

Efficient Signal Processing of Multineuronal Activities for Neural Interface and Prosthesis

H. Kaneko¹, H. Tamura², T. Kawashima³, S. S. Suzuki¹, I. Fujita²

¹National Institute of Advanced Industrial Science and Technology (AIST), Tsukuba, Ibaraki, Japan

²Graduate School of Frontier Biosciences, Osaka University, Toyonaka, Osaka, Japan

³Department of Electrical and Electronic Engineering, Toyohashi University of Technology, Toyohashi, Aichi, Japan

Summary

Objectives: Multineuronal spike trains must be efficiently decoded in order to utilize them for controlling artificial limbs and organs. Here we evaluated the efficiency of pooling (averaging) and combining (vectorizing) activities of multiple neurons for decoding neuronal information.

Methods: Multineuronal activities in the monkey inferior temporal (IT) cortex were obtained by classifying spikes of constituent neurons from multichannel data recorded with a multisite microelectrode. We compared pooling and combining procedures for the amount of visual information transferred by neurons, and for the success rate of stimulus estimation based on neuronal activities in each trial.

Results: Both pooling and combining activities of multiple neurons increased the amount of information and the success rate with the number of neurons. However, the degree of improvement obtained by increasing the number of neurons was higher when combining activities as opposed to pooling them.

Conclusion: Combining the activities of multiple neurons is more efficient than pooling them for obtaining a precise interpretation of neuronal signals.

Keywords

Information theory, correlation, spike sorting, vision, prosthesis

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1. Introduction

In neural interface/prosthesis technology, an amputated person's own neuronal activities will be used to voluntarily control his or her artificial limb. Accordingly, it is essential that the neuronal activities that provide command signals to drive the prosthetic device are recorded and decoded appropriately. Neuronal activities from sensory systems also can be used to achieve feedback control of such a device. Furthermore, when afferent neurons are artificially activated via implanted electrodes, the subject should be able to “feel” the movement of the artificial limb.

This technology requires not only techniques for recording from and for stimulating individual neurons, but also for interpreting neuronal activities. Thus it is important to develop a technique to extract transferred information from neuronal activities.

Using simultaneously recorded responses of multiple neurons in the monkey inferior temporal cortex (IT; an association area subserving visual recognition of objects) to the presentation of visual stimuli, we investigated what kind of signal processing is efficient for obtaining information about the stimuli. Here we compared two methods of extracting information from multineuronal responses: 1) by averaging spike counts of multiple neurons (pooling) to improve the signal-to-noise (S/N) ratio, and 2) by vectorizing spike counts of multiple neurons (combining) to accumulate independent information from these neurons.

2. Methods

2.1 Recording Multiple Neuronal Activities

Neuronal responses to 64 visual stimuli were recorded from IT of four anesthetized monkeys (*Macaca fuscata*; see details in [1]). All experimental procedures were based on the guidelines from the National Institutes of Health of the United States (1996). The Osaka University animal experiment committee approved the procedures.

General experimental procedures were similar to those described elsewhere [1]. Monkeys were prepared for repeated recording through initial aseptic surgery under sodium pentobarbital anesthesia. For recording experiments, monkeys were anesthetized with isoflurane. Vital signs were monitored throughout the experiments. The eyes were covered with contact lenses. For multichannel recording of neuronal activity, a 7-core electrode (seven recording sites, impedance of each site: 1–2 MΩ at 1 kHz; see Fig. 1a) was inserted into IT through a craniotomy. To ensure stable recordings, we immobilized the brain surface with paraffin and waited at least 20 min after changing the electrode's position before beginning data acquisition. To prevent eye movements, monkeys were paralyzed with pancuronium bromide.

Multichannel recordings were made at intervals of $\geq 300 \mu\text{m}$ to avoid sampling the same neuron twice as the sampling radius of the 7-core electrode is about $150 \mu\text{m}$. Neuronal activity from each recording site was amplified 10,000 times, filtered from

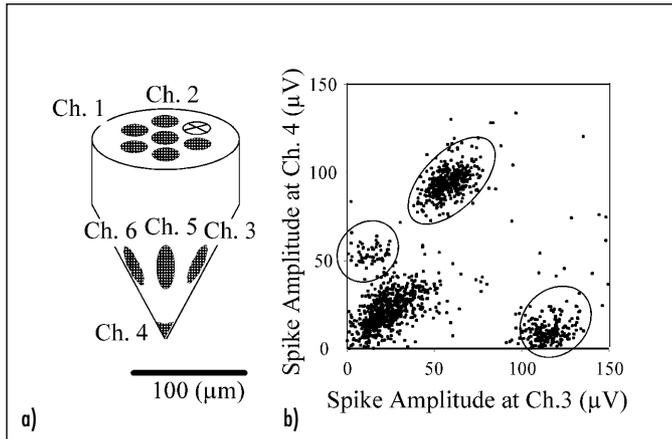


Fig. 1
Recording of multiple neuronal activities with a multisite microelectrode. Schematic diagram of a heptode (a) (Thomas Recording, Germany). Cluster distributions of spike amplitudes of multiple neurons (b). Each cluster except the cluster nearest to the origin in (b) is presumed to correspond to activities from a single neuron.

$$\Sigma(u) = \frac{1}{10-1} \sum_{k=1}^{10} (\mathbf{x}(u, k) - \mathbf{m}(u))(\mathbf{x}(u, k) - \mathbf{m}(u))^T$$

Fig. 2
Equation 4

500 Hz to 3 kHz, and digitized at 20 kHz for offline spike sorting and analysis.

Multiple single-unit recording of adjacent neurons was achieved by applying spike sorting to the multichannel recording data [2]. We employed a custom-made spike sorter that performed three procedures: spike detection, burst detection, and spike classification [3]. Multineuronal spikes were detected by matching the observed waveforms with a set of spike templates with different durations (spike detection). For each spike of a neuron, six waveforms were recorded simultaneously at the six recording sites (the tip and five lateral sites). The amplitudes of these waveforms constituted a spike-amplitude vector. Spike bursts were identified from attenuation of the spike amplitude and inter-spike intervals (burst detection). The amplitude vectors of the spikes in each burst were represented by the vector of the first intraburst spike. Finally, clusters of spike-amplitude vectors were classified by bottom-up hierarchical clustering (Fig. 1b).

2.2 Visual Stimuli

During each presentation session, each of the 64 visual stimuli (see Fig. 1B in [1]) was randomly presented at the center of the re-

ceptive field for 1 s against a homogeneous gray background (15.7 cd/m²) with inter-stimulus intervals of 1 s. The entire recording period consisted of ten sessions. The visual response of a neuron was defined as the number of spikes during a 1-s period starting 80 ms after the onset of each stimulus presentation to compensate for the response latency of IT neurons.

2.3 Amount of Transferred Information

The amount of information about the visual stimuli transferred by spike responses R , $I(S; R)$, is derived from the joint probability of the u -th stimulus and the v -th response, $p(u, v)$, as follows:

$$I(S; R) = \sum_{u=1}^{64} \sum_{v=1}^{64} p(u, v) \log_2 \frac{p(u, v)}{p(u)p(v)}, \quad (1)$$

where $p(u)$ indicates the probability of the u -th stimulus, and $p(v)$ represents the probability of the v -th response.

To obtain the joint probability, $p(u, v)$, we used the decoding procedure proposed by Gochin et al. [4]. First, we approximated the response of N neurons after the presen-

tation of the u -th visual stimulus ($u = 1 - 64$) at the k -th trial ($k = 1 - 10$),

$$\mathbf{x}(u, k) = (x(1, u, k), x(2, u, k), \dots, x(N, u, k))^T, \quad (2)$$

as a multidimensional Gaussian distribution of spike counts with the mean vector

$$\mathbf{m}(u) = \frac{1}{10} \sum_{k=1}^{10} \mathbf{x}(u, k) \quad (3)$$

and the variance-covariance matrix (see Eq. 4 in Fig. 2).

Second, we generated 640 “pseudoreponses” based on each spike count distribution $N(\mathbf{m}(u), \Sigma(u))$ by the Monte Carlo method. Instead of assuming independent responses between neurons [4], we introduced observed correlations to “pseudoreponses” [5]. Third, we classified each “pseudoreponse” into one of the 64 responses that had the minimum Mahalanobis distance. Finally, we integrated the co-occurrences of the u -th stimulus and the v -th response to obtain $p(u, v)$.

2.4 Success Rate of Estimating Visual Stimuli

Assuming that the responses of neurons after the presentation of the u -th visual stimulus were generated from $N(\mathbf{m}(u), \Sigma(u))$, we classified the neural response of each trial into one of the 64 responses that had the minimum Mahalanobis distance. Then we calculated the percentage of successfully classified trials as “success rate”.

3. Results

To evaluate the effects of pooling and combining neuronal activities, we analyzed spike trains simultaneously recorded from five to ten neurons each at seven recording sites (47 neurons in total).

3.1 Pooling Activities of Multiple Neurons

Because the correlation coefficients between activities of adjacent neurons are

higher than those of distant neurons [6-8], pooling activities of the adjacent neurons are considered to be more effective in increasing the S/N ratio and the amount of transferred information. We examined the effects of pooling activities of adjacent neurons on the amount of transferred information (closed triangles in Fig. 3a) and the success rate (closed triangles in Fig. 3b). The mean amount of transferred information increased slightly from 0.54 to 0.70 bits with the number of neurons used for pooling ($p < 0.05$, multiple comparisons). The success rate also increased from 4.2 to 4.8%. The indices for triplets or quintuplets were not always larger than those for single neurons (singles).

3.2 Combining Activities of Multiple Neurons

If each neuron encodes some information independent of other neurons, more information may be obtained by combining activities of more neurons. Figure 4 shows the histogram of the mutual information between neurons used to evaluate their redundancy and synergy [9, 10]. Because the average of 0.06 bits is slightly but significantly positive, most of these neurons appear to encode some redundant information. This redundancy is, however, much smaller than the mean amount of information of a single neuron (0.53 bits), indicating that the information of each neuron can be considered mostly independent. Thus, by combining activities of more neurons, more information about the visual stimuli could be obtained.

We examined the effects of combination on the amount of transferred information (open circles in Fig. 3a) and the success rate (open circles in Fig. 3b). The amount of information and the success rate both increased with the number of neurons combined. In the best case, we obtained about three bits of information and about 40% success rate from only five neurons.

Fig. 3 Comparison between the results of pooling and combining multiple neurons. Effects on the amount of information (a) and those on the success rate (b). The error bars are 1 SD.

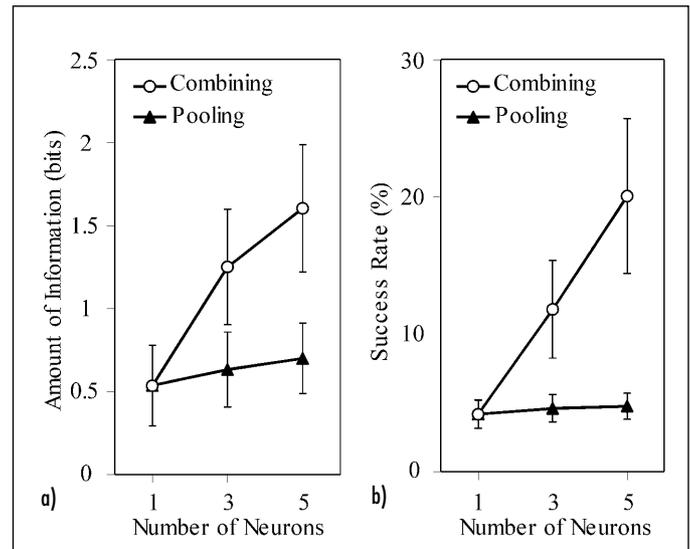
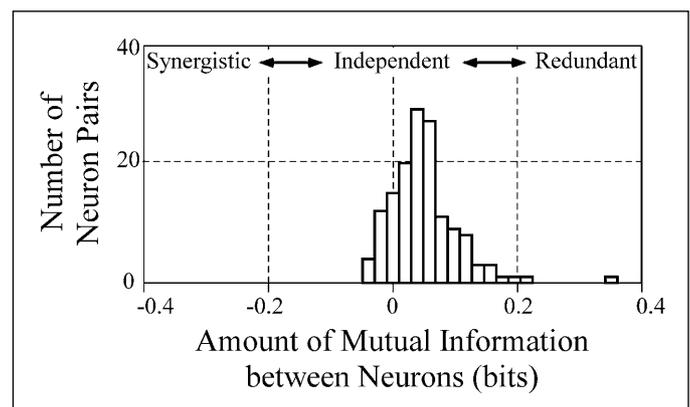


Fig. 4 Amount of mutual information between adjacent neurons. The mean amount of mutual information between neurons (145 simultaneously recorded pairs of 47 neurons) was slightly positive (mean: 0.06; SD: 0.06; $p < 0.0001$, runs-test).



4. Discussion

4.1 Efficacy of Pooling Neuronal Activities

The amount of information increased slightly but significantly with the number of neurons pooled (Fig. 3a). If a large number of neurons were pooled, the pooled activities could be related to some global indices of cortical activity such as a local electroencephalogram (EEG). Of interest here is to directly compare the relative advantage of pooled multineuronal data and EEG data from the perspective of information analysis. Similarly, electromyographic (EMG) signals as summed motor unit activities can be considered in the same context.

The pooling procedure may be improved with the use of weight coefficients for accumulating neuronal activities. We also previously discussed an improvement in the S/N ratio and in the amount of information by pooling (addition) or subtracting (differential) multineuronal activities [7]. We showed that both of these procedures could bring some improvement in the S/N ratio and the amount of information. However, the improvement was not outstanding.

4.2 Comparison of Pooling and Combining

Both the pooling and combining procedures increased the amount of information and the success rate of estimating the visual stimuli.

However, the degree of improvement obtained by increasing the number of neurons was different between these schemes (see Fig. 3). The improvement with the combining procedure (information: 0.26 bits/neuron; success rate: 4.0%/neuron) was higher than that with the pooling procedure (information: 0.04 bits/neuron; success rate: 0.14%/neuron). We conclude that the combining procedure is more effective for obtaining information than the pooling procedure.

If EEG and EMG signals can be considered as pooled activities of numerous units, their performance as control signals for driving prosthetic devices may be comparable to that of pooled neuronal activities. The present study demonstrates that a higher performance can be achieved with the combining procedure. However, as suggested by Andersen et al. [11], local field potentials representing pooled activities (e.g., excitatory synaptic potentials) of local neurons may have advantages as control signals for prosthetic devices in terms of ease of recording and robustness over time.

4.3 Realtime Interpretation of Neuronal Activities

In realtime control of prosthetic devices, ongoing neuronal activities in each trial must be processed to derive useful information. The success rate of estimating visual stimuli is a parameter for the evaluation of this feature. If we select one of the 64 visual stimuli randomly, the success rate must be 1.6%. The success rate for the pooling or combining procedure was higher than this value. Therefore, the multineuronal activities can contribute to the estimation of the visual stimuli. The combination of neuronal activities produced higher performances than the pooling procedure as shown in Figure 3b. Thus, the combination procedure

seems more promising for realtime interpretation of multineuronal activities.

How many neurons are needed to discriminate the visual stimuli perfectly? Even in the worst case in 5-neuron combinations, the success rate was over 10%. If we assume a linear increase of the success rate with the number of neurons as we saw over the range of one to five neurons, the rate would probably approach 100% when activities of about 50 neurons are combined. However, the success rate may not increase linearly over the range of greater than five neurons. This is an empirical question which should be experimentally addressed in future studies.

5. Conclusions

We demonstrate that the combining procedure is more effective than the pooling procedure. We discuss the importance of introducing the concept of combining multineuronal activities to the field of neuroprosthetic device control. With recent advances in both multichannel microelectrode fabrication technologies and multichannel signal processing techniques, we anticipate rapid progress in the field of neuroprosthetic device control.

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References

1. Tamura H, Kaneko H, Kawasaki K, Fujita I. Presumed inhibitory neurons in the macaque inferior temporal cortex: visual response properties and functional interactions with adjacent neurons. *J Neurophysiol* 2004; 91 (6): 2782-2796.
2. McNaughton BL, O'Keefe J, Barnes CA. The stereotrode: a new technique for simultaneous isolation of several single units in the central nervous system from multiple unit records. *J Neurosci Methods* 1983; 8 (4): 391-397.
3. Kaneko H, Suzuki SS, Okada J, Akamatsu M. Multineuronal spike classification based on multisite electrode recording, whole-waveform analysis, and hierarchical clustering. *IEEE Trans Biomed Eng* 1999; 46 (3): 280-290.
4. Gochin PM, Colombo M, Dorfman GA, Gerstein GL, Gross CG. Neural ensemble coding in inferior temporal cortex. *J Neurophysiol* 1994; 71 (6): 2325-2337.
5. Krzanowski WJ. Principles of multivariate analysis: a user's perspective (revised edition). New York: Oxford University Press; 2000.
6. Gochin PM, Miller EK, Gross CG, Gerstein GL. Functional interactions among neurons in inferior temporal cortex of the awake macaque. *Exp Brain Res* 1991; 84 (3): 505-516.
7. Tamura H, Kaneko H, Fujita I. Quantitative analysis of functional clustering of neurons in the macaque inferior temporal cortex. *Neurosci Res* 2005; 52 (4): 311-322.
8. Wang Y, Fujita I, Murayama Y. Neuronal mechanisms of selectivity for object features revealed by blocking inhibition in inferotemporal cortex. *Nat Neurosci* 2000; 3 (8): 807-813.
9. Gawne TJ, Richmond BJ. How independent are the messages carried by adjacent inferior temporal cortical neurons? *J Neurosci* 1993; 13 (7): 2758-2771.
10. Schneidman E, Bialek W, Berry MJ 2nd. Synergy, redundancy, and independence in population codes. *J Neurosci* 2003; 23 (37): 11539-11553.
11. Andersen RA, Musallam S, Pesaran B. Selecting the signals for a brain-machine interface. *Curr Opin Neurobiol* 2004; 14 (6): 720-726.
12. Ginter J Jr, Blinowska KJ, Kaminski M, Durka PJ, Pfurtscheller G, Neuper C. Propagation of EEG activity in the beta and gamma band during movement imagery in humans. *Methods Inf Med* 2005; 44 (1): 106-113.

Correspondence to:

Hidekazu Kaneko, Ph.D.
Institute for Human Science and Biomedical Engineering
National Institute of Advanced Industrial Science and Technology (AIST)
AIST Tsukuba Central 6
Higashi, Tsukuba
Ibaraki 305-8566
Japan
E-mail: kaneko.h@aist.go.jp