# Electrogram Coupling as a Measure of Local Conduction during Atrial Fibrillation

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## Abstract

*Epicardial wavefront conduction patterns during atrial fibrillation (AF) can be recorded using high-density contact mapping. Quantification of electrogram morphology similarity at adjacent recording sites during AF may characterize substrate complexity without the need for electrogram annotation. Electrogram coupling was quantified as the decay in reconstruction quality of a central electrogram by its neighbors at increasing distance. Coupling was computed in patients in paroxysmal AF (PAF, n=12) and persistent AF (persAF, n=9) with a 16×16 grid of electrodes (1.5mm electrode distance) with nonnegative least squares using only complete, symmetric topologies. Half-decay distance $c_{0.5}$ was compared to conventional conduction-related contact mapping parameters. Electrogram coupling was weaker in persAF than in PAF ($c_{0.5}$ (median±MAD): 2.4±0.5mm vs. 3.2±1.2mm, p<0.02). High correlation was found between mean $c_{0.5}$ and CV ( ρ=0.80, p<0.001). Other parameters showed only moderate or no correlation. Differences in AF conduction velocity between patients can be accurately described using a surrogate parameter based on the degree of electrogram coupling. This technique can for instance be applied to high-density contact recordings to quickly assess the Class I effect of antiarrhythmic drugs, both in atrial and ventricular recordings.*

## 1. Introduction

Invasive high-density contact mapping of atrial fibrillation (AF) provides detailed information on complexity of electrical conduction patterns. However, the detection and annotation of local activations in electrograms can be challenging due to electrogram fractionation [1]. Various methods have been designed to try and untangle local and remote signals to improve annotation, using for instance deconvolution [2] or the Laplacian of extracellular electrograms [3]. While these methods rely on several modelling assumptions (a uniform, constant wavefront velocity, a homogeneous, isotropic medium, etc.), the degree of similarity between electrogram morphology at adjacent sites during AF may already contain information related to AF substrate complexity and serve as a surrogate parameter to characterize conduction patterns without the need for electrogram annotation. In this study we investigated the relationship between an electrogram at a central electrode and electrograms at surrounding electrodes, expressed as the ability of surrounding electrograms to reconstruct the central electrogram. The decay in this reconstructive ability with increasing distance from the central electrode was then compared to standard invasive AF complexity parameters to better understand the implications of a higher or lower spatial coupling decay in relation to AF complexity.

## 2. Methods

### 2.1. Materials and electrogram processing

Electrogram were recorded by means of high-density contact mapping of AF using a $16 \times 16$ grid of electrodes (1.5mm electrode distance) in 21 patients during open-chest cardiac surgery. Epicardial unipolar electrograms were acquired from both the right atrial free wall and posterior left atrium at a sampling frequency of 1kHz for 10 seconds. Patients were in paroxysmal AF (PAF, n=12) or persistent AF (persAF, n=9) at the time of recording. Electrograms were not filtered before analysis, but ventricular contributions to the atrial electrograms, if present, were removed using a single beat cancellation method, by removing the first principal component as computed by principal component analysis on single ventricular beats (detected in a reference ECG), under the assumption that the first principal component represented the ventricular contribution.

## 2.2. Electrogram coupling

The degree of coupling between electrograms was defined as the spatial decay in the quality of the reconstruction of the central electrogram by surrounding electrograms at increasing distance. Given a set of electrograms at $N$ electrodes $\mathbf{x}[\mathbf{k}] = [\mathbf{x_1}[\mathbf{k}], \mathbf{x_2}[\mathbf{k}], \dots, \mathbf{x_N}[\mathbf{k}]]^{\mathbf{T}}, \mathbf{k} = \mathbf{1}, \dots, \mathbf{M}$ and Euclidean electrode distance $d_{i,j}$ between electrodes $i$ and $j$, the reconstruction of electrogram $i$ by electrograms recorded at electrodes at a distance $\delta$ was defined as the solution to the *nonnegative least squares (LS) problem* [4]

$$\min_{a} \sum_{k=1}^{M} \left\| \left( \sum_{j \in \{d_{i,j}=\delta\}} a_j x_j[k] \right) - x_i[k] \right\|_2^2, \quad a_j \geq 0.$$

The motivation behing using a nonnegative LS formulation as opposed to an unconstrained LS formulation is that we aimed to detect the instantaneous contribution of the local electrical activity present in an electrogram to the surrounding electrograms, and vice versa. This contribution was expected to have the same sign as the generating source, hence the positive constraint. Note that although the distance $d_{i,j}$ to the central electrode $i$ was required to be equal for all surrounding electrograms, the contribution $a_j$ could differ between electrodes. This was done deliberately to account for conduction pattern anisotropy [5] and to be more robust against varying electrogram quality. The degree of coupling $c(\delta)$ between electrograms was defined as 1 - the relative root mean square error of the reconstruction of a central electrogram by the positive linear combination of surrounding electrograms at a distance $\delta$:

$$c(\delta) = 1 - \frac{\|e_i^\delta\|_2^2}{\|x_i\|_2^2}, \quad e_i^\delta = \left( \sum_{j \in \{d_{i,j}=\delta\}} \hat{a}_j x_j \right) - x_i,$$

where $\hat{a}$ denotes the vector of electrogram coefficients corresponding to the optimal solution to the nonnegative LS problem. Coupling ranged from 1 (complete coupling) to 0 (no coupling), and was computed using only complete, symmetric topologies for each distance. Figure 1 shows an example of a central electrogram and corresponding optimal reconstructions using surrounding electrodes at selected distances.

For each electrode, coupling $c$ as a function of electrode distance $\delta$ was modelled by an exponential decay function: $c(\delta) = e^{-\lambda\delta}$. Half-decay distance $c_{0.5}$ was defined as $\frac{\ln(2)}{\lambda}$ and compared to conventional conduction-related contact mapping parameters, i.e. AF cycle length (AFCL), conduction velocity (CV), number of waves per AF cycle (NW) and electrode dissociation (D). Figure 2 depicts an example analysis of coupling decay and corresponding fitted decay function and half-decay distance, based on the same electrograms as in Figure 1.

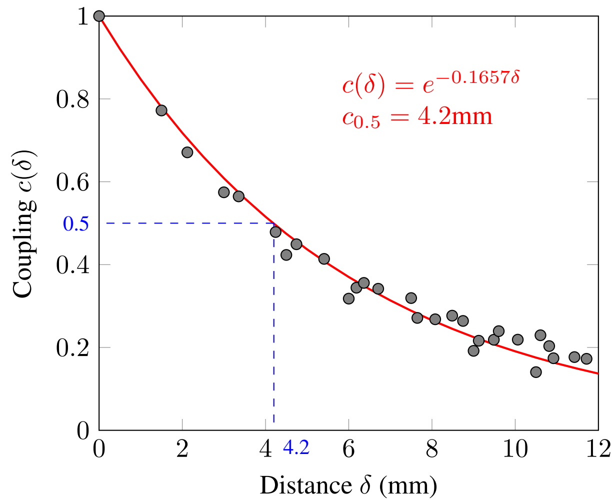


Figure 2. Example of the degree of electrogram coupling $c$ as a function of the distance $\delta$ of the surrounding electrodes to the central electrode. Half-decay distance $c_{0.5} = 4.2$mm is marked by the dashed blue line.

## 3. Results

Electrogram coupling was weaker in persAF than in PAF ($c_{0.5}$ (median±MAD): 2.4±0.5mm vs. 3.2±1.2mm, p<0.02, Wilcoxon rank-sum test, see Figure 3). High correlation (Spearman's $\rho$) was found between mean $c_{0.5}$ and mean CV ($\rho$=0.80, p<0.001, see Figure 4). Other parameters showed only moderate correlation (NW: $\rho$=-0.49, p<0.01, D: $\rho$=-0.50, p<0.01) or no correlation (AFCL: $\rho$=0.2, p=0.22). On the individual electrode level, the correlation between $c_{0.5}$ and CV was slightly less pronounced, but still present ($\rho$=0.66, p<0.001, see Figure 5).

## 4. Conclusions

Differences in AF conduction velocity between patients can be accurately described using a surrogate parameter based on the degree of electrogram coupling. Faster decay in the coupling strength between a central electrode and electrodes at increasing distance appeared to be strongly related to the conduction velocity of wavefront conduction patterns. A short-time version of the algorithm, e.g. estimating electrogram coupling on segments as long as the AFCL, may provide more detailed information on variations in conduction pattern characteristics. This technique can for instance be applied to high-density contact recordings to quickly assess the Class I effect of anti-arrhythmic drugs [6] or to identify potentially arrhythmogenic atrial regions with conduction slowing [7], and is not limited to atrial recordings, but can also be applied to ventricular recordings.

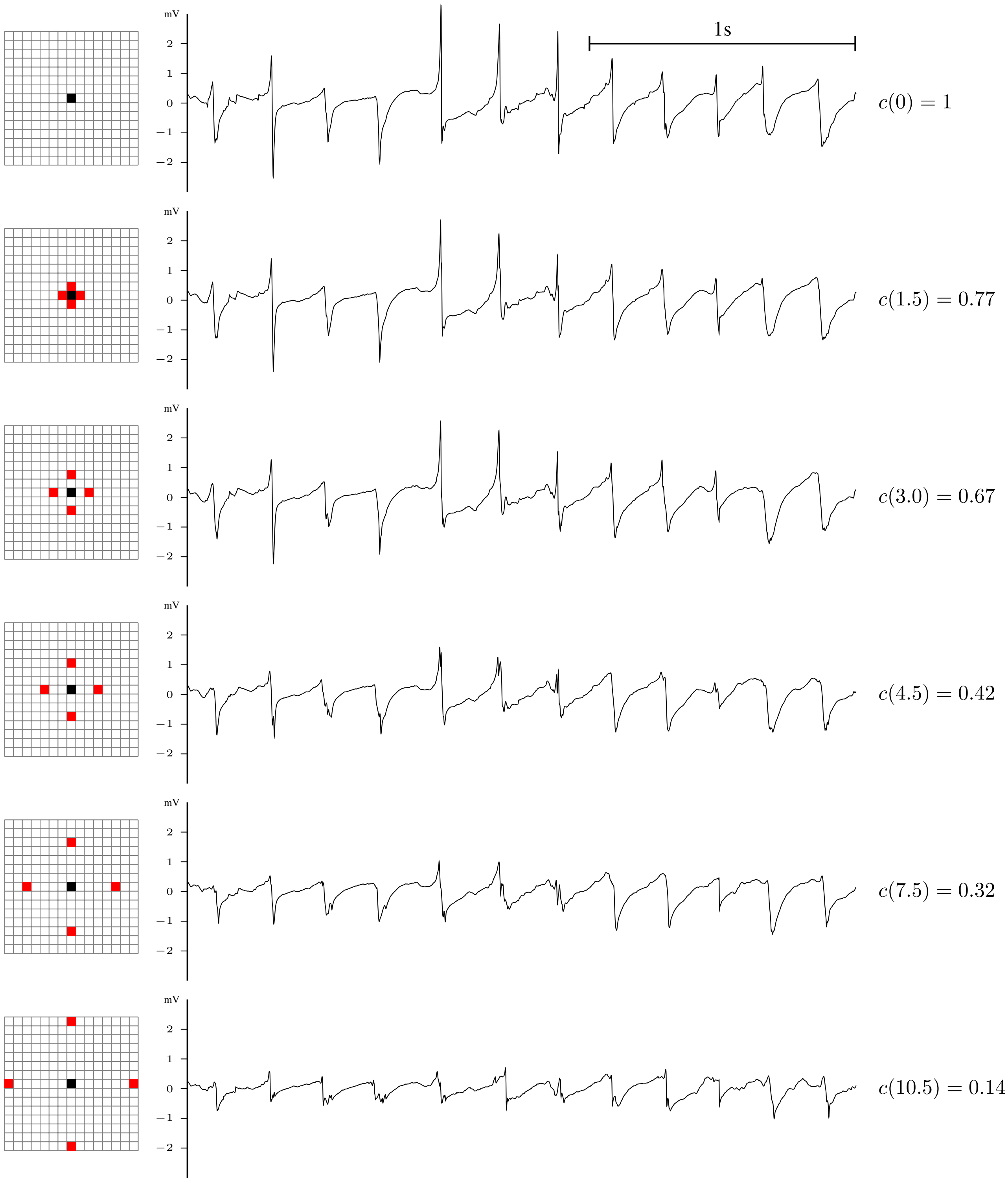


Figure 1. Example of electrogram reconstruction (paroxysmal AF) using symmetric topologies (red squares) at selected distances from the central electrode (black square). A 2.5 second segment (out of 10 seconds) of the original central electrode electrogram is shown at the top, followed by reconstructed versions using the set of electrograms at a certain distance (not all possible configurations shown). The degree of coupling $c(\delta)$ ($\delta$ in mm) of the original central electrogram and the surrounding electrograms at the selected distances is shown on the right.

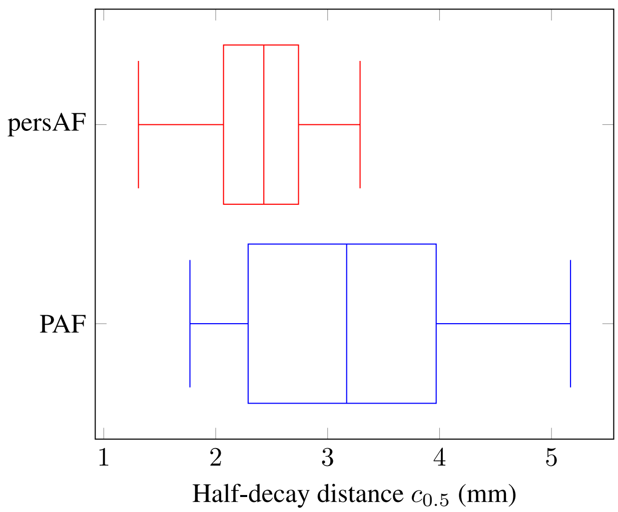


Figure 3. Box plot of distribution of average half-decay distance $c_{0.5}$ for paroxysmal (3.2±1.2mm) and persistent AF patients (2.4±0.5mm, $p<0.02$).

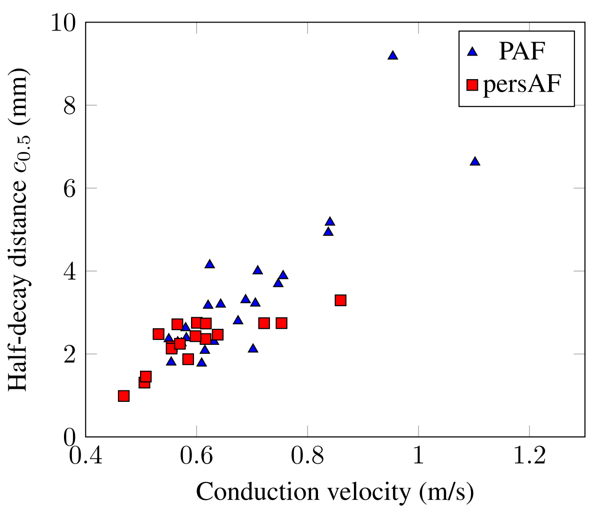


Figure 4. Relation between average wave conduction velocity of a recording and half-decay distance $c_{0.5}$ (Spearman's $\rho$: 0.80, $p<0.001$).

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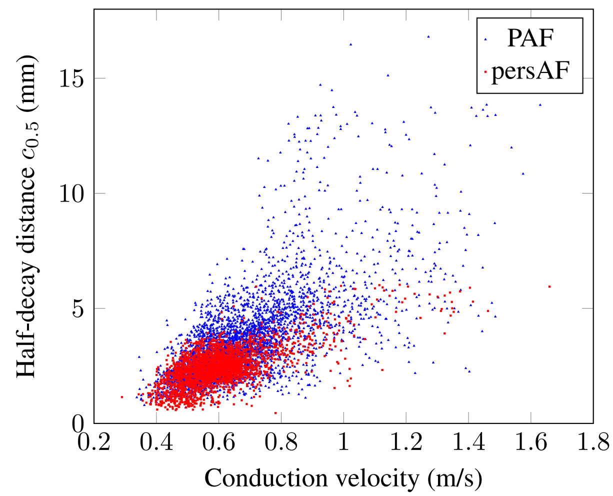


Figure 5. Relation between individual electrode wave conduction velocity for each recording and corresponding electrode half-decay distance $c_{0.5}$ (Spearman's $\rho$: 0.66, $p<0.001$).

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