Prediction of Acute Hypotensive Episodes: A Survey of Time-Series Prediction Models Used in Financial Forecasting

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ABSTRACT

Acute Hypotensive Episodes are critical ICU events that involve a period of critically low arterial blood pressure. These episodes require immediate attention to prevent the incidence of irreversible organ damage or death. Providing prompt courses of treatment appropriate for the episode may help reduce the extent of the damage. Predicting the incidence of an acute hypotensive episode before its onset can enable medical professionals with the ability to immediately begin administering care to their patients. In this paper, we survey a variety of time-series prediction methods commonly used for forecasting financial data and apply these methods to arterial blood pressure recordings to solve the acute hypotensive episode prediction problem. Our approaches achieve a best score of 10/10 for Test Set A and 32/40 for Test Set B of the PhysioNet 2009 Challenge.

Introduction

Acute hypotensive episodes (AHE) are significant periods of time during which a patient's blood pressure drops below a threshold value. AHE can be attributed to a wide variety of possible causes, and identifying the root cause of an AHE reduces the risk of irreversible damage by enabling the administration of the most optimal course of treatment. However, the time-critical nature of AHE in ICU patients often results in medical professionals prescribing a more general intervention in order to buy time for proper diagnosis. In the MIMIC II Database[1], out of the 1237 patients with arterial blood pressure (ABP) recordings, the 511 patients who experienced an AHE have a mortality rate more than twice that of the entire database population.

Predicting the occurrence of AHE in ICU patients reduces the probability of the patient sustaining irreversible damage by both providing medical professionals with sufficient time to properly diagnose AHEs, and potentially allowing the episode to be prevented altogether. For these reasons, the PhysioNet 2009 challenge involved the prediction of AHE through analysis of ABP recordings. In this paper, we present a survey of common time-series prediction models often used in predicting financial data and apply them to the AHE prediction problem. We begin by describing our methodology, including the PhysioNet Challenge in detail, and we introduce selected financial forecasting models and our application of them to the challenge criteria. Finally, we compare our results on the test set data compared to previous work, and comment on possible alterations that could improve our results.

Methods

For this challenge, 60 ABP recordings were provided for training purposes. These recordings were taken from a variety of patients, 30 of whom experienced an AHE. The objective of this challenge is, given 10 consecutive hours of recorded ABP data ending at time T_0, predict whether an AHE will occur within a 1-hour time window after T_0. The provided data sets are distributed across four groups:

- H1: 15 Patients who experienced an AHE and were treated with pressors
- H2: 15 Patients who experienced an AHE, not treated with pressors
- C1: 15 Patients who did not experience an AHE
- C2: 15 Patients who experienced an AHE outside the 1-hour forecast window

Acute Hypotensive Episode: a time period of 30-minutes or more during which 90% of the ABP readings are shown to be below 60mmHg.

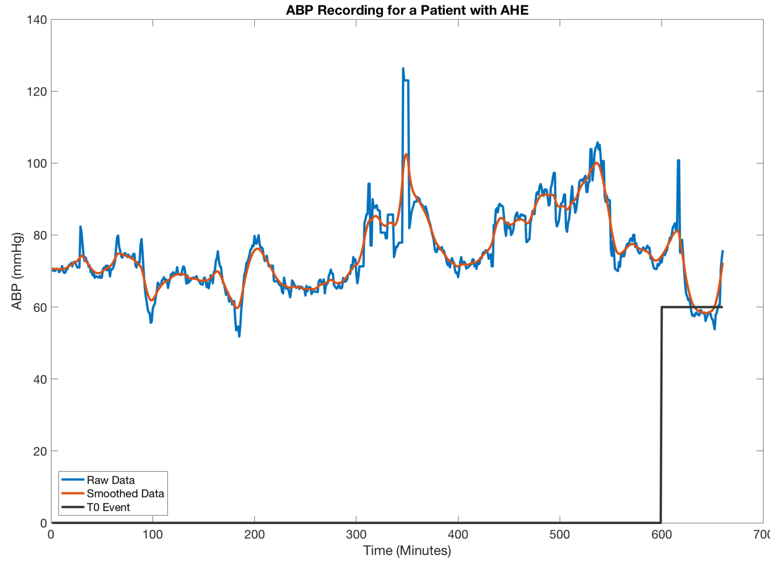

Figure 1. An example ABP training set data recording for a patient with an AHE within the forecast window.

Figure 1 shows a typical training set recording provided for this challenge. Raw data in Figure 1 is ABP data downsampled to 1 reading per minute, a resolution also used in previous work[2]. The smoothed data in Figure 1 is the data processed with a moving average to smooth out additional noise. The T_0 event indicates the end of the 10-hour data recording. All recording values provided past this point are for training purposes only, and are not available for the test set data.

As can be seen in Figure 1, the ABP recording drops below 60mmHg for a significant amount of time. For the purposes of this challenge, we define an AHE as:

Financial Forecasting Models

Forecasting is a common technique used to predict trends in financial market data. Time-series analysis is an accepted technique for performing forecasting, which is based on the premise that time-series data may inherently have autocorrelation that should be accounted for[3]. The most widely used approaches for time-series modelling include exponential moving average (EMA) and autoregressive integrated moving average (ARIMA) models, both of which we present in this section. Additionally, academic work shows a significant effort in developing neural network models for predicting financial data trends[4,5,6]. Essentially, financial

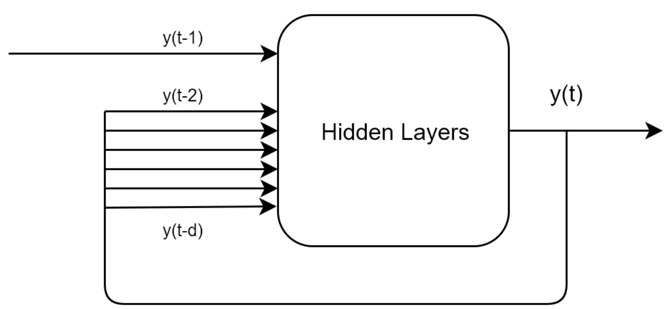

Figure 2. A simplified NAR network topology.

forecasting models predict the magnitude and the direction of trends that occur in financial data. Financial data is typically recorded as discrete samples over periods ranging from the order of seconds to the order of years. The raw ABP data we have been provided as part of the 2009 PhysioNet challenge was recorded with a frequency of 120 Hz. However, when downsampled to conform to a period of one minute, the ABP data resembled that of a typical financial chart.

The main goal of the challenge is to predict a severe drop in blood pressure. In financial data terms, this would correspond to short and sharp trend downward. The nature of the challenge, combined with the discrete nature of the ABP data provided, lead to the hypothesis that financial forecasting models can be used to predict an AHE. Based on this hypothesis, we attempt to apply neural network, ARIMA Monte Carlo Simulation, and EMA crossover techniques to this challenge. The remainder of this section presents each of these techniques, our implementations of these models, preliminary results, and some observed limitations of these techniques.

NAR Neural Network

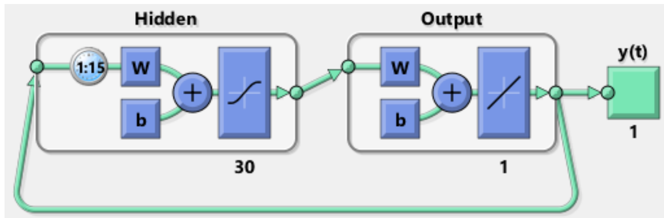

Figure 3. MATLAB Neural Network View of our implemented NARNN.

Non-linear Autoregressive (NAR) neural networks are Artificial Neural Networks (ANN) commonly used to predict time series data that have been determined to be nonlinear[7]. The use of NAR methods for data sets that rely on current and past states is well documented[8] in many fields and is often used as a less computationally expensive autoregressive model when compared to the NAR network with Exogenous inputs. The NAR network differs from this similar network, the Nonlinar Autoregressive network with Exogenous inputs (NARX), in that it does not depend on an external input to also drive the system's output. The NARX network is used extensively with financial predictions[9], and relies on past data as well as external factors that influence the response of the system. Though there is evidence that heart rate and blood pressure are related[10], it is not clear whether heart rate can be directly tied to ABP and so we instead considered a model that would only rely on past blood pressure readings as input, the NAR network.

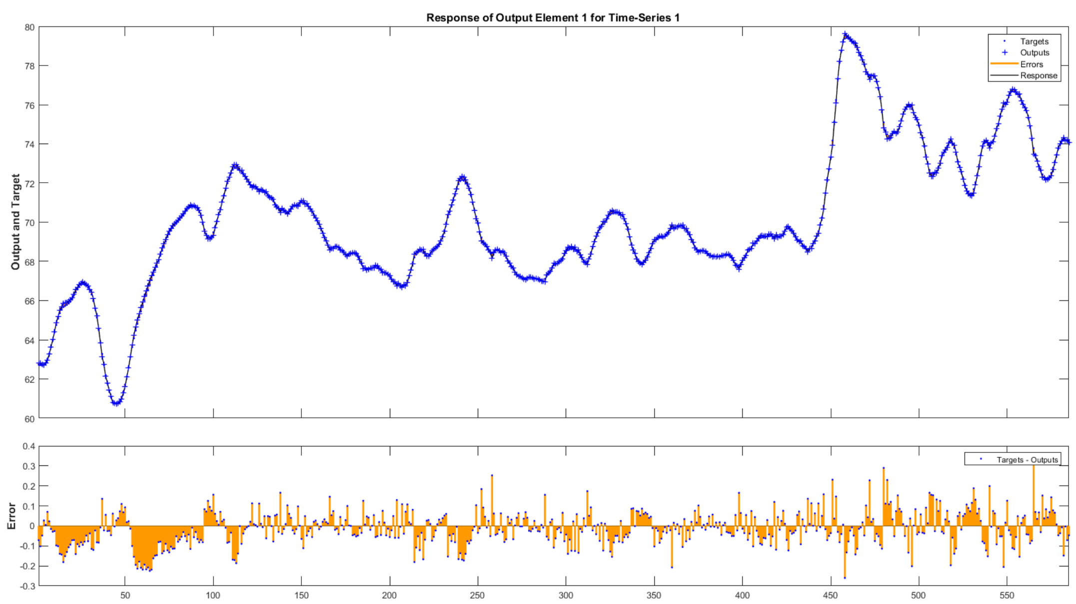

Figure 4. The Open loop response (trained) of our NARNN.

In previous work[2], neural network models were shown to be effective in predicting an AHE based on careful correlation between training and test sets. While this method achieved a 10/10 score in Test Set A and a 37/40 score in Test Set B[2], and placed very highly in the second event of the PhysioNet 2009 challenge, we looked for a method that would use a much more generalized neural network model. At this stage of work, we have used NAR Network models trained with smoothed ABP readings split in to four sub-categories as indicated in the challenge description. Our goal was to create a method that did not

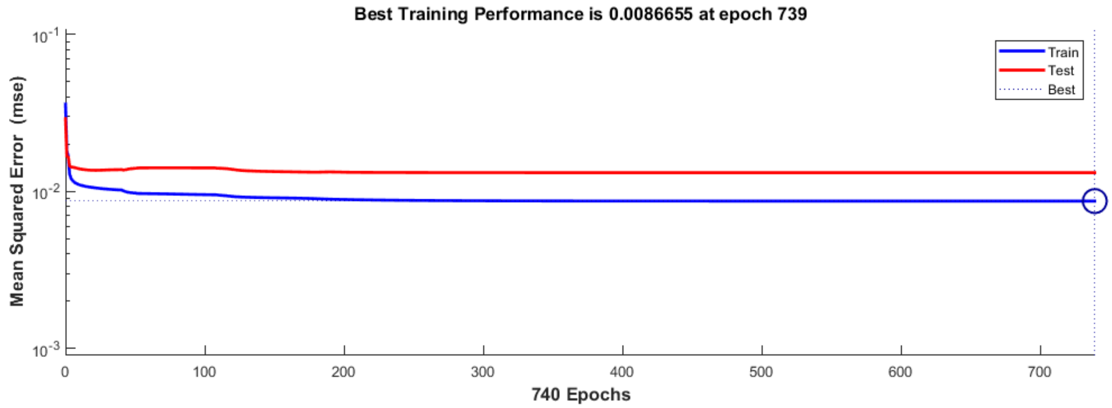

Figure 5. Training history of our open loop NARNN, showing MSE as a performance metric.

require training of many networks and correlation analysis before prediction, but instead would allow for quick testing of each patient from the testing sets provided.

The implementation of our networks was greatly simplified by the Neural Network Toolbox of MATLAB, allowing for rapid adjustments to network models, but knowledge of the topology and performance metrics of the NAR network is necessary to understand some of our results and future steps. A NAR neural network (NARNN), when applied to time series forecasting, is modeled by weighting a chosen number of past system outputs of a data set y at time t, $y(t)$, as the parameters for a function h that is determined by "training" the network[8]. The network can be described as:

$$y(t) = h(y(t-1), y(t-2), ..., y(t-p)) + \varepsilon(t) \tag{1}$$

where p is the number of feedback delays and $\varepsilon(t)$ is the error for the approximation of y[8]. The simplified topology in Figure 2 shows the feedback delays and a representation of the hidden layers. The hidden layers of a network contain the neurons that receive a weight through training and optimization that lead to a prediction. The number of layers and neurons is specific to each application and though increasing the number of neurons may increase network performance, it can also lead to over-fitting of data and increased computation time.

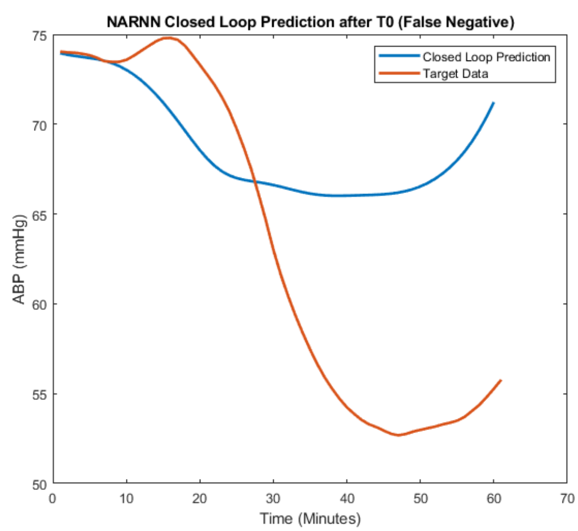

Figure 6. A prediction based on the closed loop output of our NARNN, resulting in a False Negative.

Since our data is stored in sets of 660 readings, and we are forecasting the last 60 readings after T_0, we worked with a network that has 15 delays and 30 neurons in one layer. As discussed before, the number of neurons and delays will affect the performance and generalization of our network, so these values have been determined by trial and error, and may change in the future. The network was trained with the Bayesian Regularization Backpropagation algorithm 'trainbr' provided by

MATLAB[11]. This algorithm was chosen over the default Levenberg-Marquardt algorithm (LMA) because it still implements the LMA but it favors generalization. Our network as displayed by the MATLAB Neural Network View is Figure 3.

Initially, the results of these generalized networks was very promising in the open loop (Figure 4). The Mean Squared Error (MSE), which is a network performance metric used to evaluate the performance of a network by comparing average of the squared error, of our open loop network was very low when training and testing, on the order of 10^{-2} (Figure 5). However, once the loop was closed and we began to try to predict time series after T_0, we found that the closed loop response was not sensitive to the large dips and surges that is frequently present in ABP (Figure 6). Due to the time constraints of our deadline, at this time, we are unable to achieve quantifiable results from this method as our predictions are inconclusive. A common behaviour that our closed loop predictions followed was the tendency to avoid drastic changes in ABP values, which unfortunately is the exact circumstance we are trying to predict. Future goals and considerations will be discussed later in this paper.

ARIMA Monte Carlo Simulation

ARIMA models are a combination of autoregressive (AAR), integrative (I), and moving average (MA) methods of predicting time series. These models are typically used for short-term forecasting based on the inertia of historical data[12]. ARIMA models are particularly useful for non-stationary time series. In financial data sets, non-stationarity indicates the presence of trends and seasonality in the data[13]. In our application, non-stationarity would indicate a downward trend in ABP, potentially indicating the eventual incidence of an AHE.

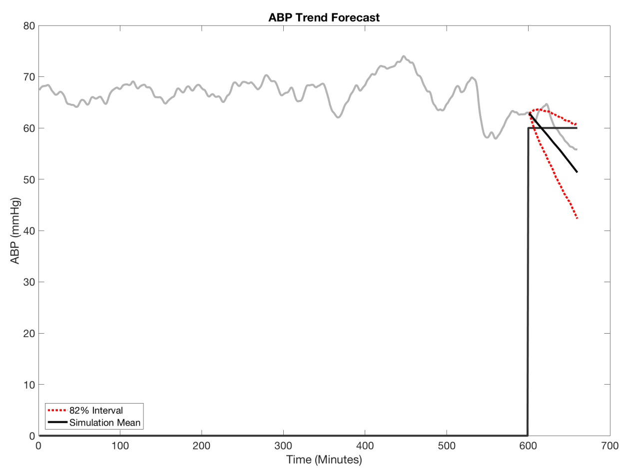

Figure 7. Results of simulating 1000 Monte Carlo Observations on a fitted ARIMA(2,2,2) model in a patient with an AHE.

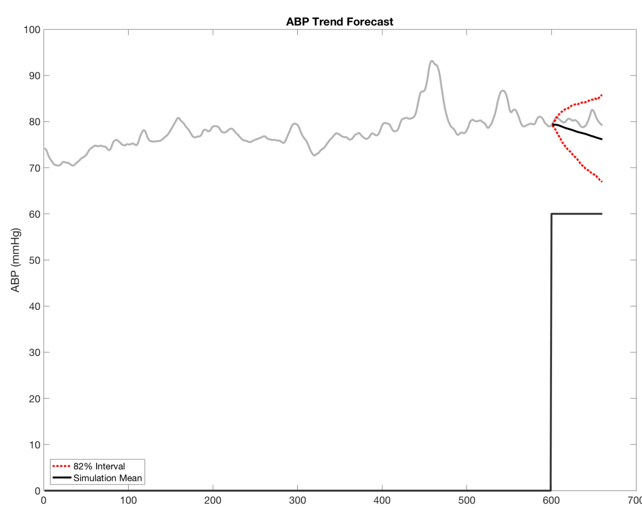

Figure 8. Results of simulating 1000 Monte Carlo Observations on a fitted ARIMA(2,2,2) model in a patient without an AHE.

Autoregression refers to the application of linear regression of current values against previous values[3], integration is the process of differencing the data to produce a forecast[12], and moving average models are also linear regression models of current series values against randomness in previous series data[3]. The combination of these models is typically referred to as a mixed model, and the ARIMA model is typically denoted as ARIMA(p,d,q), where each integer p, d, and q represents the order to the autoregressive, integrative, and moving average models, respectively[12]. By experimentation, the ARIMA(2,2,2) model resulted in the best results in forecasting training data.

In our implementation, 1000 Monte Carlo observations of the fitted ARIMA(2,2,2) model were simulated to forecast the ABP data for 60 data points (1 hour) beyond the cutoff time T_0. The simulations are then sorted on the basis of percentile. Experimentally, observing the 91st and 9th percentile bounds of simulation data resulted in the best forecasting results on training data.

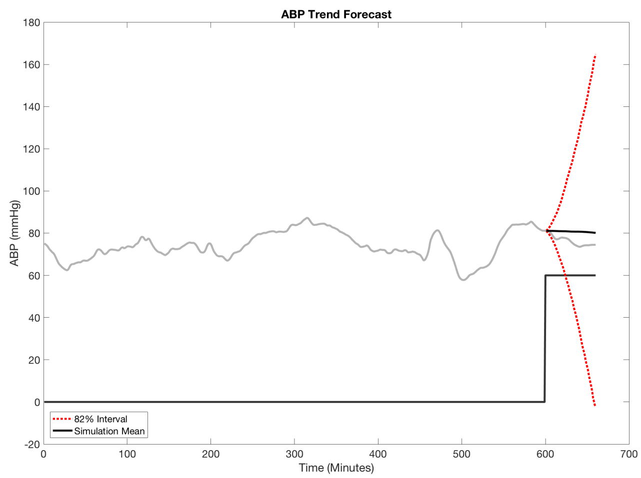

Figure 9. Failure of the ARIMA(2,2,2) model in a patient without an AHE.

Figure 7 shows the successful true prediction of an AHE based on the ARIMA Monte Carlo Simulations. The lines labelled as the 82% interval are the bounding 91st adn 9th percentile simulations. The simulation mean is also indicated. This solution is considered to forecast the occurrence of AHE as 'true' if the lower bounding simulation interval crosses the 60mmHg threshold. Similarly, Figure 8 shows the successful simulation for ABP in a patient that does not experience an AHE.

Despite these promising results, the ARIMA model is not without limitations. In select simulations, a significant divergence of the observations occurs. Figure 9 presents such a simulation.

EMA Crossover

The Exponential Moving Average (EMA) Crossover is one of the most rudimentary trend prediction techniques used in stock trading and foreign exchange. It uses two EMA plots, one with a smaller averaging window (the "faster" signal) and one with a larger averaging window (the "slower" signal).

EMA is computed with a recursive formula, where α is the degree of weighting decrease (a constant smoothing factor between 0 and 1). This formula is shown in Equation 2:

$$EMA_{today} = EMA_{yesterday} + \alpha(price_{today} - EMA_{yesterday}) \tag{2}$$

The formula could be further decomposed. The decomposed form of the formula can be seen in Equation 3

$$EMA_{today} = \alpha(p_1 + (1-\alpha)p_2 + (1-\alpha)^2 p_3 + \ldots) \tag{3}$$

Whenever the faster EMA signal is above the slower EMA signal, the data points are trending upward. If the slower EMA signal is above the faster EMA signal, the data points are trending downward. The crossover point at which the faster EMA signal meets the slower EMA signal represents a trend reversal. If the faster EMA signal is going from higher to lower relative to the slower EMA signal, the data points will go from trending upward to downward and is considered a "sell" signal in the financial industry. The opposite is true if the faster EMA signal is going from lower to higher relative to the slower signal, and such an event constitutes a "buy" signal.

Initially, we used only the upward and downward trends as predictors of AHE and non-AHE events, respectively. We made our preliminary predictions on the basis that if an ABP graph is trending downward, an AHE event will happen during the forecast window. However, while this method successfully identified AHE events, multiple instances of false positive readings were recorded. An instance of this is shown in Figure 10.

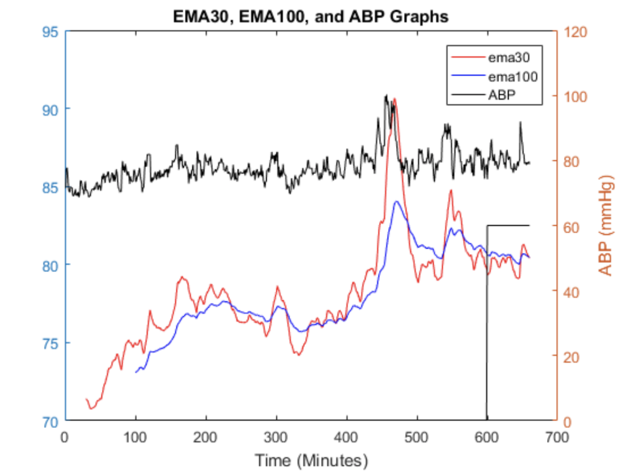

Figure 10. False positive prediction for a C1 patient.

An observation we have made regarding the ABP data shows that the mean values of the last few hours for the C1 and C2 cases are noticeably higher than that of H1 and H2. Figure 11 shows a graph from a C1 patient.

Juxtaposing Figure 11 with Figure 12, we can see that the mean of the C1 case is significantly higher than that of the H1 case. Experimentation and data sweeps shows that 80mmHg is a suitable threshold value that would differentiate the different cases.

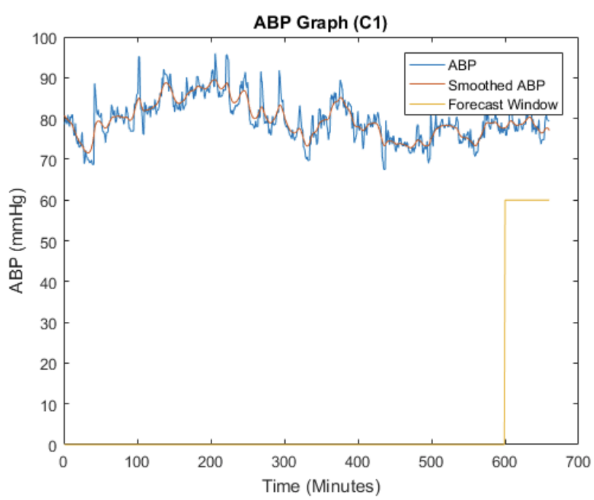

Figure 11. A graph showing the Arterial Blood Pressure for a C1 case from the training set.

Our final algorithm using the EMA approach is a simple conditional statement. If the ABP data is trending down during the one-minute period immediately before the beginning of the forecast window and the mean value of the last 50 minutes preceding the forecast window is less than 80 mmHg, the patient will undergo an AHE event. Otherwise, the patient will not experience an AHE event.

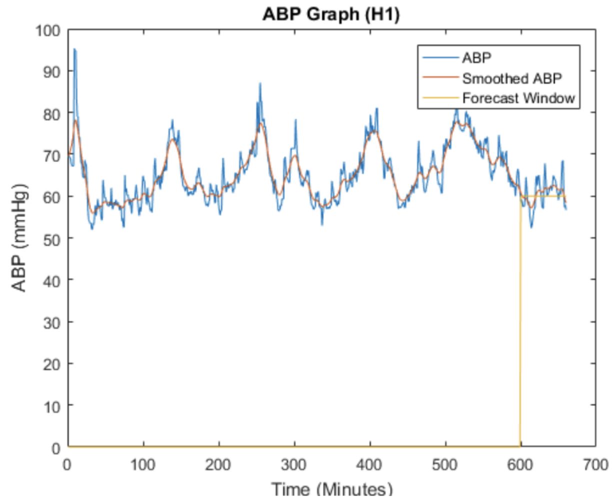

Figure 12. A graph showing the Arterial Blood Pressure for a H1 case from the training set.

Results

Our proposed models were trained on the 60 ABP recordings provided by PhysioNet and downsampled to 1 reading per minute by Henriques et al[2]. Table 1 presents our optimized sensitivty and specificity from the training data. We then evaluated the performance of our models on the two sets of test recordings provided to challenge participants.

	Sensitivity	Specificity
EMA Crossover	73%	73%
ARIMA Monte Carlo Simulation	68%	89%
NAR Neural Network	-	-

Table 1. Sensitivity and Specificity of our models based on training data results.

Test Set A, containing 10 recordings, contains 5 recordings from group H1 (patients treated with pressors who experienced and AHE), and 5 from C1 (patients who did not experience an AHE). Test Set B contains between 10-16 recordings from group C and 24-30 recordings from group H. Table 2 presents the final performance of our proposed models among the original submissions to the PhysioNet 2009 challenge.

Method	Test Set A (10 recordings)	Test Set B (40 Recordings)
EMA Crossover	10	32
ARIMA Monte Carlo Simulation	7	26
NAR Neural Network	-	-
Henriques & Rocha[2]	10	37
Mneimneh & Povinelli[14]	10	36
Chen et al[15]	10	36
Fournier & Roy[16]	10	35
Hayn et al[17]	10	34
Jin & Stockbridge[18]	10	33
Chiarugi et al[19]	10	30
Jousset, Lemay, & Vesin[20]	10	30
Ho & Chen[21]	10	-

Table 2. Legend (350 words max). Example legend text.

As indicated in Table 2, the EMA crossover model is highly competitive among the PhysioNet 2009 submissions. With 10/10 on Test Set A and 32/40 on Test Set B, EMA crossover is our best-perfroming method. The ARIMA model, with scores of

7/10 and 26/40, provides less performance than the EMA Crossover model. We hypothesize that there are some ABP recordings provided that do not exhibit non-stationarity, and therefore the ARIMA model can not be successfully applied. This is likely the cause for the simulation divergence observed in Figure 9, however no correction method has been successfully implemented at the time of submission.

Discussion

From the data presented in our results, we can see that our implementations have room for improvement. The ARIMA implementation could improve with rigorous identification and correction of the divergence observed in the failed recording forecasting. As previously discussed, the current hypothesis is that these results are likely due to stationarity within individual recordings, although no successful correction based on this hypothesis has been implemented. In future work, this method could potentially see significant improvement and become competitive with the bulk of submissions to the PhysioNet 2009 challenge.

Future work on an ANN solution will have to consider and focus on a few different topics. The first, and perhaps most important, is a method to allow for greater generalization in training. Most of the open loop response was fantastic, but in several cases the system did not respond quickly to rapid changes in ABP data, which was much exacerbated in the closed loop results. With less over-fitting, perhaps the network will be able to predict these rapid changes that we are looking for preceding an AHE. Another topic to consider is the inclusion of heart rate data into the network, creating a NARX Network. Although as discussed above, there is no clear relationship between heart rate and ABP, it is possible that through training a neural network, some small relationship can be found and used to predict future trends in ABP data similar to how stock data is predicted with many exogenous variables contributing to the final prediction. If we are able to adapt this method further, under guidance of an advisor, more concerted research into ANN predictions will be required to carefully tune the size and shape of our network, as well as choose appropriate external inputs to aid closed loop predictions.

Conclusion

The data provided in the 2009 PhysioNet challenge has lead us to the hypothesis that using Financial Forecasting Methods would allow us to accurately predict AHE events. Our results show that our approaches are viable. The ARIMA approach yielded satisfactory results, but holds a lot of opportunities for further development given the malleability of the model. The EMA Crossover method provided comparable results to more sophisticated analytical models. The Neural Network we constructed, while having little in the way of tangible predictions, had a very strong open loop response and may prove to be the most accurate method given more adjustment. We are looking towards improving our approaches with more data sets and potentially with mentorship from a qualified advisor. We aim to hone our methods into a series of academic papers for submission to scientific journals in the near future.

The code written for this project can be viewed at https://github.com/kahlanlg/physionet2009.

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Author contributions statement

A.H. contributed the neural network implementation, M.T. contributed the EMA crossover implementation, and K.G. contributed the ARIMA Monte Carlo simulation, and automated the testing of these methods. All authors reviewed and contributed to the paper.