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High-side Digitally Current Controlled Biphasic Bipolar Microstimulator

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Abstract

Electrical stimulation of nervous tissue has been extensively used as both a tool in experimental neuroscience research and as a method for restoring of neural functions in patients suffering from sensory and motor disabilities. In the central nervous system, intracortical microstimulation (ICMS) has been shown to be an effective method for inducing or biasing perception, including visual and tactile sensation. ICMS also holds promise for enabling brain-machine-brain interfaces (BMBIs) by directly writing information into the brain. Here we detail the design of a high-side, digitally current-controlled biphasic, bipolar microstimulator, and describe the validation of the device in vivo. As many applications of this technique, including BMBIs, require recording as well as stimulation, we pay careful attention to isolation of the stimulus channels and parasitic current injection. With the realized device and standard recording hardware - without active artifact rejection - we are able to observe stimulus artifacts of less than 2 ms in duration.

Keywords

microstimulation; cortex; artifact; suppression

I. Introduction

Numerous studies have shown that electrical microstimulation of neural circuits by injecting small currents from an electrode tip into the nervous tissue may evoke a variety of effects that are often similar to the functional contribution of the stimulated area [1]. In particular,

microstimulation can produce or bias sensations [2]; [3]; [4]; [5], [6]; [7] [8]. This property of bioelectrical stimulation has attracted the attention of neural engineers as the key component of sensory neural prosthetics for the restoration of sensation in patients suffering from sensory disabilities.

Microstimulation has been introduced as a sensory loop in brain-machine-brain interfaces (BMBIs), systems that both translate brain activity into commands to artificial actuators and deliver information to the brain in the form of microstimulation of sensory areas. In experiments conducted in our laboratory, we utilized temporal patterns of cortical microstimulation to create an artificial somatosensory input for the BMI that enacted arm reaching movements [9]. More recently, our laboratory has demonstrated closed-loop BMBI control for delivering artificial texture feedback through ICMS [8], where precise, rapid, and low-artifact ICMS control was essential to give feedback to the monkey without interfering with recording periods. Here we describe our custom multichannel microstimulator that enabled these BMBIs.

Intracortical microstimulation (ICMS) poses a number of exacting requirements on the experimental system. ICMS requires relatively high voltages (50–100 V) when high impedance (0.5–2M Ω) electrodes are used [10]; [11]; [12]. Furthermore, the useful stimulation waveform durations are usually very short (10 μ s to 100 μ s) [13] [2]; [11]; [7]; [12]. The waveform most frequently used is a charge balanced, symmetric, biphasic stimulation pulse, where a square cathodic pulse is followed by an anodic pulse of equal amplitude [14]. Although the second pulse can reduce the excitation of the tissue, damage to the electrode and tissue is prevented by this charge balancing pulse. The impairing effect of the second pulse can be partially counteracted by a short (100 μ s) delay between the two pulses [15]). Due to the variable electrode to tissue impedance, and response of the tissue to charge, cortical stimulation is usually performed with constant current sources [16]. In terms of safety, the range of figures quoted here – 100 μ s pulses of 100 μ A/phase – equates to 10nC/phase, well within the regions described by [17]. Charge density using our 65 μ m electrodes is 300 μ C/ cm^2 /phase, which is also within the safety limits proposed by [18].

The current, voltage and timing requirements are not difficult to achieve with modern electronic systems, and many commercial products are available that satisfy the conditions. However, for advanced ICMS studies, the complexity of the stimulus train and number of electrodes enforce more rigorous requirements on stimulation technology. There is immediate need for advanced microstimulation systems capable of operating as ICMS feedback systems in BMBIs [19]; [7]; [9]; [20]. These systems require microstimulation in multiple sites in the brain, using multiple electrodes and complex spatiotemporal stimulation patterns [7], [9], [21], delivered at low latency to enable closed-loop control [8]. It is critical for these systems to induce artifacts of minimal duration to adjacent recording sites to maximize recording quality in BMBIs.

Our stimulator is high-side current controlled, which nearly eliminates the charge and discharge current of stray capacitance between each isolated channel and animal ground. High-side means that the compliant current source is tied to the voltage rails, not ground; with a low-side current source, the current regulator develops voltage across it depending on electrode impedance, voltage that is presented to the stray capacitance of the microstimulator and experimental wiring. Since currents associated with charging and discharging voltage offsets from stray capacitance must necessarily go through the stimulation electrodes, and ultimately through the ground that connects the animal to wired recording systems, voltage offsets should be minimized for both accuracy and artifact avoidance. High-side current control is, to the best of our knowledge, unique to this design. Further artifact suppression can be achieved through close-proximity bipolar biphasic

stimulation, which restricts the spread of electric field within the tissue while remaining efficacious [7]. Finally, the described stimulator is highly flexible: both the current and duration of both phases of the biphasic stimulus waveform can be controlled continuously from a computer with tight synchrony. This computer control permits stimulus trains of arbitrary complexity to be enacted in real-time as needed for a BMBI.

It should be emphasized that the construction and testing of this device was done explicitly for a tethered research environment – that is, where the microstimulator is not mounted on or in the experimental animal – as no commercially available microstimulators were available to permit high temporal fidelity, high flexibility (any pattern can be commanded), high compliance, good current resolution, good channel isolation, minimum parasitic current injection, and a flexible number of channels. Full specifications of the described device are listed in Table I. Given these design criteria the size of the device is large and consumes 300 mW per channel. In comparison, other research into microstimulators such as the clinically-targeted Bion [22] are much smaller and lower power, but correspondingly much more expensive, less flexible due to their high level of integration, and not matched for the high compliance voltage required by our electrodes. Integrated ASIC microstimulators such as [23] and [24] offer compliance of 11V or less, which is insufficient to drive current through high-impedance (more than 100k Ω) electrodes; full systems described in [25] offer insufficient latency and bandwidth for our experimental requirements. Finally, the current-mirror topology of integrated microstimulators does not guarantee low leakage current, which is critical as DC current will gradually erode the tips of electrodes and damage neural tissue.

II. Methods

A. Microstimulation system

The full microstimulation system is comprised of four principal elements: high-level control programs (web interface, UDP sever), a low-level driver/DMA control program, stimulus isolation channels, and the stimulation electrode array (including lead system). Software control of the microstimulation system is depicted in Figure 1.

B. Software control

Interactive control of the microstimulator is through a custom driver program. This program, which runs on a dedicated computer Linux running a low-latency kernel, services a free running National Instruments PCI-6533 card, which continually outputs 16 or 32 bits of digital data at a clock rate of 100 kHz. These digital data consist of multiplexed control pulses and serial peripheral interface (SPI) commands to set the channel current. Data to be output are read by the PCI-6533 from a circular DMA buffer, the address of which is acquired through a custom Linux kernel module. The driver maintains the DMA buffer via a set of watermarks, placement of which depends on the speed of the computer and its peripheral subsystem. To prevent underflow, typically this is less than 200 samples, which translates to a delay of 2 ms at the 100 kHz clock rate. Between DMA servicing cycles – when the watermark criteria are satisfied – the driver program interprets control commands written to a common memory-mapped file.

Microstimulation commands can either be issued through a python-based web interface, or from a UDP server. The latter allows the stimulator to be controlled through Matlab or from other experimental software, such as the BMI software developed in our lab. The web interface allows easy user control of all parameters of stimulation, e.g. current amplitude, pulse width, frequency, and secondary frequency from any networked computer. The present software implementation allows the stimulation pattern to be a single pulse, a

continuous train of pulses, a pulsed stimulation train, a doubly-pulsed stimulation train corresponding to three periods and duty cycles [12], or a stochastic stimulus train derived from a gamma distribution. More complicated stimulus programs can easily be added to the driver program to provide more sophisticated feedback. In the experiments described in [8], where 50ms of BMI decoding alternated with 50ms of microstimulation, we minimized kernel overhead and tightened DMA watermarks so that the latency from BMI command to stimulation, including UDP transmission over ethernet, was $5.4 \text{ ms} \pm 180 \mu\text{s}$ (mean $\pm$ standard deviation). This low-variance latency permitted precisely timed ICMS feedback.

C. Stimulus isolation units

Four stimulator channels are assembled on a circuit board, providing independent and isolated monopolar or bipolar stimulation per electrode. Four of these boards can be stacked and serviced by one PCI-6533, for a total of 15 stimulation channels¹. An overview of a single channel is shown in Figure 2.

There are four primary elements to each channel: the power supply, digital-to-analog converter (DAC), bipolar current regulator, and an isolated monitoring circuit. The isolated power supply uses two series 1 W miniature DC-DC converters to provide 40–160 V for high compliance / high impedance electrodes. An additional 1 W DC-DC converter is used to supply 5 V for the DAC and other circuitry. Current is commanded via the SPI DAC, with separate commands for the anodic and cathodic phases; the command signals for each DAC (clock, data, chip select, load output) are multiplexed with the anodic and cathodic pulse commands so only four signals need pass through the magnetic isolator. Stimulation is enabled with the inverted DAC chip select signal; current amplitude can hence be changed whenever stimulation pulses are absent. Chip select and DAC load output signals are common among all channels, thereby requiring the total number of digital control signals to be two plus twice the number of channels; in turn this means currents on all channels must be set (but not necessarily changed) at the same time.

The core of the stimulation unit is a voltage-feedback high-side current source, shown in Figure 3. It is vital that the current source is high-side, as the topologically simpler low-side control alternative necessitates that during the anodic and cathodic phases the current needed to charge the stray capacitance from one channel to ground must pass through the output electrodes. Note the current source is a symmetric H-bridge, so for clarity only half is fully shown in the figure. Briefly, each half receives two inputs: a voltage command from the DAC into $V_{\text{dac_A}}$, and an inverted pulse command on A_{in} . Transistors Q2 and Q9 act as common-collector amplifiers to detect differences between voltage across the sense resistor, R1, and V_{dac} . Transistors Q4–Q7 act as a differential amplifier to set the current through Q11 and Q15. The latter directly controls the current into the opposite electrode in the pair, while the former supplies current to turn on the lower leg of the H-bridge, Q12. Note that base current into Q12 also goes through the sense resistor R1, so the current command is off by a fraction set by the ratio of resistors R2 and R3 $\times \beta_{Q15}$. This offset is measured below and corrected in software. Capacitor C1 controls the slew rate of the Q4–Q7 pair, and prevents feedback oscillations. Finally, Q3 and Q10 serve to turn off the output stage when the control signal goes high; Q10 is essential for draining base charge on Q12 and returning the output to a high impedance condition. Buffer U1 serves to delay this command to Q10, allowing Q12 to remain on for about $4 \mu\text{s}$ longer so as to discharge any residual charge on the electrodes, and hence between the animal ground and isolated ground. As mentioned before, this is to minimize artifact on neighboring recording electrodes. Transistor Q3 is

¹The PCI-6533 has 32 digital input/output channels, and each channel requires two lines plus two common signals for all channels, hence only 15 channels can be controlled from one PCI-6533 card.

saturated on when output is disabled, which turns Q5 on through the current mirror, hence setting the base current of Q15 to zero; this means that stimulator leakage current is dominated by the off-state current mismatch through Q15 and Q12, which is measured to be less than 300 pA. It was chosen to make the output high-impedance when off rather than short-to-ground to further minimize noise injection.

For safety, diodes D4, D5 and their mirrors serve to protect the output stage from ESD damage along with resistors R1 and R2. If this topology is used in a clinical setting, further protection will need to be added, as failure-to-short of any transistor can tie one half of the H-bridge to a supply rail, and failure of two transistors can permit unregulated DC current through the electrodes. In the implemented boards, all transistors are rated at 185V or higher, while the supply voltage is typically 50V; no semiconductor failures have been observed in several years of operation, though one channel in one stimulator was disabled prior testing due to internal PCB delamination. This is best fixed by simply using a thicker medical-grade PCB. Finally, While there are no hardware limits on the duration of delivered current, we have observed no software failures leading to DC current applied to the animals. Transistor bias currents limit total current delivered per channel to 800 μ A.

The isolated monitoring circuit stage is shown in Figure 4. Blocks U1 and U2 contain one infrared LED and two matched photodiodes. Opamps O1 and O2 regulate the LED current to match the photodiode current to that from inputs Aout' and Bout' (see Figure 3); this mirrors the current onto the non-isolated photodiode pairs. Opamp O3 converts the resulting non-isolated bipolar photodiode current to a voltage, and opamp O4 works to null DC differences due to photodiode imperfections. In turn, O6 drives indicator LEDs, and O5 the final output, which can be viewed on an oscilloscope or digitized. Because the current command and resultant voltage are known, this circuit allows electrode resistance to be easily calculated.

D. Electrodes

The electrodes used in testing this system were fabricated in-house at the Duke University Center for Neuroengineering (DUCN). The electrodes work well for both chronic multisite neural ensemble recordings and for stimulation. The DUCN microelectrode arrays consist of tungsten or stainless steel microwires with teflon, SML, or HML insulation. The overall diameter of the microwires is in the range of 25–65 μ m, and the separation of electrodes in the array is the range of 200–1000 μ m, center to center, depending on the brain area targeted, the animal species, and the experimental protocol [26]. For all testing and validation use of the system reported here, we stimulated between two of electrodes chosen from an arrays constructed with stainless steel microwires and HML insulation.

E. Assembly and Testing

Electrical schematics were designed in the open-source Kicad software suite; the PCB was designed in Kicadocaml then manufactured by Imagineering Inc. (Elk Grove, Illinois). We elected to use entirely discrete components in this device for manufacturing ease and cost; the current regulator and other parts could be integrated in a high-voltage bipolar process. The smallest components placed were 0402 chip resistors and capacitors, though the majority of the PCB is populated with 0603 scale resistors and transistors, only on the top of the board; this leads to a total PCB area for 4 channels of 187 cm^2 with a mass of 120 g. As mentioned in the introduction, this is much larger than comparable microstimulator ASICs designed for implantation, which are less than 1 cm^2 , but the device meets its intended research purposes. Four PCBs can be stacked to obtain 15 stimulation channels. A photograph of the assembled PCB is shown in Figure 5.

III. Results

A. Bench-top testing

The system was first tested using resistive loads to verify proper circuit performance and timing. Figure 6 shows the output of the simulator through a 100 k Ω resistor and the resultant isolated monitoring output. The latter has a voltage attenuation of 25 to allow headroom for measuring large-amplitude signals or high-impedance electrodes. In practice, the waveforms have much lower slew rate due to the capacitance of the wire between electrode and microstimulator and the nonlinear charge/discharge profile of the electrode-tissue interface.

The implemented system is capable of a current range of 0–400 μ A or 0–800 μ A, depending on the DAC output scaling. Output currents larger than this will require different bias currents in the bipolar current regulator, hence a few component values would need to be changed. The stimulator features a measured maximum voltage compliance of 160V, and an output parallel resistance of greater than 10 M Ω . To characterize the slew rate of the current source, rise and fall times of the pulse output were measured across a 118 K Ω resistor for varying currents. Rise and fall times are defined as the time for the voltage to increase from 10% to 80%, and to fall from 80% to 10% of the output amplitude, respectively. As can be seen in Figure 7, the rise and fall times ranged from 6–20 μ s for output voltages of 5–38 V, with longer rise and fall times at higher output amplitudes. This corresponds to a slew rate of 5 V/ μ s at larger amplitudes; this may be decreased by increasing the value of capacitor C1 in Figure 3.

As mentioned above, the current output is less than the commanded output current by the base current of transistor Q12 in Figure 3. This current was set conservatively in the present implementation to allow higher output currents, hence must be corrected in software. To calibrate the device, we tested the output across 97, 120, 180, 240, 270, 330, and 470 k Ω resistors, with current amplitudes of 50, 75 and 100 μ A. Figure 8 shows the result of this calibration, in which the trend line, found using linear regression, has slope of 0.745. The pulses measured in this test were deemed to have started when the voltage reached 50% of peak amplitude, and to have ended when the voltage dropped to 50% of peak amplitude. The output voltage amplitude is defined as the mean voltage during that interval.

Using these criteria, we also measured the distribution of pulse widths, shown in Figure 9. For a 100 μ s command pulse, the distribution of measured pulse widths was found to have a mean of 92 ± 1.3 μ s. The charge balance of each stimulation pulse was calculated, and the distribution is shown to the right. The mean charge imbalance for commanded pulses was -0.094 ± 0.56 nC. For comparison, the charge delivered in each phase is 5–10 nC, so this imbalance is only on the order of 1–2%.

B. In Vivo testing

To characterize the stimulator in intended application, we examined the effects of ICMS in a rhesus monkey chronically implanted with multielectrode arrays bilaterally in motor and sensory cortices. In the first of these tests, we applied stimulus trains consisting of 150 μ s long, 100 μ A anodic and cathodic pulse pairs separated by a delay of 25 μ s. Fifty of these pulse pairs were applied with an inter-pulse interval of 10 ms to electrodes spaced at 1 mm in the arm representation of the left primary motor cortex (M1). Simultaneously we recorded using a Plexon Inc. (Dallas, TX) Multi-acquisition processor (MAP) from electrodes implanted in the arm region of M1 of the opposite hemisphere, using standard spike (passband: 170 Hz–8 kHz, gain:1000) preamplifier boxes and custom headstages with a gain of 8 and one high-pass pole at 560 Hz.

In Figure 10, trace A was recorded from a blunt-cut 50 μm Teflon-insulated stainless electrode at +15.5 mm lateral the mid-line, +4.5 mm rostral the intra-aural line, or 32 mm from the center of the dipole created by the stimulating electrode. Trace B is from the same type of electrode, at +12 lateral, +10 rostral, making it 29.2 mm from the stimulating dipole; trace C is from a sharpened HML-insulated 65 μm stainless electrode +15 lateral, +6 rostral, hence 31.5 mm from stimulating dipole. Despite the fact that all three recordings were from about the same distance from the stimulating dipole, the top trace shows no stimulation artifact, the middle shows a small stimulation artifact, and the bottom shows a large stimulation artifact. The differences are likely due to different referencing for the three channels – channels A and B were referenced to electrodes in the microelectrode array functionally identical to the recorded electrode, while channel C was referenced to animal ground, which is connected to T-bolts implanted through the skull. In the Plexon preamplifier, reference channels are subtracted from individual electrode channels to cancel out common-mode noise; it can work well though better methods exist [27].

To further test the degree to which microstimulation interferes with neural recording, we needed to increase the artifact on channels A and B shown in Figure 10. As increasing the spacing between electrodes increases the size of the associated electric field, we made the distance between the stimulating electrodes as 5.6mm, as large as possible within one microelectrode array in the chronically implanted monkeys. Figure 11 shows the resulting traces, which indicate accordingly that the artifact has increased as compared to Figure 10.

Importantly, neuronal spikes are clearly still visible in between stimulus artifacts on Figure 11 traces A and B. Trace C shows a broader artifact that may occlude spikes. To accurately determine the width of these artifacts, we next recorded continuously for one hour, again from several microelectrodes located in the arm representation of M1 while stimulating the contralateral hemisphere with 100 μs , 100 μA anodic and cathodic pulses separated by a delay of 100 μs . These pulses were applied once a second (1Hz) to two electrodes spaced at 1 mm, the same electrodes as in Figure 10.

Figures 12 and 13 show the two extremes of the result of this test: Figure 12 shows a channel that was very minimally effected by the stimulus artifact, while Figure 13 shows the channel that was broadly affected. Figure 12 is consistent with only minor interference with spike detection and sorting, and only for those spikes whose duration spans the stimulus pulse. Figure 13, however, suggests that at least one part of the amplifier chain, most likely the high-gain preamplifier, is driven to saturation for the duration of the artifact; it is unlikely that the headstage is driven to saturation, as then the result in Figure 12 would not be possible. These two channels, other than slight differences in distance from the stimulating pair, are only different in their referencing - the channel in Figure 13 was referenced to ground. These results show that it is possible to record with very minimal stimulus artifact with the described stimulation system, proper referencing, and centimeter spacing between stimulating and recording electrodes. Note that no stimulation artifact suppression system was used.

To further characterize the duration of the artifact for much closer stimulation-recording distances, we examined the stimulus artifact on 112 channels during a closed-loop stimulation task with a rhesus macaque. Of the 112 recording electrodes, 32 were in motor cortex contralateral to stimulation, mean distance 36 ± 1.7 mm from stimulating pair; the other 80 were ipsilateral, in the same array as the stimulating electrodes, mean distance 2.7 ± 1.2 mm. Plotting stimulus artifact duration by absolute distance from stimulating pair did not yield any observable trends due to varying referencing and per channel gain, so the aggregate data is presented in Figure 14. Stimulus artifact in contralateral recording electrodes was 2.1 ± 0.8 ms, and 5.8 ± 2.3 ms for ipsilateral. Though the electrodes here are

much closer to the stimulating pair than Figures 12 and 13, this is short enough that spikes can be recorded between stimulus pulses on many channels, as can be observed from the aggregate firing rate in Figure 14 A.

C. Efficacy in Nervous Tissue

To demonstrate the efficacy of the stimulator in activating nervous tissue, we performed stimulation of the right arm representation of M1, with two stimulating electrodes consisting of HML insulated sharpened 65 μm stainless steel, centered +15mm lateral, +10mm rostral. These electrodes were the deepest of the array and penetrated the cortex by ≈ 3.4 mm. Stimulation pulses were 100 μs pulses of 75 μA , separated by 50 μs ; fifty of such pulses were applied for each trial at 100 Hz. The results of this protocol are depicted in Figure 15.

The microstimulation had a gradually increasing effect on EMG during the half-second of duration of pulses, as is evident in the Figure. More immediate responses and broader activations (including muscles of the torso) were obtained with higher currents - up to 175 μA . No other effects, harmful or otherwise, were observed in the monkey.

IV. Conclusion

We have demonstrated the design of a multi-channel high-side digitally current regulated microstimulator, and verified its function on the bench as well as in an experimental animal. The design tries to minimize current injected as a result of parasitic capacitance between the microstimulator and animal ground, and as a result is capable of introducing only very short artifacts into simultaneous neuronal recordings – less than 1ms in some configurations – which, when combined in low-latency control, is suitable for experiments where neural recording and microstimulation are tightly interleaved. Our microstimulator offers a compliance of 50V or greater for stimulating high-impedance electrodes with a very small leakage current of 300pA or less. As such, the design is immediately applicable to experiential neurophysiology; indeed, in our lab we have been using three instances of the stimulator.

Several improvements are suggested by the results. Other than further reducing parasitic capacitance, it would be useful to provide a greater range to the output current. For example, if the feedback resistor (R_1 in Figure 3) and bias currents are adjusted, the same stimulator topology can easily be used on muscles for functional electrical stimulation (FES). An alternative to the present H-bridge design is a bipolar supply totem-pole configuration with current mirroring rather than feedback stabilization, so there is no need for a feedback resistor and its attendant voltage offsets; however, this design can be susceptible to leakage current and charge imbalance, both which can damage electrodes. Even though the microstimulation artifact is short, active or forward cancellation schemes may be desired to reduce the artifact to below the noise level. Perhaps the most pressing concern, however, is size - if microstimulation with simultaneous recording is to be clinically applied, stimulation channels and controller will need to be integrated onto one chip, consume less than 1mW, and likely share a common power supply rail with recording apparatus. We believe that the topology described herein represents a step forward in microstimulator design for experimental use, that the lessons in minimizing artifact are instructive to other practitioners, and that the same compact topology may be integrated and miniaturized into a ASIC for future clinical use.

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Fig. 1.
Schematic overview of software control of the microstimulator.

Fig. 2.
Schematic overview of one stimulator channel.

Fig. 4.
Isolated monitoring circuit.

Fig. 5.
Photograph of a populated PCB featuring four bipolar channels; input is on the lower left, output on the right.

Fig. 6.

Top, output of microstimulator through a 100 k Ω resistor, current set at 200 μ A, anodic and cathodic phases set to 100 μ s, delay between pulses 50 μ s. Bottom, simultaneous output of isolated monitoring circuit.

Fig. 7.

Rise and fall times for anodic and cathodic phases. Slight differences may be due to the fact that this was measured with one oscilloscope probe, hence the anodic pulse had to charge stray capacitance whereas the cathodic did not.

Fig. 8. Expected vs. actual pulse amplitude for several current settings and resistive loads.

Fig. 9. Left, distribution of measured pulse widths for a 100 μs command pulse. Right, distribution of charge imbalance for pairs of anodic-cathodic pulses.

Fig. 10.

Three example voltage traces recorded from different electrodes in right M1 arm region of a rhesus macaque. Traces show varying amounts of stimulus artifact and simultaneous extracellular action potentials, as sorted in the Plexon software, indicated with red asterisks.

Fig. 11.

Three electrode traces recorded from right M1 arm region of a rhesus macaque. Stimulus artifact resultant 100 μ s, 100 μ A anodic and cathodic pulses separated by a delay of 100 μ s.

Fig. 12.

A, Rasterplot of spike times relative to the 1 Hz stimulation pulses; electrode and neuron were the same as shown in A of Figures 10 and 11. **B**, Peri-event time histogram (PETH) of the corresponding spike rate, binned at 1 ms. Artifact, while not visible in Figure 10, is visible here, and is ≈ 1 ms.

Fig. 13.

A, Rasterplot of spike times relative to the 1 Hz stimulation pulses; neuron was recorded from leg representation of right M1 @ +4.5 lateral, +2 rostral from 65 μ m HML insulated stainless electrode, or 21 mm from the stimulating pair. **B**, Peri-event time histogram (PETH) of the corresponding spike rate, binned at 1 ms. Artifact was 6.5 ms and was the longest of those recorded in this session.

Fig. 14.

A, Mean aggregate firing rate of 190 neurons recorded from 112 electrodes in left and right motor cortex from a rhesus macaque. Stimulus was groups of 8 $150 \mu\text{A}$ pulses separated by 5 ms. Note blanking due to stimulus artifact and rebound excitation after stimulus group. **B**, Boxplots of the stimulus artifact duration grouped by recording side. Box indicates 25% and 75% intervals, with the center line indicating mean duration, whiskers the distribution of all data, and '+' the duration of two outliers.

Fig. 15.

EMG responses to stimulation of right M1 cortex. Top trace shows the timing envelope of the stimulus; below that: LWE = left wrist extensor; LWF = left wrist flexor; LB = left biceps brachii; LT = left triceps brachii; RWE = right wrist extensor; RWF = right wrist flexor; RB = right biceps brachii; RT = right triceps brachii.

TABLE I**Microstimulator Specifications**

Parameter	Value
Compliance	50 V (160 V max)
Current	800 μ A
Current resolution	0.2 μ A
Output impedance	>10 M Ω
Leakage current	300pA
Parasitic current injection	30 pC/pulse
Charge imbalance	-0.094 $\pm$ 0.56 nC
Channel isolation	15 pF
Timing resolution	10 μ s
Timing latency	5.4 ms $\pm$ 180 μ s
Power	300mW/channel
Size	13 cm $\times$ 2.5 cm/channel
Channel count	15 (bipolar/monopolar)