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Long-term stability of neural signals from microwire arrays implanted in common marmoset motor cortex and striatum

Shubham Debnath¹, Noeline W Prins¹, Eric Pohlmeier², Ramanamurthy Mylavarapu¹, Shijia Geng³, Justin C Sanchez⁴, and Abhishek Prasad^{1,*}

¹Department of Biomedical Engineering, University of Miami, Coral Gables, FL 33146

²John Hopkins University Applied Physics Laboratory, Laurel, MD 20723

³The Center for Computational Science, University of Miami, Coral Gables, FL 33146

⁴Defense Advanced Research Projects Agency, Arlington, VA 22203

Abstract

Current neuroprosthetics rely on stable, high quality recordings from chronically implanted microelectrode arrays (MEAs) in neural tissue. While chronic electrophysiological recordings and electrode failure modes have been reported from rodent and larger non-human primate (NHP) models, chronic recordings from the marmoset model have not been previously described. The common marmoset is a New World primate that is easier to breed and handle compared to larger NHPs and has a similarly organized brain, making it a potentially useful smaller NHP model for neuroscience studies. This study reports recording stability and signal quality of MEAs chronically implanted in behaving marmosets. Six adult male marmosets, trained for reaching tasks, were implanted with either a 16-channel tungsten microwire array (five animals) or a Pt-Ir floating MEA (one animal) in the hand-arm region of the primary motor cortex (M1) and another MEA in the striatum targeting the nucleus accumbens (NAcc). Signal stability and quality was quantified as a function of array yield (active electrodes that recorded action potentials), neuronal yield (isolated single units during a recording session), and signal-to-noise ratio (SNR). Out of 11 implanted MEAs, nine provided functional recordings for at least three months, with two arrays functional for 10 months. In general, implants had high yield, which remained stable for up to several months. However, mechanical failure attributed to MEA connector was the most common failure mode. In the longest implants, signal degradation occurred, which was characterized by gradual decline in array yield, reduced number of isolated single units, and changes in waveform shape of action potentials. This work demonstrates the feasibility of longterm recordings from MEAs implanted in cortical and deep brain structures in the marmoset model. The ability to chronically record cortical signals for neural prosthetics applications in the common marmoset extends the potential of this model in neural interface research.

Keywords

electrode failure; microelectrode arrays; marmosets; neuroprosthetics

*Corresponding Author Abhishek Prasad, PhD, Department of Biomedical Engineering, University of Miami, 1251 Memorial Dr, MEA 203, Coral Gables, FL 33146, Phone: 305-243-4886, a.prasad@miami.edu.

1. Introduction

Neuroprosthetic research relies on the use of cortical recording for controlling brain-machine interfaces (BMI) to restore voluntary functions in patients with spinal cord injury (SCI), stroke, or other motor disorders of the nervous system. Control of neuroprosthetic devices has been successfully shown in rodents [1, 2], non-human primates (NHP) [3–12], and humans, where the neural signals are decoded to control a robotic limb [13–21], movement of computer cursor [6, 22–25] or trigger a functional electrical stimulation system (FES) [26–28]. Therefore, BMIs require stable, high quality recordings from chronically implanted microelectrode arrays in the neural tissue. Microelectrodes implanted in the brain tissue can be affected by multiple factors that can lead to degradation in recording quality [29–32] and result in electrode failure. Failure modes can be due to physical changes in the electrode resulting from broken electrode tips, insulation damage, or breaks in wire bundle [31, 32], while biological responses can occur from insertion damage and foreign body response [31–36] and disruption of the blood-brain barrier [37–40].

Most research to track and characterize the quality of neural recordings from chronically implanted microelectrode arrays have been performed in a rodent model [29–32, 41–44] or in cats [45–47]. However, very few studies have reported the quality of chronic neural recordings in a NHP model. Barrese *et al* [48] reported chronic impedance and signal quality along with suggested electrode failure modes in a macaque model from 78 arrays in 27 monkeys; however, not all data was available for each case due to the large number of animals and compiled data over a span of several years [48]. Suner *et al* [49] tracked signal-to-noise ratios over time in three macaque monkeys and found no significant decline over time, while Chestek *et al* [7] reported action potential changes and its effect on BMI decoder performance over time in three rhesus macaques implanted with four Utah intracortical arrays.

Compared to rodent data, these are very few studies that have reported chronic recording characteristics from intracortical microelectrodes in non-human primates. Further, chronic recording characteristics from intracortical arrays have not been reported from common marmosets. The common marmoset (*Callithrix jacchus*) is a New World primate that provides a good step between rodents and larger NHP models [50]. While macaques are the most commonly used NHP model, marmosets are easier to breed and handle with reduced zoonotic risks [51–54]. The marmoset's cortex is similarly organized to that of humans and larger NHPs [51, 54–57] making the animal model particularly useful for neuroscience and neural engineering studies. Therefore, the primary goal of this study was to show the chronic recording characteristics of electrophysiological signals recorded from intracortical microelectrode arrays (MEAs) implanted in the marmosets involved in our studies over the past seven years. Results reported are from MEAs implanted in the primary motor cortex (M1) and in striatum targeting the nucleus accumbens (NAcc). The stability and signal quality of neural recordings were characterized by tracking array yield (defined as the fraction of active electrodes that recorded neuronal activity), neuronal yield (defined as the number of isolated units during a recording session), and signal-to-noise ratios (SNR) over time. Various commonly encountered electrode failure modes with this model are also

reported. The ability to chronically record cortical signals for neuroprosthetic applications in the common marmoset suggests the potential of this model in neural interface research.

2. Methods

2.1 Overview:

All animal care, surgical and research procedures were performed in accordance with the National Research Council Guide for the Care and Use of Laboratory Animals. All work was approved by the University of Institutional Animal Care and Use Committee (IACUC). Six adult male marmosets were used in this study. Table 1 summarizes the respective implant durations and locations for all electrode arrays and the reason for termination of each experiment. Neural recordings were performed for up to 45 weeks after implantation and signal quality metrics were calculated and tracked throughout the implant duration.

2.2 Electrode Arrays Used:

Two types of microelectrode arrays (MEAs) were used in this study. Type A MEAs were 16-channel tungsten microwire arrays (Tucker-Davis Technologies, Alachua, FL), which consisted of two rows 375µm apart with eight electrodes each, spaced by 250µm. The microwire arrays, insulated by polyimide, were 50µm diameter, and they were either 5mm or 10mm long for targeting cortical and striatal brain targets, respectively. Ground and reference wires from the ZIF-connector were tied to a skull screw. Type B electrode array was a 16-channel parylene-C coated platinum-iridium (Pt-Ir) floating microelectrode array (FMA, MicroProbes for Life Science, Gaithersburg, MD). These FMAs were made up of four rows of electrodes with 250µm separation and consisted of a 4cm cable from the array to the connector. Electrodes on the FMAs were insulated by Parylene-C. FMAs used to target the hand/arm regions in the M1 had recording electrodes of 2mm, while reference and ground electrodes were 4.5mm long. FMAs to target the striatum contained recording electrodes of 8mm in length with reference and ground electrodes of 6mm.

2.3 Surgical Implantation:

Six adult male marmosets aged 2–4 years and weighing 350–480 grams at the time of surgery were implanted with one 16-channel MEA in the M1 and another MEA in the striatum. The animals ranged between two to four years old at implantation. Five animals (E, P, Du, L, and M) received type A arrays for both implant locations, while one animal (Do) received type B arrays. Detailed surgical procedures are described in Prins *et al* [50]. Briefly, animals were anesthetized with ketamine (IM, 10–50 mg/kg) and maintained under deep anesthesia by isoflurane (1–4% in 1–2 L/min O₂) through a nose cone. The animal was placed on a stereotaxic frame for small animals (Kopf Instruments, Tujunga, CA) and a midline incision was made from behind the orbital ridge to the interaural line followed by removal of the soft tissue to expose the skull. The craniotomy location corresponding to the hand-arm region in M1 and NAcc was marked based on a comparative analysis of multiple marmoset atlases [58–60]. Six to eight titanium screws were drilled into the skull to serve as anchoring screws. Upon craniotomy at each location, the dura was removed to expose the cortex, followed by surface stimulation on exposed cortex to identify the hand-arm regions. The electrode array assembly was then attached to a micro-positioner and advanced slowly

into the cortex. Each electrode array was inserted only once into the cortical tissue. Electrophysiological recordings were performed to further confirm the target implant location by listening for cues from the anatomical target. The M1 electrode array was implanted at 1.5–2.0 mm depth, and the NAcc electrode was implanted at 6.5–7.5 mm depth, relative to the cortical surface. For each MEA, the reference and ground wires were wrapped around one of the anchoring screws. The craniotomy around the implanted array was filled with Gelfoam and dental acrylic was used to cover the skull surface. Post-operative analgesics and antibiotics were used until the animal recovered.

2.4 Behavioral Training and Neural Data Acquisition:

Before surgical implantation of the MEAs, the marmosets were trained to complete reaches for a four-target center-out task or a two-target robot reaching task. Timeline for both of the tasks was similar; a trial was initiated by placing his hand on a random (0.7–1.2 seconds) hold period, followed by an audio cue corresponding with the target coming into view. The animal must reach and grasp the target accurately within 2 seconds. Animals were rewarded with a treat if the reach was made correctly. Neural signals were recorded in awake, behaving animals from the MEAs using a RZ2 BioAmp Processor (Tucker-Davis Technologies, Alachua, FL) at 24,414 Hz and 24-bits of resolution. Data were band-pass filtered from 500 Hz to 6 kHz. Recorded neural data included single unit and multi-unit signals and action potential waveforms were discriminated using online and offline sorting by waveform amplitude, waveform shape, and manually set threshold levels. Only analysis of single unit signals is presented in this study.

2.5 Neural Signal Processing and Analysis:

Online spike sorting was used to isolate single unit activity from background noise during recording sessions. Thresholds were manually set at the noise floor, and box sorts were used to distinguish individual waveforms of single units from thresholded data. These individual action potential waveforms were extracted from the data stream for offline sorting to further verify the spikes identified during online sorting. The signal amplitude of each sorted unit was defined as the average peak-to-peak amplitude (A) of all the individual action potential waveforms. The background noise for each channel was calculated by subtracting the mean waveform from each individual waveform and finding the standard deviation from this collection of residuals, σ_{noise} [49]. The signal-to-noise ratio (SNR) for a given unit was calculated using the formula:

$$SNR = \frac{A}{2 * \sigma_{noise}}$$

The signal stability was quantified by array yield and neuronal yield. Array yield was defined as the fraction of active electrodes that recorded neuronal activity during each recording session. Neuronal yield was defined as the number of isolated single units during each recording session. Both neuronal yield and array yield were calculated and combined across time for each animal for their respective implant duration. Because not every animal was recorded from every week, either due to lack of recording sessions or, for later points,

array failure, only data from available animals were aggregated for each time point. Figure 3 shows the number of arrays available for data analysis in each month after implantation.

2.6 Statistics:

Array yield, neuronal yield, and SNR values from all animals at the end of each month were compared using a one-way analysis of variance (ANOVA), to indicate if there was a significant decline in these metrics over time. A linear regression line was also used to indicate the trend for these metrics. Only p values less than 0.05 were considered significant. Tukey post hoc test was used to make paired comparisons between monthly data to identify significant changes.

3. Results

3.1 Array yield over time:

Figure 4 summarizes the array yield for all implanted MEAs for both the motor cortex and striatum implants. Each data point in 4A and B depicts the weekly array yield whereas 4C summarizes the data by each month. In the M1 (4A), animals E and L both had modulating units on 93.75% of electrodes in the early weeks post-implantation. However, the motor array in E failed within the first month due to broken array connector. The array yield in L remained greater than 70% for approximately 100 days after which it had steady decline in signal quality. Animals P, Du, and Do began with lower array yields below 50%, but the yield increased over the first two months and peaked at 87.5%, 75%, and 68.75%, respectively. The longest recording-term animals, Du and Do, had arrays in which performance steadily declined after the first four months but continued to obtain functional channels throughout the implant duration.

Five of six animals received implants in the striatum (4B). Single unit activity was recorded in animals E, P, and Du on 81.25% of implanted electrodes up to one month postimplantation. More units were observed in animal P in the second and third months, peaking at 87.5% on day 85. The MEA in animal Do recorded single unit activity in 50 to 60% of electrodes throughout the implant duration, while the implant in animal L had low yield always, only recording on approximately 12.5% of electrodes. Array yield significantly declined in the chronic period for cortical implants ($p < 0.01$) whereas the array yield for the striatal implants did not indicate a significant decline during the implant duration ($p = 0.14$), also shown by the regression lines in 4A and 4B. Figure 4C summarize the array yield from all implanted arrays from all monkeys throughout the study. The median array yield in cortical implants rose from 40.6% in the first month to 75%, before declining slowly for 6 months and remained around 25% for months 7 to 10. The striatal implants were more stable in comparison, with the median array yield being between 43.7% and 62.5% for all implants. High array yields ($> 80\%$) were still observed in some animals at 5-month time period for cortical MEAs and at 3-month for striatal MEAs.

3.2 Neuronal yield over time:

While the array yield quantified the fraction of active electrodes within a 16-channel MEA, the neuronal yield from each array represented the total number of isolated single units from

each electrode array during a recording session. Figure 5 shows the neuronal yield for all implanted arrays separated by implant location; figures 5A and 5B show data points for one recording session per week, while 5C shows summary data by month. In the cortical array (5A), similar to the array yields, animals E, L, and M had high neuronal yields where 16, 20, and 17 neurons were isolated in their first recording sessions, respectively. Animals P and Du started with low neuronal yields but the neuronal yield increased to 15 isolated single units within the first two months on days 41 and 57, respectively. Only three units remained on the cortical array in animal Du that lasted out to 10 months. Overall, the neuronal yield significantly declined over time ($p < 0.01$), shown by the regression line.

Figure 5B shows the neuronal yields in the five animals that received an implant in the striatum. Monkeys E, P, and Du had high neuronal yields, with over eight isolated single units for over 120 days. The high neuronal yield continued for animal Du throughout the implant duration. Monkey Do had a neuronal yield ranging between four and ten units through his implant duration, while the implant in animal L failed early after implantation, peaking at only two units. Nine single units could be recorded on the striatal array in animal Du up to 10 months. The neuronal yield across animals does not significantly decline ($p = 0.58$) as shown by the regression line in 5B as the neuronal yield was more stable for striatal implants. Figure 5C summarizes the neuronal yield for all implanted arrays from all the monkeys throughout the study duration. The median neuronal yield in cortical implants increased from 7 to 16 units before declining to 4–5 units in months 5 to 10. The neuronal yield for striatal implants stayed between 9 and 12 throughout the implant duration for all the implanted monkeys. High neuronal yields (>16 units) were still observed at ~5-month period for both cortical and striatal MEAs for a subset of MEAs.

3.3 Signal-to-Noise Ratio (SNR) over time:

The recorded signal quality was quantified by isolating single units through online and offline spike sorting action potentials for each neural channel. SNR values were calculated by dividing the peak-to-peak amplitude by the noise floor following methods described previously [49]. The noise floor was defined as two times the standard deviation calculated from the neural signal during the rest period. Spiking activity was removed from the signal prior to noise amplitude estimation as channels with highly active units could lead to overestimation of the noise. Figure 6 shows representative action potential waveforms extracted from three electrodes from animal Du, along with their respective SNR values. Average waveform shape is denoted by the darker blue line.

Figure 7 displays the average SNR values calculated from one recording session at the end of each month from each MEA from all the monkeys throughout their implant duration. For the cortical MEAs (Figure 7A), all animals had SNRs averaging around 4, with animals P and M having the best quality signals. The mean SNR values ranged between 2–5 throughout the lifetime of all cortical implants, aside from the rapid decay in animal M in month 5. In animal Du, SNR remained stable until month 8 after which it declined before array failure. Figure 7B shows the SNR values in the five animals implanted in the striatum. The SNR values right after implantation were very low (~2) in these implants but increased in the first 3 months in 3 monkeys. The average SNR values continued to increase further in

animals P and Du before declining towards the end of their implant duration when those MEAs failed. In general, the SNR values for the striatal arrays were more stable in the chronic period. Figure 7C summarizes the SNR values for all implanted arrays in all the animals during their implant duration. The median SNR (shown by the red line) remained at 2 over the lifetime of all implants. Very high SNR values (>6) were frequently observed even in later months, shown by the outliers denoted by red '+' signs and upper limits. The SNR did not significantly change with time for the first 7 months ($p = 0.07$) for all animals.

3.4 Waveform shapes changes over time:

Another way to track the stability and quality of signals is to track waveform shape changes over time for the action potential. Figure 8 shows three examples of units that could be described by changes in the waveform shape. Figure 8A show a unit on one channel in cortex of animal Du over 8 time points ranging from day 2 to day 293, along with the respective SNR values at those time-periods. This unit was chosen since it was recorded on this channel in every recording session and lasted the longest among all units. On day 2, the SNR for that unit was 3.33, which increased to 7.15 on day 61 before slowly deteriorating to 1.08 after 293 days. It should be noted that the signal amplitude and average waveform shape (denoted by the darker blue line) remains the same throughout. On this particular channel, the background noise floor increased over time which could be attributed to decreasing impedance of that electrode.

We also show an example of a single unit from the motor cortex channel from animal M that could be tracked over 4 time points ranging between day 23 to day 170 (Figure 8B). This unit was recorded on this channel for all recording sessions for this animal, with the SNR staying greater than 2 for about 5 months before quickly failing. The waveform amplitude varies in magnitude slightly until day 170, then declining rapidly to a SNR of only 0.51. Figure 8C displays a unit on one channel in the striatum from animal E over 4 time points, ranging between day 22 to day 127. This unit remained stable, albeit small and a SNR just over 1, for the entire implant duration. In general, background noise floor levels increased over time for all channels.

4. Discussion

In this work, we present chronic intracortical recording characteristics from microelectrode arrays implanted in the marmoset cortex. We discuss the electrode viability, design considerations, and failure modes for MEAs implanted in the motor cortex (1.5–2mm relative to brain surface) and in a deep brain (6.5–7.5mm relative to brain surface) structure. We further discuss the challenges with recording electrophysiological signals chronically from a smaller NHP model and also advantages of using this model in behavioral neuroscience research. A significant amount of literature has focused on reporting electrophysiological recordings from rodents whereas only a few studies have reported chronic recording characteristics in larger NHP model and none, as far as we know, from common marmosets.

In our studies, we were able to record single unit and multi-unit activity from the marmoset brain, with recordings from one animal for 45-weeks post-implantation. We measured the

percentage of functional electrodes over time by tracking array yield. Six out of 11 of the implanted arrays had array yields greater than 75% in the first 3-months post-implant whereas after 5-month period, the array yields remained approximately 50% for both the cortical and striatal implants (Figure 4). For longer-term implants, the yield continued to decline as commonly reported with electrodes implanted in the cortical tissue. While array yield reported in this study depicts whether electrodes were able to record single unit activity, other electrodes were still generally functional and able to record multi-unit activity. The total number of single units recorded was quantified by calculating the neuronal yield over time. Five out of 11 implanted arrays had neuronal yields of 16 single units in the first month post-implantation, beyond which the number of single units decreased following a similar trend as the array yield (Figure 5). Most channels only recorded one single unit at a time during the entire recording period. An interesting observation was that the MEAs implanted in the striatum showed more stable array and neuronal yields in the chronic periods as compared to the M1 arrays. This may be attributed to the difference in the distance between the electrode entry-point in the cortex and the recording site. MEAs in the M1 were ~2mm from the cortical surface where they entered the brain tissue whereas the striatal arrays were approximately 7mm from the brain surface. This observation is similar to that reported by Thelin *et al* [61], where they showed in NHPs that electrodes that were implanted several centimeters away from the ultimate recording location performed better than electrodes that had recording sites closer to where they entered the brain tissue.

The stability and recording quality of recorded units was also assessed by calculating signal-to-noise ratio (SNR) (Figure 7), which remained stable for most units in both MEA locations during the recording period. While the SNR for some units was high (>6) and remained high even after 10-months post-implantation, the SNR of most units remained in a range between 2 to 4 during the recording period. The SNR for striatal arrays were, in general, more stable than M1 arrays, possibly attributed to the same effect as described above for array and neuronal yields. We also tracked single units recorded by individual channels and found that these channels remained viable in the chronic period, but with an increasing noise floor, in general. An example of three such units from different animals is tracked during the implant duration (Figure 8). The same channel was tracked during the implant duration to observe how unit characteristics and background noise floor changed over time. In general, noise floor tended to increase in the chronic period and many of these units were indistinguishable from the background noise at late time points, as indicated by very low SNR.

Despite differences in the NHP model, the signal quality and time to failure was comparable with previously reported work. While Barrese *et al* [48] reported one electrode array that was functional 6-years after implant, most of the array failures (56% of 78 implanted MEAs) occurred within the first year after implantation. The array yield in their study also showed a general declining pattern as observed in this study, though their implant durations were significantly longer and consisted of a much larger cohort of animals (27 monkeys). Chestek *et al* [7] also reported action potential changes and neural decoder performance over 382 days postimplant in three rhesus macaques, where they observed a similar decline in action potential amplitude. The SNR results reported here can also be compared to previous work where Suner *et al* [49] tracked SNR over time from electrode arrays implanted in the motor cortex of three macaques, showing no diminishing trends over time or any decline in

recording reliability. Those animals were implanted for 83, 179, and 569 days, respectively. In our study, we also did not observe significant decline in the SNR in the first 7-months post-implantation. However, we did observe SNR decline after this period.

The failure modes of the implanted arrays were comparable to previous reported work. Out of 11 implanted arrays, four arrays failed due to acute mechanical failure (36%), compared to 48% in Barrese *et al* [48]. All other terminated experiments were due to signal degradation, with a mean time to failure of approximately 7 months. In this study, most of the failures were either mechanical attributed to connector issues or due to decline in signal quality over time. In addition to the difference in the NHP model, the MEAs used in this study were different compared to the other studies [7, 48, 62]. Previous studies used 100-channel Utah silicon MEAs whereas we used either a 16-channel tungsten microwire array (Tucker-Davis Technologies, Alachua, FL) or a 16-channel Pt-Ir floating microelectrode array (MicroProbes for Life Science, Gaithersburg, MD). While there are advantages of using a smaller NHP model, we are limited by the size of the MEA that can be implanted in the cortex. The size of a marmoset brain is significantly smaller than a rhesus macaque, and therefore, our electrode arrays were significantly smaller in dimensions and limited in channel counts. Despite the small size of marmoset brain, marmosets have lissencephalic cortex; they do not have the sulci and gyri otherwise present in larger NHP cortex. This is an advantage of this NHP model as one can access different cortical structures using planar MEAs since the presence of gyri and sulci poses additional challenge to target certain cortical areas. During the course of these experiments, we had to update the electrode and external connector design through iterations to suit the small marmoset brain size. The presence of two MEAs (one in M1 and another in striatum) posed additional surgical challenges, as the implant locations of both on the brain surface are very close to each other. Due to the close proximity of the two implants, it was challenging to place two ZIF-connectors such that they could be accessed later in recording sessions. In our earlier implants, we used 16-channel tungsten microwire arrays (Figure 1A) of different lengths. After implantation and during array fixation on the skull, one of the arrays was bent and fixed at an angle using the dental acrylic (Figure 1C) so as to allow access to both the MEAs during recording. This issue was due to the non-floating nature of the MEA where the external ZIFconnector was attached to the wire assembly. Therefore, in a later implant, we used floating MEAs (Figure 1B) so that the connector could be attached to the skull anywhere and was not restricted to where the array was implanted. We also went through multiple iterations of the ZIFconnector assembly, which was made of plastic and often broke in the chronic period. To avoid such failures, we worked with the manufacturer (Tucker-Davis Technologies, Alachua, FL) to custom design an aluminum shroud for the ZIF-connector instead of a plastic material to minimize mechanical failures due to connector design.

While this study proposes the use of a smaller NHP in neuroscience research and demonstrated the feasibility of achieving chronic recordings from multiple cortical locations, there are also several challenges associated with using a smaller animal model. MEA designs had to be custom built so as to accommodate the smaller brain size and recording channel counts were significantly lower than those from larger NHPs. There are also surgical challenges associated with a smaller model attributed to the small animal size and the

fragility of this model as compared to larger NHPs. However, based on our experience with this NHP model and results shown in this study suggest that marmosets can be used as a smaller NHP model in behavioral neuroscience studies.

Conclusions

This work demonstrates chronic recordings from multichannel microelectrode arrays in the marmoset model. Long-term recordings from multiple brain locations from a marmoset have not been previously described. This work shows that tungsten or Pt-Ir implants in marmosets show similar life cycles on average as reported in other test animals. Thus, researchers may be able to acquire useful chronic electrophysiological data with good yield during the first 7–10 months following electrode implantation, with a decline likely occurring in the following months. Further, with smaller MEA footprint and better connector technologies, stable recording could be achieved for a much longer period of time. Stable recordings are essential for neuroprosthetic technologies in both scientific and clinical settings and the study shows the potential of this smaller NHP model during behavioral tasks. Future work will focus on identifying histological changes that can be correlated with chronic electrophysiology.

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Figure 1. Electrode arrays and recording software. (A) Type A electrode arrays.

Type A electrode arrays were 16-channel tungsten microwire arrays (Tucker-Davis Technologies, Alachua, FL). Shown are microelectrode arrays of length 10mm and 5mm.

(B) Type B electrode array. Type B electrode arrays were 16-channel platinum-iridium floating microelectrode arrays (FMA, MicroProbes for Life Science, Gaithersburg, MD).

Substrate contains recording electrodes with length of 2 mm. **(C)** After arrays are implanted in both locations, dental acrylic was applied to anchor connectors and to cover the skull surface. Dust caps were placed over the connectors for protections.

(D) Screenshot during a recording session. Neural signals were recorded in awake, behaving animals from the MEAs using a RZ2 BioAmp Processor (TuckerDavis Technologies, Alachua, FL). Waveforms were discriminated online using box-sorting methods.

Figure 2. (A) Variation 1 of the 4-target center-out reaching task.

Targets were placed at 0° , 90° , 180° , and 270° . **(B) Variation 2 of the 4-target center-out reaching task.** Targets were placed at 45° , 135° , 225° , and 315° . **(C) Example of 2-target robot task.** The timeline for tasks A-C was similar; the task was initiated by a random hold time between 0.7 and 1.2 seconds before the target came into view. Once in view, the animal had 2 seconds to reach to the correct target. With a correct reach, a treat was given. With no or an incorrect reach, there was no reward.

Figure 3. (A) Number of cortical arrays recorded at each time point. (B) Number of striatal arrays recorded at each time point.

Because the total implant time in each animal and the number of recording sessions varied, only available arrays were included in yield and SNR analysis.

boxes represent the 75th and 25th percentiles, and the whiskers extended to cover approximately 99.3% of the data. Red '+'s are data that fall outside of this range and are considered outliers.

Figure 5. (A) Neuronal yield over time: cortical arrays.

Neuronal yield was defined by the number of isolated single units during a recording session on an implanted electrode array. The neuronal yield decayed over the implant period ($p < 0.01$). All arrays were able to record from at least 10 isolated single units within the first two months, with the highest overall yields in animals L and M. Linear fit: $-0.039x + 13.3357$

(B) Neuronal yield over time: striatal arrays. The neuronal yield in striatal arrays did not significantly decline ($p = 0.58$). All but one array were able to record from at least 10 isolated single units within the first three months, with the highest overall yields in animals E and Du. Linear fit: $y = -0.0087 + 10.7098$ **(C) Summary of the neuronal yields of all implanted electrodes over time.** The median array yield (shown by the red line) remained at 5 units or higher over the lifetime of all implants. The upper and lower limits of the boxes

represent the 75th and 25th percentiles, and the whiskers extended to cover approximately 99.3% of the data.

Figure 6. Typical action potential waveforms.

Shown are waveforms extracted from three channels from the cortical array in animal Du, with respective SNR values. The signal waveforms are in blue, while noise in grey. The average waveform shape is denoted by the darker blue line.

Figure 7. (A) SNR over time: cortical arrays.

For cortical arrays, the SNR values remained stable for the first 7 months ($p = 0.07$). There was a rapid decay in animal M, while all others have a steady SNR over 2 out to at least 8 months. The error bars represent the 75th and 25th percentiles around the mean. Linear fit: $y = -0.1188x + 3.4806$ **(B) SNR over time: striatal arrays.** The SNR values in striatal arrays remained stable for each animal, even increasing in the chronic period for animal P and Du. Linear fit: $y = 0.2035x + 1.8483$ **(C) Summary of the SNR of all units over time.** The median SNR (shown by the red line) remained at 2 or higher over the lifetime of all implants. Many single unit recordings with very high SNR values (> 5) were observed throughout the experimental period. The upper and lower limits of the boxes represent the

75th and 25th percentiles, and the whiskers extended to cover approximately 99.3% of the data. Red '+'s are data that fall outside of the range and are considered outliers.

Figure 8. Tracking waveform changes of single unit on single channel over time. (A) Unit from cortex in animal Du (B) Unit from cortex in animal M (C) Unit from striatum in animal E.

The blue lines show the individual waveform snippets, while the grey lines show levels of background noise. The darkest blue line denotes the average waveform shape for each recording session.

Table 1.

Summary of implant durations (in months) and electrode failure modes in each animal (MWA: tungsten microwire array; FMA: Pt-Ir floating microelectrode array).

Monkey	Motor Cortex Implant			Striatum Implant		
	Array Type	Duration	Failure Mode	Array Type	Duration	Failure Mode
E	MWA	1	Broken array	MWA	5	Signal degradation
P	MWA	7	Signal degradation	MWA	7	Signal degradation
Du	MWA	10	Signal degradation	MWA	10	Signal degradation
L	MWA	3	Signal degradation	MWA	1	Broken array
Do	FMA	6	Broken array	FMA	7	Signal degradation
M	MWA	5	Broken array	No implant in striatum		