Influence of the number and location of recording contacts on the selectivity of a nerve cuff electrode

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***Abstract*—A 56-contact matrix nerve cuff electrode (7 rings with 8 contacts each) was used to obtain recordings from the rat sciatic nerve, which were then discriminated as originating from one of three fascicles (tibial, peroneal, and sural branches). The influence of the number and location of the recording contacts on the classification accuracy was studied. The performance of a classifier was shown to be superior when data was available from all 56 contacts, compared to when only the 8 contacts of the middle ring were used (as in previously proposed multi-contact tripolar cuff designs). By examining the performance variations as contacts were included one at a time (in order of decreasing positive impact on performance), it was further shown that the matrix configuration could outperform the single-ring configuration with only a small number of contacts. We can therefore conclude that the performance improvement is not due to the sheer number of contacts, but rather to the possibility of selecting the most informative locations around the nerve. The results could have important implications for the design and use of multi-contact nerve cuff electrodes.**

***Index Terms*—Multi-contact cuff electrode, layout of recording contacts, nerve cuff selectivity, peripheral nerve interface, rat sciatic nerve.**

I. Introduction

DEVELOPING effective interfaces between peripheral nerves and artificial devices is crucial to the development of better implanted neuroprostheses. The nerve cuff electrode [1]–[5] has been an essential component of this endeavour for the past 30 years, in part because it can be safely implanted for extended periods of time [6]. The main drawback of the device has traditionally been the lack of spatial selectivity within the nerve: recording or stimulating from a specific fascicle or pathway was difficult, and in this respect the nerve cuff was at a disadvantage with respect to intrafascicular devices [7]–[9] and micro-electrode arrays [10]–[13], which are more invasive but also more spatially selective. As manufacturing technology progressed, larger numbers of contacts were incorporated into nerve cuff electrodes. These improvements, in combination with other novel strategies such as nerve reshaping [14]–[16], have led to several demonstrations of the fact that the activity of different fascicles can be discriminated using nerve cuff recordings [16]–[21].

In the present study, we present an evaluation of the improvement in fascicle discrimination that can be achieved with a recently proposed nerve cuff design, the "matrix" cuff [22]. This device has 56 contacts laid out in 7 rings of 8 contacts each. Our goal is to determine if this configuration leads to better discrimination accuracy than the signals from a set of contacts laid out in a single ring, as in previously employed multi-contact tripole configurations [16]. To investigate this issue, we use the matrix cuff and compare the performance of the full grid-like contact configuration (the 56-contact "matrix" configuration) to the performance when using only the 8 contacts in the middle ring of the cuff (the "single-ring" configuration). If the matrix performance is found to be superior, we will seek to determine in addition whether the improvement is due to the number of contacts used or to their position. The large number of contacts and grid layout of the matrix cuff makes it ideal to study these issues. Information about the optimal placement of contacts in a nerve cuff to maximize selectivity would have direct applications in the design and use of this type of electrode in neuroprosthetic systems.

Manuscript received October 24, 2008; revised January 9, 2009. This work was supported by the Natural Sciences and Engineering Research Council of Canada (grant #249669), the Ontario Graduate Scholarship program and the Walter C. Sumner Foundation.

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II. Methods

A. Data collection

1) Animals: Six old male Long-Evans breeders (640 g to 850 g) (Charles River Laboratories Inc., Wilmington, MA) were used. All rats were acclimatized for one week prior to use in the experiment. Food and water were provided *ad libitum*. A 12 hour lights on/off cycle was used. All animal care and use procedures conformed to those outlined by the Canadian Council on Animal Care (CCAC).

2) Anaesthesia: All animals were anesthetized with a single bolus injection of pentobarbital (60 mg/kg, intraperitoneal), and their lower backs and legs were shaved and treated with povidone-iodine. When an adequate depth of anesthesia was attained (loss of corneal reflex and loss of sharp pain sensation), the animals were positioned prone on the operating table.

3) Surgical exposure: An oblique incision was centered over the posterior (dorsal) aspect of the hip. The incision was extended proximally to the midline and distally parallel with the fibers of the gluteus maximus to the posterior margin of the greater trochanter. The incision was then directed distally, parallel with the femoral shaft to the posterior fossa of the knee.

The deep fascia was exposed and divided in line with the skin incision. By blunt dissection, the gluteus maximus was split in line with its fibers and retracted to expose the sciatic nerve and short external rotator muscles. Care was taken not to disturb the superior gluteal vessels in the proximal part of the exposure.

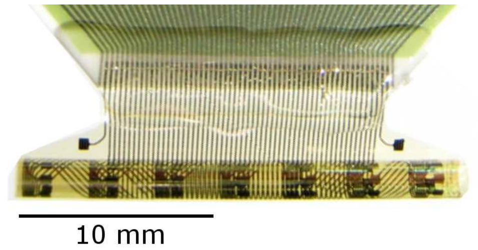
The sciatic nerve was exposed as far proximally as possible to allow adequate exposure for application of the recording cuff. The recording cuff was applied to the sciatic nerve following application of the three stimulating cuffs (see details in the next section).

The sciatic nerve was then followed distally and three branches were identified: the sural nerve, peroneal nerve, and tibial nerve. The soft tissue surrounding each of these nerves was carefully blunt dissected to allow a stimulating cuff to be applied to each nerve.

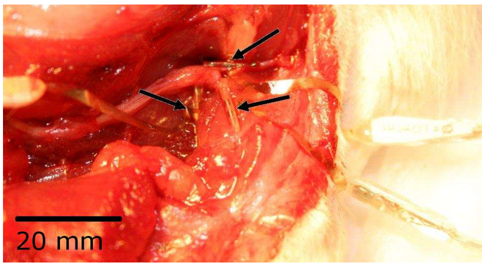
4) Experimental procedure: A matrix design polyimide spiral nerve cuff electrode [22] (Figure 1(a)) was placed on the sciatic nerve, just proximal to its division into its peroneal and tibial branches. This cuff was 23 mm long, 1 mm in diameter and contained 56 contacts, arranged in 7 rings of 8 contacts. This electrode was used to record the nerve activity during the experiments. In addition, three tripolar stimulating polyimide spiral nerve cuffs (8 mm long and 1 mm in diameter) were placed around the tibial, sural, and common peroneal nerves. The center ring of the stimulating electrodes contained 8 contacts that were shorted together, resulting in traditional tripole cuffs. The stimulating cuffs were placed first (Figure 1(b)), followed by the recording cuff (Figure 1(c)).

The measurements from the cuff on the sciatic nerve were acquired using a SynAmps2 64-channel amplifier (Neuroscan Inc., Herndon, VA, USA), with a sampling rate of 20 kHz and a gain of x2010. The signals were bandpass filtered between 300 Hz and 3 kHz. The reference for the recordings was a contact included in the matrix cuff design and located just outside the cuff. A needle electrode in the calf was used as the ground.

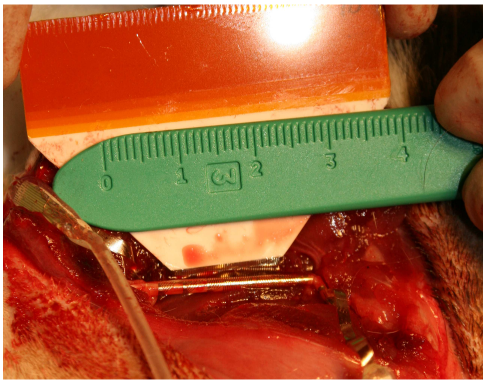
The tibial, peroneal, and sural nerves were stimulated one at a time using the 8mm cuff electrodes. The stimulation pulses were generated using Compex Motion stimulators (Compex SA, Switzerland). Although the intended stimulation parameters consisted of 10 μs 2 mA pulses (2 mA being comfortably higher than the thresholds reported in the literature for pulses of this duration [14], [17], [23], [24]), technical difficulties noticed only after the fact resulted in pulses with an estimated duration of 2-4 μs and with amplitudes in the 0.7 to 3.8 mA range approximately. Fortunately, these pulses were still able to reliably produce action potentials in the nerve (as indicated by muscle twitches and the fact that the matrix cuff recordings showed a temporal progression of activity along the cuff consistent with action potential propagation). 100 trials were conducted for each fascicle, at a frequency of 2 Hz.



(a)



(b)



(c)

Fig. 1. a) The matrix recording cuff before implantation (photo courtesy of Dr. Martin Schuettler, used with permission). b) The tibial, peroneal, and sural nerves are exposed. Each has a stimulating cuff wrapped around it, indicated by an arrow. The sciatic nerve has been exposed but the recording cuff has not yet been placed. c) The exposed sciatic nerve with the recording cuff wrapped around it.

B. Evaluation of the classification accuracy

We sought to determine whether or not the recordings from the 56-contact matrix cuff genuinely contained more useful information than measurements from a simpler configuration. We considered the case of a simple feature-based classifier for differentiating the activity of the three different fascicles, when only one of them is active at a time. In the context of our experiments this means that our goal is to determine which fascicle was being stimulated in a given randomly chosen trial, using the measurements from the recording cuff. We compared the performance of this classifier when using data from all 56 contacts to the performance when using only data from the 8 contacts in the middle ring of the cuff (ring 4 of 7). The two configurations are illustrated in Figure 2.

The classification process was conducted as follows for each animal:

1) For each trial, the data was converted to a "tripole"

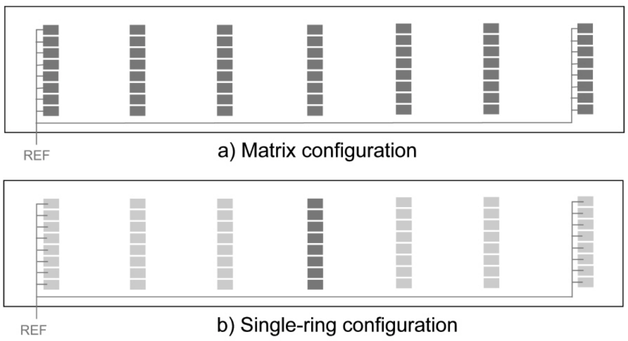


Fig. 2. Contact configurations for the matrix (a) and single-ring (b) cases. The contacts in dark gray are the ones that are available for use in the classification process. The contacts of the first and last ring are averaged to produce the reference, for both configuration.

reference, which is to say that the average of all the contacts in the first and last rings was used as the reference (the term tripole is used loosely here, since there are more than three rings in the cuff). Once this was done, the data was normalized using the largest absolute value in this trial over all contacts. Because of this normalization, the classification is based on the distribution of activity among the contacts, and therefore on spatial information, rather than on the magnitude of the activity.

2) A set S of contacts to be included in the feature vector was defined.
3) For each trial, the peak of the action potential recorded at each of the contacts in S was found (the peaks may not all occur at the same time, since the contacts can be at different longitudinal positions along the cuff). The feature vector was then defined as the potential of each contact at its peak, resulting in a vector with one entry for each element in S.
4) The trials from each nerve were partitioned into a training set and a testing set. The feature vectors from the training set were averaged for each fascicle, resulting in one mean feature vector for each of the tibial, peroneal, and sural branches. Each of these mean feature vectors was normalized. The three vectors were then collected into a matrix L.
5) For each trial in the combined testing sets, the normalized feature vector F was classified by finding the least-squares solution to the overdetermined system $LX = F$. The fascicle corresponding to the largest value in X was chosen as the one responsible for the observed activity in this trial.
6) The classification accuracy is the percentage of trials in the testing set that are assigned to the correct fascicle.

In order to ensure that the results were not biased by the choice of trials included in the training set, the evaluation of the classifier was performed using 10-fold cross-validation.

In each trial, channels with excessive variance or very small amplitude compared to the other channels were marked as bad channels and set to 0 before computing the feature vector. Trials were discarded when more than a quarter of the channels in S were bad or when the temporal spread of the peaks across all contacts was greater than 1ms.

Our main concern is whether or not the matrix cuff allows for more accurate classification than the single-ring configuration. In addition, we would like to establish whether or not all 56 contacts are needed for an improvement (if any is found). In other words, we would like to know if the benefit of the matrix cuff stems from having more channels of information, or if a small subset of contacts could also lead to better performance simply by virtue of having 56 possible contacts to choose from instead of 8. To answer these questions, both configurations were investigated by adding one contact at a time and tracking the performance as more contacts were added. The set of available contacts during this process was in one case all 56 contacts, and in the other case the 8 contacts in the middle ring (refer once again to Figure 2). At each step, the contact added was the one that improved the performance the most. In other words, we first computed the performance using each contact individually (i.e. S had a single element, and the full cross-validation procedure was performed) and retained the best one. Next, we investigated each remaining contact in combination with the first contact selected, and again retained the best one. The third contact was then combined with the first two, and so on, until all the contacts from the set of interest had been added.

C. *Evaluation of the influence of the stimulation artefact*

The interpretation of the results will be complicated by the presence of a large stimulation artefact in the recordings. An artefact is present because the amplifiers were not blanked during the stimulation (our recordings were performed using AC coupling in order to achieve the necessary gain, and the amplifier's blanking feature was not available in this mode). The amplifiers did not saturate, but they were susceptible to an impulse artefact with a time constant of approximately 0.5 ms and thus overlapping with the signal of interest. Figure 3 illustrates this with an example of one trial, showing both the raw data and the data after conversion to the tripole reference. We must consider the possibility that stimulation at different sites produces slightly different stimulation artefacts, and that the classifier is partly taking advantage of this information. If this were the case, we would expect that classification accuracy would be superior when large artefacts are present. In order to investigate this possibility, we use the fact that the magnitude of the artefact is expected to vary between rings of contacts. Indeed, theoretically, the electric field produced by sources outside the cuff should vary linearly along the length of the cuff [25]–[28]. By examining the magnitude of the signals recorded at each contact before converting the data to the tripole reference, we can estimate how the size of the artefact varies between rings. This information can then be converted to an estimate of how the artefact will vary between rings after the tripole reference is applied. Lastly, to determine whether the classifier is relying heavily on information in the artefacts, we compute the classification accuracy using each ring in turn

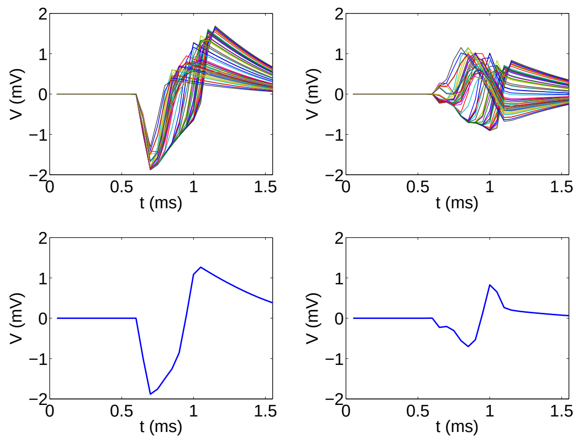


Fig. 3. Example of the recordings of one tibial branch trial in Rat 1. The upper left-hand plot shows the raw recordings for all 56 channels. The upper right-hand plot shows those same recordings after conversion to a tripole reference. The lower plots show the same data for one contact only, taken from the middle ring of the cuff.

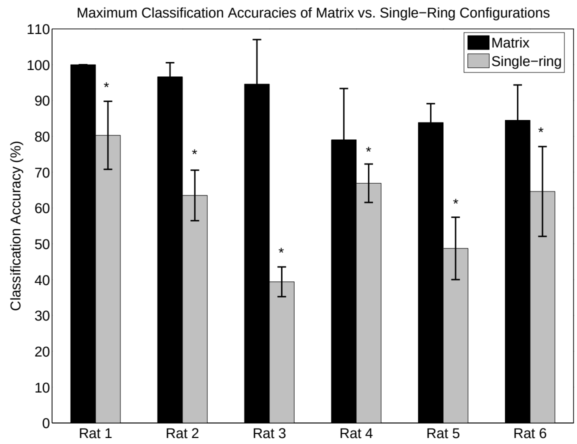


Fig. 4. Maximum classification accuracy achieved with the matrix and single-ring configurations, for each rat. The standard deviations shown are based on the set of 10 results obtained for each case during the 10-fold cross-validation process. The asterisk denotes a statistically significant difference ($p < 0.05$).

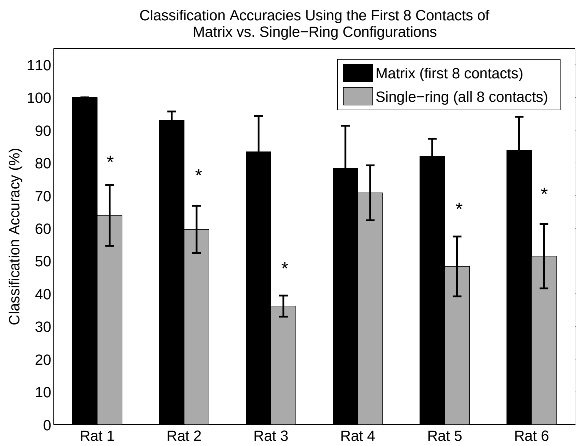


Fig. 5. Classification accuracy achieved with the first 8 selected contacts of the matrix and of the single-ring configurations, for each rat. The standard deviations shown are based on the set of 10 results obtained for each case during the 10-fold cross-validation process. The asterisk denotes a statistically significant difference ($p < 0.05$).

as the set S described above. If the classification uses the artefact, we expect that the performance using the different rings will be correlated with the estimated size of the artefact at those rings.

To estimate the artefact variations, the recordings of each contact are first averaged over all trials of all three fascicles combined, then rectified and integrated. The signals used in this step are the raw measurements, recorded with respect to the outside contact rather than using the tripole reference. The size of the artefact at each ring is estimated using the average of the obtained values of each contact in the ring. The resulting set of seven values (one per ring) is normalized using the largest value. By subtracting the mean of the first and last values and taking the absolute values of the results (to take into account the tripole reference in the classification), an estimate is obtained of how the classification performance would be expected to vary from ring to ring if the size of the artefact was the determining factor. Lastly, the correlation between this series and the performance actually obtained is computed.

III. Results

A. Comparison of the matrix and single-ring configurations

Figure 4 shows the maximum classification accuracy achieved for each animal using each method. These results demonstrate that in all cases better classification accuracy was achieved using the matrix configuration. The question now is whether the improvement is due simply to the sheer number of contacts. To resolve this issue, the classification accuracy was computed using the first eight selected contacts of the matrix configuration, versus the eight contacts of the single-ring configuration. The results are shown in Figure 5, and once again the matrix configuration results in clear improvements. For each comparison, an ANOVA test was conducted using the 10 results of the cross-validation procedure for each contact configuration. The differences in Figures 4 and 5 were shown to all be significant ($p < 0.05$), with the exception of the rat 4 comparison in Figure 5, although the matrix configuration's performance was still higher in that case.

Figure 6 plots the classification accuracy of the matrix configuration as a function of the number of contacts for each rat. Markers on each plot indicate the point at which maximum accuracy is achieved, and the point at which the accuracy exceeds the maximum accuracy achieved with the single-ring configuration. As an example of the contact selection process, Figure 7 shows the order in which the contacts were selected in the case of Rat 1 for each of the two configurations, up to the number of contacts at which maximum accuracy is reached (refer to Figure 6).

Several conclusions can be drawn from this data. First, discrimination of the activity of different fascicles is feasible, which confirms the information found in the literature [16], [20], [21]. Second, the use of the matrix cuff can significantly

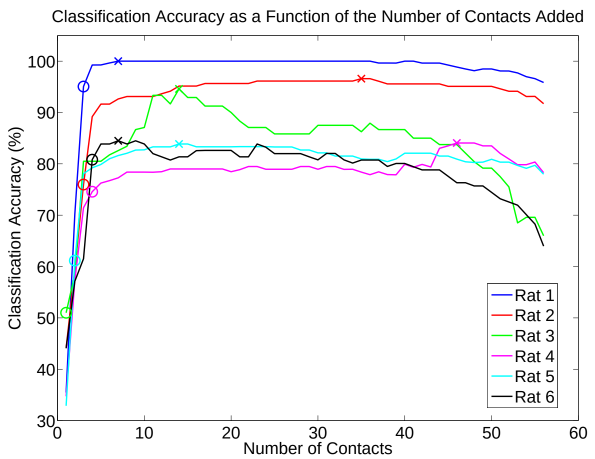


Fig. 6. Classification accuracy achieved using the matrix configuration, as a function of the number of contacts used. The first markers (o) indicate the point at which the matrix configuration starts outperforming the maximum accuracy achievable with the single-ring configuration. The second markers (x) indicate the maximum accuracy achieved with the matrix configuration.

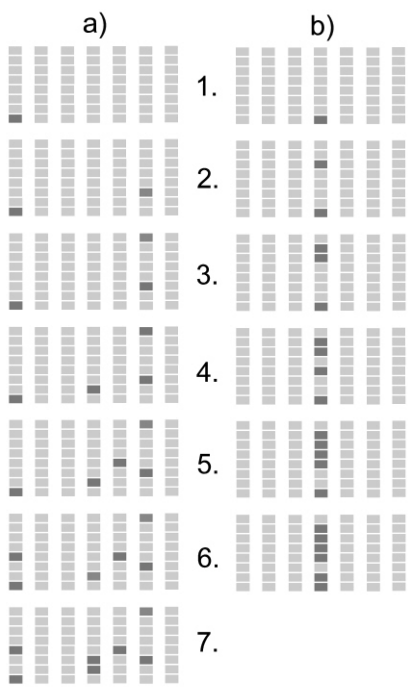


Fig. 7. a) Order in which contacts were added in Rat 1 when using the matrix configuration. Only the first 7 contacts are shown because that is the number required to reach maximum accuracy for this animal (see Figure 6). b) Corresponding results when using the single-ring configuration.

TABLE I
CORRELATION OF THE ARTEFACT AND CLASSIFICATION ACCURACY VARIATIONS BETWEEN CONTACT RINGS

Animal	Correlation	P-value
Rat1	0.07	0.880
Rat2	0.08	0.861
Rat3	0.85	0.015
Rat4	-0.57	0.177
Rat5	0.37	0.420
Rat6	0.33	0.475

improve the classification accuracy. Lastly, optimal or near-optimal accuracy can be achieved with fewer than 10 contacts. This implies that the superior performance of the matrix cuff is not due to the absolute number of contacts, but rather to the possibility of sampling the extracellular fields in locations that contain the most useful information. These results were consistent across all of the animals, but the maximum classification accuracy varied widely, with a range of 83.9% to 100%. In addition, the contacts selected as providing the most information were not consistent between animals. These variations could be due to a number of factors, mainly related to the position of the cuff on the nerve, the quality of the electrical connection established at each contact, and noise issues.

B. *Influence of the stimulation artefact*

An example of the comparison described in Section II-C is shown in Figure 8. The estimated normalized artefact distribution is shown, as well as the expected performance variations if the classification was based on the artefact, and the actual performance variations observed. The correlation between the expected and observed variations was 0.07, which corresponds to a p-value of 0.88 when considering a null hypothesis of no correlation. Table I shows the correlations and p-values for all six animals. The p-value was considerably larger than 0.05 in five of the six cases, such that we cannot conclude that the stimulation artefact plays a significant role in the classification accuracy. Although these results do not allow us to state that the stimulation artefacts have absolutely no influence on the performance, they do show that the artefacts are not the dominant factor, and that the comparisons between the different contact configurations are based on neural activity. The case of Rat 3, in which $p \leq 0.05$, suggests that there may have been an incomplete closure of the cuff in that experiment, leading to a much more predominant stimulation artefact in the recordings. All results for this rat should therefore be treated with caution.

It should be mentioned that although Figure 8 shows a roughly linear variation of the artefact, as expected, this pattern was not observed in all of the animals. The lack of linearity in the other animals can be attributed to variations in the impedances of the contacts, as well as to small shifts in the cuff position during the experiments (recall that the artefacts are estimated using an average of all the trials for a given animal). It is for this reason that we examined the correlation between the variations in artefact and in classification accuracy, rather

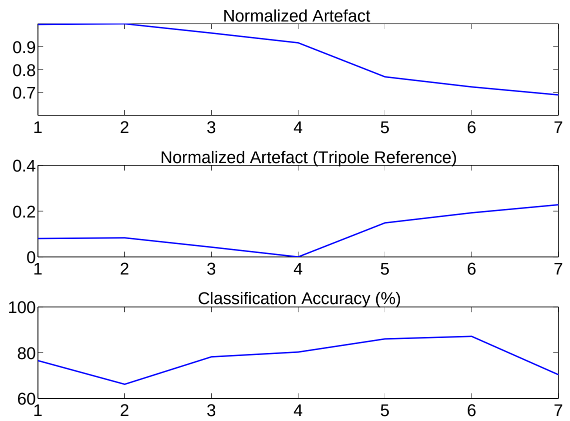


Fig. 8. Comparison of artefact variations and classification accuracy variations between contact rings in Rat 1. The top plot shows the normalized estimated variations of the stimulation artefact in the raw recordings, as a function of the contact ring. The middle plot shows the variations once the use of the tripole reference has been taken into account. The bottom plot shows the variations in the classification accuracy when each of the contact rings is used in turn. The middle and bottom plots are poorly correlated, arguing against the hypothesis that the stimulation artefact plays an important role in the classification accuracy.

than checking for a pre-determined pattern in the accuracy variations.

Computing the classification accuracies for every ring of contacts also allowed us to confirm that none of them outperformed the accuracy obtained using the matrix configuration (results not shown).

C. Layout of the most informative contacts

Having established that a small number of contacts can be used to achieve high accuracy, the question arises of whether it is possible to identify the optimal contacts, and potentially incorporate this information in future cuff designs. We therefore examined the order in which the contacts of the matrix configuration were selected, in other words which contacts proved most informative for the purposes of fascicle classification accuracy.

Establishing a common set of useful contacts among all rats proved difficult, which is not surprising given that the alignment of the contacts with the fascicles was not the same from one experiment to the next. Nonetheless, it was observed that in all cases the selection algorithm started by choosing contacts from several different radial positions along the nerve (not necessarily aligned at the same longitudinal position). The number of contacts that were added before any repetition of the radial position occurred varied between 4 and 6, with an average of 5.33 over the six animals. This result indicates that there is value in sampling different radial positions around the nerve, which of course is to be expected because it allows different contacts to be close to different fascicles. The fact that the different radial positions selected were not necessarily aligned longitudinally is also very important, because it illustrates the value of having more than one contact to choose from when attempting to record from a given fascicle. These observations are well illustrated by the Rat 1 results shown in Figure 7.

IV. Discussion

We demonstrated that by using a matrix cuff electrode it was possible to obtain better fascicle classification accuracy than when using signals only from contacts in the middle ring of the cuff. We further showed that the difference was not due to the sheer number of contacts, since the matrix cuff could outperform the single-ring configuration even with a small number of contacts. These results are in accordance with expectations, because they support the idea that classification accuracy can be improved by selecting the locations around the nerve that contain the most useful information.

The locations of the most useful contacts cannot necessarily be determined *a priori*, because they will not depend only on the locations of the fascicles. Rather, variations in the impedances of the cuff contacts, the details of interface of each one with the nerve (i.e. distance, amount of interfering tissue, etc.) and the noise level are likely to play a large role. In addition, even if the approximate placement of the fascicles can be estimated, their relative positions will not be completely constant along the length of the cuff, particularly if the device is long. As a result, how the selectivity will vary with the longitudinal position is not known in advance. Furthermore, the optimal number of contacts will depend on the number of fascicles that we are attempting to discriminate in a given nerve. Because of these issues, the results presented here cannot be used to design a cuff with a small number of optimally-placed contacts. Rather, they argue in favor of implanting a device with a large number of contacts, then conducting an optimization procedure that will indicate which subset of the contacts should actually be used. Having a large initial set of contacts available is all the more beneficial when one considers the issue of chronic implantation. With time, morphological changes will occur, in the form of connective tissue accumulation and reshaping of the nerve itself [3], [29]–[31]. The optimal subset of contacts may therefore not be constant. If the contact selection procedure could be conducted not only during the initial implantation but on a regular basis, the nerve cuff's performance could be maintained at a higher level over time. Another aspect to this issue is illustrated by Figure 6, which shows that the accuracy not only can be maximized with a modest number of contacts, but can actually decrease when too many contacts are added. We can hypothesize that certain contacts contain very little classification information, either because of their position or because of high impedance or noise. Including such contacts in the classification procedure could therefore cause more confusion than improvement. This phenomenon argues in favour of having a contact selection procedure regardless of the amount of information bandwidth that can be accommodated.

The main limitation of our study is the presence of the stimulation artefact, which casts doubt on the exact classification accuracy that could be achieved in its absence. Nonetheless, we have shown that its impact was limited. Similarly, the unintended variations in the stimulus pulses (as described in the Data Collection section) likewise raise the possibility that the classification was partially based not on the spatial position of the fascicles, but on differences in the neural activity generated in each one. The fact that the data in each trial is normalized (as described in the Methods section) helps to compensate for possible differences of this kind. Furthermore, the doubt created by this issue pertains more to the actual values of the accuracy achieved than to the difference between the matrix and single-ring configurations, and as such has little bearing on the main conclusion of our study (i.e. the benefit of choosing amongst numerous contact locations). Another small but important limitation is that the algorithm that we used to select the best contacts had the benefit of simplicity but was not necessarily optimal. Indeed, the contacts were selected one at a time, rather than exploring the entire space of possible contact configurations, which would have been computationally prohibitive. If different contact selection algorithms were explored, they would most likely have some impact on the classification accuracies. Nonetheless, the simple algorithm was quite sufficient for demonstrating that the matrix configuration was beneficial and that only a small number of contacts was needed. A more significant drawback is that the results in this study are based on recordings of compound action potentials, rather than spontaneous activity. The larger amplitudes of these signals were helpful in establishing clear measurement patterns corresponding to each nerve, achieving successful classification, and evaluating with greater certainty the influence of the number and location of the contacts. The smaller signal-to-noise ratio that can be expected in certain types of natural activity (e.g. [19]) would likely result in poorer classification accuracy. Once again, however, this limitation does not invalidate our conclusions regarding the varying usefulness of different contacts and the benefits of carrying out a selection procedure.

Lastly, it is important to keep in mind that the findings described in this study deal with a reasonably simple case, specifically the identification of the active fascicle when only one fascicle is active and a training set is available. The more complex case of identifying combinations of fascicles without a training set cannot be adequately handled with such simple techniques, evoking the need for more complex methods such as source localization algorithms [32]–[35]. Nonetheless, the comparison of the matrix configuration with the single-ring one has important practical applications. By using a matrix-type cuff and performing some preliminary training recordings, it should be possible to improve the performance over current devices while still using a small number of contacts, thereby avoiding wiring and power consumption issues stemming from using large numbers of contacts (the combination of nerve cuff electrodes with multiplexer circuits to access different contacts has previously been explored in the literature [36]). Even when multiple fascicles are simultaneously active (as will likely be the case in practice), the optimal number of contacts may not be the same for all situations, but the contact selection method proposed here will still be useful by helping to identify which contacts are most useful, by virtue of having a good interface with the nerve and positions that allow them to discriminate among different fascicles.

ACKNOWLEDGMENT

The authors would like to thank Lori Dixon, Ashlie Soko and Dr. Dimitry Sayenko for their invaluable help with the experiments, as well as Dr. Martin Schuettler and Dr. Thomas Stieglitz for providing us with the cuff electrodes.

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