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Evaluation of high-density, multi-contact nerve cuffs for activation of grasp muscles in monkeys

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Abstract

Objective—The objective of this work was to evaluate whether nerve cuffs can selectively activate hand muscles for functional electrical stimulation (FES). FES typically involves identifying and implanting electrodes in many individual muscles, but nerve cuffs only require implantation at a single site around the nerve. This method is surgically more attractive. Nerve cuffs may also more effectively stimulate intrinsic hand muscles, which are typically difficult to individually implant and stimulate without spillover to adjacent muscles.

Approach—To evaluate its ability to selectively activate muscles, we implanted and tested the Flat Interface Nerve Electrode (FINE), which is designed to selectively stimulate peripheral nerves that innervate multiple muscles [1]. We implanted FINEs and bipolar intramuscular wires for recording compound muscle action potentials (CMAPs) from up to 20 muscles in each arm of six monkeys. We then collected recruitment curves while the animals were anesthetized.

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Main Result—A single FINE implanted on an upper extremity nerve in the monkey can selectively activate muscles or small groups of muscles to produce multiple, independent hand functions.

Significance—FINE cuffs can serve as a viable supplement to intramuscular electrodes in FES systems, where they can better activate intrinsic and extrinsic muscles with less extensive surgery.

Keywords

functional electrical stimulation; electrodes; peripheral nerves; neural prostheses; nerve stimulation; macaque; brain machine interface

Introduction

Paralysis resulting from spinal cord injury (SCI) is devastating, dramatically reducing the independence of affected individuals. In addition to the direct effects, a number of secondary complications emerge as a result of disuse, such as muscle atrophy, contractures and pressure sores [2–3]. However, if the motor neurons remain intact after injury, muscles can be made to contract through functional electrical stimulation (FES) [4]. FES has been used to assist or restore gait [5]–[7], the ability to grasp objects [4], [8]–[11] and to augment bowel and bladder function [12].

While some hand grasp systems use transcutaneous muscle stimulation [13], [14] (e.g., Bioness, Myndtech, Belgrade Grasping System), FES often requires an invasive procedure where surgeons must identify and implant electrodes in every muscle of interest. In this case, the intrinsic muscles of the hand present a challenge. In addition to being difficult to implant, their small size often results in current spillover to adjacent muscles [15], rendering selective activation difficult to achieve. In the case of larger, extrinsic muscles with spatially distributed motor units, it is difficult to recruit the fibers of the entire muscle, resulting in partial and ineffective recruitment [16].

Nerve trunk stimulation is an alternative that may address these challenges, and a variety of multi-contact nerve-based electrodes exist [1], [17]–[23]. These electrodes vary in how they interface with the nerve, but are similar in that a single implant site can potentially access all the muscles innervated by that nerve. This more efficient access to muscles means a less extensive and shorter surgery, potentially improving outcomes and reducing risks. There is also about a 10-fold decrease in the required stimulation intensity for nerve cuffs compared to intramuscular stimulation, thereby simplifying stimulator design, increasing battery life, and reducing stimulation artifact in cases where concurrently recorded biosignals are used for control.

In this study, we evaluate the Flat Interface Nerve Electrode (FINE), for use in upper extremity hand grasp systems. The FINE is an extraneural electrode designed to gently reshape the nerve and thereby increase access to nerve fascicles [1]. It offers the potential to activate muscles strongly and selectively and has been shown to be stable over several years for restoring sensation in humans [24]–[26]. It is therefore an attractive candidate for use in motor recruitment for FES. In the experiments presented here, we collected recruitment

curves from FINEs implanted in six monkeys. We evaluated the ability to generate selective activation of several functionally synergistic muscle groups as well as certain individual muscles. Our ultimate goal is to use this technology in tandem with intramuscular stimulation in the development of FES systems, including a cortically-controlled FES system that uses signals in motor cortex to control the time-varying stimulation of multiple muscles [27]–[29].

Methods

We implanted and tested 12 and 16-channel FINE cuffs on the median, radial, and ulnar nerves of six monkeys: four rhesus macaques (*Macacca mulatta*, Monkeys 1, 2, 3, and 4) and two long-tailed macaques (*Macaca fascicularis*, Monkeys 5 and 6) (Table 1). We collected recruitment curves by varying either pulse amplitude or pulse width of single, biphasic, charge-balanced stimulus pulses, and recorded the evoked twitch response of all implanted muscles [17]. These twitch responses represent Compound Muscle Action Potentials (CMAPs) evoked by nerve stimulation. Four experiments, in monkeys 1–4, were 36-hour non-recovery procedures. Two experiments, in monkeys 5 and 6, were chronic experiments to evaluate the performance of chronically implanted FINE cuffs. Measurements were collected under sedation. Monkey 5 was implanted for 6 months, and was involved in 12 stimulation experiments. Stimulation experiments in Monkey 5, however, were largely exploratory and did not involve standardized stimulation parameters across sessions. The study in Monkey 6 spanned 15 weeks, and involved weekly, standardized, eight-hour recording sessions to collect a series of recruitment curves. All methods were fully consistent with the *Guide for the Care and Use of Laboratory Animals* and conducted in accordance with a protocol approved by the Northwestern University Institutional Animal Care and Use Committee.

FINE cuff implantation

We implanted up to four FINE cuffs in each arm of the acute study monkeys, on the median and ulnar nerves (Table 1). During surgery, we dissected a 2 cm length of nerve free from surrounding tissue, placed the cuff around the nerve and secured the ends with a suture (**Error! Reference source not found.** (a) and 1(b)). Contacts near the cuff hinge, especially contacts 8 and 9, did not always touch the nerve (**Error! Reference source not found.** (a–c)).

CMAP electrode implantation

We implanted pairs of multi-stranded, Teflon coated stainless steel wires (Cooner 632) in each muscle after stripping 2 to 3 mm of insulation from the end of each wire and separating the deinsulated tips by approximately 1 cm (Table 2). In surgery, we exposed and identified each muscle based on its response to electrical stimulation. For the acute experiments, we either sutured the wires to the muscle surface (epimysial) or inserted them into the muscle belly using hypodermic needles (intramuscular). We placed two needles in the shoulder to serve as the stimulation return (anode) and the CMAP reference. For the chronic experiments, we also implanted a reference wire near the elbow, along with a return electrode on the upper arm. All electrodes were intramuscular, and routed together with the

FINE leads to a percutaneous implant on the monkey's back that included three connectors (Samtec Inc., New Albany, Indiana) on a printed circuit board.

Data Collection

During the acute experiments (Monkeys 1–4), we used two battery-powered, computer-controlled stimulators (custom devices by Crisptronics, Cleveland, OH) to deliver charge-balanced, biphasic, rectangular pulses. We acquired CMAP signals at 2.4 kHz sampling rate, amplified, AC coupled (2nd order, 10 Hz HPF cutoff) and low-pass filtered (2nd order, 1 kHz) the signals.

For the chronic experiments with Monkey 6, we conducted experiments every 1–2 weeks for 15 weeks. We induced sedation with either Telazol or a ketamine-midazolam cocktail IM, and maintained an experimental level of sedation with IV propofol. A MATLAB user interface controlling a 16-channel stimulator (Tucker-Davis Technologies, Alachua, FL) sent stimulus pulses to the cuffs and collected CMAP signals. The CMAP data were sampled at 3 kHz, amplified, AC coupled (2nd order, 10 Hz HPF cutoff), low-pass filtered (2nd order, 1 kHz).

For both acute and chronic trials, we used a binary search routine to generate pulse-width and pulse-amplitude modulated recruitment curves. For each curve, we held one parameter (amplitude or width) constant and varied the other. For each session with Monkey 6, we collected up to four sets of recruitment curves per nerve: two sets with pulse amplitude values of either 0.10 mA or 0.25 mA and varied pulse width, and two sets with pulse width of either 10 μ s or 20 μ s with varied pulse amplitude. We used a stimulation frequency of 4 Hz to minimize the experimental time without fusing muscle twitches [18].

Data Analysis

We analyzed the recruitment curves to determine stimulation thresholds and the ability to selectively activate muscles. We used peak-to-peak CMAP amplitude to quantify the magnitude of muscle contraction, and normalized to the maximum peak-to-peak value recorded in a session for each muscle. We defined the selectivity of individual muscles as the percent activation of a given muscle before any other muscle reached 20% of the Recorded Max Value (Figure 2). We chose this metric because it is functionally relevant and provides insight into the level of activity of the muscles. Others have used 10% as the cutoff, which represented just palpable muscle activity [30]. The 20% of maximum activation chosen for this analysis represents a visible twitch with minor force production. Since 20% represents the lowest or just below functional output, a selectivity value of around 20% has limited functional value and is not selective as another muscle is also at 20% output. As selectivity increases above 20%, there is an increasing functional output from the selective muscle while no other muscle achieves a functional output.

To evaluate muscle selectivity over time, we used two different types of analyses. In the “Fixed Contact” analysis, we chose the contact that yielded the highest selectivity across all weeks, and computed its selectivity in each session. In the “Best Contact” analysis, we computed selectivity for each session using the most selective contact for that session.

Results

Activation Thresholds

For all monkeys, we evaluated activation thresholds for all contacts in the median nerve cuffs. As the cuffs were somewhat larger than the nerves, contacts at either end were typically the farthest from the fascicles **Error! Reference source not found.** (a–c)), and had somewhat higher thresholds. The highest thresholds were for contacts 8 and 9, located at the hinge of the cuff, and often not in direct contact with the nerve **Error! Reference source not found.** (c)). The thresholds across all muscles, regardless of monkey and nerve, were mirrored for the top and bottom of the cuff, such that opposing pairs of contacts had comparable thresholds (Figure 3). The intraoperative thresholds were initially high for Monkey 5, but decreased at five weeks and further at six months during the terminal experiment. **Error! Reference source not found.** shows thresholds for Monkey 6 in more detail for each nerve at two months post-implant. As opposed to the median and ulnar nerve results, for the radial nerve, the thresholds for contacts 1 and 16 were relatively low, a result of being in close proximity with the nerve in this particular case **Error! Reference source not found.** (b)).

Selective recruitment of muscles with FINES

We were able to achieve at least partially selective activation of muscles in all monkeys (Figure 5). In all cases where the median nerve cuff was implanted just proximal to the pronator teres (PT) branch, we could recruit that muscle with a selectivity value of 62 to 90% (Figure 5(a)). The best results for the proximal implant were in Monkey 1 (Left arm) with selective activation of four muscles: PT (Selectivity=90%), FDP (80%), FCR (70%), and FDS (30%). For Monkey 3, the selectivity of activation of intrinsic thumb muscles in the thenar eminence was 45%.

To avoid dominance of PT recruitment in Monkeys 4–6, we placed the median nerve cuffs distal to its nerve branch. This enabled selective activation of finger and wrist flexors for these three monkeys. For Monkeys 4 and 6, FDP and FDS were active selectively, which demonstrates an ability to control finger flexors. In Monkey 6, four muscles were selectively activated, including both finger: FDP (60%), FDS (40%) and wrist flexors: PL (35%), FCR (25%), at 6 days post-surgery.

The ulnar nerve cuffs in Monkeys 1–4 were implanted proximal to the elbow and activated flexor carpi ulnaris (FCU), the first muscle to branch distal to the cuff, with selectivity ranging from 54% to 100%. In Monkeys 5 and 6, the ulnar cuff was implanted just proximal to the wrist, well past the nerve branch to FCU. Using these cuffs, we recruited FDI and ADM at 55% and 34% selectivity, respectively.

Recruitment Order

Order of recruitment of multiple muscles, especially functionally synergistic muscles, affects the functional result of stimulation. Recruitment order two months post-implant in Monkey 6 shows multiple different recruitment orders from single contact stimulation (Figure 6). For example, contact 6 on the radial nerve (Figure 6(a)) first activated the finger extensors EDCu

and EDCr, then the wrist extensor, ECU, and finally thumb abductor, APL. In contrast, contact 5 first activates wrist extensors, ECRb and ECRI, then finger extensors EDCr and EDCu. For the radial nerve, there were 11 unique recruitment orders for 16 contacts. For the median nerve (Figure 6(b)), there were 10 unique recruitment orders for 16 contacts.

Four of the five muscles of the radial nerve (APL, Brad, EDC, ECR, and ECU) were activated first by at least one of the electrodes. Only the brachioradialis was not activated first by any contact. Each of the four muscles innervated by the median nerve (FDS, FDP, FCR, and FCU) were recruited first by at least two contacts. Of the four muscles in the ulnar nerve (ADM, FDMb, FDI, and First Lumbrical) all contacts always activated the muscles in the same order of ADM, FDMb, FDI, and First Lumbrical (not shown in figure). Only contact 13 reversed the order of the FDI and First Lumbrical activation.

Stability of muscle selectivity for chronically implanted cuffs

To evaluate the stability of muscle recruitment over time for Monkey 6, we obtained recruitment curves for the most selective muscle recruited by each cuff, and averaged the recruitment curves for experimental sessions 9 through 14 (Figure 7). For these recruitment curves, pulse width was held static at 10 or 20 μ s while pulse amplitude varied. Ulnar nerve stimulation selectively recruited ADM, an intrinsic hypothenar muscle, with selectivity values of $69\% \pm 6$. For the radial nerve, the muscle with the highest selectivity value was APL, ($51\% \pm 5$ at 20 μ s). For the median nerve, FDP was most selective ($83\% \pm 5$). Not only did these three muscles have the highest selectivity, they were also recruited with the highest stability across weeks, indicated by their low standard deviations. Conversely, the muscles that were activated with the least stability across sessions, FCR and PL, were only selective for 3 sessions (selectivity means of 29% and 30%, respectively). Due to external factors, FCR and PL were only tested in 5 of 6 sessions.

Achieving selectivity with more than one contact

In many cases the same muscles were selectively activated by more than one contact, and we therefore evaluated selective muscle activation across sessions using two different analyses (Figure 8). The Fixed Contact analysis (Figure 8a) shows selectivity of a single contact across all sessions for Monkey 6, while the Best Contact analysis (Figure 8b) shows results for the contact that produces the greatest selectivity in a given session. The largest difference in selectivity between the Fixed and Best contact results is seen in the wrist flexor functional group, where selectivity using the Best contact was better by more than 15% for weeks 3, 8, and 11 (Figures 8a and 8b, Median Nerve). The difference in selectivity between the Fixed and Best contact for the finger flexors was more than 10% for weeks 5, 13, and 14 (Figures 8a and 8b, Median Nerve). In another example, the wrist extensor functional group, selectivity using the Best contact was better by more than 15% at week 2. (Figures 8a and 8b, Radial Nerve). These examples demonstrate the ability to improve selectivity by switching to another contact.

Chronic cuff performance

To further evaluate chronic cuff performance for Monkey 6, who was involved in regular, standardized experiments for four months, we evaluated thresholds over time using the

contact from the “Fixed Contact” analysis. (Figure 9. **Thresholds over time.** Thresholds for selective muscles using the same “fixed” contact over time.. Thresholds for selective muscles were generally stable over time, although the thresholds for the pairs of electrodes in EDC experienced some variation throughout the experiment. We also evaluated the peak-to-peak values of the CMAP twitches across sessions for the most selectively activated muscles for each nerve (Figure 10). For each muscle, we also used the contact from the “Fixed Contact” analysis, and evaluated twitches for a pulse amplitude of 3mA and a pulse width of 20 μ s. In general, CMAP values remained stable or slightly increased over time, suggested the cuff electrode does not affect the physiology. Note that there are a few significant changes in CMAP between two successive sessions (Figure 10, Radial Nerve). The cause of these jumps is not certain, but the intramuscular recording pair consisted of two independent wires placed within the muscle. Since CMAP amplitude is dependent on interelectrode spacing, it is possible that one of the leads was displaced between sessions, especially early in the trials, before the encapsulation was fully matured.

Multiple-contact stimulation

In a brief experiment in Monkey 6, we used the FINEs to activate muscles using multiple contacts from the median and radial cuffs simultaneously. Based on recruitment curve information, we identified contacts that drove the hand from a posture with the fingers extended to a posture with the fingers closed in a fist (Supplementary Video A). In another trial, we caused the fingers to spread, an action mediated largely by the dorsal interossei (Supplementary Video B). By stimulating on multiple contacts, we were able to achieve strong wrist extension in tandem with finger flexion. In both videos, the monkey’s wrist extends, and remains extended while all fingers flex. This type of activation is crucial for restoring effective grasp.

Discussion

In the current study, we demonstrate the feasibility of using extraneural FINE cuffs for evoking muscle activity for a hand grasp activity, a promising avenue for improving FES. FINEs offer an advantage over individual muscle stimulation in part because their implantation requires much less extensive surgery. Implanting a cuff requires surgery at a single site rather the multiple sites required for all the muscles innervated by that nerve. FINEs also improve access to the small, intrinsic muscles, the size and location of which make them particularly difficult to implant with individual intramuscular electrodes. Furthermore, the small distance between intrinsic hand muscles makes them prone to current spillover, even at relatively low intensity stimulation. Another limitation of intramuscular electrodes is the limited force that may be produced through partial activation of the muscle. Activation of finger flexors during a power grasp also causes wrist flexion torque, which can overpower the torque produced by intramuscular activation of the much weaker wrist extensors. We found this not to be in the case in our multiple-contact stimulation experiment (Supplemental Videos A and B). In both videos, the monkey’s wrist extends, and remains extended while all fingers flex. This type of activation is crucial for restoring effective grasp.

Selective activation of muscles and functional muscle groups

While recent studies have demonstrated the successful chronic use of 8-channel FINEs in humans for evoking sensory percepts [25–26], here we focus on the viability of 12 and 16-channel designs for motor applications. The more closely spaced electrodes may explain why adjacent contacts often activated muscles in a similar sequence. In many cases, we could achieve similar selective activation of a given muscle or functional group using multiple contacts. This meant that for sessions where we could not achieve great selective activation using one contact, we could often instead use a neighboring contact. The high-density design provides a redundancy that allows more contact options to choose from, which is helpful for maximizing selective activation of muscles and functional groups, and could also contribute to long-term stability of selective activation.

Monkey as a model for evaluating nerve stimulation

In the current study, the monkey proved to be a valuable model to evaluate and improve stimulation algorithms more readily than would be possible with human subjects. While the experiments described here are important for exploring ways to improve stimulation techniques, they are time consuming and therefore not ideal for human experiments. Our chronic experiments spanned as much as eight hours, while the acute ones spanned as much as thirty-six hours. These long sessions permitted a comprehensive evaluation of the feasibility of the FINE cuffs, allowing us to test muscle responses to stimulation using a wide range of pulse widths and amplitudes. As reported elsewhere [31], we also developed a genetic algorithm (GA) to optimize parameters for multiple-contact stimulation, and our 8-hour experiments allowed us to run several GAs. Use of a monkey model further afforded us the ability to investigate other practical issues, including the posture dependence of the stimulation, which proved to be minimal, and the ability to form functional grasps using multi-contact stimulation.

However, anatomical differences between the monkey and human need to be understood when considering how our results will translate to the clinic. Monkeys have considerably fewer fascicles than the human, a difference that is important, given that selectivity improves with increasing number of fascicles [32] (Figure 11). It is likely then, that selectivity in humans will be better than what we report here in monkeys.

The use of FINEs for FES

There are three basic categories of peripheral nerve interfaces: extraneural, interfascicular, and intrafascicular. The FINE is an extraneural electrode, which does not penetrate the epineurium or perineurium of the nerve. Unlike circular extraneural electrodes, such as the CWRU spiral [33], cylinder electrodes [34], [35], and HMRI helix [36], the FINE reshapes the nerve into a flattened oval to increase the ratio of the surface area to volume of the nerve [1]. This improves access to the fascicles and axons within a nerve bundle to provide increased selectivity. Interfascicular electrodes, such as the SPINE [37] or groove [38], penetrate the epineurium but not the perineurium. The goal is to place contacts within the nerve, between the fascicles. Intrafascicular electrodes gain further access to the axons by penetrating both the epineurium and perineurium, placing contacts within the fascicle. Examples of intrafascicular electrodes include the longitudinal intrafascicular electrode

(LIFE) [39], thin-film LIFE (tfLIFE) [40], [41], transverse intrafascicular multichannel electrode (TIME) [19], self-opening intrafascicular neural interface (SELINE) [42], and Utah slant electrode array (USEA) [43].

Many factors must be considered in choosing a neural interface for a particular application. Selectivity, functional performance, impact on nerve health and morphology, anatomical constraints, implementation logistics, physical reliability, and serviceability of the interface are a few of the more significant considerations. The relative importance of each differs across applications. Generally, interfaces will be needed on multiple nerves, potentially complicating the surgical requirements [44]. A nerve consisting of multiple fascicles may require implantation of several LIFE electrodes, with at least one per fascicle. In feline or canine animal models, the number of fascicles is usually small, usually 15 or less. In humans, however, there are many fascicles in the nerves of interest [45]–[47]. The number of fascicles in a nerve in the arm is 20 to 40 in the target areas of implantation [47], and the sciatic nerve in the leg can have even more.

The TIME electrode transects multiple fascicles, but still requires several electrodes in each nerve in order to place contacts in close proximity to all the fascicles [48]. The USEA is designed to penetrate all fascicles of the nerve with a single device, but reaching deeper fascicles requires penetration through the more superficial fascicles. Studies indicate that penetration may not detrimentally affect long-term physiology of the animal [49], but it does cause axonal regeneration and encapsulation of the electrodes within the fascicle [50], [51]. Interfascicular and intrafascicular electrodes also need to be stabilized or anchored in the nerve [44]. A peripheral nerve is much more mobile than the central nervous system tissue and can move several centimeters during normal daily activity. Additionally, since the peripheral nervous system is not encased in a bony structure, forces from muscles and even external environmental interactions will influence and stress the interface. The SELINE [42] introduces barbs within the fascicle to anchor the electrode, but their long-term effects on encapsulation and neural health are yet to be understood.

In contrast, extraneural cuff interface approaches, such as the FINE and spiral, are implanted around each nerve and closed. A single electrode can be implanted around the whole nerve in just a few minutes. These extraneural electrodes, however, require circumneural exposure of the nerve and sufficient length along the nerve to accommodate the electrode. The neural blood supply runs along with the nerve, enabling the surgeon to free up sections of the nerve, but the longer the section of nerve that is exposed and subsequently enclosed, the more it is separated from surrounding tissue and nutrients.

Metrics related to selectivity of individual fibers or muscles are academically interesting, but the clinical goal of an interface is to restore function, which does not necessarily require selectivity even at the level of individual muscles. In fact, the ability to recruit functionally useful and distinct muscle synergies may be just as important. In studies directly comparing classes of electrodes, non-reshaping, extraneural cylindrical electrodes performed like intrafascicular electrodes for many of the muscles studied [48]. In the Miller lab, both the FINE and the USEA were evaluated independently. Both demonstrated an ability to activate muscles selectively and both produce similar functional grasps. In the supplemental videos

provided with the current study, the FINE demonstrates functional results like those reported of a USEA tested acutely on monkey nerves [20].

It is important to consider all factors related to a clinical application to choose interface technology. None of the electrode designs is likely to provide a universally best approach. The optimal systems will likely comprise a mixture of types working together to produce the best performance.

Conclusions

Here we present results from several acute and chronic experiments conducted under sedation with six monkeys. We could achieve selective activation of individual muscles, or distinct functional groups of muscles. The high-density cuff design led to overlap in the sets of muscles activated by different contacts, allowing the ability to choose contacts that provided the most selective activation. Overall, the monkey model allowed us to test a wide range of stimulation parameters, and will continue to be a valuable model for exploring FINE capabilities.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1. Experiment Setup

(a) CFINE cuff made from poly-ether-ether-ketone (PEEK) with 16 contacts sandwiched in PDMS sheeting. (b) Placement of the cuff around the radial nerve of a macaque. (c) Schematic illustrating the arrangement of contacts around the nerve. (d) Schematic illustrating the flow of experiment. The computer sent commands to the stimulator, which stimulated the appropriate contact on the FINE cuff. This produced a muscle twitch, which was amplified and sent back to the computer to be saved. (e) Examples of muscle twitches elicited by nerve stimulation on a single contact.

Figure 2. Median Nerve Recruitment Curve

These recruitment values are for the right arm of Monkey 1, who had a FINE cuff implanted around the median nerve proximal to the elbow. The dotted line at 20% shows the threshold for determining selectivity. In this example, the first muscle to reach 20% is the Pronator (PT), and it remains the only muscle above this line until it reaches 90% activation, which is when the next muscle, FDP, reaches 20%. The selectivity value for the Pronator in this example is therefore 90%.

Figure 3. Stimulation thresholds for all monkeys for the median nerve cuff

These stimulation thresholds were found across all muscles for each contact. The data from each monkey are centered around the hinge at contact 8 and 9 because not all cuffs had 16 channels. Missing data points indicate that the contact could not activate muscle, or that the data were not collected.

Figure 4. Thresholds

These plots show the mean charge at threshold (20% of CMAP value) of each muscle at each contact for all three nerves in trials collected after 2 months post implant in Monkey 6.

Figure 5. Summary of selective muscle activation for the median nerve

Each plot represents the highest selectivity value for each muscle across the range of pulse amplitudes and widths tested. Selectivity for each muscle was therefore achieved using different stimulation parameters. All data were collected intraoperatively except the data for Monkey 6, which were collected 6 days post-implantation. The background shading of each polar plot separates the muscles into functional groups, showing the ability to get functional selectivity in addition to muscle selectivity.

Figure 6. Recruitment order

The order for muscle recruitment for each contact in Monkey 6 at 2 months post implant. Muscles depicted closest to the nerve were recruited first. The muscles are grouped according to functional synergy.

Figure 7. Mean recruitment curves of selective muscles

These curves average data from trials collected after 1.5 months post-implant in Monkey 6. The dotted line indicates one standard deviation from the mean (solid line). The mean is calculated across all recruitment curves for the contact and pulse width that produced the most selective recruitment.

Figure 8. Selectivity over time

(a) Selectivity, as calculated by the Fixed Contact Analysis, for the three nerves in Monkey 6. (b) Selectivity, as calculated by the Best Contact Analysis.

Figure 9. Thresholds over time
Thresholds for selective muscles using the same “fixed” contact over time. CMAP pairs producing similar functions were grouped together for this analysis (i.e. EDCu and EDCr, and ECRl and ECRb).

Figure 10. Peak-to-peak CMAP over time

Peak-to-peak CMAP values were calculated for the most selective muscles for each nerve. The stimulation parameters evaluated were a pulse amplitude of 3mA and a pulse width of 20 μ s.

Figure 11. Fascicle count in the monkey versus the human

The fascicle count trends are similar in the human and the monkey, though the fascicle count in the monkey does not exceed 17, while the human has many more fascicles. The fascicle count locations were normalized to the elbow. Reprinted with permission (pending) [32].

Table 1**Nerves implanted with FINEs in each monkey**

This table shows the number of contacts for all the cuffs included in the current paper's analysis. The number of contacts for each cuff ranged from 12 to 16. In Monkey 6, we implanted clinical-grade CFINE nerve cuffs. All radial cuffs were implanted proximal to the elbow. The difference between the proximal and distal median cuffs is relative to the nerve branch to the pronator teres muscles. The distal ulnar cuffs were just proximal to the wrist, while the proximal cuffs were closer to the elbow.

	Median Proximal	Median Distal	Ulnar distal	Ulnar Proximal	Radial
Monkey 1 Left	16	--	--	16	--
Monkey 1 Right	16	--	--	16	--
Monkey 2	16	--	--	16	--
Monkey 3	12	--	--	12	--
Monkey 4	--	12	--	12	--
Monkey 5	--	12	12	--	--
Monkey 6	--	16	16	--	16

Table 2

Muscles implanted with electrodes for each monkey

The list of muscles for each monkey includes flexor digitorum profundus (FDP), flexor digitorum superficialis (FDS), opponens pollicis (OP), palmaris longus (PL), pronator teres (PT), abductor pollicis longus (APL), brachioradialis (Brad), extensor carpi radialis brevis (ECRb), extensor carpi radialis longus (ECRl), extensor digitorum communis (EDCr and EDCu to dictate the relative location of electrode pairs), extensor carpi ulnaris (ECU), abductor digiti minimi (ADM), adductor pollicis (AdP), flexor carpi ulnaris (FCU), first dorsal interosseous (FDI), flexor pollicis brevis (FPB), flexor digiti minimi brevis (FDMb), and first lumbrical (Lum1). Hypothenar (HT) and thenar refer to electrodes implanted in the hypothenar and thenar eminence, but that were not more specifically identified.

	Median						Radial						Ulnar									
	FDP	FDS	FCR	OP	PL	PT	APL	Brad	ECRb	ECRI	EDCu	EDCr	ECU	ADM	AdP	HT	FCU	FDI	FPB	FDMb	Lum1	Thenar
Monkey 1 Left	.	.	.			.											.	.				.
Monkey 1 Right	.	.	.			.										.	.	.				.
Monkey 2	.	.	.			.										.	.	.				.
Monkey 3	.	.	.			.											.					.
Monkey 4	.	.	.		.	.									.		.	.	.			.
Monkey 5	.	.	.											.	.		.	.	.			.
Monkey 6	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.