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MODELLING SHORT TERM VARIABILITY INTERACTIONS IN ECG: QT VERSUS RR

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Abstract: QT and RR series interactions were explored by a dynamic linear approach using AR and ARARX models with automatic orders selection. Validation with simulated data and application to real records are presented. An important QTV fraction was found to be not linearly driven by HRV.

1 Introduction

The electrocardiogram (ECG) analysis is extensively used as a diagnostic tool to provide information on the heart function. Each cardiac beat (Figure 1) is typically associated to a sequence of five principal waves denoted by P, Q, R, S and T, whose characteristics are clinically relevant. In particular, the time interval between the onset of the QRS complex and the T wave end, known as QT interval, is considered to express the duration of ventricular repolarization. Abnormal QT values have been associated with ventricular pro-arrythmicity and its beat-to-beat variations are, to some extent, driven by the autonomic nervous system through the RR interval (measured as the time interval between consecutive beats). However it has not been yet clearly quantified which fraction of QT variability (QTV) is effectively correlated with RR beat-by-beat variations (Heart Rate Variability - HRV).

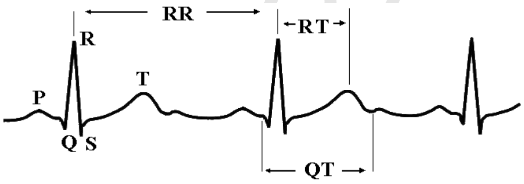

Figure 1: Schematic representation of relevant information in a cardiac beat.

The determination of RR and QT sequences requires the detection and delineation of ECG waves and limits. A wavelet transform based delineation system has proven to be quite robust against noise and morphological variations [3], even in the problematic T wave. Problems in delineation of T end lead to uncertainty in QTV measures which, allied to its smaller amplitude compared to HRV, represents the main difficulties in exploring this relation.

Many authors used alternative measures such as the RT interval (time between the peaks of the R and T waves); however, in spite of being easier to measure, the RT presents even shorter length than QT interval, additionally penalising the variability measures. A linear dynamic parametric approach was proposed by Porta et al [7] to express the interactions between the RR and RT intervals and allowing to quantify the fraction of the RT variability driven by RR. In previous work [1] we used a linear low order model similar to the one proposed by Porta to explore the short term HRV and QTV relations. A generalized and improved version of that model including automatic orders selection is now proposed and validated, defining an approach to quantify the fraction of QTV not driven by HRV.

2 Methods

2.1 Model formulation

Our approach, based on Porta [7], expresses RR and QT variability interactions in an open loop linear model (Figure 2) where A_{11}, A_{12}, A_{22} and D are polynomials in z^{-1} with coefficients $a_{11}[k]$, $a_{12}[k]$, $a_{22}[k]$ and $d[k]$, respectively. The series $W_{RR}[n]$ and $W_{QT}[n]$ are uncorrelated stationary zero-mean white noises with variances λ^2_{RR} and λ^2_{QT} and n denotes beat number.

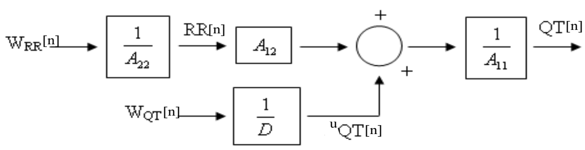

Figure 2: Schematic representation of the QTV versus HRV model.

$RR[n]$ series was modelled as an AR_p stationary random process given by

$$RR[n] = -\sum_{k=1}^{p} a_{22}[k]RR[n-k] + W_{RR}[n] \qquad (1)$$

The QT was assumed to result from two uncorrelated sources, one driven by heart rate and other resulting of an exogenous input ($ARARX_q$ model [2])

$$QT[n] = \sum_{k=0}^{q} a_{12}[k]RR[n-k] - \sum_{k=1}^{q} a_{11}[k]QT[n-k] +^{u} QT[n], \qquad (2)$$

$$^{u}QT[n] = -\sum_{k=1}^{q} d[k]^{u}QT[n-k] + W_{QT}[n]$$

Therefore, the model accounts for the possible dependence on its past values and those of the RR interval (as shown in recent studies [8]). For simplicity, the same order q was assumed for all ARARX model polynomials, while a possible different order p is allowed for the AR model. This is a generalization from previous approaches [1, 7] where the same order was considered for all polynomials in the model. In fact there is no reason to constrain the QT and RR sequences to the same memory of its own past.

The assumption of uncorrelated sources allows to compute the Power Spectral Density (PSD) of QT ($S_{QT}(f)$) as the sum of the partial spectra that express each one of the contributions

$$S_{QT/W_{RR}}(f) = \overline{RR}\lambda_{RR}^2 \left| \frac{A_{12}(z)}{A_{11}(z)A_{22}(z)} \right|^2_{z=exp(j2\pi f\overline{RR})} \tag{3}$$

$$S_{QT/W_{QT}}(f) = \overline{RR}\lambda_{QT}^2 \left| \frac{1}{A_{11}(z)D(z)} \right|^2_{z=exp(j2\pi f\overline{RR})} \tag{4}$$

where f is the frequency in Hz. As both $QT[n]$ and $RR[n]$ series are unevenly sampled the mean RR interval ($\overline{RR}$) was used as sampling rate for estimating the PSD functions, what has been shown acceptable for low frequencies far from the Nyquist frequency [4]. As usual in HRV studies, the spectral energy within each frequency band (*band*) was measured taking the areas (P^{band}) below the spectra, S,

$$P_E^{band} = \int_{f\in band} S_E(f)df; \tag{5}$$

with $E \in \{QT, QT/W_{QT}, QT/W_{RR}\}$. The ratios between $P^{band}_{QT/W_{QT}}$ and in total power P^{band}_{QT} represent the relative contribution of the QTV not driven by RR in the frequency band *band*.

2.2 Model identification and order selection

From the $RR[n]$ and $QT[n]$ interval series corrected from the mean, the polynomial A_{11} was estimated using least squares, while the ARARX model parameters were iteratively obtained using a generalized least squares methodology [2]. For adequate orders the convergence to white noise residual W_{QT} is expected in a reasonable small number of iterations and a large enough SNR guarantees that the minima of the square residue are global [2].

From $p, q \in \{6, 8, 10, 12, 14, 16, 18\}$, an order was considered to be adequate for modelling a given segment of data if the normalized autocorrelations of the residual ($W_{RR}[n]$ or $W_{QT}[n]$) satisfied a 5% significance bilateral test, both in lags lower than 40 beats and considering all lags. The optimal p and q were automatically selected from the adequate orders as the ones that better satisfied a common criteria such as FPE or AIC [2]. The uncorrelation between $W_{RR}[n]$ and $W_{QT}[n]$ was also verified for the same 5% significance.

2.3 Simulation set-up and performance evaluation

The validation of the model was based on simulated $RR[n]$ and $QT[n]$ series with known QTV fraction correlated with RR ($QT_{W_{RR}}$).

The $RR[n]$ sequences were simulated using a model IPFM (integral pulse frequency modulation) [4] following a AR_{10} modulating signal. Two models (RR1 and RR2) with different main frequency components (Figure 3) were used to simulate uncorrelated RR series realizations.

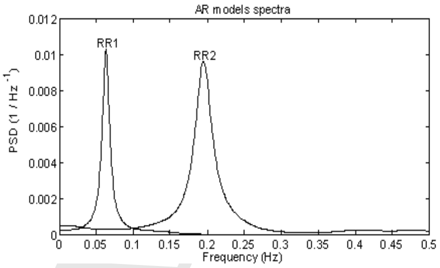

Figure 3: Spectra of the AR_{10} models used to generate data.

To obtain realistic QT series from RR sequences we considered a constant QT value qt_0, extracted from a real beat, and used the classical *Bazett's* formula as a static relation between a QT and the previous RR [8]: $QTj[n] = qt_0\sqrt{RRj[n]}$, for $j = 1, 2$. The test data was defined considering 3 cases:

A: QT and RR correlated: $RR1_i[n]$ vs $QT1_i[n]$ and $RR2_i[n]$ vs $QT2_i[n]$;

B: QT and RR uncorrelated: $RR1_i[n]$ vs $QT2_i[n]$ and $RR2_i[n]$ vs $QT1_i[n]$;

C: Mixture of the dependencies: $RR1_i[n]$ vs $QT1_i[n]+QT2_i[n]-\overline{QT2_i}$ and $RR2_i[n]$ vs $QT1_i[n]+QT2_i[n]-\overline{QT1_i}$; were $\overline{QTj_i} = (\sum_{n=0}^{N} QTj_i[n])/N$.

were i denotes realization. The $QT[n]$ fraction linearly driven by $RR[n]$ is denoted as $QT_{RR}[n]$ and calculated for each pair of test data as the projection of ($QT_i[n]$-$\overline{QT_i}$) over the subspace generated by the corresponding ($RR_i[n]$-$\overline{RR_i}$) and its delayed vectors up to order 10 (in accordance with RR simulation). The ratio between the power variability measures of this projection and of the total QTV corresponds to the fraction correlated with HRV. The reference variability measures $\tilde{P}_E^{band}$ were obtained from AR_{10} spectral model, analogously as P_E^{band} and the errors calculated as $P_E^{band} - \tilde{P}_E^{band}$.

After identification of the model (figure 2), from the estimated coefficients and the residues $W_{RR}[n]$ and $W_{QT}[n]$, we calculated explicitly the signals $QT_{W_{RR}}[n]$ and $QT_{W_{QT}}[n]$ corresponding to the two uncorrelated driving sources in QT ($QT[n] - \overline{QT} = QT_{W_{QT}}[n] + QT_{W_{RR}}[n]$). The similarity of $QT_{W_{RR}}[n]$ and the reference projection $QT_{RR}[n]$ was evaluated from the coherence between them and the same was applied to $QT_{W_{QT}}[n]$ versus the difference between $(QT[n] - \overline{QT})$ and the reference projection (corresponding to the QTV fraction uncorrelated to HRV). Both spectral coherences were calculated using an non parametric approach (Welch method with a Hanning window).

2.4 Real data set

ECG recordings of young normal subjects from POLI/MEDLAV and Politecnico Ca' Granda databases [6] were used in this study (3 leads at 500 Hz) and each lead was processed by the delineation system in [3]. Only segments with minimum length of 315 consecutive beats with valid RR and QT intervals were considered in the subsequent analysis: anomalies in RR series were identified [5] and QT intervals out of a 3-standard deviation band were rejected as possible outliers. Longer segments were carved up respecting the minimum length admitted, what allowed to obtain 29 segments from POLI/MEDLAV database and 135 segments from Politecnico Ca' Granda database, with a mean length of 415 and 402 beats ($\approx$ 292.46 and 329.24 sec), respectively.

3 Results and discussion

The methods were implemented using MATLAB and the facilities of the System Identification Toolbox. All the results are relative to the orders chosen by FPE but analogous ones were obtained using AIC. To evaluate whether the uncorrelated fraction differed for different frequencies, the measures were estimated considering separately low frequency (band = LF: 0.04-0.15 Hz) and high frequency (band = HF: 0.15-0.4Hz), frequency bands typically used in HRV studies. Total power (band = TP) was considered as the band from 0.04 Hz to the highest frequency present in each spectrum.

3.1 Simulated data

We simulated 50 uncorrelated RR realizations ($i = 1, ..., 50$) with 348 beats at 500 Hz, resulting on a test data of 300 pairs of RR vs QT series.

As expected the orders selected (figure 4, left) were mainly the lowest, as an AR_{10} was used to generated $RR[n]$ series and the IPFM model does not change revelantly the frequency components, for the considered frequency bands [4]. The errors in the calculated ratios between $P^{band}_{QT/W_{QT}}$ and P^{band}_{QT} were lower than 5% for more than 75% of the series in LF and HF frequency bands and for about 96% of the segments considering TP. In the right panel of figure 4 are presented the distribution of the errors for each case.

The mean and standard deviation of the errors in the estimated QTV fraction uncorrelated to RR can be found in the table below, for each case of simulated series and for all the data set, considering each frequency band.

CORRECTED DRAFT

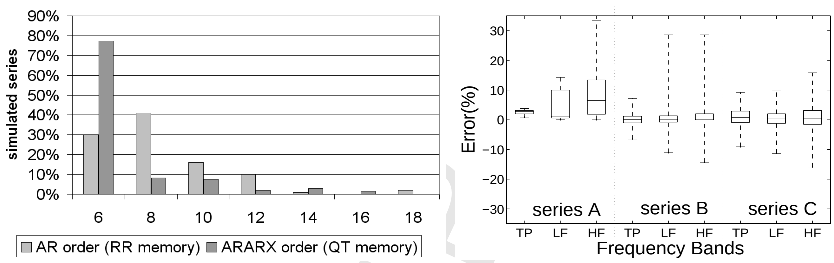

Figure 4: Simulated data: left) selected orders; right) box and whisker plots of errors in the ratios between $P^{band}_{QT/W_{QT}}$ and P^{band}_{QT}.

	series A	series B	series C	all data sets
$P^{TP}_{QT/W_{QT}}$	2.53 ± 0.76	-0.06 ± 2.11	0.88 ± 3.12	1.12 ± 2.46
$P^{LF}_{QT/W_{QT}}$	4.56 ± 5.21	1.01 ± 5.99	0.63 ± 3.22	2.07 ± 5.24
$P^{HF}_{QT/W_{QT}}$	9.45 ± 8.89	1.46 ± 7.10	0.55 ± 4.48	3.82 ± 8.10

Errors in ratios over simulated data ($\%, mean \pm std$).

Considering all data sets, the mean errors were lower that 4% for all bands. The increased error found in series A is due to the very low power of RR1 and QT1 series in HF band and of RR2 and QT2 in LF band (as illustrated in Fig. 2), resulting in a small absolute error on the estimated PSD measures holding a high percent importance. Eliminating the series A the mean results became lower that 1%, with a relevant decrease on std values (0.41 ± 2.70 for TP, 0.82 ± 4.80 for LF and 1.00 ± 5.94 for HF).

The gain (evaluated as the squared absolute value) and phase (angle) of the complex spectral coherence γ between the model estimated $QT_{W_{RR}}[n]$ and the projection $QT_{RR}[n]$ used as reference are presented in the table below, for each frequency band. The high gains reflect the degree of similarly between the variability distribution shapes and thus $QT_{W_{RR}}[n]$ has frequency contents close to $QT_{RR}[n]$ both in power as in location of peaks. The lower gains relative to $QT_{W_{QT}}[n]$ are partially related with the very low power in some regions of the simulated spectra (case A). Excluding these series the mean gain increase to 0.87 (TP), 0.93 (LF) and 0.86 (HF). The very low phases reflect the no existence of delays in the model.

	$QT_{W_{QT}}[n]$		$QT_{W_{RR}}[n]$	
	γ gain	γ phase (rad)	γ gain	γ phase (rad)
TP	0.98	0.01	0.76	-0.01
LF	0.99	-0.02	0.80	-0.01
HF	0.90	0.01	0.75	-0.01

Mean spectral coherence between QTV fractions and the references

3.2 Real data

We obtained adequate models for 28 segments in POLI/MEDLAV and 132 in Politecnico Ca' Granda database and in 4 cases for which we did not found an adequate order to the AR model part.

In the left panel of figure 5 the orders selected by FPE for each model part are presented. Lower orders are more frequent for the ARARX model than for AR, reflecting different dependence of QT from its own past (memory) and past RR intervals. This can also be seen in simulated signals (left side of figure 4) validating that the QT intervals were realistically simulated.

The fraction uncorrelated with HRV was found to be higher than 40% for 98% of the segments in TP and HF band and for 91% in LF suggesting that other factors rather than RR could drive an important part of QTV. The values found for the ratios (%) between the measures on uncorrelated fraction and total QTV spectrum were very high, as illustrated in Figure 5. It is worthwhile to remark that in this study we aimed to estimate the fraction of QTV that is not correlated with HRV. The uncorrelation between that part of QTV and HRV does not imply that there is not any physiological dependence between them, since non-linear effects are not taken into account.

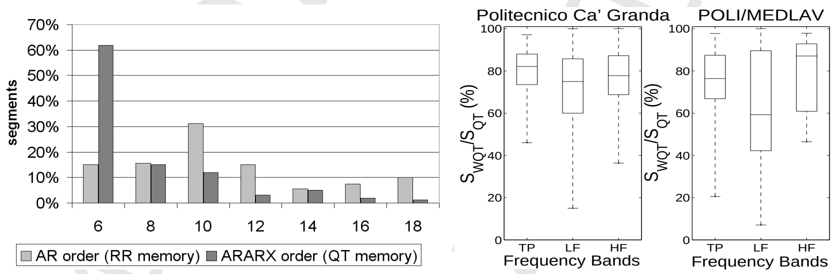

Figure 5: Real data: left) selected orders; right) box and whisker plots of the ratios between $P^{band}_{QT/W_{QT}}$ and P^{band}_{QT}.

4 Concluding remarks

This work discusses the characterization of the short term QT versus RR variabilities by applying a linear open loop model that includes an approach for order selection in each part of the model. The methodology was validated with simulated data and applied to real records. The orders selected for the RR model part are generally higher than for QT what can be associated to differences in the memory of the signals. The results point out that an important part of QTV (more than 40%) is not linearly driven by RR.

The study of the QT versus RR interactions is a complex problem. A deeper characterization requires the incorporation of additional information on the model. Identification and interpretation of the sources non-correlated with RR are the driving force for future studies.

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