Perspectives on New Electrode Technology for Stimulating Peripheral Nerves with Implantable Motor Prostheses

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Abstract—The limits of present electrode technology are being reached in current motor prostheses for restoring functional movement in paralyzed people. Improved devices require electrodes and stimulation methods that will activate muscles selectively and independently with less implanted hardware. A practical functional neuromuscular stimulation (FNS) system may need to employ extraneural, intraneural, epimysial, or intramuscular electrodes or a combination of these types. The limitations of current muscle electrodes and the anatomy of peripheral nerve innervation of muscle have pointed to stimulation of peripheral nerve trunks as a promising area for investigation. Attempts to use conventional (extraneural) peripheral nerve electrodes for selective activation of muscles in chronic applications have met with only limited success. Intraneural (intrafascicular) electrodes offer the advantages of greater selectivity and lower power requirements, but these may be offset by the difficulty of inserting delicate electrodes through the collagenous epineurium and perineurium while avoiding unacceptable amounts of trauma. Cuff electrodes require more power than intrafascicular ones but may provide more stable recruitment patterns over time, and the opportunity for retrieval and replacement.

I. INTRODUCTION:
IMPROVEMENT OF MOTOR PROSTHESES THROUGH STIMULATION OF PERIPHERAL NERVE TRUNKS

THE SUCCESS of current implantable motor prostheses in restoring functional movement to paralyzed people [1], [2] has increased demand for even more limb function, pressing the limits of present electrode technology. With at least one intramuscular or epimysial electrode used for each muscle, the number of muscles activated is limited by the number of electrodes that can be physically tolerated and the number of available stimulator channels. Anatomical features further restrict the sites and ease of implantation of muscle electrodes [2]. Finally, muscle electrodes exhibit

spill-over of activation to neighboring muscles and length-dependent recruitment characteristics that degrade the control of functional movements [3].

Improved motor prostheses require electrodes and stimulation methods that will activate muscles selectively and independently with less implanted hardware. We expect that a practical functional neuromuscular stimulation (FNS) system would employ some combination of extraneural, intraneural, epimysial, and intramuscular electrodes. The use of conventional (extraneural) peripheral nerve electrodes for applications other than on-off activation of muscles in chronic applications is essentially nonexistent. Intraneural (intrafascicular) electrodes potentially offer the advantages of greater selectivity and lower power requirements, but these may be offset by the difficulty of inserting delicate electrodes through the collagenous epineurium and perineurium while avoiding unacceptable amounts of trauma.

Work at Huntington Medical Research Institutes over the past eight years has helped to delineate the range of stimulation parameters at which peripheral nerves can be safely and effectively stimulated with extraneural electrodes [4]–[6]. These studies indicate that damage to nerves by electrical stimulation can be avoided, provided certain guidelines are followed. However, another, possibly greater, concern is the possibility of mechanical injury to nerves inflicted by the implantation and residence of stimulating electrodes.

Anatomical [7], [8] and electrical stimulation [6] studies have shown that in the more distal sections of a nerve trunk, motor axons are arranged into discrete fascicles that eventually branch from the main trunk to innervate single muscles or small groups of muscles. Thus, localizing an excitatory field to a discrete region of a nerve trunk should allow selective activation of an individual muscle without activation of other muscles served by different regions of the same nerve trunk.

An ideal extraneural electrode would need to be fabricated of soft pliable material, be able to survive indefinitely in the environment of tissue fluids, and would not induce tissue reactions or mechanical injury. At the same time, it would have adequate "claspability" to avoid dislodgment and ensure very close electrical contact with the nerve. In addition to showing the same biochemical characteristics, the ideal intrafascicular electrode would permit easy insertion through the epineurium and perineurium. Also, it would be able to flex with undulations of the nerve during muscle movement, avoiding shearing forces between the nerve fibers and the electrode.

This paper explores new approaches to electrode technology and stimulating techniques that selectively activate specific portions of a peripheral nerve trunk with much less implanted hardware than is required with present motor prosthesis systems. The first section reviews the vulnerability of nerves to both mechanical and electrical factors and considers how these findings might be utilized in future electrodes. The second section presents results on longitudinally oriented intrafascicular electrodes for both nerve stimulation and recording. The third section reviews results on nerve cuff electrodes and compares the Huntington and Case Western Reserve University designs. The fourth section raises issues of concern to clinicians and device manufacturers that investigators need to consider throughout the device development process.

II. PROBLEMS IN SELECTIVE STIMULATION OF NERVES, *William F. Agnew*

At the Neurological Research Laboratory of Huntington Medical Research Institutes, we have studied the problem of mechanical and electrical injury of peripheral nerves on or in which electrodes have been implanted.

A. Mechanically Induced Damage with Extraneural and Intraneural Electrodes

Most of our studies have been conducted with the "Huntington Helix" extraneural electrode array which has two coils of platinum or activated iridium ribbons embedded in silicone elastomer. The coils have a nonslip feature (counterdirectional coiling of the helices at either end of the array) and are self-sizing to conform snugly to the nerve. Incidence of neural damage with this electrode compares favorably to other types of extraneural cuff electrodes [9]. When our electrodes were implanted on the sciatic nerves of cats for 4–6 weeks, three of 30 electrode sites sustained slight mechanically induced damage. At autopsy, a positive correlation could usually be made between neural damage and the amount of traction exerted on the electrode by the cable, with attendant deformation of the nerve. Neural damage was characterized by endoneurial edema, subperineurial crescents of connective tissue resembling "Renaut Bodies," and, rarely, axonal degeneration and remyelinating fibers [10]. Recent work reported by Weis *et al.* [11] has indicated that the subperineurial connective tissue is an adaptive response which appears to provide a cushioning effect for the endoneurium. We have observed that lessening the tension exerted by the cable on chronically implanted electrode arrays significantly decreased the incidence and size of the connective tissue structures.

Whether for extraneural or intraneural applications, we believe that the problems presented by the electrode cable are a major challenge, particularly in electrodes implanted adjacent to muscles with large and repetitive muscle movements, a location which increases the chances for tension on the cable and traction on the electrode array. Judicious routing of the cable and the use of recurrent (or extendable) cables have been of benefit, and such modifications are still being evaluated. The problems associated with electrode cables
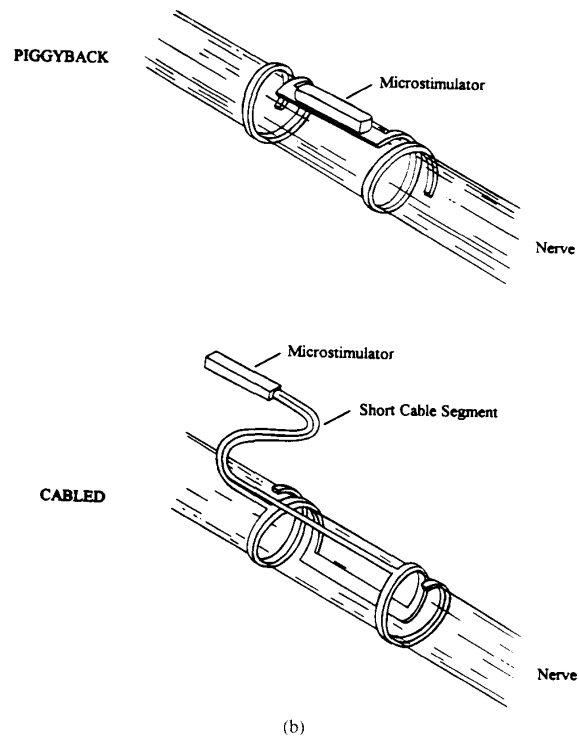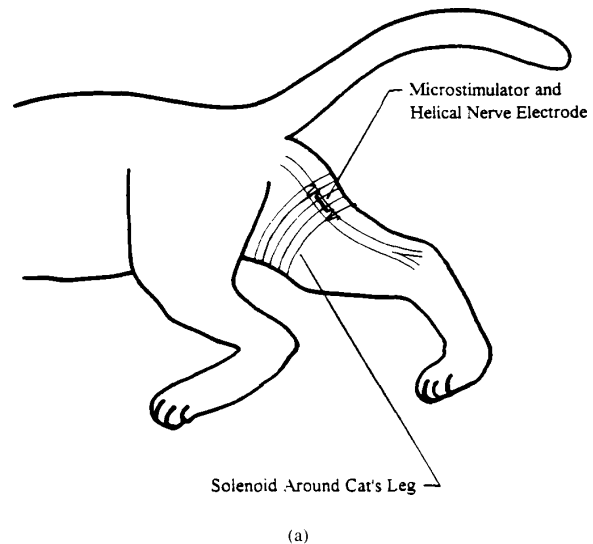

Fig. 1. Suggested utilization of implantable microstimulators to ameliorate the problems of chronically implanted cables leading to a multielectrode array on a peripheral nerve. Several stimulators can be addressed from one external antenna coil (solenoid), which also supplies the power for the implanted units (a). (b) One or more microstimulators could be integrated into the electrode array (top). Alternatively, to reduce the bulk of the array, one or more microstimulators might be connected to the array by a short cable segment (bottom). Microstimulators of this type are being developed by the NIH Neural Prosthesis Program (RFP-NIH-NINDS-94-11).

might be largely solved by the development of miniaturized cableless microstimulators that derive stimulation information and power via a transcutaneous radiofrequency link (Fig. 1).

Intraneural electrodes have been used in a few clinical applications for the control of facial pain [12] and for neuromuscular applications [13], [14]. Intraneural stainless steel coiled wires of 250 μm diameter, implanted in the sciatic nerves of rabbits and cats, produced no significant changes in nerve conduction velocities during nine weeks of implantation. However, bulbous formations of connective tissue, demyelination, and fiber loss were observed in 40% of the nerves [15]. These effects may be due to damage to the perineurium. In some acute studies, investigators have incised the epineurium and/or perineurium in order to facilitate intrafascicular placement of electrodes [16]; the long-term consequences of this very invasive procedure have yet to be determined. Sunderland [7] states that "lesions of the perineurium invariably result in neuromas and mass degeneration of axons, whereas removing the epineurium (as in neurolysis) is without harmful effects." Rydevik et al. [17] have emphasized that compromising the permeability of the perineurium results in loss of the pressure gradient across the perineurial membrane, with consequent endoneurial edema and interference with the intrinsic blood supply of the nerve.

We are currently collaborating with investigators at the University of Michigan to develop multisite, photolithographic silicon electrode arrays for intraneural use. In early experiments with these electrodes, we have encountered difficulty in inserting them through the epineurium and perineurium. There are problems with brittleness and stiffness of the electrode material. In recent experiments in our laboratory, we have used an intrafascicular electrode inserter for "depositing" multiple wire electrodes of varying lengths within the fascicle. The inserter is made of stainless steel tubing 250 μm in diameter with a sharpened (10°) tip. Up to seven wire electrodes or multisite photolithographic probes may be loaded into the inserter and deposited intrafascicularly as the inserter is passed completely through the nerve. Two weeks after the procedure, nerves through which the inserter alone was passed showed minimal damage: a linear scar through a portion of the fascicle. Nerves into which wire or silicon electrodes were deposited showed more severe damage: widespread endoneurial edema with or without degeneration of myelinated fibers. Much of the neural damage appears to be reversible and longer term implants are needed for complete histologic assessment.

B. Neural Damage Due to Electrical Stimulation

In animal studies, continuous stimulation of peripheral nerves at 50 Hz for 8–16 h using bipolar extraneural electrodes resulted in neural damage, provided that the stimulus amplitude was greater than that required to fully recruit all of the Group I and Group II axons. The damage was characterized by endoneurial edema within 48 h after stimulation and early axonal degeneration of large myelinated fibers by one week after stimulation [10]. Stimulation at a frequency of 50 Hz with lower pulse amplitude or delivered with intermittent duty cycle (1 s on, 1 s off) did not induce neural injury. Also, continuous stimulation of peripheral nerve using a frequency of 20 Hz was not damaging, even when

TABLE I
ELECTRODE POWER CONSUMPTION

PARAMETERS*	INTRANEURAL	EXTRANEURAL
• IMPEDANCE OF ELECTRODE-TISSUE INTERFACE (R)	40 KΩ	2 KΩ
• THRESHOLD STIMULUS (I)	20 μA	200 μA
• POWER: P = I^{2}R	16 μW	80 μW
• OPERATIONAL TIME: (4.5 WATT·HR, LITHIUM THIONYL CHLORIDE BATTERY)	651 DAYS	130 DAYS

*STIMULUS PARAMETERS: 50 HZ CONTINUOUS, PULSE WIDTH = 100 μS/PHASE (BIPHASIC); CALCULATIONS BASED ON A 24 HR. DAY

the pulse amplitude was many times greater than that required to recruit Group I and Group II axons [6], [10]. To date, we have no corresponding data on electrical stimulation of nerves by intraneural electrodes.

C. Selective Stimulation with Extraneural and Intraneural Electrodes

It seems fair to conclude that extraneural electrode arrays carry less risk of injury to the nerve and should be easier to implant than a large number of intrafascicular electrodes. However, extraneural electrodes for FNS have limited capacity to restrict the excitation of axons to a single fascicle or to part of a fascicle. Also, they have a strong tendency for reverse-order recruitment of motor units (the large axons tend to be recruited at the lowest stimulus current)

Several investigators have studied the activation function (the mathematical relation between the depolarization of the axon membrane, and the distribution of the voltage field in the surrounding extra-axonal compartment) both as a 3-D mathematical model and in the natural nerve [16]–[21]. Their consensus is that selective excitation of the axons within a particular fascicle may be possible with an array of extraneural electrodes, but only if the fascicle is near the surface of the nerve trunk; selective stimulation of fascicles deep within the nerve trunk will require the use of intrafascicular, or at least intraneural, electrodes.

Comparisons of acutely implanted, multiwire intraneural electrodes and the Huntington Helix extraneural electrode showed a five-fold advantage for the intraneural design in terms of power requirements, especially near the threshold current for nerve excitation (Table I).

Current knowledge suggests the feasibility of a chronically implantable electrode system that can achieve a high degree of selective excitation of the axons in a peripheral nerve [9], [15], [16], [18]–[21]. Such a system would probably include an array of extraneural electrodes close to the epineurium, and pulsed synergistically; it now seems clear that snug-fitting nerve electrodes are stable and safe, provided problems related to the cables can be overcome. The system would also probably include some intrafascicular microelectrodes to handle those situations in which it is necessary to selectively excite fascicles lying deep within the nerve trunk, or in which it is important to achieve a more natural order of recruitment of small and large motor units [16], [20], [22].

To capitalize on the capability of intrafascicular microelectrodes to achieve superior selective activation of different parts of the nerve, we will need surgical techniques that will allow a sufficient number of microelectrode arrays to be inserted into or between the fascicles without undue trauma, with reasonable ease, and in a reasonable amount of time. Animal studies are needed to assess the long-term consequences of multiple penetrations of the perineurium, and to determine if rigid silicon microprobes are acceptable for chronic implantation in a peripheral nerve, or whether a more flexible matrix is needed. Solutions to these problems should definitely be pursued, in view of the potential benefits of intraneural electrodes, particularly when used in conjunction with the appropriate extraneural arrays.

III. LONGITUDINAL INTRAFASCICULAR ELECTRODES FOR NERVE STIMULATION AND RECORDING,

Ken Horch

At the University of Utah, we have developed electrodes that are threaded longitudinally inside individual fascicles of peripheral nerves so that the active region of the electrode lies parallel to the axons in the nerve [23]. This active region is longer than the internodal distance of the nerve fibers of interest and can be used for stimulation of [24]–[26] or recording from [27]–[30] nerve fibers within the fascicle. This design was developed to provide selective activation of small sets of nerve fibers with low intensity stimuli by placing the electrode as close to the target tissue as possible, namely within the fascicle. The impedance barrier provided by the perineurium maintains good stimulus isolation between fascicles.

Placing a point source within the fascicle also allows the development of sufficiently sharp voltage gradients so that small fibers near the electrode are activated before more distant large fibers. This gives a closer approximation to the natural recruitment order of motor neurons [16], [22]. By extending a point source longitudinally, making it a line source with a length greater than the internodal spacing, we can ensure that the current source is in the immediate proximity of at least one node of Ranvier.

Proper control of FNS requires feedback from sensors about joint position, joint velocity, and skin contact. In principle, one can derive adequate feedback to control FNS by recording from a representative population of sensory nerve fibers within the fascicle. Very low impedance electrodes placed close to the nodal regions of myelinated axons can record the small extracellular potentials. Increasing the length of these electrodes decreases their impedance and increases the probability that they will lie near a node. However, the active zone must be less than one quarter the wavelength of the action potential (conduction velocity times pulse duration). Based on the relationship between nerve conduction velocity and nodal spacing, this translates to a length of around 1 mm [23].

A. Electrode Design

We are currently using two electrode designs: unipolar for nerve stimulation and bipolar for nerve recording. The unipolar
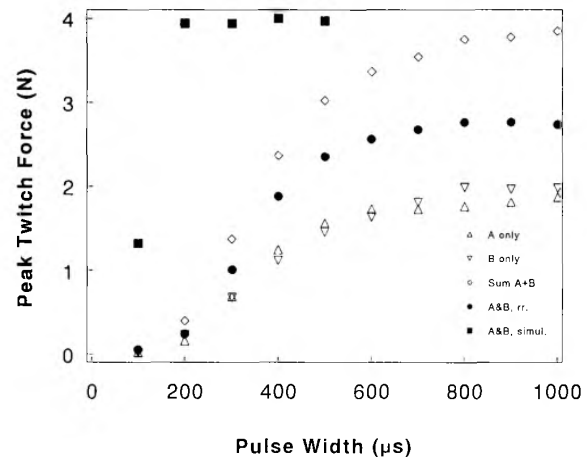

Fig. 2. Recruitment curves for pulse width modulated, constant current stimuli delivered to two unipolar electrodes implanted in a single fascicle. The current amplitudes for each electrode were selected to provide a twitch force plateau somewhat less than half the force elicited by supramaximal stimulation. Open triangle symbols show recruitment curves produced with single electrode stimulation. The open diamond symbols show their arithmetic sum, the expected force for independent electrodes. Solid symbols show recruitment with paired stimulation in which the two stimuli were delivered either simultaneously (simul.) or interleaved so that the second stimulus came during the time when the fibers activated by the first stimulus were refractory (rr.). The stimulus current applied through electrode A was 7 μA and through electrode B was 5 μA. The plateau force produced by simultaneous stimulation through the two electrodes was over 95% of the maximal force available from stimulation of the whole fascicle.

electrodes are made from 25 μm diameter, Teflon-coated, Pt-Ir wire [24]–[26], comparable in diameter to 10-0 suture. The bipolar electrodes are made from 5 μm diameter carbon fibers, twisted together and insulated with poly(oxyphenylene) to produce an electrode pair with a total diameter similar to that of the unipolar electrode [16]. In both cases, an active (recording or stimulating) site is produced by removing 1 mm of insulation some 1 or 2 cm proximal to the end of the electrode, giving a geometric surface area of about 80 × 10^3 μm^2. In the Pt-Ir electrodes, the recording or stimulating site (active zone) is coated with platinum black.

The electrode is attached to the end of a sharpened, 50 μm diameter, tungsten wire in such a way as to provide a smooth transition between the tungsten needle and the electrode and to avoid any increase in diameter at the attachment site. For implantation, enough of the overlying epineurium is dissected free of the nerve to visualize the target fascicle. The needle is used to thread the electrode inside the fascicle for a distance of about 1 cm so that the active zone of the electrode is centered between the entry and exit points. A ground or reference electrode is placed extraneurally, but parallel and adjacent to the intrafascicular electrodes.

B. Stimulation

Single pulse thresholds for activation of muscle with unipolar, intrafascicular electrodes are typically around 1 nC [24], [25] (Fig. 2). Recruitment curves with intrafascicular stimulation have modest slopes with either amplitude or dura-

tion modulation, and full fascicular recruitment occurs before there is visible activation of neighboring fascicles [24]. Using duration-modulated pulses of limited current amplitude, one can further restrict activation to a subset of fibers in the fascicle [25]. This behavior is illustrated in Fig. 2. Two electrodes were implanted in a single fascicle of the nerve innervating the gastrocnemius muscle in a cat. Pulse width modulated stimulation through each electrode alone produced forces lower than those produced by passing the same stimuli through the two electrodes together. This summation of forces shows that the electrodes were activating, in large part, different sets of motor nerve fibers in the fascicle.

We can use this ability of paired electrodes implanted in a single fascicle to activate different sets of motoneurons as a means of controlling muscle fatigue. By interleaving stimuli between the two electrodes, one can produce a fused, tetanic contraction of the muscle without tetanizing individual motor units. This significantly reduces fatigue during prolonged muscle contraction [26]. Brief, full strength contractions can be elicited when needed by simultaneous activation through both electrodes (Fig. 2).

Furthermore, we should be able to selectively activate muscles even in situations where more than one muscle is represented in a single fascicle. Anatomically, fibers tend to segregate as they course distally, well before fasciculation becomes apparent. By implanting multiple electrodes in a fascicle at a level where this segregation has occurred, we should gain separate control of the segregated populations of fibers.

C. Recording

Chronically implanted intrafascicular electrodes have recorded unit nerve fiber activity from the neurons for periods in excess of six months, the longest time tested to date [28]. This demonstrates that the potentials are recorded from intact axons and are not due to high extracellular current flows from injured nerve fibers.

The parallel, relatively closely spaced conductors of this electrode render it intrinsically more immune to electromyographic noise than other unshielded electrode configurations. In those instances where activity in overlying muscle is a problem, a water and ion-permeable, flexible, Faraday cage made from carbon fibers or other conductive polymers significantly attenuates the noise (Fig. 3). This is placed loosely around the nerve in the surrounding connective tissue and does not interfere with the normal displacement of the nerve during movement of the limbs.

In FNS applications, we need to be able to identify the sources of action potentials that occur continuously, in real time while recording from the nerve [30]. Coupling bipolar recordings to an action potential classifier makes it possible to extract detailed information about the nature and extent of external stimuli under these conditions [31].

D. Advantages and Limitations

The major advantages of the longitudinal, intrafascicular electrode for use in FNS are: the ability to use the same
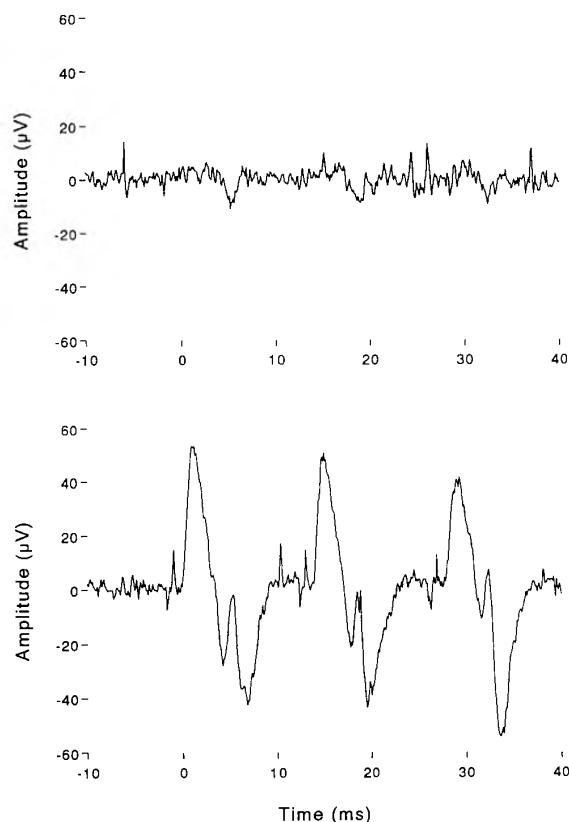

Fig. 3. Electromyographic noise rejection using a carbon-fiber Faraday cage. A longitudinal intrafascicular electrode was implanted in the tibial nerve to stimulate the lateral head of the gastrocnemius muscle, and a second electrode was implanted in the peroneal nerve directly beneath the gastrocnemius to record activity from the extensor digitorum longus muscle. The traces show two digitized neural recordings made while stimulating the tibial nerve at a level sufficient to produce nearly full activation of the motor units in the implanted fascicle (i.e., providing a contraction force on the order of 1 N). The bottom trace shows the large EMG signal present when the electrodes were unshielded. The top trace shows the signal when a conductive, freely permeable, carbon fiber shield was placed between the implanted electrodes and the overlying muscle. In both traces, the stimulating pulse train (50 μA pulses at 50 Hz) started at time 0. In the presence of the shield, the EMG noise has been reduced to a level that allows detection and discrimination of the small, positive going action potentials visible in both traces.

electrode design to record feedback information; obviation of the need for an impermeable barrier around the implant site that could become the source of a nerve entrapment syndrome; ability to activate spatially restricted populations of motor units; low charge levels for motor neuron stimulation; a means to more closely approximate normal recruitment and limit muscle fatigue without requiring high, anodal blocking currents; a simple implantation procedure (by the standards of the nerve repair community) without the need for sizing of the electrodes and; a minimal displacement of tissue at the implantation site, allowing use in areas where space is limited (e.g., in the hand).

At present, the main problem with these electrodes is a lack of a good material with which to build them. Even well proximal to the muscles they innervate, nerves are subject

to considerable stretch and bending during limb movements. Nerve tissue is tough, but very soft and flexible. We need a conductive material with an elastic modulus similar to that of the bulk nerve tissue, and a way to insulate this material with a durable but biocompatible and flexible coating. Metal is too stiff, work hardens, and becomes brittle. Woven carbon fibers are sufficiently flexible and do not work harden but they are brittle. We are currently working on a conductive Kevlar fiber with a covalently bonded, polymeric insulator coating. The active site of the electrode would be electroplated with activated Ir or Pt-Ir. When a viable electrode of this type is developed, then we will assess its tissue reaction properties.

We believe these electrodes would be particularly useful in upper limb FNS applications, especially where control is needed in several small muscles with limited room for implants. Multiply fasciculated nerves, such as the median, are particularly attractive as targets for this technology. We believe that these electrodes could also be applied in control of prosthetic limbs [18], [30].

IV. THE CASE FOR CUFF ELECTRODES,
J. Thomas Mortimer

At the Applied Neural Control Laboratory of Case Western Reserve University (CWRU), we have developed a prototype cuff electrode that allows selective and progressive activation of individual regions of a multifascicular nerve trunk [19], [32], [33] without the greater risk of trauma associated with intraneural electrodes.

Implantation of cuff electrodes should place minimal demand on both the patient and the surgeon, as large nerve trunks are relatively easy to access throughout the body. Clinical applications of earlier cuff designs have included correction of footdrop [13], [34], [35], with some implants still functioning after 12 years; pain suppression [36]–[38]; phrenic nerve pacing for respiratory assist [39]; and stimulation of the spinal roots for micturition assist [40]–[43].

Cuff electrodes overcome several disadvantages of intramuscular and epimysial electrodes [9]. The cuffs may be placed in areas of relatively low stress, minimizing the chances of mechanical failure of the electrodes or leads. Length-dependent recruitment properties are unlikely to be a problem since cuff electrodes are not likely to move relative to the motor nerve fibers. Excitation thresholds are an order of magnitude lower than those of intramuscular and epimysial electrodes. The use of lower excitation currents will permit the use of smaller electrode surfaces; the electrode's design increases selectivity without increasing the risk of corrosion. The lower power requirements of cuff electrodes make them an attractive component for a fully implanted neural prostheses system. Also, it is likely that microstimulators being developed by the NIH Neural Prosthesis Program would be suitable for use with the multiple contact cuff to produce a leadless motor prosthetic system.

Selective activation of peripheral nerve trunks using cuff electrodes has been demonstrated in acute animal studies [19]. Selectivity was highly dependent on the electrode orientation

and required that the electrode fit snugly around the nerve trunk.

In our laboratory, Sweeney et al. [32] conducted computer modeling and acute animal studies to examine the efficacy of a tripolar (cathode between two anodes) electrode configuration with an additional anode located across the nerve trunk from the tripole to steer the electric field [33]. *With careful positioning of the electrodes*, it was possible to activate selectively and maximally the fascicle innervating the medial gastrocnemius muscle in cats. Addition of the transverse, field-steering current greatly improved the selectivity [32].

Recently, investigators in our laboratory implanted a 12-contact spiral cuff electrode [33], [44] on the sciatic nerves of six cats, *without prior reference to the location of particular fascicles*. Selective and progressive control of the forces was demonstrated in four muscles that dorsiflex or plantarflex the ankle. Muscles innervated by well-defined fascicles could be recruited over their full force range before spread of activation to other muscles. To a lesser degree, selectivity was possible between muscles innervated by a common fascicle. In preliminary experiments, we have extended the four-muscle experiment to explore the control of joint torque through a multicontact cuff electrode applied to a major nerve trunk serving several muscles. Acute experiments in three animals have shown that dorsi- and plantarflexion can be controlled and that field steering can be used to improve the dynamic range of recruitment as well as selectivity [45].

Some people believe that the extraneural approach will not allow selective activation of fibers that are positioned centrally in a nerve trunk without activation of the more peripherally located fibers. We have conducted a preliminary modeling study and found that the nonlinear properties of nerve membrane provide an opportunity to activate deeper fibers without activating more superficial fibers. Using subthreshold, depolarizing prepulses to inactivate the sodium channels of fibers lying close to the electrode, we were able to selectively activate fibers far from the electrode before activating fibers close to the electrode [46], [47]. Chronic animal studies were performed and the recruitment characteristics remained stable, showing no changes that could indicate any nerve damage over a six-month period, which was the duration of the experiment [45]. Histological preparation is under way at the time of this writing.

By combining electrode geometries, field steering currents, and selective inactivation, we believe that it is possible to control the activation of individual muscles innervated by a common nerve trunk using a chronically implanted multiple contact cuff electrode.

A. Candidate Designs for Cuff Electrodes

Currently, there are two cuff electrode designs available that provide snug contact between the electrode contacts and the nerve trunk without causing neural damage: the CWRU Spiral [9] and the Huntington Helix [10]. The spiral cuff electrode design offers greater opportunity for selective activation of peripheral nerve trunks than does the open helix of the Huntington design. The insulating tube of the spiral confines

current flow within the cuff while the open design of the helix cannot prevent unwanted spill-over. The spiral design also allows placement of electrode contacts at any location on the surface of the nerve trunk, while the open helical design limits contact sites. Finally, because spiral cuffs may be fabricated in a planar configuration, they can be manufactured using the thin film fabrication techniques developed by the solid state electronics community.

The spiral nerve cuff is capable of expanding or contracting to fit very closely to the surface of a peripheral nerve without causing passive neural damage [48], [49]. The electrode can be implanted with an initial diameter between 60 and 200% of the diameter of the nerve trunk, and it will either expand or contract to fit snugly around the nerve trunk [49]. Chronic animal testing of bipolar spiral nerve cuff electrodes for electrical block of peripheral nerve [50] suggests that the cuffs are both safe and reliable [51].

V. DEVICE DEVELOPMENT AND CLINICAL ISSUES,
Paul Citron and Graham Creasey

While none of the electrode designs discussed in this paper has been tested in humans yet, it is not too soon to plan for the technology transfer that will be needed to take a feasible design into the clinical arena. Requirements for manufacture of the devices, for the surgical techniques to install them, and for acceptance by consumers must be kept in mind during the development of any implantable neural prosthesis. Many of these issues overlap with the fundamental safety and efficacy questions that are addressed in basic research studies such as the ones reported here.

Cuff electrodes, based on a very simple concept, seem to work better than many neural electrode designs in the clinical setting. The ability of cuff electrodes to selectively "steer" stimulation will open wider possibilities for this modality. The multiple contact cuff electrode may present the long sought solution. The notion of self adaptation to a range of nerve trunk diameters is obviously an advantage in the clinical setting. The health care system's increasing concern over costs would not be tolerant of a trial-and-error electrode selection process in the operating theater. The relative simplicity of positioning the cuff at the desired location is also appealing, especially in contrast to the surgical procedures required to place intrafascicular or intramuscular electrodes.

Should the capability of the CWRU cuff electrodes be shown to be repeatable and consistent in a chronic study, that would be a significant step toward system simplification while providing a level of stimulation flexibility and sophistication not previously available. However, to be viable as a commercial electrode-lead system, the CWRU cuff would have to fulfill mechanical requirements, including durability, corrosion resistance of the electrodes, integrity of thin-walled insulation, and freedom from fatigue failure in several years of use. Perhaps most important is verification that the cuff electrode does not induce inflammatory reactions or mechanical stress or irritation on the nerve trunk which result in nerve injury, or unacceptable excursions in stimulation threshold when used over long periods of time. To the extent selective activation

is a requirement, it must still be demonstrated that this aspect will maintain itself reliably in a sufficiently large percentage of patients without surgical revision.

Because of problems with surgical implementation of intrafascicular electrodes and associated costs, these electrodes may have limited applications. Also, there are many safety concerns surrounding the intrafascicular electrodes: Does mechanical breaching of the perineurium produce osmotic effects which compromise nerve function? What are the effects of repeated movement, especially in chronic motor applications? Will there be fibrosis or axonal damage? How many electrodes can be placed in a single fascicle? Can individual ones be replaced, and can additional ones be placed later on? Responses, even partial ones, to these questions will be necessary for transferring the device to medical practice.

An often overlooked aspect of peripheral nerve vulnerability is the influence of the cable portion of the lead on ultimate performance. The notion of a cableless, radio-frequency-driven stimulation system certainly merits consideration. As with a cabled system, the mass and dynamics imposed by such a distributed system will need to be modeled and tested to verify decreased propensity for nerve damage. But, will the extra procedural time and care needed for implantation of a distributed system, and its long-term reliability, outweigh the power benefit obtained?

It may well be that practical neural prostheses will need to combine extraneural and intraneural electrodes with muscle electrodes (epimysial or intramuscular) as has been done in some applications [52]. Current uses of intraneural electrodes include research, clinical research, or those clinical applications which require only one or two electrodes placed in large nerve trunks. Even with these restrictions, the results of such research are vital for building the knowledge base for the entire field of peripheral nerve stimulation.

Availability of suitable biomaterials is a concern throughout the medical device industry. The long-term physical requirements described for the intrafascicular electrode challenge the existing portfolio of biomaterial choices, which is currently shrinking rather than expanding. It remains to be seen if we can develop a combination of materials that meet the necessary requirements of flexibility, durability, absence of inflammatory reactions, and other biocompatibility requirements while having the electrical characteristics required of a chronic sensing or stimulation system.

In addition to biocompatibility, electrode and lead materials must display robustness. Electrodes are likely to be used in active individuals for whom resistance to breakage will determine the acceptance or rejection of the device. Reliability is also important in the other parts of a motor prosthesis such as cables, stimulating circuits, and especially in their connections to the electrodes. Connections are the most likely places for device failure; it is necessary to create a very gradual change in stiffness between cables and other components to avoid localized stresses and breakage.

Current FNS systems are limited in the number of muscles that can be activated, resulting from the limitation in the number of electrodes that can be tolerated and the number of available stimulator channels. Taking the example of a cuff

electrode with 12 contacts, and presumably 12 leads and 12 stimulator channels, how many muscles can realistically be controlled with such a cuff? It has been suggested that by interpolation between pairs of tripoles the number of muscles might be doubled. Possibly, selective inactivation may give access to deeper fascicles. Control of eight muscles with one cuff would simplify the surgery, but it also would make the electrical system more complicated.

Attention to nerve damage, especially mechanical damage, is particularly important in view of damage which has been seen clinically in some phrenic nerve and sacral root neural prostheses [43]. It appears that electrical damage has been easier to avoid than mechanical damage and that mechanical damage is commonly due to surgical handling rather than to long-term presence of the cuffs. It has been said that a surgeon should have the heart of a lion, the eye of an eagle, and the hand of a lady. But, in practice, what is needed are electrode designs that are easy to use and relatively standard procedures for implantation if motor prostheses are to be disseminated to the widest possible patient constituency.

There will be trade-offs between surgical complexity (and consequently, cost, risk of infection, and other complications), hardware complexity, and postsurgical tuning. It is desirable to reduce the skill required of the surgeon in order to increase the chance of surgeons accepting the technique and to decrease the chance of surgical error. There is an advantage to having a standard operation even if further time is required after the operation for tuning of the prosthesis. Although one-stage surgery is a goal, the surgical procedure should allow for revision.

While complex hardware may be expensive and difficult to make, this can be justified if it is easy to set up and use. The limit on the amount of time that can be spent in tuning the system typically will be set by the user; but if the device is genuinely useful, such limits will continue to be extended.

A critical issue to be faced in the application of neural electrodes is fulfilling expectations. Are the leads of sufficiently robust design to yield acceptable results in the spectrum of surgical circumstances (i.e., anatomical variations and surgical skill)? What constitutes an acceptable level of complication or system failure? How will those expectations be set? There have been instances in the application of medical technology where the expectations have been set too high and great difficulties were encountered in meeting them. Only by interaction with physicians, surgeons, rehabilitation specialists, and potential consumers will the developers of neural prostheses establish relevant expectations of new devices.

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