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Refined Ventricular Activity Cancellation in Electrograms During Atrial Fibrillation by Combining Average Beat Subtraction and Interpolation

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***Abstract*— Many techniques have been developed to cancel the ventricular interference in atrial electrograms (AEG) during atrial fibrillation. In particular, average beat subtraction (ABS) and interpolation are among those mostly adopted. However, ABS usually leaves high power residues and discontinuity at the borders, whereas interpolation totally substitutes the residual activity with a forecasting that might fail at the center of the cancellation segment. In this study, we proposed a new algorithm to refine the ventricular estimate provided by ABS, in such a way that the residual activity should likely be distributed as the local atrial activity. Briefly, the local atrial activity is first modeled with an autoregressive (AR) process, then the estimate is refined by maximizing the log likelihood of the atrial residual activity according to the fitted AR model. We tested the new algorithm on both synthetic and real AEGs, and compared the performance with other four algorithms (two variants of ABS, interpolation and zero substitution). On synthetic data, our algorithm outperformed all the others in terms of average root mean square error (0.043 vs 0.046 for interpolation; $p < 0.05$). On real data, our methodology outperformed two variants of ABS ($p < 0.05$) and performed similarly to interpolation when considering the high power residues left (both $< 5\%$), and the log likelihood with the fitted AR model.**

I. INTRODUCTION

During ablation routines for the treatment of atrial fibrillation (AF), atrial electrograms (AEG) are measured on the atrial surface to determine the loci responsible for the fibrillation. Depending on the position of the catheter and type of measurement (*i.e.*, unipolar or bipolar), the ventricular activity might be overlapped to the signal of interest, *i.e.*, atrial one.

Many algorithms have been developed in the last decades to reduce the interference caused by the ventricles (both on AEG and standard electrocardiogram, ECG). Such algorithms can be categorized into the following five groups: i) average beat subtraction (ABS) and its variants [1], [2]; ii) interpolation [2]; iii) adaptive filtering [3], [4]; iv) model-based filtering [5]; and v) multi-lead filtering [4]. (An extensive review may be found in [2].)

Considering the first two groups, ABS estimates a template as average of several ventricular activities and subtract it to the AEG. Several are its variants, including power correction algorithms [6], noise-dependent weights or residual-constrained template [1].

Interpolation substitutes the entire ventricular segment with a prediction obtained from a model of the nearby atrial activity. Common methods in this context are sinusoidal and autoregressive interpolations in which the residue is substituted with a prediction that minimizes the mean square error or prediction error, respectively.

All methodologies present pros and cons. ABS is simple to implement but might leave high power residue and discontinuity at the borders of the ventricular segment. Interpolation forces the frequency content of the residue to be similar to the nearby atrial activity. However, its forecasting might fail due to models poorly fitted [2] (especially at high heart rate when the duration of the nearby atrial activity, before the next ventricular artifact, is limited in time).

In this proof-of-concept, we developed and tested a new algorithm, *i.e.*, r-ABS, by combining ABS and interpolation in an unified framework. The new algorithm has been tested on both synthetic and real AEGs, while its performance compared with two variants of ABS, an autoregressive interpolation method, and zero substitution.

II. METHODS

A. The model

The common signal-plus-noise model is used to model the endocavitary recording, as follows

$$z_k = a_k + v_k,$$

where k is the sample index, v_k is the ventricular activity to remove (hence, the noise) and a_k is the activity that includes both far and near atrial field effects.

The activity a_k is modeled as a zero-mean stationary stochastic Gaussian process with autocovariance function $\rho(l)$, with l being the lag. Under the stationary and normality assumptions, the sequence of N stochastic variables $\mathbf{a} = [a_1, a_2, \cdots, a_N]^\intercal$ is distributed as a multivariate Gaussian variable

$$\mathbf{a} \sim \mathcal{N}(0, \Sigma),$$

where Σ is the Toeplitz covariance matrix, built from the values of $\rho(l)$.

B. The signal

Let us have one AEG in which the ventricular activity is clearly overlapped. In addition, let us assume that the time-positions of the ventricular complexes are known and that for each of the ventricular complex a window of N AEG samples is located such that the R-peak, as identified on the ECG, is approximately at the center. Let us also set apart the Q samples before the beginning of the window bracketing a ventricular complex (in which the ventricular activity is likely not present). Then, the two windows

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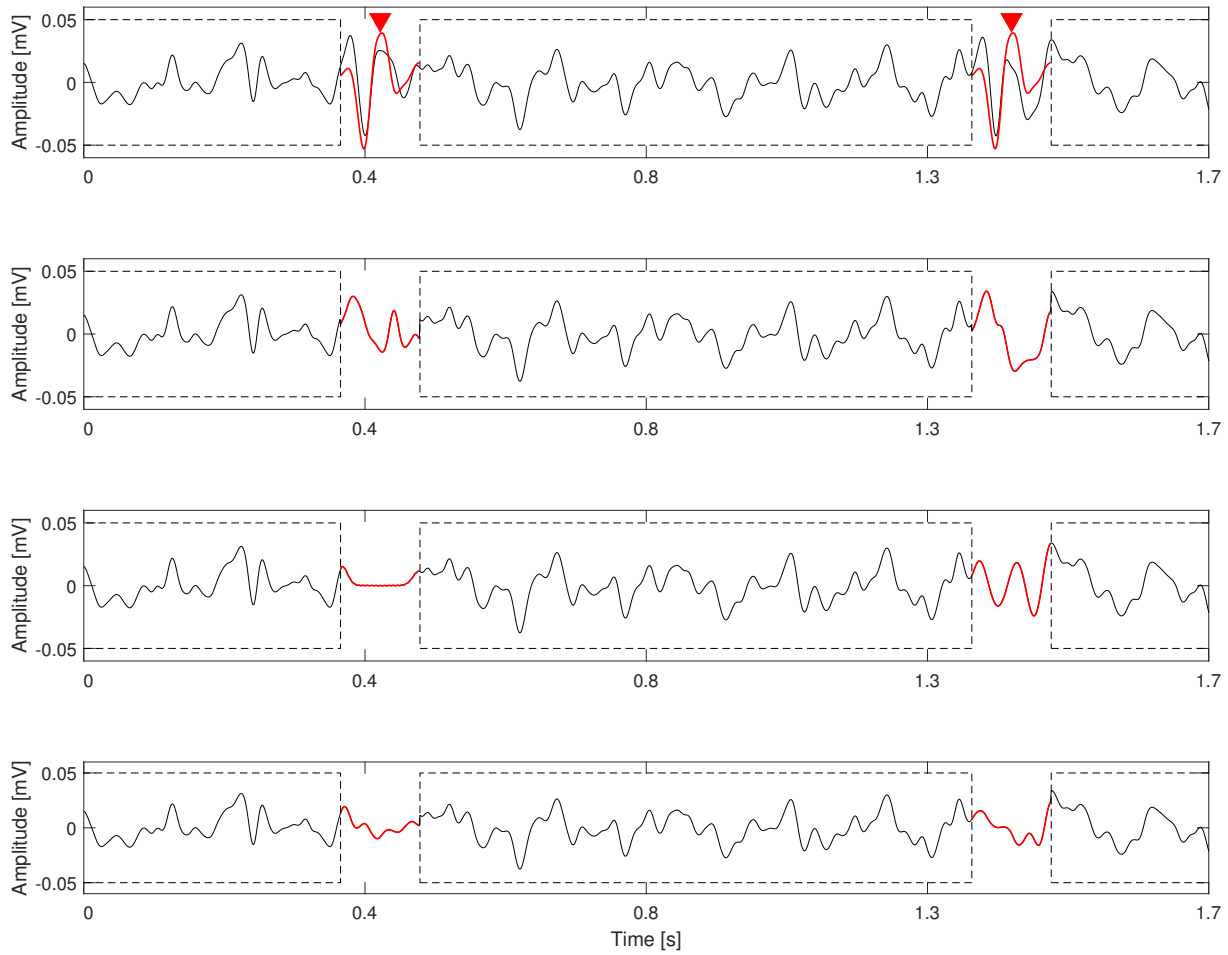

(d)

Fig. 1: Example of AEG that underwent to three different ventricular cancellation algorithms. The original AEG is shown in panel (a). Red arrow-tip markers point to ventricular activities (determined by mean of the surface ECG). Red thick signals show the ABS template (a) and residual activities of ABS (b), interpolation (c) and r-ABS (d). The dashed box encloses the portion of AEG used for fitting the AR model.

can be stored in the vector $\mathbf{z}_Q = [z_1, z_2, \cdots, z_Q]^\intercal$ and $\mathbf{z}_N = [z_1, z_2, \cdots, z_N]^\intercal$, along with the augmented signal $\mathbf{z}_A = [\mathbf{z}_Q^\intercal, \mathbf{z}_N^\intercal]^\intercal$. Let us also call these two segments as Q and N window, respectively.

C. The refined estimate

We propose to refine the ventricular activity estimate $\hat{\mathbf{t}}$ (N dimensional vector) provided by the ABS to obtain its improved version $\hat{\mathbf{v}}$. The refinement is based on the fact that the residual activity $\hat{\mathbf{a}} = \mathbf{z} - \hat{\mathbf{v}}$ should follow a specific multivariate Gaussian distribution.

First, we model the refinement of the vector $\hat{\mathbf{t}}$ by using a linear combination of basis functions

$$\hat{\mathbf{v}} = \hat{\mathbf{t}} + \Phi^\intercal \mathbf{c}, \tag{1}$$

where Φ is a $B \times N$ matrix containing B basis functions and $\mathbf{c}$ is the vector of coefficients to be estimated.

Let us now define the augmented activity $\mathbf{a}_A$ as

$$\mathbf{a}_A = \begin{bmatrix} \mathbf{a}_Q \\ \mathbf{a}_N \end{bmatrix},$$

in which $\mathbf{a}_N$ is the activity to be estimated. Such augmented vector follows a multivariate Gaussian distribution with covariance matrix Σ_A

$$\mathbf{a}_A \sim \mathcal{N}\left(\mathbf{0}, \begin{bmatrix} \Sigma_{QQ} & \Sigma_{QN} \\ \Sigma_{NQ} & \Sigma_{NN} \end{bmatrix}\right).$$

In order to estimate the coefficient vector $\hat{\mathbf{c}}$, it is possible to maximize the log conditional likelihood of the residual activity, as follows

$$\hat{\mathbf{c}} = \text{argmax}_{\mathbf{c}} \log \mathcal{L}(\mathbf{c}; \mathbf{z}_N | \mathbf{z}_Q),$$

where $\mathbf{a}_Q = \mathbf{z}_Q$, since no ventricular activity is supposed to be overlapped on the Q window.

If the atrial activity $\mathbf{a} = \mathbf{z} - \hat{\mathbf{t}} - \Phi^\intercal \mathbf{c}$ follows a multivariate Gaussian distribution with mean vector $\boldsymbol{\mu}_*$ and covariance matrix Σ_*, the maximum likelihood estimate for $\mathbf{c}$ can be obtained by solving the following optimization problem

$$\begin{aligned} \hat{\mathbf{c}} &= \text{argmax}_{\mathbf{c}} \log \mathcal{L}(\mathbf{c}; \mathbf{z}) = \text{argmax}_{\mathbf{c}} \log [P(\mathbf{z}; \mathbf{c})] \\ &= \text{argmax}_{\mathbf{c}} \left[(\mathbf{z} - \hat{\mathbf{t}} - \Phi^\intercal \mathbf{c} - \boldsymbol{\mu}_*)^\intercal \Sigma_*^{-1} (\mathbf{z} - \hat{\mathbf{t}} - \Phi^\intercal \mathbf{c} - \boldsymbol{\mu}_*) \right] \\ &= \text{argmax}_{\mathbf{c}} J(\mathbf{c}). \end{aligned}$$

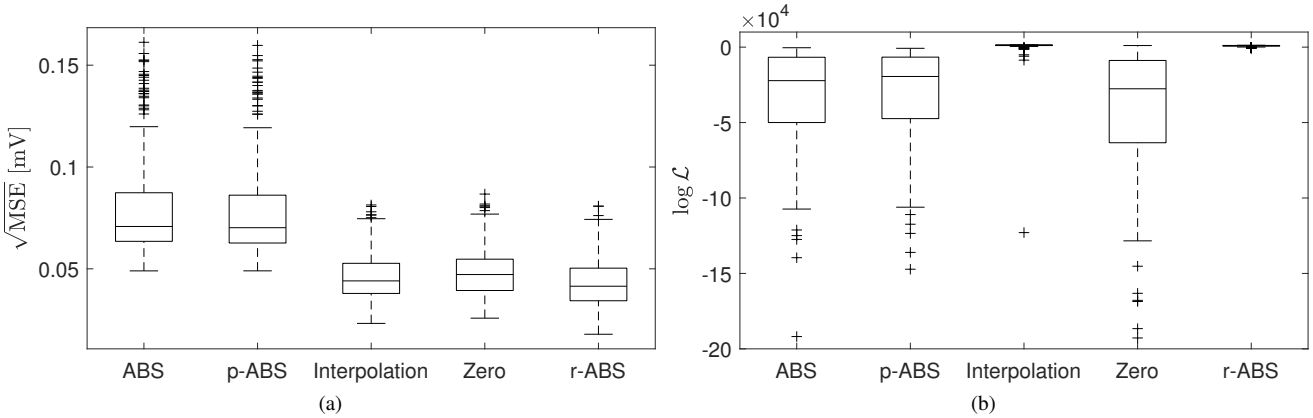

Fig. 2: Boxplots of the performance for the five algorithms. Panel (a) reports the root MSE between the residual activity and the true one on the synthetic data. Panel (b) shows the log likelihood computed on the real signal.

The derivative of $J(\mathbf{c})$ with respect to $\mathbf{c}^\intercal$ is

$$\frac{dJ(\mathbf{c})}{d\mathbf{c}^\intercal} = -2\Phi\Sigma_*^{-1}(\mathbf{z} - \hat{\mathbf{t}} - \boldsymbol{\mu}_*) + 2(\Phi\Sigma_*^{-1}\Phi^\intercal)\mathbf{c},$$

which, once set to 0, leads to

$$(\Phi\Sigma_*^{-1}\Phi^\intercal)\hat{\mathbf{c}} = \Phi\Sigma_*^{-1}(\mathbf{z} - \hat{\mathbf{t}} - \boldsymbol{\mu}_*). \tag{2}$$

It is worth noting that the conditional probability of a multivariate Gaussian variable is another multivariate Gaussian variable. In particular, the conditional probability of the activity $\mathbf{a}_N$ conditioned by $\mathbf{a}_Q$ is

$$\mathbf{a}_N|\mathbf{a}_Q \sim \mathcal{N}\left(\Sigma_{NQ}\Sigma_{QQ}^{-1}\mathbf{a}_Q, \Sigma_{NN} - \Sigma_{NQ}\Sigma_{QQ}^{-1}\Sigma_{QN}\right).$$

Therefore, the estimate of the coefficient vector $\hat{\mathbf{c}}$ can be obtained using eq. (2), by setting $\boldsymbol{\mu}_* = \Sigma_{NQ}\Sigma_{QQ}^{-1}\mathbf{a}_Q$ and $\Sigma_* = \Sigma_{NN} - \Sigma_{NQ}\Sigma_{QQ}^{-1}\Sigma_{QN}$.

D. Selection of the basis functions

In general, there is no standard rule on how to choose certain basis functions over others, and, in most of the cases, only empirical considerations guide the selection for the problem at hand. In our problem, considering that most of the ventricular energy will likely be located at the center of the N window by construction (at sample $\approx N/2$), a reasonable requirements for the basis function might be to assume the same value at the boundaries of the window. A common set of basis functions, displaying this characteristic, is the set of the sinusoidal functions, along with their harmonics, with fundamental frequency $\omega = 2\pi/N$. With this choice, which we performed, the coefficients $\mathbf{c}$ correspond to the Discrete Fourier Transform of the refinement in eq. (1). We employed the harmonics of order $0 \cdots (B-1)/2$ where B was an odd number by construction, that is, i) a constant term; ii) $(B-1)/2$ sines; and iii) $(B-1)/2$ cosines.

E. Dataset

The algorithm was validated on two datasets. The first one comprised 10 synthetic AEGs, built along the line of what described in [1]. Briefly, the far-field atrial activity was modeled using an autoregressive model, whereas the near-far atrial activity and ventricular activity were generated using an electric dipole moving along a straight line, with respect to the electrodes. The average ratio between ventricular and near-field atrial peaks was set to 4, while the average ratio between the near-field atrial peak and standard deviation of the far-field activity was 2. Each synthetic AEG signal contained the interference of 120 beats, generated independently between each other.

The second dataset was composed by a single real signal taken from the Intracardiac Atrial Fibrillation Database [7]. In particular, we used the first 2 minutes of the first signal in the dataset (iaf1_afw; CS12, sampling rate: 1000 Hz). The location of 145 beats was provided with the AEG. Figure 1a shows a portion of the signal.

F. Estimation of Σ_A

The covariance matrix Σ_A was estimated using the coefficients of an autoregressive model fitted on the atrial activity between two consecutive ventricular complexes. In particular, for the k-th ventricular activity, we fitted the model on the atrial signal between the $k-1$ and k beats. First, the covariance function was estimated using the Yule-Walker equations and then the Σ_A matrix, of dimension $(Q + N) \times (Q + N)$, was composed.

G. Estimation of Hyper-parameters

The algorithm required two parameters to be estimated: the number of basis functions B and number of samples Q in the Q-window. To do so, we used a grid search approach in which, for each combination of B and Q, the mean square error (MSE) between the residual activity after cancellation and the true activity was computed. In order to avoid overfitting when evaluating the performance, we considered only the first 5 signals of the syntethic dataset. The values of B and Q that minimized the average MSE across these 600 beats were 11 and 2, respectively.

H. Evaluation of the Performance

The algorithm was tested on both syntethic and real AEGs. In the first case, root MSE was used as indicator of performance and was determined only on the second half of the synthetic dataset (the 5 signals not used to set the hyper-parameters).

On real data, we evaluated the performance using two metrics. The first one computed the percentage of high power residues remaining in the signal after cancellation (similarly to [1]). In practice, we counted how many residual segments had a mean power higher than a certain threshold. Such threshold was estimated as the 95^{th} percentile of the mean power distribution of windows of (only) atrial activities of length 120 ms (which is the same length of the N-window we employed). With the second metric, we evaluated the log likelihood of the residual activity with respect to the fitted AR model. We first computed the prediction error between the residual activity and the $1-$step prediction, based on the AR model. Then, considering that the prediction error must be distributed as a white Gaussian noise, we computed its log likelihood with a diagonal covariance matrix, having all the entries equal to the variance provided by the model fitting procedure.

We compared r-ABS with other four methods: i) ABS; ii) ABS with adjustment of the power (p-ABS; *i.e.*, the template $\hat{\mathbf{t}}$ is multiplied by $(\hat{\mathbf{z}}_N^\intercal \hat{\mathbf{z}}_N)/(\hat{\mathbf{t}}^\intercal \hat{\mathbf{t}})$) [6]; iii) interpolation based on autoregressive models [2]; and iv) substitution with zero (the ventricular activity was set to 0).

III. RESULTS

Figure 2a reports the root MSE between the estimated atrial activity and the true one on the second half of the synthetic dataset (test-set), for each of the five considered methodologies. Both versions of ABS performed the least (even though p-ABS was 0.8% lower than ABS in terms of root MSE; Wilcoxon sign rank test; $p < 0.05$). On the other hand, r-ABS outperformed all the others, having a root MSE statistically significantly lower from that of the interpolation method ($p < 0.05$), that ranked second. Zero substitution ranked third.

Even on real data, r-ABS and interpolation resulted with the highest log likelihood, even though r-ABS ranked second in this case ($p < 0.05$). In addition, ABS and p-ABS did not show any statistically significant difference ($p > 0.05$), while the zero substitution performed the least ($p < 0.05$). Moreover, excluding zero substitution, r-ABS and interpolation resulted with the lowest percentage of high power residues (2.8% and 4.1%), while ABS and p-ABS performed the least (8.3% and 4.8%).

IV. CONCLUSIONS

In this study, we proposed a new algorithm, *i.e.*, r-ABS, for ventricular activity cancellation in AEG during AF. The methodology combines two common techniques, ABS and interpolation, in an unified framework. Such framework was able to refine and improve the ventricular activity estimate, under the stationary assumption of the atrial activity in very short time windows.

With respect to ABS-based algorithms, in which common problems [1], [2] are lack of continuity at the boundaries of the N-window and high power residues (figure 1b), our algorithm modulated the template $\hat{\mathbf{t}}$ to match the stochastic process' properties (figure 1d).

On the other hand, interpolation-based algorithms using autoregressive models tend to predict poorly the expected value of the stochastic process for long temporal horizons (figure 1c). This effect results in a flat signal around the peak of the ventricular activity (especially for low model orders), while preserving the frequency content of the process at the borders of the N-window. Although the residual power lies in the range of what expected from atrial activity and the frequency content is preserved at the borders, the reconstructed atrial activity lacks details exactly in the part of the N-window which much needed of refinement. This did not happen with r-ABS, as the algorithm was able to preserve the frequency content by considering the autoregressive model's Σ_A, while still exploiting the ABS estimate.

A limitation of r-ABS is that the covariance matrix Σ_A needs to be estimated. Even though this can be easily obtained from the samples nearby the ventricular activity, the stationary assumption might break, leading to a poor estimate. Also, to fit properly the autoregressive model, near-field atrial activity must be limited. A second limitation is that, while it is often reasonable to assume $\mathbf{a}_Q = \mathbf{z}_Q$, Q-windows might still contain ventricular activity. In this case a larger N-windows should be considered. Finally, inverting directly the matrix Σ_N or computing its determinant might be numerically challenging, and specific available numerical strategies should be adopted.

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