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Fuzzy linguistic prediction model for sinoatrial node field potential analysis in acute hyperglycemia environment

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Abstract. The objective of this study is to build a fuzzy linguistic prediction model (FLPM) for analyzing the actuation duration of acute hyperglycemia to sinoatrial node field potential. The field potential was recorded using microelectrode arrays (MEA). The experimental data were analyzed using partial least squares (PLS), support vector machine (SVM), back propagation neural network (BPNN) and the proposed method. The experimental results showed that the fuzzy linguistic prediction model could be adopted for predicting the actuation duration of high glucose to the sinoatrial node field potential. Compared with the other aforementioned models, the proposed model had higher prediction accuracy.

Keywords: Sinoatrial node field potential, acute hyperglycemia, linguistic prediction model, fuzzy rule

1. Introduction

In the biological researches, electrophysiological study is a significant field. A variety of cells such as heart cells, brain cells and retinal cells have electrophysiological characteristics. Meanwhile, sensors for recording electrophysiological signals progress rapidly. The experimental data have increased several times over because of the fast development and extensive application of multiple electrodes electrophysiological sensors [1-3]. The traditional data processing method is extracting some features artificially and using simple statistics. The method is effective when the quantity of data is small. However, when the amount of data is huge, some of the features may be hidden in the data and difficult to be found. Moreover, most existing conclusions of the electrophysiological study were statistical descriptions of the experimental results. These descriptions could not establish effective prediction models. In fact, researchers tend to pay more attention to whether the existing results and experiences can be used to evaluate the new experimental data. Therefore, accurate prediction models need to be built. So far the most common modeling methods are partial least squares (PLS) [4], support vector machine (SVM) [5] and back propagation neural network (BPNN) [6]. These methods have been used widely in electrophysiological studies [7-9]. In this paper, a fuzzy linguistic prediction

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model (FLPM) was used for sinoatrial node field potential analysis in high glucose environment. Linguistic prediction [10] can provide the human-readable description for electrophysiological data analysis. Fuzzy rules are the if-then statements which are usually adopted for linguistic modeling [11]. Sinoatrial node field potential is an important electrophysiological signal. It generates from the sinogatrial node and conducts around the heart [12]. Experimental data showed that sinoatrial node field potential was highly sensitive to acute hyperglycemia. As time went on, the signals in high glucose changed constantly and showed distinct characteristics. We used microelectrode arrays (MEA) [13] to record the changes of field potential in acute high glucose at different time points. After that, we built prediction models for high glucose duration using FLPM, PLS, SVM and BPNN. We then compared the prediction results of the models. The experimental results showed that the fuzzy linguistic prediction model had higher prediction accuracy.

2. Prediction modeling methods

2.1. PLS

The output of PLS can be written by Eq. (1):

$$Y = X\beta + r \tag{1}$$

where X is the input, β is a regression coefficient matrix, and r is a bias vector.

When a small number of principal components are defined by linear combinations of the input matrix, the output of PLS could be rewritten as Eq. (2):

$$Y = Tu + r \tag{2}$$

where vector u is corresponding to the latent variables. The matrix T could be written as Eq. (3):

$$T = XW(P^TW)^{-1} \tag{3}$$

In Eq. (3), X is the input. Loading matrix P is influenced by matrix X. Weight loading matrix W can indicate the relevance of X and Y.

2.2. SVM

The regression model of SVM can be written by Eq. (4):

$$Y = w \cdot \phi(X) + c \tag{4}$$

In Eq. (4), w is a weight coefficients matrix. Nonlinear function $\phi(X)$ can map the input X into a high dimensional space. c is a threshold vector.

The quadratic programming optimization process is used to find optimal w. If $\{(x_1, y_1), \ldots, (x_i, y_i), \ldots, (x_n, y_n)\}$ is the training dataset, the optimization problem can be written by Eq. (5):

$$\min_{(w,b)} \frac{1}{2} \| w \|^2 + C \sum_{i=1}^{n} (\xi_i + \xi_i^*)$$
$$s.t. \begin{cases} \varepsilon + \xi_i \geq y_i - w \cdot \phi(x_i) - b \\ \varepsilon + \xi_i^* \geq w \cdot \phi(x_i) + b - y_i \\ \xi_i, \xi_i^* \geq 0 \end{cases} \tag{5}$$

In Eq. (5), C is the penalty parameter, ε is the approximation accuracy, ξ_i and ξ_i^* are the slack variables.

The Lagrange function can be formed as Eq. (6):

$$L = \frac{1}{2} \| w \|^2 + C \sum_{i=1}^{n} (\xi_i + \xi_i^*) - \sum_{i=1}^{n} \lambda_i^1 (\varepsilon + \xi_i - y_i + w \cdot \phi(x_i) + b)$$
$$- \sum_{i=1}^{n} \lambda_i^2 (\varepsilon + \xi_i^* + y_i - w \cdot \phi(x_i) - b) - \sum_{i=1}^{n} (\lambda_i^3 \xi_i + \lambda_i^4 \xi_i^*) \tag{6}$$

where λ_i^1, λ_i^2, λ_i^3 and λ_i^4 are the Lagrange multipliers.

The final SVM form can be calculated and written as Eq. (7):

$$Y = \sum_{i=1}^{n} (\lambda_i^1 - \lambda_i^3) w \cdot \phi(x_i) + b \tag{7}$$

2.3. BPNN

The BPNN model has an input layer, an output layer and several hidden layers. The hidden layers are used to connect the input and output layers. The hidden layers are usually Sigmoid-type function and the number of hidden layers is decided by the characteristics of experimental data and expert knowledge. In this study, the field potentials in different high glucose concentrations made up the input layer. The high glucose actuation durations made up the output layer. The number of the hidden layers was 5.

2.4. Fuzzy linguistic prediction model

The rules of the proposed method use the IF-THEN linguistic statement for describing the knowledge. The model has an input matrix $[x_1, x_2, \ldots x_n]$ and a fuzzy set $\{L_1, L_2, \ldots L_m\}$. m is the linguistic terms number. A rule of the model can be expressed by Eq. (8):

$$\text{Rule i:}$$
$$IF \ \ x_{p_1} \in L_{q_1} \ and \ x_{p_2} \in L_{q_2} \ \ldots \ \ and \ x_{p_n} \in L_{q_n},$$
$$THEN \ \ Y = \sum_{j=1}^{n} k_j^i x_j + b_i \tag{8}$$

where b_i and k_j^i are the corresponding parameters respect to the output Y of the model's i-th rule.

The membership function can be expressed by the Gaussian function. The μ_i, which is the i-th rule's firing strength, can be written and calculated by Eq. (9):

$$\mu_i(x_j) = \prod_{j=1}^{n} \exp[\frac{(x_j - c_{ij})^2}{2\sigma_{ij}^2}] \tag{9}$$

In Eq. (9), σ_{ij} is the standard deviation, c_{ij} is the expectation. $i \in \{1, 2, \ldots, N\}$, $j \in \{1, 2, \ldots, n\}$.

The parameters can be estimated by Eq. (10):

$$\begin{cases} k_j^i = \dfrac{Y}{x_j} \cdot \dfrac{\sum_{i=1}^{N} \mu_i(x_j)}{\mu_i(x_j)} \\ b_i = Y \cdot \dfrac{\sum_{i=1}^{N} \mu_i(x_j)}{\mu_i(x_j)} \end{cases} \tag{10}$$

For a new input $[x_1', x_2', ..., x_n']$, the prediction output can be written and calculated by Eq. (11):

$$Y^* = \frac{\sum_{i=1}^{N} \mu_i Y'}{\sum_{i=1}^{N} \mu_i} \tag{11}$$

where $Y' = \sum_{j=1}^{n} k_j^i x_j' + b_i$.

3. Materials and experimental design

3.1. Animals

Male C57/BL6J mice which were fed standard diets and water were chosen for the experiments. The mice were 8-12 weeks old and weighed 20-25g. The ambient temperature was 21°C±2°C. The experimental protocols were approved by the Animal Experimentation Ethics Committee (AEEC) and were performed according to the Animal Experimentation Guidelines (AEG) of the Xi'an Jiaotong University.

3.2. Introduction of the recording instruments

The multi-electrode device 64 (MED64) recording and analysis system (Alpha Med Science, Panasonic, Japan) was used to record and analyze the experimental data. The system comprised an

MED64 amplifier, an MED64 connector, an MED64 controller, a data processing computer, an inverted microscope, a perfusion cap, a peristaltic pump and a measuring electrode. The electrode had 64 recording channels with the square 8×8 arrangement. The electrode spacing was 300 μm. Each electrode was square and the length of a side was 50 μm.

3.3. Design of experiments

The Langendorff system [14] and Tyrode's solution [15] was used for the mouse heart in vitro perfusion. The sinoatrial node is located on the right atrium [16, 17]. Tissue from this area of the heart was cut off using a vibration cutting machine (Vibratome 1000 Plus, Vibratome Company, USA). The thickness of the section was set as 1mm. The sample was then directly put into the MEA electrode for recording. During the entire recording process, Tyrode's solution with 5% carbon dioxide and 95% oxygen was provided continuously with a flowing rate of 5 ml/min. The biotic sample size of each group was 8. First, we recorded the field potentials of the control sample. After that, high glucose solutions (experimental group) and mannitol solutions (isotonic control group) were fed into the sample at 0th minute. The concentrations were 30 mM, 40 mM and 50 mM respectively and the duration was 60 minutes.

Data were recorded every five minutes beginning from the 0th minute. The sampling frequency was 20 kHz. Each recording was taken for 30 seconds. The results showed that the field potential was not sensitive to high osmotic pressure.

Fast Fourier Transform (FFT) was used to convert the field potential signals from the time domain to the frequency domain. The most power of the frequency domain signals focused at 0-50 Hz. Data from this section were selected as the experimental data. The predict duration was from the 15th minute to the 45minute since the sinoatrial node field potential evidently changed in this range. The three concentrations correspond to three dataset. Each dataset contained 426 samples. The shutter grouping strategy was used to divide every dataset into two sets. One was calibration set and the other was validation set [18]. Every two elements of the datasets were selected into the two sets respectively. The calibration set was used for setting up the prediction model. The validation set was used for estimating the predictive abilities of the models.

4. Results and discussion

In this research, PLS, SVM, BPNN and the proposed method FLPM were used for predicting the actuation duration of high glucose in the three different concentrations. Table 1 showed the predictive abilities of the four methods in 30mM high glucose environment. RMSEP and RMSECV of the proposed method were lower than that of the others. R_p^2, R_c^2 and R_{cv}^2 of the proposed method were higher than those of the others. It showed that the FLPM had the highest predictive ability and the lowest discrete degree. Table 2 showed the predictive abilities of the four methods in 40 mM high glucose environment. In the same way, the predictive result of the proposed method was the best. Table 3 showed the predictive abilities of the four methods in 50 mM high glucose environment. The RMSECV of the proposed method was slightly higher than the one of SVM and BPNN, and the R_p^2, R_c^2 and R_{cv}^2 of the proposed method was slightly lower than those of the SVM and BPNN. Nevertheless, the RMSEP of the proposed method was the lowest.

In summary, the results in the tables verified that the fuzzy linguistic prediction model could be adopted for predicting the actuation duration of high glucose to the sinoatrial node field potential. The

method had higher prediction accuracy.

5. Conclusion

In this paper, a fuzzy linguistic prediction model was used for predicting the actuation duration of high glucose to the sinoatrial node field potential. The linguistic rules of the method were human-readable and realized the actuation duration prediction successfully. Compared with classical PLS, SVM and BPNN, the proposed method had higher prediction accuracy and lower discrete degree.

Table 1

The predictive results for the actuation duration in 30 mM high glucose environment

	RMSEP	RMSECV	R_p^2	R_c^2	R_{cv}^2
PLS	5.3543	3.4171	0.4837	0.7021	0.4567
SVM	3.6961	3.0067	0.5993	0.8932	0.9662
BPNN	3.5751	5.4177	0.7147	0.8455	0.7278
FLPM	2.4302	1.5810	0.8207	0.9195	0.9899

Note: RMSEP: root-mean-squared error of prediction.
RMSECV: root-mean-square error of cross validation.
R_p^2: squared correlation coefficient of prediction.
R_c^2: squared correlation coefficient of calibration.
R_{cv}^2: squared correlation coefficient of cross validation.

Table 2

The predictive results for the actuation duration in 40 mM high glucose environment

	RMSEP	RMSECV	R_p^2	R_c^2	R_{cv}^2
PLS	7.5069	7.9670	0.0292	0.0121	0.0063
SVM	4.9835	3.0381	0.2163	0.8797	0.6097
BPNN	5.4656	3.1364	0.2664	0.6913	0.4879
FLPM	2.5291	1.5678	0.8026	0.9183	0.9894

Note: RMSEP: root-mean-squared error of prediction.
RMSECV: root-mean-square error of cross validation.
R_p^2: squared correlation coefficient of prediction.
R_c^2: squared correlation coefficient of calibration.
R_{cv}^2: squared correlation coefficient of cross validation.

Table 3

The predictive results for the actuation duration in 50 mM high glucose environment

	RMSEP	RMSECV	R_p^2	R_c^2	R_{cv}^2
PLS	6.6942	5.9300	0.6570	0.7143	0.6480
SVM	5.4741	3.0498	0.9000	0.9028	0.7838
BPNN	3.9859	3.0328	0.8447	0.9598	0.8040
FLPM	3.9596	3.2346	0.8422	0.8962	0.7081

Note: RMSEP: root-mean-squared error of prediction.
RMSECV: root-mean-square error of cross validation.
R_p^2: squared correlation coefficient of prediction.
R_c^2: squared correlation coefficient of calibration.
R_{cv}^2: squared correlation coefficient of cross validation.

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