Adaptive common average reference for *in vivo* multichannel local field potentials

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Abstract For *in vivo* neural recording, local field potential (LFP) is often corrupted by spatially correlated artifacts, especially in awake/behaving subjects. A method named adaptive common average reference (ACAR) based on the concept of adaptive noise canceling (ANC) that utilizes the correlative features of common noise sources and implements with common average referencing (CAR), was proposed for removing the spatially correlated artifacts. Moreover, a correlation analysis was devised to automatically select appropriate channels before generating the ACAR reference. The performance was evaluated in both synthesized data and real data from the hippocampus of pigeons, and the results were compared with the standard CAR and several previously proposed artifacts removal methods. Comparative testing results suggest that the ACAR performs better than the available algorithms, especially in a low SNR. In addition, feasibility of this method was provided theoretically. The proposed method would be an important pre-processing step for *in vivo* LFP processing.

Keywords Local field potential · Microelectrode array · Adaptive noise canceling · Common average reference · Spatially correlated artifacts

1 Introduction

The microelectrode array extracellular recording of neural signals typically contain activities of both action potentials and field potentials near a microelectrode site [1]. The former is often referred to as spike, and the latter is always known as local field potential (LFP). In comparison with spike activity (typically 0.25~5 kHz [2]), LFP is a low frequency signal and can be separated from the recordings by a low-pass filter with cutoff frequency around 0.25 kHz. In recent years, the LFP has received increasing attention for the following advantages. Firstly, the LFP has been shown to reflect sensory and motor-related signals that can be modulated by cognitive processes, and provides additional information to single neuron activity [3]. Secondly, the LFP appears to be more closely correlated with the BOLD signal measured with fMRI than spike activity [4]. Lastly, the LFP is relatively easy to be recorded and more stable than the spike, which is an efficient candidate signal for the control of neural prostheses [5].

Recent studies have shown that the LFP recorded in awake behaving animals against a distal reference on the skull as commonly practiced is significantly contaminated by non-local and non-neural sources arising from the reference electrode and the movement-related noise, these sources collectively account for 23–77% of total variance in unprocessed LFP [6]. Therefore, for the *in vivo* LFP recording, one of the significant problems is the global artifacts, which can be seen in multiple channels of a microelectrode array and represent/cover most of the artifacts types [7]. Due to the distance between electrodes relatively nearby (about 250 μm) [8], the global artifacts is recorded in almost all electrodes once appearing and is spatially correlated among different channels. Two typically spatially correlated artifacts were shown Fig. 1.

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Fig. 1 Example of two real spatially correlated artifacts. The *left* is the motion artifacts during the pigeon feeding period, and the *right* is the 50-Hz line noise

The removal of spatially correlated artifacts is an important step in processing multichannel LFP recordings. However, many factors make it a challenging work, especially in the less-constrained *in vivo* recording environment. Firstly, LFP is very weak (μV level) and often corrupted by the artifacts from environmental, experimental and physiological factors. Secondly, the spectral characteristics of the signal and the noise are overlap. Thirdly, the neural response bands from different types of neural events triggered by various processing pathways are unknown and variable. Although several objective, semi-automatic approaches have been proposed for defining the response frequency bands and their boundaries [9, 10, 11, 12] based on the relationship between neuronal responses and external stimulus, there is not always a clear and measurable stimulus in neural recordings, such as motor planning.

Another set of algorithms to remove the artifacts mainly use multichannel denoising methods. Although LFP has many similar properties to many other physiological signal recordings (e.g. EEG, ECG, EMG), such as narrow-band, spectral overlapping, and highly non-stationary, many available multichannel algorithms for these signals cannot be applied on the LFP, such as the BBS (blind source separation)-based methods [13, 14, 15]. One assumption of BSS is that the observations are the linear mixing of the sources and the number of sources is equal or less than the number of observations. Another assumption is that the sources have to be either independent for ICA (independent component analysis)-based methods or maximally uncorrelated for CCA (canonical correlation analysis)-based methods. However, most of the mentioned assumptions do not often match with the LFP. Because the LFP is commonly thought to reflect population synaptic potentials and other types of slow activity unrelated to synaptic events from an area around the electrode tip, it cannot be separated as an independent source [7].

This study presents a simple processing method, the adaptive common average reference (ACAR), based on a combination of the classic common average reference (CAR) and an adaptive noise canceling (ANC). The CAR has been always used in EEG/ECOG to identify the small

signal sources in noisy recordings [16, 17]. Ludwig et al. [18] has studied its effectiveness in single-unit neural recordings. In comparison with the standard CAR, we introduce two modifications: firstly, a correlation analysis was used to identify the candidate channels before generating the reference data; secondly, an adaptive filtering technique was introduced to automatically remove the undesired activity, which avoided introduction of new artifacts components. Its performance was evaluated according to the synthetic data as well as the real data from the hippocampus (Hp) of pigeons and compared with the standard CAR and several available algorithms found in the literature. In addition, a theoretical justification for the proposed method was provided.

2 Methods and materials

2.1 Common average reference

For a K channels *in vivo* LFP signal, a simple model can be given as follows [16]:

$$d_{k,t} = s_{k,t} + w_k \times n_t \quad (1)$$

where $d_{k,t}$ is the recorded signal channel k at time point t , $k = 1, 2, \dots, K$, $s_{k,t}$ is the desired signal, and n_t is the artifacts, w_k is the weighting coefficient, which decides the noise with a contribution to each channel. The CAR is taken by a sample by sample average of all the channels, which is used as a global reference to remove the artifacts:

$$\hat{s}_{k,t} = d_{k,t} - \hat{n}_t \quad (2)$$

where

$$\hat{n}_t = \frac{1}{K} \sum_{k=1}^K d_{k,t}.$$

It is assumed that the desired signals are uncorrelated among channels and the noises are identical or similar, that is $w_k \approx 1$ for each channel. Through the averaging process, only the noise that is common to all the channels remains on the reference, the signal that is isolated on one channel does not appear on the CAR, thus,

$$\hat{n}_t = \frac{1}{K} \sum_{k=1}^K (s_{k,t} + w_k \times n_t) \approx n_t. \quad (3)$$

The CAR has been proven effective under the right conditions but does have many problems in practice: the first one is that different channel characteristics can cause the noise to have unpredictable amplitudes; the second one is that, for some channels, the signal is so large that dominates the average, it causes an inaccurate reference to be generated. In other words, correspondently, if $w_k \neq 1$ in (3), then $\hat{n}_t = c \times n_t$, $c = \sum_{k=1}^K w_k / K$ is constant, $\hat{s}_{k,t} = s_{k,t} + (w_k + c) \times n_t$, it will cause introduction of new noise components, and if $s_{k,t}/K \neq 0$ or $s_{m,t}/K \neq 0$, $m \neq k$, then $\hat{s}_{k,t} = s_{k,t} - s_{k,t}/K$ or $\hat{s}_{k,t} = s_{k,t} - s_{m,t}/K$, it will cause inadequate noise reduction. Therefore, the CAR is invalid in these cases, and these cases generally exist for *in vivo* LFP recordings.

2.2 Adaptive common average reference

The method presented here, referred to as the ACAR, attempts to combine the strengths of the ANC filter and the CAR technique. If an accurate reference is available, the ANC filter will be proved to be extremely effective in removing noise [19]. In the ANC filter, the reference must be temporally correlated with the noise, although a small amount of time shift is acceptable as long as it does not exceed the length of the finite impulse response filter. In addition, for good performance, any correlation between the reference and the signal should be minimal.

The ANC filter can automatically adjust the parameters of filter through adaptive recursive algorithms to minimize the difference between $\hat{n}_t$ and n_t so that $\hat{s}_t$ converges towards s_t , i.e. $\min_{\hat{n}_t} \|s_t - \hat{s}_t\|^2$. Here, the normalized least-mean-squares method, which is a simple modification of the least-mean-squares algorithm, is chosen as the adaptive recursive algorithm of the ANC filter because of simple computation and easy realization [19]:

$$\mathbf{W}_{t+1} = \mathbf{W}_t + 2u\hat{s}_t\mathbf{x}_t / L\sigma_x^2 \quad 0 < u < 1. \quad (4)$$

where $\mathbf{W}_k$ is the filter tap coefficient at t , $\mathbf{x}_t$ is the most recent L values of the reference x , L is the filter length, u is the step size to ensure filter stability, σ_x^2 is the power of x , which can be estimated from a segment of x . For implementation, a 1-s segment of data is used as well as L is set to 10 and u is set to 0.1 for all data.

The CAR is generally able to produce a usable reference signal for spatially correlative artifacts. But for the ANC filter, the CAR might not provide a good enough reference due to the problems described above. In practice, not every dataset includes the spatially correlative artifacts, and not also every channel is considered appropriate for the CAR.

Therefore, the data is screened by the correlation between the CAR and each channel.

Let ρ_k as the Pearson's correlation coefficient between the CAR and the channel k , thus,

$$N = \sum_{k=1}^K \text{sign}(\rho_k), \quad (5)$$

where,

$$\begin{cases} \text{sign}(\rho_k) = 1, & \text{if } \rho_k \geq \alpha, \\ \text{sign}(\rho_k) = 0, & \text{else.} \end{cases}$$

where α is the threshold. For the channel k , if $\rho_k \geq \alpha$, the channel is considered as the candidate channel for the CAR. Here, we use $\alpha = 0.75$ based on the experiments. If $N \geq \beta$, the LFP is considered that it includes the spatially correlated artifacts. Here, $\beta = 0.5$. The ρ_k can be calculated as follows:

$$\rho_k = \frac{E[(s_k - \mu_k)(x - \mu_x)]}{\sigma_{s_k} \sigma_x}, \quad (6)$$

where μ is the mean of the signal and σ is the standard deviation, $E[\cdot]$ is the expectation operation, x is the CAR reference. In order to increase the quality of the CAR reference, for each channel, we calculate the CAR with the remaining channels instead of all the channels. The candidate channel is normalized by the z-score, but the mean is not removed since the artifacts could have a DC component [16]. To improve the speed and consistency of convergence, the reference data is smoothed by a moving average filter with the span of 5.

2.3 Theoretical justification

According to the adaptive filter theory, the reference which contains the desired signal causes the attenuation and distortion of the filter output signal [19]. Therefore, the effect of applying the CAR on the adaptive filter is discussed from the theory in the section. According to the above assumption and the formula (1), for the channel m , the reference $x_{m,t}$ is calculated by the CAR as follows,

$$x_{m,t} = \frac{1}{K-1} \sum_{k=1}^K (s_{k,t} + w_k \times n_t) = \frac{\sum_{k=1}^K s_{k,t}}{K-1} + \lambda_m \times n_t \quad (7)$$

where $m \neq k$, $\lambda_m = \sum_{k=1}^K w_k / (K-1)$.

Following the formula (6), the correlation coefficient between the reference $x_{m,t}$ and the desired $s_{m,t}$ can be calculated as,

$$\rho[x_{m,t}, s_{m,t}] = \frac{\sum_{k=1}^K \text{cov}(s_{m,t}, s_{k,t})}{(K-1)\sigma_{s_{m,t}}\sigma_{x_{m,t}}} = 0 \quad (8)$$

where $\text{cov}(\cdot)$ is covariance operation. Due to the desired signal of different channels is not correlated,

$\text{cov}(s_{m,t}, s_{k,t}) = 0$. The correlation coefficient between the reference and the artifacts is calculated as follows,

$$\rho[x_{m,t}, n_{m,t}] = \left(\lambda_m + \frac{1}{(K-1)^2} \frac{\sum_{k=1}^K \sigma_{s_{k,t}}}{\sigma_{n_t}} \right)^{-1} \quad (9)$$

Note that when $\sigma_{s_{k,t}}/\sigma_{n_t}$ is a constant and $w_k \rightarrow 1$, $\rho[x_{m,t}, n_{m,t}] \propto \sqrt{1 - 1/K}$. As K increases, $\rho[x_{m,t}, n_{m,t}] \rightarrow 1$. When K is a constant, the smaller the $\sigma_{s_{k,t}}/\sigma_{n_t}$, the stronger the correlation between the reference and the artifacts. In other words, with a larger σ_{n_t} , i.e., there are high-amplitude correlated artifacts among channels, the reference is particularly effective. The results have shown that the CAR technique is valid for the *in vivo* LFP recording, especially in the low SNR.

2.4 Neural recordings

2.4.1 Real data

Real data, used to illustrate the ACAR, was acquired by a 16/32-channels microelectrode array (Microprobe Inc., platinum-iridium electrode, 250 μm inter-electrode spacing, impedance at 1 kHz equals 0.5–1.0 $\text{M}\Omega$) in left Hp (AP: 4.5–5.5 mm, ML: 0–1.5 mm, DP: 1.0–2.5 mm) of 7 adult pigeons. All the experiments were in accordance with Animals Act, 2006 (China) for the care and use of laboratory animals and approved by Life Science Ethical Review Committee of Zhengzhou University. The pigeons were trained to perform a freedom-foraging task in a plus-maze or a circle open-field. During the experiment, water was available at all times; food was restricted to the period of daily testing on workdays, with additional free food available on weekends.

The pigeons could learn the behavior easily and become fully trained after 1–2 weeks. All surgeries were performed when the animals were under general anesthesia. The head was placed in the stereotaxic holder that was customized for pigeons with the anterior fixation point (that is, beak bar position) 45° below the horizontal axis of the instrument [20]. Following 5–7 days of recovery, neural signals were collected and amplified with a CerebusTM system (Blackrock Microsystem Inc., Salt Lake City, UT, USA). The sampling frequency and resolution of analog-to-digital conversion were 30 kHz and 16 bits, respectively. The LFP was extracted by a low-pass filtering (second-order Butterworth) at 0.25 kHz, and sampled at 1 kHz. The real data per pigeon is displayed in Table 1.

2.4.2 Synthesized data

To evaluate the performance of proposed algorithm, the synthetic data was simulated based on the real data. The

data synthesis process was illustrated in Fig. 2. For each pigeon, a 10-s LFP epoch was selected based on the appearance of the spatially correlated artifacts. These epochs were separated by the ACAR into the common-mode artifacts and the artifacts-less signals. Then the common-mode artifacts were averaged as the noise and the artifacts-less signals were named as the desired signals. Based on the formula (1), the noise from a pigeon was linearly added to the desired signals from the other pigeons to form a data sequence that was contaminated by the artifacts, it was referred to synthesized data.

For each trial, the weighting coefficient vector w_k was generated with each element as a random number distributed uniformly between 0 and 1. The vector was then normalized to provide a specified average SNR to ensure the value was a constant. In keeping with theoretical analysis, the average SNR was calculated as the mean signal power over the mean noise power [16]:

$$\text{SNR}_{\text{average}} = \frac{\sum_t \sum_k s_{k,t}^2}{\sum_t \sum_k n_{k,t}^2} \quad (10)$$

where $n_{k,t} = w_k \times n_t$.

2.5 Performance measures

The measurement for quantitative evaluation of the algorithm is mainly two types: one is to measure how much artifacts has been removed and the other is to measure how much distortion it brings into the signal of interest. Therefore, the amount of increase in the SNR, ΔSNR , and root mean square error (RMSE) are applied to evaluate the performance of the proposed method. ΔSNR : The ΔSNR is the difference in SNR before and after artifacts removal [7]:

$$\Delta\text{SNR} = 10 \log \left(\frac{\sum_k \sum_t s_{k,t}^2}{\sum_k \sum_t e_{k,t}^2} \right) - 10 \log \left(\frac{\sum_k \sum_t s_{k,t}^2}{\sum_k \sum_t n_{k,t}^2} \right), \quad (11)$$

where $s_{k,t}$, $n_{k,t}$ and $e_{k,t}$ is the desired signal, the noise before and after artifacts removal, respectively.

RMSE: The RMSE is calculated as follows:

$$\text{RMSE} = \frac{1}{K} \sum_k \left(\frac{1}{T} \sum_t e_{k,t}^2 \right)^{1/2}, \quad (12)$$

where $e_{k,t}$ represents the error data after artifacts removal, T is the length of the error data. The ΔSNR quantifies the amount of increase in the SNR, and the RMSE quantifies the amount of signal distortion.

Note that the above calculations can only be performed on synthesized data. For the real data, we mainly discussed the effect of applying these methods on the correlation among channels. For this reason, for a signal with K channels, the correlation coefficient matrix is,

Fig. 2 Illustration of the synthesis process to generate simulated data. w_k is the weighting coefficient of the channel k

Table 1 Real data description for the artifacts removal methods

Pigeon ID	No. of channels	No. of trials	Task	Electrode types
P070	16	27	Plus-maze	4 × 4
P001	32	22	Circle	4 × 8
P009	32	101	Circle	4 × 8
P022	16	47	Circle	4 × 4
P046	16	44	Circle	4 × 4
P048	16	8	Circle	4 × 4
P349	16	87	Circle	4 × 4

$$\rho = \begin{bmatrix} \rho_{1,1}, \rho_{1,2}, \dots, \rho_{1,K} \\ \vdots \\ \rho_{K,1}, \rho_{K,2}, \dots, \rho_{K,K} \end{bmatrix}_{K \times K}, \quad (13)$$

where $\rho_{k,k} = 0$, $k = 1, 2, \dots, K$. The correlation before and after artifacts removal is defined,

$$\Delta\rho = [(|\rho_1| - |\rho_2|)z_1]^T z_2, \quad (14)$$

where ρ_1 and ρ_2 are the correlation coefficient matrix before and after artifacts removal, respectively. z_1 and z_2 are the $1 \times K$ matrix, in which each element is $1/(K-1)$ and $1/K$, respectively.

All results were tested with a Wilcoxon rank sum, the significance level was set to 5%, i.e. $P < 0.05$ was considered significant [21]. Statistical calculations were carried out using the MATLAB Statistics and Machine Learning Toolbox (The Mathworks, Inc., USA). The rank sum test is a rank-based method, as an alternative to the parametric t -test, which only assumes that the distribution of differences within pairs be symmetric without requiring normality [21].

3 Results

3.1 Results from synthesized data

For the synthesized data, the results of the ACAR were firstly compared with the three established artifacts removal algorithms, the CAR, the FACAR, and the ARX methods. The FACAR algorithm proposed by Rehbaum and Farina is a

modified CAR [17], it can adaptively select channel subset based on the channel-wise signal intensity to generate the reference; The ARX algorithm is proposed by Wang and Roe [22], an automatic method based on the ANC and the autoregressive model with exogenous input can remove the power line noise. Figure 3 shows an example of multichannel LFP signals denoised by different methods. Compared to the original signals, these methods can clean the artifacts for much of the time for most channels. However, the CAR introduced the artifacts to channels where it was not initially presented, such as 7, 8 and 14. The FACAR and the ARX had no detrimental effects on cleaning noise of channels, but they still failed to remove much of the contamination, such as 10, 12 and 13. By contrast, the ACAR suppressed the spatially correlated artifacts obviously and avoided disturbing the channels where the artifacts was not presented.

The artifacts removal performance of the proposed method has also been evaluated at different SNR. As the results shown in Table 2, the reconstructed data based on the proposed method performs with a higher Δ SNR and a smaller RMSE, comparing to the reconstructed data using the other three methods. For the Δ SNR, an average of the proposed method is 1.5 times more than that of the CAR method, 4.1 times of the FACAR, and 2.8 times of the ARX method. For the RMSE, an average of the proposed method is less than other three methods, 30.3% of the CAR method, 74.2% of the FACAR method, 66.7% of the ARX method. However, the Δ SNR decreases and the RMSE increases slowly with the increase of SNR, which indicates the denoised performance of the proposed method in a lower SNR may be much better than that in a higher SNR, this is in agreement with theoretical analysis. An example

Fig. 3 Example of LFP artifacts removal for synthesized data (SNR = 0.50)

Table 2 Quantitative comparison of proposed method with other methods on artifacts removal for different SNR

SNR	CAR	FACAR	ARX	ACAR
<i>ΔSNR</i>				
0.50	4.4 ± 0.8**	1.6 ± 1.1**	2.3 ± 3.4*	6.6 ± 1.1
0.75	3.4 ± 0.3*	0.9 ± 0.7**	2.9 ± 2.9	4.9 ± 0.9
1.00	2.6 ± 0.3	0.8 ± 1.1*	2.5 ± 3.0	3.5 ± 1.7
1.25	1.9 ± 0.1	0.3 ± 1.0*	1.1 ± 1.8	1.8 ± 1.6
1.50	1.2 ± 0.1	0.2 ± 0.6	0.4 ± 2.4	0.4 ± 0.7
<i>RMSE</i>				
0.50	8.6 ± 1.1**	11.5 ± 1.4**	11.0 ± 3.0*	6.6 ± 0.7
0.75	7.8 ± 0.5*	10.1 ± 0.9**	8.2 ± 2.4	6.4 ± 0.7
1.00	7.3 ± 0.5	8.8 ± 1.2*	7.4 ± 2.4	6.4 ± 1.1
1.25	7.1 ± 0.3*	8.4 ± 1.1*	7.5 ± 1.5	6.9 ± 1.3
1.50	6.7 ± 0.3	7.4 ± 0.6	7.2 ± 1.6	7.2 ± 1.4

Values for Δ SNR and RMSE are: mean ± standard deviation

* $p < 0.05$

** $p < 0.001$. Note that the asterisks indicate statistically significant difference compared to outcome of the ACAR method. $n = 49$, all synthesized data sets

of ACAR denoised performance under different SNR was shown in Fig. 4.

3.2 Results from real neural recordings

Next the proposed method was applied to the real data and compared with the CAR, the FACAR, and the ARX methods, the results had been shown in both Figs. 5 and 6. Compared to the other three methods, the spatially correlated artifacts was clearly eliminated by the proposed method. But similar to the synthesized data, the CAR introduced the new artifacts to some channels, such as 1 and 4 in Fig. 5, and also failed to provide much improvement to the artifacts at some channels, such as 6 and 15 in

Fig. 5. The FACAR performed better than the CAR, but still failed to remove much of the contamination. The ARX and the ACAR consistently removed most of artifacts and avoided disturbing the channels where the artifacts was not presented. In comparison with the ARX, the ACAR removed all spatially correlated artifacts and most of the large artifacts, although a small spike is still noticeable which is most likely due to the result of the filter adapts not quickly enough to such a large artifacts.

To quantify the artifacts removal performance, we measured the correlation of LFP before and after artifacts removal and compared its results with those obtained by the other methods. For the original signals, the correlation among the channels was strong, most were above 0.9 (Fig. 7a). Compared with the original signal, the correlation coefficients of denoised LFP had an obvious decrease. Moreover, compared with the CAR and the FACAR methods, the ARX and the ACAR methods eliminated the 50 Hz line noise (Fig. 7b). It should be noted that in addition to the power line noise, the ACAR was able to remove the DC offset and correlated drift (Fig. 7b inset figure). Figure 7c shows the correlation coefficients change before and after denoised for all the animals. In general, for all datasets, most of artifacts removal methods significantly decrease the correlation among the channels. Note that the $\Delta\rho$ obtained by the ACAR was significantly more than other three denoised methods for all subjects except the P009 pigeon. The results further indicated the effectiveness of the ACAR for the spatially correlated artifacts.

4 Discussion

In this study, a spatially correlated artifacts removal method for the LFP based on the ANC using the reference data from the CAR technique was proposed. In the method,

Fig. 4 Artifact removal example by the ACAR method for synthesized data with different SNR. **a** Original data; **b** Denoised data; **c** Error data. Note that although the denoised data is different under different SNR, the error data were similar, the RMSE from left to right is 4.1, 5.7, 7.5, 6.9, and 6.6

Fig. 5 Example of LFP artifacts removal for real data recorded from Hp of a pigeon (16 channels)

Fig. 6 Example of LFP artifacts removal for real data recorded from Hp of a pigeon (32 channels)

a channel was firstly selected by the correlation with the data between the channel and the CAR before generating the reference data, then the reference data was smoothed to improve the speed and consistency of convergence. Moreover, the reference was calculated for each channel

with the remaining channels instead of all candidate channels, the modification did improve the quality of the reference. Although it looked similar to many previous reports, the method provided a more practical solution to artifacts removal for the *in vivo* LFP recorded from

Fig. 7 Results for real data. **a** The correlation coefficients of LFP obtained by different methods. **b** The corresponding mean power spectrum ($n = 16$, all channels). The *inset* illustrates the greater detail which was marked by the *black rectangle*. **c** The $\Delta\rho$ for the denoised LFP using different methods. *Error bars* indicate the standard deviation of the mean $\Delta\rho$

microelectrode arrays. We quantified its performance with synthesized data and real data recorded from the Hp of pigeons.

For the synthesized data, compared with the other three methods, the reconstructed data based on the proposed method performed a higher ΔSNR and a smaller RMSE (see Table 2). In addition, the proposed method had a better performance in a lower SNR, this was in agreement with theoretical analysis. For the real data, compared with the original signal, the proposed method was able to remove the spatially correlated artifacts and avoid disturbing the channels where the artifacts was not presented (see Fig. 4). In addition, the ACAR was also able to remove the DC offset and correlated drift (see Fig. 5b). Compared with the original signal, the correlation coefficients of denoised LFP had an obvious decrease (see Fig. 5a), and the correlation coefficients changed before and after denoised by the ACAR significantly more than that by the CAR, the FACAR, and the ARX methods (see Fig. 5c).

Closer to the ACAR method, Kelly et al. [16] also applied the ANC and the CAR (KACAR) to remove the common-mode artifacts in multichannel ECoG neural recordings. The difference between the two methods was that the KACAR used the weighted CAR as a reference signal. More specifically, for the KACAR method, the correlation between the reference and the ANC output was as a weight for each channel in calculating CAR, and for

the ACAR method, the correlation between the CAR and each channel signal was applied to select the appropriate channels to generate the reference, and for each channel, the reference was calculated with the remaining channels instead of all channels. Compared with the KACAR, the ACAR had the slight computational burden and was easy to realize. Moreover, in theory, based on the formula (1), the $\hat{n}_t = c \times n_t$, $c = \sum_k w_k / K$, whether $w_k = 1$ or other constant, it has hardly any effect on the results. We think whether the signal includes the spatially correlated artifacts is important for the performance of the methods. In addition, in the ACAR, both the signal normalized by the z-score before generating the reference data and the reference smoothed by a moving average filter improved the speed and consistency of convergence as well as provided a more ideal reference for the adaptive filter.

Moreover, the proposed method does not require any subjective input and can be seamlessly integrated with any recorded LFP processing algorithm as long as multiple recording sites are presented. However, there are situations where it might not be the best choice for common-mode artifacts removal. When the noise had no amplitude change among the channels, the standard CAR performed better. In addition, the proposed method is only a basic common-mode artifacts removal technique, because the background noise of *in vivo* LFP recordings is too complex, it is not realistic to remove all noise. However, compared with the established artifacts removal methods, the ACAR is a

reliable technique, whose performance more closely approximates the theoretical differential recording. It is therefore possible that this method can provide a fundamental processing technique to be applied to LFP data before further analyses are carried out.

5 Conclusion

In summary, this study proposed a spatially correlated artifacts removal method, named as adaptive common average reference, combining the strengths of the ANC filter with the CAR technique. Before generating the reference using the CAR, the correlation between the CAR and each channel signal was calculated to automatically select candidate channels. Moreover, for each channel, the reference was calculated with the remaining channels instead of all candidate channels. The performance was evaluated in both synthesized data and real data, and the results were compared with the standard CAR, the FACAR, and the ARX methods. The results demonstrate that the ACAR performs better than the other three algorithms, especially in a lower SNR. What's more, feasibility of this method was provided theoretically. This method removes the correlated artifacts, thus allows the study of functional connection analysis among recording channels. It can be also applied for brain machine interfaces (BMI) to provide an effective preprocessed method. Further research in distortion or correlation between denoised LFP and original LFP is necessary for fully demonstrating the effectiveness of the proposed method. Improving the computational efficacy of the ACAR and proposing an extension of the method to pure online scenarios will also be further studied.

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Compliance with ethical standards

Conflict of interest The authors confirm that this article content has no conflict of interest.

References

- Belitski A, Panzeri S, Magri C, Logothetis NK, Kayser C. Sensory information in local field potentials and spikes from visual and auditory cortices: time scales and frequency bands. *J Comput Neurosci*. 2010;29(3):533–45.
- Liu XY, Wan H, Shang Z, Shi L. Automatic extracellular spike denoising using wavelet neighbor coefficients and level dependency. *Neurocomputing*. 2015;149:1407–14.
- Scherberger H, Jarvis MR, Andersen RA. Cortical local field potential encodes movement intentions in the posterior parietal cortex. *Neuron*. 2005;46(2):347–54.
- Magri C, Schridde U, Murayama Y, Panzeri S, Logothetis NK. The amplitude and timing of the BOLD signal reflects the relationship between local field potential power at different frequencies. *J Neurosci*. 2012;32(4):1395–407.
- Hwang EJ, Andersen RA. The utility of multichannel local field potentials for brain-machine interfaces. *J Neural Eng*. 2013;10(4):1–12.
- Whitmore NW, Lin S. Unmasking local activity within local field potentials (LFPs) by removing distal electrical signals using independent component analysis. *NeuroImage*. 2016;132:79–92.
- Islam MK, Rastegarnia A, Nguyen AT, Yang Z. Artifacts characterization and removal for in vivo neural recording. *J Neurosci Methods*. 2014;226:110–23.
- Paralikal KJ, Rao CR, Clement RS. New approaches to eliminating common-noise artifacts in recordings from intracortical microelectrode arrays: inter-electrode correlation and virtual referencing. *J Neurosci Methods*. 2009;181:27–35.
- Zareen M, Yin H. Information quantification of empirical mode decomposition and applications to field potential. *Int J Neural Syst*. 2011;21(1):49–63.
- Magri C, Mazzoni A, Logothetis NK, Panzeri S. Optimal band separation of extracellular field potentials. *J Neurosci Methods*. 2012;210(1):66–78.
- Siegel M, König P. A functional gamma-band defined by stimulus-dependent synchronization in area 18 of awake behaving cats. *J Neurosci*. 2003;23(10):4251–60.
- Belitski A, Gretton A, Magri C, Murayama Y, Montemurro MA, Logothetis NK, Panzeri S. Low-frequency local field potentials and spikes in primary visual cortex convey independent visual information. *J Neurosci*. 2008;28(22):5696–709.
- Sweeney KT, Ward TE, McLoone SF. Artifacts removal in physiological signals-practices and possibilities. *IEEE Trans Inform Technol Biomed*. 2012;16(3):488–500.
- Sweeney KT, McLoone SF, Ward TE. The use of ensemble empirical mode decomposition with canonical correlation analysis as a novel artifacts removal technique. *IEEE Trans Biomed Eng*. 2013;60(1):110–23.
- Safieddine D, Kachenoura A, Albera L, Birot G, Karfoul A, Pasnicu A, Biraben A, Wendling F, Senhadji L, Merlet I. Removal of muscle artifacts from EEG data: comparison between stochastic (ICA and CCA) and deterministic (EMD and wavelet-based) approaches. *EURASIP J Adv Signal Proc*. 2012;2012(127):1–15.
- Kelly JW, Siewiorek DP, Smailagic A, Wang W. Automated filtering of common-mode artifacts in multichannel physiological recordings. *IEEE T Biomed Eng*. 2013;60(10):2760–70.
- Rehbaum H, Farina D. Adaptive common average filtering for myoelectric applications. *Med Biol Eng Comput*. 2015;53(2):179–86.
- Ludwig KA, Miriani RM, Langhals NB, Joseph MD, Anderson DJ, Kipke DR. Using a common average reference to improve cortical neuron recordings from microelectrode arrays. *J Neurophysiol*. 2009;101(3):1679–89.
- Widrow B, Glover JR, McCool JM, Kaunitz J, Williams CS, Hearn RH, Zeidler JR, Done E, Goodlin RC. Adaptive noise cancelling: principles and applications. *Proc IEEE*. 1975;63(12):1692–716.
- Wan H, Shi L, Liu XY, Chen SL, Qin ST, Wang ZL, Hai X, Li XL. A brain stereotaxic atlas with four positioning points for pigeon. *China Patent 201510264896.9*, 2015-09-23.
- Oyeka ICA, Ebuh GU. Modified wilcoxon signed-rank test. *Open J Stat*. 2012;2(2):172–6.
- Wang Z, Roe AW. Trial-to-trial noise cancellation of cortical field potentials in awake macaques by autoregression model with exogenous input (ARX). *J Neurosci Methods*. 2011;194(2):266–73.