Risk Assessment Model for Diabetic Cardiovascular Disease Via Personality and Time-Aware LSTM Network

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Abstract: Diabetic cardiovascular disease is one of the leading causes of disease death in the diabetic population and its prevention and treatment has become a major social challenge. It has attracted the attention of many scholars and experts around the world, and a lot of research work has been done on it. Most of them use cox proportional risk models to investigate the correlation between risk indicators and the risk of developing cardiovascular disease based on statistical methods, which lack attention to the heterogeneity of individual patient characteristics and disease contextual information. To fill this gap, we propose a new deep learning model, the Personality and Time-Aware LSTM (PT-LSTM), which is based on individual characteristics and time perception to assess the risk of developing cardiovascular disease in diabetes. The model is able to take into account the characteristics of chronic metabolic disease in diabetes, using information from long-term patient visits as input. The model uses the individual feature interaction layer to reweight the hidden information of disease information learned in the T-LSTM unit, resulting in a more accurate representation of disease information for the risk assessment task. We realistically evaluate our proposed model on this task and the experimental results show that our proposed model exhibits better performance. Compared to the baseline model, PT-LSTM achieves 93.49% AUROC on the dataset for this task, which is on average around 8.75% higher than the comparison model.

1 INTRODUCTION

Diabetes is a chronic metabolic disease that causes a variety of serious health complications, including heart disease, kidney failure and cardiovascular disease (CVD), and has become one of the most significant disease burdens in our country and worldwide (Forbes, 2013). Death due to cardiovascular diseases as a complication of diabetes is one of the leading causes of death in this population (Grøntved, 2011). Therefore, the search for an effective diabetic cardiovascular disease risk assessment method for early prevention and treatment of the disease could greatly improve the survival rate of diabetic patients.

Most of the existing studies have used statistically relevant experimental analyses such as cox proportional risk models, logistic regression tests or simple machine learning to calculate the correlation between risk indicators and CVD risk or disease risk scores. For example, Domanski M J et al (Mjd, 2020) used Kaplan-Meier method estimates to assess the association between low-density lipoprotein (LDL-C) and CVD risk. Most of these methods are based on statistical correlation of risk characteristics with disease, treating both the important disease context of diabetes and important individual characteristics such as patient gender as simple risk characteristics. As a result, most of them lack attention to the heterogeneity of individual patient characteristics and ignore the important information carried by the disease context.

Based on the above issues, we propose a model for assessing cardiovascular disease risk in diabetes based on individual interaction and time perception, namely the Personality and Time-Aware LSTM (PT-LSTM). PT-LSTM takes into account the chronic metabolic disease characteristics of diabetes and is inspired by the TLSTM model proposed by Baytas I M et al (Baytas, 2017), which is applied on top of the T-LSTM to design an individual feature interaction layer that uses individual features to correct the hidden information of disease information obtained from learning Time-aware LSTM units to obtain a more accurate representation of disease information. Finally, we use a fully connected layer to assess the

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patient's current risk of developing cardiovascular disease.

In summary, the main contributions of this paper are as follows.

(1) Considering the chronic metabolic disease characteristics of diabetes mellitus, we adopt the modelling idea of T-LSTM. For the diabetic cardiovascular disease risk assessment task, we regard patients' long-term medical visit data as time-series information as the input to the model.

(2) An individual feature interaction network was designed to incorporate individual patient features into the model learning, resulting in a more accurate representation of disease information features.

To demonstrate the effectiveness and superiority of our model, we evaluated and compared the model with traditional machine learning methods (LR, RF and GBDT) and deep learning methods (RNN, GRU and LSTM) on this task. The experimental results show that our proposed model performs better in real-world tasks, outperforming the compared baseline models in terms of metrics such as AUROC.

2 RELATED WORK

Cardiovascular disease, as the leading cause of death worldwide, is an important public health issue (Yang, 2020) and its associated disease risk research has been a hot issue over the years, attracting the attention of many scholars and experts at home and abroad. For example, Bode E D et al (Bode, 2021) studied the risk factors for cardiovascular disease in US firefighters by BMI category based on statistical methods using the Wald test and logistic regression models. D'Agostino RB Sr et al (D'Agostino Sr, 2008) constructed a predictive model for cardiovascular disease in Framingham, USA, based on the general population. Elley CR et al (Elley, 2010) used a cox proportional risk regression model to construct a New Zealand diabetes cohort based on patients with type 2 diabetes, assessing multiple risk factors such as glycated haemoglobin associated with cardiovascular disease. Conroy R M et al (Conroy, 2003) used the Weibull proportional risk model to develop a risk scoring system for the clinical management of cardiovascular risk in European clinical practice.

These risk prediction algorithms are typically developed using multivariate regression models and often assume that all these factors are linearly related to cardiovascular disease prognosis, allowing existing algorithms to typically exhibit modest predictive performance (Alaa, 2019). This has led some scholars to propose data-driven techniques based on machine learning (ML) to improve the performance of risk prediction. For example, Mohan S et al (Mohan, 2019) combined random forest (RF) and linear methods (LM) to propose a hybrid random forest (HRFLM) heart disease prediction model with linear models for improving the accuracy of predicting cardiovascular disease. Dinh A et al (Dinh, 2019) used multiple supervised learning models to classify high-risk patients to obtain better performance than a single algorithm.

All of these efforts have contributed to the study of cardiovascular disease risk in diabetes. But these models treat all relevant factors as the same, lack attention to the clinical significance of individual patient characteristics, and ignore important information carried by the disease context. Such as patient age, gender and the disease context of diabetes. Patients with diabetes are at greater risk of developing cardiovascular disease and the correlation cannot be ignored (Einarson, 2018; Strain, 2018). Therefore, it is important to further explore and exploit diabetes information for cardiovascular disease risk prediction tasks.

3 PT-LSTM METHOD

3.1 Overview

As shown in Fig.1, the PT-LSTM model is a three-stage architecture consisting of three components: (1) a feature learning module based on Time-aware LSTM; (2) an interaction module of individual characteristics based on attention; (3) a prediction module with Fully Connected Network (FNN) for disease risk assessment.

The PT-LSTM model uses the visit records and visit time intervals in patients' EHR information as inputs to the T-LSTM module to obtain the hidden state h_i and c_i at the first moment. In the attention-based individual feature interaction module, the observation window size is set to K, and the sequence of disease hidden feature information $h_{T-K:T}$ ($h_{T-K:T} = [h_{T-K}, \ldots, h_{T-1}, h_T]$) output in the previous stage is used as input to the module together with the individual patient features q. The module outputs the reweighted weights β ($\beta = [\beta_{T-K}, \ldots, \beta_{T-1}, \beta_T]$) of $h_{T-K:T}$ based on the interaction of the individual patient features q with the temporal hidden information $h_{T-K:T}$. Finally, the disease risk information u is obtained based on the corrected temporal hidden information $\tilde{h}_{T-K:T}$ and individual characteristics q to predict the risk of disease occurrence $\hat{y}$.

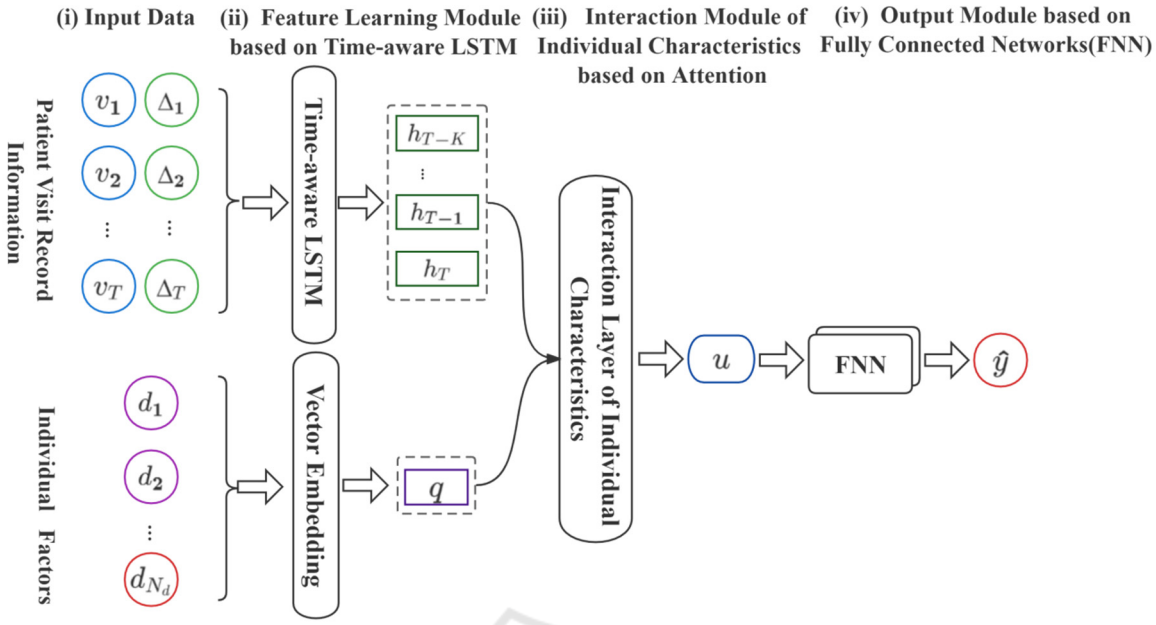


Figure 1: Overall architecture of Personality and Time-aware LSTM model

3.2 Time-Aware LSTM Module

T-LSTM is proposed based on the architecture of LSTM, which merges runtime information into the standard LSTM architecture and is able to focus on the information dependencies between two adjacent visit records (e.g. v_{t-1} and v_t) to capture the temporal dynamics of sequential data with temporal irregularities. Therefore, in order to capture long-term information in patient medical data, in this paper we use a Time-aware LSTM module to process the temporal medical features in patient data, as shown in Fig.2, which is computed as follows.

$$C_{t-1}^S = tanh(W_s C_{t-1} + b_s) \qquad \hat{C}_{t-1}^S = C_{t-1}^S * g(\Delta_t) \qquad \text{(New short term memory)}$$

$$C_{t-1}^L = C_{t-1} - C_{t-1}^S \qquad C_{t-1}^T = C_{t-1}^L + \hat{C}_{t-1}^S \qquad \text{(New previous memory)}$$

$$f_t = \sigma(W_f v_t + U_f h_{t-1} + b_f) \qquad i_t = \sigma(W_i v_t + U_i h_{t-1} + b_i)$$

$$o_t = \sigma(W_o v_t + U_o h_{t-1} + b_o) \qquad \text{(Gate cell calculation)}$$

$$\tilde{C} = tanh(W_c v_t + U_c h_{t-1} + b_c) \qquad C_t = f_t * C_{t-1}^T + i_t * \tilde{C} \qquad \text{(Current memory)}$$

$$h_t = o_t * tanh(C_t) \qquad \text{(Current hidden state)}$$

Here, v_t represents the current input, h_{t-1} and h_t are the hidden states of the previous and current steps respectively. C_{t-1} and C_t are the unit memory of the previous and current steps respectively. C_{t-1}^S represents the short-term memory, C_{t-1}^T is the short-term memory after adjustment, C_{t-1}^L represents the long-term memory. Similarly, as with standard LSTM units, $\tilde{C}$ is the current candidate memory, f_t, i_t and o_t are the input, forget and output gates respectively. In addition, W, U and b are the network parameters to be trained, Δ_t is the access interval between v_{t-1} and v_t, and $g()$ is a heuristic decay function based on the value Δ_t, i.e. the larger the value of Δ_t, the smaller the effect on short-term memory.

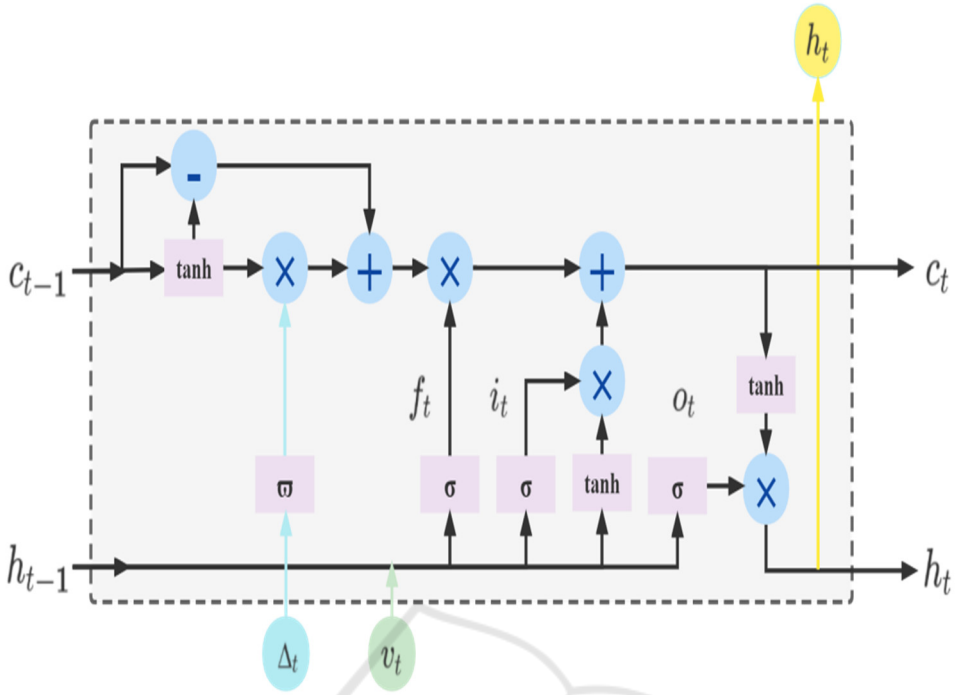


Figure 2: The structure of Time-aware LSTM cell.

3.3 Attention-Based Feature Interaction Module

In order to obtain more accurate information about the characteristics that can represent the patient's current risk of disease occurrence, we developed an attention-based individual factor interaction layer applied on the Time-aware LSTM cell, as shown in Fig.3 (a), whose specific process can be represented as the following three stages.

(1) Individual Feature Representation Layer

First, we count the discrete number of discrete individual features as the word table size, and according to the size of the number of possible values of discrete features, we set the word vector dimension size to N_s. Subsequently, the discrete individual features $[d_1,\ldots,d_{N_d}]$ are input to the embedding layer, and the embedding vector $[e_1,\ldots,e_{N_d}], e_i \in \mathbb{R}^{N_s}$ of individual features is obtained based on Word2Vec. Then, the matrix representation $\hat{q}$ ($\hat{q} \in \mathbb{R}^{1\times(N_d*N_s)}$) of individual features is obtained by vector stitching through the concat layer, and then multiplied with the parameter matrix W_q ($W_q \in \mathbb{R}^{(N_d*N_s)\times N_h}$) to obtain the latest representation $q(q \in \mathbb{R}^{1\times N_h})$ of individual features by matrix variation.

(2) Activation Unit

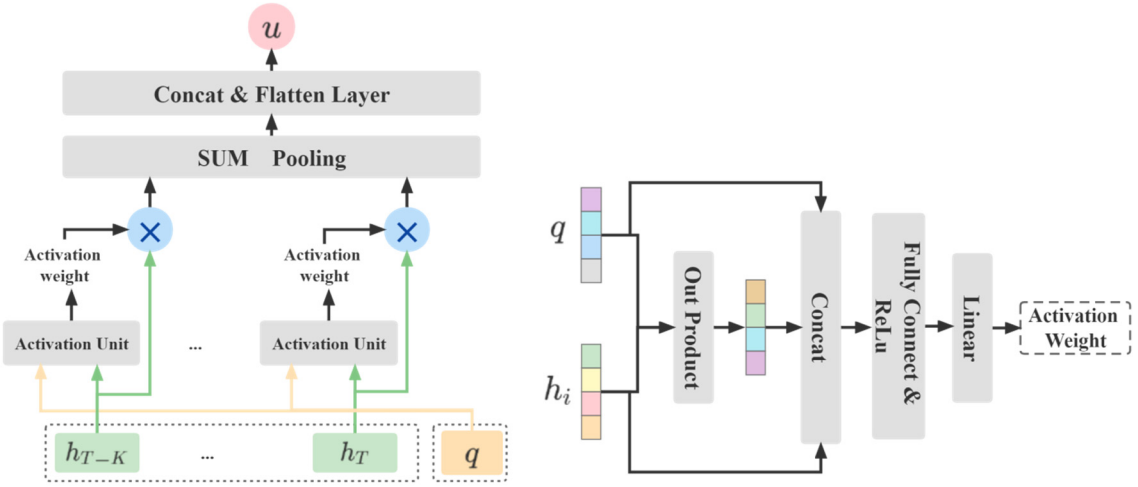
The individual feature q and the hidden state sequence $h_{T-K:T}$ are used as the input of this layer, and the outer product p of the two features is calculated, which is then concatenated with these two features to obtain the new feature representation. The attention weights β are obtained by multi fully connected network and linear layer. Here is an example of the calculation process for a single h_i with q, as shown in Fig.3 (b), and the formula is expressed as follows.

$$p = q * h_i$$
$$R_1 = ReLu\{W_{r1}(q \oplus p \oplus h_i) + b_{r1}\}$$
$$R_2 = ReLu(W_{r2}R_1 + b_{r2}) \quad (1)$$
$$\beta_i = SoftMax(W_{r3}R_2 + b_{r3})$$

(3) Feature Interaction Layer

Based on the attention weights in the previous layer, the modified disease hidden information $\tilde{h}_{T-K:T}$ is obtained, which is input to the SUM Pooling layer for summation according to the 1st dimension, and then concatenated with the individual feature information to obtain the final disease information feature representation u.

$$u = q \oplus \sum_{j=0}^{K} \beta_{T-j}\, h_{T-j} \quad (2)$$



(a) Overall structure (b) The process of the Activation Unit

Figure 3: The construction of the Individual Factors Interactive Attention Layer.

3.4 Disease Risk Assessment Module

The disease risk assessment module takes the output u from the previous stage as input and obtains a binary label indicating the patient's current risk of developing cardiovascular disease via a Fully Connected Network. In addition, we choose the cross-entropy function to calculate the loss, which is calculated as follows.

$$\hat{y} = \sigma(W_y u + b_y)$$

$$\mathcal{L}(y, \hat{y}) = -(\hat{y}\log(y) + (1-\hat{y})log(1-y)) \quad (3)$$

Where W_y ($W_y \in \mathbb{R}^{N_h}$) is a network parameter, y represents the true value of the patient's risk of developing cardiovascular disease, and $\hat{y}$ is the output value of the model's disease risk assessment function.

4 EXPERIMENT

4.1 Dataset Description

The study was approved by the Ethics Committee of Ruijin Hospital and written informed consent was obtained from each participating patient in accordance with the Declaration of Helsinki. Patient information is shown in Table 1.

Table 1: Details of Patient Information.

	Statistic	Value
DataSet	# patients	33048
	# visit	61646
	# positive label	12680
	# negative label	20368
	% male	60.21%

Our dataset was selected from biochemical index data of diabetic patients in Shanghai Ruijin Hospital from August 1, 2009 to July 30, 2021, with a total of 33,048 patients and 61,646 visit records, including 19,899 men and 13,149 women. Combining domestic and international literature and clinical recommendations, we selected high-density lipoprotein, low-density lipoprotein, cholesterol, glycated hemoglobin, two-hour glucose and triglycerides as inputs in terms of medical characteristics. Also, for individual patient characteristics, we selected patient gender, age and history of the remaining four common complications of diabetes (here, diabetic foot disease, diabetic nephropathy, diabetic peripheral neuropathy and diabetic eye disease).

4.2 Experiment Setting

We implemented our proposed baseline and target models on tensorflow 2.2.0 and scikit-learn 1.0.2, and trained them using the Adam optimizer. Through

parameter tuning, we set the learning rate to 0.001, the dimensionality of the individual feature embedding vector used in the deep learning baseline and PT-LSTM models to 64, and the dimensionality of the hidden vector to 128. In addition, we randomly divided the dataset into ten sets, and all experimental results were averaged by ten cross-validations, using seven training sets, one validation set, and two testing sets each time. Finally, we compared the performance of all methods using four metrics: the area under the receiver operating characteristic (AUROC) curves, Accuracy, Recall and F1-Score in the test set as measures.

To validate the effectiveness of our proposed model, we evaluated our proposed PT-LSTM model on different baseline models, including three traditional machine learning methods, LR, RF, and GBDT, and four deep learning methods, RNN, GRU, LSTM, and T-LSTM. Among them, in order to demonstrate the availability of individual feature interaction, we also implemented three versions of PT-LSTM and LSTM, namely PT-LSTM_Metabo, PT-LSTM_Add, PT-LSTM_Concat, LSTM_Metabo, LSTM_Add, and LSTM_Concat, respectively. Notably, there are many advanced clinical prediction models that use attentional mechanisms to extract long-term dependencies in patients' historical visits (Kamal, 2020; Lee, 2018), and they are orthogonal to our contribution. We focus on taking into account the heterogeneity of individual patient factors into the model, and our model PT-LSTM can be easily combined with attentional mechanisms.

4.3 Comparison Methods

To obtain the best performance of the model, all models used in our experiments were involved in parameter tuning. In this subsection, the PT-LSTM model is used as an example to discuss and compare the different effects of the number of patient medical visits T and the observation window size K of the individual-specific interaction layer on the model performance.

4.3.1 Comparison of Parameter Selection

(1) Parameter Selection of T

Diabetic disease is a chronic metabolic disease, and to accurately assess the risk of cardiovascular disease in diabetic patients, it is important to effectively follow up and learn the long-term health status of patients. Setting K = 1, an experimental comparison of our proposed PT-LSTM model regarding the number of patient medical visits T was conducted.

As shown in Fig.4, the experimental results show that each assessment index of the model improves as T increases. Thus, we believe that tracking and learning information about patients' long-term visits can effectively improve the accuracy of patients' cardiovascular disease risk assessment. We consider that this is brought about by diabetes itself as a chronic metabolic disease. Therefore, we should collect as much information on patient visits as the amount of data allows as a way to improve the accuracy of the disease risk assessment task. In addition, we observed that the model metrics reached their best and started to stabilize when T was greater than equal to 5. In order to reduce the impact of too small a data volume on other model comparison experiments later, we selected T of 5 as the parameter for our later experiments.

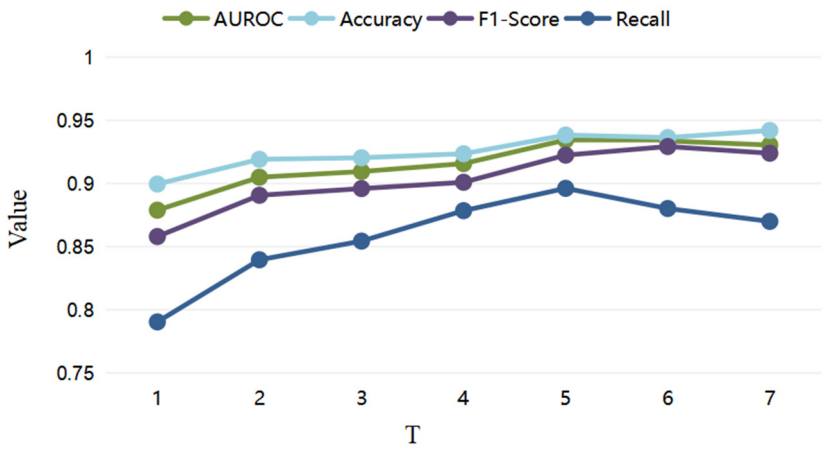


Figure 4: Parameter selection of T.

(2) Parameter Selection of K

Here, we set T=5 and discuss the influence and role of the parameter K in the individual feature interaction module on the use of the model. The experimental results are shown in Fig.5. When K=2, the model achieves the best performance, and when it is larger than 2, the model performance decreases, which is due to the long-term dependency of information that has been modeled and learned in the PT-LSTM. When T = 5, the observation window K is set too large, e.g. K is greater than 2, which can lead to the model focusing excessively on the repetitive and redundant part of the feature information, thus reducing the performance of the model. This also confirms the advantage of our LSTM unit in learning long-term dependence of information from a certain perspective.

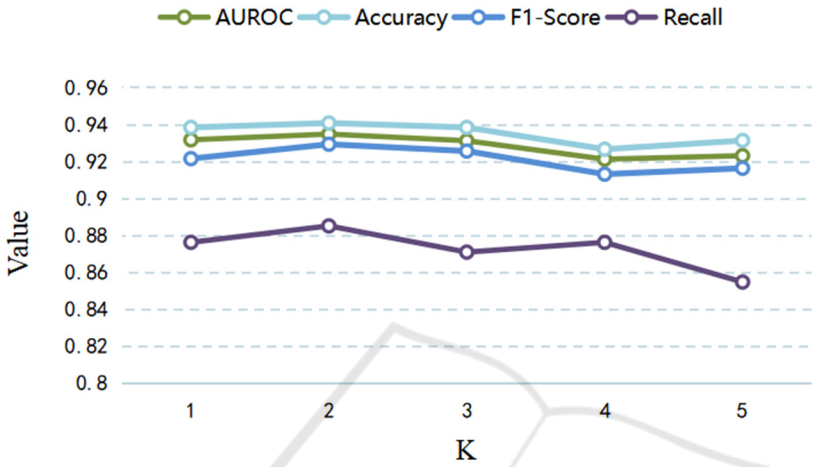


Figure 5: Parameter selection of K.

4.3.2 Comparison of Individual Feature Fusion Methods

From the experimental results in Table 2, we can find that the traditional LSTM model and our proposed model can also have relatively good results with only metabolic metrics, and their AUROC metrics can reach 85.87% and 88.66%, respectively. Subsequently, we added individual feature learning to the models using the traditional feature fusion methods concat and add, and both models showed significant improvements in various metrics such as AUROC, accuracy and F1-Score. This reflects the importance of individual feature learning in disease risk tasks. When we employ the interactive fusion method of individual features based on attention mechanism on LSTM and T-LSTM (i.e., LSTM_At and PT-LSTM), the accuracy and other evaluation metrics are significantly better than other models and fusion methods, which can reach 91.02% and 94.09%, respectively.

The experimental results demonstrate the effectiveness of our proposed individual feature interaction network and support the superiority of our model. In addition, comparing the LSTM and PT-LSTM models and their respective improved models, we can also find that effectively focusing on the medical information carried by the irregularity of visit time in medical data is of great significance and value for our assessment of disease risk.

Table 2: Comparison of feature fusion methods.

Model[a]	Feature Fusion[b]			Evaluation Index			
	Metabo	Indifac	Interfus	Accuracy	F1-Score	AUROC	Recall
LSTM_Metabo	√			0.8747	0.8359	0.8587	0.7258
LSTM_Add	√	√		0.9007	0.8793	0.8923	0.8226
LSTM_Concat	√	√		0.8913	0.8678	0.8827	0.8118
LSTM_At	√	√	√	0.9102	0.8889	0.9002	0.8172
PT-LSTM_Metabo	√			0.8936	0.8725	0.8866	0.8280
PT-LSTM_Add	√	√		0.9291	0.9128	0.9199	0.8441
PT-LSTM_Concat	√	√		0.9314	0.9169	0.9238	0.8602
PT-LSTM	√	√	√	**0.9409**	**0.9291**	**0.9345**	**0.8817**

[a] "Metabo" here means that the model only uses patient visit data as input data. "Concat" and "Add" represent the fusion mode of medical characteristic information and individual factors.
[b] Here, we defined the patient visit data as "Metabo", individual factor as "Indifac", and individual characteristic interaction as "Interfus".

4.3.3 Comparison of Different Producttion Models

To further validate the superiority of our proposed model, we evaluated our proposed PT-LSTM model on different baseline models. The experimental results are shown in Table 3, where the disease risk assessment task almost always performs worse than the deep learning model on machine learning. We consider that it is because the machine learning model loses the temporal information of medical visits and the information of individual patient characteristics. The T-LSTM outperforms the LSTM model, demonstrating the importance of irregular visit timing information in patient medical data in our diabetic cardiovascular disease risk assessment task. It should be noted that the individual feature fusion methods used here for both the LSTM and T-LSTM models are the ones they performed better in the previous section, and in this case, our proposed model PT-LSTM also shows significant advantages.

Table 3: Comparison of different models.

	Model	Accuracy	F1-Score	Recall	AUROC
Baseline	LR	0.7626	0.7483	0.721	0.7617
	RF	0.7857	0.7839	0.794	0.7859
	GBDT	0.7899	0.7863	0.7897	0.7899
	RNN	0.8960	0.8736	0.8172	0.8875
	GRU	0.8960	0.8771	0.8441	0.8904
	LSTM	0.9007	0.8793	0.8226	0.8923
	T-LSTM	0.9214	0.9069	0.8602	0.9138
Proposed	PT-LSTM	**0.9409**	**0.9294**	**0.8852**	**0.9349**

In summary, we have experimentally analyzed and compared each important module of the model and its overall performance. In addition, we compared the parameter selection of the training model and selected the optimal hyper-parameters. The experimental results of the comparison with the baseline model provide evidence for the effectiveness and superiority of our proposed model.

5 CONCLUSION

In this study, we propose a new deep learning model (PT-LSTM), for the task of assessing the risk of developing cardiovascular complications in the context of diabetes. Our can model is divided into three phases. In the first stage, patient visit records and visit intervals are used as input, and a time-aware LSTM module is employed to learn disease information carried by temporal data from patient medical visits. In the second stage, individual patient factors are interacted with the disease information features obtained in the previous stage to obtain a more comprehensive and accurate representation of disease risk features. In the third stage, a fully connected layer is used for our final disease risk assessment. The experimental results show that our model, based on the design of individual feature interaction fusion, can learn patient information better and make it consistently better than the base model. Our model also shows better performance in this task compared to other models.

Our proposed model effectively addresses the problem of personalised assisted diagnosis in the diabetic cardiovascular disease risk assessment task. In clinical practice, we hope that our model can help physicians identify patients at greater risk of diabetic cardiovascular disease in order to prevent or delay the onset of adverse outcomes. In the future, our model needs to be further validated on a larger scale for its adaptability and effectiveness in cross-hospital and cross-disease problems to better advance the application of Artificial Intelligence models in the field of diabetic complication risk prediction.

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