Soft-sensing Modeling Based on MLS-SVM Inversion for L-lysine Fermentation Processes

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Abstract: *A modeling approach 63 based on multiple output variables least squares support vector machine (MLS-SVM) inversion is presented by a combination of inverse system and support vector machine theory. Firstly, a dynamic system model is developed based on material balance relation of a fed-batch fermentation process, with which it is analyzed whether an inverse system exists or not, and into which characteristic information of a fermentation process is introduced to set up an extended inversion model. Secondly, an initial extended inversion model is developed off-line by the use of the fitting capacity of MLS-SVM; on-line correction is made by the use of a differential evolution (DE) algorithm on the basis of deviation information. Finally, a combined pseudo-linear system is formed by means of a serial connection of a corrected extended inversion model behind the L-lysine fermentation processes; thereby crucial biochemical parameters of a fermentation process could be predicted on-line. The simulation experiment shows that this soft-sensing modeling method features very high prediction precision and can predict crucial biochemical parameters of L-lysine fermentation process very well.*

Keywords: *L-lysine fed-batch process, Mass balance relations, Differential evolution algorithm, Soft-sensing.*

Introduction

As the indispensable first limiting amino acid in the production process of such sectors as medicine, feedstuff and foodstuff, L-lysine has experienced an ever growing market demand in recent years [7, 9, 13, 18, 21]. However, L-lysine fermentation process goes with a complicated mechanism, featuring strong non-linear property, time variance, uncertainty, etc., so it is hard to make on-line or fast measurement of some crucial biochemical parameters (such as mycelia concentration, sugar concentration and chemical potency) that directly reflect quality during the fermentation process. Currently, they are mostly obtained by way of laboratory off-line analysis and assay following timing sampling, and they come with a substantial time delay in measurement, making it hard to meet the requirements on real-time control and greatly limiting the application of advanced technology in L-lysine fermentation process [1, 10, 11, 22]. Soft-sensing technology is an effective way to solve this problem. Therefore, research in the soft-sensing of L-lysine fermentation process is of great theoretical significance and application value.

As the inverse system method features a clear concept, a simple method and so on, it has been extensively applied in non-linear system soft-sensing. However, the application of the inverse system method requires the associated object's mathematical model and specific system parameters to be already known; moreover, the analytic expression of the inverse system should be accurately determined. All these greatly limit the application of the inverse system

method in the soft-sensing of complicated non-linear systems. Specific to the foregoing "bottlenecks", some scholars have introduced the idea of intelligent control into inverse system method [3], have used neural network to get inversion models of non-linear systems, and have applied that to the soft-sensing of fermentation. However, in this method, the process system model for inverse system analysis is based on a simplified model of Monod equation which ignores many non-linear components, making it inconsistent with the practice of fermentation processes and unreasonable to the original non-linear coupling system. Also, traditional neural network method is based on the asymptotic theory of sample approximates to infinite, while in such a complicated non-linear system as a biological fermentation process, it is hard to obtain accurate sample data, in addition to such problems as model structure selection, algorithm convergence, uniqueness of solution, etc.

On the basis of this, in this work, with the use of a mechanism modeling approach, a dynamic system model is developed based on the material balance relation in L-lysine fermentation processes. With respect to the multi-variable non-linear model, the inverse system method is combined with the support vector machine theory, and a modeling approach based on multiple output least squares support vector machine (MLS-SVM) inversion is presented. The theoretical analysis and the simulation result have demonstrated that the approach provides higher accuracy in predicting crucial biochemical parameters during L-lysine fermentation process.

Fermentation processes modeling

In this work, where L-lysine fed-batch fermentation process is taken as an example, the concentrations of mycelia and metabolite in various feeding liquids are assumed to be 0. According to the material balance relation (1) Eq. (1) of various substances (mycelia, substrate, metabolite, oxygen, H+ and so on) in the fermentation process, a dynamic system model [2] is developed.

$$\frac{dx}{dt} = \mu(X, S, P, C_L, pH)X - \frac{x}{V}\frac{dV}{dt} \tag{1}$$

where $x \in \{X, S, P, C_L, pH\}$ and X, S, P, C_L, pH, V are mycelia concentration, sugar concentration, chemical potency, dissolved oxygen concentration, *pH* value and the volume of the fermentation liquor, respectively; μ is the specific rate of various substances.

During the fermentation of L-lysine fed-batch, various nutrient solutions are added at a certain speed rate, which aims to supplement the necessary carbon source, nitrogen source, inorganic salt, precursor substances and biotin, as well as adjust and control the *pH* value of the fermentation liquor within an optimal range. Fermentation volume V and *pH* vary with the addition of various nutrient solutions. Their balance equations are expressed respectively as:

$$\frac{dV}{dt} = f_c + f_{nh} + f_s + f_{asp} + f_{csl} \tag{2}$$

$$\frac{dpH}{dt} = \gamma(X, S, P, C_L, pH)X - \frac{pH}{V}\frac{dV}{dt} + \frac{S_{nh} f_{nh} - S_c f_c - S_{asp} f_{asp} - S_{csl} f_{csl}}{V} \tag{3}$$

where f_c, f_{nh}, f_s, f_{asp} and f_{csl} are respectively the liquid feeding speeds of glucose, aqueous ammonia, monopotassium phosphate, aspartic acid (precursor substance) and corn steep (biotin); S_c, S_{nh}, S_{asp}, S_{csl} are respectively the liquid concentrations of glucose, aqueous ammonia, aspartic acid and corn steep; γ is the specific consumption of H+.

As a restrictive substrate medium of L-lysine fermentation, the carbon source is required in a relatively large quantity and will be consumed at a comparatively fast speed. Considering the influence of carbon source (glucose) addition on the fermentation process, the balance equation of substrates is expressed as:

$$\frac{dS}{dt} = -\nu(X,\ S,\ P,\ C_L,\ pH)X + \frac{S_c}{V} f_c - \frac{S}{V}\frac{dV}{dt} \tag{4}$$

where ν is the specific consumption rate of various substrates.

In the L-lysine synthesis stage, in order to raise the production volume of L-lysine, refrain synthesis of by-product glutamic acid, precursor substances and biotin should be added in large volume. The influence of aspartic acid and corn steep added on the fermentation process has been considered in the balance equation of chemical potency.

$$\frac{dP}{dt} = \rho(X,\ S,\ P,\ C_L,\ pH)X + \frac{K_{asp} f_{asp} + K_{csl} f_{csl}}{V} - \frac{P}{V}\frac{dV}{dt} \tag{5}$$

where: K_{asp} and K_{csl} are saturation coefficients; ρ is the specific production rate of the product.

With respect to the aerobiotic characteristic of L-lysine fermentation and in consideration of the influence of the reactor size on the dissolved oxygen level of the fermentation liquor, the volume oxygen-transferring coefficient (K_{La}) is introduced into dissolved oxygen balance equation:

$$\frac{dC_L}{dt} = -\eta(X,\ S,\ P,\ C_L,\ pH)X + K_{La}(C_L^* - C_L) - \frac{C_L}{V}\frac{dV}{dt} \tag{6}$$

where C_L^* is the dissolved oxygen concentration in saturation status; $\left[f_c \ f_{nh} \ f_s \ f_p \ f_{paa} \right]^{\mathrm{T}}$ is the specific consumption rate of oxygen.

Mycelia concentration, sugar concentration and the chemical potency $\left[X \ S \ P\right]^{\mathrm{T}}$ are selected as non-direct immeasurable directly measurable variables; dissolved oxygen concentration, *pH* value and fermentation liquor volume $\left[C_L \ pH \ V\right]^{\mathrm{T}}$ are selected as directly measureable variables; the feeding speeds of various substrates $\left[f_c \ f_{nh} \ f_s \ f_{asp} \ f_{csl} \right]^{\mathrm{T}}$ are selected as input. Its system status Eq. (7) can be expressed as:

$$\begin{cases} \dot{x}_1 = \mu(x_1, x_2, x_3, x_4, x_5)x_1 - \dfrac{x_1}{x_6}\sum_{i=1}^{5} u_i \\ \dot{x}_2 = -\nu(x_1, x_2, x_3, x_4, x_5)x_1 + \dfrac{s_1 u_1}{x_6} - \dfrac{x_2}{x_6}\sum_{i=1}^{5} u_i \\ \dot{x}_3 = \rho(x_1, x_2, x_3, x_4, x_5)x_1 + \dfrac{s_2 u_4 + s_3 u_5}{x_6} - \dfrac{x_3}{x_6}\sum_{i=1}^{5} u_i \\ \dot{x}_4 = -\eta(x_1, x_2, x_3, x_4, x_5)x_1 - s_4 x_4 + s_5 - \dfrac{x_4}{x_6}\sum_{i=1}^{5} u_i \\ \dot{x}_5 = \gamma(x_1, x_2, x_3, x_4, x_5)x_1 + \dfrac{s_6 u_2 - s_1 u_1 - s_7 u_4 - s_8 u_5}{x_6} - \dfrac{x_5}{x_6}\sum_{i=1}^{5} u_i \\ \dot{x}_6 = \sum_{i=1}^{5} u_i = u_1 + u_2 + u_3 + u_4 + u_5 \end{cases} \quad (7)$$

where $\boldsymbol{x} = [x_1, x_2, x_3, x_4, x_5, x_6]^{\mathrm{T}} = [X, S, P, C_{\mathrm{L}}, pH, V]^{\mathrm{T}}$ is the status vector; $\boldsymbol{u} = [u_1, u_2, u_3, u_4, u_5]^{\mathrm{T}} = [f_c, f_{nh}, f_s, f_{asp}, f_{csl}]^{\mathrm{T}}$ is the input vector; $\mu, \nu, \rho, \eta, \gamma$ are the analytical functions of the respective status variables; $s_i (i = 1, 2, \cdots, 8)$ are all constants other than zero.

Reversibility analysis

Specific to the dynamic system model of L-lysine fermentation process, soft-sensing modeling for multi-variable nonlinear system is made based on inverse system theory.

Suppose there is a "multi-dimension sensor" existing in L-lysine fermentation process: Take the non-direct measurable variable $\hat{\boldsymbol{x}} = (x_1, x_2, x_3)^{\mathrm{T}}$ as its input, and the directly measurable variable $\boldsymbol{z} = (x_4, x_5, x_6)^{\mathrm{T}}$ as its output, and $\boldsymbol{u} = (u_1, u_2, u_3, u_4, u_5)^{\mathrm{T}}$ as parameters (dynamic coupling existing between variables). If it can be proven that the "multi-dimension sensor" is reversible, and its inverse model can be built, then, by serial connection of it as a dynamic compensator and a "multi-dimension sensor", a unit compound system is constructed. As the input and the output of the unit compound system present a decoupling identical mapping relation, it is possible to realize dynamic compensation to the "multi-dimension sensor", and go further to realize true reappearance of x_1, x_2, x_3 (i.e. soft-sensing)

Below, reversibility analysis will be made on the "multi-dimension sensor" in the L-lysine fermentation process, and its inverse system model will be developed.

Lemma 1. The necessary and sufficient condition for reversibility of System Σ within certain realm of Point (x_0, u_0): The system meets $rank\left(\partial \boldsymbol{Z}_m^{\mathrm{T}} / \partial \hat{\boldsymbol{x}}^{\mathrm{T}}\right) = r_m = l$, l is the dimension number of non-direct measurable variable.

Use Interactor algorithm to analyze the reversibility of the "multi-dimension sensor" [2], with the analysis process as follows:

Calculate all-order derivatives of the directly measurable variable $z_i(i=1, 2, 3)$ to the time $\dot{z}_i, \ddot{z}_i, \cdots, z_i^{(k_i)}$, and select function's derivative information to constitute the vector $\boldsymbol{Z}_m$. From Eq. (7):

$$\begin{cases} \dot{x}_4 = -\eta(x_1, x_2, x_3, x_4, x_5)x_1 - s_4 x_4 + s_5 - \dfrac{x_4}{x_6}\sum_{i=1}^{5} u_i \\ \ddot{x}_4 = g_1(\boldsymbol{x}, \boldsymbol{u}) + g_2(x_4, x_6, \boldsymbol{u}, \dot{\boldsymbol{u}}) \\ \dot{x}_5 = \gamma(x_1, x_2, x_3, x_4, x_5)x_1 + \dfrac{s_6 u_2 - s_1 u_1 - s_7 u_4 - s_8 u_5}{x_6} - \dfrac{x_5}{x_6}\sum_{i=1}^{5} u_i \end{cases} \tag{8}$$

where $g_1(\boldsymbol{x}, \boldsymbol{u}) = \left(\dfrac{\partial \eta}{\partial x_1}x_1 + \dfrac{\partial \eta}{\partial x_2}x_2 + \dfrac{\partial \eta}{\partial x_3}x_3 + \dfrac{\partial \eta}{\partial x_4}x_4 + \dfrac{\partial \eta}{\partial x_5}x_5\right)\dfrac{x_1}{x_6}\sum_{i=1}^{5} u_i - \mu\eta x_1 + \dfrac{2\eta x_1}{x_6}\sum_{i=1}^{5} u_i +$

$+\eta x_1 s_4 - (\dfrac{\partial \eta}{\partial x_1}\mu - \dfrac{\partial \eta}{\partial x_2}\nu + \dfrac{\partial \eta}{\partial x_3}\rho - \dfrac{\partial \eta}{\partial x_4}\eta + \dfrac{\partial \eta}{\partial x_5}\gamma)x_1^2 +$

$+\dfrac{\partial \eta}{\partial x_5}\dfrac{x_1}{x_6}(s_1 u_1 + s_7 u_4 + s_8 u_5 - s_6 u_2) + \dfrac{\partial \eta}{\partial x_4}x_1(s_4 x_4 - s_5) - \dfrac{\partial \eta}{\partial x_2}\dfrac{x_1 u_1 s_1}{x_6} - \dfrac{\partial \eta}{\partial x_3}\dfrac{x_1(s_2 u_4 + s_3 u_5)}{x_6}$;

$g_2(x_4, x_6, \boldsymbol{u}, \dot{\boldsymbol{u}}) = \dfrac{2s_4 x_4}{x_6}\sum_{i=1}^{5} u_i + \dfrac{2x_4}{x_6^2}(\sum_{i=1}^{5} u_i)^2 + s_4^2 x_4 - \dfrac{s_5}{x_6}\sum_{i=1}^{5} u_i - \dfrac{x_4}{x_6}\sum_{i=1}^{5} \dot{u}_i - s_4 s_5$.

From Eq. (8), it is obvious that $\partial \ddot{z}_1 / \partial x_i = \partial g_1(\boldsymbol{x}, \boldsymbol{u}) / \partial x_i$ $(i=1, 2, 3)$, $m=3$. Let Jacobian matrix $\boldsymbol{J} = \partial \boldsymbol{Z}_3^{\mathrm{T}} / \partial \hat{\boldsymbol{x}}^{\mathrm{T}} = \partial(\ddot{z}_1, \dot{z}_1, \dot{z}_2)/\partial(x_1, x_2, x_3)$, then

$$\boldsymbol{J} == \begin{bmatrix} \dfrac{\partial g_1(\boldsymbol{x}, \boldsymbol{u})}{\partial x_1} & \dfrac{\partial g_1(\boldsymbol{x}, \boldsymbol{u})}{\partial x_2} & \dfrac{\partial g_1(\boldsymbol{x}, \boldsymbol{u})}{\partial x_3} \\ -\dfrac{\partial \eta}{\partial x_1}x_1 - \eta & -\dfrac{\partial \eta}{\partial x_2}x_1 & -\dfrac{\partial \eta}{\partial x_3}x_1 \\ \dfrac{\partial \gamma}{\partial x_1}x_1 + \gamma & \dfrac{\partial \gamma}{\partial x_2}x_1 & \dfrac{\partial \gamma}{\partial x_3}x_1 \end{bmatrix} \tag{9}$$

Make elementary row transformation for $\boldsymbol{J}$ and obtain the following:

$$\tilde{\boldsymbol{J}} = \begin{bmatrix} g_5(\boldsymbol{x}, \boldsymbol{u}) - \dfrac{g_6(\boldsymbol{x}, \boldsymbol{u})}{g_4(\boldsymbol{x}, \boldsymbol{u})}g_3(\boldsymbol{x}, \boldsymbol{u}) & & \\ & 0 & 0 \\ g_3(\boldsymbol{x}, \boldsymbol{u}) & g_4(\boldsymbol{x}, \boldsymbol{u}) & 0 \\ \dfrac{\partial \gamma}{\partial x_1}x_1 + \gamma & \dfrac{\partial \gamma}{\partial x_2}x_1 & \dfrac{\partial \gamma}{\partial x_3}x_1 \end{bmatrix} \tag{10}$$

where $g_3(\boldsymbol{x},\boldsymbol{u})=\left[(\frac{\partial\gamma}{\partial x_1}x_1+\gamma)\frac{\partial\eta}{\partial x_3}\right]\Big/\frac{\partial\gamma}{\partial x_3}-\frac{\partial\eta}{\partial x_1}x_1-\eta$; $g_4(\boldsymbol{x},\boldsymbol{u})=\left(x_1\frac{\partial\gamma}{\partial x_2}\frac{\partial\eta}{\partial x_3}\right)\Big/\frac{\partial\gamma}{\partial x_3}-\frac{\partial\eta}{\partial x_2}x_1$;

$g_5(\boldsymbol{x},\boldsymbol{u})=\frac{\partial g_1(\boldsymbol{x},\boldsymbol{u})}{\partial x_1}-\left[(\frac{\partial\gamma}{\partial x_1}+\frac{\gamma}{x_1})\frac{\partial g_1(\boldsymbol{x},\boldsymbol{u})}{\partial x_3}\right]\Big/\frac{\partial\gamma}{\partial x_3}$; $g_6(\boldsymbol{x},\boldsymbol{u})=\frac{\partial g_1(\boldsymbol{x},\boldsymbol{u})}{\partial x_2}-\left(\frac{\partial\gamma}{\partial x_2}\frac{\partial g_1(\boldsymbol{x},\boldsymbol{u})}{\partial x_3}\right)\Big/\frac{\partial\gamma}{\partial x_3}$.

If $\det\left(\tilde{J}\right)=\left(g_5(\boldsymbol{x},\boldsymbol{u})-\frac{g_6(\boldsymbol{x},\boldsymbol{u})}{g_4(\boldsymbol{x},\boldsymbol{u})}g_3(\boldsymbol{x},\boldsymbol{u})\right)g_4(\boldsymbol{x},\boldsymbol{u})\frac{\partial\gamma}{\partial x_3}x_1$ is constantly not zero in the whole real vector space, it can be known from **Lemma 1** that $\boldsymbol{J}=\partial\boldsymbol{Z}_m^{\mathrm{T}}/\partial\hat{\boldsymbol{x}}^{\mathrm{T}}=\partial(\ddot{z}_1,\dot{z}_1,z_2)/\partial(x_1,x_2,x_3)=3$, meeting the system reversibility condition, i.e. the system is globally reversible. However, as far as $\det\left(\tilde{J}\right)$ is concerned, it is hard to ensure that the condition of not being zero is met everywhere in the whole real vector space *R*.

Based on the foregoing, and in consideration of the current operation of L-lysine fermentation process (always operating in a certain specific working area and such an area is only a very small part of the real vector space *R*), let us first assume that $\det\left(\tilde{J}\right)$ in the working area of L-lysine fermentation process is constantly not zero, meeting the reverse condition for the "multi-dimensional sensor". Afterwards, use the method herein to build the inverse soft-sensing model, and then use the actual test result to judge whether such an assumption is reasonable.

If we assume that the system meets the inversion conditions in the working area of L-lysine fermentation process, then, according to the inverse function existence theorem and the Eqs. (7) and (8), the structure of the inverse model of "multi-dimensional sensor" for L-lysine fermentation process is:

$$\hat{\boldsymbol{x}}=\begin{pmatrix}x_1\\x_2\\x_3\end{pmatrix}=\begin{pmatrix}\varphi_1\left(x_4,x_5,x_6,\dot{x}_4,\ddot{x}_4,\dot{x}_5,\boldsymbol{u},\dot{\boldsymbol{u}}\right)\\\varphi_2\left(x_4,x_5,x_6,\dot{x}_4,\ddot{x}_4,\dot{x}_5,\boldsymbol{u},\dot{\boldsymbol{u}}\right)\\\varphi_3\left(x_4,x_5,x_6,\dot{x}_4,\ddot{x}_4,\dot{x}_5,\boldsymbol{u},\dot{\boldsymbol{u}}\right)\end{pmatrix} \tag{11}$$

L-lysine fermentation process is a complicated non-linear system featuring strong coupling and great time variance, while expression (7) is a so-called "grey box" model built based on balance relationship of various materials during the fermentation process, presenting the following assumption: 1) During fermentation, temperature and pressure in the fermentation tank remain constant; 2) Fermentation liquor and various materials concentration as well as other factors are not influenced by fermentation heat. Thereby, the inverse model Eq. (12), obtained from the assumption conditions does not reflect fermentation temperature, air flow volume, waste oxygen content, waste CO_2 content and so on, which are parameters exerting remarkable influence over L-lysine fermentation process. As a result, the prediction result of the soft-sensing comes with a deviation and the prediction precision can hardly meet the requirements for an actual fermentation process. Therefore, based on the inverse model's basic structure express (12), 4 parameters, namely, fermentation temperature (W_t), air flow volume (F_a), waste oxygen content (O_c) and waste CO_2 (R_c) are introduced into it for building the soft-sensing model. The structure expression of the extended inverse model goes as follows:

$$\hat{\boldsymbol{x}} = \begin{pmatrix} x_1 \\ x_2 \\ x_3 \end{pmatrix} = \begin{pmatrix} \varphi_4\left(x_4, x_5, x_6, \dot{x}_4, \ddot{x}_4, \dot{x}_5, \boldsymbol{u}, \dot{\boldsymbol{u}}, W_t, F_a, O_c, R_c\right) \\ \varphi_5\left(x_4, x_5, x_6, \dot{x}_4, \ddot{x}_4, \dot{x}_5, \boldsymbol{u}, \dot{\boldsymbol{u}}, W_t, F_a, O_c, R_c\right) \\ \varphi_6\left(x_4, x_5, x_6, \dot{x}_4, \ddot{x}_4, \dot{x}_5, \boldsymbol{u}, \dot{\boldsymbol{u}}, W_t, F_a, O_c, R_c\right) \end{pmatrix} \quad (12)$$

As crucial parameters of L-lysine fermentation process are introduced into Eq. (13) for building an inverse system, hence more characteristic information of the fermentation process being obtained, the inverse system features stronger adaptation to parameter variation during fermentation and stronger restraining ability against interference, thus improving adaptability of the inverse system.

However, it is hard to get the analytical expression of the extended inverse model Eq. (12). But in recent years, support vector machine algorithm has become a popular research subject, breaking the thinking limitation of the empirical risk minimization inductive principle, providing a brand-new perspective for machine learning based on empirical risk minimization inductive principle, and, additionally, solving such problems as learning and local minimum arising out of neural network algorithm, featuring good generalization ability and system identification ability, thus suitable for solving non-linear identification problem of a complicated non-linear system [4, 6, 8, 12, 14, 19, 20]. Based on this, this work uses support vector machine's strong approximation ability towards non-linear function to identify the three non-linear functions $\varphi_4, \varphi_5, \varphi_6$ in Eq. (12).

Inverse model identification and soft-sensing modeling

MLS-SVM algorithm

Traditional LS-SVM is built upon multi-input/single-output, so it is hard to realize identification of a multi-input/multi-output system. To meet the requirement for identification of L-lysine fermentation (multi-input/multi-output) inverse model, this work improves the algorithm.

Traditional LS-SVM defines the following optimization problems, given L pairs of a sample set $\{(\boldsymbol{x}_i, y_i)\}_{i=1}^{l}$:

$$\begin{aligned} &\min J(\boldsymbol{w}, b, \boldsymbol{\xi}) = \frac{1}{2}\boldsymbol{w}^{\mathrm{T}}\boldsymbol{w} + \gamma\frac{1}{2}\sum_{i=1}^{l}\xi_i^2 \\ &s.t.\ \ y_i = \boldsymbol{w}^{\mathrm{T}}\varphi(\boldsymbol{x}_i) + b + \xi_i,\ \ i = 1, 2, \cdots, l \end{aligned} \quad (13)$$

where a is Lagrange multiplier, ξ is relaxing factor, and γ is penalty parameter.

In this work, the relaxing factor in optimization problem (13) is replaced by a quadratic loss function of error, and based on the original LS-SVM problem, the original problem of MLS-SVM is presented:

$$\begin{aligned} &\min J(\boldsymbol{w}, b, \boldsymbol{\xi}) = \frac{1}{2}\sum_{i=1}^{n}\boldsymbol{w}_i^{\mathrm{T}}\boldsymbol{w}_i + \frac{1}{2}\gamma_i\sum_{i=1}^{n}\boldsymbol{\xi}_i\boldsymbol{\xi}_i^{\mathrm{T}} \\ &s.t.\ \ y_i = \boldsymbol{w}_i^{\mathrm{T}}\varphi_i(\boldsymbol{x}) + \boldsymbol{\gamma}^{\mathrm{T}}b_i + \boldsymbol{\xi}_i,\ \ i = 1, 2, \cdots, l \end{aligned} \quad (14)$$

where $\xi \in \boldsymbol{R}^{l\times n}$, n is the number of output variables, $\varphi_i(\boldsymbol{x}) = [\varphi_i(\boldsymbol{x}_1), \cdots, \varphi_i(\boldsymbol{x}_l)]$.

With the introduction of Lagrange multiplier $\boldsymbol{a}, \boldsymbol{a} \in \boldsymbol{R}^{m\times l}$, m being input vector number, and problem (14) becomes:

$$\max L = \frac{1}{2}\sum_{i=1}^{l} \boldsymbol{w}_i^{\mathrm{T}} \boldsymbol{w}_i + \frac{1}{2}\sum_{i=1}^{l} \xi_i \xi_i^{\mathrm{T}} - \sum_{i=1}^{l} \boldsymbol{a}_i^{\mathrm{T}} (\boldsymbol{w}_I^{\mathrm{T}} \varphi_i(\boldsymbol{x}) + \boldsymbol{\gamma}^{\mathrm{T}} b_i + \boldsymbol{\xi}_i - \boldsymbol{y}_i) \tag{15}$$

According to KKT optimization conditions,

$$\begin{cases} \dfrac{\partial L}{\partial \boldsymbol{w}_i} = 0 \Rightarrow \boldsymbol{w}_i = \varphi(\boldsymbol{x}_i)\boldsymbol{a}_i^{\mathrm{T}} \\ \dfrac{\partial L}{\partial b_i} = 0 \Rightarrow \boldsymbol{\gamma}^{\mathrm{T}} \boldsymbol{a}_i^{\mathrm{T}} = 0 \\ \dfrac{\partial L}{\partial \boldsymbol{\xi}_i} = 0 \Rightarrow \boldsymbol{a}_i = \boldsymbol{\xi}_i, i = 1, 2, \cdots, l \\ \dfrac{\partial L}{\partial \boldsymbol{a}_i} = 0 \Rightarrow \boldsymbol{w}_i^{\mathrm{T}} \varphi_i(\boldsymbol{x}) + \boldsymbol{\gamma}^{\mathrm{T}} b + \boldsymbol{\xi}_i - \boldsymbol{y}_i = 0, i = 1, 2, \cdots, l \end{cases} \tag{16}$$

Considering Eq. (16), ξ_i and $\boldsymbol{w}$ are removed, and the optimization problem is transformed into solving the following equation set:

$$\begin{bmatrix} b_i & \boldsymbol{a}_i \end{bmatrix} \begin{bmatrix} 0 & \boldsymbol{\gamma}^{\mathrm{T}} \\ \boldsymbol{\gamma} & K_i(\boldsymbol{x}_i, \boldsymbol{x}) + I \end{bmatrix} = \begin{bmatrix} 0 & \boldsymbol{y}_i \end{bmatrix} \tag{17}$$

where $K(\boldsymbol{x}_n, \boldsymbol{x})$ meets the kennel function of Mercer conditions; in this work, RBF kennel function $K(\boldsymbol{x}_i, \boldsymbol{x}_j) = \exp[-\left|\boldsymbol{x}_i - \boldsymbol{x}_j\right|^2 / (2\sigma^2)]$ is used, with σ being kennel width.

The matrix $\begin{bmatrix} 0 & \boldsymbol{\gamma}^{\mathrm{T}} \\ \boldsymbol{\gamma} & K_i(\boldsymbol{x}_i, \boldsymbol{x}) + I \end{bmatrix}$ is non-singular, so

$$\begin{bmatrix} b_i & \boldsymbol{a}_i \end{bmatrix} = \begin{bmatrix} 0 & \boldsymbol{y}_i \end{bmatrix} \begin{bmatrix} 0 & \boldsymbol{\gamma}^{\mathrm{T}} \\ \boldsymbol{\gamma} & K_i(\boldsymbol{x}_i, \boldsymbol{x}) + I \end{bmatrix}^{-1} \tag{18}$$

So, the *i*-th output of MLS-SVM is:

$$f_i(\boldsymbol{x}) = \boldsymbol{a}_i K(\boldsymbol{x}_i, \boldsymbol{x}_j) + b_i \tag{19}$$

Regarding MLS-SVM system identification, the selection of kennel function parameter $\boldsymbol{\sigma}$ and penalty parameter $\boldsymbol{\gamma}$ exerts great influence over the building of the inverse model. Traditional parameter selection methods are mostly based on experience and trial-error methods, making it hard to ensure precision and computing speed. In order to obtain a soft-sensing model with

a relatively high prediction effect, this work applies a differential evolution algorithm to make on-line optimization and adjustment of MLS-SVM.

Differential evolution algorithm

Differential evolution (DE) algorithm is a simple but very effective real parameter random optimization algorithm [5, 15-17]. DE uses computing steps similar to the standard evolution algorithm, including three operations: variation, crossover and selection. However, unlike the traditional evolution algorithm, DE uses proportional difference vectors generated by varied individuals randomly selected to interfere with the population individuals of the current generation, hence no need for using singular probability distribution to generate the offspring. In DE algorithm, *D*-dimension real parameter vectors $X_i^t = \{x_{i1}^t, \cdots, x_{iD}^t\} \in S(i = 1, \cdots, NP)$ in the number of *NP* constitute a generation of population $P^t = \{X_i^t, \cdots, X_{NP}^t\}$ and make parallel direct search in the search space; here $t = 0, 1, \cdots, T_{\max}$ represents the evolved generation.

In variation operation, variation vector $V_i^t = (v_{i1}^t, \cdots, v_{iD}^t)$ is generated by way of carrying out variation operation on every target individual X_i^t, i.e. on the basis of Eq. (20).

$$V_i^t = X_{r1}^t + F \cdot (X_{r2}^t - X_{r3}^t) \tag{20}$$

where r_1, r_2, r_3 are integers randomly selected from the set $\{i = 1, 2, \cdots, NP\}$ and different from each other; F is the scale factor with a value range being [0.4, 1], used for controlling scaling of the differential vector.

To enhance the potential diversity of population, the target vector X_i^t and its variation vector V_i^t make a cross-operation, i.e. generating a test vector $U_i^t = (u_{t1}^t, \cdots, u_{tD}^t)$ according to Eq. (21).

$$u_{ij}^t = \begin{cases} v_{ij}^t, & \text{rand}_{ij} \le \text{CR or } j = j_{\text{rand}} \\ x_{ij}^t, & \text{otherwise} \end{cases} \tag{21}$$

where rand_{ij} is the randomly selected dimension number index, which ensures that at least one element of the test vector U_i^t is contributed by the variation vector; V_i^t is a probability constant.

Greedy strategy is used for selection operation. Use Eq. (22) to compare the objective function value (fitness) of the test vector with the objective function of the target individual; if the former is smaller or equal to the latter, the test vector will take the place of the corresponding target individual and enter the next generation, otherwise the target vector is kept unchanged.

$$X_i^{t+1} = \begin{cases} U_t^i, & f(U_i^t) \le f(X_i^t) \\ X_i^t, & \text{otherwise} \end{cases} \tag{22}$$

where *f* is objective function; the objective function selected in this work for DE operation is the square of the deviation between MLS-SVM output value and off-line analysis value.

DE algorithm features simple theory, a small number of controlled parameters and fast convergence speed, hence an effective global optimal search algorithm. It is comparatively suitable for solving complicated optimization problems, so the use of DE's global search capability to make on-line optimization and adjustment on performance parameters $\boldsymbol{\sigma}$ and $\{x_1, x_2, x_3\}$ of MLS-SVM will definitely result in a relatively accurate inverse system model.

Inverse model identification based on MLS-SVM

Use MLS-SVM to identify the extended inversion model (12) of L-lysine fermentation process, with specific steps of the identification process as follows:

1) Data acquisition. In the working area of L-lysine fermentation process, an adequate excitation signal is applied to the system; on the precondition of meeting the sampling theorem, make timing sampling on excitation input signal, directly measurable $\{x_4, x_5, x_6\}$ and relevant parameter $\{W_t, F_a, O_c, R_c\}$, thus obtaining the original data sample $\{u_1, u_2, u_3, u_4, u_5, x_4, x_5, x_6, W_t, F_a, O_c, R_c\}$. Non-direct measurable variable $\{x_1, x_2, x_3\}$ can be obtained by way of laboratory off-line assay.

2) Data Processing. To calculate all-order derivatives in need, according to the inverse model structure determined with Eq. (12), use the method of higher order numerical differentiation (five points derivation method is used herein) on $\{x_4, x_5, \boldsymbol{u}\}$ obtained from sampling, to get its all-order derivatives $\{\dot{x}_4, \ddot{x}_4, \dot{x}_5, \dot{\boldsymbol{u}}\}$. Also, use polynomial interpolation method to process off-line data $\{x_1, x_2, x_3\}$ into data of the corresponding sampling period. As a result, a data sample set $\{x_1, x_2, x_3\}$ and $\{x_4, x_5, x_6, \dot{x}_4, \ddot{x}_4, \dot{x}_5, \boldsymbol{u}, \dot{\boldsymbol{u}}, W_t, F_a, O_c, R_c\}$ will be obtained, with the former serving as the output of the extended inversion model (i.e. a crucial biochemical parameter) and the latter is the input for the extended inversion model.

3) Off-line fitting and on-line correction. Based on the input/output data set, have MLS-SVM undergo off-line training and learning, and use crossover verification method to determine the corresponding initial parameters ($\boldsymbol{\sigma}$ and $\boldsymbol{\gamma}$), thus building the initial extended inverse model. According to the analysis value of an actual fed-batch fermentation process and the deviation information output by the extended inversion model, go further to use DE algorithm to optimize MLS-SVM performance parameters and make on-line correction on the initial extended inversion model. Fig. 2 shows the on-line correction figure of the extended inversion model of L-lysine fermentation process.

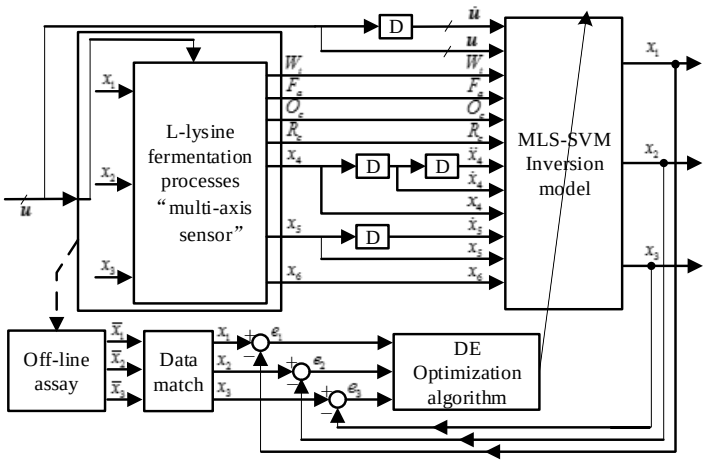


Fig. 2 On-line correction figure of the extended MLS-SVM inversion model

Soft-sensing modeling method based on MLS-SVM inversion

To ensure high-quality input data obtained from soft-sensing, it is necessary to process error of the input data ($x_4(pH)$, $x_5(CL)$, $\boldsymbol{u}$ in particular, if the noise pollution is not effectively filtered out, it will cause frequent data variation of $\dot{x}_4, \ddot{x}_4, \dot{x}_5, \dot{\boldsymbol{u}}$ and a substantial variation amplitude). To effectively filter out random errors, this work proposes an improved method to process error. Take *pH* as example. Firstly, make data pretreatment of the input values to refrain strong noise as the initial step; afterwards, make secondary treatment on the processed data (moving average filtering method) to further refrain noise error. The specific steps are as follows:

1) Judge whether $x_n(k)$ is pathological data. Method: If *k* is 1, directly go to Step 2); otherwise, make calculation of $\left|x_n(k)-\hat{x}_n(k-1)\right|$; if the value is bigger than the threshold value ($\max\left|\bar{x}_n(k)-\bar{x}_n(k-1)\right|+\max\left|\bar{s}_n(k)-\bar{s}_n(k-1)\right|, (k=2,3,\cdots)$), go to Step 2); otherwise, the measured value is reliable, so make $\hat{x}_n(k)=x_n(k)$ and go to Step 3).

2) According to Eq. (23), confirm whether it is pathological data and make a correction.

$$\hat{x}_n(k)=\begin{cases}\bar{x}_{n-1}(k)-s_{n-1}(k), & x_n(k)-\hat{x}_n(k-1)<-s_{n-1}(k)\\ \bar{x}_{n-1}(k)+s_{n-1}(k), & x_n(k)-\hat{x}_n(k-1)>s_{n-1}(k)\\ x_n(k), & \text{otherwise}\end{cases} \tag{23}$$

3) According to Eqs. (24) and (25), update $\bar{x}_n(k)$ and $s_n(k)$ at moment *k*.

$$\bar{x}_n(k)=\frac{(n-1)\bar{x}_{n-1}+\hat{x}_n(k)}{n} \tag{24}$$

$$s_n(k)=\sqrt{\frac{n-1}{n}s_{n-1}^2(k)+\frac{1}{n-1}(\bar{x}_n(k)-\hat{x}_n(k))^2} \tag{25}$$

where $\bar{x}_{n-1}(k), \bar{x}_n(k)$ – average *pH* values of batch $n-1$ and batch n at moment *k*; $\hat{x}_{n-1}(k)$ and $\hat{x}_n(k)$ – corrected *pH* values of batch $n-1$ and batch *n* at sampling moment *k*; $s_{n-1}(k)$ and $s_n(k)$ – *pH* standard deviation of batch $n-1$ and batch *n* at sampling moment *k*.

4) Make moving average filtering processing according to Eq. (26).

$$\tilde{x}_n(k) = \frac{1}{15}\hat{x}_n(k-4) + \frac{2}{15}\hat{x}_n(k-3) + \frac{1}{5}\hat{x}_n(k-2) + \frac{4}{15}\hat{x}_n(k-1) + \frac{1}{3}\hat{x}_n(k) \tag{26}$$

where $\tilde{x}_n(k)$, $(k = 5, 6, 7, \cdots)$ is the result of moving average filtering.

Fig. 2 is the figure of error processing results of *pH* value of Batch 9.

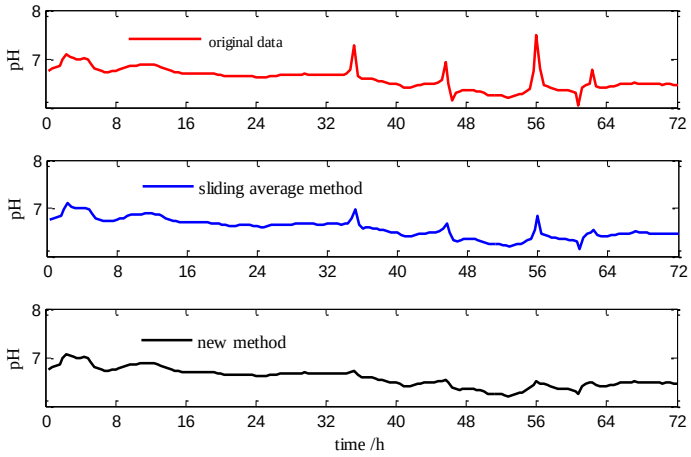


Fig. 2 Comparison of error processing results of the *pH* value of Batch 9

According to Fig. 2, after error processing by use of the improved method, pathological data of *pH* are eliminated and data become smoother, thus reducing the negative impact on the model exerted by the first derivation of *pH* with a relatively big variation amplitude and enhancing the soft-sensing precision.

After connecting the improved error processing module and the extended MLS-SVM inversion model of L-lysine fermentation process, a unit compound system is formed; make the compound system's input/output to present an identical mapping relationship and realize on-line prediction of crucial biochemical parameters. Fig. 3 shows a combined pseudo linear system chart.

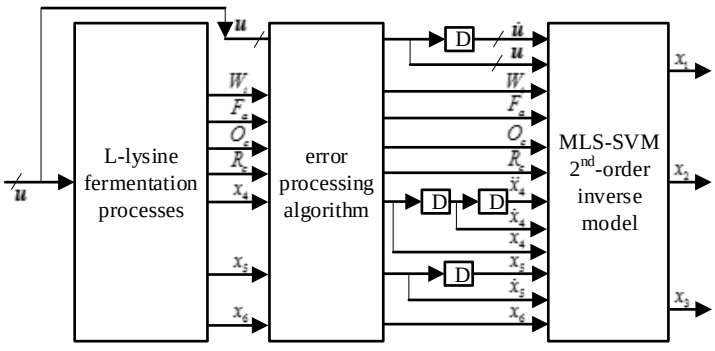


Fig. 3 Combined pseudo linear system chart

Simulation test and analysis

Take the fermentation process of L-lysine fed-batch as the object for experimental verification. To bring the experiment close to an actual production process, the experiment process is designed as follows:

1) The fermentation period for each batch is 72 h, the sampling period is 15 min, the tank pressure is controlled between 0-0.25 Mp, and the temperature in the early and the middle stage of fermentation is controlled at about 32 °C, while that in the late stage of fermentation is about 30 °C; mark the reference reading of the dissolved oxygen electrode when the mixing motor speed is 400 r/min before the fermentation. Non-direct measurable variable $\{x_1, x_2, x_3\}$ is obtained every two hours by sampling and off-line assay. Among that, X is obtained by calculation based on the dry cell weight method, i.e. taking 10 ml fermentation liquor in a centrifugal tube, running centrifugal operation for 5 min at 3000 r/min, abandoning the supernatant, washing with distilled water twice, and after drying it at 105 °C till it becomes dry and its weight is constant, weighing it. Use SBA-40C multi-functional biosensor for measurement of S. P uses improved ninhydrin colorimetry for measurement, i.e. use 2 ml supernatant and add 4 ml ninhydrin reagent for mixing; use a boiling water bath for heating for 20 min; after cooling, measure the optical density at the 475 mm position by use of an ultraviolet spectrophotometer; and get the value by reference to a standard L-lysine curve.

2) During the experiment, only 10 batches of medium are considered to check the identification ability of MLS-SVM inversion over small samples. The initial conditions of various batches are set to be different, with the flow strategies of various nutrient solutions varying correspondingly to enlarge batch differences. Among them, the fermentation data of the first 6 batches are selected as a training sampling set, which are off-line trained to obtain the initial extended inversion model of the fermentation process, then the data of the 7th batch and the 8th batch are used to correct on-line the initial extended inversion model, and the data of the 9th batch and the 10th batch are used to examine the identification precision of the extended inversion model.

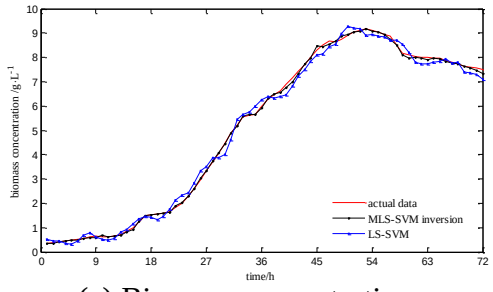
To verify the performance of this method, compare it with the traditional LS-SVM method and calculate the relative error of the soft-sensing results. The initial performance parameter of MLS-SVM uses empirical values: $\boldsymbol{\sigma}^2 = [1.0, 1.0, 1.0]$, $\boldsymbol{\gamma} = [10, 10, 10]$. Following DE calibration, the performance parameters of MLS-SVM are: $\boldsymbol{\sigma}^2 = [0.53, 1.61, 0.48]$, $\boldsymbol{\gamma} = [10.2, 6.4, 8.2]$.

Fig. 4 shows the comparison figure of crucial biochemical parameter soft-sensing results in the 10th batch fermentation. Fig. 5 is the relative error figure of the corresponding soft-sensing values and the off-line assay values. Table 1 lists the maximum relative error MRE of the soft-sensing results of the two data batches.

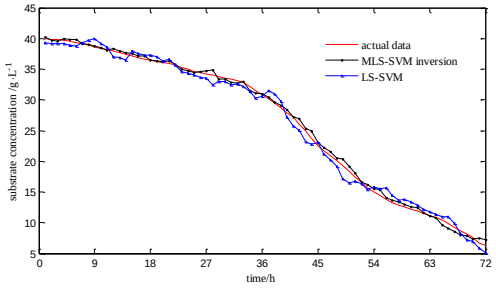
Results and discussion

As shown in Fig. 4, Fig. 5 and Table 1, in comparison with the use of the traditional LS-SVM soft-sensing method, MLS-SVM inverse soft-sensing method produces prediction results that are closer to actual assay values; in particular, the prediction effect of its sugar concentration is very remarkable, adequately indicating that this work's assumption that $\det(\tilde{J})$ is constantly not equal to zero in the penicillin (the fermentation process working area) is totally reasonable. During the logarithmic phase and the stationary growth stage (15-55 h) of L-lysine fermentation, when LS-SVM method is used, the average RMSE of the soft-sensing of mycelia concentration, sugar concentration and chemical potency are 0.216, 0.149 and 0.182 respectively, while when MLS-SVM inverse method is used, the soft-sensing RMSE of the three results are respectively 0.0436, 0.0385 and 0.0402. This shows that the use of MLS-SVM inverse method is effective and reliable, capable of enhancing soft-sensing

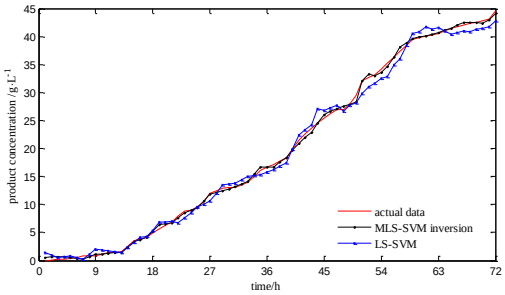
precision of mycelia concentration, sugar concentration and chemical potency, and reaching the expected goal relatively satisfactorily.



(a) Biomass concentration

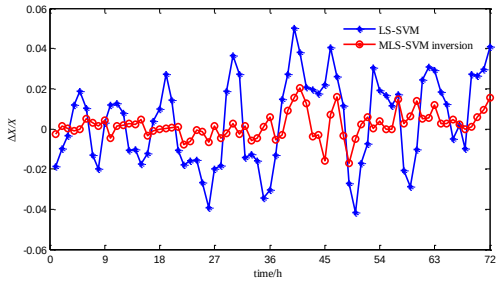


(b) Substrate concentration

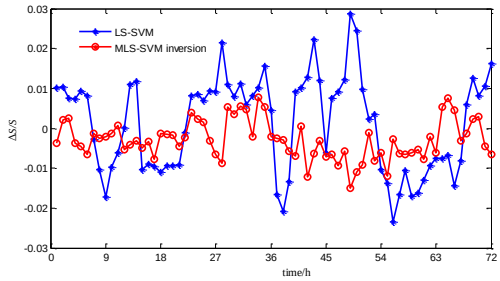


(c) Product concentration

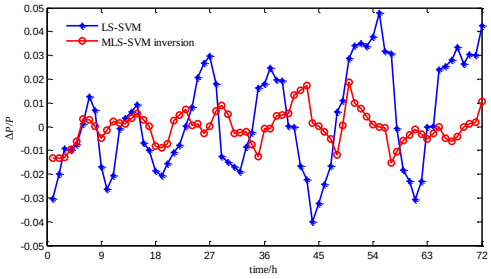
Fig. 4 Comparison figure



(a) Biomass concentration



(b) Substrate concentration



(c) Product concentration

Fig. 5 RE Comparison of the prediction results

Table 1. MRE comparison by two models

Fermentation batch	MLS-SVM Inversion			LS-SVM		
	X, [g·L^{-1}]	S, [g·L^{-1}]	P, [g·L^{-1}]	X, [g·L^{-1}]	S, [g·L^{-1}]	P, [g·L^{-1}]
The 9th batch	1.96%	1.35%	2.04%	6.23%	3.07%	4.82%
The 10th batch	2.01%	1.51%	1.87%	5.02%	2.84%	4.77%

In order to solve the difficulties in on-line measurement of crucial biochemical process variables in L-lysine fed-batch fermentation process, a modeling approach of L-lysine fermentation process soft-sensing based on MLS-SVM inversion is presented in this work by a combination of inverse system and support vector machine theory. On the basis of building a dynamic system model for fed-batch fermentation process, reversibility analysis is made on a non-linear model based on the inverse system method; also MLS-SVM system identification and DE algorithm on-line optimization are used to build an extended inversion model, and in this way on-line prediction of crucial biochemical parameters during fermentation is realized. Simulation research has shown that the system dynamic model is reasonable and that MLS-SVM inverse soft-sensing method is effective for L-lysine fed-batch fermentation process.

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