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GMDH ALGORITHM IMPLEMENTED IN THE INTELLIGENT IDENTIFICATION OF A BIOPROCESS

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Abstract. *The concentration of biomass is one of the main variables in fermentative processes that exist in the biotechnology industry. There are several techniques for estimating it. It is very difficult and expensive to measure it continuously and on line. This paper presents an alternative for estimating biomass concentration using a neural network – based model, applied to a batch-feed type operation fermentative process. A modified GMDH algorithm (Group Method of Data Handling) was applied, using a new structure based on the combination of a genetic algorithm and the use of a negative feedback loop. The model was tested in the fermentation of yeast Pichia pastoris for the production of a recombinant. The stability and capacity of generalization is demonstrated. Using the mean square error behaviour as criterion the proposed method was compared with other neural networks - based structures.*

Keywords*: modeling, fermentation, GMDH, negative feedback, genetic algorithm*

1. INTRODUCTION

The methodology of systems identification has been developed to determine mathematical models of process based on known data of a system. In this area, the general guidelines for the design of classifiers and / or predictors are widely known, however there is consensus on the need for a particularized approach for each application.

The models used in the area of bioengineering problems are complex because of the characteristics of these processes (Passoni, 2005). This concept becomes the fact that the biological activity generates information with special features, most notable being the following:

• The obtained information from process presents a non-homogeneous structure since of the complexity of the objects alive.

• The information is emerging from the dynamics of change associated with the functional properties of the studied phenomena.

The techniques of Artificial Intelligence, AI, is being applied in this field significantly in recent decades, and among them those known as Artificial Neural Networks, ANNs, are characterized by their properties of learning and generalization, (Leiva, 2006). It's often necessary to take into account their potential for induction, which can be implemented by software, (Miroslav Šnorek, 2006). There are several methods to obtain inductive models. The Group Method of Data Handling methods, GMDH, (Ivakhnenko AG, 1971) is well known.

Solla (1989) shown the probability that a given RNA shows a certain behavior depends not only on the learning algorithm of the network, but also its architecture. The procedure for increasing the probability of correct correspondence between inputs and outputs often lies in learning but, as argued in (Happel and Murr, 1990), to increase correspondence between neural network model and process is necessary to impose restrictions on its topology, which should corresponds to the maximum extent possible with the structure of the process. Thus, for complex processes with intermediate or output variables in internal feedback loops require neural network models with similar features. These models have better efficiency in the long-term prediction (Yuan and Vanrolleghem, 1999).

Feedforward neural networks, FFNN, have several design-related limitations that can be improved with a change in its architecture. On the other hand, recurrent neural networks, RNN, have several characteristics that make them superior. First, RNN can converge quickly to a target value for a given performance with a certain margin of error, meaning less iterations. Another advantage, RNN presents a better non-linear behavior during learning. (Lau, 1992) However, these advantages are a significant cost: processing time is increased. This feature becomes a principal difficulty in applications involving a large number of neurons. Hence the use of this architecture should be a compromise between performance and speed.

Another tool of AI is expanding currently. The use of genetic algorithms, AG, based on the theory of biological evolution as applied in the optimization of mathematical models of systems (Holland, 1975) (Ferreira, 2001, 2004).

In this paper an identification of a fermentation process is developed using the concept of Evolutionary Identification Systems combining methodologies developed by several authors: Functional Networks and self GMDH (Ivakhnenko, 1999, Ivakhnenko et al. 1998; Ivakhnenko GA, 2001 ; Kondo and Ueno, 2009) Genetic Programming (Mark and Xin, 2002) (Ferreira, 2001, 2004) and GMDH-.Type with negative feedback (Kondo and Ueno, 2006).

The structure of this paper is as follows: In section 2 describes the basic features of the GMDH algorithm. Section 3 is devoted to representation of a GMDH neural network using AG and then move on to Section 4 to describe the steps

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required to design the model proposed. Section 5 provides an example of applying the model in a Feed-Batch Fermentation type. These results are compared with other algorithms in Section 6. Finally a section with conclusions is presented.

2. THE GMDH ALGORITHM

The algorithm was developed for identifying nonlinear relationships between inputs and outputs. The algorithm provides an optimal structure, obtained in an iterative procedure of partial descriptions of the data by adding new layers. The number of neurons in each layer, the number of layers and the input variables are automatically determined to minimize a criterion of prediction error and thus organizes an optimal neural network architecture using a self-heuristics, the which is the basis of the GMDH algorithm. (Ivakhnenko, 1971). This method is particularly successful in solving problems of modelling multiple entries for a single output (Mutasem, 2004). The neural networks developed using this algorithm are called GMDH Type Neural Networks and are classified within the group of Polynomial Neural Networks, PNN.

The used data set to design of the network contains vectors consisting of independent input variables ($x_1, x_2, \ldots x_n$), and a variable output S_t.

The first step to implement a GMDH algorithm is to divide the data into two groups, one for training, which is used to estimate parameters of each neuron to obtain a partial description of the process, and the second one to evaluate the results and to select those neurons that describe the process more efficiently. In this way it's obtained a structure that allows a full description of the process.

The n input variables are grouped in pairs (xi, xj) such that:

$$\{(x_1, x_2), (x_1, x_3), \cdots, (x_1, x_n), \cdots, (x_{n-1}, x_n)\}$$

Resulting $n\,(n\text{-}1)\,/\,2$ combinations.

These combinations are entries to similar number of polynomial equations, describing the process partially.

$$y = a_0 + \sum_{i=1}^{n} a_i x_i + \sum_{i=1}^{n} \sum_{j=1}^{n} a_{ij} x_i x_j \tag{1}$$

The coefficients can be calculated by regression analysis for the training data set.

An external criterion, usually the mean square error, MSE, also known as Criterion for Regularity, CR, is calculated using the equation for each set of test data.

$$CR = \frac{1}{T} \sum_{n=1}^{T} (\hat{y}_n - y_n)^2 \tag{2}$$

Where

T number of vectors composing the test data set,

$\hat{y}_n$ actual output variable, such that $\hat{y}_n$ = St,

y_n model output variable.

Only those equations meeting a minimum *CR* survive. Others equations are eliminated. This method ensures that only units having the greatest ability to approximate will be selected.

Subsequently a new layer is created using the selected outputs from previous layer as inputs and the process starts again forming pairs of entries. These steps are repeated to generate new layers until the error criterion stops decreasing. When this happens the output will be one with the obtained lowest *CR* value in previous layer above and so will complete the design process. Figure 1 shows how a GMDH-type network is structured from the optimum selection of units.

S_{t-1} is feedback as input variable. Once neurons best meeting the criterion of regularity are selected the model is evaluated using the test data. (Kondo 2003, Kondo and Ueno, 2006).

3 REPRESENTATION WITH GENETIC ALGORITHM

Incorporating Genetic Algorithm to GMDH-type neural networks, each neuron is represented as a string, which can be mutated or crossed with each other to form new generations. The procedure to define a chromosome as described in (Nariman-Zadeh et al., 2003) can be modified easily be included in the proposed GMDH algorithm, which is achieved by repeating the name of the neuron, moving directly from a layer to the another. This means that in GMDH-type neural

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network with genetic structure connections between neurons may occur through different non-adjacent layers. (Bagheri et al., 2007). In conventional GMDH neural networks connections occur only between adjacent layers.

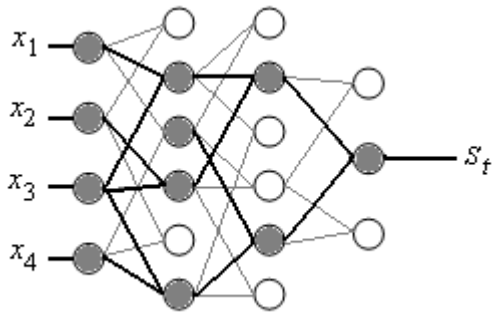
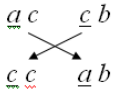
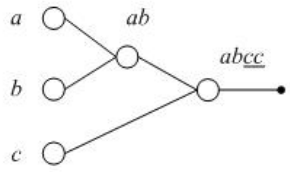


Figure 1. Example of neural network structure obtained by GMDH algorithm.

Figure 2 shows an example, where the connection of the neuron c is established directly with the output. This connection is represented including the entry *c* twice *abcc*, which generates a virtual neuron whose entries are equal *cc*. (Nariman-Zadeh et al., 2005) In other words the crossover and mutation among populations new virtual neurons with repeated inputs are generated, moving directly to the new layer. Considering $\tilde{n}$ the number of layers moving on, the number of repetitions is calculated as $2^{\tilde{n}}$.



(a). Crossover



(b). Alter crossover

Figure 2. Generation of a virtual neuron through crossover

The quality of each generation (Φ) is represented by

$$\Phi = 1 / CR \tag{3}$$

Where *CR* is represented by equation (2). This value is minimized through the selection process for increasing the quality of the generation (Φ).

Considering only those descendants that are new generations, *M* new descendants are obtained. This number is equal to the maximum number of layer input. This increases the number of input variables of the next layer, expressed as:

$$n = F + n_{ant} \tag{4}$$

Where n_{ant} is a number of input in previous layer and *F* is the number of selected outputs. This causes the number of input variables are increased from one layer to another, so it is necessary to provide a stopping criteria for not over sizing the network. Two stopping criteria can be defined:

- Minimum value of CR.
- Maximum number of layers N.

Figure 3 shows this behaviour in one layer. Similar occurs in the others layers.

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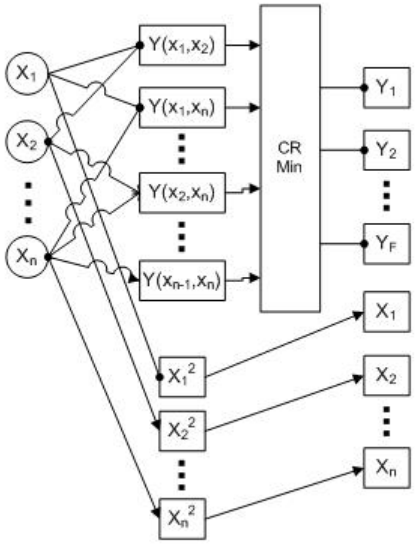

Figure 3 Diagram of distribution of input variables of the adjacent layer.

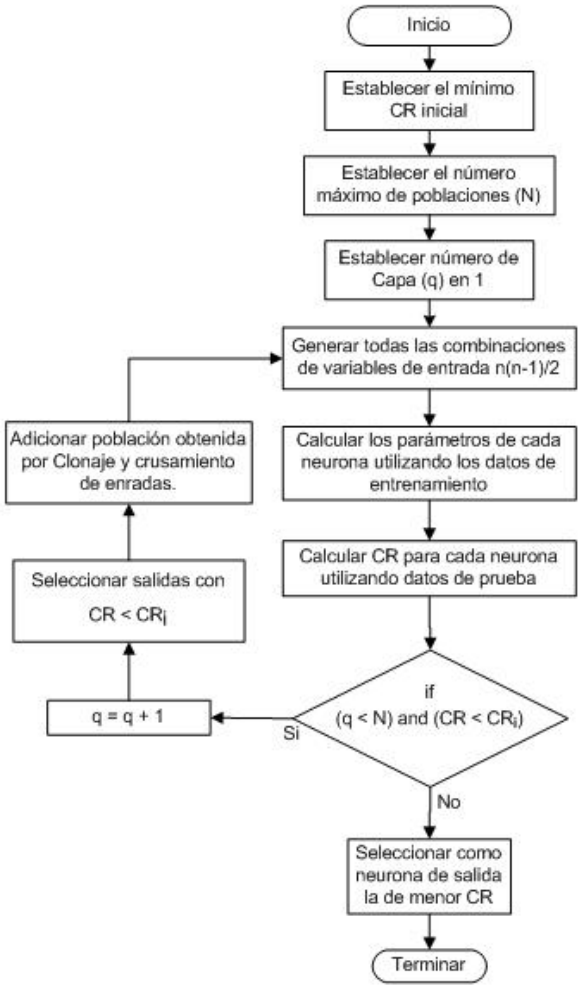

Figure 4 Algorithm .

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4 STEPS FOR THE DESIGN OF THE MODEL

Before starting the design process the initial values of the feedback variable S_{t-1} for training and testing must be established. Then the following steps are executed:

Step 1: To establish value for stopping criteria, initial minimum *CR* and maximum value of populations or layers *N*.

Step 2: To generate all possible combinations of inputs $m = n\,(n\text{-}1) / 2$.

Step 3: To calculate the parameters of each neuron using the training data.

Step 4: To check stopping criteria: *N* and CR_{min}.

Step 5: To select the output meeting CR_{min} and to form the input population for next layer, plus combinations obtained by cloning and crossover (virtual neurons).

Step 6: To set CR_{min} = lower *CR* obtained.

Step 7: Go to Step 3 and repeat until satisfying a stopping criterion.

Figure 4 show a detailed diagram of the proposed algorithm.

5 APPLICATION IN THE PROCESS OF MODELING OF FERMENTATION.

5.1 Description of the process.

Getting maximum concentration of biomass is a principal objective in a biotechnological production. By measuring this variable it's possible to control the cell growth and to optimize the process. Therefore a precise, continuous and on-line measure of the concentration of biomass is an objective for any control and supervision system in biotechnological process. Among the most known methods for determining the concentration of biomass are samples for gravimetric (dry weight of cells) and test of spectroscopy (optical density) (Reed et al., 2000; Känsäkoski et al., 2006) . These methods don't allow appropriate actions to control since they are executed off line of the process (off-line), implying loss of information, delay in obtaining results and human effort (Royce, 1993) .

The fermentations are different. For this reason it's required a robust system for the estimation and a good capacity of generalization, allowing for strict control of the initial conditions, substrate and instrumentation (Jenzsch et al., 2006). The use of models is an important alternative for application in these cases.

The studied process in this application was a type of feed-batch fermentation for production of a vaccine using recombinant yeast Pichea pastoris, which has two stages in its growth in response to the supply of substrate (Figure 5). The first stage occurs in glycerol where no substrate is added, and the second one takes place in methanol, with a controlled flow of substrate in correspondence with the rate of cell growth.

The measured variables are: Flow Substrate (*F*), Temperature (*Temp*), pH (*pH*), Dissolved oxygen (O_2) and Stirring Speed (*Speed*) (McNeil and Harvey, 1990). Considering S_{t-1} the output value a step backwards, then the input variables are expressed as follows:

$x_1 = F$ $\quad x_2 = Temp$ $\quad x_3 = pH$

$x_4 = O_2$ $\quad x_5 = Speed$ $\quad x_6 = S_{t-1}$

S_t is the concentration of biomass (output variable). It's measured by the technique of wet weight, out of the process, which reduces at 24 samples per fermentation the number of data.

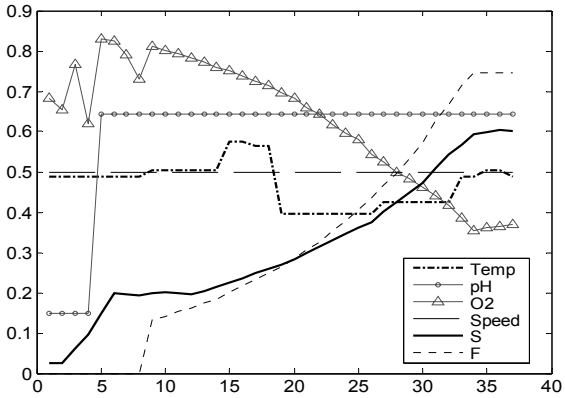

Figure 5. Typical behaviour of the process variables

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3.2 Design of the network:

After establishing the values of S_{t-1} for training and test data respectively, the initial values of the following stopping criteria are adopted:

$CR = 0.01$ and $N = 5$.

Then all input combinations are formed according to the proposed model and the parameters of polynomial equations (3) are calculated. Because of the characteristics of the process the polynomial was restricted to order 2. Criteria are evaluated and selected the combination more representative of the process. Those combinations over minimum CR are rejected. The selected outputs are part of the input population in the intermediate layer. Then the new population of input variables is formed adding the input of the previous layer. Once selected the output neuron the network can be constructed following the input combinations involved in the process. For this case the model results as shown in the Fig. 6:

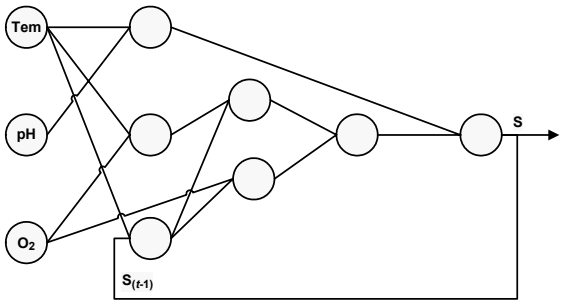

Figure 6. Network architecture design

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The input variables that do not appear in the model were rejected during the design process. Table 1 shows the parameters obtained by regression methods. These parameters belong to the intermediate layer equations. There are only those equations that describe the process efficiently. To calculate these parameters the training data set was used.

Table 1: Coefficients for equations of the intermediate layer.

Ne	a_1	a_2	a_3	a_4	a_5	a_6
5	3.22E-01	1.25E+00	-8.59E-01	-1.22E+00	0.00E+00	6.08E-01
6	1.62E-03	5.50E-01	0.00E+00	0.00E+00	0.00E+00	0.00E+00
7	1.62E-02	-6.57E-02	1.56E+00	-5.11E-01	0.00E+00	-2.85E-01
16	-9.69E-04	1.42E-02	1.00E+00	-6.82E-02	0.00E+00	3.08E-02
18	1.08E-03	9.92E-01	0.00E+00	0.00E+00	1.11E-02	0.00E+00
34	2.79E-02	4.57E+01	-4.49E+01	-3.28E+04	1.63E+04	1.65E+04
57	1.73E-04	9.57E-01	4.35E-02	9.35E-01	-3.95E-01	-5.41E-01

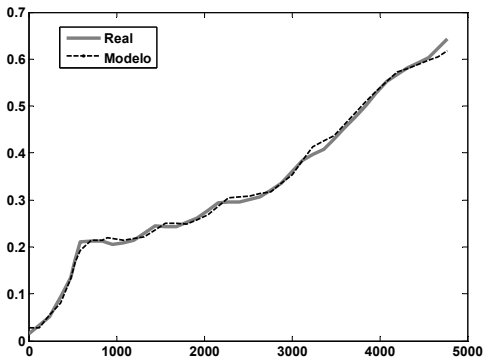

Figure 7. Simulation of a model

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5.3 Analysis of results.

Figure 7 shows the behaviour of the network during the fermentation process. A satisfactory model performance was obtained. Stability in the modelling and its ability to absorb the nonlinearity associated with fermentation processes are demostrated. A best evidence of stability is obtained introducing white noise as input. See Figure 8.

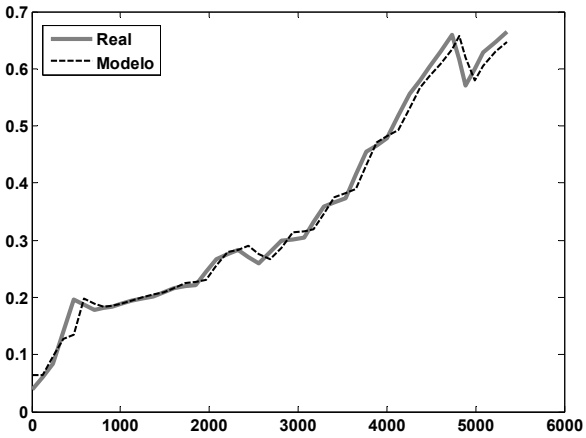

Figure 8. Response in the presence of noise.

6. COMPARISON WITH OTHER ALGORITHMS

The mean square error (MSE) (Ramsey, 1994; and Ekonomou Pappas, 2006) was used as criterion for comparison with other algorithms. Figure 9a shows the results using a classical GMDH algorithm, and the comparison with error convergence is presented in Fig. 9b.

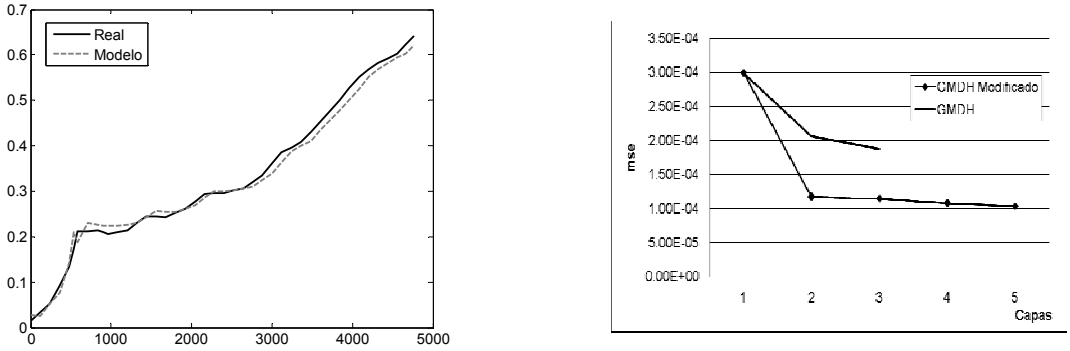

Figure 9. Comparing Classic GMDH and Modified CMDH.

In Figure 10 shows a comparison of the proposed model with other methods. Among them, the GMDH algorithm in its classical form, the Elman neural network, which contains a recurrent loop too and a classic feed-forward neural network. For the studied process, it's clear that the proposed GMDH algorithm with negative feedback has better performance, showing a lower average error than the others methods.

The neural network developed using the GMDH algorithm, have an important difference compared to the models whose neurons are determined beforehand, because of their processing units have an active role as the algorithm is executed within the unit, representing a new variable, which is generated by selection, (Balance et al., 1998).

7. CONCLUSIONS

This paper presented a neural network using the GMDH algorithm, incorporating a negative feedback loop and increasing the number of input combinations by Genetic Algorithm. It was demonstrated its ability to estimate the cell growth in a Batch Feed type fermentation. This allows the implementation of a virtual sensor (Soft-sensor) to estimate on-line the biomass concentration and to enable in this way, an appropriate control of the variables and to optimize the results.

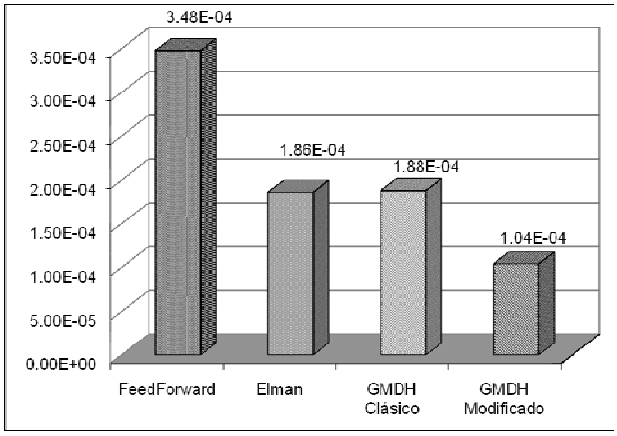

Figure 10. Comparing average error

The number of feedback loops as well as the input variables are automatically determined satisfactory manner that minimizes the criterion RC. In comparison with other methods of neural modeling, you can see a better performance, demonstrating its ability to be successfully used in modeling of a batch fermentation process.

The use of recurrent loops and Genetic Algorithms applied to neural network design using the GMDH algorithm, opens new horizons.

It's possible work with multiple internal loops, which allows to define in the GMDH algorithm, neurons that are able to link in several directions forward and backward. Therefore it's possible to develop complex systems with greater potential for identifying non-linear processes such as the fermentation process

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