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Wavelet analysis of cardiac optical mapping data

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ABSTRACT

Background: Optical mapping technology is an important tool to study cardiac electrophysiology. Transmembrane fluorescence signals from voltage-dependent dyes need to be preprocessed before analysis to improve the signal-to-noise ratio. Fourier analysis, based on spectral properties of stationary signals, cannot directly provide information on the spectrum changes with respect to time. Fourier filtering has the disadvantage of causing degradation of abrupt waveform changes such as those in action potential signals. Wavelet analysis has the ability to offer simultaneous localization in time and frequency domains, suitable for the analysis and reconstruction of irregular, non-stationary signals like the fast action-potential upstroke, and better than conventional filters for denoising.
Methods: We applied discrete wavelet transformation for temporal processing of optical mapping signals and wavelet packet analysis approaches to process activation maps from simulated and experimental optical mapping data from canine right atrium. We compared the results obtained with the wavelet approach to a variety of other methods (Fast Fourier Transformation (FFT) with finite or infinite response filtering, and Gaussian filters).
Results: Temporal wavelet analysis improved signal-to-noise ratio (*SNR*) better than FFT filtering for 5–10 dB *SNR*, and caused less distortion of the action potential waveform over the full range of simulated noise (5–20 dB). Spatial wavelet filtering produced more efficient denoising and/or more accurate conduction velocity estimates than Gaussian filtering. Propagation patterns were also best revealed by wavelet filtering.
Conclusions: Wavelet analysis is a promising tool, facilitating accurate action potential characterization, activation map formation, and conduction velocity estimation.

1. Introduction

Optical mapping is a very important tool to study cardiac electrophysiology ex vivo. This technique has the advantages of high spatiotemporal resolution of intracellular signals, which traditional intracellular and extracellular recording methods lack [1]. Optical action potentials (APs) have individual properties that differ from single cell measurements recorded with intracellular electrodes [2,3]. Given the benefit of high spatial resolution, optical imaging can record the propagation of the electrical wavefront over the surface of the heart to study electrical properties in normal and pathological conditions. Even though there have been great advances in imaging devices and voltage-sensitive dyes, challenges to recording high quality optical signal remain. In particular, transmembrane fluorescence signals emitted by voltage-sensitive dyes typically have low signal-to-noise ratio (*SNR*), which can hamper analysis [1]. Processing of optical mapping data can degrade the waveforms and alter physiologically relevant properties, leading to misinterpretations of physiological significance [1].

Wavelet analysis is an interesting method applied in many fields like mathematics, physics, engineering, and computer science [4–6]. The method, based on decomposing the signal into basic forms at different positions and scales, can be used for subsequent signal reconstruction with high precision. The main advantage of the wavelet approach is its ability to offer simultaneous localization in time and frequency domains, whereas the standard Fourier transformation is only specified in the frequency domain. Consequently, wavelet analysis has advantages in analyzing irregular and non-stationary waveforms. Cardiac APs generally have sharp upstrokes, for which the high frequency components are very rich over a very short period. Wavelet analysis might

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provide a powerful tool for the characterization of electrophysiological optical mapping data.

The objective of this study was to investigate the use of wavelet analysis as a temporal and spatial processing method for cardiac optical mapping data. Here, we first compare the temporal wavelet approach to Fourier filtering methods, specifically the Finite Impulse Response (FIR) and Infinite Impulse Response (IIR) filtering methods, on simulated optical APs and real canine atrial optical data. We then follow with a comparison between 2D spatial wavelet processing of activation maps and conduction velocity estimation with Gaussian kernel approach. Our results suggest that wavelet analysis is a promising technique for the processing and analysis of cardiac optical mapping data.

2. Methods

2.1. Temporal wavelet transformation

The wavelet transform and its multi-resolution implementation provide an analysis of the signal that is localized in both time and frequency. Given a mother wavelet $\psi(t)$, the wavelet series will be

$$\Psi_{a,b}(t)=\frac{1}{\sqrt{a}}\psi\left(\frac{t-b}{a}\right), \tag{1}$$

where $a,b\in R$, and $a\neq 0$. Here a and b are the dilating and translating coefficients respectively. The continuous wavelet transform (CWT) of the function $f(t)\in L^2$, is expressed as

$$W_{f(a,b)}=|a^{-1/2}|\int_R f(t)\psi^*\left(\frac{t-b}{a}\right)\mathrm{d}a\mathrm{d}b. \tag{2}$$

Practically, $W_{f(a,b)}$ is sampled on a dyadic grid, i.e., $a=2^{-m}$ (dyadic dilation) and $b=n\cdot 2^{-m}$ (dyadic position), with $m,n\in Z$.

2.2. Mallat's discrete fast wavelet transform algorithm

The discrete fast wavelet transform can be computed efficiently by using Mallat's algorithm with series of conjugate mirror filter pairs [7]. The decomposition level is obtained by using two complementary high-pass ($g[n]$) and low-pass ($h[n]$) filters under the following condition:

$$g[L-1-n]=(-1)^n h[n], \tag{3}$$

where L is the filter length. The high-pass and low-pass filters used in the algorithm are determined according to the mother wavelet [4]. The outputs from the $h[n]$ filter are refered to as approximation coefficients $a(n)$ and the outputs from the $g[n]$ filters are referred to as detail coefficients $d(n)$. The two filtering and sampling operations can be expressed by

$$a_{j+1}[k]=\sum_n a_j(n)\cdot h[2k-n], \tag{4}$$

$$d_{j+1}[k]=\sum_n a_j(n)\cdot g[2k-n], \tag{5}$$

where, $j>0$ represents the jth decomposition level. For $j=0$, $a_0(n)$ is the original signal to be analyzed.

2.3. Discrete wavelet transform to denoise temporal fluorescence AP signals

The denoising procedure consisted of the following three steps: (1) Wavelet transform to obtain the approximation and detail coefficients $a(n)$ and $d(n)$ for levels j up to j_{max}; (2) Selection of an optimal thresholding value to determine the set of detail coefficients; and (3) Reconstruction of the signal from the thresholded detail coefficients. With $f_{s/2}$ being half of the sampling frequency, each level j roughly corresponds to the frequency band between $2^{-j}f_{s/2}$ and $2^{-j+1}f_{s/2}$.

For orthogonal or biorthogonal wavelets, the maximum decomposition level is determined by the length of the signal (N) and of the decomposition filter (L). Generally, the decomposition level j is selected at a level smaller than j_{max} (Eq. (6)), as long as the characteristic frequency of the signal is covered by the band $[2^{-j}f_{s/2}, 2^{-j+1}f_{s/2}]$ [8], where

$$j_{max}=\mathrm{floor}(\log(N/(L-1))/\log(2)). \tag{6}$$

For the simulated data and experimental data shown in the paper, j_{max} was in the range between 4 and 8. The waveform of the synthesis and the analysis filters are identical, except for a time reversal.

Therefore, the reconstruction formula for each layer becomes

$$\hat{a}_j[n]=\sum_{k=-\infty}^{\infty}\left(\hat{d}_{j+1}[k]\cdot g[-n+2k]+\hat{a}_{j+1}[k]\cdot h[-n+2k]\right). \tag{7}$$

Here $\hat{a}_{j+1}$ and $\hat{d}_{j+1}$ represents the reconstructed approximation and detail coefficients of the level $j+1$. A soft thresholding operation, done before the reconstruction step, is applied to the detail coefficient based on the function ρ_T presented in Eq. (8). For example, for the level j, the thresholding operation is done by setting $d_j[k]$ to zero if its absolute value is below a certain level, denoted by T_M (by Eqs. (9) and (10)), or reducing by the difference with the threshold value of the coefficient, as in Eq. (8),

$$\rho_T(d_j[k])=\begin{cases}\mathrm{sgn}(d_j[k])(|d_j[k]|-T_M) & d_j[k]>T_M\\ 0 & d_j[k]\le T_M\end{cases}. \tag{8}$$

T_M, the threshold value, is a very important parameter for the reconstruction and is related to the noise level. The first step to calculate T_M is to estimate the noise level $\hat{\sigma}$. The noise estimation method proposed by Donoho and Johnstone [9] was adopted and $\hat{\sigma}$ calculated with Eq. (9)

$$\hat{\sigma}=\frac{\mathrm{median}(\{|d_1[k]|\})}{0.6745}. \tag{9}$$

The minimax method was then applied as a thresholding estimation method to obtain the threshold value T_M as

$$T_M=\hat{\sigma}(0.3936+0.1829\log_2(N)). \tag{10}$$

A note should be taken that the thresholding process is only applied to the detailed coefficients for the denoising application [4].

The use of different mother wavelets to analyze the same signal could produce varying results. Usually, a mother wavelet is characterized by properties such as orthogonality, symmetry, compact support and vanishing moment. The selection of the mother wavelet is determined by similarities between the properties of the signal and of the mother wavelet [10]. In this paper, four popular types of mother wavelet functions, Daubechies, Biorthogonal, Coiflets and Symlets, were used to filter fluorescence-intensity signals. When performing denoising, the thresholding value was calculated by the method of minimax thresholding (Eq. (10)), and soft thresholding (Eq. (8)) was the cut-off method for high frequency components [11–13]. Daubechies wavelets are the extreme phase wavelets. Symlet wavelets are more symmetric than Daubechies. In the biorthogonal approach, analysis wavelets are orthogonal to the synthesis wavelets [14]. Coiflets are discrete wavelets with scaling functions that have vanishing moments. All four types of wavelets have been used in biomedical signal and image processing [15–19]. Symlet functions have the disadvantage of generally slower processing than other wavelet-based methods including Daubechies filtering [13–17].

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