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Predicting the Risk of Heart Failure With EHR Sequential Data Modeling

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ABSTRACT Electronic health records (EHRs) contain patient diagnostic records, physician records, and records of hospital departments. For heart failure, we can obtain mass unstructured data from EHR time series. By analyzing and mining these time-based EHRs, we can identify the links between diagnostic events and ultimately predict when a patient will be diagnosed. However, it is difficult to use the existing EHR data directly, because they are sparse and non-standardized. Thus, this paper proposes an effective and robust architecture for heart failure prediction. The main contribution of this paper is to predict heart failure using a neural network (i.e., to predict the possibility of cardiac illness based on patient's electronic medical data). Specifically, we employed one-hot encoding and word vectors to model the diagnosis events and predicted heart failure events using the basic principles of a long short-term memory network model. Evaluations based on a real-world data set demonstrate the promising utility and efficacy of the proposed architecture in the prediction of the risk of heart failure.

INDEX TERMS Electronic health records, heart failure, risk prediction.

I. INTRODUCTION

Heart failure, also referred to as congestive heart failure, occurs when the heart cannot pump enough blood to meet the body's needs [1]. The risk factors for heart failure include [2] high blood pressure, a prior heart attack, obesity, smoking, alcohol abuse, vitamin deficiencies, sleep apnea, heavy metal toxicity, an unhealthy diet (including animal fats and salt), and being sedentary. Heart failure is more common among people over the age of 65, overweight people, and those with a previous heart attack. The diagnostic method for heart failure is primarily based on the patient's medical and family histories, a physical examination, and test results. The signs and symptoms of heart failure are also common in other conditions. Thus, physicians identify any damage to a patient's heart and check how well the patient's heart pumps blood. These diagnostic methods provide massive sequential data, and it is a non-trivial task to perform accurate diagnosis with such massive data, particularly in the early stages. Indeed, a method for early diagnosis of heart failure that has a low-error rate is critically needed for clinical trials and

treatments [3]. By analyzing these sequential datasets, we have an opportunity to provide early diagnoses and treatments for people who are likely to have heart failure and help them have longer, more active lives.

A preferred strategy to resolve the problems of accurate diagnosis and the delivery of targeted therapies is the frequent performance of complete physical evaluations [4]. However, complete and frequent physical evaluations would lead to data overload. Heart failure patients and society would benefit if we could provide an accurate, systematic diagnostic service for the population. To this end, this paper develops a new approach to this vital task using an enhanced long short-term memory networks (LSTM) method and a data-driven framework.

Specifically, we treat each patient as a dynamic system that can be measured by a set of time series, such as the results of different lab tests, records and medical indicators. Our key idea is to analyze these time series. A time series is a sequence that provides the value of a statistical indicator in the order of time [5]. A time series indicates the

trend of the numerical value of the statistical index of the study object over a certain period. The traditional prediction methods based on time series primarily comprise the exponential smoothing method [6], the autoregressive integral moving average model (ARIMA) [7], recurrent neural networks (RNN) [8], and the long short-term memory network (LSTM) [9]. Currently, however, researchers often infer the diagnosis events with vectors in an unsupervised manner. In contrast, it is extremely valuable to model the diagnosis events with similarity learning. In this paper, we propose a novel method for diagnosis event modeling that combines one-hot encoding and word vectors and employs LSTM approach for heart failure prediction with the modeled diagnosis events as the input. Experimental results on a real-world dataset demonstrate the performance of the improved diagnosis prediction method.

The rest of the paper is organized as follows. In Section 2, we introduce the background of the time series analysis. Section 3 introduces the proposed modeling architecture, and we evaluate it using real-world data in Section 4. We discuss the related work in Section 5 and conclude our work and highlight future research directions in Section 6.

II. BACKGROUND

A. AUTOREGRESSIVE INTEGRAL MOVING AVERAGE MODEL (ARIMA)

The ARIMA model and exponential smoothing model exhibit better performances with short-term time series data prediction [10] and are thus suitable for numerical sequences. For non-numeric time series, a neural network can be constructed to solve the problem. In most time series data predictions, the depth-learning method provides better predictions than the ARIMA model or the exponential smoothing model. The depth-learning algorithm is based on a traditional neural network.

B. RECURRENT NEURAL NETWORK (RNN)

With today's increasing computational power, deep learning has been used to build many complex neural networks, such as convolutional neural networks (CNNs) [11], recurrent neural networks (RNNs) [12], and depth neural networks (DNNs) [13]. These networks have enabled breakthroughs in natural language processing (NLP), image recognition (IR), speech recognition (SR) and other fields. RNNs are suitable for dealing with time-series prediction problems. RNNs consist of an input layer, a hidden layer, and output layer. The result of the hidden layer is related to the input of the current layer and the output of the previous layer. Using this mechanism, an RNN gains the ability to remember historical results. Through transfer between the hidden layers, the previous information is passed to the next sequence, which establishes the relationship across the time series.

C. LONG SHORT-TERM MEMORY NETWORK (LSTM)

Hochreiter *et al.* [14] proposed the LSTM model, which is a special RNN model, in 1997. To achieve long-term memory, the RNN needs to hook the state of the current hidden layer to the state of a previous n -level hidden layer. This results in an exponential increase in the amount of computation, which in turn increases the time cost of the model. Thus, RNNs are not directly used for long-term memory calculations. The layers of the LSTM are added to the valve node on the basis of the original RNN network, which is conducive to overcoming the problems of RNN with long-term memory calculations. Moreover, this approach has been widely used. LSTM adds three gates to the basics of the original RNN network, i.e., an input gate, a forget gate, and an output gate. In recent years, many researchers have made minor changes to the LSTM model. One popular LSTM variant, introduced by Gers *et al.* [15], involves the addition of "peephole connections" (i.e., we let the gate layers look at the cell state). Another larger variant is the threshold cyclic unit (GRU) model, which was proposed by Chung *et al.* [16]. Here, the forget gate and the input gate are combined as a single update gate. Chung also merges the cell states and hidden states and makes some other changes. The GRU can increase the persistence of the memories of RNNs and thus support longer sequences. Moreover, the GRU model is both simpler and more popular than the standard LSTM model.

III. METHODS

In contrast to the abovementioned methods, we develop a word-vector-enhanced LSTM framework that can jointly construct the LSTM model with a word-to-vector method learned with available supervising constraints. Our work is based on the basic LSTM model. We present the details of our approach in the following section.

A. DIAGNOSTIC EVENT SEQUENCE PREPROCESSING

The input of our framework is the patient's diagnostic event sequence. In this paper, we use two methods to process the diagnostic event sequence into the form of the model input. The first method is the one-hot method [17], and the second one is the word vector method [18].

The one-hot method represents each diagnostic event as a vector whose length is equal to the number of different diagnostic events. The weight of the vector contains a single one, and the other cells are all 0s. The 1 corresponds to the current diagnostic event. One-hot coding is currently the most widely used method. This method is most convenient for use with only a few dimensions. However, one-hot encoding is not good at characterizing similarities between different words. For example, consider a vocabulary V inside which each word w_i has a label. The word w_i can be expressed as a vector of length $|V|$ with the one-hot method. The i -th element is 1, the others are all 0s. Assuming that the second word is "Cardiac Failure" and the third word is

“Heart Failure”, then:

$$\begin{aligned} \mathbf{w}_2 &= [0, 1, 0, \dots, 0]^T \\ \mathbf{w}_3 &= [0, 0, 1, \dots, 0]^T \end{aligned} \quad (1)$$

“Cardiac Failure” and “Heart Failure” are semantically the same, but the one-hot expression does not reflect the similarity between the two words.

Another method is the word vector model. As one of the distributed expression methods, the word vector model provides a method for directly calculating the similarity between two words. The basic idea of the model is to map each word into a fixed-length vector by studying a large number of expected corpora. In general, the vector length is much smaller than the length of the dictionary in the language. The vector length is usually between tens to hundreds of dimensions. All vectors make up the word vector space. Moreover, each vector represents a point in the space such that the distance between points can be used to measure the similarity between two words. We use a three-layer neural network to construct a language model whose structure is illustrated in Figure 1.

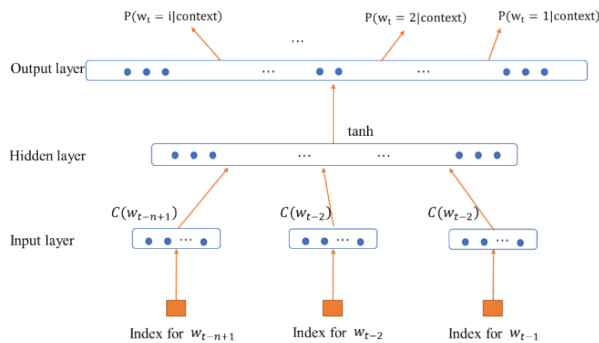


FIGURE 1. Three-layer neural network language model.

C is a matrix of $|V| * m$. $|V|$ represents the total number of corpora. m represents the dimension of the word vector. $C(w)$ denotes the word vector of word w . The entire model uses a unique set of word vectors that essentially consists of the following three layers:

Input layer: Splices the word vector $C(w_{t-n+1}), \dots, C(w_{t-2}), C(w_{t-1})$ and obtains the input vector x .

Hidden layer: Updates the state by calculating $d + Hx$ directly, where d is the offset item, H is the hidden layer weight of the $h * (n - 1)m$ vector, and h represents the number of elements selected from the word vector.

Output layer: There is $|V|$ nodes in all. Each node y_i represents the probability of the next word, i , which is not the normalized \log . The softmax activation function is then used to normalize the output value y_i according to the following formula:

$$y = b + Wx + U \tanh(d + Hx) \quad (2)$$

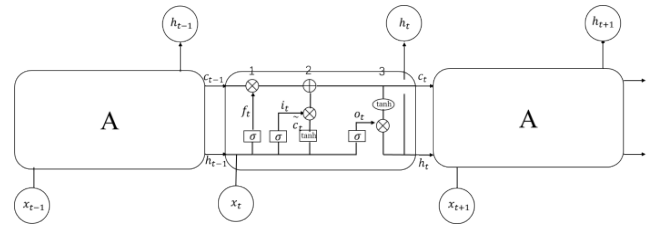


FIGURE 2. LSTM network structure.

B. RISK PREDICTION

The LSTM model for heart failure risk prediction is illustrated in Figure 2. The valve node uses the sigmoid function (σ symbol) for calculation based on the memory state of the network as input. The output ‘0’ of the sigmoid layer corresponds to the closed state of the gate, and the output ‘1’ corresponds to the open state. If the value of output gate exceeds the threshold, this output would multiply the output of the current layer and is taken as the input of the next layer. Otherwise, it should be forgotten. By controlling the closing of the valve, the effect of the previous sequence on the final result can occur.

The first part of Figure 2 (labeled “1”) determines which information is discarded from the cell state. Here, h_{t-1} represents the state of a hidden layer at moment $t - 1$, and x_t represents the output at moment t . This decision is performed by the input gate. The gate reads the values of h_{t-1} and x_t and outputs the values of 0 to 1 to the state c_{t-1} of each cell through the σ function. A “1” means all reserved, and a “0” means all discarded. Equation (1) indicates the state of the cell:

$$f_t = \sigma(W_f \cdot [h_{t-1}, x_t] + b_f) \quad (3)$$

The second part of Figure 1 (labeled “2”) is used to update the cell status and includes the sigmoid layer and the **tanh** layer. The sigmoid layer determines what value needs to be updated. A new value is created through the **tanh** layer. i_t and \tilde{c}_t can be calculated from the sigmoid layer and the **tanh** layer:

$$\begin{aligned} i_t &= \sigma(W_i \cdot [h_{t-1}, x_t] + b_i) \\ \tilde{c}_t &= \tanh(W_C \cdot [h_{t-1}, x_t] + b_C) \end{aligned} \quad (4)$$

The third part is used to update the cell state. This part updates \tilde{c}_t to c_t . Next, c_{t-1} and f_t are multiplied, and the information that needs to be dropped is discarded. Then, add $i_t * \tilde{c}_t$, and obtain the value c_t of the new state:

$$c_t = f_t * c_{t-1} + i_t * \tilde{c}_t \quad (5)$$

The last part is used to get the output value. The sigmoid function is implemented to determine the part that needs to be output. The cell state is **tanh**-treated (to obtain a value between -1 and 1) and multiplied by the sigmoid output. Then, the part h_t that needs to be output is obtained:

$$\begin{aligned} o_t &= \sigma(W_o \cdot [h_{t-1}, x_t] + b_o) \\ h_t &= o_t * \tanh(c_t) \end{aligned} \quad (6)$$

IV. DATA ANALYSIS

This paper used the electronic health record (EHR) data from real-world datasets related to congestive heart disease to perform the experiment. First, we extracted the records of patients who had heart failure disease for more than four years. The dataset consists of two parts: dataset A and dataset B. Dataset A contains the diagnostic records of 5000 patients who have been diagnosed with heart failure. The records mainly includes recording times, diagnosis events, and diagnosis times. Dataset B contains the diagnostic records for 15000 patients who have not been diagnosed with heart failure. The records mainly include recording times, and diagnostic events.

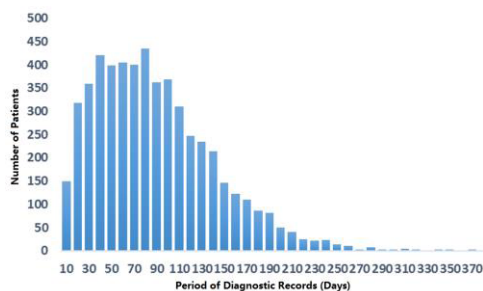


FIGURE 3. Distribution of patients in dataset A.

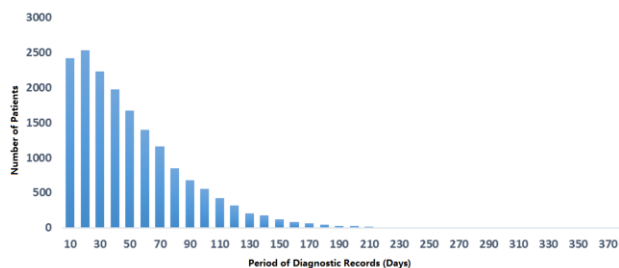


FIGURE 4. Distribution of patients in dataset B.

Figure 3 illustrates the distribution of patients in dataset A according to the period of diagnostic records. The number of days diagnosed in Figure 3 refers to the number of elapsed days from when the patient began the diagnosis process and treatment until the illness was determined. Figure 4 shows the same distribution for the patients in dataset B. As illustrated in Figure 3 and Figure 4, the diagnostic times of the patients in dataset A mainly occurred within six months, whereas the times of diagnosis in dataset B mainly occurred within 3 months.

Next, we extract the dataset for each patient’s diagnostic record, including the patient number, diagnostic event number, diagnostic time, and time of illness. For dataset B, the time of illness is unknown. Thus, the time of the last diagnosis was taken as the time of illness. Then, each patient was given a sick label; those in dataset A were marked as sick, and those in dataset B were marked as not sick.

V. EXPERIMENTAL RESULTS

In this paper, phrases “embedded vector” and “one-hot encoding” refer to the manner in which diagnostic events were handled. “Embedded vector” uses the word2vec tool to perform word vector training on the patients’ diagnostic events and represents the 1864 diagnostic events by the word vector. “One-hot encoding” represent each diagnostic event directly with an 1864-dimension vector. The corresponding event in the vector is set to 1, and the others are set to 0. The data were divided into five copies using a 5-fold cross validation method. Four copies were used as the training set and one copy was used as the proof set. The training set was rotated, and this process was repeated 5 times for verification. Similarly, the word vector also processed five training sets and five proof sets.

To evaluate the performance of the proposed model, we compared it with several state-of-the-art alternatives as baselines, including logistic regression (LR), random forest (RF) and AdaBoost. We used the receiver operator characteristic (ROC), precision-recall (PR), area under the curve (AUC) and F1 score metrics to evaluate the proposed method [19]. The experimental results are presented in Tables 1 and 2.

TABLE 1. Experimental results for the one-hot processing.

Model	ROC-AUC	PR-AUC	F1 Score
LSTM	0.6483	0.2401	0.2787
LR	0.5335	0.1456	0.0012
RF	0.5480	0.1589	0.0022
AdaBoost	0.5955	0.1780	0.0473

TABLE 2. Experimental results for the word vector embedding processing.

Model	ROC-AUC	PR-AUC	F1 Score
LSTM	0.6827	0.2678	0.2186
LR	0.6633	0.2251	0.0394
RF	0.6270	0.2025	0.0060
AdaBoost	0.6302	0.2124	0.1336

The average results of the proposed method and the other three baselines (i.e., ROC-AUC, PR-AUC and F1 score) were obtained after 5-fold cross validation. From the experimental results, we can draw the following conclusions:

- The accuracy of LSTM disease prediction is higher than those of LR, RF and AdaBoost algorithms, which indicates that the LSTM model is superior.
- A comparison of the two tables shows the LSTM model using word embedding vector to represent the patient diagnostic event outperforms the model using one-hot processing.

VI. RELATED WORKS

Traditional time series methods using linear models for low-dimensional data have been widely applied to EHRs; e.g., modeling the progression of chronic kidney disease to kidney failure using the Cox proportional hazard model [20], modeling the progression of Alzheimer’s disease using the

hidden Markov model [21] and the fused group Lasso [22], modeling the progression of glaucoma using a 2-dimensional continuous-time hidden Markov model [23], modeling the progression of lung disease using graphical models with the Gaussian process [24], modeling the progression of chronic obstructive pulmonary disease using the Markov jump process [25], and modeling the progression of multiple diseases using the Hawkes process [26]. These previous works were not able to model high-dimensional non-linear relations.

Deep learning methods have recently led to a renaissance of neural network-based models. Hochreiter and Schmidhuber [14] proposed long short-term memory (LSTM), which exhibited impressive performance in numerous sequence-based tasks such as handwriting recognition, acoustic modeling of speech, language modeling, and language translation. Hammerla *et al.* [27] applied restricted Boltzmann machines to time series data collected from wearable sensors to predict the state of Parkinson's disease patients. Lipton *et al.* [28] used LSTM for multilevel diagnosis prediction using pediatric ICU time series data (e.g., heart rate, blood pressure, glucose level, etc.). Both these latter studies used multivariate time series data from patients but focused on very different clinical conditions with the continuous time series data.

The prediction and earlier detection of heart failure could lead to improved outcomes through patient engagement and more assertive treatment. Previous work on the early detection of heart failure has relied on conventional modeling techniques such as logistic regression (LR) and support vector machines (SVM), using features that represent the aggregation of events in an observation window and exclude the temporal relations among events in the observation window. In contrast, recurrent neural network (RNN) methods capture temporal patterns that are present in longitudinal data. RNN models have proven effective in many difficult machine-learning tasks, such as image captioning [29] and language translation [30]. Extending these methods to health data is sensible.

We borrowed from the prior work to leverage similar representations of medical concepts through word vectors, but we focused on temporal modeling in the use of LSTM to predict heart failure.

VII. CONCLUSIONS

In this paper, we propose a novel predictive model framework for heart failure diagnosis using LSTM methods. Compared to popular methods such as LR, RF, and AdaBoost, our method exhibits superior performance in the prediction of heart failure diagnosis. In the experimental data analysis and preprocessing, we used one-hot encoding and word embedding vectors to represent the patient diagnostic events. By analyzing the results, we reveal the importance of respecting the sequential nature of clinical records. Future work will include incorporating expert knowledge into our framework and expanding our approach to additional health care applications.

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B. Jin and C. Che contributed equally to this work.

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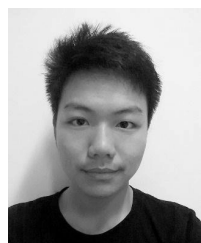
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