

Multilayer Perceptrons for Time Series Prediction: A Case Study on Heart Signals

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Abstract

The study of the dynamicity of the response of the heart ventricles to external stimuli is of major interest to assess the risk of sudden death. The given task is to predict the changes of the so called QT duration in function of the instantaneous changes of the RR interval. The QT interval measures the duration of activation and inactivation of the heart ventricles while the RR interval represents the heart rate. These two intervals are measured on the body-surface Electrocardiogram (ECG). In this paper multilayer perceptrons (MLP) are used to create predictive models of the QT-RR relationship. It's however difficult to obtain good quality signals covering all possible values of RR and QT, making the choice of the learning set a major challenge. Therefore, in addition to real data, simulated data are used for the design of the MLPs and the assessment of their performances. Learning and predicting the simulated data allowed to understand the generalization behavior of MLPs outside learning zones. These data also permitted to test the predictive quality of MLP trained on real signals allowing, in case of differences between predicted QTs and measured ones, to understand if the differences are due to a model dysfunction or a physiological phenomenon.

Introduction

In Europe, 40% of all deaths of individuals who are 25-74 years of age are caused by cardiovascular disease. Cardiac disease is the underlying cause in two-thirds of out-of-hospital sudden deaths [1]. 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 [1]. A non-invasive method for early detection of heart pathologies becomes an important challenge for public health interest. Among the different measurements that are performed on the Electrocardiogram (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 abnormalities in the adaptation to heart rate changes may facilitate the development of ventricular arrhythmia that might lead to SCD [2]. The duration of QT is influenced principally by the inverse of the heart rate, measured by the RR duration between two successive heart beats [3]. QT duration is also influenced by gender, age, the central nervous system and circadian cycles [4]. Bazett already proposed a variation model of the QT-RR relationship in 1920 [5]:

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

Since then many other formulas were proposed [3]. 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.

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 [6]. Predictive modeling to the QT dynamic behavior using RR may be a very precious diagnosis tool. The conception of such models would allow detecting life-threatening variations of the QT duration by comparing the predicted value to the real measured one. But up to now invasive techniques are the only ways for studying the ventricle response to sudden heart rate changes [6].

Much of what is known about physiological systems has been learned using linear system theory. However, many biomedical signals are apparently random or aperiodic in time. Nonlinear methods such as neural networks may be a powerful tool to reveal the characteristics and mechanism of biosignals because systems are basically nonlinear by nature [7]. Global techniques such as the multilayer perceptron may, thus, be the preferred choice for modeling time series as they employ a limited set of kernel functions (nodes in the hidden layer) to represent the input space, and in theory can approximate any nonlinear function with arbitrary accuracy [8]. MLPs were initially introduced for the purpose of pattern recognition utilizing the attribute that the nodes of the hidden layer capture characteristic

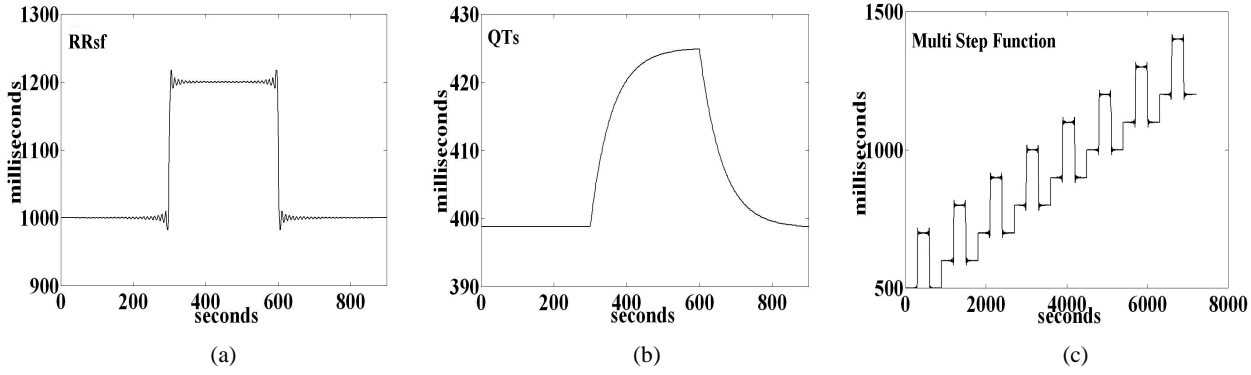


Fig 1. Artificial data: a- The filtered step function. b- The first order response with a time constant of one minute. c- Eight step functions centered on several RR values.

features of the input presentation vector. Early attempts to use an MLP for time series prediction were carried out by Lapedes and Faber [9].

In this paper we propose to model the QT dynamic behavior in function of the history of RR intervals by means of multilayer perceptrons. The networks will learn the following non-linear patient specific relationship:

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

where M is a time delay.

Materials and Methods

Real Data

The ambulatory ECGs are recorded by means of a 3-channel analog Holter recorder [10]. RR and QT sequences were chosen over the 24H recording using as a selection criterion the richness in variations of the RR interval. Sequences were selected for twelve 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 [11].
- 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 sympathetic (LF) activities [4].
- The filtered RR and QT sequences are down sampled to 0.5 sample per second by keeping one point over eight.
- The RR interval ranging from 400 to 1500 milliseconds and the QT interval ranging from 250 to 600 milliseconds were transformed for the network to the interval ranging from -0.9 to 0.9.

Artificial Data

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 minute 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. An example of the filtered signal RRs_f is given in figure 1-a.
- Computation of QTs (figure 1-b), the simulated QT, according to the following function [21]:

$$QTs_i = 8.7 * \sqrt{RRresp_{i-1}} + 123.7 \quad (2)$$

The data used for the training and the testing of the ANN are the RRs_f and QTs (fig. 1-a,b).

The generalization capabilities of the MLP is studied through predicting eight step functions, equally spaced by 100 ms and centered on different values between 600 ms and 1500 ms as shown in figure 1-c.

Multilayer Perceptrons

For the modeling of the QT dynamics we have chosen a multilayer perceptrons architecture with NbE entries, k sigmoid hidden neurons and one linear output neuron as shown in figure 2.

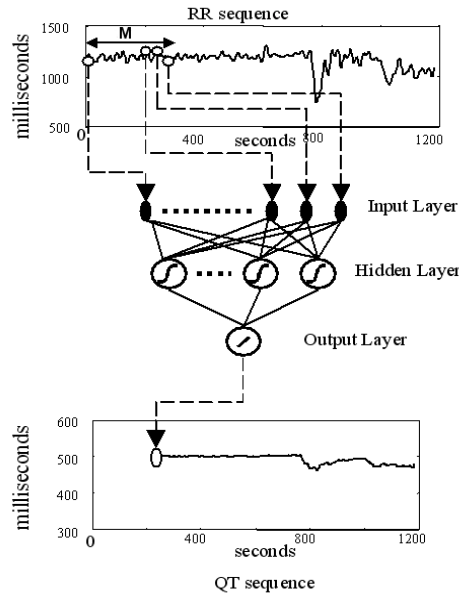


Fig 2. Multilayer Perceptrons architecture used for the prediction of the QT in function of the RR.

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:

$$NbE = M \times 30 \quad (3)$$

To determine the value of the delay M necessary for a good learning of the QT-RR relationship, two ECG sequences belonging to subject "Clav" were selected. These sequences, recorded at 4:25 am and at 6:05 am, were used respectively as training and test sets. The mean square error (MSE) is taken as a measure for evaluating the performance:

$$MSE = \sum_{i=1}^N \frac{(QTp_i - QTm_i)^2}{N} \quad (4)$$

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

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 (SD) over the prediction error is used as a complementary criterion.

Results

MLP Dimensioning

The delay M was set to vary from one minute up to eight minutes, with 5 hidden neurons and 10.000 training iterations. For a delay greater than 4 minutes no significant

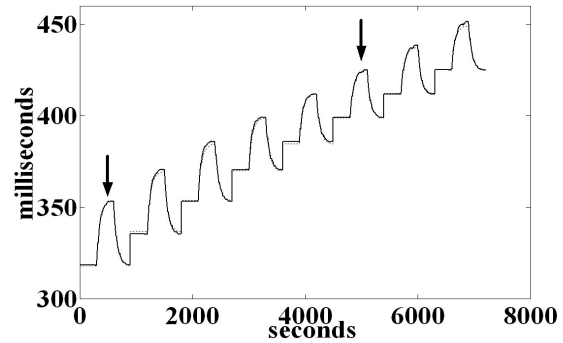


Fig. 3. Expected QT (QTs in dotted line), and the ANN response for the multi steps function (in solid line). The two arrows indicate the step functions used for the training.

improvement was noticed on the learning quality and the MSE in equation (4) stayed constant.

Therefore the number of neurons in the input layer was set to 120, using equation (3).

The number of hidden neurons was determined experimentally by training several architectures embedding from 1 to 22 neurons. The MLP with 10 hidden neurons gave the best results in learning the training set and in predicting the test set.

Prediction Capacity of MLP outside Training Zones

The training set is composed of two step functions. The first set has a RRsf centered around 1100 ms, and the second set has a RRsf centered around 600 ms. They correspond respectively to the first and the sixth step functions in figure 1-c. Training was stopped after 22.000 iterations when the learning error had reached a steady state and did not improve any more.

Figure 3 shows the close dynamic behavior between the predicted signal and the expected one. The multilayer perceptrons succeeded in learning the transient dynamic behavior of the first order, one-minute response of the step impulse. It succeeded also in learning the steady state, non-linear QT-RR relationship defined in equation 2. Choosing specific variation zones for learning set avoid using huge amount of data covering all possible values for input and output.

Training MLP with RR and QT Time Series

To train the MLP, we have chosen a "Clav" sequence recorded at 4:25 am. The training was stopped after 4000 iterations using the sequence recorded at 6:05 am as a test set.

Figure 4 shows the result of the network prediction for the RR sequence recorded at 7:35 am. The upper tracing of Figure 4-b corresponds to the measured QT interval (QTm) and the lower to the QT predicted by the MLP (QTp). The dynamic behavior of QTp follows closely the real QT variations, with a standard deviation on the prediction error

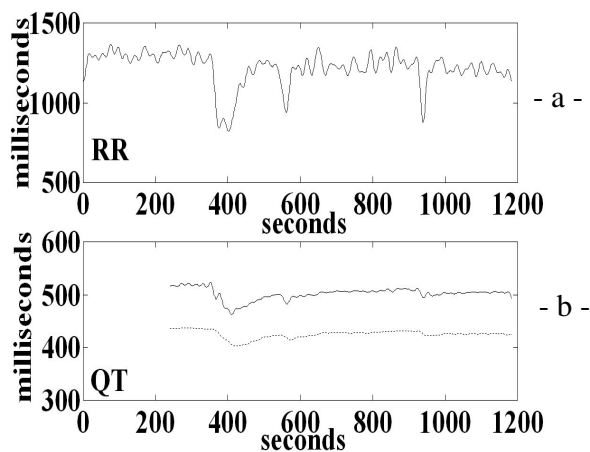


Fig 4. Real RR and QT sequences (in full line) and the predicted QT (in dotted line) produced by the MLP.

of 3.5 ms. The vertical shift between the two signals is due to a different time recording and to different activities of the sympathetic and parasympathic systems [4].

From figure 5, it can be noticed that the step response predicted by the MLP is very close to a first order step response for QT varying from 380 ms to 520 ms. The quality of the predicted signal is worsening when getting closer to the upper limit of the QT values.

In addition to sequences belonging to the “Clav” used for training, the neural model will also predict sequences of other subjects. A standard deviation 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. The SD for night sequences is 3.85 ± 0.73 ms and is 7.21 ± 2.5 ms for day sequences.

Discussion

Predicting data outside the learning window is a big challenge for MLPs. As noticed in figure 5, the amplitude variation doesn't closely follow the variations of the expected theoretical signal all over the range of the QT variations. It's hard to imagine that the MLP could “invent” a QT-RR relationship as in equation 2, when only a small part of RR and QT variations is used for the training. Using only two step functions but far away at the borders of the range of variation, we could, as shown in figure 3, approximate both the static and the dynamic behavior of the expected signal. The ECG sequence used for the training must contain a big amount of RR and QT variations, and using a 24H signal for the training won't solve this problem. Automatic methods need to be developed to select RR and QT sequences covering a wide range of variation.

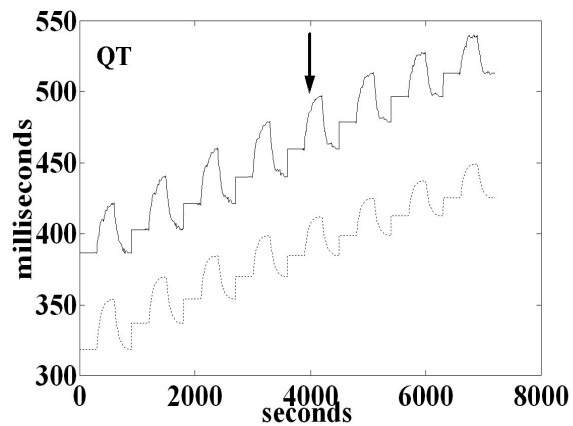


Fig. 5. Expected QT (QTs in dotted line) and the MLP's response for the multi steps function (in solid line). The two arrows indicate the step functions used for the training.

The capability of multilayer perceptrons to learn and to correctly predict non-linear functions depends essentially on the architecture dimensioning (i.e. the number of entries and hidden neurons) and on the number of iterations. To minimize the training cost and the risk of over-design, the number of entries must be the lowest possible. But in the same time, the time delay M must be long enough to approach the non-linearity (1 minute time constant) of the studied signal. 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. On the other hand, given the 0.05Hz low-pass filter cut off frequency, it would be difficult to reduce the sampling rate below 0.5 Hz if we want to have a good quality of signal representation.

Another concern is the vertical shift between the predicted and the measured QT. This shift depends on the time of the day and the activity of the central nervous system, and is in itself an important measurement that is expected to have a diagnostic importance. The same yields for the amplitude of the step impulse response, the time constant of the response and the symmetry of the rising and the falling edges.

The results on the day sequences show that the MLP model established on a night sequence is not appropriate to predict day signals. These results confirm that the QT-RR relation is influenced by the circadian cycle [4].

Conclusions

Although preliminary, our results indicate that multilayer 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 impulse) 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. Our first results indicate the possibility of the universality of a night model for healthy subjects. Further studies must be carried out to determine if such models are dependent on gender and age. To approach day models additional parameters might be used in the entry of MLPs such as sympathetic and parasympathetic activities measured by the LF/HF ratio.

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