

Do Nonlinearities Play a Significant Role in Short Term, Beat-to-Beat Variability ?

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Abstract

Numerous studies of short-term, beat-to-beat variability in cardiovascular signals have not resolved the debate about the completeness of linear analysis techniques. The aim of this paper is to evaluate further the role of nonlinearities in short-term, beat-to-beat variability. We compared linear autoregressive moving average (ARMA) and nonlinear neural network (NN) models for predicting instantaneous heart rate (HR) and mean arterial blood pressure (BP) from past HR and BP. To evaluate these models, we used HR and BP time series from the MIMIC database. Experimental results indicate that NN-based nonlinearities do not play a significant role and suggest that ARMA linear analysis techniques provide adequate characterization of the system dynamics responsible for generating short-term, beat-to-beat variability.

1. Introduction

Numerous analyses of hemodynamic signals have been performed to understand cardiovascular regulatory mechanisms. Previous studies of heart rate variability have relied mainly on linear methods such as spectral methods or linear parametric approaches [1,2]. Although linear methods provide a comprehensive view of characterizing fluctuations in hemodynamic signals, these techniques cannot identify the presence of nonlinear coupling. It is also reported that there are nonlinear interactions between the parasympathetic and the sympathetic nervous systems with respect to heart rate control.

Despite numerous studies involving the analysis of beat-to-beat variability in cardiovascular signals, there continues to be a debate on the appropriateness of linear methods. At least one previous study has attempted to settle this debate [3]. This study attributed the importance of the nonlinear analysis to the description of the effect of instantaneous lung volume and arterial blood pressure on

heart rate fluctuations. However, it only considered the significance of second-order nonlinearities. Thus, the role of nonlinear contributions in hemodynamic variables has not been fully explored. In this paper, we aim to evaluate further the role of nonlinearities on short-term, beat-to-beat variability in a clinical patient population, using neural networks that can account for higher-order nonlinearities.

Multilayer neural networks, an important class of neural networks, have been applied to solve complex problems in diverse fields. These networks are commonly referred to as multilayer perceptrons. A multilayer perceptron trained with the back-propagation algorithm may be viewed as a practical vehicle for performing a nonlinear input-output mapping. According to the universal approximation theorem for multilayer perceptrons [4], a single hidden layer is sufficient for a multilayer perceptron to approximate any given training data set. This approximation theorem provides the theoretical background that the multilayer NN approximating the higher-order continuous functions can evaluate the role of nonlinearities in short-term, beat-to-beat variability. In this paper, a recurrent neural network (RNN) is used as the multilayer neural network.

In order to verify that the RNN is able to approximate higher-order polynomials, we tested the prediction of time series generated from linear and nonlinear systems. It showed that the normalized root mean square errors were almost zero (4.9543×10^{-4} for linear system, 4.2×10^{-3} , 1.1312×10^{-4} , and 1.5×10^{-3} for the second, third, and fourth order nonlinear systems). Recently a study has shown that multilayer neural networks can realize linear and some nonlinear systems [5]. A paper [6] has also compared RNN prediction with ARMA prediction on nonlinear and nonstationary signals such as Mackey-Glass time series and speech signals, in which RNN prediction is superior to the ARMA. Thus, it can be said that the RNN is capable of predicting higher order nonlinear polynomials including linear signals.

This paper describes neural network-based nonlinear prediction and compares it with the performance of a

linear model in order to evaluate the role of nonlinearities in the analysis of short-term, beat-to-beat variability. We constructed and compared linear and nonlinear models for predicting instantaneous HR and BP from past values of HR and single-beat mean arterial BP. The former is the ARMA model, and the latter is based on Elman type recurrent NN. To evaluate these models, we compared their mean-squared HR and BP prediction errors using the MIMIC database.

2. NN-based HR prediction

Figure 1 shows the block diagram of a linear prediction system.

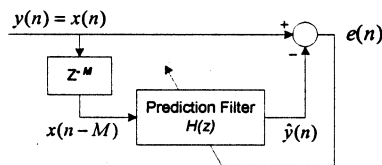


Figure 1. Block diagram of a linear prediction system

The prediction $\hat{y}(n)$ of the future $y(n)$ is estimated using only the delayed inputs $x(n-M)$. Most linear prediction models, which estimate the future value using a linear combination of input values, use the ARMA model for finding all zeros and poles of the system transfer function $H(z)$ of the prediction filter. The system transfer function of the prediction filter is described by the following equation.

$$H(z) = \frac{\sum_k b_k z^{-k}}{\sum_k a_k z^{-k}} \quad (1)$$

The impulse response of the prediction filter is determined by the error signal $e(n) = y(n) - \hat{y}(n)$. The coefficients a_k and b_k of the IIR filter are computed by minimizing error $\sum_n |e(n)|^2$.

The linear model works well for signals generated by linear systems. However, it is not appropriate for the prediction of nonlinear and nonstationary signals. For the higher order nonlinear signal processing, dynamic neural networks such as time-delay neural networks and recurrent neural networks are adequate models. They use feedback loops or delay elements as memories in order to process temporal information, and can perform more complex signal processing well. Thus, our approach for dealing with the inherent nonlinearity of cardiovascular signals is to replace the linear adaptive prediction filter with the NN-based nonlinear adaptive filter. The neural network used as a nonlinear filter in this paper is the Elman type recurrent neural network (RNN) shown in Figure 2. It consists of three layers. All the units in a layer are fully connected to all the units in the following layers,

i.e. they are one-to-many variable connecting weights. The input layer has external inputs $x(k)$ and additional inputs $h(k)$ that are fed from the outputs of all neurons of the hidden layer with one-to-one weight connections. These recurrent connections improve the dynamics of the network.

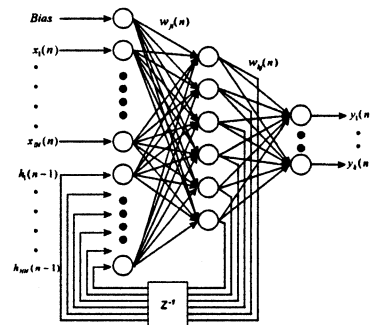


Figure 2. Structure of recurrent neural networks

The “learning” of the network is an extension of the gradient descent algorithm. It is modified to enhance the convergence speed. The connecting weights as well as the parameters of the node activation function are updated using the error backpropagation algorithm. All neurons in the hidden and output layers use sigmoid transfer functions. The output of the each node is as follows:

$$y(n) = \frac{g(n)}{1 + e^{-s(n)(v(n)-v'(n))}} \quad (2)$$

where $g(n)$, $s(n)$, $v(n)$, and $v'(n)$ represent the gain, slope, input, and delay of the activation function, respectively. The cost function, the error of the neural networks, is defined as

$$E(n) = \frac{1}{2} \sum_k e_k^2(n) = \frac{1}{2} \sum_k \{d_k(n) - y_k(n)\}^2. \quad (3)$$

The purpose of the adaptive algorithm is to reduce the error $E(n)$ by adaptively adjusting weights $w(n)$ and parameters $p(n)$. The $p(n)$ represents $g(n)$, $s(n)$, and $v'(n)$. Changes of the weights $\Delta w(n)$ and the parameters $\Delta p(n)$ of the network are defined as

$$\Delta w(n) = -\eta_w \frac{\partial E(n)}{\partial w(n)}, \quad \Delta p(n) = -\eta_p \frac{\partial E(n)}{\partial p(n)}. \quad (4)$$

The equations above show the incremental weights and function parameters of the layers. And η_w and η_p represent the update rates for the weights and the function parameters. The momentum term is added to change only the weights to speed up the learning. The incremental connecting weights ($\Delta w_{ij}(n)$, $\Delta w_{ji}(n)$) and the parameters ($\Delta g_j(n)$, $\Delta s_j(n)$, $\Delta v'_j(n)$ for hidden neurons, $\Delta g_k(n)$, $\Delta s_k(n)$, $\Delta v'_k(n)$ for output neurons) of the activation function are updated at every iteration in the training process. An adaptively tuned multi-layer neural network is used to predict the nonlinear, time-varying heart rate and blood pressure.

3. Experimental Results

To investigate the nonlinearities, we used HR and BP time series from patients without diagnosed autonomic dysfunction from the MIMIC database (www.physionet.org [7]). The data sets were sampled at 125 Hz. A study [8] has shown that the choice of sampling rate may affect accurate detection of the QRS complexes, especially if a low sampling rate is chosen. However, the sampling rate of 125 Hz used in this study is high enough to allow for accurate detection of QRS complexes. Several studies have shown that dynamics of HR fluctuations are located at frequencies below 0.5 Hz. Thus, instantaneous HR and BP signals are downsampled by 3 resulting in a sampling rate of 125/3 Hz and then these decimated signals are used for prediction. In this paper the prediction is performed in two ways. First, current HR is predicted based on past HRs and BPs. Next, current BP is also predicted using past BPs and HRs.

$$HR(n) = \sum_{k=1}^M a(k)HR(n-k) + \sum_{k=1}^N b(k)BP(n-k) + e(n) \quad (5)$$

$$BP(n) = \sum_{k=1}^N c(k)BP(n-k) + \sum_{k=1}^M d(k)HR(n-k) + e(n) \quad (6)$$

M and N represent the delays of HR and BP. Figure 3 shows the structure for predicting HR. We used the ARMA structure as a linear model and the RNN as a nonlinear model in prediction filter. Then, their prediction results are compared to evaluate relative performance of the RNN model.

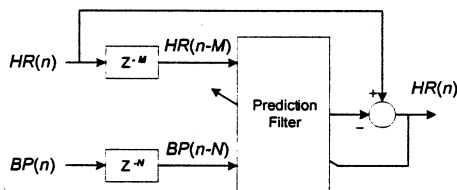


Figure 3. Structure for HR prediction

We tested the prediction on 10 different segments from MIMIC database. Average segment length is about 13 minutes. Each segment was divided into two equal parts. The first half of the segment was used to train the prediction filter, and the second half was used to test the predictive quality of both models. The structure of the NN consists of the input layer with neurons of external inputs (delayed HR and BP) and with additional inputs of feedbacks from the hidden layer, the hidden layer with 10 neurons, and one output neuron. The parameters of the network are determined experimentally and the values of the parameters are slightly different for each segment. Typical values are as follows: learning rate of 0.02, momentum rate of 0.0015, update rate of 0.01 for both gain and slope, and 0.001 for delay in activation function. The network is trained for 10000 iterations to reach a

stable error level, beyond that iteration the error does not reduce much as iteration continues. The delays (N , M) of the HR and BP in the input of the network are set equal and tested for $N=M=1, 3, 5, 7$, and 9 . The best delay for each record is determined when the rate of error change does not reduce significantly. The error is the average of five experiments with different initial values of the neural networks. For the linear ARMA model, the model order for each data segment is determined by use of the Akaike information criterion.

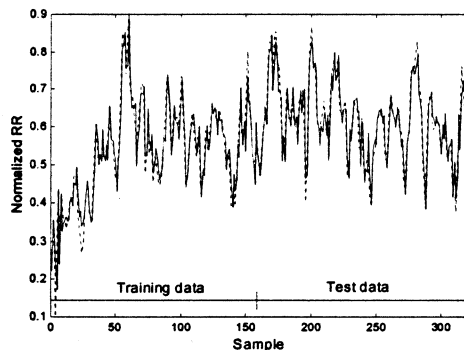


Figure 4. Example of NN-based HR prediction (Record: 408, $N=M=9$)

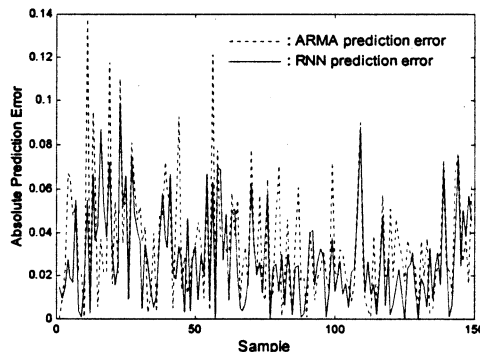


Figure 5. Example of absolute prediction errors in HR prediction (Record: 411, $N=M=9$)

Figure 4 shows an example of RNN-based HR prediction. In this figure, the dotted and solid lines represent the original and predicted signals for both training and test data. Figure 5 shows an example of absolute prediction errors in ARMA and RNN-based HR prediction on test data. For the quantitative evaluation of the prediction error only on the test data, we define the normalized root mean square error ($NRMSE$) as follows.

$$NRMSE = \sqrt{\frac{\sum_{n=1}^N [e(n) - \bar{E}]^2}{\sum_{n=1}^N [y(n) - \bar{Y}]^2}} \quad (7)$$

where, $e(n) = y(n) - \hat{y}(n)$, $y(n)$ and $\hat{y}(n)$ are the sample values of the original and the predicted signals, \bar{E} and \bar{Y} are averages of $e(n)$ and $y(n)$, N is the number of samples to be evaluated. This $NRMSE$ represents fractional error with respect to what is predicted. Table 1

compares the prediction error of HR and BP for all segments. The value in the table is the best prediction result for given delays and function parameters in the test data set.

Table 1. Summary of *NRMSE* in HR and BP prediction

Record	HR		BP	
	ARMA	RNN	ARMA	RNN
411	0.5025	0.4332	0.7795	0.5020
408	0.4160	0.3965	0.4996	0.4854
401	0.3585	0.3558	0.2354	0.2625
224	0.3508	0.3953	0.1022	0.1378
240	0.3626	0.3336	0.3910	0.3687
055	0.4165	0.3776	0.3883	0.3792
211	0.3940	0.3629	0.3462	0.3674
041	0.2228	0.1401	0.2719	0.2317
417	1.1156	0.7896	0.4707	0.2963
218	0.5716	0.5416	0.1891	0.2119
AVG	0.4711	0.4126	0.3674	0.3243
STD	0.2447	0.1657	0.1909	0.1178

The linear ARMA model is able to represent 52.89% +/- 24.47% of the HR variations, but the nonlinear NN accounts for 58.74% +/- 16.57%. For the BP variations, the linear and nonlinear models can represent 63.26% +/- 19.09%, 67.57% +/- 11.78%, respectively. These results show that the NN-based nonlinear model is about 6% and 4% better in representing the nonlinearities of HR and BP variations than the linear ARMA model in terms of *RNMSE*. Based on paired T-tests, however, there is no significant difference between linear and nonlinear prediction ($p=0.098$ for HR prediction and $p=0.2156$ for BP prediction).

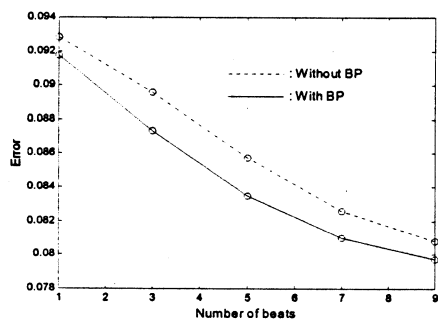


Figure 6. HR prediction error versus number of beats

From the experimental results, we found that the more delays the better the prediction for both HR and BP in both training data and test data. It was also found that the HR (or BP) prediction using past BP (or HR) is better than the prediction without using past BP (or HR). Figure 6 shows the NN-based HR prediction error versus number of beats for test data. The error in the figure is computed based on eq. (7) assuming $\bar{Y} = 0$. We found similar results in the BP prediction.

4. Conclusions

The aim of this study is to evaluate further the role of nonlinearities in short-term, beat-to-beat variability in cardiovascular signals. We compared the linear ARMA and nonlinear NN models in predicting instantaneous heart rate and mean arterial blood pressure. Experimental results indicate that NN-based nonlinearities do not play a significant role in short-term, beat-to-beat variability in the MIMIC patient population. This means that linear analysis techniques provide adequate characterization of the system dynamics responsible for generating short-term, beat-to-beat variability. We conclude that the linear techniques are appropriate to analyze cardiovascular signals for these patients even though there exist weak nonlinearities. Further investigations on the appropriateness of linear analysis techniques should be carried out in other patient populations and with other nonlinear techniques.

Acknowledgements

The National Aeronautics and Space Administration supported this work through the NASA Cooperative Agreement NCC 9-58 with the National Space Biomedical Research Institute.

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