REVAMPING SIGNAL PROCESSING FOR ADAPTIVE, REAL TIME, BI-DIRECTIONAL BRAIN MACHINE INTERFACE SYSTEMS

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ABSTRACT

Brain Machine Interfaces (BMIs) have recently received significant attention from the neuroscience and engineering communities as a result of striking advances in monitoring, processing, and modeling brain function at multiple temporal and spatial resolutions. These advances, however, have also raised significant challenges to both communities that are becoming the focus of numerous ongoing research efforts.

Broadly categorized based on their level of invasiveness, BMIs relying on implantable microelectrode arrays (MEAs) have received the most attention. This paper briefly reviews some fundamental concepts underlying the operation of MEA-based BMIs and highlights in particular the signal processing challenges faced by these systems in light of their resource-constrained operation. Finally, we summarize some of our recent progress in this area and suggest some open questions for future research.

Index Terms— Nervous system, brain machine interface, wavelets, decoding, spike trains

1. INTRODUCTION

At the crossroad of neurophysiology and psychology, brain-machine interfaces (BMIs) stand as a promising technology for linking and translating neurophysiological signals to actual behavior, and vice versa. Some 140 years ago, neuronal signaling was artificially induced in the motor cortex using a stimulating electrode placed in the vicinity of small groups of neurons [1]. Nowadays, inducing a network-wide pattern of neural activity across targeted cortical and subcortical areas is becoming a standard technique for evoking distributed brain responses that can mediate an entire motor behavior, such as treating the debilitating symptoms of Parkinson's Disease [2].

Much research has focused over the years on developing devices for sensing large scale neural activity. The objective is to enhance our basic understanding of the dynamic operation of the functional brain and characterize any causal relationships between the measured neural activity and the observed behavior. This research has progressed enormously in recent years, owing largely to technological advances in brain imaging methodologies such as functional Magnetic Resonance Imaging (fMRI), Diffusion Tensor Imaging (DTI), Electroencephalographic (EEG) and Magnetoencephalograophic (MEG) recordings. Perhaps the most promising among all is the advent of high-density microelectrode arrays (MEAs) that can be implanted in the vicinity of small populations of cortical neurons [3, 4]. These devices permitted monitoring the collective activity of ensembles of neurons with temporal and spatial resolution far exceeding what is offered by surface EEG electrodes or fMRI. The technology is already paving the way to improve the lifestyle of many patients with severe neurological diseases and disorders or traumatic brain injury following stroke [5].

MEA-based BMIs, however, are severely resource-constrained in the face of numerous signal processing tasks that need to be performed to extract relevant biological information. These constraints may preclude their usage in many future applications that require high precision, ubiquitous and real time computations to take place. This paper is exclusively focused on reviewing some of these challenges, and summarizes our most recent effort to alleviate them. Non-invasive BMIs (e.g. EEG or fMRI-based) are outside the scope of this paper [6].

2. BMI SYSTEM OPERATION

Single neuron firing pattern is believed to be the primary carrier of information essential for functional brain networks. Penetrating MEAs implanted in cortical tissue are capable of recording the activity of multiple neurons as well as local filed potentials (LFPs) [3, 4]. The later is believed to represent the collective, synchronized activity of much larger and more distal neuronal populations. Because of this lack of precision about the origin of LFP sources, multi-neuron activity has received more attention in BMI applications, largely due to the increased temporal and spatial resolution.

2.1. Spike Detection and Sorting

The signals recorded with MEAs are typically an instantaneous mixture of signals from multiple neurons contaminated by large degrees of noise. The noise is presumably from numerous other biological sources that may or may not be representing the observed behavior, in addition to sources of instrumentation noise and electromagnetic interference. The multi-neuron activity is typically represented by sequences of 1-2 ms action potentials -or *spikes*- that have to be detected in the noisy observations prior to any further processing. Spike detection can be a challenging task given the high levels of time-varying neural noise that may obscure spikes of interest from neighboring neurons, particularly in stimulus driven activity [7].

The spikes, once detected, have to be sorted out to segregate the response of each neuron in the recorded population. This is one of the most challenging tasks in BMI system operation. Spike waveforms from different neurons can be largely correlated as illustrated in Fig.1a, precluding the usage of classical blind source separation algorithms to separate individual neurons' responses. Moreover, spike waveform shape can be highly nonstationary over millisecond time scales (particularly during bursting periods) to even hours and days [8-10].

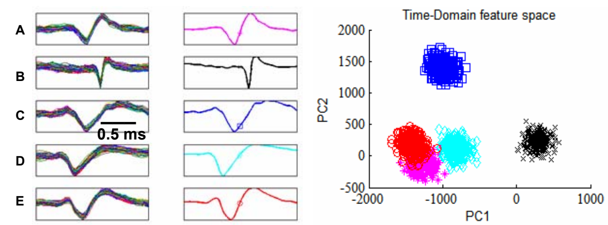
Sparse representation using wavelets was shown to provide a powerful solution to the spike detection and sorting problems under highly nonstationary conditions [11-15]. The idea stems from the ability of wavelets to provide very compact, class-dependent representations of spike waveforms. When used in conjunction with subspace-based array processing techniques, complex event structures such as those resulting from simultaneous firing of two or more neurons can be efficiently resolved [14]. Fig. 1b shows example feature space of the sparse representation for 5 spike classes and quantitative analysis of the resultant "clusters" (the true class of each spike is known in this case). Fig. 1c shows quantitatively the *spike class separability*, defined as the ratio of the cluster separation to the cluster spread in the reconstructed signals after *hard-thresholding* their wavelet transform coefficients at various threshold levels. This illustrates that spike detection and sorting is simultaneously enhanced along with data compression. The later feature is highly desirable for a fully implantable BMI system with wireless data telemetry [11].

In cortical areas such as the motor cortex, firing rate is predominantly believed to carry all the information about movement intentions [16]. Direct estimation of the instantaneous firing rate of individual neurons is a critical feature for real time BMI operation [17]. We have shown that the sparsely-represented spikes can be regarded as irregular samples of the instantaneous rate function. Therefore, estimating the rate is feasible by extending the wavelet decomposition of the thresholded transform to levels where the basis support becomes comparable to the time constant of the firing rate functions of the recorded neurons (Fig. 1c). This step substantially alleviates the complexity that would arise due to the need to decompress the data (through inverse wavelet transformation) followed by time-domain spike sorting in the classical sense.

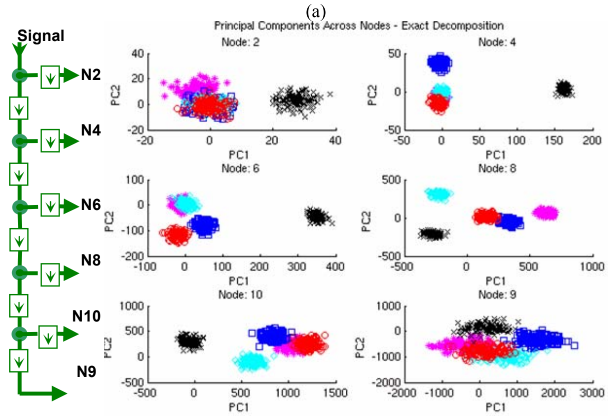
2.2. Ensemble spike train analysis

Associations among constituent groups of neurons thought to be orchestrating the processing of stimuli or representing behavior have to be identified in the ensemble spike trains. The complexity of this task stems from the variable time scale at which neurons interact [18]. For example, synchrony is thought to play an important role in stimulus encoding in the visual and auditory cortices, while its role in motor cortex remains highly debated. In addition, cortical neurons are consistently observed to vary their receptive fields (or tuning functions) as a result of cortical plasticity [19]. This complexity increases dramatically with modest increase in the number of neurons and with the number of elements in the stimulus vector.

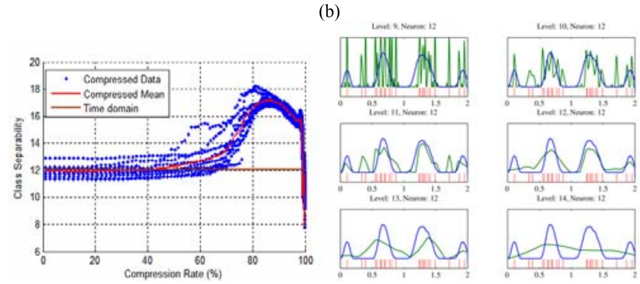
From a system identification standpoint, identifying the neural circuit involved in dynamically encoding the observed behavior is an important but nontrivial task. An unknown number of neurons is typically recorded in a given session and that number seem to vary substantially over recording sessions. The source of this variability may be caused by either physiological changes in the extracellular medium surrounding the electrode array (e.g. electrode drift, cell death or migration, electrode encapsulation due to adverse tissue reaction), or can be attributed to the reorganization of cortical representations that accompany learning and development. These observations seem to reinforce Hebb's original hypothesis that *each neuron can participate in different cell assemblies at different times*, indicating variable degrees of involvement in encoding stimuli parameters that is a function of the behavioral state, the particular brain area, and the subject's level of experience with the stimuli [20]. It can be argued that temporary computational demands may activate relatively *short-lasting* clusters of spatially distributed -but functionally interdependent- neurons to inform the brain about a specific behavioral state and hence optimize cortical resources to carry out instantaneous biological computations.



(a)



(b)



(c)

Figure 1: (a) Representative sample of spikes from five well-isolated neurons and their template waveforms. (b) Time domain feature space for the spikes in (a), wavelet decomposition tree path and feature space for the sparse representation across 5 decomposition levels. (c) (Left) Class separability versus compression rate compared to time domain separability, (Right) true (blue) and estimated rate (green) for spike events (red) of a sample neuron across wavelet nodes.

We have recently developed a new algorithm to adaptively determine these functionally-interdependent neurons from the observed ensemble activity [21]. The algorithm relies on computing a similarity measure across multiple time scales between pairwise neurons and fusing these measures using SVD to connect neurons (objects) in a graph representation. Spectral clustering is performed in this representation to identify neurons with similar firing patterns in a probabilistic sense. In Figure 2, we demonstrate a 16-neuron/4-cluster cortical network model in which various inhibitory and excitatory synaptic connections were created over time between neurons across clusters that were otherwise independent. Each neuron's firing rate was modeled as inhomogeneous Poisson process with firing probability that depends on H_t, defined as the neuron's own firing history and those of other neurons connected to it as [22]:

$$\lambda_i(t|\boldsymbol{\alpha}_i, H_t)\Delta = \Delta.\mathbf{exp}\left(\beta_i + \sum_{j=1}^{P}\sum_{m=1}^{M_{ij}} \alpha_{ij}(m\Delta) I_j(t-m\Delta)\right)$$

where α_{ij} is the synaptic coupling between neurons i and j, β_i denotes the background rate of neuron i, $I_j(t\text{-}m\Delta)$ is the spike count of neuron j in window m, Δ is the bin width used to sample the spike train, M_{ij} indicates the interval length (in bins) of past interaction between the two neurons, and P is the total number of neurons in the population. Synaptic coupling was modeled as a damped sinusoid: $\alpha_{ij}(t) = \pm A_{ij}\,\mathbf{sin}(2\pi f_{ij} t / M_{ij})\,\mathbf{exp}(-B_{ij} t / M_{ij})$, where (+/-) indicates excitatory/inhibitory interactions, respectively. The terms A_{ij}, f_{ij}, B_{ij} are experimentally-derived, Gaussian-distributed parameters governing the temporal and spectral characteristics of the synapse strength. Figure 2b demonstrates the clustering accuracy is maximized at a time scale matching the history of interaction (chosen to be 100 ms) in the model, while Figure 2c demonstrates the compactness of the clusters as the connectivity between neurons in the same cluster is strengthened.

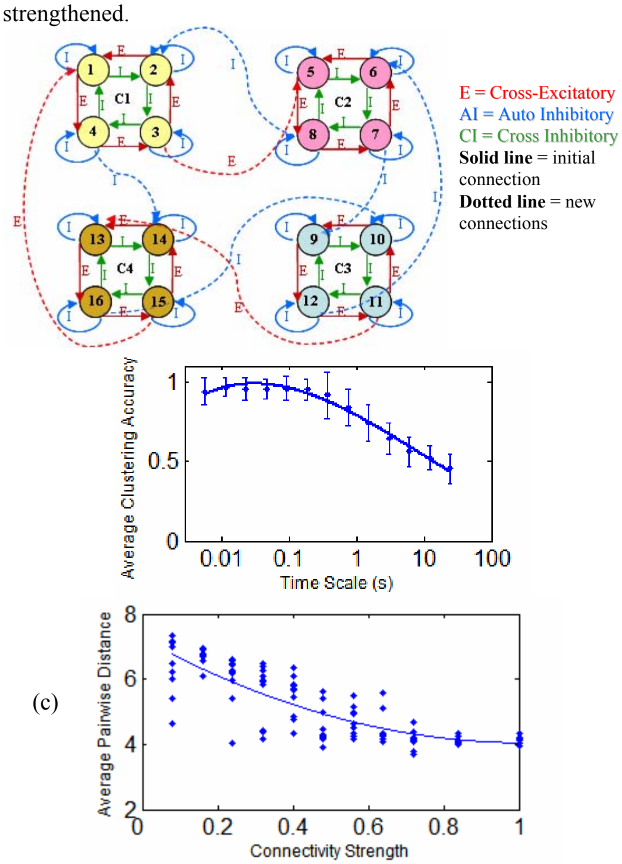


Figure 2: (a) 16-neuron network. (b) Clustering accuracy vs time scale (c) Neuronal Pairwise distance vs connectivity strength

2.3. Decoding the Ensemble Activity

The outcome of the spike sorting step is a collection of neuronal response properties (precise spike time, rate, correlation, etc…) expressed in the spike trains that can be used to describe a cortical network "state". Decoding this state is a key step to relate the observed spike trains to the subject's behavior. Decoding algorithms fall in two broad classes: 1) Linear algorithms: based on the well-known minimum variance best linear unbiased estimator (MVBLUE) [23]; 2) Nonlinear algorithms (Bayesian): uses the prior distribution of observed responses given stimuli to estimate the posterior distribution of the stimuli given the observed response in a maximum likelihood sense [24]. In all existing decoding algorithms, neuronal responses consist of the firing rates estimated over a fixed bin width (typically 50-100 ms) and these are the sole response property indicative of the network state. As a result decoding filters poorly generalize to other types of non-stereotypical behavior. These algorithms require extensive periodic "calibration", even when recordings are stable and the subject's performance remains steady [25].

The large variability in individual neuron response across repeated trials underlines an inherent varying spectrum of temporal and spatial interactions among cortical neurons. An ultimate goal is to design these filters to faithfully decode neural signals observed when the subject is freely behaving and naturally interacting with the surrounding. We hypothesize that improved adaptive decoding can be achieved in this case by restricting the input to the decoder to a *spatiotemporal neural subspace* where the *relevant* task information resides. Thus, spike train clustering algorithms may constitute an important pre-decoding step to enable continuous assessment of the cortical network state by detecting any variations in the spatiotemporal patterns of interaction reminiscent of plastic changes in the cortex.

3. PRACTICAL CONSIDERATIONS

For MEA-based BMIs to be a viable augmentative or replacement technology to normal human function, it needs to be fully implanted, operate wirelessly to minimize patient's risk of infection and discomfort, and continuously perform the above operations in real time to allow the patient to experience natural behavior when interacting with the surrounding. There are many technical challenges to these objectives. The shear amount of data that MEA-based BMIs record well exceeds 1 Mbps/channel. This is a major challenge to state-of-the-art biotelemetry systems, considering that arrays can be >100 electrodes. The problem is exacerbated by the need for real time signal processing with limited chip size and power consumption. Much research is currently devoted to optimize signal processing for real time processing within area-power efficient hardware. We have recently demonstrated the feasibility of area-power efficient circuitry for the sparse representation [25]. In addition, low-power wireless telemetry seems to be feasible [26]. Taken together, a fully implantable, completely wireless, MEA-based BMI system seems to be in the horizon.

A closed loop BMI system relies mainly on visual feedback signals to inform the brain about behavioral states, of a prosthetic limb for example. Feedback signals need to be augmented to include other sensory information (such as tactile) to allow the patient to experience more natural behavior. These signals should be processed and delivered with the "correct format" in the appropriate cortical sites. Intra-cortical electrical micro-stimulation therefore can play a fundamental role in this regard if its parameters are optimized to evoke the desired pattern of neural activity representing sensory experience.

4. CONCLUSION

BMIs seem to be a promising technology to help achieve a better lifestyle for people who suffer from many motor disorders, depression, chronic pain, epilepsy and many others. We have reviewed some of the numerous challenges facing this technology from a signal processing perspective and provided some approaches to overcome them. Much research needs to be done for this technology to better serve human welfare.

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