

High-Coverage and High-Resolution Mapping of Repetitive Patterns During Atrial Fibrillation

Ozan Özgül¹, Ben Hermans¹, Arne van Hunnik¹, Sander Verheule¹, Ulrich Schotten¹, Pietro Bonizzi², Stef Zeemering¹

¹ Department of Physiology, Maastricht University, The Netherlands

² Department of Data Science and Knowledge Engineering, Maastricht University, The Netherlands

Abstract

Localized AF drivers with repetitive activity are candidate ablation targets for patients with persistent atrial fibrillation (AF). High-density mapping electrodes cover only a fraction of the atria but combining sequential recordings could provide a more comprehensive picture of common repetitive atrial conduction characteristics and enable AF driver localization. We developed a novel algorithm to merge overlapping local activation maps into larger composite maps using recurrence plots. The proposed algorithm was applied to atrial recordings in a goat model of AF (249-electrode mapping array, 2.4 mm inter-electrode distance, $n=16$). Sequential, overlapping recordings were generated by segmenting the mapping region into four spatially overlapping regions. Repetitive activation patterns were detected from recurrence plots generated from the recorded electrograms, and reconstructed with the proposed algorithm. Reconstruction quality was measured as the Pearson correlation between original and reconstructed activation patterns. The average correlation was 0.86. Among pattern properties, such as duration, area, complexity and cycle length, only duration was significantly correlated with the composite map quality ($r=0.125$, $p < 0.01$). The percentage of the cases where a composite map could be generated was 75.30% which was significantly higher for larger patterns ($p < 0.01$).

1. Introduction

In patients with atrial fibrillation (AF), regular sinus rhythm is disrupted by electrical activities originating from other arrhythmogenic mechanisms. Pulmonary vein isolation (PVI) stands as the main non-pharmacological treatment option for AF and aims at electrical isolation of the AF triggers located near pulmonary veins. This therapy is highly efficient in early phases of the disease as most of the sources are located near pulmonary veins [1]. In later stages, sources exhibit more complex spatial patterns and

therefore, more comprehensive ablation strategies are required.

Mapping of AF is performed to localize extra-PV drivers of AF which are hypothesized to be spatially localized. These drivers are thought to reflect diverse mechanisms such as rotors, breakthrough or focal activity and could be efficient ablation targets [2]. Localized patterns, even if they are mechanically distinct, are expected to dominate the conduction characteristics of their vicinity and exhibit repetitive patterns that are observed through intracardiac recordings. Therefore, repetitiveness could be an indicator of localized drivers in atria.

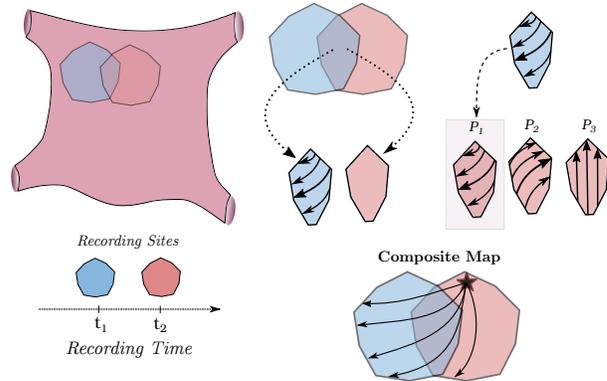


Figure 1. Two regions (blue and red) are recorded sequentially. A repetitive pattern detected on the reference site (blue) is compared with all repetitive patterns on the other site (P_1, P_2, P_3). If a matching pattern is captured, regions are merged to form a composite map.

Intrinsic properties of repetitive atrial conduction patterns can enable realization of efficient mapping approaches that are not feasible with current clinical settings. A pattern which is repetitive and intermittently observed during a recording can be observed from different locations with a high-density electrode grid. With the help

of a suitable temporal anchor signal, these asynchronous recordings can be aligned and fused to form a virtual high coverage and high density atrial activation map. These maps can provide a more complete picture of atria during AF and aid a better understanding of the role of specific mechanisms in initiation and perpetuation of AF. Activation maps that are formed by fusing asynchronous information from multiple overlapping regions into high-coverage maps are called composite atrial activation maps, or in short, composite maps. A substantial problem in composite map generation is the absence of the temporal anchor signal for aligning asynchronous recordings. This can be tackled through usage of spatial overlaps between sequentially recorded sites. A composite map can be generated whenever two spatially overlapping recordings show a common pattern in the overlapping area (see Fig. 1).

This study introduces an algorithm for generation of composite maps based on overlapping asynchronous recording sites. Proposed algorithm encapsulates a recurrence plot (RP)-based systematic approach of detecting repetitive patterns on distinct recordings sites and aligning these using cross-recurrence plots. The proposed approach was evaluated based on its ability to detect repetitive patterns over asynchronous recordings and the quality of the generated composite maps. Lastly, how pattern properties such as duration, size, complexity and cycle length affect composite mapping process was explored and statistically evaluated.

2. Materials and Methods

2.1. High-Density Contact Mapping of AF

High-density contact mapping was performed on 16 goats during an open-chest experiment using a 249-electrode spoon-shaped catheter with 2.4 mm inter-electrode distance. 40 seconds-long unipolar atrial electrograms were recorded on right atrial and left atrial epicardial wall. Ventricular far field artefacts were detected and eliminated using single beat QRST-template cancellation.

2.2. Detection and Visualization of Repetitive Patterns with Recurrence Plots

Recurrence plots (RPs) are visual tools enabling systematic detection of repetitive patterns in multivariate time series. An RP is a two-dimensional scatter plot having time on both of its axes. If the system visits the same state on two time points t_i and t_j (with $i \neq j$), the respective coordinate on this plot $[t_i, t_j]$ is filled with 1. State encoding strategies (embedding), utilized distance functions and thresholding approaches vary greatly among different applications [3].

Figure 2. illustrates the recurrence plot-based framework we have utilized to detect repetitive patterns in intracardiac signals which was previously described in [4]. First, local activation time detection was performed using a probabilistic template matching-based approach. This was followed by activation phase interpolation where intervals between consecutive activations were interpolated with phase values between $-\pi$ to π (Fig 1A). Each time-point was represented by the activation phase snapshot it was associated with (Fig 1B). Then, a recurrence plot was generated based on the similarities of snapshots. If a repetitive pattern was present for multiple AF cycles, this formed a square block oriented on the diagonal of the recurrence plot. These diagonally oriented square blocks were detected (Fig 1C). At the last step, static average activation maps were extracted as follows: a time point with minimum average phase snapshot value was chosen around the vicinity of the midpoint of the repetitive pattern (t_{min}). All time points showing recurrence with t_{min} were extracted and average to yield an average activation snapshot.

Cross-recurrence plot is a special form of recurrence plots which capture recurrences between two different recordings. If a cross recurrence plot is constructed using a number of shared electrodes between two asynchronous recordings, repetitive patterns that are common on both recordings can be captured. If any block structure is revealed on the cross recurrence plot, then this implies a common repetitive pattern present on two different sites and two different time intervals. Using this information, it was possible to generate average activation snapshots for both X and Y sites and fuse these maps into a larger composite map. This operation was extended to more than two regions by using a single region as the reference (Fig 1E).

2.3. Study Design

A fundamental problem in composite mapping is the lack of ground truth to quantify efficiency of the proposed approach. To overcome this, an artificial data segmentation framework was designed. We artificially segmented 17x17 high density grid recordings into four quarters that are spatially overlapping (approximately 50% overlap). We used 10 sec. recordings from each quarter, with no time overlap.

Each repetitive pattern in the dataset was characterized by: (i) Duration: measured in terms of how many AF cycles a repetitive pattern lasted, (ii) Size: percentage of electrodes, (iii) Complexity: electrogram sample entropy during the time course of repetitive pattern, (iv) Cycle length of the pattern. The proposed approach was evaluated based on its capability to: (i) efficiently capture repetitive patterns from all four asynchronously recorded quarters with cross-recurrence plots, (ii) obtain a composite map as similar as possible to the ground truth.

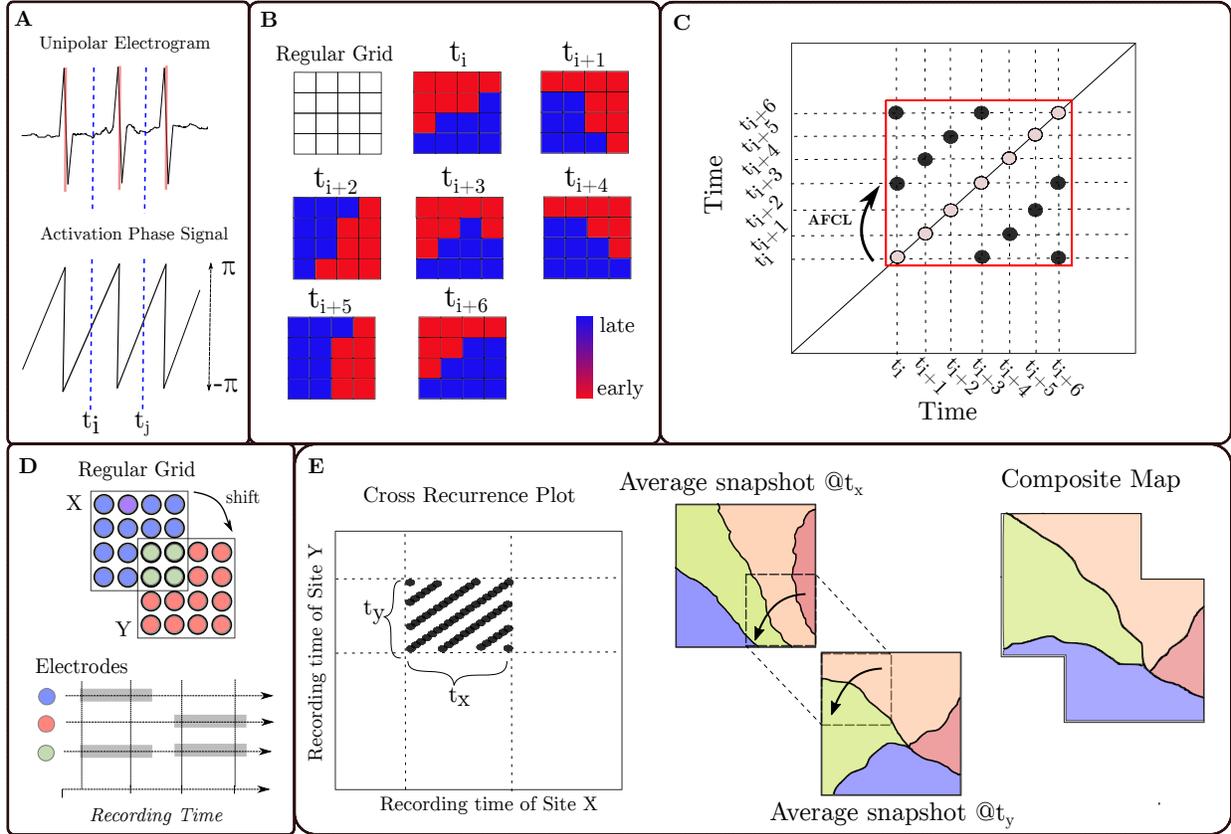


Figure 2. Repetitive pattern detection and composite mapping framework. (A,B) Generation of activation phase signals and snapshots, (C) Recurrence plot construction, (D) Sequential recordings with overlapping sites, (E) Usage of cross recurrence plots for composite map generation.

3. Results

1021 repetitive patterns were identified in the dataset (31.91 ± 13.38 repetitive pattern per each 40 seconds-long recording). Among these, 328 (32.13% of the total) were repetitive in all four artificially segmented time intervals-making them suitable to test the proposed composite mapping algorithm. Each repetitive pattern in the data set was classified as captured if it could be detected from at least two quarters or missed, otherwise. As shown in Table 1, the method detected 247 patterns (75.30%) and missed 81. The differences between pattern properties among these classes were statistically analyzed using Kruskal-Wallis non-parametric test. Captured patterns were larger in size than the missed patterns while no significant effect was observed for the other pattern properties ($p < 0.01$).

As the second step, each composite map was compared with the actual average pattern. In Fig. 3A, distribution of actual pattern-composite map correlations is given. The distribution was highly skewed to large correlation values with a median value of 0.86. Pattern properties were analyzed in order to reveal the effect of pattern properties

Table 1. Count and pattern properties of captured and missed patterns.

Case	Missed	Captured
Count	81	247
Duration (Cycles)	7.05	9.37
Area (% of electrodes)	0.67	0.71(*)
Complexity (Sample Entropy)	0.63	0.60
Cycle Length (msec)	95.25	100.92

(*) $p < 0.01$

on the quality of reconstructed composite maps. The relation was characterized by the Spearman rank correlation test which revealed a significant but weak positive correlation between pattern duration and composite map quality ($r=0.125, p<0.01$). No significant effect was observed for other pattern features (Fig. 3B).

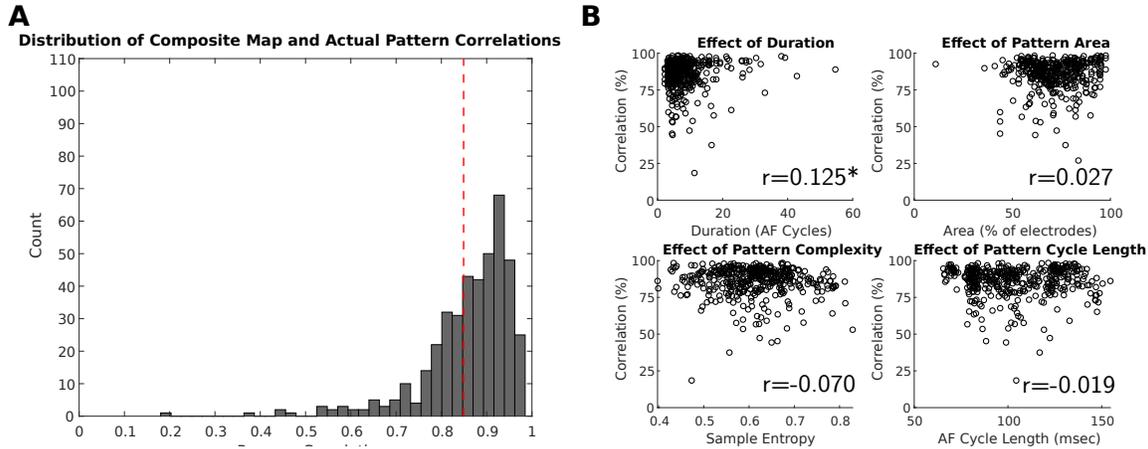


Figure 3. (A) Pearson Correlation between composite maps and actual patterns, (B) Effect of input pattern properties on correlations.

4. Discussion

The proposed approach successfully generated composite maps in 75.30% of all cases by capturing similar repetitive patterns over asynchronous recordings. The main modulator of this capturing capability was the size of the patterns. As a pattern shrinks, the number of electrodes it was observed would decrease and the pattern would be less likely to be present in the overlapping electrodes. This absence hampered pattern's representation in the cross recurrence plot and consequently, a composite map could not be produced. On the other hand, duration was found as the one and only pattern feature showing significant correlation with the composite map quality, although the effect was weak. This was expected as more durable patterns produce more entries in the recurrence plot that could be used for average activation map generation. As averaging suppresses random noise, resulting average activation maps are less noisy and consequently, more similar to the ground truth.

A notable finding was the statistical independence of the results from pattern complexity and cycle length as given in Table 1 and Figure 3B. This manifests our algorithm's suitability for AF patterns which are rich in terms of highly complex patterns with diverse cycle lengths.

5. Conclusion

A novel recurrence plot-based approach for generation of high-coverage and high-density atrial activation maps was introduced. The proposed scheme framework was shown to be capable of successfully aligning asynchronously recorded repetitive patterns over different areas and also producing high-quality composite maps. These properties were minimally affected by pattern properties enabling potential use in highly variable patterns of AF. A

possible extension of this work would be an application of the proposed algorithm in a clinical setting.

Acknowledgments

This work was supported by PersonalizeAF project. This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 860974.

References

- [1] Haissaguerre M, Jaïs P, Shah DC, Takahashi A, Hocini M, Quiniou G, Garrigue S, Le Mouroux A, Le Métayer P, Clémenty J. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *New England Journal of Medicine* 1998;339(10):659–666.
- [2] Hansen BJ, Csepe TA, Zhao J, Igozzi AJ, Hummel JD, Fedorov VV. Maintenance of atrial fibrillation: are reentrant drivers with spatial stability the key? *Circulation Arrhythmia and Electrophysiology* 2016;9(10):e004398.
- [3] Marwan N, Romano MC, Thiel M, Kurths J. Recurrence plots for the analysis of complex systems. *Physics reports* 2007;438(5-6):237–329.
- [4] Zeemering S, Van Hunnik A, Van Rosmalen F, Bonizzi P, Scaf B, Delhaas T, Verheule S, Schotten U. A novel tool for the identification and characterization of repetitive patterns in high-density contact mapping of atrial fibrillation. *Frontiers in physiology* 2020;11:1304.

Address for correspondence:

Ozan Özgül
 Universiteitssingel 50, UNS50, 6229 ER Maastricht, Netherlands
 o.ozgul@maastrichtuniversity.nl