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Full Length Research Paper

Comparison of v-support vector regression and logistic equation for descriptive modeling of *Lactobacillus plantarum* growth

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Due to the complexity and high non-linearity of bioprocess, most simple mathematical models fail to describe the exact behavior of biochemistry systems. As a novel type of learning method, support vector regression (SVR) owns the powerful capability to characterize problems via small sample, non-linearity, high dimension and local minima. In this paper, we developed a v-SVR model with genetic algorithms (GA) in the pre-estimate in *Lactobacillus plantarum* fermentation by comparing the predicting capability of logistic model and SVR model. 5-fold cross validation technique was applied in the SVR train to avoid over-fitting. The information of SVR parameters were obtained in the generation of 150 and the optimal parameters were C= 235.8935, σ= 8.3608, v=0.7587. Correspondingly, the logistic model parameters $\mu_{\max}$ and x_{max} were estimated as 0.4791 and 0.3498, respectively. The experimental results demonstrated that, SVR model excelled the logistic model based on the normalized mean square error (NMSE), mean absolute percentage error (MAPE) and the Pearson correlation coefficient R. We found that the v-SVR model optimized by genetic algorithms could be a potential monitoring method for prediction of biomass.

Key words: Support vector regression, genetic algorithm, logistic model, prediction of biomass.

INTRODUCTION

Because microorganism fermentation process is complex and non-linear, many parameters such as the concentration of bacteria, substrates and products are difficult to measure on-line (Wang et al., 2006). In order to optimize bioprocess and put the advanced algorithms of control into practice, it is necessary to monitor and diagnose the bioprocess parameters.

Kinetic models are generally experimentally derived mathematical formulas that can agree well with the cultivation data (Bessaou and Siarry, 2001). Kinetic models can be linear or nonlinear, such as ordinary (or partial) differential equations, cellular automata (Xiao et al., 2005; Xiao et al., 2006) and logistic model. The logistic model firstly, proposed by Verhulst in the eighteenth century(Liu et al., 2002), has been demonstrated to be the most illustrative model of microbial growth dynamics in a habitat of finite resources (Fujikawa et al., 2002; Peleg et al., 2007; Schepers et al., 2000). Logistic equation is based on the notion that the momentary growth rate of a given population inoculated into a virgin environment is proportional to the momentary population's size.

Recently, a statistical learning theory based on formalism known as the support vector machines (SVMs) emerged as a novel powerful tool for data classification and regression, which are called support vector classification (SVC) and support vector regression (SVR).

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SVMs could solve the problems resulted from small samples, nonlinearity, high dimension and local minimum (Vapnik, 1995; Borin et al., 2006; Cai et al., 2003; Moreira et al., 2007). Therefore, SVR is gradually accepted in the data-driven nonlinear modeling applications (Desai et al., 2006).

Unfortunately, for the generalization performance of SVR which depends on SVR parameters, how to set these parameters by a given set of data is the main issue for the application of SVR. Cherkassky (2004) described ε-support vector regression (ε-SVR) for setting meta-parameters. However, as the parameter ε influences the solution indirectly and lacks intuitionistic means, it is difficult to give appropriate value for ε. To overcome this problem, a new parameter v was introduced to control the fitness and predication accuracy instead of parameter C in SVR (Schepers et al., 2000). Chalimourda et al. (2004) studied optimal v in SVR for different noise models using the data from sine function and Boston housing problem. Recently, the performance of SVR in bioprocess was also researched (Li et al., 2006a; Li and Yuan, 2006b). However, v-SVR coupled with genetic algorithm has not been investigated in fermentation process.

In this study, v-SVR was applied to determine the concentration of cell via the data from fermentation process. We aimed to find a suitable method for the simulation of microbial growth by comparing different modeling strategies in process simulation and fermentation control. The organism used in the model was *Lactobacillus plantarum*.

MODEL STRUCTURE

Logistic model

As unstructured kinetic model, logistic model is the most frequently employed for modeling microbial systems, because it is simple and good enough for technical purposes ((Kiviharju et al., 2006; Mu et al., 2006). The logistic model can describe the kinetics of the microbial growth as follows:

$$\frac{dx}{dt} = \mu_{max}\left(1-\frac{x}{x_{max}}\right)x \qquad (1)$$

Where, x (g l^{-1}) is the cell concentration, t (h) is the fermentation time, μ_{max} (h^{-1}) is the maximum specific growth rate and x_{max} (g l^{-1}) is the maximum cell concentration. Using $x = x_0$ (t = 0), integration of equation 1 gives the following equation for microbial biomass:

$$x = \frac{x_0 x_{max} e^{\mu_{max} t}}{x_{max} - x_0 + x_0 e^{\mu_{max} t}} \qquad (2)$$

Support vector regression

Support vector regression

The v-support vector regression (v-SVR) is a promising method for solving non-linear regression problem, which depends on the theory of support vector machines (SVMs). In this section, a brief introduction of SVR is given.

Given a set of data points: $T=\{(x_i, y_i)\}_{i=1}^{l} \in R^N \times R$, where $x_i \in R^m$ is the input vector, $y_i \in R$ is the desired value and l is the total number of data points. SVR estimation aims to seek for a function using the following formula:

$$y = w^T \cdot \Phi(x_i) + b \qquad (3)$$

Where, w is the weight, b is the coefficient, and $\Phi(x_i)$ denotes the data in high dimensional feature space mapped by applying nonlinear kernel function from the input space x_i.

The coefficients (both *w* and *b*) could be optimized only by minimizing the regularized risk function:

$$\frac{1}{2}\|w\|_k^2 + C\frac{1}{l}\sum_{i=1}^{l}(\zeta_i + \zeta_i^*) \qquad (4)$$

Where, $\frac{1}{2}\|w\|_k^2$ is called the regularized term. $\frac{1}{l}\sum_{i=1}^{l}(\zeta_i + \zeta_i^*)$ is the empirical risk measured by the $\varepsilon-$insensitive loss function. The slack variable ζ_i, is called the upper training error and ζ_i^* represents the lower training error subject to the "ε-radius-tube" where $|y_i - ((\omega \cdot \Phi(x_i) + b)| \le \varepsilon$. C is the regularization factor which has the ability of determining the trade-off between the empirical risk and the regularized term.

As a consequence, the ε-SVR problem can be

described as the following quadratic optimization problem:

$$\min_{\omega,\zeta,b} \quad \left[\frac{1}{2}\|w\|_k^2 + C\cdot\frac{1}{l}\sum_{i=1}^{l}(\zeta_i+\zeta_i^*)\right] \tag{5}$$

$$subject\ to \quad ((\omega\cdot\Phi(x_i)+b)-y_i \le \varepsilon+\zeta_i,$$
$$y_i-((\omega\cdot\Phi(x_i)+b) \le \varepsilon+\zeta_i^*,$$
$$\zeta_i,\zeta_i^* \ge 0,\ i=1,2,3\cdots l$$

However, the varied value of the ε could be selected from all values in real number and would deeply influence the solution of quadratic optimization problem. Fortunately, Schölkopf et al. (2000) cited a weight parameter (v) multiplied by ε in the ε-SVR problem to control the tube size, which avoids exhausting search of the ε parameter in the real number range. After this transition, the optimization problem is as follows:

$$\min_{\omega,\zeta,b} \quad \left[\frac{1}{2}\|w\|_k^2 + C\cdot\left(\upsilon\varepsilon+\frac{1}{l}\sum_{i=1}^{l}(\zeta_i+\zeta_i^*)\right)\right] \tag{6}$$

$$subject\ to \quad ((\omega\cdot\Phi(x_i)+b)-y_i \le \varepsilon+\zeta_i,$$
$$y_i-((\omega\cdot\Phi(x_i)+b) \le \varepsilon+\zeta_i^*,$$
$$\zeta_i,\zeta_i^* \ge 0,\ i=1,2,3\cdots l$$

Usually, the problem stated earlier could be successfully solved in its dual form by exploiting the Lagrange multipliers approach (Vapnik, 1995; Belousov et al., 2004). Through the Karush-Kuhn-Tucker (KKT) conditions of solving quadratic programming problem, the dual Equation 5 leads to the solution by maximizing the α_i^*, α_i, which are Lagrange multipliers

.

$$\max_{\alpha,\alpha^*} \quad \frac{1}{2}\sum_{i,j=1}^{l}(\alpha_i^*-\alpha_i)(\alpha_j^*-\alpha_j)K(x_i,x_j)+\sum_{i=1}^{l}y_i(\alpha_i^*-\alpha_i) \tag{7}$$

$$subject\ to \quad \sum_{i=1}^{l}(\alpha_i-\alpha_i^*)=0$$
$$0\le\alpha_i,\alpha_i^*\le\frac{C}{l},\ \forall i=1,2,3\cdots l;$$
$$\sum_{i=1}^{l}(\alpha_i^*+\alpha_i)\le C\cdot\upsilon$$

They satisfy the condition of $\alpha_i^*\times\alpha_i=0, x_i\ge 0, \alpha_i^*\ge 0$. Where $i=1,2...l$.

Parameters determination of the v-SVR model

To construct an efficient v-SVR model, SVR's parameters are crucial and should be set carefully (Fujikawa et al., 2004). These parameters include:

Kernel function: The term $k(x_i,x_j)$ in Equation 7 is defined as kernel function. Generally speaking, as the key in the SVM theory, kernel function is used to map the input feature data x_i into a higher-dimensional feature space via non-linear mapping (Bessaou and Siarry, 2001). Three typical examples of kernel functions are polynomial, radial basis function (RBF) and linear kernel. As a kind of RBF kernel functions, Gaussian function yielding better prediction performance was used in this study (Samanta et al., 2003).

Penalty parameter C: As mentioned earlier, C determines the trade off between margin maximization and error minimization.

Bandwidth of the kernel function (σ^2): In this paper, sigma square (σ^2) denotes the variance of the Gaussian kernel function.

Parameter v: v represents an upper bound on the fraction of errors and a lower bound on the fraction of parameters to build the regression function and the range is from 0 to 1.

In general, the accurate estimation of *v*-SVR model is based on the hyper-parameters (*C*, σ, *v*), these parameters need to be selected in *v*-SVR. But now it is still a complex problem and hard to obtain the optimized parameters value in an effective algorithm. Heuristic search techniques are usually used to find the optimal SVR parameter settings, such as genetic algorithm (GA) or simulation annealing algorithm (SA). Thereinto, GA is better for robust optimization in a complex search space (Potocnik and Grabec, 1999; Ustun et al., 2005). In this study, the coupled-model of GA-SVR was proposed to find the optimal values of v-SVR parameters.

GA-SVR optimization procedure

Genetic algorithm (GA), which was formerly introduced by Holland (1975), employs the biological techniques of

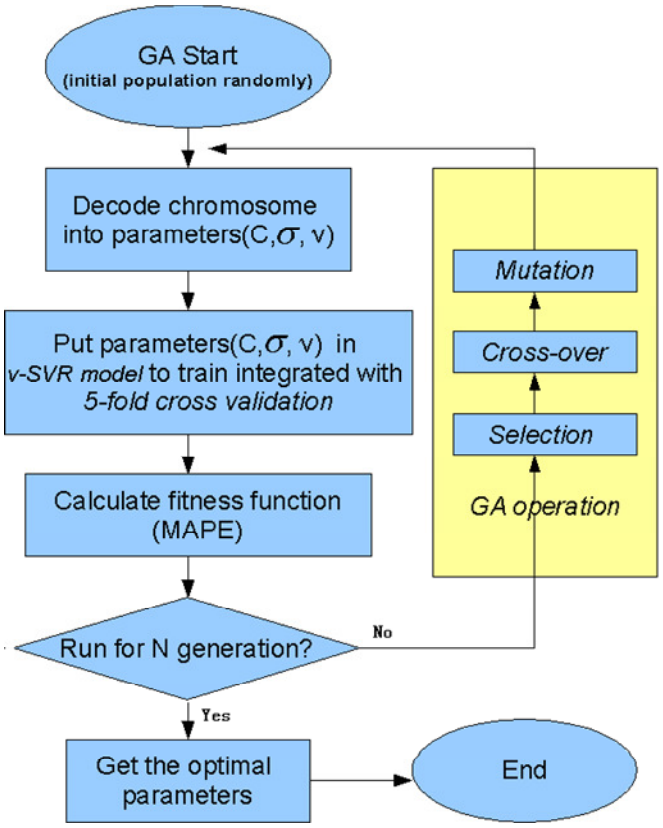

Figure 1. GA-v-SVR model.

mutation and crossover to search the local optimal solutions. Figure 1 illustrates the algorithm of the GA-SVR model. Our proposed GA- SVR is described as follows in detail:

Step 1. Population initialization: In this process, the three v-SVR parameters (*C*, σ, *v*) were converted decimal code into a binary format. The chromosome X was represented as X = p1, p2, p3, where p1, p2 and p3 denote the regularization parameters C, σ and *v*, respectively. One population contains n sizes of such kind chromosomes and is randomly generated. In this study, we used 100 sizes of such chromosomes and when the chromosomes were put into SVR to train, the binary format was translated into decimal once again.

Step 2. Evaluate the fitness function: The fitness of training data set is easy to be calculated, but also, it is prone to be over-fitting. The 5-fold cross validation technique was applied in the SVR train to avoid over-fitting and to make the result generalized and reasonable (Holland, 1975; Browne, 2000). The fitness function of the parameter set is measured as the criteria of minimizing the MAPE (mean absolute percentage error):

$$\text{MAPE}=\frac{\sum_{i=1}^{n}\left|a_i-p_i\right|/a_i}{n}\times 100\%$$

Where, p_i denotes the predicted value in SVR model, a_i represents the actual experimental observation and n is the number of experimental observations. The smaller the values of MAPE in the regression, the better the prediction performance would be.

Step 3. Genetic operation: The genetic operators (Figure 2) which contain selection, crossover and mutation are mainly illustrated as follows:

Selection: A spin of a weighted roulette wheel is applied to choose chromosomes in the current population with the possibility of selection frequency rate.

Crossover: Crossover is a typical genetic operation in genetic algorithm which allows new population to be created in the search space. This mechanism operation aims to create a crossover point randomly in a pair of parental chromosomes and then, exchange genes between these two chromosomes. This situation occurs between two chromosomes and the crossover rate could be described with the frequency of crossover.

Mutation: Mutation process is the same genetic operator of crossover which also alters the solution of parental chromosome. However, it happened in one chromosome and the genes may occasionally be altered. In binary code, one mutation means genes changing code from 0 to 1 at one random point.

After these operators, if the minimum fitness value of the new population is smaller than that of the old population, the offspring chromosome could replace the old chromosome and create a new population.

Step 4. Termination criteria: The process was repeated from the genetic operation and fitness function evaluation until the number of generations was up to termination. After that, the best chromosomes would be presented as a solution. Of course, the information of parameters in the chromosomes could be acquired and the best MAPE could be represented. In this study, we defined 150 generation.

MATERIALS AND METHODS

Strain

L. plantarum C263, originally isolated from diary food were

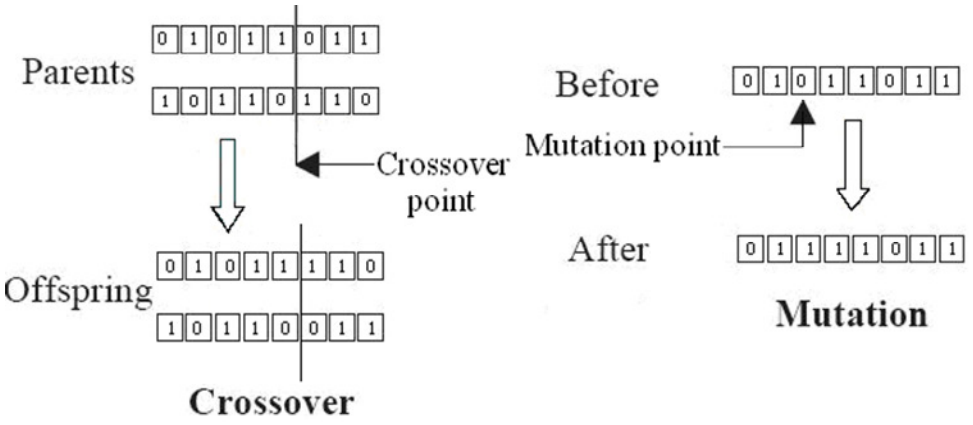

Figure 2. Genetic operation.

rendered by China Center of Industrial Culture Collection (CCICC) and cultured in MRS broth (Difco). Culture stocks were inoculated into MRS medium at 5% and incubated for 24 h at 37°C. This culture was propagated twice under the same conditions.

Fermentation experiment

The optimized fermentation medium consisted of (g l^{-1}): glucose, 2; peptone, 1; beef extract, 1; yeast extract, 1; $Na_3C_6H_5O_7 \cdot 2H_2O$, 0.1; $(NH_4)_2HPO_4$, 1; K_2SO_4, 0.2. The seed culture was inoculated at 5% into 250 ml Erlenmeyer flasks containing 150 ml MRS medium cultured at 37°C. For batch cultures in a bioreactor, 150 ml seed culture was added to a KF-5l fermentor (KBT, Korea) with 3 L production medium at 37°C anaerobically. The samples were fetched at intervals and the pH was recorded.
The microbial growth was measured by recording the optical density (OD) at 660 nm. The glucose concentration in the fermentation broth was determined by the DNS method (Zhang et al., 1997).

Data scaling

Because original data may disturb each other during the training process, which could mislead the predicting result, data re-scaling plays an important role to improve the predicting accuracy. Another advantage for data scaling is to avoid numerical difficulties during the calculation. All the data sets are scaled within the range of 0 and 1 in this formation shown as follows:

$$x_{N,i} = \frac{x_i - x_{\min}}{x_{\max} - x_{\min}}$$

Where, x_i is the feature vector which influences the *L. plantarum* growth in the batch fermentation, $x_{N,i}$ is the normalized value of the ith process variable after the process of scaling, $x_{\max}$ is the maximized value of the feature vector x_i, $x_{\min}$ is the minimized value of the feature vector x_i and N is the number of experimental observations.

RESULTS AND DISCUSSION

Variables selection

Variables selection is necessary for the *v*-SVR model with a good prediction. In this paper, we selected the most important features to describe the fermentation process, which included temperature, pH value, glucose concentration and fermentation time. We set the four vectors as the input variables and the cell concentration as output variables.

Performance criteria

In the statistical prediction, the following three cross-validation methods are often used to examine a prediction model for its effectiveness in practical application; independent dataset test, subsampling (K-fold cross-validation) test and jackknife test. However, among the three cross-validation methods, the jackknife test is deemed the most objective which can always yield a unique result for a given benchmark dataset and thus, has been increasingly used and widely recognized by investigators to examine the performance quality of various predictors (Chou, 2009; Lin et al., 2009; Wu et al., 2010; Xiao et al., 2008a; Xiao et al., 2008b; Xiao et al., 2009a; Xiao et al., 2009b; Xiao et al., 2009c; Xiao et al., 2010). In this work, we used 5-fold cross-validation to examine the performance quality of the two models and chose some statistical metrics such as normalized root mean square error (NRMSE), MAPE and R. Table 1 shows these performance metrics and their calculations. NRMSE, MAPE were used to measure the deviation between the measured and predicted values. The smaller

Table 1. Performance metrics and their calculations.

Metric	Calculation
MAPE	$\text{MAPE}=\frac{\sum_{i=1}^{n}\lvert a_i - p_i\rvert / a_i}{n}\times 100\%$
NRMSE	$\text{NRMSE}=\sqrt{\frac{\sum_{i=1}^{n}(a_i - p_i)^2}{\sum_{i=1}^{n} a_i^2}}$
R	$R=\frac{\sum_{i=1}^{n}(a_i-\bar{a})(p_i-\bar{a})}{\sqrt{\sum_{i=1}^{n}(a_i-\bar{a})^2}\sqrt{\sum_{i=1}^{n}(p_i-\bar{a})^2}}$

the values of NRMSE and MAPE were the closer the predicted values were to the measured values. The Pearson correlation coefficient R was adopted to measure the correlation of the experimental and predicted values.

Growth models obtained by v-SVR

The GA was used for searching the optimal parameter sets when the MAPE was at its minimum. The searching process of optimal parameters was operated with 150 generations in total. The genetic process was recorded. Figure 3 shows that the tendency of the optimal and average fitness of population varied during genetic process. We found that when the generation of population rose to 60, the optimal fitness value (MAPE) became steady. The information of the best parameters were acquired in the generation of 150 and the corresponding optimal ones were C = 235.8935, σ = 8.3608 and *v* = 0.7587. The mean error applied to describe the average MAPE in the total chromosome population was 0.068969.

After the GA method was applied to search for the optimal parameter of v-SVR, the predicting model for the batch fermentation with *L. plantarum* was constructed. The graphical comparison of the measured and predicted value modeling by GA-v-SVR is shown in Figure 4.

Growth models obtained by logistic model

The logistic model is an approximation of the microbial growth curve for the batch experiments in this study. Figure 5 showed the relationship between the cell concentration and cultivation time, including both experimental data and predicted values obtained based on the logistic model. Correspondingly, the logistic model parameters $\mu_{\max}$ and x_{max} were estimated as 0.4791 and 0.3498.

Performance comparison of SVR and logistic model

As shown in Table 2, the values of MAPE and NRMSE generated from GA-v-SVR model were smaller than those from logistic model, which indicated smaller deviations between the measured and predicted values. Moreover, the Pearson correlation coefficient R was higher.

To illustrate the better performance of the SVR model, we compared the measured value with the predicted one. The plots between the measured value and the predicted value are shown in Figures 6 and 7. The predicting simulation was performed with the testing data. From Figures 6 and 7, the proposed GA-v-SVR model qualified this particular data set very well (Pearson correlation coefficient was 0.9966), while two particular points lacked accuracy in the logistic model (Pearson correlation coefficient was 0.9828). Therefore, the performance of GA-v-SVR model was better than that of the logistic equation.

Conclusions

Fermentation process is very complex and it is very difficult to obtain a complete picture of what is actually going on in a particular fermentation. In order to estimate the biomass online, the models presented in this work can be use to predict fermentation process of microbes.

In this paper, a relatively easy strategy was given based on the investigation of v-SVR parameters, which determined the value of v beforehand and then, selected other two parameters(C and σ). From the results of MAPE, NRMSE and Pearson correlation coefficient, we concluded that, the approximation ability and generalization of v-SVR model were better than the logistic model for the on-line monitoring of biomass. SVR models could be considered as intracellular metabolic pathways, which are described by four variables (temperature, pH value, glucose concentration and fermentation time), while the logistic model has only one variable to describe the biomass. In conclusion, GA v-

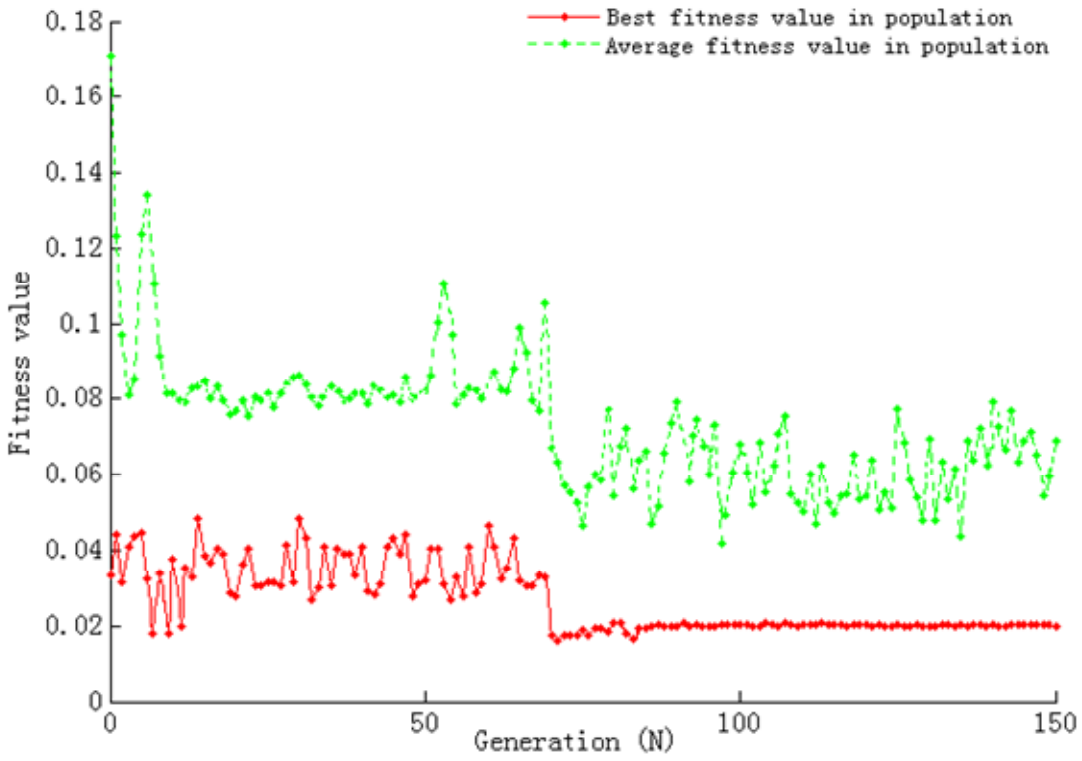

Figure 3. The fitness alternation during the evolutionary process.

Table 2. Comparison of the predicted results from GA-v-SVR and logistic models.

Model	R	MAPE	NRMSE
GA-v-SVR	0.9966	0.0185	0.0209
Logistic	0.9828	0.0375	0.0465

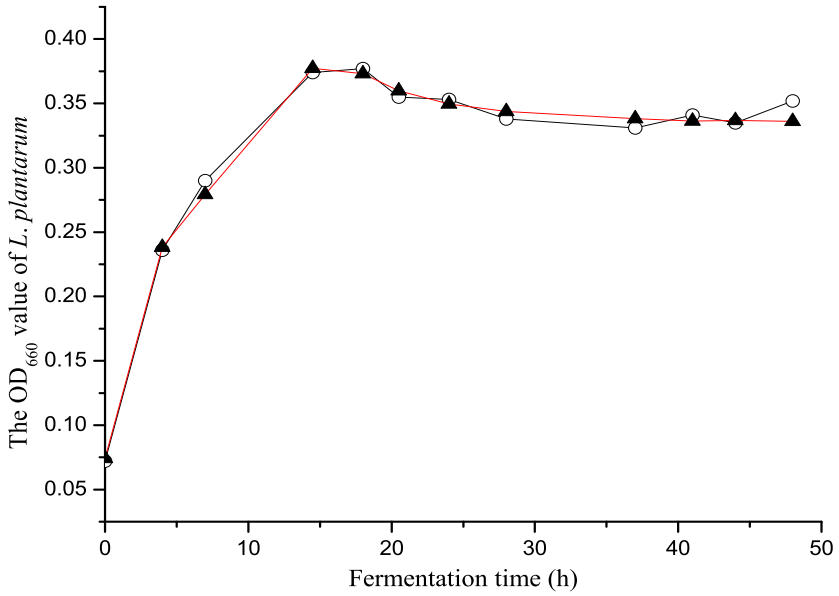

Figure 4. Measured and estimated cell concentration by v-SVR (○-measured value ▲-predicted value).

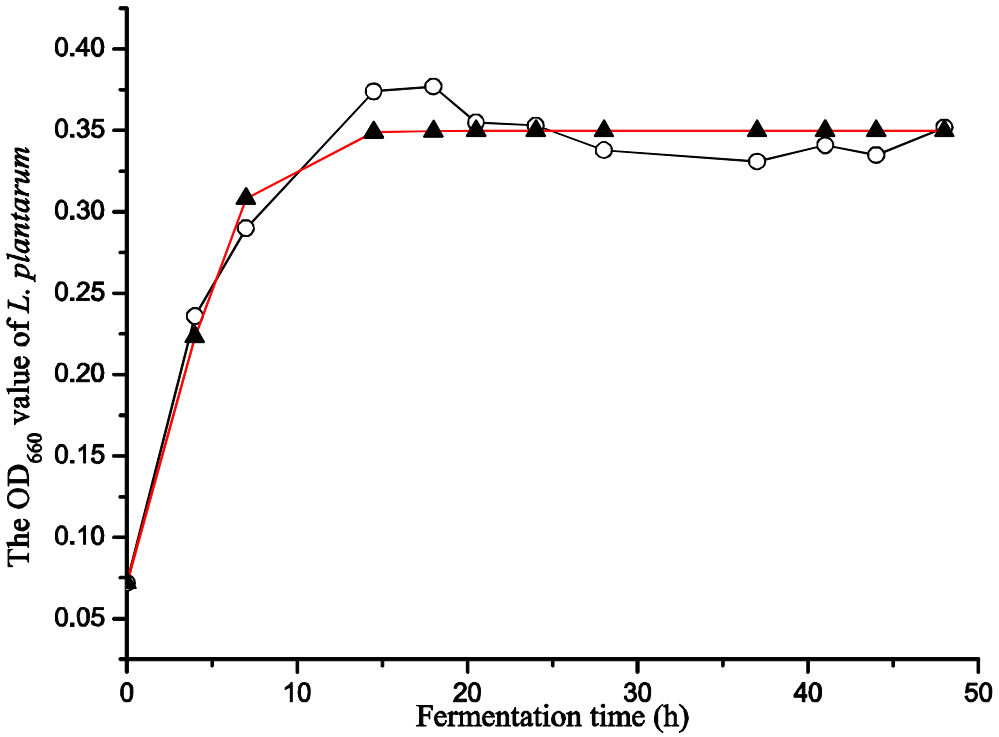

Figure 5. Measured and estimated cell concentration by logistic model (○-measured value ▲-predicted value).

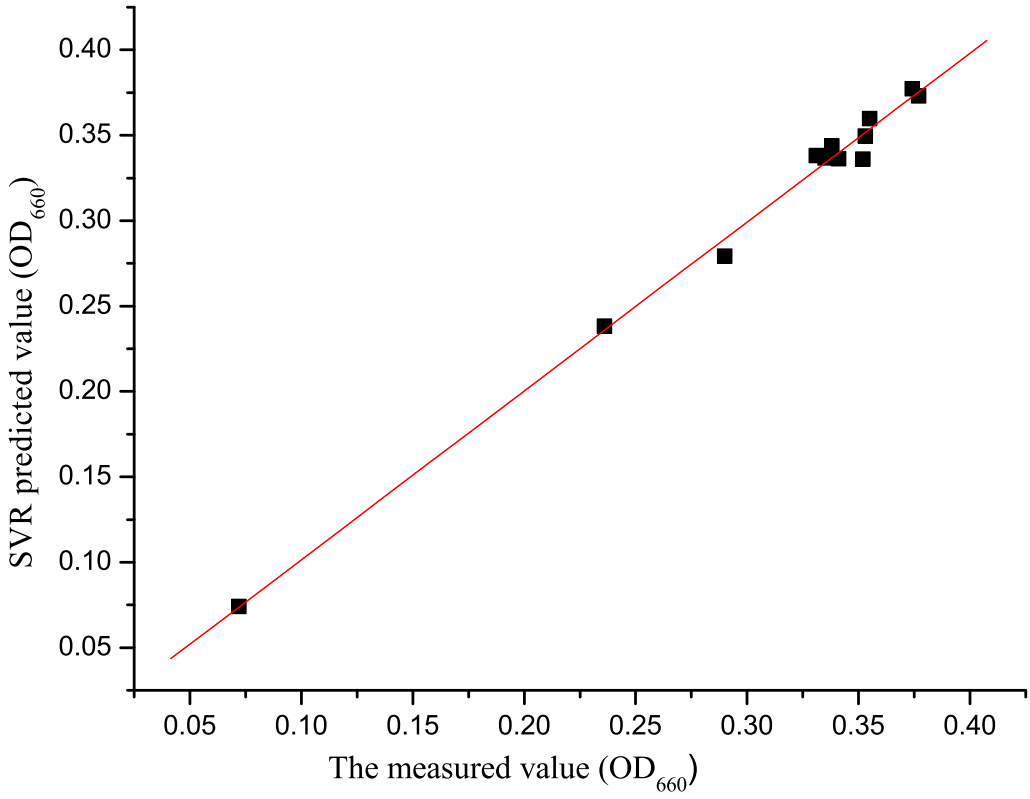

Figure 6. The plots of measured cell concentration vs. predicted value by the v-SVR model.

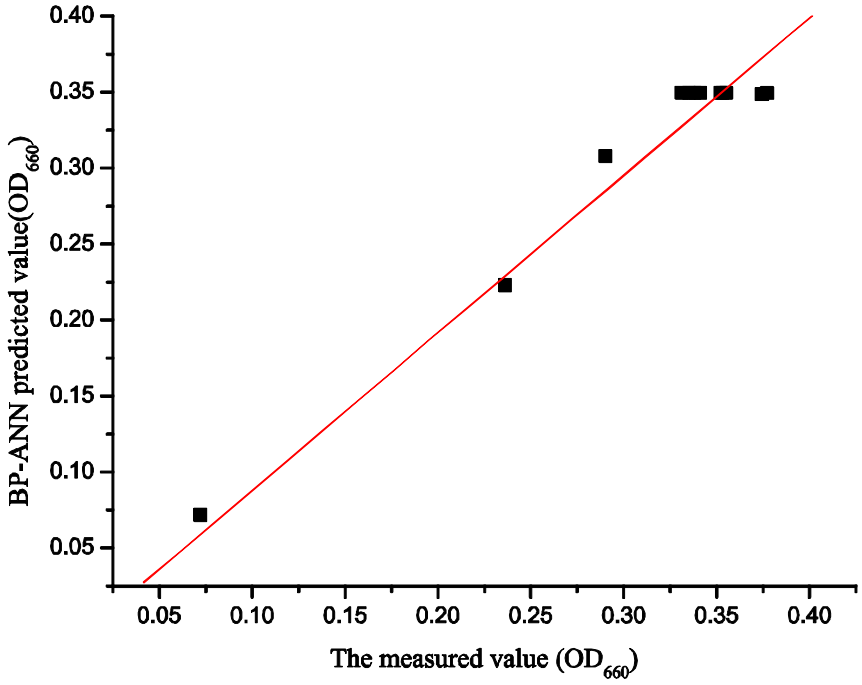

Figure 7. The plots of the measured cell concentration vs. predicted value by logistic model.

SVR has better predicting capacity on simulating bacteria biomass than logistic model and is a promising method for estimating the microbial growth.

Acknowledgements

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