TIME SERIES PREDICTION USING PARAMETRIC MODELS AND MULTILAYER PERCEPTRONS: CASE STUDY ON HEART SIGNALS

Rajai El Dajani[1,2], Maryvonne Miquel[1,2], Pierre Maison-Blanche[3] and Paul Rubel[1,2]

[1] Institut National des Sciences Appliquées de Lyon (INSA), Laboratoire d'Ingénierie des Systems d'Information (LISI), Bat 501, 20 avenue Albert Einstein, 69621 Villeurbanne
[2] INSERM ERM107, 28 avenue Doyen Lepine,69500 Bron
[3] Hopital Lariboisiere, Paris, France

ABSTRACT

Physiological signals are usually patient specific, and they are difficult to predict, especially for the cardiovascular system. New methods capable to be adapted to each case and to learn the singular behavior of heart functions should be developed to support physicians in their decision-making. One of the most widely studied relations is the QT-RR one, between the total duration of the ventricle activation and inactivation, and the heart rate. In the past, different studies were made to approach this relation in the steady state. In this paper, a new method for modeling and predicting the transient dynamic behavior of QT interval in relation to changing RR intervals is presented using parametric models and multilayer perceptrons (MLP).

1. INTRODUCTION

Cardiac disease is the underlying cause in two-thirds of out-of-hospital sudden deaths. Despite expanding insight into the mechanisms causing sudden cardiac death (SCD), the population at high risk is not yet going to be effectively identified, and mechanisms of SCD in subjects with apparently normal hearts are poorly understood. A non-invasive method for early detection of heart pathologies becomes an important challenge for public health interest.

New methods of signal processing and Quantitative Electrocardiology made the electrocardiogram (ECG) a privileged way to detect heart arrhythmias and acute myocardial ischemia that might lead to SCD. Among the different measurements that are performed on the ECG, one of the most studied one is the QT interval. It measures the time after which the ventricles are again repolarized. One of the main reasons for the great interest in measuring the QT interval is that its prolongation has been related to cardiac arrhythmia, like ventricular fibrillation and *torsades de pointes*. The study of the dynamicity of ventricular repolarisation in ambulatory patients is of major interest to assess the risk of sudden death [1].

The duration of QT is influenced principally by the inverse of the heart rate, measured by the RR duration between two successive heart beats. QT duration is also influenced by gender, age, the central nervous system and circadian cycles [2].

Bazett already proposed a variation model of the QT-RR relationship in 1920 [2]:

$$QT_i = k\sqrt{RR_{i-1}}$$

Since then many other relationships were proposed. These non-linear models are valid only for heart beats corresponding to steady rhythm periods lasting almost one minute. In the absence of the steady state situation, the study of the QT-RR relationship becomes more complex and usual methods are not adapted [3].

It has been shown by invasive studies that the QT interval has a delayed adaptation to sudden changes in heart rate in normal subjects. The QT-RR relationship seems to behave like a first order system with a time constant of about one minute [3]. Abnormalities in the adaptation of the QT interval to changes in the RR interval may facilitate the development of ventricular arrhythmia.

In this paper we propose to model the QT dynamic behavior in function of the history of RR intervals by means of parametric models and multilayer perceptrons.

2. MATERIALS AND METHODS

Time series prediction is based on the idea that the time series carry within them the potential for predicting their future behavior. Linear models (such as MA, AR, and ARMA) have been most frequently used for time series analysis, although often there is no inherent reason to restrict consideration to such models. Linear models have two particularly desirable features: they can be understood in great detail, and they are straightforward to implement. Linear models can give good prediction results for simple time series but can fail to predict time series with a wide band spectrum, a stochastic or chaotic time series, in

which the power spectrum is not a useful characterization. The analysis of such series requires a long history of the series, which results in a very high order linear model.

A number of new nonlinear techniques, such as neural networks (NNs) and wavelets, promise insight that traditional linear approaches cannot provide. Some recent work shows that a feed-forward NN, trained with back-propagation and a weight elimination algorithm, outperforms traditional nonlinear statistical approaches in time series prediction [4]. The simplest approach for learning a time series model by means of an NN is to provide its time-delayed samples to the input layer of the NN. The more complex the series are, the more information about the past is needed, so the size of the input layer and the corresponding number of weights are increased.

2.1. Pre-Processing on RR and QT Signals

The ambulatory ECGs are recorded by means of a 3-channel analog Holter recorder [5]. RR and QT sequences were chosen over the 24H recording using as a selection criterion the richness in variations of the RR interval. Several twenty minutes length ECG sequences were selected for six patients without heart diseases and the following steps are performed:

- The RR intervals and the QT duration are calculated using the "Lyon System" and the "Caviar" methods [6].
- Because of the variability of the heart rate, an over-sampling of 4Hz with linear interpolation is used to pass from an unequally sampled to an equally sampled time series sequence.
- The RR and QT time series are low-pass filtered at 0.05Hz to eliminate the high frequencies (HF) and low frequencies (LF) components due to the parasympathic (HF) and the sympathic (LF) activities.
- Finally the filtered RR and QT sequences are down sampled to 0.5 sample per second by keeping one point over eight.

2.2. Artificial Data Description

The complexity of physiological signals makes difficult to finalize and to validate the predictive models. Therefore we will also use, in addition to real data, simulated data for the assessment of the models performances. The quality of the predictive models learned on real data will also be tested on artificial sequences covering the usual RR and QT situations. The artificial data are used to simulate data that could have been recorded in invasive electrophysiology.

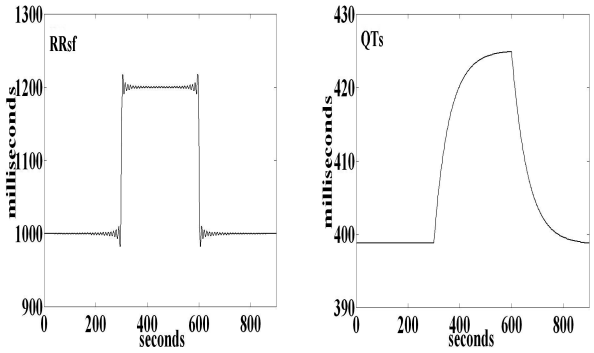

Figure 1: Artificial data used to assess prediction capacities of the models.

To simulate a first order one-minute time constant behavior of the QT-RR relationship, the following steps are performed:

- Generation of RRs, a RR sequence simulating a step function. RRs is composed of a 5 minutes baseline, an abrupt change in amplitude of 200 milliseconds that is maintained for 5 minutes, a return to the baseline that is kept for 5 minutes. The total duration of the step function is 15 minutes.
- Computation of RRresp, the first order one minute time constant response to RRs:

$$RRresp_i = RRs_1 + [RRs_i - RRs_1] \times \left[1 - \exp\frac{1-i}{td}\right]$$

where *td* is the one minute time constant and RRs_1 is the first sample of RRs.

- Filtering RRs using the same low-pass filter used for the real RR and QT data, RRsf is the filtered signal.
- Computation of QTs, the simulated QT, according to the following function where all values are in milliseconds [2]:

$$QTs_i = 8.7 * \sqrt{RRresp_{i-1}} + 123.7$$

RRsf is presented to the entry of the models and their output is compared to the expected QTs (fig. 1).

2.3. Multilayer Perceptrons

The MLP model will learn the following patient specific relationship:

$$QT_i = f(RR_i, RR_{i-1}, ..., RR_{i-M+1}, RR_{i-M}) \qquad (1)$$

where M is a time delay.

For the modeling of the QT dynamics we have chosen the MLP architecture with *NbE* entries (RR values), *k* sigmoïdal hidden neurons and one linear output neuron (QT value) as shown in figure 2.

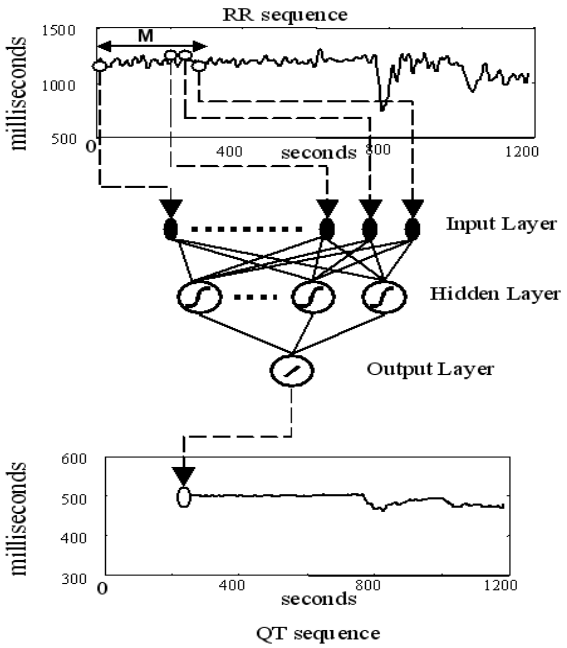

Figure 2: MLP architecture with NbE entries, k hidden neurons and 1 output neuron

The number of entries *NbE* in the input layer will depend on the time delay M to be taken into account for modeling the relationship described in equation (1). The number of entries NbE is determined by equation:

$$NbE = M \times 30 \qquad (2)$$

where M is the time delay expressed in minutes.

2.4. Parametric Models

There are several elaborations of the basic ARX model, where different disturbance models are introduced. These include well known model types, such as ARMAX, Output-Error (OE), and Box-Jenkins (BJ). All these models have been tested on the real sequences and only the results of the best model are presented in this paper.

After validation of the parametric models on real data, the Akaike's Final Prediction Error (FPE) criterion will be used to select the best model.

2.5. Prediction Quality Evaluation

Beside the visual criterion, another criterion is needed to compare only the dynamical behavior of real and predicted signals. Therefore, the standard deviation over the prediction error is used as a complementary criterion.

3. RESULTS AND DISCUSSION

To determine the appropriated models, night ECG sequences recorded at 4:25 am and belonging to patient "Clav" were selected. The RR and QT signals are used respectively as input and output values in the learning phase for the parametric models and the MLP.

3.1. Parametric Models

The best parametric model obtained was the OE with the following parameters nb=2, nf=1 and nk=0, where nb and nf are the orders of the output error model and nk is the delay. The FPE value for this model is 23.4

The QT-RR relationship is:

$$QT(t) = 0.99 * QT(t-1) + 0.034 * RR(t) - 0.023 * RR(t-1)$$

3.2. MLP Architecture

To determine the value of the delay M necessary for a good learning of the QT-RR relationship, an additional ECG sequence recorded at 6:05 am and belonging to "Clav" is selected. This sequence is used as a test set to stop the training when no further amelioration on the prediction performance is noticed. The mean square error (MSE) is taken as a measure for evaluating the performance:

$$MSE = \sum_{i}^{N} \frac{(QTp_i - QTm_i)^2}{N} \qquad (3)$$

where QTp_i is the i-th network output, and QTm_i is the i-th target output out of *N* instances.

The delay M was set to vary from one minute up to eight minutes [2], and the number of hidden neurons from 2 to 22 using 10.000 training iterations. For a delay greater than 4 minutes no significant improvement was noticed on the learning quality and the MSE in equation (3) stayed constant. Therefore the number of neurons in the input layer was set to 120, using equation (2). The best MLP was the one with 120 entries and 10 hidden neurons.

3.3. Results on Artificial and Real Data

The responses of the OE model and the MLP were tested on the step function as shown in figure (3). The dynamical behavior of the MLP response is much closer to the expected one than the OE model. The result is also noticed on figure (4) where an RR sequence belonging to the same patient used in learning phase is presented to the entry of the two models. The superiority of the MLP model is clearly shown where the dynamical behavior of the predicted QT by the MLP follows closely the real measured QT even after fast variation of the RR signal. All RR sequences are then presented to the MLP model and the predict QT signal is compared to the real measured one. A standard deviation (SD) on the prediction error less than 5 milliseconds is considered as an acceptable result. This value was chosen experimentally by watching sequences one by one.

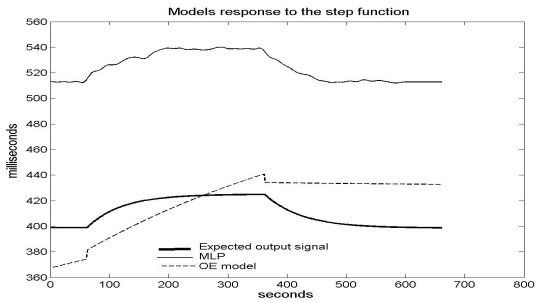

Figure 3: Prediction results of OE and MLP models compared to the expected signal in response to the step function.

The SD for night sequences is 3.85 ± 0.73 ms and 7.21 ± 2.5 ms for day sequences is. The results on the day sequences show that the MLP model established on a night sequence is not appropriate to predict day signals. This might be due to differences between the QT-RR relationship between night and day. The MLP training on day sequences didn't give good results in generalization, this is probably due to a more complex relationship in the day. Additional parameters might be used in the entry of the day models, such as sympathetic and parasympathetic activities measured by the ratio LF/HF.

The number of entries can be reduced by changing the time delay value M or reducing the sampling rate. The time delay of 4 minutes found in this study is coherent with the findings that can be derived from invasive physiological tests: the step response of a one minute time constant first order system will reach 98% of the expected amplitude after 4 minutes.

4. CONCLUSION

Although preliminary, our results indicate that Multi-Layer Perceptrons are able to approach the non-linear aspects of the QT-RR relationship, and can model both the dynamic behavior (response to a step function) and the steady state dynamic behavior QT=f(RR) (response to different, fixed RR intervals).

The predictive models can measure the difference between the measured QT interval and the predicted one and could trigger an alarm each time a given threshold is passed. Further studies are needed to determine such thresholds and to assess the predictive value of the step impulse responses.

Further studies must be carried out to determine the influence of gender and age over the prediction quality. Predictive models could be established depending on gender, age or patient specific models.

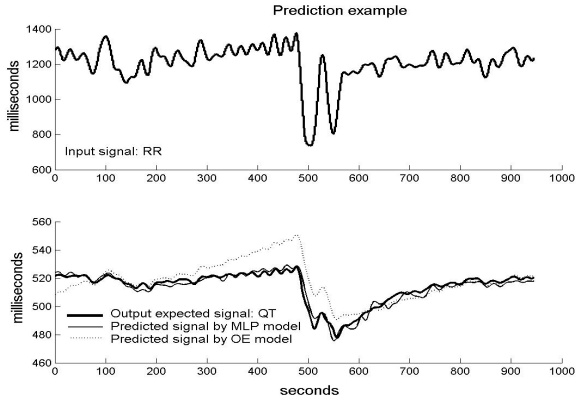

Figure 4: Predicted QT signal of OE and MLP models compared to the measured QT (figure below) in response to the RR signal (figure above). The standard deviation on the prediction error is 3.6ms.

5. REFERENCES

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