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A simulation study of information transmission by multi-unit microelectrode recordings

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Abstract

To analyse the information content of multi-unit signals, cases of two and three superimposed neural responses to a stimulus were simulated. The multi-unit Shannon information rates were compared with those of the constituent single-unit spike trains and also with those of corresponding labelled line signals.

The mutual information in the multi-unit response was found to depend on the degree of similarity in the attribute-specific information of the single-unit spike trains. As long as the units were encoding similar attribute-specific information, the multi-unit signal had greater information than any of the individual units. If the units' responses were confounded by different amounts, the multi-unit response could not recover the maximal single-unit information. Labelled line and pooled responses had similar mutual information when the information in the constituent units was similar. However, the normalized gain in information of a labelled line response over a pooled response increased from 27% to 84%, relative to the maximum single-unit information rate, as the difference in constituent single-unit information increased to 100%.

Information in single-unit responses is not completely lost when multiple units are superimposed. There are cases in which the union of single-unit spike trains can fully conserve single-unit information and even reduce the effect of confounding information present in the individual responses. More information is available in pairs of responses when the identities of the units are maintained. Summed responses can be used at low informational cost in redundantly encoding clusters of neurons. Higher information losses are incurred as the encoding becomes more independent.

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1. Introduction

Since the late 1990s, arrays of microelectrodes have been used to record extracellular responses from many neurons simultaneously both to study the nature of encoding in populations of neurons and to further development of the brain–machine interface (BMI). An electrode detects a superposition of responses from more than one neuron, 2–3 units on average in various cortical and subcortical regions [1, 2]. Typically, these multi-unit responses are sorted into single-unit signals before being used in computational analysis. Two main questions arise from this processing of multi-unit recordings: (1) What information is available in the multi-unit signals? (2) What information can be extracted after a spike sorting process that introduces error? Here, we focus on describing the available multi-unit information.

Different types of information can be measured. Total or formal information would describe the overall capacity of the neural response to encode at all; it quantifies how many 'code words' can be formed from the 'alphabet' of responses which neurons can output. Attribute-specific or mutual information quantifies how much of a particular stimulus parameter, e.g. magnitude, can be extracted from the output; it quantifies how many code words are formed which encode that stimulus parameter. Also, different methods of calculating information can be used. Direct methods require knowledge of the joint stimulus–response probability distributions or computation of the empirical likelihood distributions, whereas an indirect method can approximate information decoded from the neural response about a continuous time-varying stimulus without the need for probability estimates. In this study, attribute-specific information was calculated using an indirect method. The appropriateness and relevance of this approach can be seen in the framework of a BMI. The goal in a BMI is to recover as much of the stimulus information as possible in real time using some computational algorithm to decode the neural response. The information to be recovered may be about the stimulus that elicited the response or the behaviour that was to be elicited by the neural activity.

In general, we seek to analyse the multi-unit signal's ability to encode stimuli (or control resultant behaviour) and understand how this ability can be affected. In the process, we test the theoretical necessity and benefits of spike sorting. The responses of individual neurons have been observed to carry information about external stimuli. Neurons output responses that covary with the stimulus, or have characteristics that depend on the input stimulus. A summation of these responses would also have characteristic properties that depend on the stimulus. However, details would be lost in the summation which might prevent the multi-unit signals from carrying as much information as the single-unit signals. One question we would like to eventually address is how much information would be lost and whether that loss is worth the savings that would be achieved by eliminating spike sorting. The long-term goal of this and subsequent studies is to develop a model of the information available to real-time decoders of neural population activity. Here, we attempt to answer two questions: (1) How much attribute-specific information in individual spike trains is lost by pooling the responses? (2) How much of that information is recovered by maintaining the individual responses' identities in a labelled line response? To do so, we calculate Shannon information in simulated multi-unit responses and observe the effects of basic encoding properties of the spike trains that are combined.

2. Methods

Multi-unit spike trains were created by superimposing two or three simulated single-unit spike trains. The transmission rate of Shannon information about a particular stimulus, also referred to as attribute-specific information [2, 3], was analysed. An integrate-and-fire neuron generated a stochastic single-unit neural response $\rho(t)$ [4, 5]. The mean threshold was adjusted to 15 mV

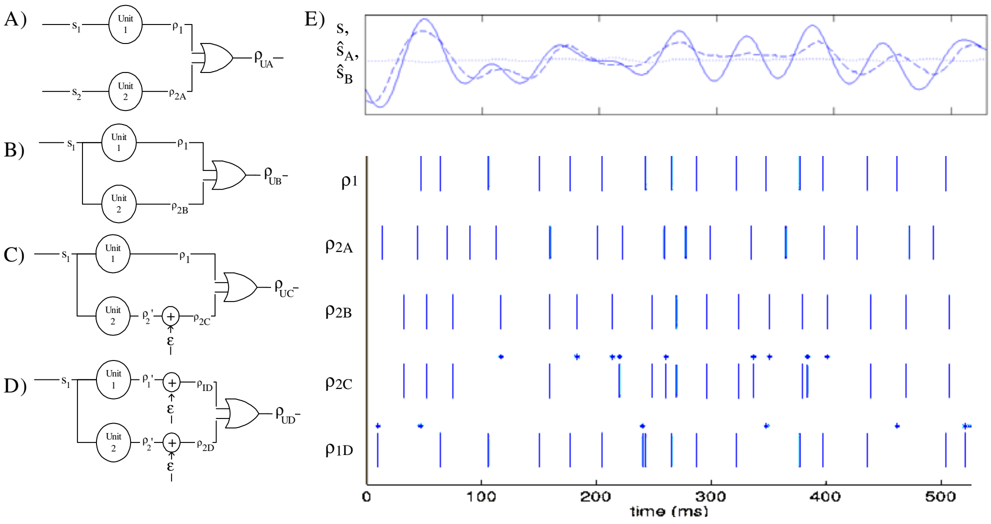


Figure 1. Generation of four types of multi-unit signal. (A) A spike train independent of the stimulus is added. (B) The added spike train is the same as ρ_1 in its encoding but uncorrelated. (C) A spike train with less correlation to the stimulus is added to ρ_1. (D) Both units in the multi-unit signal are similarly less correlated with stimulus. (E) Examples of spike trains used in each of the four cases. Asterisks indicate spikes added or removed in cases C and D to decrease correlation between the two combined units. The upper panel shows the original stimulus s, and reconstructions from ρ_{2A} (dotted) and ρ_{2B} (dashed).

to produce an average firing rate of 32 spikes s^{-1}. Each time the neuron fired, the threshold voltage was set to a new value chosen from a normal distribution with a standard deviation equal to 5% of the mean threshold.

A 1000 sample s^{-1} Gaussian signal was band-limited with a 12-pole low-pass filter with a 20 Hz cut-off. This signal simulated the stimulus $s(t)$ into the neuron. Each trial was defined by the creation of a unique 100 s duration stimulus signal. Ten trials were performed, with each trial consisting of multiple presentations of the stimulus. Every presentation of the stimulus generated a unique spike train. For each response generated, the optimal linear estimate of the stimulus $\hat{s}(t)$ was computed by applying Wiener–Hopf filtering to $\rho(t)$ [6]. From the error between s and $\hat{s}$, the signal-to-noise ratio (SNR) was computed using a Bartlett-windowed periodogram estimate of the signal and input-referred noise power spectra, $P_s(f)$ and $P_{n_{\mathrm{eff}}}(f)$, respectively. The gain G for calculating input-referred noise, $n_{\mathrm{eff}} = \hat{s}/G - s$, was found using a linear regression between power spectra of s and $\hat{s}$, as in [7]. The mutual information rate between s and $\hat{s}$, $\dot{I}(s, \hat{s})$, was then calculated according to [4, 7]:

$$\dot{I}(s, \hat{s}) = \frac{1}{2} \int_0^\infty \log 2(1 + \mathrm{SNR}(f))\, \mathrm{d}f \leqslant \dot{I}(s, \rho), \qquad (1)$$

where $\mathrm{SNR}(f) = P_s(f)/P_{n_{\mathrm{eff}}}(f)$. This serves as the lower bound on $\dot{I}(s, \rho)$, the rate of mutual information between s and ρ.

Four different cases (A–D) were considered in which the activities of two and three neurons are detected on the same electrode. The union of the individual units' responses was represented by the multi-unit signal $\rho_{U\theta}$, where θ = A, B, C, or D indicates to which of the four cases the multi-unit signal belongs. Each of the individual spike trains was a binary signal, making $\rho_{U\theta}$ a binary signal which masked the overlap of spikes occurring within the same millisecond. The four combinations are shown schematically in figures 1(A)–(D) and described as follows:

(A) *Unit 2 independent of the stimulus.* Two spike trains responding to different stimuli were generated, ρ_1 responding to s_1 and ρ_2 responding to an independent stimulus s_2 (figure 1(A)). ρ_1 and ρ_2 had mean spike rates within 5% of each other. The union ρ_{UA} simulated a multi-unit recording of two unrelated, uncorrelated neurons. For each trial, a unique s_2 was presented to unit 2 ten times to create ten different unit 2 responses.

(B) *Unit 2 completely dependent on the stimulus.* ρ_2 was generated from a second presentation of s_1; i.e., ρ_2 was a different observation of the same stochastic point process as unit 1 encoding s_1. The output ρ_2 was combined with ρ_1 to produce multi-unit signal ρ_{UB} (figure 1(B)). As in case A, ten different unit 2 responses were generated for each trial.

(C) *Unit 2 partially dependent on the stimulus.* To look at the case intermediate between complete dependence and independence of ρ_2 on s_1, ρ_1 was combined with $\rho_{2\mathrm{C}}$, a corrupted version of the ρ_2 in case B; thus, $\rho_{2\mathrm{C}}$ responds to s_1 but carries less information about the stimulus than $\rho_{2\mathrm{B}}$. We have observed that random addition and deletion of spikes will decrease the mutual dependence of the spike train on the stimulus [5]; therefore, the spike train $\rho_{2\mathrm{C}}$ was created by adding random spikes to and deleting original spikes from ρ_2 (figure 1(C)) while maintaining a constant average firing rate. Error was defined as the ratio of the number of random spike additions and deletions to the number of stimulus-generated spikes. Error was added until the attribute-specific information $\dot{I}(s_1, \rho_{2\mathrm{C}})$ reached a minimum beyond which adding random error did not decrease the information; we later define this point as the baseline level.

(D) *Both neurons partially dependent on the stimulus.* The final case looked at a multi-unit signal comprised of two spike trains both responding to s_1 but decreasing similarly in their dependence on s_1 (figure 1(D)).

Signal ρ_1 is present in ρ_{UA}, ρ_{UB}, and ρ_{UC} but is corrupted to create $\rho_{1\mathrm{D}}$ for case D. This signal ρ_1 is the ideal single-unit spike train with maximal information content about stimulus s_1. The relation of unit 2 to the stimulus s_1 and to unit 1 varies in each of the four cases as described. One time segment of the spike trains from each case is displayed in figure 1(E). Corresponding three-unit cases were simulated by adding a third unit which behaved like unit 2. We considered cluster sizes of two and three only because the number of neurons discriminated on the same electrode is most often two or three [1, 2].

Information about s_1 in ρ_2 and $\rho_{\mathrm{U}\theta}$, was calculated relative to information in ρ_1. The ratio of $\dot{I}(s_1, \rho_2)$ to $\dot{I}(s_1, \rho_1)$, is denoted by $\dot{I}_2/\dot{I}_1$. The relative change in information in $\rho_{\mathrm{U}\theta}$ compared to ρ_σ was calculated as

$$\Delta\dot{I}_{\mathrm{r}} = \frac{\dot{I}(s_1, \rho_{\mathrm{U}\theta}) - \dot{I}(s_1, \rho_\sigma)}{\dot{I}(s_1, \rho_\sigma)}, \tag{2}$$

where σ here indicates the single-unit response to which the multi-unit response is being compared (1, 2(A), 2(B), 2(C), 1(D), or 2(D)).

Although the stimulus reconstruction method has been accepted as a method to study information in neural spike trains [4, 7, 8], one caveat regarding the information estimate derived from a Gaussian channel assumption is that there is strictly a non-zero dependence of $\hat{s}$ on s, unless $s = 0$ or the gain G of the system from the input s to the output $\hat{s}$ equals 0. When ρ is independent of s, mutual information should equal 0 as the length of the signals observed approaches infinity; hence, the true gain must be 0. The measured gain was estimated to be very small under this condition but not exactly equal to 0, due to random correlations between s and ρ which results in a non-zero Wiener–Hopf filter. The consequence of $G \neq 0$ is an erroneously finite $P_{n_{\mathrm{eff}}}(f)$, resulting in the calculated SNR and information being greater than

0 even in the case of unrelated s and $\hat{s}$. In order to be able to speak of information on a more intuitive scale, information rates were normalized to range from 0 at random guessing to 100% at the maximal single-unit information rate, $\dot{I}(s_1, \rho_1)$. For this purpose, the baseline level of information was defined to account for random correlations between finite length signals and the non-negative nature of the SNR. The baseline was defined as the average information rate for which the coding fraction = 0. Coding fraction γ is a measure of the variability in the stimulus which is encoded in the variability of the output and should equal 0 for a random-guess estimate; it is the fraction of the standard deviation of the stimulus which is not accounted for by the mean square error of the stimulus estimate:

$$\gamma = 1 - \frac{\frac{1}{N}\sqrt{\sum(\hat{s} - s^2)}}{\sigma_s}. \tag{3}$$

The subscript bl used hereafter denotes that information rates were adjusted by the baseline levels of information before calculations were carried out. Ten trials were performed, with each trial involving the generation of a unique signal for s_1 and/or s_2. Similar calculations were performed for all four cases.

The amount of attribute-specific information in a pair of responses was then calculated in a labelled line approach. The stimulus was reconstructed from a multivariate optimal linear decoder operating on labelled line two-unit responses as opposed to one pooled multi-unit response; hence, one filter was constructed for the pair, but each unit was considered a separate entity. The optimal filter for the two-unit cluster still satisfied the Wiener–Hopf equations for a one-dimensional response [6]:

$$C^{\bar{\rho}s} = h \cdot C^{\overline{\rho\rho}}, \tag{4a}$$
$$C^{\bar{\rho}s} = \bar{\rho}^{\mathrm{T}} s, \tag{4b}$$
$$C^{\overline{\rho\rho}} = \bar{\rho}^{\mathrm{T}} \bar{\rho}, \tag{4c}$$

where C is the specified covariance matrix and $\bar{\rho}$ is the Toeplitz response matrix comprised of one row for each time lag in the filter. Thus, the jth row of $\bar{\rho}$ holds the response $\rho(t)$, for $t = j, j+1, \ldots, j+L$ for a filter with L time lags. To compute a filter for a labelled line response instead of the pooled multi-unit response, the response matrix $\bar{\rho}$ was expanded for two units by concatenating the response matrix of each unit. The filter and the estimate of s were created following the methods detailed in [9] with the exception that the filter used here had negative as well as positive time lags. The mutual information was then calculated from the labelled line estimate using equation (1) and compared to the information in pooled responses.

3. Results

We studied the effects of non-discriminately using clusters of two and three units, first comparing information in multi-unit signals to single-unit signals, then comparing multi-unit signals to labelled line signals. Results from the two-unit scenarios are described first, followed by an extension of the two-unit cases to three-unit cases.

3.1. Independent unit

A spike train was derived directly from the stimulus s_1, with $\dot{I}(s_1, \rho_1) = 28.6$ bits s^{-1}. When ρ_2 was generated in response to a stimulus independent of s_1, $\dot{I}_{\mathrm{bl}}(s_1, \rho_{2\mathrm{A}}) = 0$ by definition. When unit 1's response to stimulus s_1 was contaminated by a response ρ_2 which was unrelated to s_1, the multi-unit response ρ_{UA} transmitted 28% of the $\dot{I}_{\mathrm{bl}}(s_1, \rho_1)$.

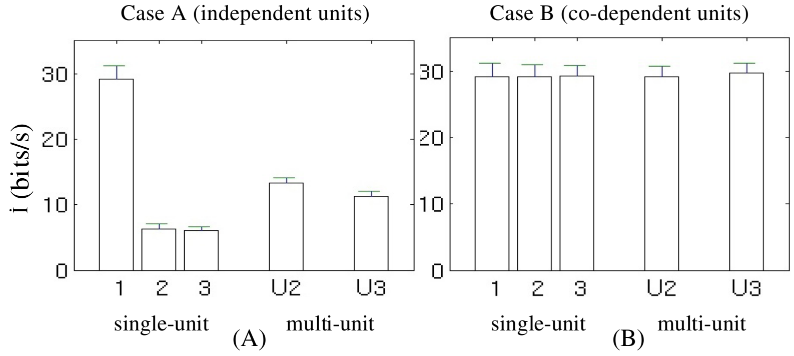


Figure 2. The average information rate and standard deviation of the original single-unit spike train (1) and of the added spike trains (2, 3) are shown alongside those of the multi-unit signals comprised of two (U2) and three (U3) responses. (A) Case A—units 2 and 3 are independent of s, and therefore have low mutual information. Contaminating ρ_1 with the other spike trains that carry information independent of s_1 decreases the mutual information about s_1. (B) Case B—when the spike train is combined with spike trains carrying insignificantly different information, the multi-unit spike train also maintains the same information rates. The average firing rate of all single units is 32 ± 0.1 spikes s^{-1}, that of two-unit signals is 64 ± 0.2 spikes s^{-1}, and that of three-unit signals is 95 ± 0.4.

Figure 2(A) shows the mean information rates and standard deviations across all trials and stimulus presentations. Results showed non-significant differences among trials at a 5% significance level (one-way ANOVA). Adding the second independent neuron decreased the mean information rate by 72%; the third independent neuron decreased the information by another 7%.

3.2. Co-dependent units

Because of the stochastic nature of neurons, different neurons may not respond identically even if they are responding to the same stimulus with the same encoding scheme. Likewise, the same stimulus presented to the integrate-and-fire neuron used here will not yield an identical response on every stimulus presentation. For scenario B, the outputs of separate stimulus presentations simulated the outputs of neurons distinct from ρ_1 but co-dependent on s_1 with ρ_1.

Despite the variability in spike timing in case B (figure 1(E)), the information rates of ρ_1 and ρ_2, $\dot{I}(s_1, \rho_1)$ and $\dot{I}(s_1, \rho_2)$, showed non-significant differences (paired t-test, $p = 0.25$). It was found that combining these signals also caused a non-significant difference in information rate; the average $\Delta\dot{I}_\mathrm{r}$ over the ten trials was less than a 1% gain ($p = 0.80$, 95% confidence interval: $-0.015 < \mu_{\Delta\dot{I}} < 0.031$).

Figure 2(B) shows the mean and standard deviation of the information rates of the multi-unit and constituent single-unit signals. The two-unit response carried the same information as the mean constituent single-unit response (mean per cent change $<1\%$, $p = 0.80$). The information rate of the three-unit response did increase significantly but only by 2.1% ($p = 0.01$).

3.3. Varying dependence of one unit (sub-optimally encoded neuron)

Random spike error was added to ρ_2 to decrease the mutual information between ρ_2 and s_1. The open circles in figure 3 show how much of the information in ρ_1 is retained when combined with ρ_2 as it decreases in its dependence on s_1. Information was normalized to $\dot{I}(s_1, \rho_1)$ because ρ_1

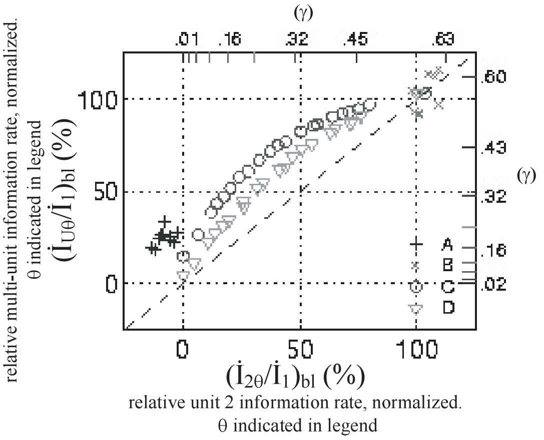


Figure 3. Comparison of relative information rates of multi-unit signals to that of corresponding single-unit signals ρ_2 for each case θ = A, B, C, or D, as indicated in the legend. Normalization rate $\dot{I}(s_1, \rho_1) = 29$ bits s^{-1}. Corresponding coding fractions of ρ_U are given for reference on the right axis, and the coding fraction of ρ_2 is shown on the upper axis.

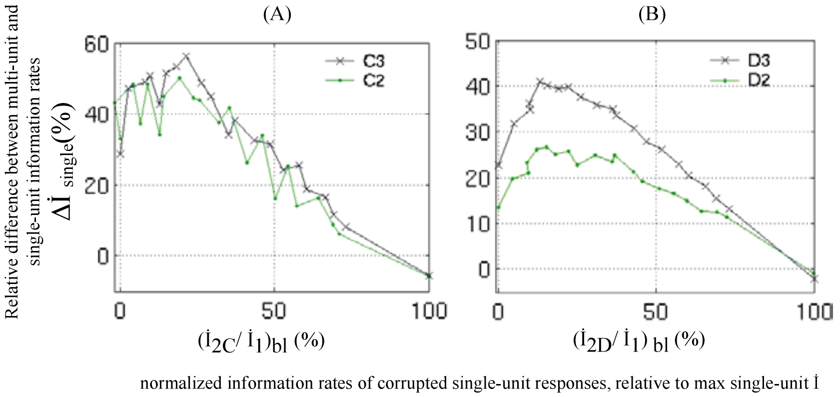


Figure 4. The effect of superimposing two and three neural responses on the information content as a function of average normalized information rate of the corrupted single-unit responses ($(\dot{I}_2/\dot{I}_1)_{\text{bl}}$). (A) Case C. The positive per cent change in information rate with respect to $(\dot{I}_2/\dot{I}_1)_{\text{bl}}$ indicates an increase in information over the corrupted single-unit responses as two and three single-unit responses are combined. This improvement increases as the single-unit responses become more corrupted until more improvement cannot be made because of the extent of corruption. Adding the third unit decreases the variability in information. (B) Case D. Information improves over the average single-unit response as more units are combined.

had maximal information. For each case, the normalized multi-unit information is shown as unit 2's information changed. The dashed line indicates the values that would be obtained if the multi-unit signal, in this case ρ_{UC}, carried as much information as unit 2's response. The information in ρ_{UC} remained above this line as it decreased nonlinearly from 100% to 20% with decreasing $\dot{I}_{2\text{C}}$.

Figure 4(A) (dotted curve) also shows the increase in information in the two-unit signal over the corrupted single-unit spike train. When the third unit was added (figure 4(A), crosses), the attribute-specific information did not change significantly even though the number of corrupting spikes had increased.

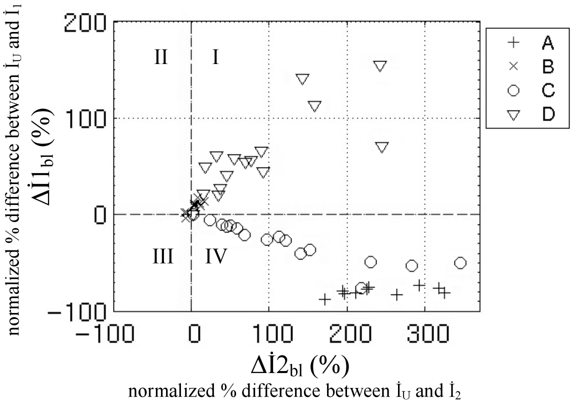


Figure 5. The per cent change in information rate between the multi-unit signal and each of the constituent single-unit signals. Data points are not shown for information gain greater than 10. Such large increases occur as $\dot{I}_{bl}(s_1, \rho_{2C})$, $\dot{I}_{bl}(s_1, \rho_{1D})$, and $\dot{I}_{bl}(s_1, \rho_{2D})$ approach 0.

3.4. Varying dependence of both units

In this scenario, neither neuron was completely dependent on s_1, and the mean difference between $\dot{I}(s_1, \rho_{1D})$ and $\dot{I}(s_1, \rho_{2D})$ was 0.30 bits s^{-1} ($p = 0.30$, two-tailed paired t-test). The relationship between $\dot{I}(s_1, \rho_{UD})$ and $\dot{I}(s_1, \rho_{2D})$ is shown in figure 3 (triangle markers). The pattern of information decay was similar to that of case C, but as expected, ρ_{UD} had less information than ρ_{UC}, in which only one of the two neurons was sub-optimal. As in case B, the information in all constituent signals of ρ_{UD} was insignificantly different (two-tailed paired t-test, $p = 0.30$). When two spike trains had similar information ($\dot{I}(s_1, \rho_{1D}) \approx \dot{I}(s_1, \rho_{2D}) = \dot{I}_2$), the dual-unit signal was found to have at least as much information as the constituent single-unit signals, i.e., $\dot{I}(s_1, \rho_U) \geqslant \dot{I}_2$. $\dot{I}(s_1, \rho_{UD})$ increased by as much as 7.3 bits s^{-1} over $\dot{I}_2$, or equivalently, the change in mutual information was 41% of $\dot{I}_2$ and 36% of $\dot{I}(s_1, \rho_1)_{bl}$ (95% CI: $\dot{I}_{UD} - \dot{I}_2 > 3.0$ bits s^{-1}). The attribute-specific information increased by another 15% when the third unit was added.

When the single-unit spike trains had similar rates of information about the stimulus, the combined signal contained more information than either of the single-unit spike trains alone. Figure 4(B) shows that as the average single-unit information $(\dot{I}_2/\dot{I}_1)_{bl}$ decreased from 100% to about 20%, the two-unit information rate increased by more than 25%. As $(\dot{I}_2/\dot{I}_1)_{bl}$ decreased further, the improvement in ρ_{UD}'s information rate over the single-unit information was reduced. The information rates improved to a greater degree in the three-unit case, reaching a maximum increase of 41% when $(\dot{I}_2/\dot{I}_1)_{bl}$ was 20%.

Several outcomes were possible in the relation of the multi-unit information to the single-unit information, as illustrated in figure 5. Figure 5 plots the per cent difference between information in ρ_U and unit 1's response against the per cent difference between information in ρ_U and unit 2's response. This shows the change in information due to combining the two single-unit signals from the perspective of each of the individual units. The horizontal dashed line indicates where the multi-unit signal carries as much information as unit 1 and the vertical line where ρ_U carries as much as unit 2.

Quadrant IV holds the instances in which the multi-unit signal has greater information than unit 2 but less than unit 1. This was the situation for ρ_{UC} and ρ_{UA}. In case A, the multi-unit signal obviously carries less information than the ideal spike train. Combining ρ_2 with ρ_1 can be viewed as adding on average 97% error to ρ_1; yet, ρ_{UA} retains 20% of the information (mean $\Delta \dot{I}1_{\mathrm{A,bl}} = -79.7\%$). Furthermore, it has a 200%–300% increase in $\dot{I}_{\mathrm{bl}}$ over unit 2. Adding in a spike train whether or not it encoded s_1 might have been expected to completely degrade information because of the loss of uniqueness of each unit's response. In case A, even though the spike trains were completely uncorrelated and independent, the multi-unit signal did not lose all the information. It lost 80% of the information with respect to ρ_1 but gained information with respect to the independent neuron and remained above baseline levels. The amount of information ρ_{UA} retained, 28% of $\dot{I}_{\mathrm{bl}}(s_1, \rho_{\mathrm{U1}})$, is as much information as a spike-sorted response carries when it has 15% sorting error [5].

The cluster of crosses at the origin for case B indicates negligible change in information with respect to either single unit, which both have the maximal attribute-specific information. No information was lost from any of the individual spike trains although they were uncorrelated and their spikes were unlabelled, or unidentified, in the multi-unit signal. The combined signal in case D transmits more information than either of the individual sub-optimally related neurons, ρ_{1D} and ρ_{2D}, as shown by the location of ρ_{UD}'s markers in the first quadrant of figure 5. In case C, once a response was corrupted by confounding information, 100% of the attribute-specific information $\dot{I}(s_1, \rho_1)$ could not be retrieved in a pooled response, but more of the information in ρ_{2C} could be retrieved by reinforcing it with another response transmitting $\dot{I}(s_1, \rho_1)$.

When comparing the three-unit information rates $\dot{I}_{\mathrm{U}\theta,3}$ to the single-unit information rates of ρ_1 and ρ_3, the results are analogous to the two-unit case. Although the details differ, the ordinal relationship between the three-unit and single-unit information rates are the same as in the two-unit cases. Thus, the three-unit cases yield a plot similar to figure 5.

Summary of multi-unit versus single-unit results. In multi-unit recordings, the goal is to retain as much of the relevant information as possible in the original spike trains. If the spike output from the neurons are reproduced at the output of the acquisition system, the information transmitted to the computational decoders remains unchanged. Thus, for the purposes of multi-unit recordings, it is sufficient to keep the identity of the spike trains separate, assuming the use of an appropriate decoder capable of extracting the information available at its input. The question remains of whether this separation is necessary and whether information is lost when neurons' responses are used in the combined form.

Thus far, our model of information decoded from pairs and triplets of neurons would state the following:

- When information about a stimulus attribute is encoded in common in each of the individual neurons, all the information is retained in the combined response.
- Information independent of the stimulus attribute of interest will corrupt the information encoding that stimulus attribute. In such cases, less than 100% of the maximal single-unit information is retrieved in the multi-unit signal.
- However, corruption of this sort is reduced in the multi-unit signal.

Now, we consider what information is available in a labelled line response of two units. Instead of taking the union of the two unit responses, the optimal filter used maintained the separate identity of the units.

Comparing labelled line and pooled information. Although a pooled multi-unit response can provide more attribute-specific information than either of the two units alone, the results in this section show that even greater information is available in two perfectly discriminated signals considered jointly in a labelled line response. Figure 6 shows reconstructions of the

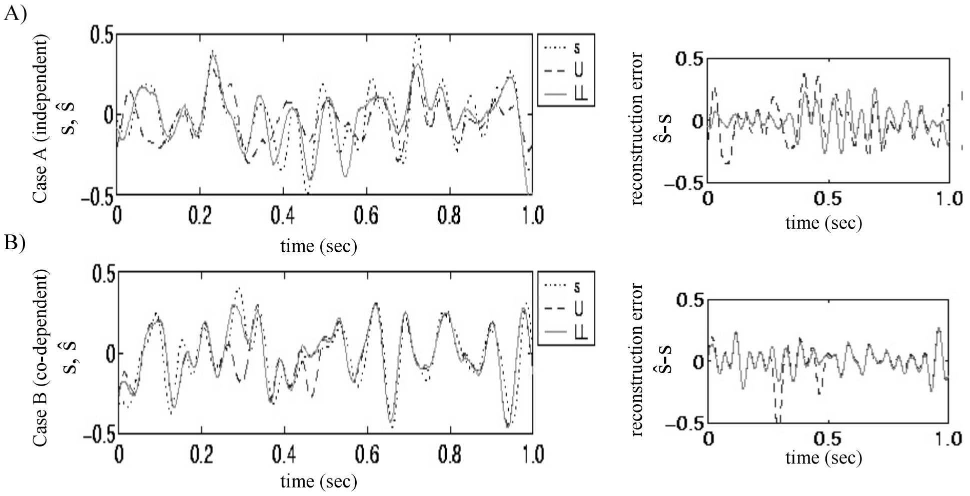
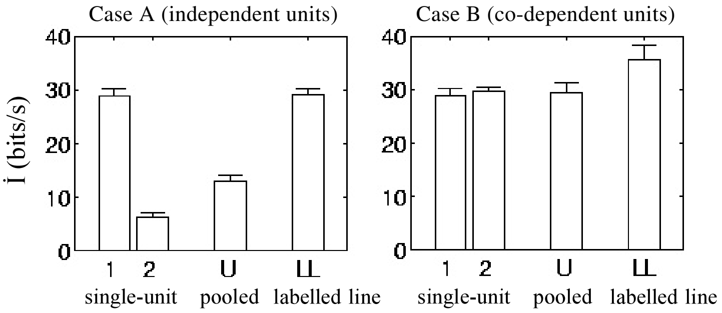


Figure 6. Reconstruction of the stimulus from two unit responses, using pooled and labelled line approaches, when units are independent (top) and when they are co-dependent (bottom). s (dotted): the original stimulus. U (dashed): $\hat{s}_{\mathrm{U}}$ reconstructed from the union of the two responses. LL (solid): $\hat{s}_{\mathrm{LL}}$ labelled line reconstruction of s.

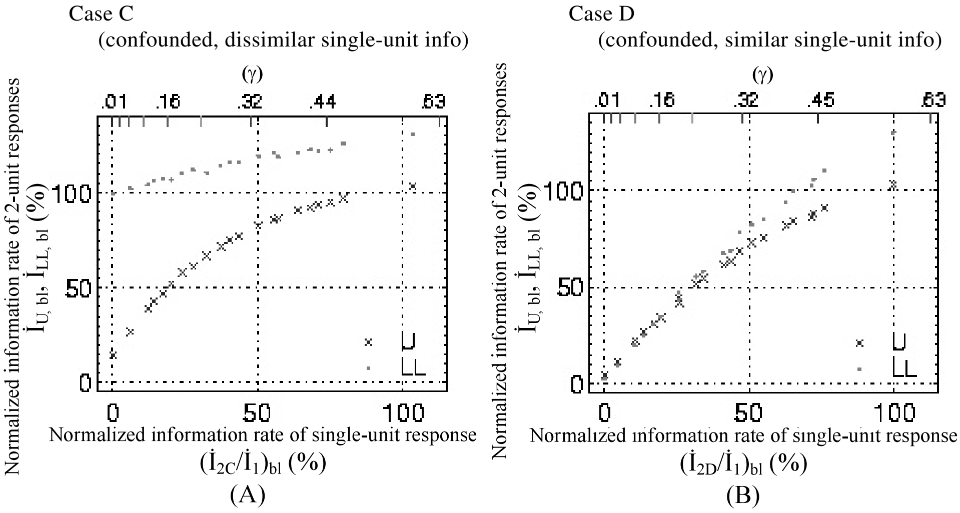


(A) (B)

Figure 7. Average information rates and standard deviations of the two single-unit spike trains ρ_1 (1) and ρ_2 (2) are shown alongside those of the pooled signals (U) and labelled line (LL) responses. (A) Case A—unit 2 is independent of s. ρ_{LL} is able to maintain all the information in unit 1. Pooling the responses causes significant loss of that information. (B) Case B—when the spike trains combined carry similar information, the pooled response can maintain that information. A labelled line response can extract even more information about s.

stimulus from the union of two unit responses ($\hat{s}_{\mathrm{U}}$) and from the labelled line response ($\hat{s}_{\mathrm{LL}}$). The labelled line estimate tracked the stimulus (s) much better than the pooled estimate when the units were independent (case A, figure 6(A)) and had less reconstruction error. When the units were co-dependent (case B), the two estimates tracked the stimulus with similar accuracy most of the time, but the pooled estimate occasionally had much larger error (figure 6(B)). In case A, the mean information in $\hat{s}_{\mathrm{LL}}$ was greater than that in $\hat{s}_{\mathrm{U}}$ by a factor of 2.2 (figure 7(A)). In case B, the information in $\hat{s}_{\mathrm{LL}}$ was a factor of 1.2 times that in $\hat{s}_{\mathrm{U}}$ (figure 7(B)).

Likewise, for case C, in which the two units had dissimilar information, the labelled line response transmitted significantly more information than the pooled response (figure 8(A)). The labelled line and pooled responses had much closer information rates in case D, for which



(A) (B)

Figure 8. Normalized information rates of pooled responses ($\dot{I}_{\mathrm{U,bl}}$) relative to maximum single-unit information and labelled line ($\dot{I}_{\mathrm{LL,bl}}$) responses versus normalized information rate of constituent single-unit responses. (A) Information of the pooled and labelled line responses in case C as unit 2 is increasingly corrupted. (B) Information of the two-unit responses in case D as units 1 and 2 are increasingly corrupted. The corresponding coding fraction of ρ_2 is shown on the upper axis.

the two constituent units also transmitted similar information (figure 8(B)). The labelled line information in case C decreased with relative linearity as the information in $\rho_{2\mathrm{C}}$ decreased; when the responses were pooled, the information decreased more rapidly. The pooled response could not achieve much more than 100% of the information in a single-unit response, whereas the labelled line response was able to transmit as much as 30% more information than the single-unit response ($\dot{I}(s_1, \rho_{\mathrm{U1}})$) and transmitted 100% of the relative information when unit 2's information $(\dot{I}_{2\mathrm{C}}/\dot{I}_1)_{\mathrm{bl}}$ was 0. In case D, $\dot{I}_{\mathrm{U}}$ and $\dot{I}_{\mathrm{LL}}$ increased together as the average single-unit information increased to 50%; beyond 50%, $\dot{I}_{\mathrm{U}}$ increased with a lower slope.

This comparison of $\dot{I}_{\mathrm{U}}$ to $\dot{I}_{\mathrm{LL}}$ as the single-unit information increases demonstrates that as expected, using both neurons as separate entities without discrimination error provides at least as much information as is obtainable from the pooled multi-unit response. However, the amount by which $\dot{I}_{\mathrm{LL}}$ exceeds $\dot{I}_{\mathrm{U}}$ varies from case C to case D, and neither $\dot{I}_{\mathrm{U}}$ nor $\dot{I}_{\mathrm{LL}}$ increase in the same manner in case C as in case D. Thus, we considered the factor that distinguishes case C from case D—the difference in the information rates of the constituent single-unit signals.

The differences between $\dot{I}(s_1, \rho_{1\mathrm{D}})$ and $\dot{I}(s_1, \rho_{2\mathrm{D}})$ were randomly distributed about 0. The difference $\dot{I}_{\mathrm{LLD}} - \dot{I}_{\mathrm{UD}}$ did not depend on these differences in information between the constituent units (figure 9) but rather on the average constituent single-unit information. From figure 8(B), it can be seen that $\dot{I}_{\mathrm{LLD}} - \dot{I}_{\mathrm{UD}}$ increased as $\dot{I}_2/\dot{I}_1$ increased. In contrast, the difference between $\dot{I}(s_1, \rho_{1\mathrm{C}})$ and $\dot{I}(s_1, \rho_{2\mathrm{C}})$ was systematically increased. As this difference increased, the difference between labelled line and pooled multi-unit signals increased monotonically in an exponential fashion (figure 9).

Information in a labelled line response ($\dot{I}(s_1, \rho_{\mathrm{LL}})$) is in general greater than that in a pooled response ($\dot{I}(s_1, \rho_{\mathrm{U}})$). However, in our simulations, the information gained by using discriminated unit responses varied for the different cases. The gain in information due to using a labelled line instead of a pooled response was greater overall for cases A and C (27%–84% increase) than in cases B and D (−2.6% to 27%). Figure 8 shows

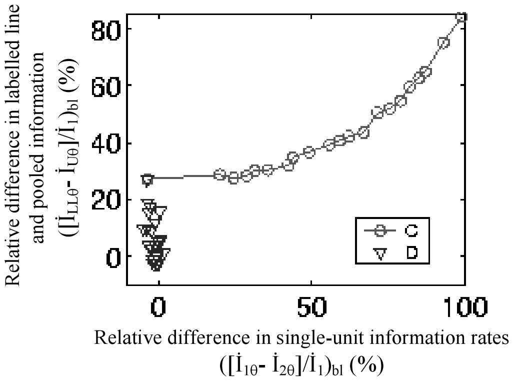


Figure 9. The difference in information rates of the labelled line and pooled responses as a function of the relative difference between unit 2 and unit 1's information rates. Case C (circles)—as differences between unit 1 and 2 information increase gradually, differences between two-unit response information rates increase exponentially. Case D (triangles)—differences between unit 1 and 2 information are clustered around 0. Differences in the two-unit response information vary from 0 to 20%.

that the reason the labelled line extracts even more information in case C than D is not related to the total amount of information available in the sum of the individual units' information. The gain $\dot{I}(s_1, \rho_{\mathrm{LL}}) - \dot{I}(s_1, \rho_{\mathrm{U}})$ increased as the sum of single-unit information in case D, $\dot{I}(s_1, \rho_{1\mathrm{D}}) + \dot{I}(s_1, \rho_{2\mathrm{D}})$, increased, but actually decreased as the sum in case C, $\dot{I}(s_1, \rho_1) + \dot{I}(s_1, \rho_{2\mathrm{C}})$, increased.

Figure 9 indicates that the labelled line gain over pooled responses is due to dissimilarity between the two constituent units. The difference in gain between cases C and D can be explained by the units having disparate information in case C and similar information in case D. The variability between spike trains in case D was due to random noise; thus, differences between units 2 and 1 did not systematically encode information about s. However, when the variability was due to systematic differences in information between the units, keeping the units separate allowed more attribute-specific information to be extracted from the cluster, and summing the responses was no longer comparable to the labelled line approach.

We have seen that more attribute-specific information can be extracted by pooling the responses than using any one of the responses alone. However, attribute-specific information in an individual unit's spike train can be degraded in a multi-unit signal that pools its response with a unit that carries disparate information. A labelled line response is more robust than a pooled response against such corruption. In general, information about the stimulus (or target signal) in the population as a whole will be lost by pooling the responses. If the differences in the responses are due to non-random differences in $\dot{I}(s_1, \rho_\sigma)$, those differences can actually encode information about s, and the identities of the spikes would need to be maintained to avoid losing significant amounts of information. The amount of information that can be retained by pooling responses will depend on the degree of similarity in information of the constituent single-unit responses.

4. Discussion

Multi-neuron recordings enable efforts to decipher the language by which neural ensembles process information and control behaviour. Computational algorithms are being developed to interpret these population signals, with the long-term goal of restoring motor control to movement-impaired patients. Since the dawn of multi-unit recordings, spike sorting was deemed necessary because the original goal of such recordings was to observe the individual waveforms of single neurons and the interactions between them [10, 11]. Despite the different goals of current high-density recording applications, the purported requirements of the acquisition and processing system have remained unchanged. One of our long-term aims is to test the assumption that neglecting to spike sort multi-unit signals is detrimental because the information in the individual spike trains would be confounded. Being able to bypass spike sorting in BMI applications would allow reductions in both size and complexity of high-demand signal conditioning, digitizing, and telemetry hardware. Instead of acquiring and transmitting high-resolution streams of data, all that would be needed is a simple detector and transmission of a bit when an action potential occurs. Therefore, it is worth questioning the necessity of spike sorting and whether the loss of information from labelled line to pooled responses outweighs the cost of spike sorting.

We started by asking the more fundamental question of how much of the information in each of the constituent single-unit signals is retrievable in a multi-unit signal. We have shown that the information in each unit is not necessarily compromised in the multi-unit signal. Being able to at least maintain the information content in each neuron provides motivation to consider using multi-unit signals without the cost of sorting. It should be noted that $\dot{I}(s_1, \rho_1)$ is the information transmitted by an ideal single-unit spike train, with no spike sorting error, and $\dot{I}(s_1, \rho_U)$ is the information transmitted by a multi-unit spike train in a system not optimized for multi-unit spike trains. In practice, the discriminated spike trains will contain error. From the results obtained in [5], it can be expected that a spike train with a reasonable 15% discrimination error [11, 12] will have as much information as an accurate non-discriminated two-unit signal with a completely independent neuron corrupting it (case A). Lower discrimination errors have been reported for complex, supervised spike sorting algorithms; error can be expected to be higher in a fully unsupervised spike sorter. The results presented here combined with the results in [5] indicate the possibility that multi-unit electrograms provide as much, if not more, information as a *single-unit* waveform with sorting error.

Whereas summing two signals which are variable in amplitude due to random noise increases the SNR by $\sqrt{2}$, the effect of summing spikes which are variable in time is unknown. It may be the case that if the signal about which information was measured had been the mean value of s over longer time intervals and the neural response was defined by the total number of spikes in the interval, as in a Poisson signal, the SNR would increase by $\sqrt{2}$. However, the signal of interest in the present study is a continuous time-varying signal, and the spike train is a temporal sequence of binary words. It should be noted that the stimulus estimate, from which information is calculated, results from convolving the spike train with a filter response by which temporal information is incorporated into the information measure. Including higher-order terms of the Volterra expansion [13] in the filter response may reveal the presence of information in higher-order interactions between spikes within a spike train; in the present study, only a first-order filter response was used, as in [4, 7, 8].

The results obtained for case B show that the union of spike responses, in which spikes from one are correlated with spikes from the other (ρ_1 and ρ_{2B} in figure 1(E)), has the same information as one of the responses alone. When two units are similar in mutual information but generate spikes unrelated to s (case D), the information content in the multi-unit signal of ρ_1 and ρ_2 combined is greater than the information in either of the single-unit responses alone. The effects of variation in amplitude are reduced by summing signals which have the same underlying ‘signal amplitude’; it appears that the analogy for a temporal spike train is that the effects of variation in spike times *unrelated* to the underlying ‘signal spikes’ are reduced by combining spike times (cases C and D).

In the case of two units having dissimilar information (case C), if ρ_{2C} had been identical to ρ_1, then ρ_{UC} would exactly equal ρ_{2C}, and the multi-unit information would exactly follow the dashed line in figure 3. However, when spike trains were combined whose spike timing showed slight variation, the information rate increased. It appears that when the individual units encode information about s_1 but their responses are confounded by extraneous information, the spikes actually resulting from s_1 in the individual responses can reinforce one another. This synergism should reduce the conditional entropy, thus increasing the mutual information. Thus, pooling the responses seems to reduce the effects of confounding information when summing causes reinforcement of stimulus-related spikes in a redundant code. The pooled information of units with similar information (case D) is also comparable to information in discriminated responses considered jointly.

Two studies have already compared information between pooled responses to labelled line responses *in vivo*, and can be interpreted in our theoretical framework. Although they calculate information by a different method, their results can still be interpreted in line with our simulation study. Reich *et al* [2] compared information in pooled and labelled line responses in primate primary visual cortex (V1). Their results indicate that as long as the neuron identity is not lost, the information in each of the neurons can be preserved. However, we must exercise caution when attempting to apply their results to the question of whether spikes detected from the same electrode need to be discriminated in order to preserve sufficient information for a BMI. Reich *et al* show that *independent* information cannot always be retained when a population sum is used. One aspect that our simulations did not seem to model is that information in the population activity can be as high as the sum of the individual information rates. The information in the neuron cluster would reach this maximum only if the conditional probability distributions were independent; and the neuron cluster could encode more than any one of the neurons only if the neurons were not exclusively mutually dependent [3]. In other words, the summed population activity only loses information that a discriminated population response would not if the neurons are either encoding independent attributes of the same stimulus or are encoding independent stimuli. In this study, we look only at the problem more relevant to a BMI of what the population response encodes about one stimulus attribute of interest (represented by the amplitude of s_1), not multiple stimulus attributes of the same stimulus. Thus, the Reich *et al* results could indicate that when neurons are encoding *independent* information, information is lost by summing the responses, as in case A of our simulations. However, it is likely that the neurons detected on the same electrode respond to similar stimulus attributes [2, 14] and have correlated tuning curves [15].

The Panzeri *et al* [14] results can also be generalized in the light of our conclusions. Units responding to stimulation of whiskers with similar responses could be pooled without loss of information while the units that responded most differently lost the most information when pooled. Furthermore, the more distant the units were physically, the more their responses differed and the more the information each carried about stimulus location differed. Nearby neurons converged to case B, in which the units carry similar information and thus have as much information when pooled as when kept separate, while distant neurons converged to case A. Such *in vivo* results, together with the results from cases B and D, imply that two- or three-neuron multi-unit signals may provide all the precision needed for computational decoding.

For the purposes of a BMI that restores motor capabilities, we would still need to know how these results from the primate V1 [2] and rat barrel cortex [14] would compare to M1 responses in primates. We still need empirical findings on whether differences between information in each pooled response and its labelled line counterpart equate to changes in qualitative performance of a BMI. Perhaps also, *populations* of pooled signals fare better against labelled line populations. Differences among multi-unit signals may exist within a population that provide information in much the same way as differences between single-unit signals provide information in a labelled line response. This would allow recovery of some of the information compromised by pooling single-unit responses.

We have found that information is preserved in multi-unit signals in cases that we believe to be more probably based on the literature. We have also found in a previous study that information content has a low tolerance for spike sorting error. These findings argue for further examination of the encoding capacity of discriminated versus non-discriminated extracellular neural responses, so an efficient multi-neuron recording and processing system utilizing multi-unit signals could be made possible.

5. Conclusion

In this study, we observed the effects of combining pairs and triplets of single-unit spike trains on encoding information about a stimulus of interest. Spikes independent of the stimulus can corrupt mutual information in single-unit responses. The noise may be reduced by pooling the responses of neurons if they are mutually dependent on the stimulus. However, when the single-unit spike trains have disparate information about the stimulus, some of the attribute-specific information is lost by combining them.

A pooled two-unit response cannot carry more information than a perfectly sorted pair of single-unit responses. For a BMI application, we expect that whether multi-unit signals can carry as much information as the discriminated single-unit signals will depend mainly on two characteristics of the BMI system *in vivo*: (1) whether neighbouring neurons found on the same electrode are redundantly encoding the same attribute or encoding independently, and (2) whether and how much spike sorting error degrades the labelled line information. Whether the loss in information from a labelled line to a pooled response outweighs costs of spike sorting is still to be determined. Nevertheless, an understanding of the information in multi-unit signals is beginning to be formed which will provide the grounds for making claims about what is and is not gained by using spike-sorted signals.

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