Relationship between Microelectrode Array Impedance and Chronic Recording Quality of Single Units and Local Field Potentials

JingLe Jiang, Francis R. Willett, and Dawn M. Taylor

Abstract— **Practical application of intracortical microelectrode technology is currently hindered by the inability to reliably record neuronal signals chronically. The precise mechanism of device failure is still under debate, but most likely includes some combination of tissue reaction, mechanical failure, and chronic material degradation. Impedance is a measure of the ease with which current flows through a working electrode under a driving voltage. Impedance has been hypothesized to provide information about an electrode's surrounding tissue reaction as well as chronic insulation degradation. In this study, we investigated the relationship between an electrode's impedance and its chronic recording performance as measured by the number of isolatable single units and the quality of local field potential recordings. Two 64-channel electrode arrays implanted in separate monkeys were assessed. We found no simple relationship between impedance and recording quality that held for both animals across all time periods. This suggests that future investigations on the topic should adopt a more fine-grained within-day and within-animal analysis. We also found new evidence from local field potential spatial correlation supporting the theory that insulation degradation is an important contributor to electrode failure.**

I. Introduction

The recording performance of intracortical microelectrodes has been commonly observed to decrease over time. This decrease is a major hindrance for clinical usage of microelectrode-based technology (e.g., brain-machine interfaces). The precise mechanism of chronic device failure is still under debate, but several mechanisms have been proposed, including tissue reaction resulting in a neuron 'killing zone' [1], electrode mechanical failure, and chronic degradation of the insulation material [2], among others. Impedance is a measure of the ease with which current flows through a working electrode under a sinusoidal, driving voltage at a fixed frequency. On the one hand, it is believed that the brain's foreign body response or 'tissue reaction' encapsulates the electrodes, resulting in an increased barrier to ionic diffusion and therefore an increase in measured impedance [3]. Consequently, impedance has been hypothesized to be an indicator of the tissue reaction surrounding an electrode [4-7,9]. On the other hand, impedance is also thought to reflect the amount of insulation material degradation by correlating with the amount of exposed surface area [2, 8]. In this study, we used 1 KHz impedance to investigate the failure mechanism of two microelectrode arrays implanted in motor-related cortical areas of two Rhesus Macaques.

Previous investigations of long-term microelectrode performance have exclusively used single-unit (SU) recording quality as a measure of microelectrode performance (i.e., number and signal-to-noise ratio of isolatable neural units) [2,4-9]. Here, we extend those results by also incorporating the electrode's local field potential (LFP) recording quality. LFPs are not typically used as an electrode performance measure due to the difficulty of defining a metric of 'quality' for LFP signals. Unlike SU recordings where an electrode's recording quality can be assessed based on the number of isolatable neurons it records, an electrode will always record some LFP activity whose power magnitude alone is not indicative of performance [5]. Here, we quantify LFP quality by calculating the amount of movement-related information contained in the recorded LFPs as well as the spatial uniqueness of the gamma band (γ-band) activity on different electrodes.

This paper reports assessments of the 1 KHz impedance, SU recording quality, and LFP recording quality from two monkeys that each had a 64-channel BlackRock array chronically implanted. We expand on previous work by analyzing within-day differences across different contacts of the same arrays to further tease out temporal changes in the complex relationship between impedance and recording quality. Our results suggest that there is no simple relationship between impedance and recording quality that holds for all monkeys at all time periods. Our results also yield new evidence supporting the theory that insulation degradation could be a main cause of significant long-term signal deterioration.

II. Methods

A. Electrode Placement

Two adult Rhesus monkeys (*Macaca mulatta*) were chronically implanted with BlackRock 64-channel microelectrode arrays in primary motor cortex (Monkey W) or dorsal premotor cortex (Monkey N) contralateral to the arm used to complete the motor task.

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B. Data Collection

Data was collected from post implant days 31-400 for Monkey N and 16-160 for Monkey W. Data collection for both monkeys included 1 KHz impedance and neural signals collected while the monkeys were sitting quietly. Additionally, neural signals plus hand position was collected from Monkey N while it performed a target-directed reaching task.

When the animals were sitting quietly, two minutes of neural data was collected at 24 KHz via a TuckerDavis Technologies RZ2 recording system (Alachua, FL). These signals were processed via two paths and recorded separately. On one path, a real-time 300–3K Hz filter was applied (intended for spike sorting). On the other path, a real-time 1 KHz low-pass filter was applied prior to down sampling to 3051Hz (intended for LFP analysis). During target-directed reaching (monkey N), neural data was collected in a similar manner, but the LFPs were filtered between 0-500Hz and down sampled to 1220Hz. Hand position was measured at 50 Hz via an Optotrak Certus motion capture system (Northern Digital Inc.) [11]. In both cases, bad channels (i.e. channels recording very large, aberrant voltages with extreme impedance values) were excluded from analysis [10]. This left 50 working electrodes in monkey N and 63 working electrodes in monkey W.

C. Data Analysis

All offline processing was performed in Matlab (Mathworks, Natick, MA). Single Unit waveforms were extracted from the 24 KHz data stream using a custom-written sorting algorithm based on principle component analysis. The algorithm and definition of signal-to-noise ratio (SNR) were similar with [9]. The number of isolatable neurons that had an SNR>1.2 was used as a measure of SU recording quality for each electrode.

The LFP data stream was assessed for quality in two ways. One assessment used LFP γ-band spatial correlation. γ-band LFP are thought to contain neural activity from local sources and should be somewhat distinct from each other [10]. Therefore, a time series of signal power in the 70-110Hz band was computed every 300ms for each channel (300ms hamming window and fast Fourier transform). The correlations of these γ-band power time series were then calculated between each pair of electrodes. The mean value of the correlation between each electrode and all others was assigned as the average degree of γ-band LFP recording spatial correlation for that electrode.

As another measure of LFP recording quality, the amount of movement-related information contained in the LFP was quantified for monkey N using data collected while monkey N completed a standard, two-dimensional, eight-target, center-out movement task using methods similar to [11]. Linear models were generated to predict (decode) hand position and velocity from LFP power. LFP power was computed every 20ms using overlapping 300ms windows of data. The window's leading edge was aligned at each time point with the monkey's hand kinematics sampled at 50 Hz. Power in six frequency bands (0-4, 7-20, 20-70, 70-115, 130-200, 200-300) was calculated and log transformed. Overall LFP decoding quality was assessed using a greedy search algorithm [11] that limited the number of electrodes used for decoding to 30. In addition, a metric of γ-bands decoding performance was calculated for each individual electrode using the top three frequency bands (70-115, 130-200, 200-300). Ten-fold cross validated fraction of variance accounted for (FVAF) was used to quantify decoding accuracy.

III. Results

A. Decline in Performance over Days

Figure 1 shows the overall trend in 1 KHz impedance, single unit (SU) recording quality, and LFP recording quality for both Monkey N and Monkey W. Figure 1A illustrates that although there seems to be a 1 KHz impedance decline in both arrays, the decline in Monkey N is stronger and less variable than that in Monkey W. The array implanted in Monkey N also had smaller impedance values overall compared to that implanted in W.

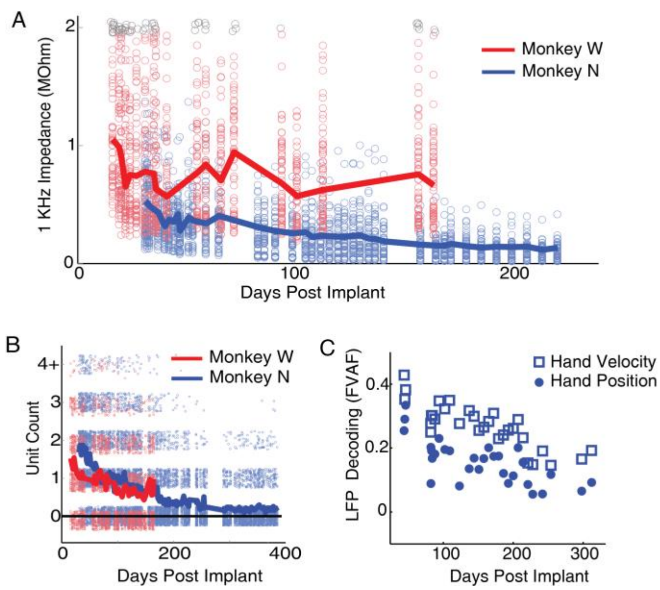

Figure 1. Trends in 1 KHz impedance, single unit recording quality, and LFP recording quality across time. (A) 1 KHz impedance magnitudes for all functioning electrodes (n=50 for monkey N and n=63 for monkey W) are plotted as open circles. Lines illustrate the median value. Individual impedance magnitudes larger than 2MOhm were clipped at 2MOhm for better visualization and plotted in gray. (B) Thick lines show the mean recording unit count across all functioning electrodes while dots in the background illustrate the unit count for each channel on a given day (note overlapping data points are offset in the y direction around each possible integer value for better visualization). (C) Monkey N LFP quality as assessed by offline decoding of hand velocity and hand position during a motor task (see Methods) revealed consistent LFP signal quality deterioration over time.

Figure 1B shows that on early days, electrodes from both arrays recorded ~two neurons on average, with several good channels recording four or more isolatable units. As expected, unit count consistently declined over time for both arrays, ending at an average of 0.29 (Monkey N) and 0.98 (Monkey W) neurons/electrode at the close of the study.

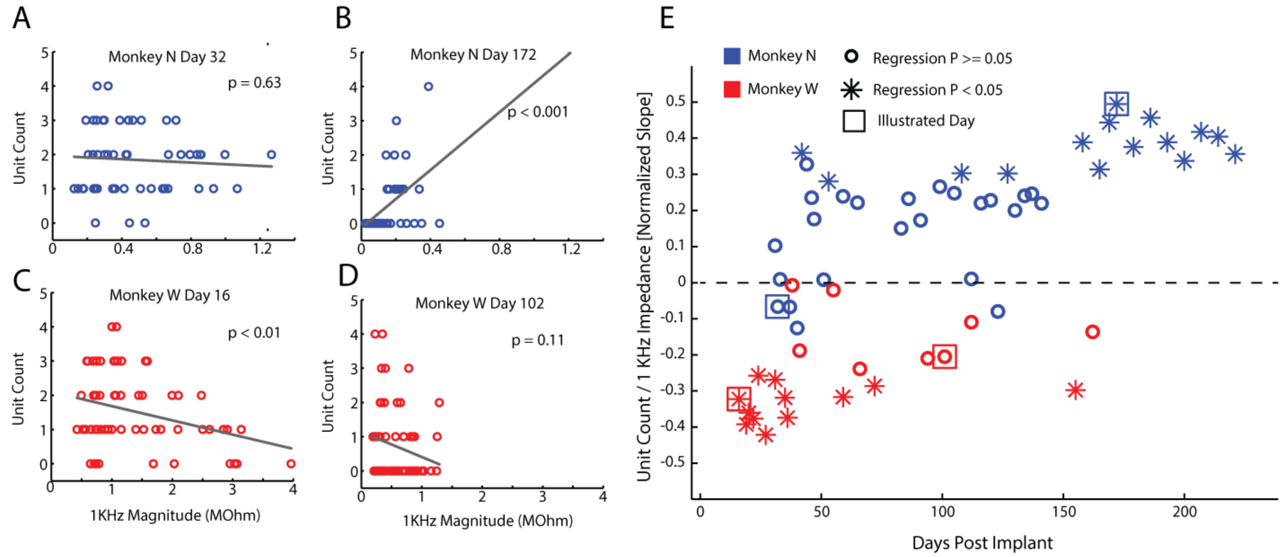

Figure 2. Within-day relationship between impedance magnitude at 1 KHz and the number of single units recorded (unit count) on each electrode is assessed on four example days for two monkeys (A-D) and the regression slope trends are plotted across time for all days (E). On day 32 (A), 1 KHz impedance did not correlate with unit count (linear regression p-value = 0.63), but was significantly correlated at day 172 (p-value < 0.001, B). The linear regression lines are plotted in gray, while data from each electrode are plotted with open circles. Note that both unit count and 1 KHz impedance decreased in (B) compared to (A). (C, D) same as (A, B) but for monkey W. Plot (E) summarizes the normalized slope of each individual day's linear regression. Normalized slopes were plotted so that the two animal's slopes were comparable. This was obtained by linear regression on z-scored 1 KHz impedance and z-scored unit count. A star denotes that a linear relationship between impedance magnitude and unit count was significant on that day (p<0.05); an open circle denotes the opposite (p>=0.05).

However, the decline of Monkey W is slower than that of Monkey N (note the crossover of the two thick lines on Figure 1B at around day 160). Since the two arrays also exhibit different impedance trends, there may be different failure mechanisms at play between the two arrays. Figure 1C shows that LFP recording quality of Monkey N consistently declined as well, as measured by the declining ability to reconstruct the animal's hand velocity and position.

B. Within-Day Analysis of inter-electrode differences

We assessed the correlation between the 1 KHz impedance of each electrode and that electrode's SU recording quality on each individual day. Figure 2A and 2B show two example days for Monkey N where 1 KHz impedance is plotted against unit count. In earlier days (Figure 2A), there was no 'preferred impedance'; electrodes with any value of 1 KHz impedance were equally likely to record a good number of units. For a later example day, however, a positive relationship between impedance and unit count emerged (Figure 2B). Figure 2E summarizes this developing relationship by plotting normalized linear regression slopes from all days. Here, a clear trend of both increased value and an increased statistical significance of the slope suggest that, for Monkey N, 1 KHz impedance indeed became associated with the electrode recording quality in later days. These later time points include many electrodes with very low impedances and no recordable units, which suggests extensive insulation breakdown.

Similarly, Figure 2C and 2D show two example days (early and late) of Monkey W where 1 KHz impedance is plotted against unit count. Unlike Monkey N, an early negative correlation was observed, which became less significant at later time points. Figure 2E contrasts the difference between the two animals across days.

Within-day relation between impedance and LFP quality is shown in Figure 3. Figure 3A illustrates that, in monkey N's early days, the individual electrodes' 1 KHz impedance was not correlated with the 'distinctness' of each electrode's recorded LFP γ-band (see Methods). Over time, however, electrodes with relatively small impedance were more likely to record a spatially-blurred γ signal, suggesting those electrodes were recording from a larger surface area. Similarly, these small impedance electrodes tended to have worse LFP decoding performance in later days, but not in early days (Figure 3C). That is, lower impedance electrodes did not contain as much movement-related information in their recorded γ-band as did higher impedance electrodes.

Figure 3B shows an early and late day example LFP analysis for Monkey W. Monkey W also had a negative relationship between 1 KHz impedance and γ-band spatial correlation. However, unlike Monkey N, the relationship was stronger at earlier time points but became less significant over time. Figure 3D summarizes these temporal results.

IV. Discussion

Reports of 1KHz impedance are common in the literature when discussing intracortical electrode performance [2,4-9]. Impedance has been hypothesized to be related to electrode performance based on the following:

• The glial scar produced by the brain's foreign body response both increases impedance and presumably pushes neurons away from the electrode. The resulting chemical environment may also kill or degrade function of neighboring neurons. In this case, higher impedance values

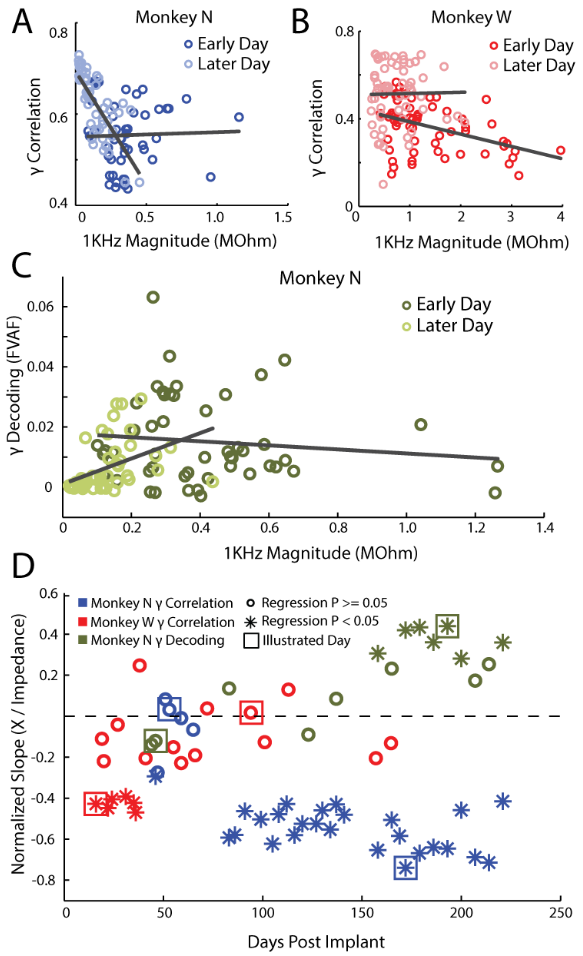

Figure 3. Relationship between impedance magnitude at 1 KHz on each individual electrode and that electrode's (i) LFP gamma band spatial correlation and (ii) hand velocity decoding performance. In (A) and (B), the relationship between 1 KHz impedance and the average pair-wise gamma correlation on each electrode is plotted for both an early day and a later day for monkeys N and W respectively. Open circles plot the data for each electrode and gray lines show the linear regression fit. In (C), the relationship between 1 KHz impedance and gamma band decoding performance in Monkey N is shown for an early and later day. In (D), the regression slope and p-value for each day is plotted across time for both gamma band decoding performance and gamma band spatial correlation. For Monkey N, a strong correlation develops in later days for both metrics, such that lower impedance electrodes are likely to contain less movement-related information and are more likely to be correlated with other electrodes. This trend is further evidence of insulation degradation in Monkey N. For Monkey W, there are no clear trends.

are hypothesized to correlate with a lower observed unit count. [4, 6, but see 9 for a special case.]

• Insulation degradation increases the electrode contact area and reduces impedance. The cause of insulation degradation is unclear but may also be tied to the brain's foreign body response due to the reactive oxygen species produced [2]. Here, lower impedances are hypothesized to correlate with a reduced ability to isolate individual neurons from the background noise. [2,8]

The fact that measured impedance is a summation of both the electrode impedance and the surrounding tissue encapsulation impedance highlight the complexity of the relationship between impedance and recording quality. The relative contribution of each of these two parts likely varies across time, across animals and even across individual electrode contacts. Therefore we adopted a detailed case-by-case, day-by-day analysis rather than collectively analyzing all data from different animals at different time points. We also extend previous results by taking LFP recording quality into consideration.

We did not see a simple relationship between 1 KHz impedance and recording quality that holds for both animals and across all time points. Results from Monkey N support the theory that insulation degradation can be a major cause of chronic failure, as suggested by Monkey N's strong correlation between low 1 KHz impedance and high LFP γ-band spatial correlation at later time points. This degradation was harmful to SU recordings as well.

No evidence of insulation breakdown was observed on Monkey W over her more-limited time span. Contrary to Monkey N, a negative correlation between impedance and unit count was observed, especially for early time points (Figure 2E). Negative slopes are consistent with what one would expect when impedance values are determined mainly by the surrounding tissue reaction. However, there was also an early relationship between 1 KHz impedance and LFP γ-band spatial correlation with Monkey W (Figure 3D), whose meaning we do not understand.

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