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Iterative Covariance-based Removal of Time-Synchronous Artifacts: Application to Gastrointestinal Electrical Recordings

Jonathan C. Erickson,

Department of Physics and Engineering, Washington and Lee University, Lexington, VA 24450 USA

Joy Putney,

Department of Physics and Engineering, Washington and Lee University, Lexington, VA 24450 USA

Douglas Hilbert,

Departments of Mathematics and Biochemistry, Washington and Lee University. He is now with Thomas Jefferson Medical College, Philadelphia, PA USA

Niranchan Paskaranandavivel,

Auckland Bioengineering Institute, University of Auckland, New Zealand

Leo K. Cheng,

Auckland Bioengineering Institute and the Department of Surgery, Vanderbilt University, Nashville, TN, USA

Greg O'Grady, and

Auckland Bioengineering Institute and the Department of Surgery, University of Auckland, New Zealand

Timothy R. Angeli

Auckland Bioengineering Institute, University of Auckland, New Zealand

Jonathan C. Erickson: ericksonj@wlu.edu

Abstract

Objective—The aim of this study was to develop, validate, and apply a fully automated method for reducing large temporally synchronous artifacts present in electrical recordings made from the gastrointestinal (GI) serosa, which are problematic for properly assessing slow wave dynamics. Such artifacts routinely arise in experimental and clinical settings from motion, switching behavior of medical instruments, or electrode array manipulation.

Methods—A novel iterative COvariance-Based Reduction of Artifacts (COBRA) algorithm sequentially reduced artifact waveforms using an updating across-channel median as a noise template, scaled and subtracted from each channel based on their covariance.

Results—Application of COBRA substantially increased the signal-to-artifact ratio (12.8 ± 2.5 dB), while minimally attenuating the energy of the underlying source signal by 7.9% on average (-11.1 ± 3.9 dB).

Conclusion—COBRA was shown to be highly effective for aiding recovery and accurate marking of slow wave events (sensitivity = 0.90 ± 0.04 ; positive-predictive value = 0.74 ± 0.08) from large segments of *in vivo* porcine GI electrical mapping data that would otherwise be lost due to a broad range of contaminating artifact waveforms.

Significance—Strongly reducing artifacts with COBRA ultimately allowed for rapid production of accurate isochronal activation maps detailing the dynamics of slow wave propagation in the porcine intestine. Such mapping studies can help characterize differences between normal and dysrhythmic events, which have been associated with GI abnormalities, such as intestinal ischemia and gastroparesis. The COBRA method may be generally applicable for removing temporally synchronous artifacts in other biosignal processing domains.

Index Terms

Artifact removal; Biomedical signal processing; Noise cancellation; Gastrointestinal; Slow wave

I. Introduction

The stomach and small intestine exhibit electrical activity known as slow waves (SWs), which help regulate the coordinated contractions of the gastrointestinal (GI) system [1]. Recently, high-resolution (HR) mapping techniques have been used to capture SW activity *in vivo* using hundreds of electrodes applied directly to the organ surface of the stomach and small intestine [2], [3], [4]. Such recordings enable the accurate spatiotemporal characterization of SW initiation and propagation, and have now been applied to study the normal and dysrhythmic, large-scale spatial organization of such activity in the porcine [5], feline [6], and canine [7] small intestine, as well as the porcine [8], canine [9], and human stomach. SW dysrhythmias have been associated with a number of health disorders [10], [11], including spatially-complex SW propagation abnormalities in humans with gastroparesis [12]. Such findings have further fuelled clinical interest in the area of GI high-resolution mapping and dysrhythmia assessment [11], [13], [10], motivating algorithm development to meet experimental and clinical demand.

Because HR mapping techniques require massive amounts of data accumulation, automated algorithms are necessary for processing and analyzing experimental results. Algorithms for detecting SW activation times (ATs) [14] and grouping them into individual wavefronts [15], [16] have already been developed, which allow for the automated production of the isochrone activation maps that quantify propagation patterns. These algorithms and others have been incorporated into a framework known as GEMS, or the Gastrointestinal Electrical Mapping Suite [17], which has facilitated recent large-scale and human GI mapping studies (e.g., [12], [5]). However, the accuracy of these algorithms is negatively impacted when noise corrupts the data, making the activation times of the low amplitude SW events undetectable. This problem is particularly pertinent to procedural human recordings, where

the busy clinical environment and tight recording windows mean that clinically important data may be compromised or lost.

Various types of noise are commonly found in experimental data which are time-synchronous (spatially correlated) across most or all of electrode array. These are most commonly introduced as motion artifacts including respiration and/or a sudden change in tissue-electrode impedance, typically due to repositioning cables or electrode arrays, which is often necessary during experimental recording periods [18]. Because these artifact waveforms are orders of magnitude larger than the SW signals, they mislead the automated detection algorithm and interfere with the detection of SW ATs.

Several algorithms for the identification and removal of time-synchronous artifacts have previously been developed for other applications, but they are suboptimal when applied to GI SW recordings. For example, an approach based on combined Empirical Mode Decomposition and Independent Component Analysis [19] has been demonstrated to successfully remove high frequency common-mode interference from a sparse set of electrograms, but is computationally expensive. The objective of this work, therefore, is to present a novel, computationally inexpensive, fully automated algorithm to eliminate such artifacts while retaining the underlying signal corresponding to GI electrical activity. The core idea is to iteratively process an electrogram to sequentially remove artifacts using an updating noise template generated by filtering a common median reference. Validation was performed using synthetic data and serosal recordings in an established *in vivo* porcine model [20]. The developed artifact removal process recovered large portions of data segments even in the presence of heavily corrupting waveforms that otherwise prevented further SW propagation mapping analysis.

II. Materials and Methods

A. Data Acquisition and Segment Selection

Ethical approval for this data collection was obtained from the University of Auckland Animal Ethics Committee. Serosal recordings (mean duration 27.3 ± 6.1 min) were collected from the proximal porcine jejunum, *in vivo* from 5 pigs. The surgery and recording methods have been described previously [20]. Recordings were performed using validated flexible printed-circuit-board (PCB) electrode arrays [2] encompassing 128 or 256 electrodes (4 mm spacing; 8×16 or 8×32 arrangement; ≈ 17 or 34 cm²), and were acquired at 512 Hz using an ActiveTwo system (Biosemi, Netherlands). Time-synchronous artifacts were intrinsic in the data set, i.e., not introduced artificially. We emphasize that such artifacts arise from extrinsic, non-GI biologic noise sources, not from intrinsic GI contractile activity [21].

After initial visual inspection, a total of 11 data segments, each 40 s in duration, were selected for further analysis based on the criterion that they contained artifact waveforms representative of those most commonly observed during extensive manual analysis. Fig. 1 illustrates three types of artifact typically encountered:

1. Multiple individually short-lived, high-frequency, large amplitude transients with relatively large temporal spacing (Fig. 1, trace i)

2. Prolonged duration, high frequency, large and variable amplitude burst of noise otherwise surrounded by cleanly recorded SW signal (Fig. 1, traces ii and iv)
3. Relatively low amplitude noise, longer time-scale dips related to respiration occurring at an approximately known rate (Fig. 1, trace iii)

Of 11 total segments selected for analysis, four were type 1, two were type 2, and five were type 3, approximately matching their relative rate of occurrence over 5 complete *in vivo* porcine experiments. In addition, expert reviewers manually identified time windows in which type 1 and 2 artifacts occurred for further quantitative performance (section II-G) and SW marking validation analysis (section II-H). Identification of type 3 segments was aided by visual inspection of data segments prior to artifact removal in which false-positive SW events (marked with the FEVT algorithm, see II-H) occurred with a periodicity consistent with the approximately known respiration rate. Given that precise manual identification of the artifact-corrupted time windows in type 3 signals was relatively difficult, they were used for SW marking validation analysis only, i.e., not for quantifying performance metrics. Overall, nine selected data segments were from 256-electrode recordings, and the other two from 128-electrode recordings.

B. Synthetic Data Sets

Synthetic intestinal SW signals were utilized to further validate and quantify the extent to which the COBRA method could reduce artifacts. They were generated using a method developed by Alcaraz and Rieta [22], which has previously been applied to generate synthetic gastric SW signals [23]. One hundred synthetic electrograms representing a 10×10 grid with 5 mm interelectrode spacing were generated at a sampling rate of 30 Hz. Manually identified artifacts from the six porcine *in vivo* serosal recordings characterized as Type 1 or 2 (see Section II-A) were superposed onto the synthetic SW electrograms, thus preserving variation in the polarity, amplitude, and shape of actual recorded artifacts. The advantage of using synthetic data is that the true underlying signals were known, which is in contrast to *in vivo* recordings.

C. Signal pre-processing

For each channel, data was re-sampled at $f_s = 30$ Hz and centered to remove any DC offset. The SALPA (Subtraction of Artifacts by Local Polynomial Approximation) algorithm [24] was implemented to remove baseline wander on a per-channel basis, since it has previously been validated with intestinal recordings for this purpose [25]. The SALPA half-window size was empirically set to 0.5 s. Additionally, a Savitzky-Golay low-pass filter of order 9 and window width 0.5 s (6.8 Hz cutoff) was implemented to remove high-frequency noise. Whereas a 1.7 s window (1.98 Hz cutoff) has previously been validated for optimally preserving SW waveforms in GI serosal recordings [26], [20], we used 0.5 s in this study to minimize distortion of sharp deflections characteristic of common mode artifacts such that they could be properly subtracted at a later step.

D. Artifact Removal Theory

The major steps of the iterative covariance-based removal of artifacts (COBRA) process are summarized in Fig. 2. For each channel i , we assume our electrical recordings Y_i can be modeled as containing the true underlying physiological signal S_i corrupted by a noise template common to all signals N , which is scaled to each channel by a covariance parameter α that describes how much noise is coupled into the experimental data:

$$Y_i = S_i + \alpha_i N \quad (1)$$

To estimate α_i , it is assumed that $S_i N^T = 0$, which asserts that the signal is uncorrelated with the noise:

$$\hat{\alpha}_i = Y_i N^T (N N^T)^{-1} \quad (2)$$

$$\hat{S}_i = Y_i - \hat{\alpha}_i N \quad (3)$$

where $\hat{S}_i$ is the estimate for the true underlying signal S_i . The assumption of $S_i N^T = 0$ is justified on biological grounds. Given the propagating nature of the SW signals, constructing a common average reference noise template using a sufficiently large number of channels (see section III-A) leads to $N \approx 0$ in artifact-free time windows. When an artifact is present, $N \neq 0$ characterizes the corrupting waveform. In such a time window, the assumption of uncorrelatedness may not be strictly true, but given the independent origins of the physiological signal and contaminating artifact, it is still reasonable to expect that $S_i N^T \approx 0$.

E. Noise Template Generation

The common reference template is computed as the median across all channels, with a Savitzky-Golay filter implemented to remove high frequency noise:

$$R[k] = \text{SGfilt}\{\text{Med}_i Y[k]\} \quad (4)$$

where k denotes the integer time index, SGfilt denotes the Savitzky-Golay filtering, and Med_i indicates the median taken across all channels. When a time-synchronous artifact is present, the median will have a large amplitude. At all other instances, the median will be close to zero, assuming that the majority of recordings are mutually uncorrelated across all channels. The choice to use the median instead of the mean was motivated by seeking to avoid undue influence of “bad” channels, with very large instantaneous amplitude, in the computation of the reference signal, as well as artifacts with inverted polarity from cancelling out. The same issues can harm the computation of the common median reference,

but typically to a much lesser extent. Note that it is difficult to differentiate between bad channels and good ones corrupted by artifacts prior to artifact reduction.

High frequency noise in the template can cause a higher baseline energy due to noise amplification. Therefore, high frequency noise was removed using a 9th order Savitzky-Golay filter with a window size of 0.5 s, since this filter has previously been shown to work in GI recordings for this purpose [23], [20]. Large deflections in the reference template $R[k]$ corresponding to the (potential) presence of time-synchronous artifacts were detected using the non-linear energy operator (NEO) transform, which accentuates high-frequency and high-energy signal components [27], [25]:

$$\text{NEO}\{R[k]\} = R[k]R[k] - R[k+1]R[k-1] \quad (5)$$

The detection threshold was set to $\eta\hat{\sigma}$, where η is a user-selectable constant multiplying the estimated standard deviation of the reference template $\hat{\sigma}$, computed using the median of the absolute deviation [28]. Based on extensive user experience, as well as analyzing the performance of COBRA as a function of the threshold value, $\eta = 2$ was determined to be optimal (Section III-A).

The minimal time between two successive and independent suprathreshold events was empirically set to 0.125 s, which allows the algorithm to distinguish successive artifacts which may occur closely in time. For each large deflection in the NEO signal, which may correspond to a time-synchronous artifact, a cleaning window centered on the suprathreshold time points was opened with a half-window size of $T_w = 2$ s. In testing, the half-window size did not affect the end result of cleaning significantly, but a smaller window size (e.g., $T_w = 1 - 2$ s) allowed for more accurate removal of an artifact than larger windows (e.g., $T_w = 5 - 10$ s), especially when multiple artifacts were present in the recording segment being analyzed.

Finally, in order to compute the noise template, the time-windowed reference signal was filtered with a zero-phase forward-reverse digital high-pass Butterworth filter of order 2, with the cutoff frequency set at 0.5 Hz, values which were chosen based on extensive user experience:

$$N = \text{HPF}\{R[k_{\text{win}}]\}, \quad k_{\text{win}} \in [N_c - N_w, \dots, N_c + N_w] \quad (6)$$

where N_c denotes the center of the cleaning window of integer-indexed width $N_w = f_s T_w$.

High-pass filtering at 0.5 Hz (30 cycles per minute) preserved high-frequency content of the artifact waveform and removed any DC offset, such that no step discontinuities were introduced when the scaled noise signal was subtracted from a finite-length data segment. The scaled noise template was subtracted from the recording to return an estimate of the signal using the model described in Equations 1-3. All individual windows containing an

energy spike were processed sequentially, with the partially artifact-reduced (cleaned) signal updating prior to cleaning the next window. When all windows were cleaned, subsequent rounds of noise template generation and cleaning were reinitialized. On each pass of this iterative processing, the size and number of interfering artifacts was reduced without degrading signal quality in segments that did not require cleaning in the first place.

F. Iterative Processing and Stopping Criteria

The process of artifact detection, noise template generation, and cleaning repeated itself until one of the following conditions were met:

- No more large pulses of energy were identified in the reference signal $R[k]$. Formally, there did not exist a time index k for which $\text{NEO}\{\hat{R}[k]\} > \eta\hat{\sigma}$.
- The median value across channels of the covariance parameter was so low that it could be assumed no noise was present in the signal ($\alpha = 0.2$).
- The number of cleaning iterations reached a user-selected maximum number of times allowed, empirically set to 20 in this study.

Iterative processing was necessary when there were multiple artifacts in a recording segment. For example, one artifact may have a much larger amplitude than another. In a single iteration cleaning process, only the first, large artifact would be identified and removed, with the smaller artifact undetected because it was under the noise threshold. However, on a second cleaning iteration, the smaller artifact would now be significantly above the new noise threshold and would be removed as well. In addition, iterative processing allowed for subsets of channels to be cleaned at different iterations, as the noise template continually converged toward the largest uncleaned artifacts remaining.

G. Performance Metrics for Artifact Reduction and Source Signal Attenuation

To quantify the effectiveness of the COBRA method for preserving the underlying source signal and removing artifacts, two well-known metrics were computed—the signal-of-interest attenuation (*SIA*) and the change in signal-to-artifact ratio (*SAR*) [29]. These performance metrics were computed for the 6 *in vivo* data segments in which artifacts were clearly identifiable by manual analysis (Type 1 and 2; see Section II-A), as well as the corresponding synthetic data sets.

The signal-of-interest attenuation was defined as in [29]:

$$\text{SIA} = 10 \log_{10} E \left\{ \frac{(\hat{S}_i[k_c] - Y_i[k_c])^2}{Y_i^2[k_c]} \right\} \text{ (dB)} \quad (7)$$

where $E\{\cdot\}$ indicates the mean value averaging over all electrodes in the array, and k_c denotes the subset of integer time points during which the data segments were inherently clean—i.e., no artifact was manually identified in the pre-processed (filtered-only)

electrograms. Examples of time windows corresponding to k_c are illustrated by gray/overlaid-black regions of electrograms in Fig. 1. Larger magnitude negative values for SIA are achieved when natively clean time segments in the electrograms $Y_i[k_c]$ are minimally distorted after application of the artifact removal method. For example, a SIA value of 0 dB would result from (undesired) complete removal of the signal of interest $\hat{S}_i[k_c]$; a value of -10 dB can be interpreted as 10% distortion of the underlying source signal; and a value of $-\infty$ would mean perfect preservation of it. Note also that the SIA metric essentially indicated the level of decorrelation between the noise template and an electrogram in artifact-free regions.

The metric SAR quantifies the ratio of time-averaged energy of SW signal and artifact signal, pre- and post-application of COBRA:

$$\Delta SAR = 10 \log_{10} E \left\{ \frac{\langle \hat{S}_i^2[k_c] \rangle}{\langle \hat{S}_i^2[k_d] \rangle} / \frac{\langle Y_i^2[k_c] \rangle}{\langle Y_i^2[k_d] \rangle} \right\} \text{ (dB)} \quad (8)$$

Higher values for SAR indicate stronger artifact reduction. In Eqn. 8, the $\langle \cdot \rangle$ operator indicates a time-averaged value, and k_d denotes the subset of integer time points for dirty windows—i.e., where artifacts were manually identified in the pre-processed (filtered-only) electrograms. Examples of artifact-corrupted time windows corresponding to k_d are illustrated by light blue regions of electrograms in Fig. 1. This analysis assumed that the amplitude of the underlying SW signal remained approximately constant regardless of whether a time window was artifact-corrupted. The validity of this assumption relies on the fact that artifacts are extrinsic to underlying GI signals, and that there is no physiological reason to expect large variations in SW amplitude over only tens of seconds under experimental conditions of these studies. In sum, computing SAR using complementary time windows delineating natively clean and artifact-corrupted portions of electrograms, for which the true underlying signal cannot be known, allowed the COBRA method to be evaluated on actual recorded data, which can be considered as the “final testbed” for an artifact removal approach [29].

H. Validation: Slow Wave Marking of in vivo Data

For each of 11 *in vivo* data segments cleaned with COBRA, the FEVT algorithm [14], with parameter values previously optimized for small intestine serosal recordings [20], was used to detect activation times of SWs. All FEVT marks were removed from dead channels, heuristically defined, on biophysical grounds, as having very small average absolute deviation, i.e.,

$$\frac{1}{N_{\text{samps}}} \sum_k |Y_i(k)| < V_{\text{thresh}}. \quad (9)$$

We empirically chose $V_{thresh} = 2 \mu V$. Note that removing marks from dead channels is more accurately performed post-artifact removal, as it may not be possible to identify *a priori* dead channels which also contain large amplitude artifacts. The automated FEVT activation times obtained were compared to manually verified activation times in order to determine true positives (TP), false positives (FP), and false negatives (FN). To assess the performance of the algorithm, the Sensitivity (*Sens.*), Positive-predictive value (*PPV*), and an overall measure $A_{roc} = Sens. \times PPV$ were computed as previously defined in [14]. Note that the range of all 3 validation metrics is 0–1, with a value of 1 indicating perfect performance. The value of *Sens.* decreases with increasing FNs; *PPV* decreases with increasing FPs.

I. Dependence on Detection Threshold and Number of Electrodes

In order to more fully characterize the performance of COBRA, analysis was carried out using all 11 *in vivo* data sets using a range of detection threshold values ($\eta = [1, 2, 3, 5, 7, 10]$) and channel numbers ($N_{chans} = 2$ –256, in powers of 2). All possible parameter value combinations for η and N_{chans} were tested. For statistical power, a total of $\sqrt{N_{array}/N_{chans}}$ trials were repeated, where N_{array} is the number of channels in the recording array (either 128 or 256). For cases when $N_{chans} < N_{array}$, subsets of electrode channels were chosen at random. Note that $N_{chans} = 1$ was not tested during validation because implementing COBRA with only a single channel would subtract a bandpass-filtered version of the signal from itself, guaranteeing significant distortion of the SW waveform.

III. Results

A. Performance Metrics

As illustrated in Fig. 1, substantial reduction of artifacts was achieved with application of COBRA to *in vivo* data sets. Plausible SW waveforms were recovered in time windows where large artifacts were present, and conservation of the desired signal components was excellent in non-artifact corrupted regions.

Similar outcomes were observed for synthetic data sets. Fig. 3 shows an example synthetic signal before and after application of the COBRA method, highlighting strong suppression of the artifact as well as minimal attenuation of the SW waveform. Analyzing all synthetic data segments with $\eta = 2$, SAR was 8.9 ± 4.7 dB (mean $\pm$ s.d.), and SIA was -14.3 ± 5.0 dB. These values are in reasonable accord with *in vivo* data set analysis done with $N_{chans} = 128$, for which values of $SAR = 11.1 \pm 3.5$ dB and $SIA = -12.3 \pm 3.7$ dB were achieved.

For *in vivo* data, Fig. 4A-B summarizes how SW signal attenuation and artifact reduction strength depended on the detection threshold and channel count. Not surprisingly, performance of the COBRA method increased monotonically with channel count. Higher channel counts allowed for better decorrelation of SW waveforms as well as averaging out other fluctuations in the electrograms, thereby generating a noise template in which the artifact was well-isolated. Both SIA and SAR showed rapid gains up to $N_{chans} = 32$, leveling off for higher channel counts. Performance of the COBRA method was fairly insensitive to the detection threshold value for $\eta \leq 3$, but degraded for larger values tested ($\eta = 5$). When the threshold is set too high, some candidate artifact-corrupt windows were not

detected and subsequently removed. Setting η to a lower value ensured small artifacts would be detected and removed. In the event that the detection step was triggered by a statistical fluctuation in the NEO detection signal for small values of η , the value for α was small, such that the electrogram signal was distorted only slightly during the cleaning process.

B. Slow Wave Marking Validation

The accuracy of SW marking with the FEVT increased with channel count (Fig. 4C-E), attributed to the stronger artifact suppression and lower signal distortion achieved with larger values of N_{chans} . In general, when using all channels ($N_{chans} = N_{array}$), artifact removal produced sufficiently clean data windows such that the sensitivity was very high across all trial data segments (0.90 ± 0.04). PPV was lower (0.74 ± 0.08) because FPs could occur where small remnants of a large artifact still dominated the FEVT SW identification, even when cleaning substantially increased the SAR. As an overall measure, A_{roc} attained a value of 0.68 ± 0.08 , which compared reasonably well to the value of 0.77 reported for electrograms inherently free of any common-mode artifacts [14].

In practice, the COBRA algorithm's performance was highly beneficial for recovering useful data from artifact-corrupted recordings in which SWs were otherwise undetectable, even by manual analysis carried out by an experienced investigator. This overall benefit is illustrated in Fig. 4E via comparison of A_{roc} values before (open black circles) and after application of COBRA with $\eta = 2$ and using the full electrode array (green triangles). In all instances, COBRA improved the ability of the FEVT method to properly mark SWs ($PPV = 0.19 \pm 0.18$; $Sens. = 0.32 \pm 0.30$; $A_{roc} = 0.31 \pm 0.25$). Drastic performance gains were noted for data segments which suffered from more severe contamination with multiple, very large amplitude Type 1 and 2 artifacts ($PPV: 0.31 \pm 0.16$; $Sens. = 0.60 \pm 0.21$; $A_{roc} = 0.52 \pm 0.15$), with more modest gains observed for data segments with Type 3 artifacts, which had an initially higher SAR ($PPV = 0.04 \pm 0.03$; $Sens = 0.04 \pm 0.03$; $A_{roc} = 0.06 \pm 0.05$). Overall, application of COBRA to reduce artifacts significantly increased the accuracy of SW mapping over long time periods.

C. Effect of Removing Dead Channels

Dead channels were identified in 6 of 11 data segments. For these data segments, $\approx 5\%$ of channels were identified as being dead (mean $\pm$ s.d. = 14 ± 10 ; median = 18; range = 1-23), with 61 ± 44 SW marks removed that would have otherwise been tallied as FPs. A total of 536 ± 148 FPs remained, and there were 1561 ± 291 TPs marked across all electrodes. Identification of dead channels therefore realized a small positive gain in PPV from 0.72 to 0.74. The total average increase in PPV with application of the COBRA method was 0.21 (0.53 ± 0.09 before vs. 0.74 ± 0.08 after). Thus, the majority of the gain realized was due to actual artifact reduction. Note that sensitivity is not affected by removal of FEVT SW activation marks from dead channels, as they are all FPs.

D. Computational Efficiency

Using a standard Intel® Core™i7, 2.4 GHz CPU with 8 GB of RAM running MATLAB 2014a (The Mathworks, Inc., Natick, MA), application of COBRA to HR mapping data sets consisting of $256 \text{ channels} \times 1200 \text{ samples/channel} \times 64 \text{ bits/sample}$ required only 0.24

± 0.16 s of processing time. The variability reflects the number of individual artifacts and iterations needed to clean a particular data segment.

We compared the computational efficiency of our method to a combined empirical mode decomposition (EMD) and independent component analysis (ICA) approach for reducing high-frequency artifacts in the electroenterogram developed by Ye-Lin et al [19]. In our hands, the total computation time required was 310 ± 7 s (≈ 26 s for EMD [30] and 284 ± 7 s for fast fixed-point ICA [31]). The variability reflected that the ICA objective function optimization depended on a randomly chosen initial condition as well as the variability in number and nature of the artifacts in each data segment.

Based on this empirical evaluation, COBRA was about $1000\times$ faster overall. Theoretically, the computational complexity of COBRA is dominated by generation of the noise template using the across-channel median. For an $N_{chans} \times N_{samps}$ data matrix, the upper bound on computational complexity is $O(N_{samps} \cdot N_{chans} \log N_{chans})$. All other linear arithmetical operations scale as $O(N_{samps} N_{chans})$. Computational efficiency is likely to be a major benefit, particularly for real-time clinical analysis and for larger data sets.

E. Illustrative Examples of COBRA

Fig. 5(a) illustrates a single electrode signal that was cleaned over multiple iterations, progressing from raw (top) to fully cleaned (bottom). The largest two artifacts were cleaned on the first pass, then remaining smaller artifacts were cleaned at later iterations. The second large artifact (at $t \approx 16$ s) is sufficiently cleaned, enabling the FEVT algorithm to accurately mark the surrounding ATs, but a noticeable dip is a vestige of the cleaning process.

To emphasize the process and performance of the artifact removal method, Fig. 5(b) shows 12 electrograms oriented in linear fashion on a 256-channel array, shown in a stacked configuration to emphasize the propagating nature of SWs. Uncleaned (gray) and artifact reduced signals (black) are shown. The two most prominent artifacts are plainly visible (at $t \approx 1$ and 16 s). The iterative artifact removal process recovered the underlying SW waveforms, enabling further post-processing and analysis, even in situations where an artifact was superimposed directly on a SW AT.

Fig. 5(c) shows a ladder plot of FEVT marks made on an entire 256-channel electrode array before and after artifact reduction. The false positives in the pre-cleaned electrograms arise from the four time-synchronous artifacts indicated by blue arrowheads in Fig. 5(b). Due to these artifacts, it is not possible to generate meaningful isochronal contour SW maps from the original data. However, proper marking of ATs is dramatically improved following artifact removal, as seen in Fig. 5(a) and (b). The sloping nature of the ladder plot in Fig. 5(c) indicates the propagation of successive SWs, as observed in Fig. 5(b). While some false positives persisted, generally manifesting in the ladder plot as marks made in the “white space” between true positive marks, the combination of fully automated COBRA and FEVT performed admirably, with $Sens. = 0.96$, $PPV = 0.73$, and $A_{roc} = 0.70$.

Fig. 6(a) shows COBRA applied to a particularly difficult case with an electrode recording corrupted by a prolonged, high frequency artifact that began abruptly at $t \approx 18$ s. The SW

activity in the uncleaned signal was impossible to accurately discern in the presence of the artifact. Additionally, the artifact also caused missed detection of ATs in the uncorrupted window prior to the onset of the artifact. Following cleaning, 5/5 ATs were correctly identified by FEVT in the uncorrupted data segment, and SW activity originally swamped by the artifact is plainly visible with the majority of AT marks (4/6) correctly identified. Note that successive iterations improve the quality (signal to artifact ratio) of the electrogram. While the first iteration largely removes the artifact, subsequent passes further reduce the continued interference near where the artifact originally began ($t = 18$ s). The relatively large rising deflection at the end of the data segment is due to the noise template filtering step on the edge of a finite data segment. The largest artifact in the uncleaned signal at $t \approx 28$ s leaves behind a relatively sharp downward deflection likely responsible for the FP/FN pair observed. On net, prior to artifact reduction there were 0 TPs, 11 FNs, and 5 FPs identified; after cleaning there were 9 TPs, 2 FNs and 2 FPs.

Even when extreme artifacts were present, the COBRA algorithm was able to successfully recover a data segment that was otherwise unusable. For example, Fig. 6(b) shows a ladder plot of FEVT marks across all 256 electrodes before and after COBRA-cleaning. Prior to cleaning, the large artifact in the latter half of the data segment scaled up the FEVT detection threshold such that true SW ATs could not be properly identified. Additionally, FEVT incorrectly marked the sharpest downward transients in the artifact-corrupted portion as FPs. After cleaning, data recovery and SW marking in the uncorrupted portion of the data segment were excellent ($Sens. = 0.99$, $PPV = 0.82$, $A_{roc} = 0.81$). Furthermore, SW AT identification was greatly improved in the artifact-corrupted portion ($t = 18$ s) post-cleaning ($Sens. = 0.88$, $PPV = 0.54$, $A_{roc} = 0.48$). In summary, COBRA was able to recover useful data from a badly corrupted data segment, albeit imperfectly.

F. Application to Small Intestine

To demonstrate the applicability of the COBRA method, we investigated the SW rate vs. time in a porcine model during baseline mapping conditions. The SW rate was computed by summing ATs identified by the FEVT algorithm across 256 electrodes in successive 10 s intervals. Fig. 7 shows a comparison of results with and without artifact removal. The baseline rate remained relatively stable (1190 ± 107 SWs per 10 s) for artifact reduced data, but not uncleaned data (688 ± 242 SWs per 10 s; values are mean $\pm$ s.d.). Local minima in the rapidly fluctuating array-wide SW rate for non-artifact reduced data were characteristic of time domains for which an artifact blinded proper identification of ATs for one time period, and subsequent local maxima were due to the presence of a large common mode artifact being incorrectly marked as a false positive. Such fluctuations could confound further analysis and interpretation. For instance, the sustained, artifactual $\approx 40\%$ decrease in SW rate that occurs after 310 s (Fig. 7, top, blue trace) could potentially be confused with the precipitous decrease in SW activity that is commonly observed with the onset of ischemia [32], [33].

To further highlight the practical utility of the COBRA method, we investigated the quality of isochronal maps generated in a data window originally contaminated by artifacts which were subsequently removed (Fig. 7, bottom). Three successive SWs propagated in the

retrograde direction across the entire mapped area (124×28 mm) at a velocity of 12.9 ± 0.1 mm/s. Successive SWs were initiated 3.6 ± 0.1 s apart, which corresponds to 16.7 cycles per minute (cpm). These results are consistent with previously reported data for SW frequency (16.4 ± 0.3 cpm), velocity (13.4 ± 1.7 mm/s), and propagation patterns in the porcine proximal jejunum [20]. Consistently sensible and accurate isochronal maps could be generated from such data segments only after reduction of artifacts. Therefore, the COBRA method can be highly beneficial for the proper analysis of SW activity, which can serve as an important indicative factor of intestinal health.

IV. Discussion

We have developed an algorithm for artifact reduction in electrograms, and applied it to analyze GI recordings. The COBRA method is computationally efficient and flexible in terms of the type of contaminating waveforms that can be effectively removed. A key innovative feature of the COBRA method is its iterative construction, which allows for artifacts to be identified and removed in a sequential manner. Making multiple passes at subtracting a noise template has been shown in this study to be highly beneficial for strongly reducing various interfering waveforms spanning a wide range of morphologies, amplitudes, and durations. The largest artifacts are removed first such that smaller artifacts can be more easily detected in subsequent iterations. In addition, the iterative construction allows for the NEO detection threshold to automatically adjust with each successive cleaning step, and yields good estimates of α for each individual artifact waveform. Therefore, user-adjustable algorithm parameters need not be finely tuned.

A. Comparison to Previous Work and Related Methods

The problem of common mode artifact reduction has been previously recognized and addressed in various biomedical fields. For example, a similar fully automated regression-based method for removing ocular artifacts from the EEG was described in [34] using a single pass of subtracting a scaled noise template from the data. In contrast, our method works iteratively, which is a crucial feature.

Sophisticated signal processing techniques using empirical mode decomposition (EMD) and independent component analysis (ICA) have been developed specifically for reducing high-frequency interference in cutaneous recordings of GI SW activity. For instance, Liang et al. applied a semi-automated EMD method to the 3-channel electrogastrogram, whereby the frequency spectra of intrinsic mode functions were used to manually determine which corresponded to artifacts or gastric activity [35]. While good performance was demonstrated, there were two issues that may be problematic for more general applicability: 1) a hard-thresholding used to pre-condition recordings for EMD presumes knowledge of the amplitude of the signal of interest as well as the artifact; and 2) EMD computation time may become prohibitively long for HR arrays with several hundred electrodes.

More recently, Ye-Lin et al. presented a combined EMD with the fast fixed-point variant of ICA to reduce high-frequency artifacts in the 4-channel electroenterogram [19]. A hard threshold on the kurtosis index was used to automate identification of ICA sources corresponding to high frequency interference. Although this fully automated artifact

reduction method produced satisfactory results, there are two potential issues: 1) the outcome of the fast ICA algorithm depends on the initialization, and therefore is not deterministic; and 2) the computational time involved with EMD-ICA is burdensome, given typical finite computing resources.

The COBRA algorithm avoids these potential pitfalls by using a detection threshold that update with each successive iteration, and by using simple matrix operations to compute the noise template N and scaling parameter α . The reduced computational complexity and fast execution time of our algorithm may be particularly beneficial for real-time clinical analysis (e.g., [36], [37]). Whereas the EMD-ICA method applied to surface electrode intestinal recordings was shown to increase the SAR (5.38 dB) by eliminating the cardiac component of high frequency noise [19], COBRA achieved a stronger reduction when applied to both synthetic (8.9 dB) and porcine *in vivo* (11.1 dB) data sets. It must be recognized that one limitation with this comparison is that SAR was computed in the present study using only data segments contaminated with a variety of large amplitude waveforms, not the cardiac waveform.

Another related approach is the method of Kelly et al., which bootstraps a common average reference technique with adaptive noise cancellation to remove common mode artifacts (ACAR) [38]. Whereas ACAR subtracts the noise template in a single pass within a sliding window, our method works iteratively, making multiple passes to remove residual interference. An appealing feature of both ACAR and our COBRA method is that a wide variety of artifact waveform morphologies can be successfully removed as the only assumption is that the noise template be uncorrelated with the underlying physiological signal. This assumption is readily realized in practice for high-resolution recordings of propagating GI electrical activity because the SW waveform is time-shifted between adjacent electrodes. Similar to ACAR, our method uses a common reference that is further filtered—although not adaptively—to generate a noise template. While the ACAR method was shown to increase the SAR of noise corrupted data sets from -5 to about 10.5 dB ($SAR \approx 15.5$ dB), it was also reported to be poorly suited for cleaning sudden, large artifacts because the learning rate is typically too slow to appropriately adapt the filter tap coefficients [38]. By contrast, COBRA was demonstrated to be very effective and efficient for this task.

Lastly, we note that Liang and Lin previously developed a method to reduce stimulus artifacts during gastric pacing based on the wavelet-transform and fuzzy set theory [39]. This method was designed to remove specific stimulus artifact waveforms characterized *a priori*, thus may not generalize well to removing a wide variety of artifacts. By contrast, the COBRA method does not build in such assumptions, and was shown to successfully remove a variety of artifact waveform types.

B. Limitations and Future Work

While the overall performance of COBRA was highly satisfactory in general, there are some known limitations to the method. Outcomes were relatively poor when two common mode artifacts with different waveforms were present in subsets of electrodes—for instance one group recorded a certain artifact waveform, while the other group recorded a completely

different artifact waveform (e.g., not just inverted polarity). A related problem occurred when a single artifact waveform was present across only a few channels. In this case, the artifact will be essentially ignored when computing the common median.

The outcome of cleaning was also poor when subsets of artifacts are closely spaced in time, but not synchronous across the entire electrode array, a scenario which may occur when manipulating a subset of tessellated electrode arrays [2]. In this instance, the universal noise template is poorly correlated to both subsets of artifacts.

Of all artifacts identified upon manual review of 5 complete porcine experiments (about 140 min total of recording time) about 8% occurred over small subsets of electrodes; 92% of artifacts occurred array-wide. Therefore, manual correction in a semi-automated process could be used to address the relatively rare problematic cases. In the future, it is worth pursuing a fully automated process to clean all artifact types.

One possible solution to these current limitations would be to compute the reference signal using the common mean across channels. Doing so might be beneficial in some cases, but harmful to the overall performance of the COBRA method, as previously remarked (Section II-E).

Another possible solution would be to cluster artifact waveforms—a problem akin to neural spike sorting (e.g., [40])—before applying COBRA separately to groups of channels contaminated with the same artifact waveform.

Another option would be to employ a blind source separation approach, such as PCA, eliminating all automatically identified artifact sources prior to reconstructing the underlying physiological signal. Mullen et al. have previously developed and successfully applied such an “Artifact Sub-space Reconstruction” (ASR) technique to 64-channel EEG recordings for cognitive monitoring [41]. In the future, it would be worthwhile to investigate implementing COBRA and ASR in tandem. Solely applying ASR to GI HR-recordings may be problematic because each of the time-lagged SW waveforms may be separated as an individual component by PCA, a process that would compete with proper separation and elimination of artifact components.

While we have specifically applied COBRA to serosal SW recordings from the porcine small intestine in this study, we have also obtained some promising preliminary results when applying it to remove a range of time-synchronous artifacts for automated analysis of GI spike burst recordings (e.g., [25]). With only a single assumption built into the method—that the time-synchronous artifact is uncorrelated with the underlying physiological signal—we also expect this iterative method can be successfully applied to gastric recordings as well. This is important because multi-electrode gastric mapping is currently receiving substantial attention due to its ability to define normal and dysrhythmic SW propagation patterns in humans and animal models [42], [9], [12]. In addition, the sensitivity and positive predictive value of the COBRA and FEVT algorithms may be anticipated to be superior in gastric recordings due to the higher intrinsic signal-to-noise quality [4].

The COBRA method could potentially be adapted for and utilized in other biosignal processing domains where a similar common-mode artifact problem arises, such as removal of the eye movement artifact from the EEG neural recordings (e.g., [43]), which have recently been used for brain-machine interfaces (e.g., [44]). Another possible application would be to remove motion artifacts in electrohysterography recordings to map the spread of electrical activity coordinating uterine smooth muscle contractions during pregnancy [45], [46], similar to how SWs coordinate contractions in the GI system.

V. Conclusion

Overall, application of COBRA has been shown to transform GI electrical recordings suffering from severe common-mode artifacts into data in which SW activation times are accurately identified by the FEVT algorithm, from which propagation maps can be made. COBRA is computationally inexpensive, and was shown to remove artifacts of widely-varying morphologies. While covariance-based approaches to artifact reduction (applied to the EEG) have been previously described [34], the COBRA method is the first to incorporate the novel iterative step. This iterative step was crucial, as it allowed artifacts of significantly different amplitudes and morphologies to be sequentially removed.

The strong performance of COBRA for removing artifacts while conserving the underlying GI signal was validated through both *in vivo* and synthetic data studies. The increase in signal-to-artifact ratio increased by >10 dB, while the signal of interest was attenuated by <-10 dB.

The experimental and clinical value of this new algorithm was furthermore established by using it in a demonstration study to quantify SW rates and propagation patterns in the porcine small intestine, *in vivo*. This algorithm extends the front end of an existing analysis pipeline [17], and improves the applicability of complementary analysis algorithms [14], [15] by removing problematic artifact interference. In addition, the COBRA method might be utilized more generally in other biomedical domains where common-mode noise and/or artifact removal problems are encountered. A MATLAB implementation of the code is freely available for academic use upon request.

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Fig. 1.

Sample electrograms illustrating various types of artifacts typically encountered during recording sessions. Waveform amplitude was rescaled for clarity of display; vertical scale bars indicate $75 \mu\text{V}$. Gray traces: filtered electrograms prior to artifact removal. Sections highlighted in light blue indicate manually identified artifact-corrupted time windows. Black traces: electrograms after application of COBRA artifact removal. The periodic slow wave waveform was sufficiently recovered in most cases. Significant overlap of gray and black traces indicates that the underlying SW waveform was well-preserved in non-artifact corrupted regions following application of COBRA.

Fig. 2.

Flowchart summarizing main steps of the artifact removal method. The iterative step returning to compute an updated common reference signal is a key feature which allows artifacts to be removed sequentially. Stopping criteria are described in Section II-F.

Fig. 3.

Illustration of synthetic data corrupted by a common-mode artifact extracted from real data set before (red) and after (black) application of COBRA artifact reduction. The width of the light gray box highlights the duration of the added artifact, and the height denotes the peak-to-peak noise in that window after artifact removal. The point of steepest descent was preserved for both SW waveforms, which occur ≈ 5 s apart.

Fig. 4.

Validation performance metrics for *in vivo* data. The shape and color coded legend at bottom indicates the threshold value η . Data points represent the trial-averaged mean across 6 data segments for *SIA* and *SAR*, and all 11 data segments for *Sens*, *PPV*, and *A_{roc}*. Error bars represent the standard error of the mean. Data points shown are jittered along the abscissa for visual clarity. *A_{roc}* results are shown for data segments not cleaned with COBRA (open black circles) to illustrate the net benefit of artifact removal.

Fig. 5.

Illustration of removal of multiple artifacts in a 40 s duration data segment. (a) Iterative cleaning on a single electrogram. Red circles indicate FEVT marks. Note the seven consecutive false negatives in the signal prior to artifact removal (top) resulted from the two large artifacts dominating the SW detection process, both of which were initially identified by FEVT as false positives. Following artifact removal (bottom electrogram), 10 out of 10 SWs were properly marked as true positives by the FEVT algorithm. (b) Recordings from 12 electrodes pre- (gray) and post-cleaning (black). For visual clarity, traces have been normalized to have uniform peak-to-peak range. Traces are vertically stacked to emphasize the propagating nature of the SW as illustrated with orange arrow. A copy of an uncleaned signal is provided at bottom for clarity. Blue arrowheads mark common mode artifacts that swamp the underlying SW activity, leading to data loss. (c) Ladder plots before (blue +) and after (red O) artifact cleaning of data segments shown in (b). The former is offset by +0.5 s for visual clarity. Prior to cleaning, the artifacts swamped correct marking of SWs throughout the data segment.

Fig. 6.

Illustration of removal of long time-scale artifact beginning abruptly in the middle of a 40 s duration recording. (a) Successive iterations of COBRA artifact removal improved the ability of the FEVT algorithm to properly mark SWs. Red circles indicate FEVT marks, thickened on the uncleaned trace (top) for clarity. Initially, 5 FPs were marked (also indicated by blue marks in (b)). After artifact removal, 9 TPs and 2 FPs (1st and 3rd arrowheads, dark blue) were marked, with 1 FN (2nd arrowhead, cyan) identified by FEVT. (b) Ladder plots corresponding to signals shown in (a), with formatting as described in Fig. 5(c). Prior to cleaning, the SW ATs could not be identified in the clean or artifact-corrupted segments of the recordings. After cleaning, the SW pattern could be discerned from ATs marked by FEVT.

Fig. 7.

Top panel: Array-wide SW rate with (red) and without (blue) COBRA artifact reduction. The presence of large artifacts often led to missed detection of true SW events, obscuring the true SW rate throughout the baseline analysis period. Bottom panel: Isochronal maps for 3 successive SWs measured from *in vivo* porcine jejunum following artifact removal in a time window ($45.3 \leq t \leq 63.1$ s) indicated by gray rectangle. Dots spaced on a square lattice correspond to electrode sites. Isochrones are drawn at 0.5 s intervals. Red and blue color-code the earliest and latest activation times, respectively, and the white arrow indicates the retrograde direction of SW propagation.