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# Study of glutamic acid fermentation process hybrid modeling

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## ABSTRACT

Fermentation process of glutamic acid is a very complicated industry process, which needs different environment parameters and has seriously nonlinear and instability. Studying the kinetic model and neural network model combining hybrid modeling of glutamic acid fermentation process, hybrid model consists of two parts, one is the mechanism model, through reasonable assumptions and limitations, simplifying the kinetics of biochemical reaction process, it is basis of hybrid model, describes the basic characteristics of glutamic acid fermentation process; the other part is a neural network model, using neural network training function of knowledge, and establishing glutamic acid fermentation process between the input and output mapping, this mapping only depends on the actual production data, and has nothing to do with the actual process, it is a secondary part of the hybrid model for correction kinetic model. Through simulation, respectively, glutamic acid fermentation process kinetic model and hybrid model to compare the results to prove the value of hybrid model predictions closer to the system actual output, the model is more accurate. 

## KEYWORDS

Glutamic acid fermentation process;
Hybrid modeling;
Kinetic model;
Neural network.

## INTRODUCTION

Glutamic Acid is the world's largest amino acid products, China is the large producer of glutamic acid fermentation, but now MSG industry in China have some serious bottleneck problems which restricting industrial development, there is lack of modern biotechnological methods transform the fine strains of high-yielding, the main technical index in fermentation were significantly lower than the level of advanced manufacturers, utilization ratio of materials and running cost of operating needed to raise; existing extraction process not suited to the nature of high glutamic acid fermentation fluid, cause the phenomenon of increasing output without increasing income; existing cleaning production still needed to improve, to solve the low-strength wastewater reuse issues, in order to save process water ;lack of online testing of fermentation process in industrial-scale and systems research of optimization control, etc. Constraints raise the level of factors in addition to the acid production rate, conversion rate of sugar acid, glutamic acid production strength fermentation technology indicators as well as production stability, raw material and operating costs, and wastewater emissions and environmental pollution problems.

The fermentation process is a typical intermittence

industry process in production process which is a highly nonlinear of complex dynamic process. And compared with the general physical and chemical process, the fermentation process has a unique and very different dynamic characteristic, such as dynamic model is highly nonlinear and strong time-varying, the majority of state variable is difficult to online measurement, the process slow response rate is slow, the significant time lag in the online measurement, etc[1]. Therefore application of hybrid knowledge of process data, process knowledge and experience build process model this is suited to fermentation process characteristics. It will play a crucial role to improve the overall performance of the fermentation process, improve the yield of the product purpose, yield and conversion of raw material.

Currently, there are many methods of fermentation process modeling existing, such as analysis and identification based on mechanism modeling and neural network modeling methods, and so on. But for the two models, it is difficult to overcome the shortcomings of their own. The modeling method of mechanism analysis and identification is based on the general reaction mechanism, and to deduce the dynamic model of cell, substance and the product. Due to the complex mechanism of the fermentation process, and the large number of factors[2,3], it usually requires a lot of derivation to simplify the kinetic model, and needs to set some restrictions, simultaneously it results in a narrow scope of application of the model, and the control accuracy is not high. Neural network modeling is essentially taking a neural network as the "black box" model of the actual object. It uses the input and output data of the object, obtained in the actual production process, to train a neural network. This model can not only reflect the impact of external disturbance and noise on the system, but also can reflect the impact of disturbance within the system on the actual system performance. While this model is based on the actual measurement data, and the formatted network model is empirical, and lack of physical infrastructure. Thus the use of extrapolation is not satisfactory, and the generalization ability is poor.

Then the thought of Hybrid Modeling emerge as the times require[4]. It can be combined with the mechanism model of practical reaction and the black box model of fitted sample data, and the comprehensive advantages of both accurately show object model. Therefore, it appeared by all the favor of scholars. For example, hybrid modeling of penicillin fermentation process based on chaos and SVM form Wang Xian Fang in 2009, hybrid modeling are built with penicillin dynamic model and SVM. The Result Show That, the predictive effect of this modeling method is obviously better than single modeling method, so the hybrid modeling method has a certain application value[5]. In hybrid modeling of penicillin fermentation process, a new hybrid modeling method which is based on mechanism model and described the system unknown factors through the RBF neural network is proposed by Chen Jin Dong in 2010. The experiments results show that, for penicillin fermentation process, this method achieved good results and prove the validity of the proposed method[6].

For the specific biochemical reactions of glutamic acid fermentation process, in order to describe the actual process more accurately and to improve control accuracy through the accurate modeling of the system, this paper propose a hybrid model structure, which is based on kinetic model and neural network model. The hybrid model consists of two parts: kinetic model and neural network model. The kinetic model is the core while the neural network model is the complement. The output of the kinetic model is fixed with the neural network model to make the final model output results closer to the real system production data.

## GLUTAMIC ACID FERMENTATION PROCESS

### Process description

Glutamic acid fermentation process is batch Fermentation, and is a metabolic process that mixes nutrient of carbon source, nitrogen source, phosphorus source, inorganic salts with a certain number of bacteria, who can grow and product glutamic acid in a suitable conditions of culture medium, PH, temperature ventilation and stir in fermentation tank. Specific process is as follows. Glutamic acid culture medium (sugar, etc.), who come from sterilizing column, and is controlled by the flow, is added to the glutamic acid fermentation cylinder that has a bactericidal finish, and is cooled to 32 degrees when it through the coil heat exchanger in the fermentation cylinder, and then is mixed

with germ and bactericidal air. Until now the glutamic acid is begin gradually. Glutamic acid bacteria (glutamate coryneform bacteria) absorb the nutrition of material, and through the body of the enzyme in complex specific biochemical reactions. In the process, will continue to produce all sorts of primary metabolites, and secondary metabolites, and so on, make the product concentration increasing. At the same time, the interior of the matrix will be constantly consumption, to ensure that all kinds of metabolic product in the form and the activity of bacteria.

Glutamic acid Fermentation process can be divided into four periods which are germ growth, transition stage, and acid stage, nearly put cans of order. The essence of the fermentation process is that the reactants through into the cells the body from cell wall and cell membrane in culture, will convert into a product. The fermentation process is divided into three periods, which are adaptive phase (or phase of adjustment, lag phase), logarithmic growth phase and decline phase. Therefore, in the fermentation process, respectively meet the conditions of the temperature, PH, ventilation rate as well as complemented glucose[7]. When acid yield, residual sugar, bacteria light density OD value index reaches a certain requirement can put pot, fermentation process will be end in a fermentation period of about 32 hour.

Glutamic acid fermentation is a complex process of microbial growth, for the purpose of rapid cell growth, normal metabolism, and more products, it is necessary to provide a good growing environment. General speaking, ventilation quantity or dissolved oxygen, PH, fermentation temperature, tank pressure, complemented material etc. are the main control parameters. And the monitoring of germ concentration is particularly significant[8,9].

## Process parameters

In a narrow sense, the state variables of the fermentation process are those parameters of the reflect process state and the characteristics. Such as cell concentration, substrate concentration, metabolic concentration, dissolved oxygen concentration (DO), enzyme activity, cell proliferation rate, generation rate of $CO_2$, etc. There's this very tight causal connection between operation parameters and these. Usually, this relationship can be through the ordinary differential equations to describe and expression.

The typical operation variables of fermentation process include temperature, pressure, pH value, matrix speeding rate of flow, dilution rate, agitation rate, ventilation and so on. In the fermentation processes, typical directly measured variables have pH value; DO viscosity, nutrient additives, cell concentration, substrate concentration, metabolite concentration and so on. And indirect measurement variables have $CO_2$ generated rate, $O_2$ consumed rate, respiratory quotient (RQ), and bacteria specific growth rate, metabolites than generation rate, acid yield rate, and transformation rate, which generally use directly measured variables, the soft measurement method calculated according to a certain formula. Generally measured variables are used directly to calculate according to a soft measurement method.

## GLUTAMIC ACID FERMENTATION PROCESS HYBRID MODELING

### Process kinetic model

1) Stage of germ growth

Empirical model of the bacterial growth rate of ventilation caused by the evaporation of liquid such as glutamic acid fermentation process in terms of the fed-batch fermentation, only without the discharge of other substances, which can be drawn from the system, is

$$\frac{dX(t)}{dt} = \mu(t)X(t) \quad (1)$$

where $X(t)$ is cell concentration in $g/L$, $\mu(t)$ is than generation rate in $h^{-1}$.

In batch fermentation process, cell growth is influence by cell concentration and bacteria concentration themselves, and the relationship of bacteria growth and the substrate concentration are observed by Contois equations.

$$\mu = \frac{\mu_m S}{K_S X + S} \quad (2)$$

where $\mu_m$ is maximum than generation rate in $h^{-1}$, $S$ is substrate concentration in $g/L$, $K_S$ is Contois saturation constant in $g/g$. And the relationship between cells is observed by Logistic equations.

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$$\mu = \mu_m (1 - \frac{X}{X_{max}}) \quad (3)$$

where $X_{max}$ is maximum cell concentration in $g/L$. Taking all these factors, the influence of cell than generation rate can get following formula.

$$\mu = \mu_m \frac{S}{K_S X + S} (1 - \frac{X}{X_{max}}) \quad (4)$$

Meanwhile, the influence of cell is showed by the change of PH value and temperature T.

$$X(t) = F(PH) \quad (5)$$

$$X(t) = A(T) \quad (6)$$

where $A(T) > 0$ and $F(PH) \le 1$. Substituting (4), (5), (6) into equation (1) obtains the following.

$$\frac{dX(t)}{dt} = \mu_m \frac{S}{K_S X + S} (1 - \frac{X}{X_{max}}) F(PH) A(T) X \quad (7)$$

Equation (7) is the dynamics model of bacteria growth to find that bacteria concentration is the function of temperature T and PH value.

2) Stage of nutrient consumption

In the fermentation process of glutamic acid, the main restrictive matrix is glucose, and consumption model can be expressed as

$$\frac{dS(t)}{dt} = -m_S X - \frac{1}{Y_{X/S}} \frac{dX}{dt} - \frac{1}{Y_{P/S}} \frac{dP}{dt} + \frac{S_F}{V} \quad (8)$$

where $m_S$ is maintenance factor in $(g/g)/h$, $Y_{X/S}$ is grow rate coefficient in $g/g$, $Y_{P/S}$ is Product yield coefficient in $g/g$, $P$ is product concentration in $g/L$, $S_F$ is supplement sugar content in $g$, $V$ is fermented liquid volume in $L$. In the whole process of fermentation, these fermented liquid volumes keep constant. In equation (8), the first is the meaning of a matrix maintains bacteria growth consumption, the second is bacteria to grow the consumption of matrix, and the third is the product of the consumption of matrix generated.

3) Stage of product generation

The product model of Glutamic acid fermented is shown in the following.

$$\frac{dP(t)}{dt} = \beta X - KP \quad (9)$$

Where, $\beta$ is Product synthesis constant of bacteria growth association in $g/(gh)$, $K$ is degradation rate constants in $h^{-1}$. And specific growth rate $\beta$ can be expressed as

$$\beta = \mu_p \frac{S}{K_P + S + S^2/K_I} \quad (10)$$

where $\mu_p$ is maximum than generation rate in $h^{-1}$, $K_P$ and $K_I$ are inhibition constant in $g/L$. Equation (10) into equation (9), the product generation model of glutamic acid fermentation process is

$$\frac{dP(t)}{dt} = \mu_p \frac{S}{K_P + S + S^2/K_I} X - KP \quad (11)$$

4) $O_2$ content of tail gas

Similarly shows, other companies also can be transformed into the difference equations.

$$\frac{dO_2(t)}{dt} = k_L a(DO^* - O_2) - (m_o + \frac{1}{Y_{X/O}} \frac{dX}{dt} + \frac{1}{Y_{P/O}} \frac{dP}{dt}) X(t) \quad (12)$$

where $k_L a$ is a volumetric oxygen transfer coefficient in $g/g$, $O_2$ is dissolved oxygen concentration in $g/L$, $m_o$ is maintain coefficient of bacteria for oxygen in $(g/g)/h$, $Y_{X/O}$ is yield coefficient of bacteria for oxygen in $g/g$, $Y_{P/O}$ is yield coefficient of product for oxygen in $g/g$, $k_L a$ is ventilation rate function, as

$$g(q) = k_L a \text{ and } g(q) > 0. \quad (13)$$

In summary, the dynamic model of the glutamic acid fermentation process for

$$\begin{cases} \frac{dX(t)}{dt} = \mu_m \frac{S}{K_S X + S} (1 - \frac{X}{X_{max}}) F(PH) A(T) X \\ \frac{dS(t)}{dt} = -m_S X - \frac{1}{Y_{X/S}} \frac{dX}{dt} - \frac{1}{Y_{P/S}} \frac{dP}{dt} + \frac{S_F}{V} \\ \frac{dP(t)}{dt} = \mu_p \frac{S}{K_P + S + S^2/K_I} X - KP \\ \frac{dO_2(t)}{dt} = k_L a(DO^* - O_2) - (m_o + \frac{1}{Y_{X/O}} \frac{dX}{dt} + \frac{1}{Y_{P/O}} \frac{dP}{dt}) X(t) \end{cases} \quad (14)$$

The mechanism model often firstly needs discrimination. The dynamic model of the above can be transformed into the following difference equations.

$$\frac{X[(k+1)T] - X(kT)}{T} = \mu_m \frac{S(kT)}{K_S X(kT) + S(kT)} \times (1 - \frac{X(kT)}{X_{max}}) F(PH) A(T) X(kT) \quad (15)$$

Arranging the above equation and the following

equation can be obtained.

$$X[(k+1)T] = T \times [\mu_m \frac{S(kT)}{K_S X(kT) + S(kT)} \times$$

$$(1 - \frac{X(kT)}{X_{max}}) F(PH) A(T) X(kT)] + X(kT) \quad (16)$$

Similarly shows, other companies also can be transformed into the difference equations.

$$S[(k+1)T] = T \times [-m_S X(kT) - \frac{1}{Y_{X/S}} \frac{X[(k+1)T] - X(kT)}{T} -$$

$$\frac{1}{Y_{P/S}} \frac{P[(k+1)T] - P(kT)}{T} + \frac{S_F}{V}] + S(kT) \quad (17)$$

$$P[(k+1)T] = T \times [\mu_p \frac{S(kT)}{K_P + S(kT) + S^2(kT)/K_I} X(kT) -$$

$$KP(kT)] + P(kT) \quad (18)$$

$$O_2[(k+1)T] = T \times [k_L a(DO^* - O_2) - (m_o + \frac{1}{Y_{X/O}} \times$$

$$\frac{X[(k+1)T] - X(kT)}{T} + \frac{1}{Y_{P/O}} \times$$

$$\frac{P[(k+1)T] - P(kT)}{T}) X(kT)] + O_2(kT) \quad (19)$$

## Parameters determining

The above model has a certain number of undetermined parameter including maximum specific growth rate $\mu_m$, Contois saturated constant $K_S$, maximum cell concentration $X_{max}$, maintenance factor $m_S$, grow rate coefficient $Y_{X/S}$, product yield coefficient $Y_{P/S}$, maximum product than producing rate, inhibition constants $K_P$ and $K_I$, degradation rate constants $K$, volumetric oxygen transfer coefficients $k_L a$, The concentration of oxygen saturation $DO^*$, bacteria rate for oxygen coefficient $m_o$, bacteria rate for oxygen coefficient $Y_{X/O}$, product rate for oxygen coefficient $Y_{P/O}$, the following explain some parameters.

1) Cells yield coefficient $Y_{X/S}$

Bacteria growth relative to the consumption of matrix yield, expressed as

$$Y_{X/S} = \frac{X - X_0}{S - S_0} = \frac{\Delta X}{\Delta S} \quad (20)$$

where $Y_{X/S}$ is grow rate coefficient in $g/mol$ or $g/g$, $\Delta X$ is stem cell growth in $g$, $\Delta S$ is matrix consumption in $mol$ or $g$.

2) Product yield coefficient $Y_{P/S}$

The relic product relative to the yield of consumption matrix, expressed as

$$Y_{P/S} = \frac{P - P_0}{S - S_0} = \frac{\Delta P}{\Delta S} \quad (21)$$

where $Y_{P/S}$ is actual product yield in $g/mol$ or $g/g$, $\Delta P$ is product cargoes in $mol$ or $g$.

Similarly shows, formula of bacteria rate for oxygen coefficient $Y_{X/O}$ and product rate for oxygen coefficient $Y_{P/O}$ can be got. Ultimately determining the model parameters is shown in TABLE 1.

**TABLE 1: Model Parameters**

| Parameter | Value | Parameter | Value |
|---|---|---|---|
| $\mu_m(h^{-1})$ | 0.12 | $\mu_p(h^{-1})$ | 1.4 |
| $K_S$ $(g/g)$ | 0.15 | $K_P$ $(g/g)$ | 0.02 |
| $X_{max}$ $(g/L)$ | 1.2 | $K_I$ $(g/g)$ | 0.12 |
| $m_X$ $((g/g)/h)$ | 0.014 | $K$ $(g/g)$ | 0.04 |
| $Y_{X/S}$ $(g/g)$ | 0.38 | $Y_{P/S}$ $(g/g)$ | 0.667 |
| $m_o$ $((g/g)/h)$ | 0.891 | $V$ $(L)$ | 2*105 |
| $Y_{X/O}$ $(g/g)$ | 0.0396 | $Y_{P/O}$ $(g/g)$ | 0.0972 |
| $DO^*$ $(g/L)$ | 0.171 | | |

## Secondary variable selection

In glutamic acid fermentation process, developing and metabolism of cell are influenced by the change of parametric variables of the temperature, PH, ventilation rate as well as complemented glucose, too big or too small all will become bacteria growth and the limiting factors of organic synthesis, and finally affects glutamate production efficiency. So the choice of parametric variables of the temperature, PH, ventilation rate as well as complemented glucose set instrumental variables of glutamic acid fermentation dynamic model.

## Neural network model

Through to the analysis and study of the glutamic acid fermentation process, obtain the process data[9], and establish the BP neural network model of the system. The input of neural network are selected by parametric variables of the temperature, PH, ventilation rate as well as complemented glucose, and bacteria con-

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centration X, substrate concentration S and product concentration P as the output of the network, the number of hidden nodes identified as 13, the neural network convergence speed faster than the traditional BP algorithm by Levenberg-Marquardt learning algorithm.

## HYBRID MODELING

### Hybrid modeling methods

In the process of glutamic acid fermentation, the hybrid Model Methods of kinetic model and neural network model is that, the mechanism model as the foundation of the mixture model, with the neural network model to correction mechanism model output error. In the hybrid Modeling Methods, mechanism model of the fermentation process from glutamic acid various practical mechanism of dynamics equation change, obtain the mathematical model. And mechanism modeling is the premise of glutamic acid to fully grasp the fermentation process mechanism, and can be exactly to the mathematics description[10].

This mechanism model is the basis of the whole mixture model, and in mechanism modeling, fermentation process of glutamate brought forward many assumptions and restrictions, make the mechanism model is simplified, and the assumption and restrictions also to the established model and the practical process of the mechanism between certain deviations. In order to recognize these deviations, the output of the neural network model is added to the output of the mechanism model, make the output of the hybrid model more close to the real output of glutamate fermentation process. Mixed model output is by the output of mechanism model and output of the neural network model to form two parts.

### Hybrid model structure

The hybrid model of fermentation process of glutamic acid consists of two parts; the one is kinetic model, it is a kind of simplified equation, through giving a lot of reasonable assumptions and limitations to biochemical reaction kinetic equation. It describes the basic characteristics of the glutamic acid fermentation process and it is the basement of the hybrid model. The other part is the neural network model, which uses the training function of the neural networks, and establishes

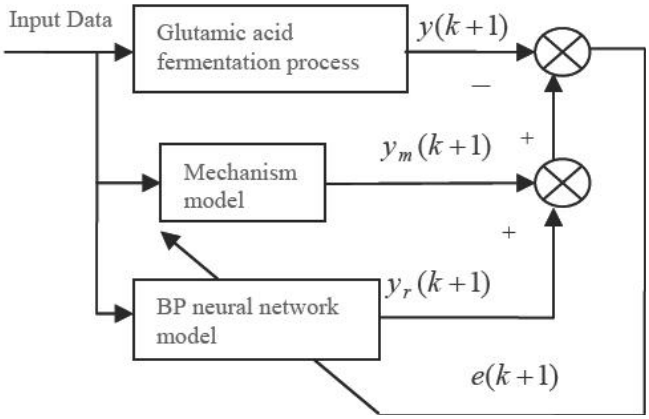



**Figure 1: Hybrid model structure**

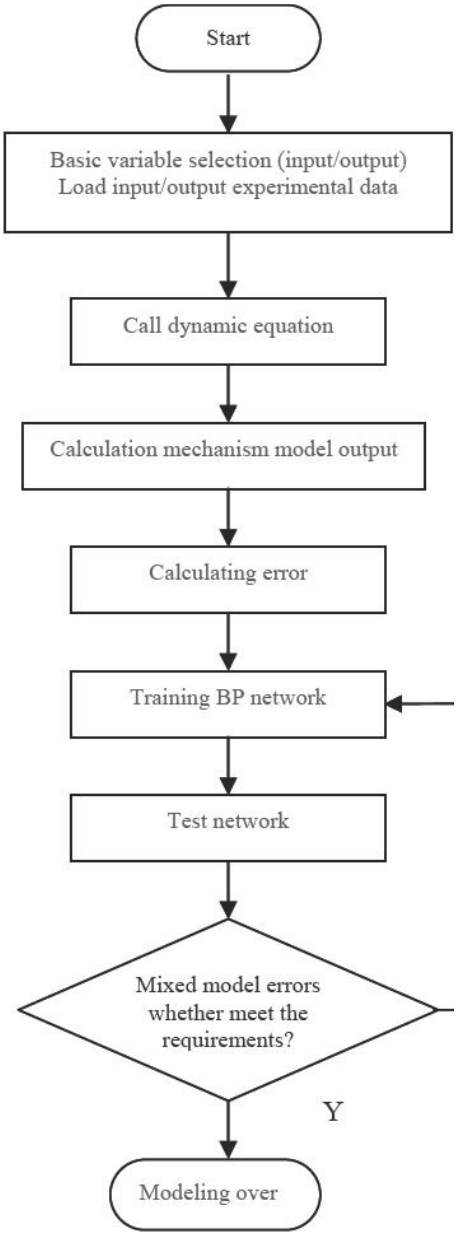



**Figure 2 : Hybrid modeling flow chart**

the mapping relationship between input and output of the glutamic acid fermentation process. This mapping depends only on the actual production data, and it is independent of the actual mechanism process. The neural network model is the auxiliary part of the hybrid model, and is used to correct the error resulted by kinetic model. Hybrid Model Structure is presented in Figure 1. The system error in Figure 1 is

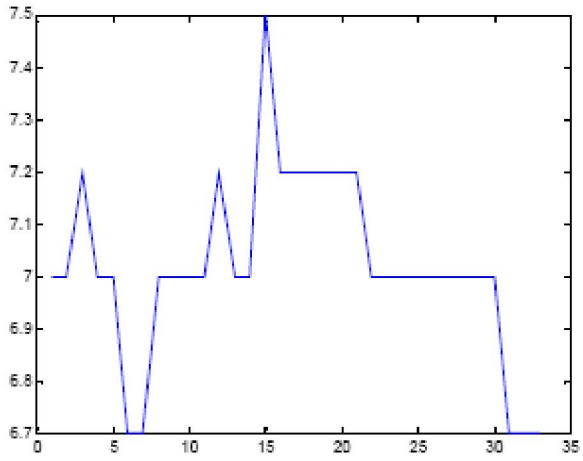
$$\mathbf{e(k+1) = y(k+1) - y_m(k+1) - y_r(k+1)} \quad \textbf{(22)}$$

where $y(k+1)$ is the real output of glutamic acid fermentation process, $y_m(k+1)$ is the mechanism model output of glutamate fermentation process, and $y_r(k+1)$ is the neural network model output of glutamic acid fermentation process.

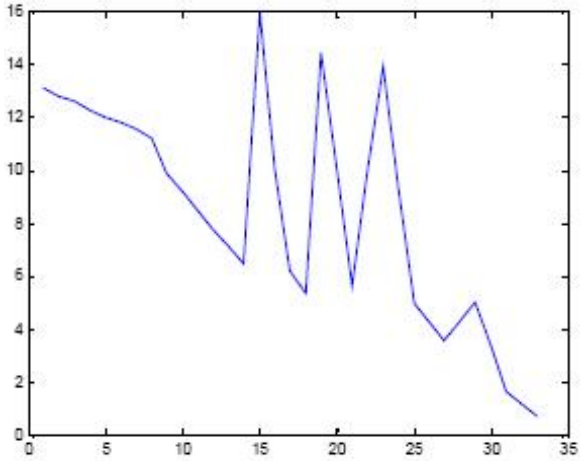
According to the above ideas, the hybrid modeling flow chart is shown in Figure 2.

## Hybrid model simulation

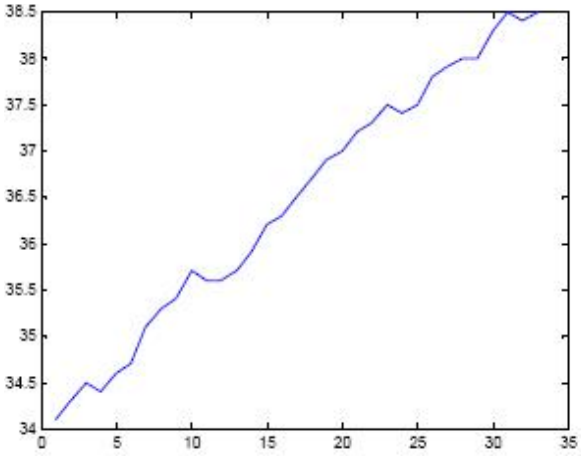
To verify the advantages of the proposed method, methods simulation of mechanism model and hybrid model are built respectively in fermentation process. Field data are provided from a certain gourmet powder factory, fermentation time is 32 hours. Every hour PH value, filling sugar content, temperature, ventilation, process parameters can be got by online measurement. Sampling value of Bacteria concentration, substrate concentration and product concentration can not be got through online measurement methods; artificial sampling is needed on average every hour. 64 sample data are selected from a lot of sample data, including 32 groups used to model fitting, another 32 group used to model test. Need to explained, According to the data of the choice should be moderate, and not the more the better. Although more sample data may make the model



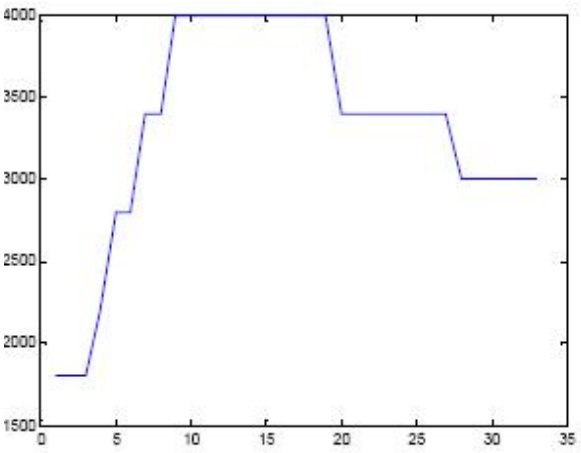
(a) PH value



(b) Filling sugar content



(c) Temperature



(d) Ventilation

**Figure 3 : Data samples trend of process parameters**

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more close to the actual process of fermentation glutamic acid, but too much sample data may also cause data redundancy phenomenon, that some of the data model correction function slowly diminish, almost disappear, it has lost its fixed meaning. In addition, excessive sample data will no doubt make the simulation experiment workload increase. PH value, filling sugar content, temperature and ventilation, the data samples trend of process parameters is shown in Figure 3.

Model simulation results are shown in Figure 4 and Figure 5, respectively training samples and verification samples, they are the actual production data, the output curve of mechanism model and hybrid model output curve of product concentration P. In simulation results, Sign x indicates the actual production data, the dotted line indicates the output of mechanism model, and the solid line indicates the output of hybrid model.

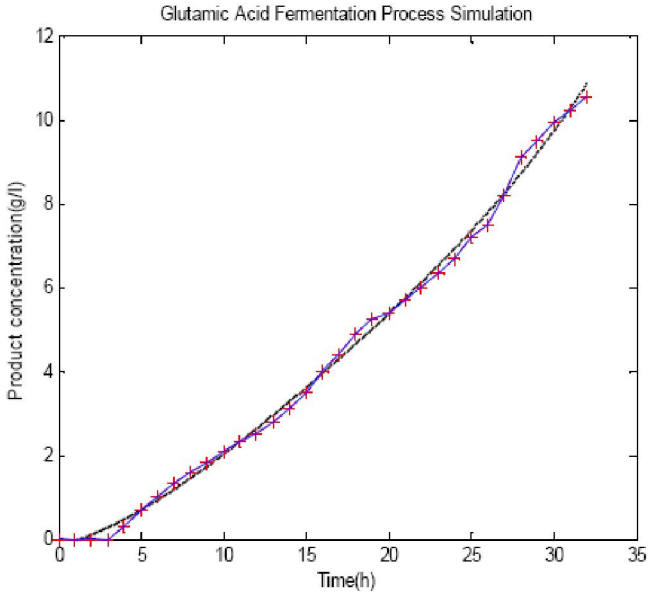


**Figure 4 : Simulation result of product concentrates P by training samples**

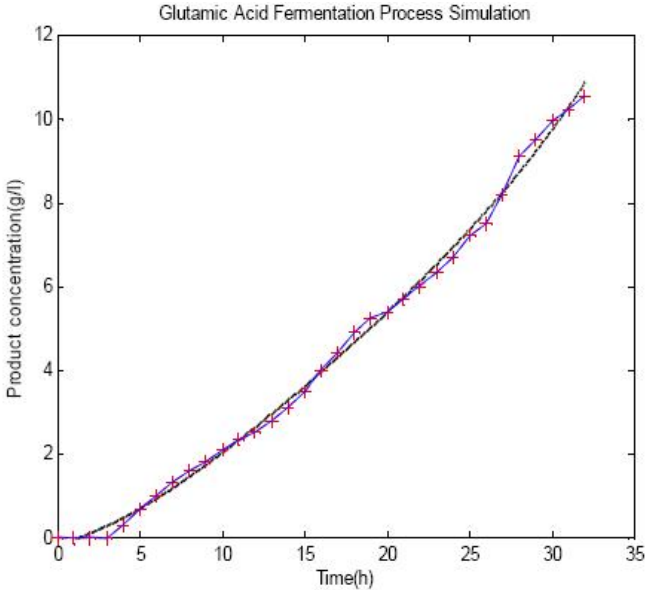


**Figure 5 : Simulation result of product concentrates P by verification samples**

## CONCLUSION

For the specific biochemical reactions of glutamic acid fermentation process, in order to describe the actual process more accurately and to improve control accuracy through the accurate modeling of the system, the paper proposes a hybrid model structure, which is based on kinetic model and neural network model. The kinetic model is the core while the neural network model is the complement. Though the simulation result indicate, the output of the kinetic model is fixed with the neural network model to make the final model output results closer to the real system production data, the fitting effect is better.

## ACKNOWLEDGMENT

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