a high-level amputee a number of different limb parameters could be monitored by sensors in the prosthesis (e.g., grip force, angular position, velocity), encoded as stimulus pulse trains, and fed into different severed nerves via separate cuff electrodes implanted in the brachial plexus.

Motor signals from severed nerves may or may not be recordable in amputees. Since severed fibers undergo considerable shrinkage, extracellular neural potentials may be reduced beyond resolution from background EMG and noise. However, since regenerated axons increase in diameter again after forming new functional connections with muscle, nerve–muscle grafting is a method available for signal enhancement. Severed nerves of interest in the brachial plexus could be grafted to neighboring regions of muscle, which in turn would be denervated to provide an appropriate target for cross-reinnervation. In animal cross-reinnervation experiments, neural signals are indeed enhanced after successful grafting (1,2,4).

Alternatively, this grafting technique might allow for the recording of EMG signals directly from a mosaic of cross-reinnervated muscles, thus taking advantage of the signal amplification properties inherent in the neuromuscular system. However, it is likely that such grafts would also undergo considerable self-reinnervation, a process which is in general very difficult to prevent completely and which would in this case render complex, multimodal EMG patterns. In contrast, neural motor signals recorded from nerves grafted to a muscle mosaic would show no such cross-talk, since the central connectivity of cross-reinnervated nerve cells does not appear to change substantially (2). Discharge patterns recorded from crossed peripheral nerves remain appropriate for the original functions of those fibers, regardless of any changes in distal connectivity introduced by cross-reinnervation.

The situation is different in spinal cord injury patients. In attempting to reestablish functional continuity between the central nervous system and the peripheral neuromuscular system, several chronic recording techniques may be applied at the peripheral end to obtain somatosensory and proprioceptive information from limbs: force transducers on tendons, length gauges across joints, nerve cuffs to record afferent traffic along cutaneous or motor nerve branches, and, in theory but probably not currently feasible in practice, single-unit electrodes inserted in spinal ganglia to record afferent activity. (The latter technique is less appealing since at this time it cannot guarantee long-term coupling to signal sources, and it requires riskier surgery.) Signals obtained from force or length transducers or from nerve cuffs could be used directly in the servoregulation of neuromuscular electrical stimulation, thus reestablishing some semblance of a spinal reflex loop. In addition, it would be desirable to make sensory information available directly to the patient. This could be done using skin surface stimulation or stimulation via electrodes implanted in body regions above the level of lesion.

To provide motor control of paralyzed musculature, functional electrical stimulation might be better achieved using several electrodes inside cuffs implanted on nerve branches to muscles of interest, rather than using conventional percutaneous wire electrodes (15). Direct stimulation of axons via cuff electrodes would reduce or eliminate typical problems of electrode drift, electrode breakage, and spontaneous threshold changes, although the added risks of invasive techniques must be kept in mind.

REFERENCES

1. Davis, L.A., T. Gordon, J.A. Hoffer, J. Jhamandas, and R.B. Stein. Compound action potentials recorded from mammalian peripheral nerves following ligation or resuturing. *J. Physiol.* 285: 543-559, 1978.
2. Gordon, T., J.A. Hoffer, J. Jhamandas, and R.B. Stein. Effects of axotomy on neural activity during cat locomotion. *J. Physiol.* 303:243-263, 1980.
3. Hoffer, J.A. Long-term peripheral nerve activity during behaviour in the rabbit: The control of locomotion. Ph. D. thesis, Johns Hopkins University, November 1975. Publ. No. 76-8530, University Microfilms, Ann Arbor, Michigan; 124 pp.
4. Hoffer, J.A., T. Gordon, and R.B. Stein. Differential atrophy of sensory and motor fibers following ligation or resuture of cat hindlimb nerves. In: *Nerve Repair: Its Clinical and Experimental Basis,* edited by D.L. Jewett and H.R. McCarroll. St. Louis: C.V. Mosby, 1980, pp. 163-165.
5. Hoffer, J.A., W.B. Marks, and W.Z. Rymer. Nerve fiber activity during normal movements. *Neurosci. Abstr.* #300, 1974.

6. Hoffer, J.A., M.J. O'Donovan, and G.E. Loeb. A method for recording and identifying single motor units in intact cats during locomotion. *Neurosci. Abstr.* 5:1248, 1979.
7. Hoffer, J.A., M.J. O'Donovan, C.A. Pratt, and G.E. Loeb. Recruitment order and firing patterns of identified cat hindlimb motor units during unrestrained walking. *Neurosci. Abstr.* 6:761, 1980.
8. Hoffer, J.A., R.B. Stein, and T. Gordon. Differential atrophy of sensory and motor fibers following section of cat peripheral nerves. *Brain Res.* 178:347-361, 1979.
9. Loeb, G.E., M.J. Bak, and J. Duysens. Long-term unit recording from somatosensory neurons in the spinal ganglia of the freely walking cat. *Science* 197:1192-1194, 1977.
10. Loeb, G.E., M.J. Bak, M. Salcman, and E.M. Schmidt. Parylene as a chronically stable, reproducible microelectrode insulator. *IEEE Trans. Biomed. Eng.* 24: 121-128, 1977.
11. Loeb, G.E. and J. Duysens. Activity patterns in individual primary and secondary muscle spindle afferents during normal movements in unrestrained cats. *J. Neurophysiol.* 42:420-440, 1979.
12. Loeb, G.E., J. McHardy, E.M. Kelliher, and S.B. Brummer. Neural prosthesis. In: *Uniscience Series–Biocompatibility in Clinical Practice,* Vol. II, edited by D.F. Williams. Boca Raton, FL: CRC Press, in press.
13. Loeb, G.E., B. Walmsley, and J. Duysens. Obtaining proprioceptive information from natural limbs: Implantable transducers vs. somatosensory neuron recordings. In: *Solid State Physical Sensors for Biomedical Applications,* edited by M.R. Neuman, D.G. Fleming, P.W. Cheung, and W.H. Ko. Cleveland, Ohio: CRC Press 1980.
14. Marks, W.B., and G.E. Loeb. Action currents, internodal potentials, and extracellular records of myelinated mammalian nerve fibers derived from node potentials. *Biophys. J.* 16:655-668, 1976.
15. Peckham, P.H. and J.T. Mortimer. Restoration of hand function in the quadraplegic through electrical stimulation. In: *Functional Electrical Stimulation,* edited by F.T. Hambrecht and J.B. Reswick. New York: Marcel Dekker, 1977.
16. Prochazka, A., R.A. Westerman, and S.P. Ziccone. Remote monitoring of muscle length and EMG in unrestrained cats. *Electroencephalogr. Clin. Neurophysiol.* 37:649-653, 1974.
17. Prochazka, A., R.A. Westerman, and S.P. Ziccone. Discharges of single hindlimb afferents in the freely moving cat. *J. Neurophysiol.* 39:1090-1104, 1976.
18. Schecter, D.C. Application of electrotheraphy to noncardiac thoracic disorders. *Bull. N. Y. Acad. Med.* 46:932, 1970.
19. Schmidt, E.M., M.J. Bak, and J.S. McIntosh. Long-term chronic recording from cortical neurons. *Exp. Neurol.* 52:496-506, 1976.
20. Stein, R.B., D. Charles, T. Gordon, J.A. Hoffer, and J. Jhamandas. Impedance properties of metal electrodes for chronic recording from mammalian nerves. *IEEE Trans. Biomed. Eng.* 25:532-537, 1978.
21. Stein, R.B., D. Charles, J.A. Hoffer, J. Arsenault, L.A. Davis, S. Moorman, and B. Moss. New approaches to controlling powered arm prostheses, particularly by high-level amputees. *Bull. Prosthet. Res.* BPR 10-33:51-62, 1980.
22. Stein, R.B., T. Gordon, J.A. Hoffer, L.A. Davis, and D. Charles. Long-term recordings from cat peripheral nerves during degeneration and regeneration: Implications for human nerve repair and prosthetics. In: *Nerve Repair: Its Clinical and Experimental Basis* edited by D.L. Jewett and H.R. McCarroll. St. Louis: C.V. Mosby, 1980, pp. 166-176.
23. Thomas, J.S., E.M. Schmidt, and F.T. Hambrecht. Facility of motor unit control during tasks defined directly in terms of unit behaviors. *Exp. Neurol.* 59:384-395, 1978.
24. Walmsley, B., J.A. Hodgson, and R.E. Burke. Forces produced by medial gastrocnemius and soleus muscles during locomotion in freely moving cats. *J. Neurophysiol.* 41:1203-1216, 1978.
25. Frank, K. Some approaches to the technical problem of chronic excitation of peripheral nerve. *Am. Otol. Rhin. Laryng.* 77:761-771, 1968.
26. Salcman, M. and M.J. Bak. A new chronic recording intracortical microelectrode. *Med. Biol. Eng.* 14:42-50, 1976.