Wavelet Time Entropy, T wave morphology and myocardial ischemia

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Abstract

Using wavelets, we computed the entropy of the signal at various frequency levels (Wavelet Time Entropy) and thus find an optimal measure to differentiate normal states from ischemic ones. This new indicator is independent from the ST segment and yet provide a conclusive detection of the ischemic states.

1 Introduction

In electrocardiology, myocardial ischemia is typically detected by a shift of the ST segment as measured at the J+60 ms or J+80 ms markers ([1], [2], [11] and Figure 1). This paper examines the information content of the complete morphology of the combined ST segment - T wave through the *Fast Wavelet Transform* and Shannon's entropy proposing a new indicator of myocardial ischemia. Wavelets have already been used successfully in various areas of electrocardiology (for examples [4] and [12]) namely to identify the markers from a multiscale approach [13], detect ischemia in the QRS complex [9], and characterize the *time-frequency signature* of heart rate variability [15]. It has already been shown that the scale entropy of the wavelet coefficients could successfully differentiate various states in medical applications [8]. The present paper however, illustrates why the time entropy of the wavelet coefficients is more likely to be a good indicator of myocardial ischemia.

2 Signal Processing Theory

The general objective of this paper is to extract additional information from the ST segment - T wave in order to characterise myocardial ischemia. What is the minimal condition on a given set of functions $\{\psi_i\}_i$ such as a decomposition of the signal in terms of this set contains all the information of the signal? From a mathematical point of view, the answer is that the set $\{\psi_i\}_i$ must be a *frame*. A frame is a set of functions

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$\{w_i\}_i$ for which there exist $A > 0$ and $B < \infty$ such that for any square-integrable function f, $A\|f\|^2 \leq \sum_k |\langle f \mid w_k\rangle|^2 \leq B\|f\|^2$ where $\langle f \mid g\rangle = \int fg$ is the scalar product and $\|f\| = \sqrt{\langle f \mid f\rangle}$. Being a frame is a weaker condition than being an orthonormal basis; however, it is still sufficient to provide a meaningful decomposition of a signal : one can recover the original signal from the decomposition. Indeed, for any frame $\{w_i\}_i$, there exists a corresponding dual frame $\{\tilde{w}_i\}_i$ such that for any square-integrable function f, $f = \sum_k \langle f \mid \tilde{w}_k\rangle w_k$. Moreover, this decomposition is the most *economical* in the sense that whenever $f = \sum_k c_k \psi_k$, $\quad \sum_k c_k^2 \geq \sum_k \langle f \mid w_k\rangle^2$ ([6] and [14]).

Wavelets are examples of *frames* and they don't have to be an orthogonal basis. The scalar values $\langle f \mid \tilde{\psi}_k\rangle$ are called wavelet coefficients (see above). The wavelets must be chosen to have good time and frequency localization. In this particular application, since signals are short (a little over a hundred sampled values per T wave), a good time localization is extremely important. Moreover, since wavelet theory generally assumes that signals are infinite, special filters must be used at the beginning and end of the signal. Otherwise most of the transformation becomes meaningless ([5], [7], [10]). That is, the ratio of the length of the signal to the largest scale of interest is too small to ignore the boundaries. In the context of short signals and large amount of data (thousands of heartbeats), the *Fast Wavelet Transform* (FWT) ([6], [14]) must be used both for performance considerations and mathematical modeling (the *Continuous Wavelet Transform* assumes long signals or smooth models). To make the analysis easier, the wavelets used should be symmetrical so that the transform is time-reversal invariant. The Cohen–Daubechies–Feauveau (CDF) biorthogonal (linear) spline-wavelets were used [3]. They have compact support and are known to have optimal time localization for a given number of null moments (frequency localization) ([6], [14]). Splines-wavelets are extremely regular and unlike other wavelets, they are symmetric in time. The corresponding scaling functions are B-splines which have the shortest support and best regularity for a given number of null moments. In other words, spline-wavelets have the best approximation properties among known wavelets for a given number of null moments.

3 Shannon's entropy and cellular synchronization

Given a non-zero signal $\{x_i\}_i$, its entropy is computed by first transforming it into a new array having unitary mass using the formula $w_i = |x_i| / \sum_i |x_i|$. The entropy of the signal $\{x_i\}_i$ is defined by the positive value $\sum_i w_i \ln w_i$, where we use the convention that $0 \times \ln 0 = 0$. Notice that the entropy is invariant under the multiplication of the signal by a constant.

Application of the entropy concept to ST segment - T wave analysis can be stated as follows. From a cellular point of view, the T wave is a summation of *out-of-phase localized* myocardial action potential. If time dispersion of T waves is increased, as it is assumed to be the case during ischemia, synchronization between these superposed waves is lost. It is then hypothesized that a good indicator of synchronization (and ischemia) would be the entropy of the position in time of each superposed wave.

Ischemia would then be detected by a significant increase in this entropy.

Unfortunately, it is highly improbable that we will ever be able to directly measure this entropy by non-intrusive methods because the myocardial action-potential waveforms are unknown; even if we knew the waveforms (from eventual numerical computations for example), they will most probably not constitute a frame (hence they could not be used to decompose mathematically and analyze the signal).

Therefore, we have to approximate this entropy. It is often observed that in a time-frequency representation (as computed with wavelets) localization increase along with the frequency up to a level of noise saturation. Selecting this frequency level makes *time entropy* computations optimal.

One can compute the *wavelet coefficients entropy* at different scales (*time entropy*). Through a multiscale approach like the wavelet transform, one is able to automatically and easily detect the relevant scales (and frequencies) without *a priori* choices. Moreover, it allows to compare various scales (or frequencies) in order to differentiate various cases.

4 Data processing

Most of data processing steps have to do with denoising and increasing the robustness of the indicator. See Figure 2 for a flowchart of the algorithm.

4.1 The data

The data comes from the orthogonal ECG of five pigs using the Frank lead system. Pigs NHJ and NHQ received 10 mg/kg of metformine in 15 ml D5W at pH 12, and pigs NHB and NHI received respectively 0.3 mg/kg and 3 mg/kg of Glyburide in 1 ml DMSO in 14 ml D5W at pH 12, the other pig (NHA) received a placebo (15 ml D5W at pH 12). The cardiac rate is kept constant by atrial pacing while there is a controlled acute partial ($\cong 75\%$) coronary artery occlusion. The coronary blood flow and other relevant hemodynamic signals are continuously recorded before and during the occlusion at 500 samples/sec/channel. The pigs were also given one of two drugs or a placebo (P) before the occlusion and the effect of one of these drugs (glyburide) on the morphology will be briefly discussed.

4.2 Preprocessing and markers

The R_{max} marker (maximum of the R wave) is found by a 5 samples moving average applied on the vector magnitude. From R_{max}, R_{off} is defined as the first negative zero crossing of lowpass filtered (cut-off frequency of 40 Hz) spatial velocity vector amplitude. T_{off} is defined as the first inflexion point on spatial velocity vector amplitude after T_{max}.

On the orthogonal ECG used for this study, keeping only the R_{off}-T_{off} interval, an average of 95 % of the energy was projected onto the principal vector defined as the eigenvector of the correlation matrix corresponding to the highest eigenvalue in absolute value [16]. The *Fast Fourier Transform* (FFT) is used to denoise the signal at

60 Hz. In all pigs, some data contains short peaks caused by the artificial pacing to keep the heart rate constant. These are removed by a moving median filter with a window of 3 sampled values and a threshold of 2 % of the difference between the maximum of the signal and its minimum between T_{off} and R_{off}.

4.3 Fast Wavelet Transform (FWT)

The FWT is then applied on the last 113 sampled values in the R_{off}-T_{off} interval noted $\{U_k\}_{k=0,\ldots,112}$. The result is 4 different sets of wavelet coefficients; each one, corresponding to a different scale (see at the bottom of Figure 2). The scales are noted $\{w_s\}_{s=1,2,3,4}$. The entropy of each set of coefficients at each scale is then computed and corresponds respectively to the approximate frequency ranges 125 Hz to 250 Hz, 60 Hz to 125 Hz, 30 Hz to 60 Hz, and 15 Hz to 30 Hz. Explicitly, the wavelet coefficients can be written as summations $w_{1,i} = \sum_k h_{i,k} U_k, w_{2,i} = \sum_k h_{i,k} \sum_{k1} g_{k,k1} U_{k1}, \ldots$ The filters h and g are taken from [7].

4.4 Entropy calculation and postprocessing

We define the *Wavelet Time Entropy* at scale s by the equation

$$WTE_s = \sum_k \frac{|w_{s,k}|}{\sum_i |w_{s,i}|} \times \ln\left(\frac{|w_{s,k}|}{\sum_i |w_{s,i}|}\right) \tag{1}$$

where the w_s are the wavelet coefficients at scale s.

Remark 1. *WTE_s is invariant under the addition of a constant to the signal and under the multiplication of this same signal by a constant(different from zero).*

A moving median filtering of the WTE_s, with a window of about 1 minute (131 heartbeats), tends to improve difference between control and occlusion states. It doesn't discard valuable information because all experiments lasted more than an hour.

5 Results

The best scale is clearly the third one (30 Hz to 60 Hz) presented in Figure 3 The fourth scale (15 Hz to 30 Hz) is also interesting because some increase in entropy is observed with all pigs except NHB (the only one which received 3 mg/kg of glyburide before the occlusion) (see Figure 4) It was also found that some differentiation is also possible in all pigs for lower frequencies and higher frequencies (60 Hz to 125 Hz).

6 Discussion

From a mathematical point of view, these indicators are independent from the ST segment amplitude (see Remark 1). WTE_3 can serve to differentiate convincingly the occlusion state from the control state. There are various ranges of values from one pig to another, but except for pig NHI, a threshold of 2.29 was able to differentiate the

occlusion period from the control period that is, the value 2.29 was never exceeded in the control periods and always exceeded at least once in the occlusion periods. One observes that for some of the pigs, there is a delay (about 10 minutes) between the occlusion and a significant increase in WTE_3 (NHB and NHI) while for the other pigs (NHA, NHJ, and NHQ), it is almost instantaneous. This prolonged delay criteria matches the pigs which received glyburide but the size of the sample is not sufficient to establish a relationship between the two. This phenomenon is also observed with the ST-VM at J+60ms indicator. In all pigs except maybe NHI, there is a period of 5 to 15 minutes following the occlusion where WTE_3 is high (above 2.29 except for pig NHJ) followed by lower values for about 10 minutes. Such a systematic low frequency phenomena might be significant in terms of cellular synchronisation.

Concerning the lower frequencies (15 Hz to 30 Hz) and WTE_4, results are inconclusive because pig NHB show no significant increase in WTE_4 during the occlusion (see Figure 4). This might tend to indicate that glyburide makes the ischemia harder to identify (especially at low frequencies). Some differentiation is possible in all pigs at high frequencies. No particular changes in high-frequency components above 125 Hz could be identified [9] which might be caused by a lower signal to noise ratio.

7 Conclusion

The Wavelet Time Entropy indicators show that more information concerning myocardial ischemia is contained in the ST segment - T wave different than the amplitude of the ST segment (at J+60 ms or J+80 ms). This information is found in the morphology of the T wave considered from a time-frequency representation. In particular, it was shown that information is contained in the distribution of the energy (entropy) at specific frequency ranges (below 125 Hz) independently of possible energy transfers between frequencies.

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CAPTIONS

Figure 1 : Basic definitions

Direct relationship between an acute coronary artery occlusion causing ischemia and the ST segment amplitude. Interval between R_{off} and T_{off} is the region of interest in this study.

Figure 2 : Algorithm

The algorithm used is presented together with an example of processing on one heartbeat. The first step involves projecting the three leads on a single one by using the Karhunen-Loève transform and denoising the data. The FWT is then applied on the resulting signal and the entropy is computed at each scale. The WTEs plots are filtered with a 131 heartbeats median filter.

Figure 3 : WTE_3

The occlusion is indicated by a vertical line. The dotted line is a measure of blood flow from which the beginning of the occlusion is identified. The figure suggests a common approximate threshold of 2.29 to differentiate between normal states and occlusion states (this threshold is indicated by an horizontal dashed line).

Figure 4 : WTE_4

The occlusion is indicated by a vertical line. The dotted line is a measure of blood flow from which the beginning of the occlusion is identified.

FIGURES

Figure 1 : Basic definitions

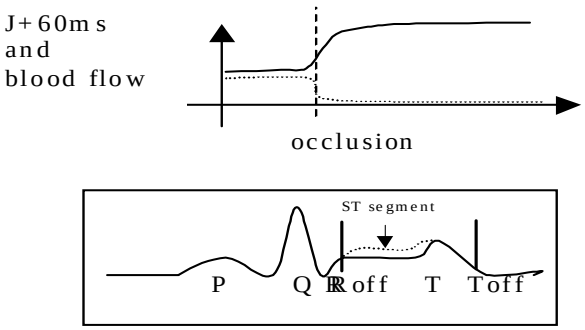

Figure 2 : Algorithm

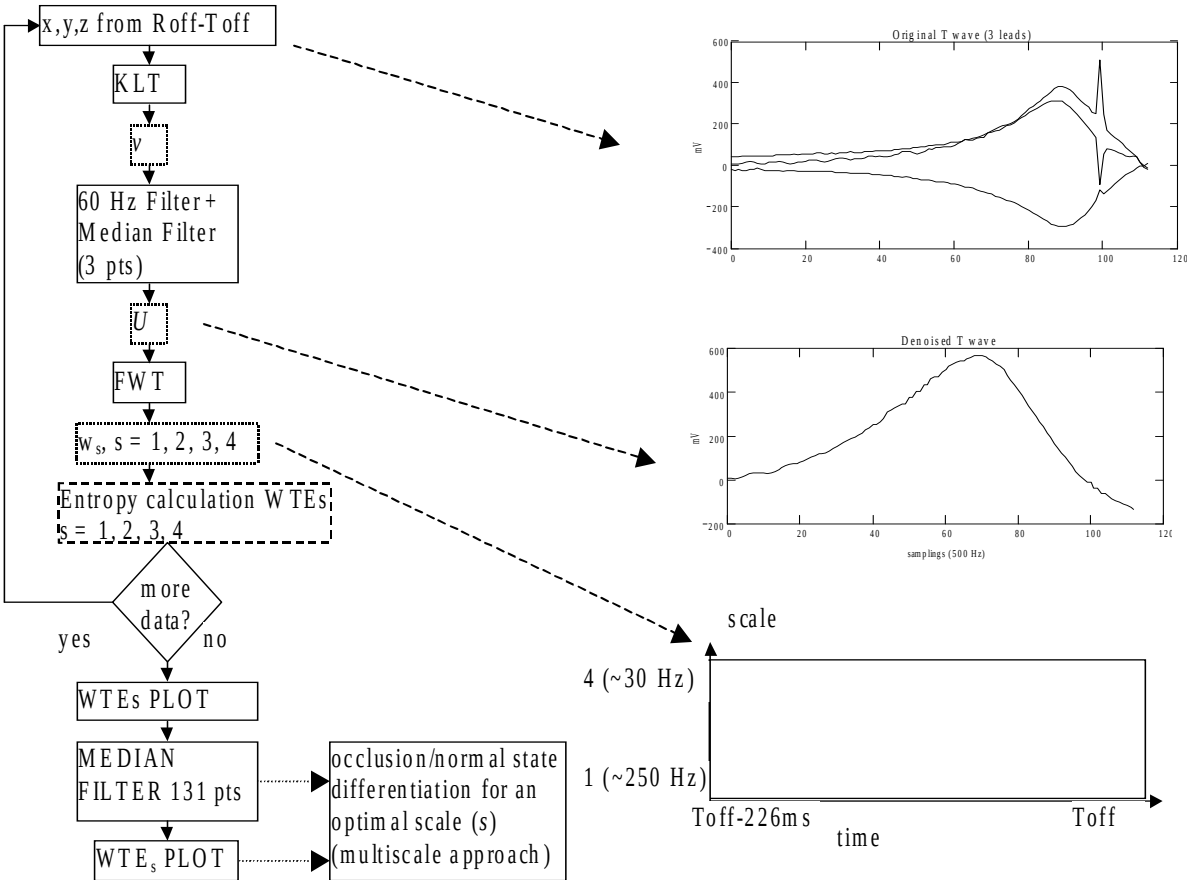

Figure 3 : WTE_3

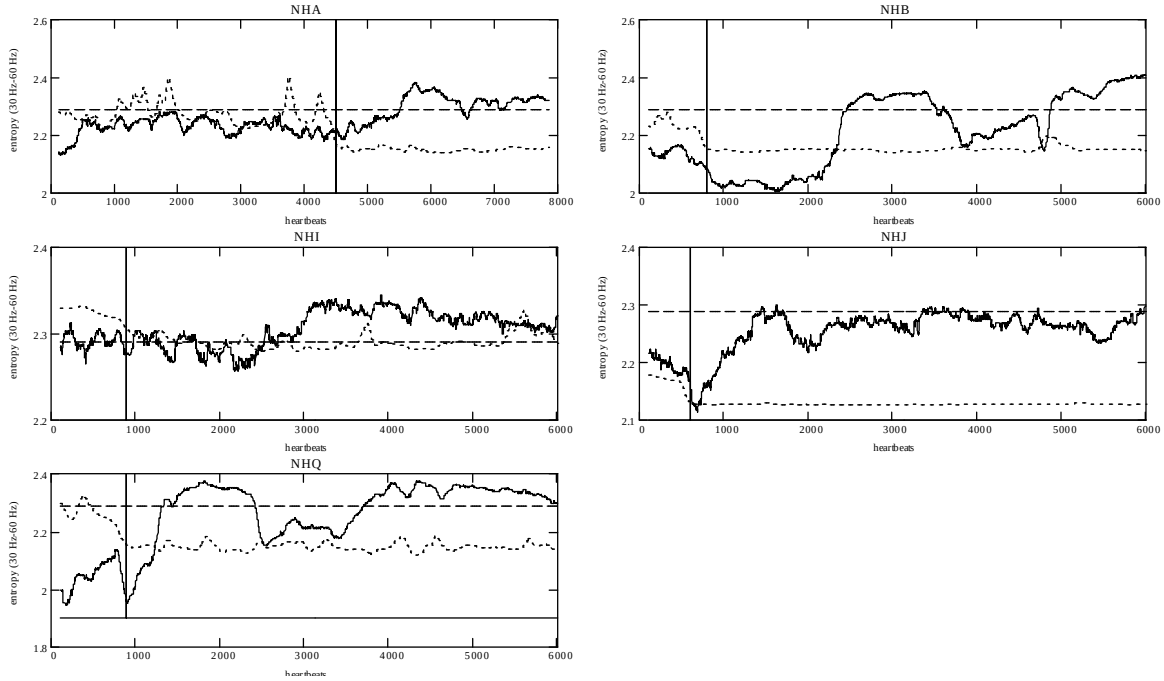

Figure 4 : WTE_4