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Correction to "Statistically Reconstructed Multiplexing for Very Dense, High-Channel-Count Acquisition Systems"

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The goal of the SRMA algorithm in our paper [1] is to estimate and reduce the spectral contribution of aliased thermal noise, to improve the signal-to-noise ratio (SNR) for heavily multiplexed neural recording systems, where implementing adequate antialiasing filters is a challenge.

Here we report on corrections pertaining to Section III.G in our paper [1]. These corrections address the incorrect statements regarding the effects of thermal noise aliasing, the consequence of this error on the general applicability of our processing strategy, and our revised recommendations on processing under-sampled spike (action potential) recordings. The discussion of the trade-off between area and noise for multiplexed acquisition systems, the quantifications on SNR improvements for sinusoid signals using our reported processing strategy, and the hardware descriptions provided in [1] remain valid. We will also show here that SRMA does improve SNR for action potential recordings from highly multiplexed acquisition systems with incomplete antialiasing in typical scenarios, the primary application domain of [1]. However, when the spectral characteristics of the signal are known, it may deliver little utility over a linear filter in many cases.

There were two errors made in Section III.G in [1] that affect the treatment of both the amplitude and phase of noise estimates. These have implications on the efficacy of the SRMA algorithm.

The first of these errors was the assumption that the under-sampled thermal noise averages in the first Nyquist zone during aliasing, when it in fact *sums*. This error affects the amplitude estimates of the aliased noise. During aliasing, the complex Fourier terms $\hat{x}_{f,i}$ in the second (*i* = 2) to the *n*'th Nyquist zone fold down into the first Nyquist Zone (*i* = 1),

where *f* is the frequency in the first Nyquist zone into which the aliased terms fold. We denote the sum of these aliased complex terms as x_f

$$x_f = \sum_{i=2}^n \hat{x}_{f,i} \tag{1}$$

Given the stationarity and the flat spectrum of thermal noise, these complex terms are independent. Both $\text{Re}(\hat{x}_{f,i})$ and $\text{Imag}(\hat{x}_{f,i})$ have zero mean. Thus, the variance of the sum of the aliased Fourier terms is the sum of the variances of these Fourier terms for n - 1 foldings into the first Nyquist zone:

$$\operatorname{Var}(x_f) = \operatorname{Var}\left(\sum_{i=2}^n \hat{x}_{f,i}\right) = \sum_{i=2}^n \operatorname{Var}(\hat{x}_{f,i})$$
(2)

The variance of the aliased Fourier terms for each frequency increase with aliasing. The power arising from aliasing is $|x_{f}|^{2}$. This, therefore, also grows with *n*.

The second consequential error affects the phase estimation of aliased noise. The SRMA algorithm uses the phase information from the aliased recording (y_m in Section III.G of [1]) to construct complex vectors to represent the aliased thermal noise. Specifically, it uses, for some first-Nyquist-zone frequency f, the phase θ_{f} .

$$\theta_f = \arg\left(s_f + t_f + x_f\right) \tag{3}$$

where $s_{f_i} t_{f_i}$ and x_f are the vectors representing the signal, the non-aliased noise, and the aliased noise, respectively, at frequency f. The true phase for the aliased noise is $\arg(x_f)$. The additional terms s_f and t_f add errors to the phase estimate. The aliased and non-aliased noise are written separately in Equation (3) for completeness, but are otherwise identical in characteristics and indistinguishable from each other in practice.

In Section III.G of [1], it is stated that aliasing causes a convergence to zero phase for thermal noise folded into the first Nyquist zone, which is incorrect. If this were true, then θ_f in Equation (3) would have been able to correctly isolate the phase of the signal plus non-aliased noise. Because the angular distribution of thermal noise is uniform, the circular mean of aliased and non-aliased thermal noise is undefined. Furthermore, as noted above, aliasing sums, rather than averages, the down-folded complex terms.

Finally, as a consequence of the foregoing errors, the SRMA algorithm, therefore, does not mimic the uniform spectral spreading of aliased contents by compressive sensing, through randomized sampling, as mentioned in Section III.G.

The SRMA algorithm subtracts, for each first-Nyquist-zone frequency f, a vector v_f comprised of the average voltage ρ' contributed by aliasing and the phase θ_f from the postaliasing data:

$$\nu_f = \rho' e^{j\left(\theta_f\right)} \tag{4}$$

For frequencies containing no signal content, the amplitude for the aliased thermal noise vector, at frequency f, after SRMA processing is $|x_f - v_f|$. It may be smaller than, equal to, or greater than (with an accompanying 180° phase change for the post-processed complex term) the pre-processed amplitude $|x_f|$. The first two conditions will cause partial and complete noise amplitude suppression, respectively. The last, noise-increasing condition

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occurs if we subtract more than twice the amplitude at frequency *f*, that is, when $\rho' > 2|x_f|$ or equivalently $|x_f| < \frac{1}{2}\rho'$.

We generated simulated, aliased thermal noise, for a system with 5 MHz bandwidth and under-sampled at 10 kHz, analogous to the CMOS-based recording system we presented in [1]. The frequency-domain amplitude distribution of this aliased noise has a skewed distribution (Fig. 1). As indicated by Equation (4), we use the average amplitude ρ' from this distribution as the amplitude for the aliased thermal noise estimate.

In Fig. 1 approximately 82% of the amplitudes are greater than or equal to $\frac{1}{2}\rho'$, while the

remaining 18% are less than $\frac{1}{2}\rho'$, implying that SRMA would reduce the noise amplitude in approximately 82% of the frequencies. Repeating this simulation experiment 10 times, we find that SRMA had an 82.12 \pm 0.04% (mean \pm standard error of mean) chance of suppressing the amplitude at frequencies containing only noise, suggesting that we can expect SRMA to generally suppress noise at frequencies containing insignificant signal content.

To ensure SNR improvement for the significant-signal-containing frequencies, the SRMA algorithm should ideally suppress the voltage contributed by aliasing, as above, and also correct the phase change due to aliasing. As indicated by Equation (3), SRMA uses for noise estimation the phase information from the post-aliasing data. Here, because the phases of the signal s_f and the non-aliased thermal noise t_f are not known *a priori*, SRMA is unable to recover the phase of the aliased noise x_f . Due to this additional uncertainty, the algorithm has decidedly poorer performance in the significant-signal-containing frequencies comparing to those frequencies containing primarily noise.

The foregoing analysis implies that SRMA favors signals with a narrow frequency spectrum, such as, in the limiting case, the sinusoids we used in [1]. As the signal bandwidth broadens, one would typically expect a decrease in performance.

We showed that the SRMA algorithm improved SNR for under-sampled sinusoids with thermal noise [1]. Does it also improve the SNR of under-sampled spike recordings? Given the foregoing amplitude and phase estimation errors, how does it compare to a band-pass filter for such spike recordings?

For these tests, we constructed a 5-MHz dataset consisting of action potentials, band-limited to 300 - 3k Hz (Fig. 2(a)), and computationally generated thermal noise, with a SNR of 5:1. The gold-standard data λ is generated by band-pass filtering the 5-MHz traces between 300 – 3k Hz, followed by decimation to 10 kHz. This simulates conventional sampling. The aliased data α is generated by decimating the 5-MHz traces to 10 kHz. The aliased, SRMA-processed data β is generated by decimation to 10 kHz, followed by applying SRMA. For comparison with a band-pass filter, data γ is generated by decimating the 5-MHz traces to 10 kHz, followed by filtering between 300 – 3k Hz. To assess SNR performance, we compared the sum-of-square-error (SSE) for α , β , and γ against the gold standard λ .

In total, the comparison statistics encompass 222 spikes, each with 28 comparison points, for SSE calculation. Two observations are apparent in Fig. 2(b). First, SRMA improves the SNR of these under-sampled spike recordings. The reduction in SSE is significant (p < 0.001, 2-sample t-test). Second, while the SRMA-processed data has lower mean SSE than that of the band-pass filter, the difference is not significant (p = 0.073, 2-sample t-test).

Here we show that the SRMA algorithm improves the SNR for under-sampled spike recordings, just as it does for sinusoids [1]. However, SRMA does not improve the SNR of under-sampled spike recordings beyond those achieved by a bandpass filter in a statistically significant manner. Since bandpass filters are routinely used as part of electrophysiological analysis, this suggests that SRMA may have limited utility over a linear filter here, when the bandwidth of the target signals is known.

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Frequency-domain amplitude distribution of simulated thermal noise, for a system with 5 MHz bandwidth and under-sampled at 10 kHz. The mean amplitude is denoted ρ' .





Fig. 2.

SNR improvement of spikes by SRMA and comparison to a bandpass filter. (a) Action potentials of 300 - 3k Hz bandwidth. (b) Comparison of sum-of-square-error (SSE) between processing conditions.