Prediction of Acute Hypotensive Episodes Using Neural Network Multi-models

JH Henriques[1], TR Rocha[2]

[1]CISUC, Center for Informatics and Systems, University of Coimbra, Coimbra, Portugal
[2] Instituto Politécnico de Coimbra, Dep. de Engenharia Informática e de Sistemas, Coimbra, Portugal

Abstract

This work proposes the application of generalized regression neural network multi-models to the prediction of acute hypotensive episodes (AHE) occurring in intensive care units. Contrasting with classical auto regressive representations, multi-model schemes do not recursively use model outputs as inputs for step ahead predictions. As result, prediction errors are not propagated over the forecast horizon and long-term predictions can be accurately estimated. The effectiveness of this strategy is validated in the context of PhysioNet-Computers in Cardiology Challenge 2009. The dataset considered consists of arterial blood pressure signals, obtained from MIMIC-II Database. A correct prediction of 10 out of 10 AHE for test set A and of 37 out of 40 AHE for test set B was achieved.

1. Introduction

Hypotension, a clinical condition characterized by abnormally low blood pressure values, is one of the recurrent situations occurring in intensive care units. If not promptly treated, acute hypotensive episodes may result in irreversible organ damage and, eventually, death. Therefore, the development of methodologies able to detect not only the presence of this condition but also to predict their occurrence is of extreme importance concerning appropriate clinical interventions. In fact, since clinical interventions to treat such events are usually invasive and aggressive, a prediction system that identifies an imminent event would be a significant benefit to timely support non-invasive and preventive treatments.

In general, the development of automatic hypotensive predictive solutions explore the correlation of patient clinical information, such as arterial blood pressure (ABP), heart rate (HR) and oxygen saturation (SO2) with the onset of the hypotension episode. Bassale [1] proposed the use of parametric and non-parametric methods to analyze and characterize ABP before hypotensive episodes. He concluded that ABP variability and shape features have the potential to predict such events. Crespo *et al* [2] also suggested the use of changes in the ABP morphology occurring immediately before an episode of hypotension. In particular, they suggested the variance of the ABP signal and the variance of the wave slope as the most relevant features to consider when predicting AHE. Recently, Lehman *et al* [3] proposed a similarity-based searching and pattern matching algorithm, applicable to classification and forecasting tasks. Using real physiological measurements they employed the methodology to forecast hypotensive episodes in intensive care units. Frolich *et al* [4] suggested the use of baseline HR as a significant predictor of obstetric spinal hypotension. Basically, they showed that higher baseline HR may be a useful parameter to predict postspinal hypotension.

Using spectral analysis of HR and ABP variability Pelosi *et al* [5] have identified precursors of hypotensive episodes during renal dialysis. Also using frequency analysis techniques, Reich *et al.* [6], investigated the correlation of HR variability analysis with hypotension events. Chamchad *et al* [7] found a significant correlation of nonlinear HR variability dimension analysis with the presence of hypotension, occurring after spinal anesthesia for cesarean delivery. Hanss *et al* [8] also concluded that HR variability analysis could be used to predict the occurrence of hypotension during spinal anesthesia. In particular, they investigated the ratio of low to high frequency peaks of the HR variability power spectrum (LF/HF) to the prediction of hypotension events after spinal anesthesia, for the specific cases of pregnant women [9] and elderly men [10]. More recently, Mancini *et al* [11] showed the potential of SO2 short-term variability in anticipating the hypotension onset.

This work addresses the forecast of acute hypotensive episodes through the development of predictive multi-models, applicable to ABP time-series. Multi-models do not recursively use model outputs as inputs for step ahead predictions. Therefore, prediction errors are not propagated and long-term predictions can be accurately estimated. Among regression models, neural networks have shown considerable capabilities to learn and to generalize from non-linear environments, enabling to capture the fundamental data dynamics. In particular, generalized regression neural network (GRNN) structures are employed here.

Moreover, multi-models can be trained by means of standard backpropagation algorithms. In fact, each independent neural sub-model is used for each sampling instant and does not depend on previous predictions. In this work neural sub-models were trained using arterial blood pressure signals, obtained from MIMIC-II "*numerics record*" dataset (H and C datasets). No information from "*clinical records*" was used.

The paper is organized as follows. In section 2 the proposed methodology is described. In section 3 the results using PhysioNet-Computers in Cardiology challenge 2009 datasets are presented and discussed. Finally, in section 4, some conclusions are drawn.

2. Methods

Figure 1 depicts the methodology proposed in this work.

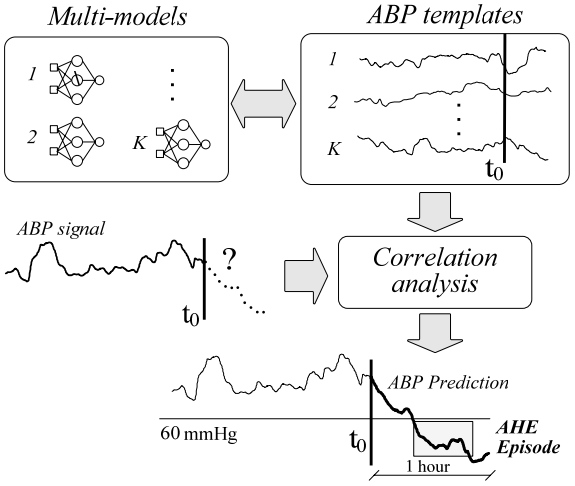

Figure 1 - Proposed scheme.

The input consists of a discrete *ABP signal* (sampled once per minute) considering the information available before t0, the instant where the forecast period starts. This signal passes through a set of pre-processing techniques, namely to deal with missing information, noise reduction and normalization. Then, a correlation analysis procedure is carried out considering the processed *ABP signal* and a series of *ABP templates*, representative of historical ABP trends evolution. From this correlation analysis the most similar templates are identified and the correspondent multi-models, previously trained, selected. These specific neural models are then employed to predict the future evolution of the particular ABP input signal, from instant t0 until the end of the forecast window (one-hour). Finally, an AHE is identified if at least 90% of the ABP prediction signal during a period of 30 minutes or more is at or below 60 mmHg.

2.1. Multi-models

This step involves modeling each ABP template signal, based on a GRNN multi-model approach, with the aim of prediction. Consider a time-model series described by the following discrete-time nonlinear auto regressive representation

$$y(k) = f_1\left(y(k-1), y(k-2), ..., y(k-n)\right) \quad (1)$$

where $y(k)$ is the value of the ABP signal at minute k, n is the *order* of the model and f_1 is a mapping such that $f_1 : \Re^n \rightarrow \Re$. Assuming the knowledge of mapping f_1, and considering the current instant k, it is possible to predict one step ahead ABP value by

$$y(k+1) = f_1\left(y(k), y(k-1), ..., y(k+1-n)\right) \quad (2)$$

Considering the instant $k+2$

$$y(k+2) = f_1\left(y(k+1), y(k), ..., y(k+2-n)\right) \quad (3)$$

This description can be reformulated [12], and expressed as a function of past observed values

$$y(k+2) = f_1(\ f_1(y(k), ..., y(k+1-n)), \\ y(k), ..., y(k+2-n)\ ) \quad (4)$$

$$y(k+2) = f_2\left(y(k), y(k-1), ..., y(k+1-n)\right) \quad (5)$$

In general, a particular future time instant P can be expressed in a compact form by

$$y(k+P) = f_P\left(y(k), y(k-1), ..., y(k+1-n)\right) \quad (6)$$

Thanks to this structure, predictions do not depend on previous predictions, but only on information available at current instant k. However, using multi-models, one independent model (f_i) has to be used for each sampling instant within the prediction horizon. As result, if a future instant P has to be predicted, P distinct regression models have to be derived.

2.2. Neural-network multi-models

Each regression sub-model (f_i) is here described by a distinct GRNN, a type of radial basis function network. The principal advantages of GRNN are that it enables a fast learn and it is suitable for smooth function-approximation problems [13]. The main drawback of GRNN is that, like kernel methods, it suffers from the curse of dimensionality. Although the multi-model can be used for long-range prediction, each neural network is trained by means of a *standard backpropagation* algorithm (actually, training a GRNN involves the estimation of kernels location and hidden-to-output layers weights). This is viable since the structure of multi-models is not recursively used and, therefore, predictions do not depend on previous predictions.

2.3. Templates and correlation analysis

To define the ABP templates a representative historical dataset composed of past and future tendencies has to be considered. The dataset consists of the 60 training records (H and C), available in Physionet/CinC challenge [14]. Actually, one signal (C1#4, a40234) was excluded, since it presents a significant discontinuity in the neighborhood of the instant t0.

For each signal an appropriate period of time, immediately before and after the beginning of the defined forecast window (instant t0), respectively 6 hours and 1 hour, is considered. To address future predictions, each of these time series templates (H and C) is modeled using the GRNN multi-model approach. These models are trained using past information available (before t0), while validation is performed based on future information (after t0).

Given a new ABP testing dataset, truncated at time instant t0, the ABP forecast is predicted based on previous trained GRNN multi-models. To select the specific multi-models a correlation analysis procedure takes place. Basically, correlation coefficients between new ABP data and stored ABP templates are firstly computed. Then, the ABP templates that present correlation coefficients verifying a given threshold value are selected. In particular, being *CC* a vector composed of all positive correlation coefficients (sorted in descending order), the first *k* templates are selected if equation (7) is verified.

$$\frac{sum(CCi)}{sum(CC)} > tolerance \quad i = 1 \,..\, k \tag{7}$$

The occurrence of an AHE, within the forecast window (one hour), is finally assessed according to the AHE definition [14].

3. Results

3.1. Neural network multi-models

When modeling each ABP signal template, the selection of the *order* (*n*) and the *size* are of particular importance. The parameter *size* is defined as the period before the starting of the forecast window, from where information is used for training purposes. In order to estimate the parameters (*order* and *size*) an optimization procedure was followed, through the minimization of the least square prediction error over the forecast window.

$$\min_{size,order} \sum_{k=t0}^{k=t0+60} (y(k) - \hat{y}(k))^2 \tag{8}$$

Variables $y(k)$ and $\hat{y}(k)$ define, respectively, the actual and the approximated ABP signal. This minimization procedure was carried out considering different values for the *order* and for the *size* parameters, namely $order \in [60...90]$ and $size \in [120...180]$, with increments of 10 minutes.

The GRNN structures have been defined and trained using the *newgrnn* function [15], available in Matlab toolbox. Figure 2 presents the training results for the record #H1_4 (*a40834*). For this specific signal the *order* and *size* values are, respectively, 80 and 140 minutes.

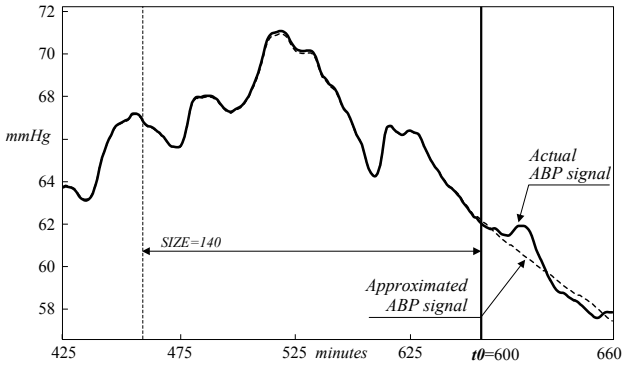

Figure 2. GRNN modeling and predicting, #H1_4 (*a40834*).

It is important to stress that the neural multi-models predict future behavior over the whole prediction horizon only using information before the starting of the forecast window (instant t0). Moreover, to reduce the number of sub-models, each GRNN structure was trained to deal with 15 step ahead predictions. As result, for each ABP template 4 neural sub-models have been trained.

3.2. Acute hypotensive episodes

Using the present strategy, testing dataset available in Physionet/CinC challenge (10 records for A dataset, and 40 records for B dataset) was used for validation purposes. Firstly, each of these 50 datasets was correlated with the ABP templates, considering a specific period of *size* minutes before instant t0. The correspondent GRNN models, determined from the correlation analysis procedure, are used to predict future ABP values. The global prediction signal is computed as the weight average of all estimated predictions, being the identification of AHE straightforward computed. Figure 3 shows the prediction of the specific ABP signal #A1_10 (*110bnm*) over the forecast horizon (one hour) and the respective AHE.

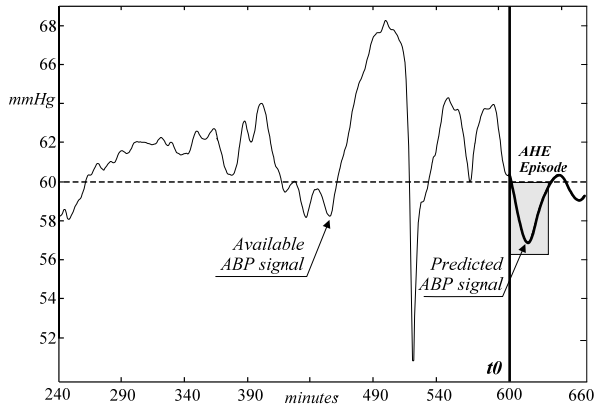

Figure 3. Prediction and AHE identification - signal #A1_10.

Table 1 presents the occurrences where AHE episodes have been identified for A and B records. A correct prediction of 10 out of 10 AHE for test set A and of 37 out of 40 AHE for test set B was achieved.

Table 1. *AHE detection*

	AHE detection
Dataset A	1, 2, 4, 9, 10
Dataset B	2, 3, 5, 7, 9, 14, 17, 18, 22, 23, 25, 26, 34, 38, 39

Although these results are relevant, the experiments performed have showed that the robustness of forecasting methodology is highly dependent on several parameters, namely *order, size,* and *tolerance*. Future work will focus on deriving compact template sets that characterize the dynamics that distinguish different ABP evolution. In this case, a PCA strategy could be easily used to capture the major characteristics of the testing dataset, reducing the number of templates and, consequently, the number of multi-models involved. Additionally, other sources of information (such as clinical record data) can be included.

4. Conclusions

This work proposed a methodology to predict acute hypotensive events over a specific time period. Using arterial blood pressure time series, a modeling strategy based on GRNN multi-models was implemented, enabling to estimate predictions over a forecast horizon. Applied to ABP time-series, considered in the PhysioNet/CinC challenge 2009, the referred strategy allows to adequately capture its dynamics and, then, to predict the onset of hypotensive events.

The reduction of the number of historical templates, and therefore of the number of neural-networks, is a possible direction of future work.

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Address for correspondence:
Jorge Henriques, jh@dei.uc.pt
Department of Informatics Engineering, DEI-FCTUC, Pólo II, 3030-290 Coimbra, Portugal