Bulgarian Chemical Communications, Volume 47, Number 4 (pp. 1204 – 1210) 2015

Soft-sensing modeling of crucial parameters for penicillinfed-batch fermentation process

B. Wang[1*], X. F. Ji[1], Y. K. Sun[2]

[1]*School of Electrical and Information Engineering, Jiangsu University, 212003Zhenjiang, China*
[2]*Nanjing Institute of Technology, 211167Nanjing, China*

Received April 7, 2015

A modeling approach for soft-sensing based on PSO-LSSVM inversion was presented to solve the problem of penicillin fed-batch fermentation being a non-linear, large time-delay and multivariable dynamic coupling process in which crucial bioprocess parameters are difficult to be measured online in real-time. First, a non-linear dynamic model of the system was developed based on the material balance relation of the penicillin fed-batch fermentation process, and the existence of an inverse system was checked. Second, an initial inverse model was off-line developed by using the fitting capacity of a least square support vector machine, online corrected by using the particle swarm optimization algorithm. Last, a combined pseudo-linear system was formed by a corrected inverse model being cascaded behind the original fermentation process; thereby non-direct measurable crucial bioprocess parameters could be online predicted. A penicillin fed-batch fermentation process was investigated as an example. The modeled soft-sensing method was demonstrated to be effective and practicable.

Key words:Penicillin fed-batch fermentation,material balance relations, inverse model, soft-sensing.

INTRODUCTION

As the first kind of antibiotic that was purified and clinically used on a large scale, penicillin has initiated a new era of antibiotic therapy and is still the most commonly used antibiotic. Penicillin fermentation is a highly non-linear and tight coupling dynamic process with characteristics of a non-linear system such as time variance, relevance and uncertainty. Moreover, in the fermentation process, some crucial bioprocess parameters cannot be measured online in real-time and there is no accurate mechanism model to be used. Now crucial bioprocess parameters are obtained through offline analysis and laboratory tests; there exist a big time-delay in data measurement, and thus it is difficult to meet real-time control requirements for the penicillin fermentation process. Therefore, the research on how to obtain crucial status information of fermentation processes in time is significant for optimizing penicillin fermentation process and thus improving penicillin yield and quality [1-5].

In recent years, the inverse system approach has offered an effective way for soft-sensing of non-direct measurable parameters of a non-linear system. There exist two application restrictions in traditional inverse-system approaches when used for practical engineering: 1) the mathematical models of relevant objects and the specific system parameters should be known; 2) the analytic expression of the inverse model can be accurately determined. With respect to the limitations of the inverse system approaches, an ANN dynamic soft-sensing method was presented by employing artificial neural network to identify the inverse model and an excellent application result was obtained [6]. But in this paper, the system model used in inverse system analysis is a simplified model based on Monod equation which ignores many nonlinear components and does not cover the actual fermentation process. Thus, it is not applicable to an original nonlinear coupled system.Moreover, the identification approach of a neural network is based on the asymptotic theory when a sample approximates to infinite. Practical samples, however, are always limited, especially in tight coupling and large time-delay of non-linear systems such as biological fermentation processes, in which it is very difficult to obtain accurate sample data. There still exist some other difficulties such as the selection of model structures, the convergence of arithmetic and the uniqueness of solution. Compared with neural network, the support vector machine theory based on the statistical theory presents an excellent performance when used in the study of small samples. It provides good generalization ability and non-linear identification ability, and is thus suitable for the identification of non-linear, tight coupling and large time-delay systems [7-13].

In this work, by applying a mechanism modeling approach, a dynamic model of a fed-batch penicillin

* To whom all correspondence should be sent:
E-mail: wangbo_jsu@163.com

fermentation system was developed based on the material balance relation in fermentation processes. With respect to the multi-variable non-linear model,the existence of its inverse system and constructing a method of an inverse model were analyzed. The inverse model was obtained through offline identification by a least square support vector machine (LSSVM) and online optimization applying the particle swarm optimization algorithm (PSO). The inverse model was cascaded behind the original fermentation process as soft-sensing model, so that the online prediction of crucial bioprocess parameters which are non-direct measurable can be realized. The theoretical analysis and simulation results demonstrated that the approach provides higher prediction accuracy than common modeling approaches such as PSO-LSSVM.

FERMENTATIONPROCESSMODELING

The concentrations of mycelia and metabolite in various fed-batch liquids were assumed to be 0. According to the material balance relation eq. (1) of various substances (mycelia, substrate, metabolite, oxygen, H^+ and so on) in the fed-batch fermentation process, a system dynamic model was developed [2]:

$$\frac{\mathrm{d}x}{\mathrm{d}t} = \mu(X,S,P,C_L,pH)X - \frac{x}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \quad (1)$$

where $x \in \{X,S,P,C_L,pH\}$, X,S,P,C_L,pH,V are the concentrations ofmycelia, substrate, product, dissolved oxygen, *pH* value and volume of the fermentation liquor, respectively; is the specific rate of the various substances.

In the fed-match fermentation process of penicillin, various substrates were flowingly fed as per specific concentrations to provide the necessary carbon source, nitrogen source, inorganic salt and precursor substances, as well as to adjust and control the *pH* value of the fermentation liquor to be maintained in an optimal range. Fermentation volume *V* and *pH*were varied by the addition of various substrates. Their balance equations are expressed as:

$$\begin{aligned} \frac{\mathrm{d}V}{\mathrm{d}t} &= f_1 + f_2 + f_3 + f_4 + f_5 \quad (2) \\ \frac{\mathrm{d}pH}{\mathrm{d}t} &= \gamma(X,S,P,C_L,pH)X - \frac{X}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \\ &\quad + \frac{S_2 f_2 - S_1 f_1 - S_4 f_4 - S_5 f_5}{V} \quad (3) \end{aligned}$$

where f_1, f_2, f_3, f_4 and f_5 are the feeding rates of glucose, aqueous ammonia, monopotassiumphosphate (KDP) and phenylacetic acid (PAA), respectively; S_1, S_2, S_4, S_5 are the flow liquidconcentrations of glucose, aqueous ammonia, KDP and PAA, respectively; and γ is the specific consumption rate of H^+.

As the only restrictive substrate of penicillin fermentation, the carbon source was required in a large quantity and would 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:

$$\frac{\mathrm{d}S}{\mathrm{d}t} = -\nu(X,S,P,C_L,pH)X + \frac{s_1}{V}f_1 - \frac{S}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \quad (4)$$

where ν is the specific consumption rate of the various substrates.

In the stage of penicillin synthesis, the hydrolysis reactions of precursor substance (PAA) and penicillin would remarkably affect the penicillin yield. The influence of PAA addition and hydrolysis rate K on the fermentation process is considered in the following balance equation of product concentration:

$$\frac{\mathrm{d}P}{\mathrm{d}t} = \rho(X,S,P,C_L,pH)X - KP + \frac{K_1}{V}f_5 - \frac{P}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \quad (5)$$

where K_1 is inhibition constant and ρ is specific production rate of the product.

With respect to the aerobiotic characteristic of penicillin fermentation and considering the influence of reactor size on the dissolved oxygen level of the fermentation liquor, the volume oxygen-transferring system (K_2) was introduced into the dissolved oxygen balance equation:

$$\frac{\mathrm{d}C_L}{\mathrm{d}t} = -\eta(X,S,P,C_L,pH)X + K_2(C_L^* - C_L) - \frac{C_L}{V}\frac{\mathrm{d}V}{\mathrm{d}t} \quad (6)$$

where C_L^* is the oxygen saturated concentration and η is the specific consumption rate of oxygen.

The concentrationsof mycelia, substrate and product $\hat{\boldsymbol{x}} = [X,S,P]^{\mathrm{T}}$ were selected as non-direct measurable parameters; the dissolved oxygen concentration, the pH value and the fermentation liquor volume $\boldsymbol{z} = [z_1,z_2,z_3] = [C_L,pH,V]^{\mathrm{T}}$ were selected as direct measurable parameters; and the feeding rates of the various substrates $\boldsymbol{u} = [f_c, f_{nh}, f_s, f_p, f_{paa}]^{\mathrm{T}}$ were selected as input. The state equations are given by (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 a state vector, $\boldsymbol{u} = [u_1,u_2,u_3,u_4,u_5]^{\mathrm{T}} = [f_1, f_2, f_3, f_4, f_5]^{\mathrm{T}}$ is an input vector, μ,ν,ρ,η,γ are smooth functions of various state variables, and $s_i (i = 1,\cdots,8)$ are all non-zero constants.

$$\begin{cases} \dot{x}_1 = \mu(x_1,x_2,x_3,x_4,x_5)x_1 - \dfrac{x_1}{x_6}\sum_{i=1}^{5}u_i \\ \dot{x}_2 = -\nu(x_1,x_2,x_3,x_4,x_5)x_1 + \dfrac{s_1u_1}{x_6} - \dfrac{x_2}{x_6}\sum_{i=1}^{5}u_i \\ \dot{x}_3 = \rho(x_1,x_2,x_3,x_4,x_5)x_1 - s_2x_3 - \dfrac{x_3}{x_6}\sum_{i=1}^{5}u_i + \dfrac{s_3u_5}{x_6} \\ \dot{x}_4 = -\eta(x_1,x_2,x_3,x_4,x_5)x_1 - s_4x_4 - \dfrac{x_4}{x_6}\sum_{i=1}^{5}u_i + s_5 \\ \dot{x}_5 = \gamma(x_1,x_2,x_3,x_4,x_5)x_1 - \dfrac{x_5}{x_6}\sum_{i=1}^{5}u_i \\ \quad + \dfrac{s_6u_2 - s_1u_1 - s_7u_4 - s_8u_5}{x_6} \\ \dot{x}_6 = \sum_{i=1}^{5}u_i = u_1+u_2+u_3+u_4+u_5 \end{cases} \quad (7)$$

SYSTEM REVERSIBILITYANALYSIS

In view of the system dynamic model of penicillin fermentation, the soft-sensing model of nonlinear multivariable system was established based on the inverse system method. The inverse system method has a good effect in soft-sensing modeling of nonlinear systems, which is a kind of feedback linearization method of nonlinear systems.Under the condition that the original system is invertible, the inverse system, with the function of dynamic compensator, is cascaded with the original system to transform the input-output relationship of the compound system to be a decoupled identity mapping relation. This realizes the mirror of some crucial bioprocess variables. The reversibility analysis and the corresponding inverse model are given as follows.

Lemma 1: System Σ is invertible in a certain (x_0,u_0) neighborhood, only if the relative order of this system equals $rank\left(\partial \mathbf{Z}_m^{\mathrm{T}}/\partial \hat{\mathbf{x}}^{\mathrm{T}}\right) = r_m = l$ [6],where l is the number of variables impossible to be directly measured.

By using the Interactoralgorithm[6], the reversibility analysis of penicillin fermentation dynamic model is given as follows:

The derivative of direct measurable parameters to time should be calculated primarily until the useful information for structuring the inverse model could be obtained. Eq. (7) leads to:

$$\begin{cases} \dot{x}_4 = -\eta(x_1,x_2,x_3,x_4,x_5)x_1 - s_4x_4 \\ \quad + s_5 - \dfrac{x_4}{x_6}\sum_{i=1}^{5}u_i \\ \ddot{x}_4 = g_1(\boldsymbol{x},\boldsymbol{u}) + g_2(x_4,x_5,x_6,\boldsymbol{u},\dot{\boldsymbol{u}}) \\ \dot{x}_5 = \gamma(x_1,x_2,x_4,x_5)x_1 - \dfrac{x_5}{x_6}\sum_{i=1}^{5}u_i \\ \quad + \dfrac{s_6u_2 - s_1u_1 - s_7u_4 - s_8u_5}{x_6} \end{cases} \quad (8)$$

where $g_1(\boldsymbol{x},\boldsymbol{u}) = s_7\dfrac{\partial\eta}{\partial x_5}\dfrac{x_1}{x_6}u_4 - s_6\dfrac{\partial\eta}{\partial x_5}\dfrac{x_1}{x_6}u_2 - \dfrac{\partial\eta}{\partial x_3}\dfrac{x_1}{x_6}u_5$

$$+\left(\frac{\partial\eta}{\partial x_1}x_1 + \frac{\partial\eta}{\partial x_2}x_2\right)\frac{x_1}{x_6}\sum_{i=1}^{5}u_i + \frac{x_1}{x_6}\sum_{i=1}^{5}u_i$$

$$+\left(\frac{\partial\eta}{\partial x_3}x_3 + \frac{\partial\eta}{\partial x_4}x_4 + \frac{\partial\eta}{\partial x_5}x_5\right)\frac{x_1}{x_6}\sum_{i=1}^{5}u_i$$

$$+\left(\frac{\partial\eta}{\partial x_1}\mu - \frac{\partial\eta}{\partial x_2}\nu + \frac{\partial\eta}{\partial x_3}\rho\right)x_1^2 - \frac{\partial\eta}{\partial x_4}s_5x_1$$

$$-s_1\left(\frac{\partial\eta}{\partial x_2} - \frac{\partial\eta}{\partial x_5}\right)\frac{x_1}{x_6}u_1 - \eta\mu x_1 - \frac{\partial\eta}{\partial x_5}\gamma x_1^2$$

$$+\frac{\partial\eta}{\partial x_3}x_3 + \frac{\partial\eta}{\partial x_4}s_4x_1x_4 + s_4\eta x_1 - \frac{\partial\eta}{\partial x_4}\eta x_1^2$$

$$g_2(x_4,x_6,\boldsymbol{u},\dot{\boldsymbol{u}}) = \frac{2s_4x_4}{x_6}\sum_{i=1}^{5}u_i - \frac{s_5}{x_6}\sum_{i=1}^{5}u_i - \frac{x_4}{x_6}\sum_{i=1}^{5}\dot{u}_i$$

$$+\frac{2x_4}{x_6^2}\left(\sum_{i=1}^{5}u_i\right)^2 - s_4s_5 + s_4^2x_4$$

Let matrix $\boldsymbol{J} = \partial\mathbf{Z}_m^{\mathrm{T}}/\partial\hat{\mathbf{x}}^{\mathrm{T}}$, then

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

Through elementary transformation of $\boldsymbol{J}$, we obtain:

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

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

$$g_4(\boldsymbol{x},\boldsymbol{u}) = \left(x_1\frac{\partial\nu}{\partial x_2}\frac{\partial\eta}{\partial x_3}\right) \Big/ \frac{\partial\nu}{\partial x_3} - \frac{\partial\eta}{\partial x_2}x_1 ; g_5(\boldsymbol{x},\boldsymbol{u}) = \frac{\partial g_1(\boldsymbol{x},\boldsymbol{u})}{\partial x_1}$$

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

$$-\left(\frac{\partial v}{\partial x_2}\frac{\partial g_1(\boldsymbol{x},\boldsymbol{u})}{\partial x_3}\right)\Big/\frac{\partial v}{\partial x_3}.$$

If $\det(\boldsymbol{J})$ is not zero in the real vector space, this system is globally invertible by using Lemma 1. However, it is very difficult to give such a condition under which this variable is not zero anywhere. Note that the practical working state of penicillin fermentation process is only in a small sub-region of the real vector space. With this consideration, we can first assume this system to be invertible in the working area and then construct the inverse-based soft measurement model for some crucial biochemical process variables in the penicillin fermentation model. The experimental result is finally used to verify the rationality and reliability of this assumption.

We were working on the assumption that the system model satisfies the reversible conditions in the work area of the penicillin fermentation process. From the inverse-function existence theorem and eqs. (7-8), the inverse model expression of penicillin fermentation process may be developed as:

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

It is difficult to determine the analytic expression of the inverse model.However, the support vector machine algorithm[11,12] based on the statistical theory provides a new perspective of machine learning from the risk minimization principle, it provides good generalization ability and non-linear identification ability, and is thus suitable for the identification of non-linear systems, From that point, three non-linear functions $\varphi_1, \varphi_2, \varphi_3$ of eq. (12) were identified using least square support vector machine(LSSVM).

As for LSSVM system identification, the selection of kernel function σ and penalty parameter C exerts an important effect on the developing of the inverse model. Most of traditional parameter selection approaches, however, are based on experience and trial-error method so that the regression precision and computation speed cannot be guaranteed. In order to obtain an inverse model with a better prediction effect, this work applies particle swarm optimization algorithm to the online optimization and adjustment of LSSVM parameters[14-17].

SOFT-SENSING MODELING

The inverse model of a fermentation process was identified applying PSO-LSSVM, following the three steps:

(1) Samples obtaining

In order to stimulate the non-linear characteristic within the penicillin fed-batch fermentation, we selected the random signals in the field of practical work as input to real-time measurement of the response of the fermentation process. From eq. (11) we can see the training sample set of the inverse model in penicillin fermentation process as $\{\bar{x}_1, \bar{x}_2, \bar{x}_3\}$ and $\{x_4, \dot{x}_4, \ddot{x}_4, x_5, \dot{x}_5, x_6\, \boldsymbol{u}, \dot{\boldsymbol{u}}\}$. The former is the output of the inverse model, i.e. desired output; and the latter is the input, where the direct measurable parameters $\{x_4, x_5, x_6\}$ and input parameters $\boldsymbol{u} = \{u_1, u_2, u_3, u_4, u_5\}$ could be obtained by direct sampling; and the various-order derivative information of the direct measurable parameters $\{\dot{x}_4, \ddot{x}_4, \dot{x}_5, \dot{\boldsymbol{u}}\}$ was offline determined by using high-precision five-point numerical algorithm. The non-direct measurable parameters $\{\bar{x}_1, \bar{x}_2, \bar{x}_3\}$ were determined by offline analysis and chemical test. The obtained data were differentially fitted using the least square method to obtain the training sample corresponding to the input.

(2)*Offline modeling*

The three SVM were offline studied applying the least square method based on input/output training sample data, to obtain corresponding a_k and b , and develop the initial inverse model of a fermentation process.

(3) Online correcting

There exist unmodeled dynamic and static errors in an initial inverse model. In order to improve the identification accuracy of the inverse model so that its soft-sensing model can fit the variation of the object based on the deviation information between the input of the fermentation process and the output of the inverse model, LSSVM performance parameters were online optimized applying the particle swarm optimization algorithm and the initial inverse model was online corrected.

The series connection of corrected PSO-LSSVM inverse model following the original fermentation process constituted a pseudo-linear combined system. This made the input and the output of the combined system display a decoupled identical mapping relation; therefore we could realize the online prediction of crucial parameters. The three non-linear functions $\varphi_1, \varphi_2, \varphi_3$ were offline identified by 3 static LSSVM and online optimized by PSO.

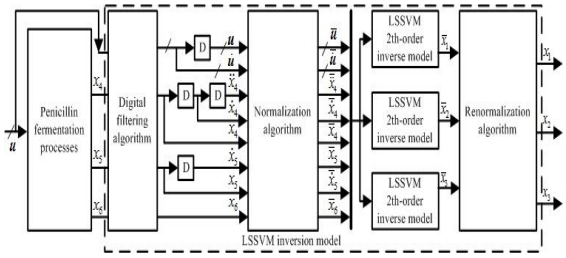


Fig. 1. Combined pseudo linear system structure

Fig.1 is a combined pseudo-linear system chart, in which the PSO-LSSVM inverse model serves as soft-sensing model and digital filtering pre-processing approach.

SIMULATION AND ANALYSIS

The experimental research was undertaken to the penicillin fed-batch fermentation process in the laboratory fermentation tank. The experimental process was designed to be close to practical productive processas follows:

(1)Penicillin fed-batch fermentation period of each batch was 200h and the sampling period T was 30min. $C_L, pH, V, \boldsymbol{u}$ were collected by sensors, X, S, P were sampled each 4h and offline analyzed. X was measured by high-performance liquid chromatography (HPLC), S was measured by SBA-40C type multi-functional biosensor and P was measured using enzyme linked immunosorbent assay (ELISA).

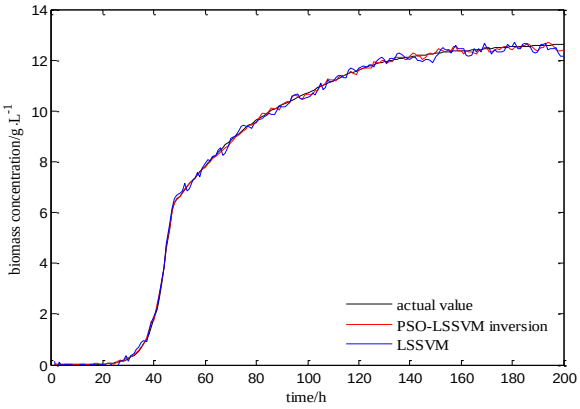
(2)Only 10 batches of medium were considered to examine the modeling ability of PSO-LSSVM inversion with respect to small samples. The initial conditions of the various batches were set to be different, the fed-batch strategies of the various substrates varying correspondingly to enlarge batch differences. The pressure of the fermentation tank was controlled between 0～0.07 MPa and the pH of the fermentation liquor between 6.8 ～ 7.2, the temperature in the early period and the medium period was set at about 26℃ and in the late period was set at about 24℃, the stirring speed was 150~250rpm, and the concentration of the precursor PAA <1kg/m^3.

The fermentation data of the first 6 batches were selected as a training sampling set, and were offline trained to obtain the initial inverse model of the fermentation process, then the data of the 7th and 8th batch were used to online correct the initial inverse model;and the data of the 9th and 10th batch were used to examine the identification precision of the inverse model.

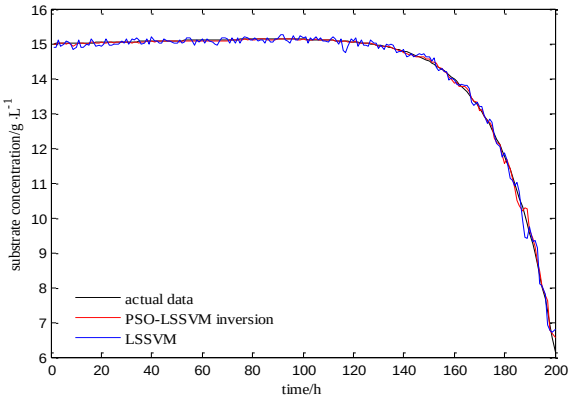
PSO-LSSVM inverse algorithm was compiled using MATLAB language. In order to verify the performance of the method, we compared it with purely data-driven algorithm LSSVM and computed the relative error of soft-sensing results. The three initial performance parameters of LSSVM were selected as empirical values: $\boldsymbol{C}=[12,12,12]$ and $\boldsymbol{\sigma}^2=[1.0,1.0,1.0]$. The three performance parameters of LSSVM corrected by PSO were $\boldsymbol{C}=[11.6,7.3,9.8]$ and $\boldsymbol{\sigma}^2=[0.67,1.33,0.59]$.

Fig.2 shows the comparison of result predictions based on PSO-LSSVM inversion and the soft-sensing model of LSSVM. Fig.3 shows the relative errors of the soft sensing values to the corresponding offline analysis values. Table 1 lists the maximum relative errors of the soft-sensing results using the two approaches.

(a) Biomass concentration



(b) Substrate concentration



(c) Product concentration

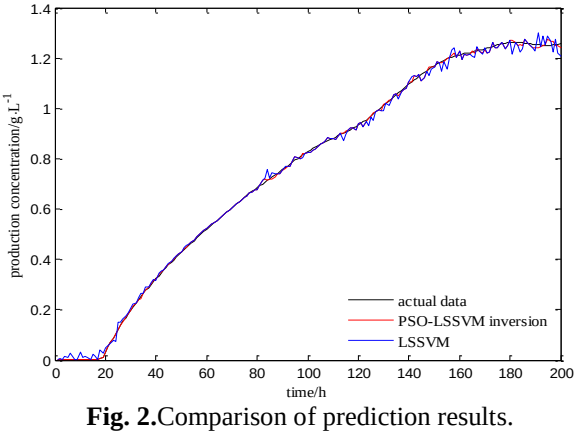


Fig. 2. Comparison of prediction results.

From Figs.2 and3 we can see that compared with the soft-sensing result applying LSSVM approach, the soft-sensing values applying PSO-LSSVM inversionapproach are more approximate to the practical offline laboratoryvalues, especially the effect of substrate concentration being notable, thus, the hypothesis that $\det\left(\frac{\partial y}{\partial u}\right)$ is not zero constantly inthe work area is entirely reasonable. In the main stage of penicillin fermentation (50h-180h), by applying LSSVM soft-sensing approach, the RMSE average values of soft-sensing of mycelia concentration, substrate concentration, and product concentration are 0.0292, 0.0189 and 0.0472, respectively; while with PSO-LSSVM inversion they are 0.0133, 0.0125 and 0.0178 respectively.

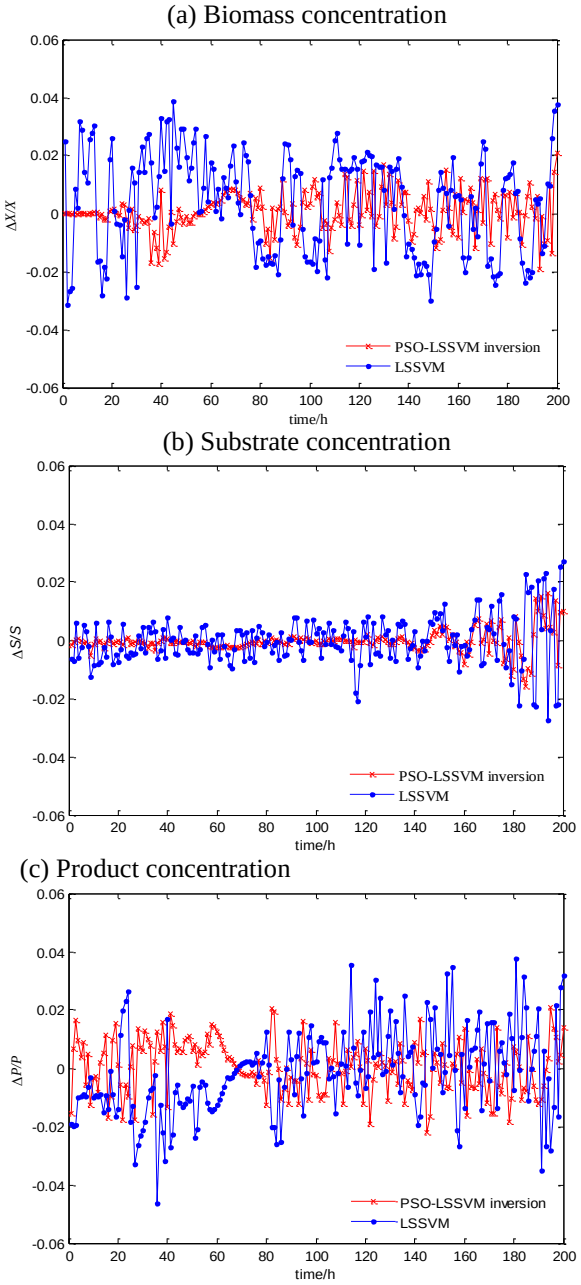


Fig. 3. Comparison of relative errors.

This meansthat the PSO-LSSVM inversion soft-sensing approach is effective and reliable with an ability to improve the soft-sensing precision of mycelia, substrate and product concentrations. We have achieved the anticipated objective, solved the problem of the low precision of online soft-sensing of crucial biomass parameters in penicillin fermentation process, and thus laid a solid foundation for applying optimization control of fermentation processes.

CONCLUSIONS

In this work, by applying PSO-LSSVM inverse model identification and soft-sensing principle, the soft-sensing was undertaken with respect to crucial biomass parameters in a penicillin fed-batch fermentation process. The simulation experiment indicates that:

(1)LSSVM can successfully perform inverse model identification regarding the penicillin fermentation process, as well as online correcting the inverse model based on PSO algorithm. This eliminated the non-linear modeling errors, making the inverse model fit with the variations in the fermentation process.

(2)The inverse model is no longer corresponding to the structure form of direct analysis of the inverse system. It not only retains all advantages of LSSVM inverse model that apply the fundamental structure, but also remarkably enhances the function of LSSVM inverse model, and therefore gives a play to the advantage of the inverse soft-sensing approach and makes the LSSVM inverse soft-sensing more suitable to practical engineering application.

(3) This approach needs no*a priori* knowledge about penicillin fermentation process; it only needs the relative order and a few input/output sample sets in the fermentation process, to obtain ideal identification effect. That broke through the two limitations of traditional approaches.

The above results can be developed to fit complex non-linear process modeling and high precision prediction such as biochemical reactions. PSO-LSSVM inversion system approach is also suitable to the modeling and soft-sensing of common non-linear reversible systems, and thus provides a new way for the soft-sensing of multi-variable non-linear systems.

Acknowledgements:*This work is supported by the Natural science fund of Jiangsu province under Grant BK2014042351 and the Natural science fund for colleges and universities in Jiangsu province Grant 14KJB510007.*

REFERENCES

1. M.Pcolka, S.Celikovsky, *Bioprocess Biosyst. Eng.*, **37**(1), 71 (2013).
2. Z. P. Shi, F. Pan, Fermentation Process analysis, control and detection technology, **126**, Beijing: Chemical Industry Press, 2010.
3. J. D. Chen, F. Pan, *Chinese Journal of Chemical Engineering(CIESC.)*,**61**(8), 2092 (2010).
4. Y. H. Liu, J. X. Bi, A. P. Zeng, *Bioprocess and Biosystems Engineering (Bioprocess Biosyst. Eng.)*, **30**(10), 1464 (2008).
5. P. V. D. Kerkhof, G. Gins, J. Vanlaner, *Computers and Chemical Engineering(ComputChem Eng.)*, **40**(3), 12 (2012).
6. X. Z. Dai, W. C. Wang, Y. H. Ding, *Computers and Chemical Engineering (ComputChem Eng.)*, **30**(8), 1203 (2006).
7. W. J. Chen, Y. H. Shao,*Journal of Control and Decision*, **28**(12), 1817 (2013).
8. X. J. Chen, Y. H. Shao, *Control and Decision*,**28** (12), 1817 (2013).
9. X. F. Wang, J. D. Chen, C. B. Liu, F. Pan, *Chemical Engineering Research and Design (CEHM ENG RES DES.)*,**88**(4), 415 (2010).
10. W. Liu, C. H. Liu, L. Zheng, *Transactions of the Chinese Society of Agricultural Engineering (Transactions of the CSAE.)*, **30**(10), 145 (2014).
11. X. D. Wang, C. J. Zhang, *Chines Journal of Scientific Instrument*, **27**(7), 730 (2006).
12. K. Desai, Y. Badhe, B. D. Kulkarni, *Biochemical Engineering Journal (BIOCHEM ENG J.)*,**27**(3), 225 (2006).
13. G. H. Liu, D. W. Zhou, X. H. Xu, C. L. Mei, *Expert Systems with Applications (EXPERT SYST APPL.)*, **37**(4), 2708(2010).
14. Q. L. Ye, C. X. Zhao, *Pattern Recognition Letters*, **31**(13), 2006 (2010).
15. X. M. Yang, W. Q. Liu, J. Yang, *Chinese Journal of Chemical Engineering (CIESC.)*, **46**(9), 3262 (2013).
16. W. H. Chih, J. L. Chih, *IEEE Transactions on Neural Networks (IEEE T NEURAL NETWOR.)*, **13**(2), 415 (2002).
17. X. G. Zhang, *ActaAutomaticaSinica*,**26**(1), 32(2000).

17. W. Li, H. Y. Su, R. L. Liu, *Chinese Journal of Chemical Engineering (CIESC.)*, **61**(8), 1927 (2010).

.

SOFT-SENSING МОДЕЛИРАНЕ НА КЛЮЧОВИ ПАРАМЕТРИ ПРИ ПОЛУ-НЕПРЕКЪСНАТА ФЕРМЕНТАЦИЯ НА ПЕНИЦИЛИН

Б. Уанг[1*], Кс. Ф. Джи[1], И. К. Сун[2]

[1]*Училище по електро-инженерство и електронна информация, Университет Джиянгсу, Женджиянг, Китай*

[2]*Технологичен институт в Нанджинг, Нанджинг, Китай*

Постъпила на 5 април, 2015 г.

(Резюме)

Подходът на soft-sensing моделиране, основан на PSO-LSSVM инверсия е използван за решаване на нелинейната многомерна задача за полу-непрекъснатата ферментация с продукт пеницилин. Процесът е с времево закъснение и ключови биопроцесни параметри се измерват трудно online и в реално време. Най-напред е съставен нелинеен модел на базата на материалния баланс за този ферментационен процес, а който инверсия е известна, но не е анализирана. След това началният инверсионен модел е разработен за off-line изпълнение с помощта на метода на най-малките квадрати, както и чрез online-корекция чрез оптимизационен алгоритъм. Накрая е образувана псевдо-линейнасистема, почиваща на коректен инверсионен модел с каскадно представяне на ферментационния процес. По този начин става възможно online-предсказването на не-пряко определяните ключови параметри на ферментацията.Като работен пример е дадено получаването на пеницилин по полу-непрекъснат начин. Показано е, че soft-sensing-моделирането е ефикасно и практично за експерименталната практика и анализ на опитните данни.