Behavioral Demonstration of a Somatosensory Neuroprosthesis

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***Abstract*—Tactile sensation is critical for effective object manipulation, but current prosthetic upper limbs make no provision for delivering somesthetic feedback to the user. For individuals who require use of prosthetic limbs, this lack of feedback transforms a mundane task into one that requires extreme concentration and effort. Although vibrotactile motors and sensory substitution devices can be used to convey gross sensations, a direct neural interface is required to provide detailed and intuitive sensory feedback. In light of this, we describe the implementation of a somatosensory prosthesis with which we elicit, through intracortical microstimulation (ICMS), percepts whose magnitude is graded according to the force exerted on the prosthetic finger. Specifically, the prosthesis consists of a sensorized finger, the force output of which is converted into a regime of ICMS delivered to primary somatosensory cortex through chronically implanted multi-electrode arrays. We show that the performance of animals (Rhesus macaques) on a tactile task is equivalent whether stimuli are delivered to the native finger or to the prosthetic finger.**

***Index Terms*—Artificial limbs, brain computer interfaces, microelectrodes, neural prosthesis, prosthetic hand, sensors.**

I. Introduction

ADVANCES in modern medicine allow an increasing number of civilians and veterans to emerge from catastrophic injury with lives intact, but bodies broken. Victims of limb amputation or spinal cord injury resulting in para- or tetraplegia often mitigate their loss with prosthetic devices to assist in performing the activities of daily living (ADL) [1]–[5]. A large body of literature demonstrates that devices (ranging from cursors on a computer screen to sophisticated armatures) can be controlled by filtering cortical output and using that output to control the speed, direction, and motion of the device [6]–[18]. One approach consists of implanting multielectrode arrays in cortical regions involved in motor planning and control, recording the neuronal activity elicited over the array during various motor tasks, and developing algorithms that decode motor intention from this neuronal activity [7], [8], [17]. Near-instantaneous cortical control of a virtual limb is now possible, greatly reducing or eliminating the need for extensive training in the use of the device [7], [10], [15], [18]. The end result is that, over the past decade, human patients are able to coarsely manipulate prosthetic devices through mere thought. With intense concentration, these patients can effect precise movements of a device comprising multiple degrees of freedom.

However, even equipped with a neuroprosthesis under full cortical control, performing ADLs without rich sensory feedback becomes burdensome to the point of being ineffective [2], [19]–[21]. Indeed, picking up a glass, tying one's shoes, or holding a pen requires continuous information about which parts of the hand are in contact with the object and how much force each exerts on the object [19]–[22]. Without this information, these ADLs have to be performed under visual control, which is less natural and sometimes inadequate, especially when the forces applied are isometric and visual feedback is uninformative.

Electrical stimulation of both the peripheral nerve [8], [23] and the somatosensory cortex [24]–[27] can elicit reproducible percepts. However, while behavioral responses can be elicited through intracortical microstimulation (ICMS) of somatosensory cortex [27], [28], the nature of these sensations, and the degree to which these can be used to guide the dexterous manipulation of objects, has yet to be demonstrated. Here, we describe the implementation of a somatosensory prosthesis with which we can deliver percepts whose magnitude is graded according to the force applied to the prosthesis. We demonstrate that animals can detect mechanical indentations delivered to the prosthesis as well as when these same indentations are delivered to their native finger. We also discuss how this sensory prosthesis could be incorporated into a dexterous and sensorized upper-limb neuroprosthesis.

Manuscript received July 17, 2012; revised November 21, 2012; accepted January 26, 2013. Date of publication March 06, 2013; date of current version May 04, 2013. This material is based upon work supported by the Defense Advanced Research Projects Agency under Contract N66001-10-C-4056. The work of G. A. Tabot was supported by the National Science Foundation under Grant DGE-0903637. The work of S. J. Bensmaia was supported by the National Institutes of Health under Grant NS18787.

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Digital Object Identifier 10.1109/TNSRE.2013.2244616

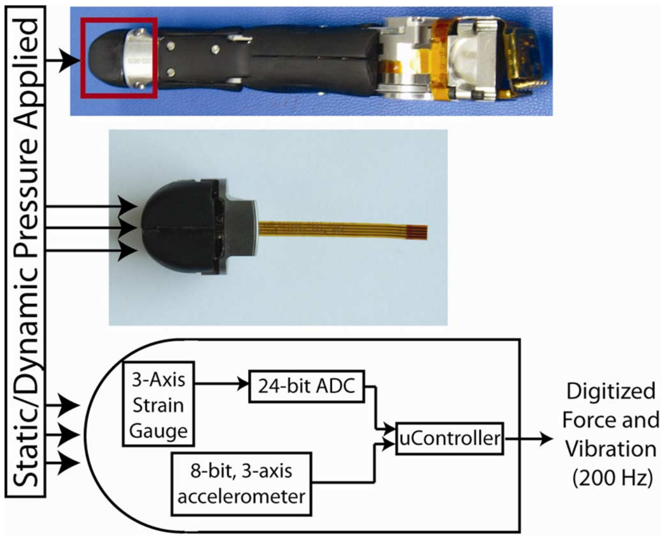

Fig. 1. Top: Photograph of the fully integrated finger of a highly dexterous prosthetic hand (Modular Prosthetic Limb, MPL). Middle: Photograph of the MPL's fingertip sensor node (FTSN). Bottom: Block diagram of FTSN.

II. Prosthesis Design

A. Sensorized Finger

The Fingertip Sensor Node (FTSN, JHUAPL, Laurel, MD) consists of a suite of sensors, electronics, and software that reside on the distal end of each finger of the Modular Prosthetic Limb (MPL, JHUAPL, Laurel, MD) and is used to provide haptic feedback, advanced control and sensory stimulation to the patient. As shown in Fig. 1 the suite of sensors includes force and vibration sensing elements. For the purposes of the experiments described here, only the force sensors were used.

In order to measure the amount of force applied to the fingertip, three sets of strain gauges are embedded into the FTSN to sense forces along three orthogonal axes (only the axis normal to the surface of the prosthetic finger was used in these experiments). The strain gauges are configured in a standard Wheatstone bridge configuration where the resistance of the strain gauges changes in proportion to the level of strain, thus creating a voltage potential. This voltage is then amplified, filtered and digitized using a low power, 24-bit analog-to-digital converter (ADC) with a built-in tunable amplifier. The ADC interfaces with an 8051 microcontroller (Silicon Labs, Austin, TX) over a Serial Peripheral Interface (SPI) bus. The 8051 microcontroller samples each channel of the force sensor at 200 Hz and drives only one channel at a time in order to minimize power consumption.

Ultimately, the 8051 microcontroller sends the digitized sensor data at 200 Hz via an RS485-like serial bus to a module known as the limb controller (LC), a processor housed in the palm of the MPL hand for high rate signal processing. The LC then sends the sensor data at 50 Hz to external nodes for sensor processing outside of the physical limb system.

The mechanical stimulator we used in the behavioral experiments described above is driven by commanding position rather than force. The stimulator is thus ill-suited to stimulate a non-deformable substrate such as the sensorized finger. In order to replicate the mechanical detection and discrimination tasks with the prosthetic finger, it was covered with a deformable elastomer. In preliminary experiments, we measured the force exerted on the sensor when the elastomer was indented at different depths, and the relationship between these and indentation depth was characterized. The force output was then converted into an equivalent indentation depth before it was fed into the sensory encoding algorithm.

B. Electrode Arrays

Each animal was implanted with three arrays. One Utah Electrode Array (UEA) (Blackrock Microsystems, Salt Lake City, UT) was implanted in the hand representation of Brodmann's area 1. These hybrid arrays consist of 96 1.5-mm long electrodes with 400-μm spacing across a 10×10 (4 mm $\times$ 4 mm) square grid. The arrays are coated with Parylene-C, with a 2000 μm^2 Sputtered Iridium Oxide Film (SIROF) tip, allowing for stable neural recordings as well as electrical stimulation. Each animal was also implanted with two Floating Microelectrode Arrays (FMAs, MicroProbes for Life Sciences, Gaithersburg, MD), flanking the UEA (medially and laterally) along the central sulcus and targeting Brodmann's area 3b. Each array consists of 16 3.0-mm long electrodes staggered across four rows by 5 long in a rectangular array measuring 2 mm $\times$ 4 mm. These hybrid arrays are coated with Parylene-C, with a 2000 μm^2 activated iridium oxide tip, allowing for stable neural recordings as well as electrical stimulation. One was implanted medially and posteriorly to the UEA along the central sulcus, the other was lateral and anterior. All implantation procedures were carried out aseptically, under veterinary observation, and in compliance with the guidelines of the Animal Care and Use Committee of the University of Chicago and of the National Institutes of Health Guide for the Care and Use of Laboratory Animals.

We verified after implantation that the receptive fields (RFs) were located in the hand. Because of the limited area of the hand representation in area 3b, only one of the two FMAs impinged upon the hand representation (the other was in the arm in both monkeys), so only that FMA was used in stimulation experiments (Fig. 2).

C. Neurostimulator

We delivered electrical stimulation using a 96-channel fully programmable biphasic pulse current generator (CereStim96, Blackrock Microsystems, Inc., Salt Lake City, UT), gated through a 128-channel electrode control switch (CereStim Switch, Blackrock Microsystems, Inc., Salt Lake City, UT). The switch allows specialized headstages to be rapidly toggled between stimulation and recording modes. When in stimulation mode, the switch passes currents from the electrical stimulator through the headstages, which interface directly with the Cereport percutaneous connector. We controlled the electrical stimulator via a C++ application programming interface invoked by custom-made programs written in C++ and Java.

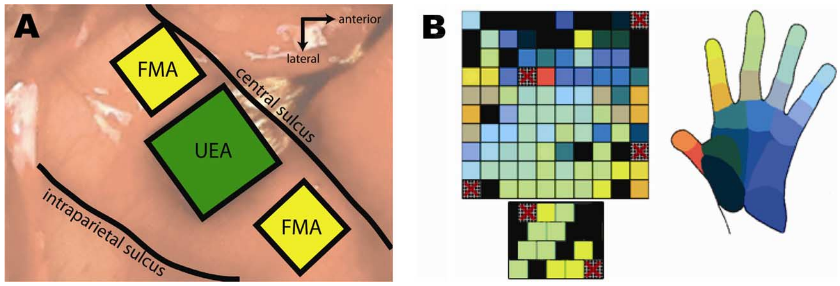

Fig. 2. (A) Chronic electrode implants in one of the two animals, showing the UEA, impinging upon area 1, flanked by two floating microelectrode arrays (FMAs), impinging upon area 3b. UEA and the lateral-anterior FMA impinged on the hand representation; the medial-posterior FMA impinged on the arm representation in all three animals and so was not used in the experiments. (B) Map of the receptive field locations for the UEA (top) and one of the FMAs (bottom) of one of the animals (the other FMA impinged upon the arm representation). The somatotopic organization of primary somatosensory cortex is readily apparent in these maps. The electrodes impinged upon the representations of the middle and index fingers. Black squares indicate electrodes from which signals were too weak to discern.

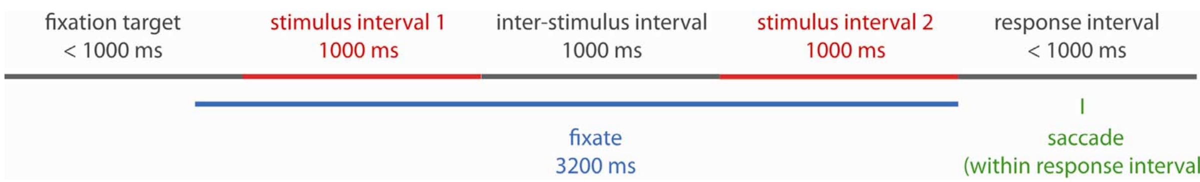

Fig. 3. Trial structure. A fixation target is presented for up to 1000 ms. The animal acquires the target and fixates for 200 ms to initiate a trial. The animal maintains fixation through the first and second stimulus intervals and the interstimulus interval (each 1000 ms), after which the fixation target disappears and two answer targets (left and right) appear for up to 1000 ms. A saccade to one of the targets, followed by a fixation on that target that lasts 50 ms or more, constitute a behavioral response. If the animal responds correctly, a juice reward is delivered during an intertrial interval of variable length (lasting between 1500 and 3000 ms). If the animal responds incorrectly, no reward is delivered. If the animal fails to acquire the initial fixation target or breaks fixation at any point during the trial, the trial is aborted, and a new trial begins after the intertrial interval.

III. Methods

A. Subjects

Two male Rhesus macaques, weighing 11.5 and 8.8 Kg and 6 years of age, were used in these experiments.

B. Behavioral Training and Preliminary Testing

Animals were trained to detect mechanical indentations delivered to the skin. Once the animals were trained to perform this task on the basis of mechanical stimulation of the skin, their ability to detect electrical stimuli was tested using identical protocols.

C. Mechanical Detection

Mechanical stimuli were delivered to the glabrous skin of the hand using a linear stage (Parker Hannifin Corporation, Cleveland, OH) that drove a metallic probe with a tip diameter of 2 mm. The stage allows for the delivery of stimuli with micrometer precision and was controlled using in-house software written in C++. Each trial began with the animal fixating on a central target (Fig. 3). After 200 ms of fixation, the animal was presented with two stimulus intervals, each indicated by a light on the screen and by a simultaneously presented auditory tone. The animal maintained fixation throughout both intervals or the trial aborted. After the second interval, the central fixation target was replaced by two response targets, left and right. The stimulus intervals lasted 1 s each and were separated by a 1-s interstimulus interval. On each trial, a mechanical indentation was presented during one of the two intervals. Mechanical stimuli

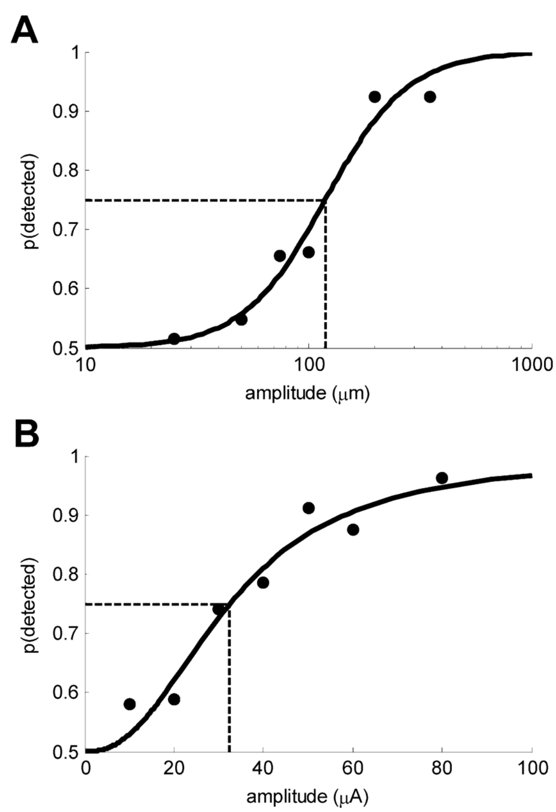

Fig. 4. Detection of mechanical and electrical stimuli for one monkey. (A) Mechanical detection performance at one skin location (middle fingerpad of the third digit, $\mathrm{N} = 387$ trials). (B) Electrical detection performance on one electrode implanted in area 1 $(\mathrm{N} = 994)$ with a receptive field on middle fingerpad of the third digit.

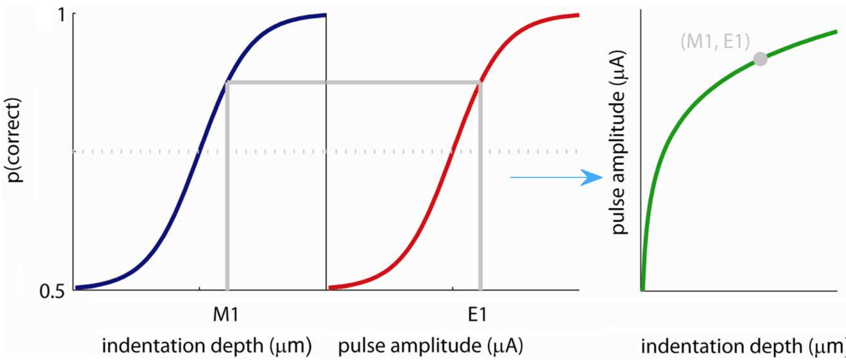

Fig. 5. Illustration of psychometric functions relating discrimination performance to the amplitude of a mechanical (blue trace) and an electrical (red trace) stimulus. The green trace shows the form of the algorithm for encoding indentation depth (proxy for contact force).

were delivered relative to a baseline pre-indentation of 500 μm and ranged in amplitude from 50 to 350 μm (the indentation and retraction rate was 100 mm/s). The animal's task was to indicate which of the two intervals contained the stimulus: A left saccade indicated the first interval and vice versa. Correct responses were rewarded with juice. White noise was delivered through speakers to mask any noise the stimulator might make, and the monkey's hand was obscured from its sight. Loci of stimulation on the hand were selected to match the receptive fields of individual electrodes used in the electrical detection experiments. Fig. 4(A) shows the mechanical detection performance of one monkey, stimulated on the distal pad of the fourth digit. As expected, stimulus detectability increases as amplitude increases and the animal's mechanical threshold (that yields 75% detection performance) at this hand location is 120 μm. Mechanical thresholds ranged from 40 to 300 μm across monkeys and hand locations (including the palm and the digits).

D. Electrical Detection

The trial structure of the mechanical detection task was duplicated, but instead of presenting mechanical stimuli, we delivered electrical stimuli. All stimuli consisted of 1-s-long 300-Hz trains of symmetric biphasic pulses, anodic pulse first, with phase durations of 200 μs and an interphase interval of 53 μs. Pulse amplitudes varied from 5 to 100 μA. Fig. 4(B) shows the electrical detection performance for one monkey at an electrode implanted in area 1 with RFs on the distal pad of the fourth digit. As expected, stimulus detectability increases as amplitude increases. Electrical thresholds ranged from 10 to 70 μA. There were no systematic differences in sensitivity to ICMS in areas 3b and 1 (mean thresholds were 34 and 39 μA for areas 3b and 1; $\mathrm{t}(52) = 1.5, \mathrm{p} > 0.1$), a result that is somewhat difficult to interpret given that different electrodes were used to stimulate the two areas.

E. Sensory Encoding Algorithm

Using detection data obtained from both mechanical and electrical trials, we developed a psychometric equivalence function that relates electrical to mechanical stimuli that are equally detectable (Fig. 5). To obtain this function, we first fit the following psychometric functions to the mechanical detection and discrimination data:

$$p(a) = \frac{1}{2} + \frac{\gamma}{1 + e^{-\frac{a-\mu}{\sigma}}}$$

where $p(a)$ is the probability that the interval in which a stimulus of amplitude a was correctly identified, μ, σ, and γ are the mean, slope, and asymptote of the function, respectively. From these functions, we paired mechanical and electrical stimuli that were equally detectable and used these functions to convert, in real time, the output of the force sensors, into an electrical ICMS pulse train that yielded a percept of equal sensory magnitude (Fig. 5). Importantly, in computing psychometric equivalence functions, we paired mechanical and electrical detection performance corresponding to the same location on the hand. For example, we paired mechanical detection on the index fingertip with electrical detection based on stimulation through an electrode with a receptive field on the index fingertip. The details and validation of this approach are beyond the scope of the present paper, whose objective is to describe its implementation.

F. Behavioral Testing With Prosthesis

After establishing psychometric equivalence functions for each animal, we wished to test whether the animal could perform the detection task based on stimulation of the prosthetic finger. The psychometric equivalence approach sketched previously allows us to produce a percept whose sensory magnitude can be matched to that evoked by indenting the skin. Thus, we can compare the performance on trials with indentations delivered to the skin to that on trials with the same indentations delivered to the prosthesis.

With this in mind, we repeated the mechanical detection task described in Section III-B1, but, rather than (mechanically) stimulating the animal's hand, we stimulated the prosthetic hand (Fig. 6). We replicated specific stimulation conditions that we had used in mechanical discrimination experiments, converting the output of the force sensors into electrical pulse

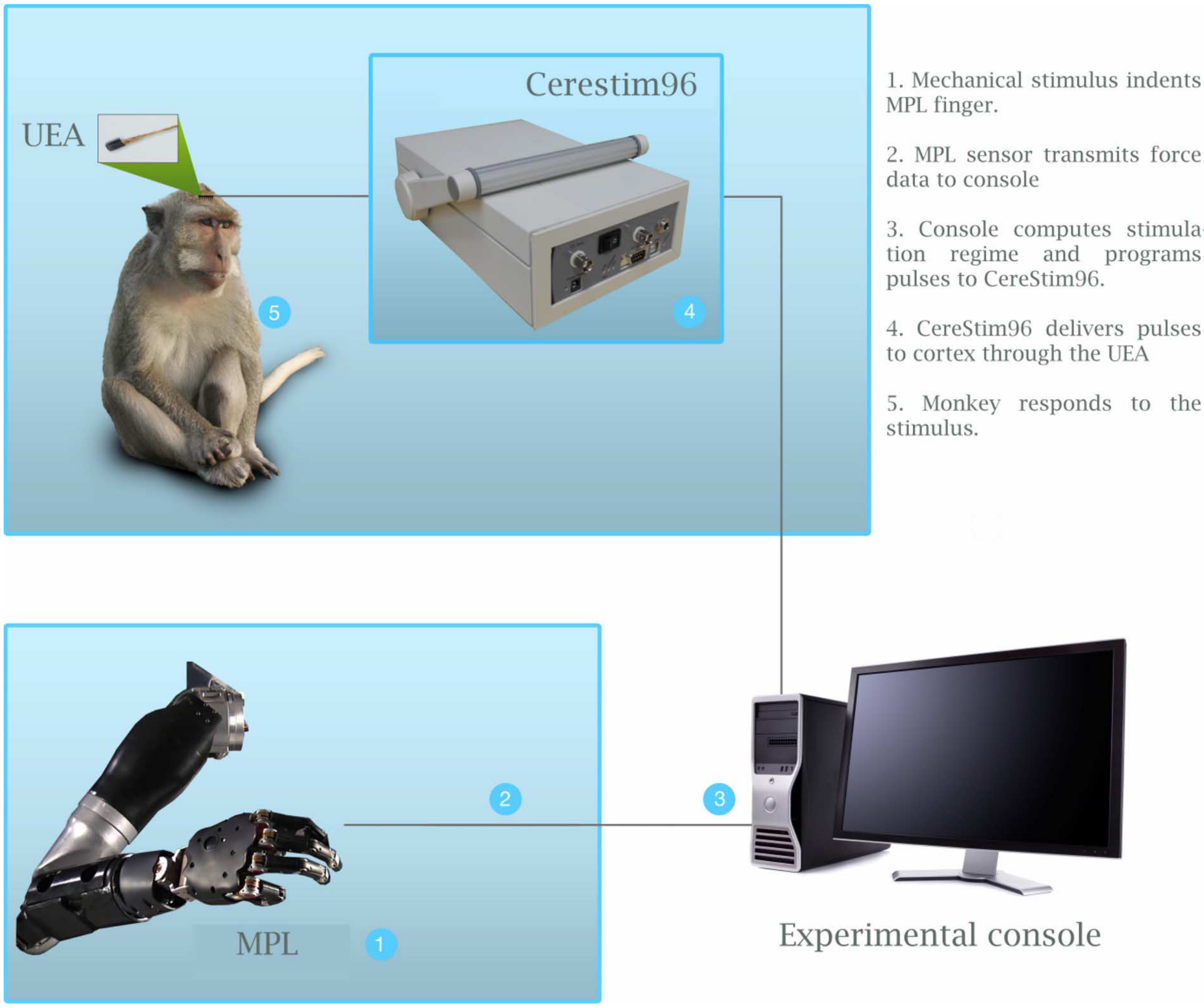

Fig. 6. Diagram of somatosensory prosthesis.

trains in (quasi-) real time (Fig. 7). Specifically, we converted the time-varying output of the sensor into an equivalent indentation depth (based on the relationship shown in Fig. 8), which was then converted into an electrical pulse train using the psychometric equivalence function (Fig. 5).

IV. Results

Fig. 8 shows the mean force, measured using the force sensors on prosthetic finger, as a function of indentation depth, for trials over three different experimental sessions. As can be seen, over the range of indentation depths tested, the relationship between indentation depth and applied force was linear. Importantly, the measured force was highly consistent from indentation to indentation (with standard deviations less than 5 g), attesting to the reliability of both the stimulator and the force sensor. Note that these forces may not match those applied to the native finger, since indentations were delivered to the prosthetic finger covered with an elastomer, the mechanical properties of which do not match those of the skin. Because the elastomer was much stiffer than skin, the magnitudes of the forces applied to the prosthesis were likely higher than those applied to the native finger [based on previously published work, [29], for example]. Over the range tested, however, force has been shown to increase linearly with the indentation depth on the skin, so the shape of the function shown in Fig. 8 matches that obtained when similar measurements are made on the skin [29].

Fig. 9 shows the performance of two animals on a detection task performed based on mechanical stimulation of the prosthetic finger using four different electrodes (run in separate experimental blocks), two in area 1, two in area 3b. As can be seen, the detectability of indentations applied to the prosthesis increases as the indentation depth and thus the force measured by the sensor increase. Detection thresholds obtained through the prosthetic finger ranged from 110 to 125 μm, which falls within the range of those obtained when the native finger is stimulated (40 to 300 μm). Thus, the performance of the animals when the prosthesis is stimulated is indistinguishable from that when the native finger is stimulated. By construction, then, the animal is equally sensitive to mechanical indentations, whether these are applied to its hand or to the prosthesis. To our knowledge, this constitutes the first demonstration of a somatosensory neuroprosthesis, in which an animal perceives a tactile stimulus through an artificial sensor.

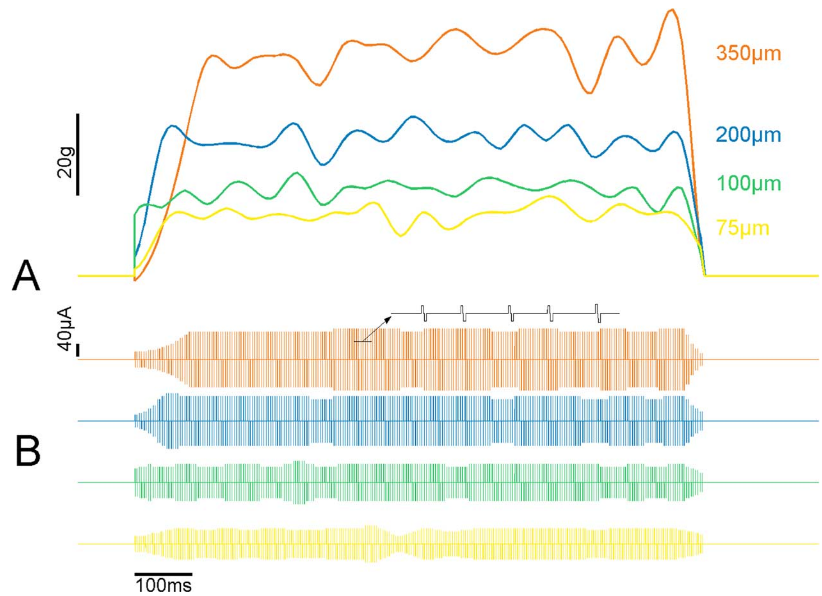

Fig. 7. Conversion from time-varying force to ICMS pulse trains of varying amplitude. (A) Time-varying force output of the prosthetic finger on four detection trials with four different amplitudes. (B) Resulting electrical stimulation pulse trains.

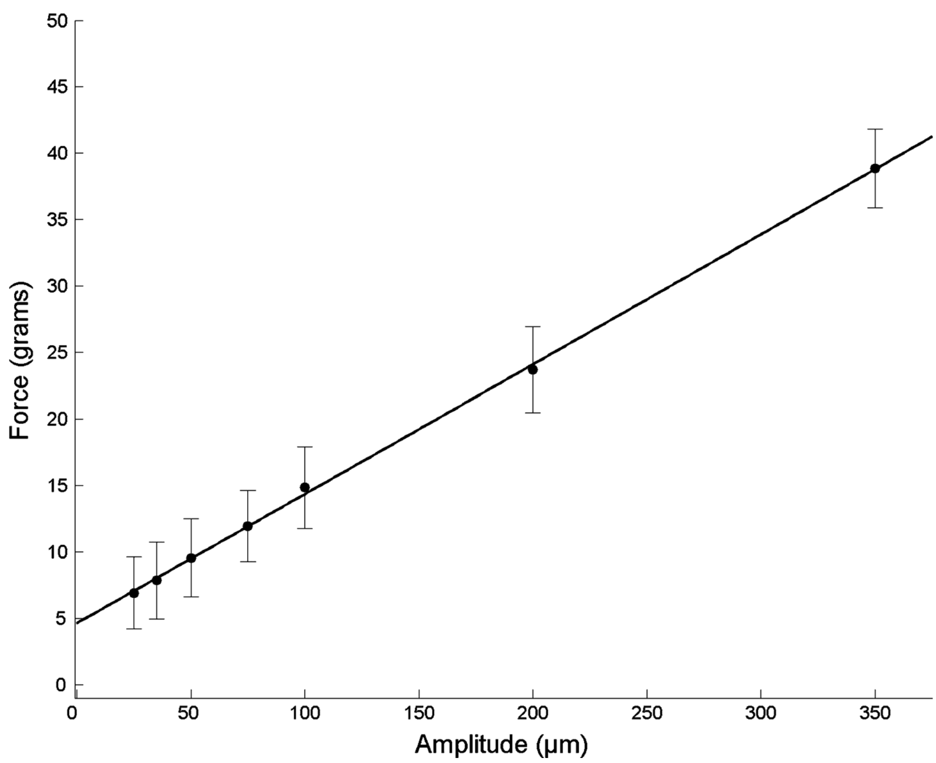

Fig. 8. Mean force recorded from the prosthetic finger as a function of indentation depth. Over the range of indentations tested, force is a linear function of stimulus amplitude. Each point represents 1430 measurements; error bars denote standard deviation. Measured force was highly consistent from trial to trial, with standard deviations less than 5 g.

V. Discussion

We describe an implementation of a somatosensory prosthesis and demonstrate it in behavioral experiments with nonhuman primates. We show that we are able to deliver graded percepts over a range of sensory magnitudes from sub- to supraliminal. We expect and have data to suggest that if we were to increase the force applied to the prosthesis beyond the range used in the detection experiments described here, we would elicit supraliminal percepts that increase in magnitude. We envision that the approach described here can readily be combined with the decoding of motor intention to convey information about force in a closed-loop cortical upper-limb neuroprostheses, particularly targeted towards patients affected by tetraplegia.

Here, we propose an approach to intuitively convey information about force. Indeed, as the force exerted on the sensor increases, the sensory magnitude of the electrically elicited percept increases. While we cannot establish that the percept is one of graded force, we can state with certainty that it scales

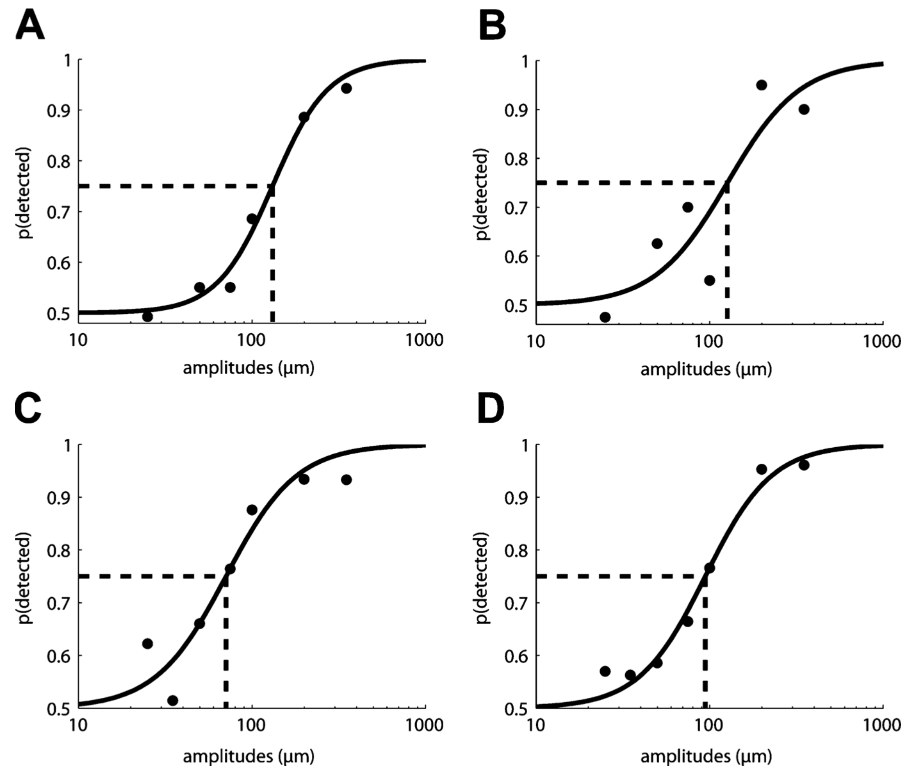

Fig. 9. Performance of two monkeys on detection experiments with mechanical stimuli delivered to the prosthetic finger (each trace represents 480 trials). (A), (B) Detection of mechanical stimuli applied to the prosthetic finger; with ICMS applied to two different electrodes in area 1. (C), (D) Detection of mechanical stimuli applied to the prosthetic finger; with ICMS applied to area 3b. Thresholds were 130, 127, 71, and 95 μm for those four electrodes.

perceptually in a way that is analogous to the perceptual scaling of force. This mapping between force level and perceptual magnitude seems intuitive and should require less training than one based on a less intuitive mapping. For instance, mapping force onto percepts of graded vibrotactile pitch, as is often done in sensory substitution paradigms [but can also be achieved through intracortical microstimulation, see [30]], would require training and the deployment of attentional resources.

The most intuitive approach to conveying information about contact location would be to elicit tactile percepts that are projected to the appropriate location on the prosthesis. Electrical stimulation of individual afferents elicits percepts that are projected to a highly localized patch of skin [23]. To the extent that stimulation of a spatially restricted population of somatosensory cortical neuron evokes a spatially localized percept, the somatotopic organization of the somatosensory cortex can be exploited to create a mapping between the sensorization of the prosthesis and the neural representation in cortex.

For a tetraplegic patient or amputee, one could electrically stimulate each electrode individually in an array implanted in somatosensory cortex and have the patient report where on the native or phantom limb the sensation is projected. The output of the sensor on the prosthetic hand corresponding to that location would then determine the electrical stimulation delivered through that electrode. The mapping between force output and electrical stimulation would then be determined using a function that converts the force into an ICMS pulse train that elicits a tactile percept of the appropriate magnitude. Neuronal populations are differentially sensitive to electrical stimulation but the shape of the function relating equally detectable electrical to mechanical (see Fig. 5) is consistent across electrodes (data not shown). In a human prosthesis, then, one might tune the gain of the function by having the patient match the perceived magnitude of an electrically elicited percept to that of a standard mechanical stimulus applied to an intact patch of skin (e.g., on the face of a tetraplegic, on the intact arm of an amputee).

What contrasts the approach sketched out here to that described in other studies (see [31], e.g., [32]) is that we seek to convey sensory feedback by mimicking, to the extent possible given our scientific and technological limitations, the manner with which sensory feedback is conveyed in the native limb. Specifically, the strength and spatial extent of the neural activity evoked by stimuli of increasing force increases [33], as does that elicited by increasing the ICMS intensity [34], [35]. The latter is thus a natural proxy for the former. Furthermore, stimulation of a spatially restricted patch of skin produces a spatially restricted pattern of activation in each area of somatosensory cortex. ICMS of a spatially restricted population of somatosensory neurons may thus produce sensations localized to a spatially restricted patch of skin. Providing information about contact location may thus be relatively straightforward. Given the intuitive nature of this ICMS-elicited feedback, we anticipate that less training will be necessary for the patient to be able to interpret this feedback and use it to guide the prosthetic limb. Furthermore, the approach presented here can readily be translated into an existing prosthesis, with little to no additional testing or development.

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Author photographs and biographies not available at time of publication.