HermesC: Low-Power Wireless Neural Recording System for Freely Moving Primates

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Abstract-Neural prosthetic systems have the potential to restore lost functionality to amputees or patients suffering from neurological injury or disease. Current systems have primarily been designed for immobile patients, such as tetraplegics functioning in a rather static, carefully tailored environment. However, an active patient such as amputee in a normal dynamic, everyday environment may be quite different in terms of the neural control of movement. In order to study motor control in a more unconstrained natural setting, we seek to develop an animal model of freely moving humans. Therefore, we have developed and tested HermesC-INI3, a system for recording and wirelessly transmitting neural data from electrode arrays implanted in rhesus macaques who are freely moving. This system is based on the integrated neural interface (INI3) microchip which amplifies, digitizes, and transmits neural data across a $\sim 900 \mathrm{~MHz}$ wireless channel. The wireless transmission has a range of $\sim 4~\mathrm{m}$ in free space. All together this device consumes 15.8 mA and 63.2 mW. On a single

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2 A-hr battery pack, this device runs contiguously for approximately six days. The smaller size and power consumption of the custom IC allows for a smaller package ($51 \times 38 \times 38 \text{ mm}^3$) than previous primate systems. The HermesC-INI3 system was used to record and telemeter one channel of broadband neural data at 15.7 kSps from a monkey performing routine daily activities in the home cage.

Index Terms—Brain-machine interface, low power, neural prosthetics, telemetry, wireless.

I. INTRODUCTION

ORTICAL neural prostheses extract signals from the brain in order to control prosthetic devices such as limbs and computer cursors [1]. This is a rapidly growing field with the potential to provide treatment for amputees or patients suffering from neurological injury and disease. After several proof-of-concept studies [2], [3], subsequent studies have demonstrated improving performance in monkeys [4]–[6] and even humans [7]. However, several obstacles stand in the way of translating these experiments into a clinical system. Two obstacles are reasonably well recognized while a third, which we focus on in this report, has to date been somewhat underappreciated. First, multielectrode array lifetime is approximately a year or less, which seriously limits the potential clinical usefulness of cortical implants. Second, current systems require a percutaneous connector, which is associated with infection risk as well as aesthetic concerns. This issue can be addressed with implantable electronics to record neural activity and wirelessly transmit this data through the skin to an external device [8]-[14]. In this study, however, we will focus on a third major obstacle to clinical adoption: neural prosthetics experiments to date have occurred in highly controlled settings over a short time span with immobile or nearly immobile animals or humans. Consequently, it is possible that posture, body movement, head movement, or brain movement within the skull could have a strong effect on performance. Also, many experiments have been done in environments with reduced visual, auditory, and tactile stimulation over limited periods of time. In some experiments, animals were trained to fixate their gaze on a specific point, which may significantly improve the performance of decoders [15]. In a human clinical setting, particularly for active amputees, these are not realistic constraints.

Therefore, one important next challenge for neural prosthetic systems is to release these constraints, and attempt to replicate previous high performance results in this more practical, yet complex setting. To address this challenge, our overarching goal is to establish an animal model of freely moving humans. To do so requires the ability to transmit neural data wirelessly from a subject. Rhesus macaque monkeys are appropriate subjects since they can make the coordinated arm movements that one would like to decode. Also, the rhesus brain is substantially homologous to the human brain, and there is a large body of neuroscience and neural prosthetics research in macaques. In addition to the neural prosthetic application, such a system could be used to study complex voluntary behaviors that have been previously difficult to access for researchers, such as aggression, vocalization, social behavior, and locomotion. Also, the large quantity of neural data that could be obtained using a wireless device over many days might be useful to computational neuroscientists studying general properties of the cortex.

There has been substantial previous work on systems that record neural data during free movement in many different animal models. Several systems have been developed for freely moving rats. Farshchi et al. has reported a rodent system using an off the shelf microcontroller and radio transceiver [16]. Other systems have been built with both custom circuitry, and commercial off the shelf (COTS) electronics. Cheney et al. developed the Pico Neural Data Collection system using a custom bioamplifier front end, and commercially available processing and wireless circuits [17]. A similar approach was taken by Chae et al. [18]. There is also a commercial system available for wirelessly recording 31 channels of neural data from freely moving rodents, which runs for 6 h contiguously before requiring a new battery (Triangle Biosystems Inc., Durham, NC). It is notable that packaging of these systems in general can be very specific to the particular animal model and cage system. For example, Takeuchi *et al.* have developed a wearable neural recording system for insects using a 15- μ m-thickness flexible polyimide cable which wraps around the insect's body between the circuitry and the electrode [19].

While the use of COTS components reduces cost and development time compared to a fully integrated approach, a major disadvantage is high power consumption, which makes it very difficult to run freely behaving experiments for extended periods of time. The first biotelemetry system integrated onto a single chip was demonstrated by Song et al. [20]. More recently, several development efforts have been underway to increase the number of channels, decrease the power, and integrate all the electronics and electrodes into a single implantable package. DeMichele and Troyk developed a 16 channel system that consumed 18 mW [21]. Yin et al. have reported a 15 channel system that draws only 4.5 mW [11]. Moving closer to freely moving primates, Mohseni et al. have developed and used a 4 channel, 2.2 mW biotelemetry system to record from awake restrained marmoset monkeys [12]. In freely moving rats, Sodagar et al. have developed a 64-channel fully integrated wireless system and successfully recorded in vivo neural data while supplying power through a nearby inductive link [13]. However, it appears that none of these systems have yet been adapted for freely moving primates, possibly due to surgical or packaging difficul-

A small number of systems have been implemented for freely behaving primate experiments. Prior to wireless systems, tethered recordings have been used to study natural behaviors such as spatial navigation [22]. However, chronic experiments would be highly challenging using such a system since the animal would have access to the tethering wire. Therefore, several selfcontained wireless systems have been developed. Two systems record 1-2 channels of neural data to onboard memory, which can be subsequently downloaded when the device is retrieved [23], [24]. It would be difficult to scale these systems up substantially since memory can fill rather quickly with broadband neural data. Also, it can be difficult to synchronize neural data with behavioral measures such as video, and impossible to access the data in real time to look at task modulation or to do BMI experiments. Several systems use COTS electronics to transmit neural data wirelessly [25], [26]. However, all of these systems have relatively high power consumption, running for 1–8 h before requiring a new battery. We would like to record for several days without servicing the device. Finally, COTS systems would be difficult to scale up to many channels in the future, since the size of the electronics for 1–2 channels is already at the limit of what a large animal can carry in an unobtrusive device. We seek to develop a system with a clear development path to 96-channel wireless neural recording.

To that end, we have developed HermesC-INI3, a wireless system for recording neural data from freely moving primates. This system uses the custom Integrated Neural Interface (INI) microchip, which is part of a larger project to develop a fully implantable 96-channel system [14] and is described in detail in the companion paper [29]. The INI3 chip digitizes the signal from one electrode on a 96-electrode array (Cyberkinetics Inc., Salt Lake City, UT) and transmits those data wirelessly to a receiver outside of the cage. HermesC refers to the system of connecting this device to the chronically-implanted electrode array, encapsulating the circuitry in a small wearable enclosure, and additional electronics for the specific needs of this primate research system, such as acquiring data from receivers placed outside the cage. HermesC-INI3 has been used to record data from a rhesus macaque performing many unconstrained regular activities. This device differs from previous primate systems by having lower power consumption, a smaller form factor, and the capability to expand to more channels in the future as part of a planned development path. Portions of this work have been previously presented in conference form [27], [28].

II. METHODS

The system consists of a neural connector and a printed circuit board (PCB) with a custom microchip to record, digitize, and transmit the data, all of which are housed in a protective enclosure. Data is recorded using an external receiver.

A. Physical Design

Fig. 1 shows a diagram of the physical design. Neural data are obtained through a 96-channel cortical array implanted in macaque motor and premotor cortex (Cyberkinetics Inc., Salt Lake City, UT). Layers of preclude and duragen help protect the dura and array, and help avoid material adhesions. A silicone elastomer fills the craniotomy and allows a flexible ribbon cable to connect to a zero-insertion force (ZIF) connector on the skull (Cyberkinetics Inc., Salt Lake City, UT). The entire implant is

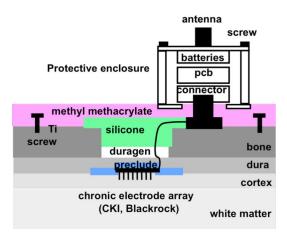


Fig. 1. Physical design of HermesC. 100-electrode arrays are implanted in macaque motor and premotor cortex. Preclude, duragen, a silicone elastomer, and methyl methacrylate protect the brain, skull, and array. ZIF connector attaches to skull (CKI). Custom connector provides 32 of 96 channels to PCB which includes INI3 microchip. Aluminum housing embedded in methyl methacrylate protects electronics and batteries.

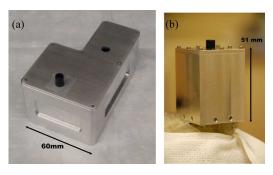


Fig. 2. Aluminum enclosure with stub antenna in lid for (a) larger prototype system and (b) final design.

protected with methyl metacrylate (dental cement). Three different custom head-stages provide access to three banks of 32 channels with connectors that attach directly to the PCB. The entire system, which includes the percutaneous connector, the PCB, and a lithium battery pack, is housed in an aluminum enclosure attached to the implant with titanium hardware and methyl methacrylate. Initial testing with a larger prototype PCB was completed in aluminum enclosure identical to the HermesB system [24], which measured $60 \times 70 \times 45 \text{ mm}^3$. However, the final design was verified in a smaller enclosure that measured $51 \times 38 \times 38 \text{ mm}^3$. For each enclosure, a stub antenna protrudes 8 mm through a hole in the lid, as shown in Fig. 2. This antenna is immobilized and sealed with epoxy. The total weight of this system including the batteries is 114 g.

B. Electronics

Table I summarizes the design parameters for this system. The electronics for HermesC consist primarily of the INI3 chip packaged in a 64-pin low profile quad flat package (LQFP), which is described in detail in the companion paper [29]. Briefly, it includes three stages: a bioamplifier, an ADC, and an FSK wireless transmitter. A block diagram of the design is shown in Fig. 3(a), and the PCBs with the INI chip are shown in Fig. 4. At the input to INI3, a wired connection was soldered by hand

TABLE I DESIGN PARAMETERS

Design Parameters	
Current # channels	1
Connector	96
accessible channels	
Wireless data rate	345.6 kbps
ADC sampling rate	15.7 ksps
ADC precision	10-bit
High pass filter	~0.1 Hz
Low pass filter	5 KHz
Battery capacity	1120 (2240)
	mA-hr
Typical battery life	2.9 (5.8) days
Enclosure size	51x38x38 mm ³
Total mass	(60x70x45 mm ³) 114 g (201 g)

Measured Results

Wireless data loss 0.05% Input referred noise 19.8 μVrms (Numbers in parentheses refer to larger initial prototype)

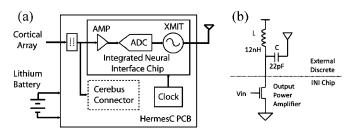


Fig. 3. Block diagram of electronics. (a) Complete system with Cerebus connector only present on the larger prototype board. (b) Modified output circuit for stub antenna.

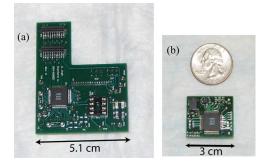


Fig. 4. PCB with INI chip. (a) Prototype board for HermesC-INI3. (b) Final design.

to one of the 32 neural channels accessible on the headstage connectors. While the chip was designed to have programmable channel selection, a known design error made it necessary to use this work around for this version of the chip.

In the special context of a freely moving primate system, several changes were made in how the chip was used for HermesC compared to [29]. Specifically, providing a power supply, clock, and initial programming command through a wireless coil connection would be difficult since a monkey cannot wear a power coil, and unnecessary since the animal is sufficiently large to carry a battery. Therefore, the PCB includes a clock oscillator as

well as connectors for a battery and a wired connection for initial programming. The device can be programmed in ~ 50 ms with an 836 bit command (which includes many parameters not yet fully implemented on this device). After device programming, this 4-wire connection can simply be removed for the rest of the experiment. Another difference is the wireless range required for freely moving monkeys. While the INI chip can transmit at a range of 5 cm at 8 mW, in the HermesC system, a single discrete resistor is added to the final RF amplifier to increase the transmit range, which results in a total power consumption of 63.2 mW. Finally, since this device is using a different antenna than described in [29] several 0603 components are used. The modified output circuit is shown in Fig. 3(b). The output stage uses a discrete inductor to bias the amplifier, and an addition capacitor to provide a dc block to the antenna. This system, HermesC "nano," is small enough to be used on any large animal with a Cyberkinetics neuroport connector.

In an earlier iteration, a larger PCB was used for initial design and testing, as shown in Fig. 4(a). In addition to the components described above, this PCB also provides an alternate data path to a traditional head-stage connector for a commercial neural recording system, Cerebus (Cyberkinetics Inc., Salt Lake City, UT). In this way, data can be obtained simultaneously and then compared. It also includes fuses, various test points for accessing the chip, and larger components for easier removal and testing. This version represents a general *in vivo* test platform for the INI chip, in which signals can be easily accessed, and the external circuitry can be rapidly reconfigured.

The power consumption of this system is adjustable in two ways. First, a bias resistor can control the gain of the wireless amplifier, which allows the user to adjust the range. Second, an optional 6 dB attenuator can be used at the output to the antenna to minimize the effect of environmentally-induced changes in antenna impedance on the transmit frequency. Due to power constraints, the INI does not include a phase lock loop (PLL) [29], which would better stabilize the transmitting frequency. In the current configuration, HermesC consumes 15.8 mA at 4.0 V, for a total of 63.2 mW. Of that amount, $\sim 28 \text{ mW}$ is required by the RF transmitter on the INI chip, and 21 mW is required by the off chip clock. The INI chip itself can run on a voltage source between 3-4 V. This represents a large improvement over HermesB, which recorded from two broadband channels, and consumed 71 mA at 4.0 V, for a total of 284 mW [24]. Despite the smaller enclosure size, HermesC can run for 2.9 days on one 1120 mA-hr battery or ~ 4 times longer. Alternatively, using the larger HermesB enclosure and a second battery pack due to the smaller electronics, it can run for 5.8 days contiguously. In the typical usage mode with the smaller enclosure, the device runs for over three days on two disposable Li-ion ½AA batteries. To our knowledge, this is the longest running wireless neural system reported that has been implemented in freely moving animals.

At the output RF stage, data are transmitted in 16-sample frames at 345.6 kb/s with one parity bit computed for each 10-bit ADC sample. The wireless data were collected with a commercial FSK transceiver, the ADF7025 development board (Analog Devices), receiving in the 902–928 MHz range. To compensate for small fluctuations in the transmitting frequency,

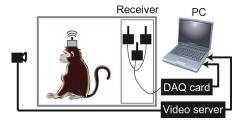


Fig. 5. Experimental setup with animal in metal home cage and receiving antennae on plastic cage window.

three receivers were used, as shown in Fig. 5. These were programmed to the main frequency and 100 KHz on either side. These receivers were connected to half-wave whip antennae and were powered and controlled by a USB-6259 DAQ (National Instruments, Austin, TX). To obtain video data, an Axis 241QA video server (Axis Communications, Inc., Chelmsford, MA) was used to capture and digitize video from an analog day/night camera. The video server provides four digital input lines for a 4-bit synchronizing clock and produces $\sim 30 \text{ JPEG}$ compressed frames per second at a 640 × 480 resolution. Each frame header includes the state of the digital input lines, facilitating synchronization with the neural data. The system was tested with a single camera, but can accommodate up to four simultaneous camera views. Neural and video data were collected and stored on a dual core Xeon 3.25 GHz PC running Windows XP using custom C code and analyzed using MATLAB (Mathworks, Natick, MA). All together, this system produces 3.6 GB of neural data and 80 GB of video data every 24 h of operation.

C. Experimental Setup

On 16 occasions this system was tested with a freely moving primate. One 6.9 kg rhesus macaque was implanted with a 96-electrode array using standard neurosurgical techniques 2.75 years prior to the current study as reported in Santhanam et al. 2007 [19] (Monkey D) as well as the larger aluminum enclosure which had been used for HermesB. All of the surgical procedures were approved by Stanford University's Institutional Animal Care and Use Committee (IACUC). Even 2.75 years following implantation into the arm area of premotor cortex (PMd), this array continues to provide many large neural units. A second monkey, Monkey L, was implanted with a similar 96-electrode array in PMd for a separate study. A small aluminum base for the HermesC enclosure was added around the Neuroport connector and immobilized with methyl methacrylate. Unlike the larger HermesB enclosure, this smaller enclosure did not interfere with normal usage of the connector. For both animals, the HermesC PCB was placed inside the aluminum enclosure on the head while the animal was seated in a primate chair. With the lid removed, the device was programmed using a wired connection. The device was programmed to transmit data at a center frequency of 919-923 MHz with an FSK frequency spacing of 460 kHz. The lid with the protruding stub antenna was replaced, and the animal was returned to the home cage.

The receivers were placed outside the animals' home cages with the antenna attached to a plastic window on the cage's

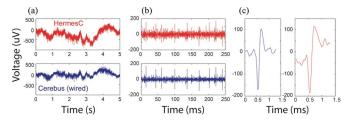


Fig. 6. Comparison of neural recordings from HermesC and commercial Cerebus system (CKI). (a) Unfiltered data from HermesC (top, right) and Cerebus (bottom, left). (b) Spike train high pass filtered at 250 Hz from both. (c) Individual action potentials unfiltered from both.

sidewall, as shown in Fig. 5. The transmit frequency was measured within 50 kHz using a portable spectrum analyzer (Protek, Tempe, AZ, model 3290N). Data were recorded as described above. In early sessions where the video system was not used, general notes on the animal's behavior were taken.

III. RESULTS

A. System Validation

Before initiating freely-moving experiments, we validated the neural data collection by simultaneously recording from the HermesC-INI3 wireless link as well as a wired neural data acquisition system, Cerebus, and comparing the waveforms. For this recording, the animal was seated in a primate chair inside an electromagnetically shielded neuroscience "rig." An electrode with a relatively large neural unit was chosen. Neural data were recorded from both during a 2 min period, and aligned precisely by hand. Fig. 6(a) shows a 5 s snippet of raw data in which the data from the commercial system (bottom) correspond with the data recorded with HermesC. Similarly, Fig. 6(b) shows a spike train created by high-pass filtering the raw broadband data from both devices at 250 Hz. Fig. 6(c) shows one action potential, unfiltered, from both. The in-band noise is somewhat higher for HermesC, at 27.4 μ Vrms compared to 17.4 $\mu Vrms$ in the commercial Cerebus system from the same electrode inside of the shielded rig.

After verifying the data acquisition, we also exercised the wireless link prior to use with the animal. The circuitry was tested in an unimplanted aluminum enclosure with the same lid and stub antenna, shown in Fig. 2(b). The device was programmed to transmit at 918 MHz and data were received at various distances with the receiving half-wave whip antenna in three different orientations. In the preferred orientation where the two antennae were parallel, the estimated bit error rate (BER) stayed below 10^{-5} up to 5 m away. In both of the two nonoptimal orientations with the antennae at right angles or end to end, the BER stayed below 10^{-5} up to 3.5 m away. The device was also tested inside an empty 105 cm x 87 cm x 91 cm metal housing cage with walls composed of a 1-in pitch wire grid. The receiving antenna was placed at the top of a plastic window on the cage wall. The device was placed in three points along each of three directions and three heights, for a total of 27 positions within the cage. The BER remained below 10^{-5} for all locations. However, it was noted that the signal could be lost when the antenna was touching or nearly touching the metal cage wall.

B. Neural Data From a Freely Moving Primate

To demonstrate the functionality of this system in a freely moving primate, neural data were recorded wirelessly from a monkey while in the home cage. Fig. 7 shows examples of two neurons from Monkey D, each recorded during six day contiguous recording sessions. Neural data are high-pass filtered at 250 Hz to reveal the spiking activity. Periods with active spiking were detected with simple voltage thresholds. The average in-band noise level (between 250 Hz-5 kHz) across 24 h of continuous recording from both neurons was 19.8 $\mu Vrms$ with action potential amplitudes of 190 μ Vrms and 264 μ Vrms for neurons 1 and 2, respectively. This is slightly lower than the simultaneous recording in the rig shown in Fig. 6 presumably because the metal lid was shut while recording during free behavior. This noise is within the range that would be expected based on the circuit design, given the tradeoff between noise and power consumption. Fig. 8 shows similarly filtered neural data aligned with video data during a time when the animal was actively reaching. Bursts of activity correspond to individual reaches, which is a typical result for implants targeted towards the arm representation in motor and premotor cortex. With the freely behaving animal, a small amount of data was lost due to RF transmission errors. These errors can be mitigated by detecting incomplete frame headers and removing that entire frame, and also by removing words with incorrect parity bits. Using this approach 0.05% of the data on average were lost during six days of contiguous recording. In addition to data obtained from Monkey D using the larger system, the final HermesC "nano" design was tested with a second animal, Monkey L. Neural data from one unit is shown in Fig. 9. Performance was similar to the results from the prototype system.

To demonstrate the experimental capabilities of HermesC-INI3, we recorded from one neuron at a time to identify correlations between patterns of neural activity and certain common behaviors in the homecage. Fig. 10(b) shows examples of raster plots of neural activity along with autocorrelation functions during inactivity, reaching (nonrhythmic bursts) and swaying (rhythmic bursts) in Fig. 10(a). Mean firing rates during those activities were $31.8 \pm 29.2 \text{ Hz}$, $53.5 \pm 43.0 \text{ Hz}$, and 46.3 ± 26.6 Hz, respectively. Fig. 10(c) shows a power spectrum for LFP during active versus inactive periods. The dotted line denotes the standard deviation, which suggests that these states could be accurately decoded using LFP only. This is consistent with previous results [24], [30] and suggests that LFP could be used as an enabling on-off signal for a neural prosthetic or another similar medical device. With more neural channels and more quantified behaviors, it may be possible to more accurately decode more precise behavioral states from the neural activity alone

IV. DISCUSSION

A. Wireless Performance

A small amount of data, 0.05% were lost during contiguous recording. One likely cause for the errors is large changes in antenna impedance when the device is touching the metal cage wall and lower signal amplitude when the antenna is oriented such that it is shielded from the receivers. A plexiglass cage

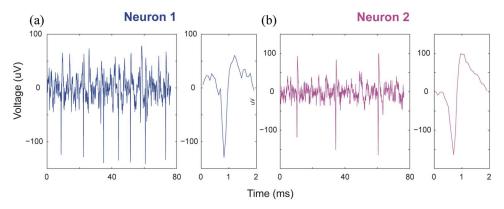


Fig. 7. Neural data from monkey freely moving in a home cage from two different cells (left and right) at two different time scales. Data high pass filtered at 250 Hz

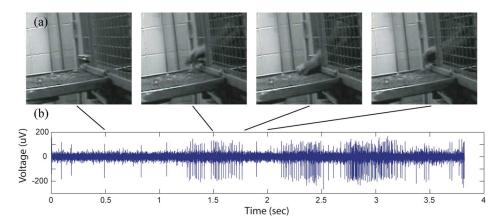


Fig. 8. Neural data from monkey freely moving in a home cage. (a) Synchronized video of reaching. (b) Bursts of neural activity corresponding to reaching movements.

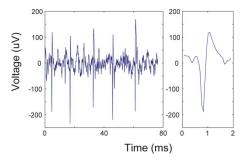


Fig. 9. Neural data from final "nano" PCB at two different time scales. Data high pass filtered at 250 Hz.

would presumably mitigate both of these effects. This primarily results in brief and detectable periods where the signal is dropped. This can be taken into account during offline analyses, by implementing a matched filter that seeks the signature of such events. The remainder of the errors are primarily single bit errors in similar quantity to those measured without the animal. These can be detected using a parity check. While this BER of $\sim 10^{-5}$ would be unacceptably high for most wireless applications, neural signals are particularly sparse and noisy, and require a specific waveform template to be matched in order to detect a spike, such as those shown in Fig. 7. Also, for most neuroscience applications, the value in question is the average firing rate of the cell over time, which is a particularly

noisy signal. In this context, we believe that a BER of 10^{-5} has an effectively negligible effect on the estimated firing rate. Therefore, with the current noise level and BER, this system can already provide useful data for neuroscience experiments.

B. Future Work

The HermesC system provides a significant improvement over similar primate systems in terms of power consumption and system size. Compared to HermesB which consumed 284 mW (142 mW per channel), the new system consumes 63 mW for one channel. The reduced size of both the required batteries and the circuitry enables a volume reduction of 60% from HermesB. With this smaller footprint, it would likely be possible to put multiple enclosures on a single macaque with multiple arrays. Also, this design should enable wireless experiments with nearly any large animal who has a 96-channel Cyberkinetics neuroport connector. Since the PCB by itself weighs only 9 g, which is on par with several previous systems [16], it might be possible to create a rat system with a shorter battery life than the current implementation.

This system would be of more general use to the community if it could provide more neural channels. Towards that end, this system has been designed to take advantage of planned future capabilities of the INI microchip. Currently, the chip includes several features that are not yet used, discussed in detail in [29]. It includes 100 separate amplifiers and each channel also

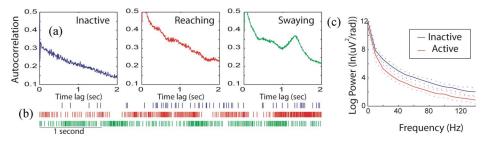


Fig. 10. Neural activity during various activities in the cage. (a) Autocorrelations of spike rasters convolved with a Gaussian window. (b) Example spike rasters for each behavior. (c) Comparison of LFP during active/inactive periods. Dotted line denotes standard deviation.

has its own programmable threshold-crossing detector, which will be latched and sampled at 982 Hz. The additional transmit bandwidth beyond 172.7 kb/s required for the ADC data is reserved for this multichannel data. The current power consumption includes powering these 100 amplifiers and wirelessly transmitting their threshold crossing information in addition to one channel of 10-bit ADC data [29]. However, these capabilities can only be accessed on the benchtop until small design changes are made in the chip. While these additional channels would only provide threshold crossing information, a small microcontroller could be added to the PCB to cycle the single broadband channel to all the available channels every few minutes to periodically provide waveforms sampled at 15.7 kS/s. In addition to waveform shape, this data could be used to periodically verify that the thresholds continue to be picking up individual action potentials from the largest unit on a channel. With such a device, wireless overnight neural unit tracking could become a routine part of experiments in both neural prosthetics and systems neuroscience.

For prosthetics, several important experiments can now be completed. While these experiments would be substantially easier with a multichannel system, preliminary data can be obtained with the current single channel system. First, similar to the HermesB system, it can be used to study how the neural population on the array changes over time. During long experiments and preliminary multiday recordings, it has become clear that neural waveforms can change over time, presumably due to small movements of the electrode array [24]. However, it has not been practical to quantify this effect across a large population and long periods of time due to the limitations on channel count, flash memory size, and battery life. Second, neural prosthetic algorithms can be tested in a far less constrained environment. Using a freely behaving animal eliminates many restrictions on head position, eye position, and body position that have been controlled in most prosthetic experiments, but are unrealistic constraints for human amputees. Also, by using neural data to control an in-cage device that the monkey may access continuously, it may be possible to observe learning effects that were not revealed in short rig experiments in which the algorithm was retrained daily [31]. Previous experiments have shown that animals readily modulate the activity of a single neural unit to obtain a reward [32]. Third, by correlating neural activity with general behavioral states, such as eating or handling a toy, it may be possible to decode the general context of an activity and use this information to inform a prosthetic algorithm. With only a single channel, this device can be used to examine the usefulness of LFP as a gating signal for a neural prosthetic device. Finally, moving towards human devices, HermesC provides a good test bench for a planned fully implantable version of a 96-electrode wireless system [14], which should have important implications for clinical neural prosthetics by eliminating the percutaneous connector that poses both aesthetic concerns and infection risks.

For systems neuroscience, the understanding of visual processing was transformed a decade ago when vision neuroscientists began recording from behaving animals without eye fixation and with naturalistic scenes, and found that neurons respond differently in this more natural visual context [33], [34]. HermesC will make it possible to observe neural activity during complex behavioral states that are difficult or impossible to observe in an experimental rig. These include foraging, social behaviors, aggression, vocalization, locomotion, and spatial navigation, which are all complex voluntary activities that could conceivably involve qualitatively different activation of the cerebral cortex. Also, the large quantity of contiguous neural recorded by such a system may be of interest to computational neuroscientists studying general properties of biological neural networks. If successful, such studies could advance our understanding of cortical motor control across a wide range of motor contexts.

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REFERENCES

- A. B. Schwartz, "Cortical neural prosthetics," Annu. Rev. Neurosci., vol. 27, pp. 487–507, 2004.
- 2] D. M. Taylor, S. I. Tillery, and A. B. Schwartz, "Direct cortical control of 3D neuroprosthetic devices," *Science*, vol. 296, pp. 1829–32, Jun. 2002.
- [3] M. D. Serruya, N. G. Hatsopoulos, L. Paninski, M. R. Fellows, and J. P. Donoghue, "Instant neural control of a movement signal," *Nature*, vol. 416, pp. 141–2, Mar. 2002.
- [4] J. M. Carmena, M. A. Lebedev, R. E. Crist, J. E. O'Doherty, D. M. Santucci, D. F. Dimitrov, P. G. Patil, C. S. Henriquez, and M. A. L. Nicolelis, "Learning to control a brain-machine interface for reaching and grasping by primates," *PLOS Biol.*, vol. 1, pp. 193–208, 2003.
- [5] G. Santhanam, S. I. Ryu, B. M. Yu, A. Afshar, and K. V. Shenoy, "A high-performance brain-computer interface," *Nature*, vol. 442, pp. 195–8, Jul. 2006.
- [6] M. Velliste, S. Perel, M. C. Spalding, A. S. Whitford, and A. B. Schwartz, "Cortical control of a prosthetic arm for self-feeding," *Nature*, vol. 453, pp. 1098–1101, 2008.

- [7] L. R. Hochberg, M. D. Serruya, G. M. Friehs, J. A. Mukand, M. Saleh, A. H. Caplan, A. Branner, D. Chen, R. D. Penn, and J. P. Donoghue, "Neural ensemble control of prosthetic devices by a human with tetraplegia," *Nature*, vol. 442, pp. 164–71, Jul. 2006.
- [8] R. R. Harrison, "The design of integrated circuits to observe brain activity," *Proc. IEEE*, vol. 97, no. 7, pp. 1203–1216, Jul. 2008.
 [9] K. D. Wise, D. J. Anderson, J. F. Hetke, D. R. Kipke, and K. Na-
- [9] K. D. Wise, D. J. Anderson, J. F. Hetke, D. R. Kipke, and K. Najafi, "Wireless implantable Microsystems: High-density electronic interfaces to the nervous system," *Proc. IEEE*, vol. 92, no. 1, pp. 76–97, Jan. 2004.
- [10] Y. K. Song, W. R. Patterson, C. W. Bull, N. J. Hwang, A. P. Deangelis, C. Lay, J. L. McKay, A. V. Nurmikko, J. D. Donoghue, and B. W. Connors, "Development of an integrated microelectrode, microelectronic device for brain implantable neuroengineering applications," in *Proc. IEEE Eng. Med. Biol. Soc.*, 2004, pp. 4053–4056.
 [11] M. Yin, R. Field, and M. Ghovanloo, "A 15-channel wireless neural
- [11] M. Yin, R. Field, and M. Ghovanloo, "A 15-channel wireless neural recording system based on time division multiplexing of pulse width modulated signals," in *Proc. Int. Conf. Microtech. Med. Biol.*, Okinawa, Japan, 2006, pp. 297–300.
- [12] P. Mohseni, K. Najafi, S. J. Eliades, and X. Wang, "Wireless multichannel biopotential recoding using an integrated FM telemetry circuit," *IEEE Trans. Neural Syst. Rehabil. Eng.*, vol. 13, no. 3, pp. 263–71, Sep. 2005.
- [13] A. M. Sodagar, K. D. Wise, and K. Najafi, "A fully integrated mixed-signal neural processor for implantable multichannel cortical recording," *IEEE Trans. Biomed. Eng.*, vol. 54, no. 6, pp. 1075–88, Jun. 2007.
- [14] R. R. Harrison, P. T. Watkins, R. J. Kier, R. O. Lovejoy, D. J. Black, B. Greger, and F. Solzbacher, "A low-power integrated circuit for a wireless 100-electrode neural recording system," *IEEE J. Solid State Circuits*, vol. 42, no. 1, pp. 123–133, Jan. 2007.
- [15] A. P. Batista, B. M. Yu, G. Santhanam, S. I. Ryu, A. Afshar, and K. V. Shenoy, "Cortical neural prosthesis performance improves when eye position is monitored," *IEEE Trans. Neural Syst. Rehabil. Eng.*, vol. 16, no. 1, pp. 24–31, Feb. 2008.
- [16] S. Farshchi, P. H. Nuyujukian, A. Pesterev, I. Mody, and J. W. Judy, "A TinyOS-enabled MICA-2based wireless neural interface," *IEEE Trans. Biomed. Eng.*, vol. 53, no. 7, pp. 1416–1424, Jul. 2006.
- [17] D. Cheney, A. Goh, K. Gugel, J. G. Harris, J. C. Sanchez, and J. C. Principe, "Wireless, in vivo neural recording using a custom integrated bioamplifier and the pico system," in *Proc. 2007 EMBS*, Kohala Coast, HI, 2007, pp. 4387–4391.
- [18] M. Chae, K. Chen, W. Liu, J. Kim, and M. Sivaprakasam, "4-Channel wearable wireless neural recording system," in *Proc. IEEE Int. Symp. Circuits Syst. (ISCAS)*, Seattle, WA, May 2008, pp. 1760–1763.
 [19] S. Takeuchi and I. Shimoyama, "A radio-telemetry system with a shape
- [19] S. Takeuchi and I. Shimoyama, "A radio-telemetry system with a shape memory alloy microelectrode for neural recording of freely moving insects," *IEEE Trans. Biomed. Eng.*, vol. 51, no. 1, pp. 133–137, Jan. 2004
- [20] H. J. Song, D. R. Allee, and K. T. Speed, "Single chip system for biodata acquisition, digitization, and telemetry," in *Proc. IEEE Int. Symp. Circuits Syst. (ISCAS)*, Hong Kong, 1997, vol. 3, pp. 1848–1851.
- Circuits Syst. (ISCAS), Hong Kong, 1997, vol. 3, pp. 1848–1851.

 [21] G. A. DeMichele and P. R. Troyk, "Integrated multi-channel wireless biotelemetry system," in *Proc. IEEE Eng. Med. Biol. (EMBS)*, Cancun, Mexico, 2003, pp. 3372–3375.
- [22] N. Ludvig, J. M. Botero, H. M. Tang, B. Gohil, and J. G. Kral, "Single-cell recording from the brain of freely moving monkeys," *J. Neurosci. Meth.*, vol. 106, pp. 179–187, 2001.
- [23] J. Mavoori, A. Jackson, C. Diorio, and E. E. Fetz, "An autonomous implantable computer for neural recording and stimulation in unrestrained primates," *J. Neurosci. Meth.*, vol. 148, pp. 71–7, Oct. 2005.
- [24] G. Sanathanam, M. D. Linderman, V. Gilja, A. Afshar, S. I. Ryu, T. H. Meng, and K. V. Shenoy, "HermesB: A continuous neural recording system for freely behaving primates," *IEEE Trans. Biomed. Eng.*, vol. 54, no. 11, pp. 2037–50, Nov. 2007.
- [25] U. Jurgens and S. R. Hage, "Telemetric recordings of neuronal activity," *Methods*, vol. 38, pp. 195–201, 2006.
- [26] N. L. Sun, Y. L. Lei, B. H. Kim, J. W. Ryou, Y. Y. Ma, and F. A. W. Wilson, "Neurophysiological recordings in freely moving monkeys," *Methods*, vol. 38, pp. 202–209, 2006.
- [27] C. A. Chestek, V. Gilja, P. Nuyujukian, R. J. Kier, F. Solzbacher, S. I. Ryu, R. R. Harrison, and K. V. Shenoy, "HermesC: RF wireless low-power neural recording for freely behaving primates," in *Proc. IEEE Int. Symp. Circuits Syst. (ISCAS)*. Seattle, WA 2008, pp. 1752-1755.
- Int. Symp. Circuits Syst. (ISCAS), Seattle, WA, 2008, pp. 1752–1755.

 [28] R. R. Harrison, R. J. Kier, C. A. Chestek, V. Gilja, P. Nuyujukian, S. I. Ryu, B. Greger, F. Solzbacher, and K. V. Shenoy, "Wireless neural signal acquisition with single low-power integrated circuit," in Proc. IEEE Int. Symp. Circuits Syst. (ISCAS), Seattle, WA, 2008, pp. 1748–1751
- [29] R. R. Harrison, R. J. Kier, C. A. Chestek, V. Gilja, P. Nuyujukian, S. I. Ryu, B. Greger, F. Solzbacher, and K. V. Shenoy, "Wireless neural recording with single low-power integrated circuit," *IEEE Trans. Neural Syst. Rehabil. Eng.*, vol. 17, no. 4, Aug. 2009.

- [30] J. Donoghue, J. Sanes, N. Hatsopoulos, and G. Gyngyi, "Neural discharge and local field potential oscillations in primate motor cortex during voluntary movements," *J. Neurophysiol.*, vol. 79, pp. 159–173, 1998.
- [31] E. E. Fetz, "Volitional control of neural activity: Implications for braincomputer interfaces," *J. Physiol.*, vol. 579, pp. 571–579.
- [32] E. E. Fetz, "Operant conditioning of cortical unit activity," *Science*, vol. 163, pp. 955–958, 1969.
- [33] M. S. Livingstone, D. C. Freeman, and D. H. Hubel, "Visual responses in V1 of freely viewing monkeys," in *Cold Spring Harbor Symp. Quant. Biol.*, 1996, vol. 61, pp. 27–37.
- [34] J. L. Gallant, C. E. Connor, and D. C. Van Essen, "Neural activity in areas V1, V2 and V4 during free viewing of natural scenes compared to controlled viewing," *NeuroReport*, vol. 9, pp. 2153–2158, 1998.



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