CONTROL OF THE PENICILLIN PRODUCTION WITH ADAPTIVE IMC USING FUZZY NEURAL NETWORKS

M.J. Araúzo Bravo[*], E. Gómez Sánchez[**], J.M. Cano Izquierdo[***], J. López Coronado[***], M.J. López Nieto[†], A. Collados de la Vieja[†]

[*] *Dept. of Electromechanical and Civil Engineering, University of Burgos, Spain*
[**] *Cedetel, Valladolid, Spain*
[***] *NEUROTECNO, University of Murcia*
Paseo Alfonso XIII,34, Cartagena, Murcia, Spain
e-mail: coronado@plc.um.es
[†] *Process Technology Department, Antibióticos, S.A.U., León, Spain*

Abstract: This paper introduces the use adaptation in IMC strategy for the control of a simulated penicillin plant. The plant model and control modules are built using FasBack neuro-fuzzy system, featuring fast stable learning guided by matching and error minimisation and good identification performance. Control results show good general performance both in the nominal case and in the presence of noise. FasBack on-line adaptation capabilities are used to develop an adaptive IMC, which shows to improve performance in realistic cases of time varying parameters. Furthermore, real data coming from pilot plants are used to train fuzzy neural networks with satisfactory identification results, and obtained modules are used within IMC with similar results to those build from simulated data.

Keywords: Process control, adaptive control, biotechnology, fuzzy systems, neural networks

1. INTRODUCTION

Biochemical processes are very difficult to control due to their strong non linear dynamics and time varying parameters. Moreover, many variables are of difficult measurement, and usually involve expensive laboratory analyses. For these reasons experts knowledge and heuristics are used for the control of such processes. However, biochemical products, in particular penicillin, have a significant added value, thus being of great industrial interest. For this reason during the last decades many researches have been making a careful laboratory study of these processes (Mou, 1979; Tiller *et al.*, 1994).

Dealing with non linear systems with variable parameters is a most difficult task in the systems control field. Traditional approach has been to search for an equivalent linear system, i.e. adjusting control parameters according to a linearization of the system transfer function near its equilibrium state, so that the equilibrium state is an attractor of the state space of the system. Processing of non linearities is avoided due to its complex mathematical nature. This solution simplifies the problem, but loss of information may be critical in the penicillin production problem, due to the fact that large perturbations and non linearities can take the system outside the equilibrium state.

Internal Model Control (IMC) structure permits a rational control design procedure, allowing considering control quality and robustness in design decisions (Garcia and Morari, 1982). The basic IMC structure (see figure 1) comprises a plant model, and the inverse model, to control the actual plant. Though any feedback controller can be structured as an IMC, and conversely an IMC can be transformed into feedback form, the design of the controller associated to IMC is easier than the design of that associated to a feedback structure, due to the fact that IMC structure allows including explicitly robustness as a design objective, with the use of perturbation estimation as feedback signal. This allows (Garcia and Morari, 1982) IMC to have dual stability, perfect control and zero offset properties. Furthermore, it has been proved that IMC can be extended to control of non linear plants (Economou-86).

Despite these advantages, the lack of a plant model or the inverse model can be a serious drawback. If valid analytical models are not available, or is not enough accurate, which is often the case for bioprocesses, neuro-fuzzy methods provide a solution to build model and control modules by learning direct and inverse dynamics, and are well suited for non linear plant identification. FasBack neuro-fuzzy system (Cano *et al.*, 1997a) feature fast stable learning guided by matching and error minimisation, fuzzy representation of the knowledge which allows the inclusion of expert rules, and good MIMO identification performance which makes it very appropriate for building IMC strategies. Furthermore, FasBack on-line stable adaptation capabilities permit the design of an adaptive IMC, (AIMC) which is of great interest for the control of a penicillin plant, in which not only parameters vary with time due to production degradation or strain mutations, among other effects, but also production results vary among fermentations even under the same conditions.

The rest of this paper is organised as follows: section 2 briefly describes FasBack as a neuro-fuzzy system, and explains how to build FasBack modules for an AIMC. Section 3 presents AIMC applied to a simulated penicillin plant, in the cases of nominal plant, presence of noise and time varying plant parameters. In section 4 the same experiments are carried out with neuro-fuzzy modules trained with real data. Finally, section 5 presents the conclusions.

2. FasBack: AN ON-LINE ADAPTIVE FUZZY NEURAL NETWORK

2.1. FasBack description

FasBack architecture (Cano *et al.*, 1997a) is a hybrid system based on Adaptive Resonance Theory (ART) (Grossberg, 1976) family of neural networks, also combining the advantages of fuzzy sets theory (Zadeh, 1965). It is initially based on Fuzzy ARTMAP (Carpenter *et al.*, 1992) architecture, which has two unsupervised modules (ART_A and ART_B) which cluster input and output respectively, while another module contains the relations between them. FasArt neural network (Cano *et al.*, 1996a) was proposed to overcome the several ambiguities observed on Fuzzy ARTMAP supervised neural networks, by the introduction of fuzzy logic in a

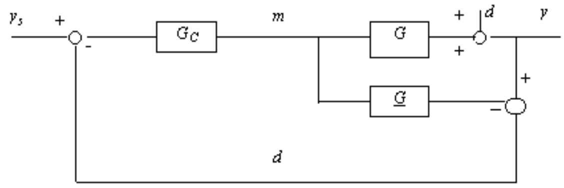

Fig. 1: Basic IMC structure, where G is the plant, $\underline{G}$ is the model, G_c is the controller; d and $\underline{d}$ are the perturbation and its estimation.

formal way, so that learning is equivalent to generating a base of fuzzy rules, and prediction consists of the use of a fuzzy inference engine with such rules. Due to the duality between neural network and fuzzy system present in FasArt, the universal approximation principle obtained for fuzzy systems (Wang, 1994) can also be applied to FasArt. Also due to this duality, inversion of the rules is straightforward, i.e. inversion of the model can be made by reverting the knowledge of direct dynamics. Furthermore, in (Cano *et al.*,1997b) rules partial inversion is used for the control of a simulated penicillin plant, in which the consequents (outputs) and some of the antecedents (state variables) are used to obtain the rest of the antecedents (control signals).

Besides these improvements, FasBack makes use of backpropagation algorithm (McClelland and Rumerlhart, 1986) to refine learning in order to reduce global error, by locally relearning the wrong input/output relations. This is carried out by using the descending gradient method, which vary parameters (weights) in the direction indicated by the derivative of error with respect to the parameters vector (Wang, 1994). Furthermore, a penalty method is used to reduce the influence of wrong rules, although these rules are not completely forgotten and can be recalled if they become valid again. Due to the fact that this refining is local, and old rules are not completely forgotten, adaptation is stable and can be carried out on line, without the need of storing previously learned patterns, as it would be the case with multilayer perceptrons using backpropagation learning algorithm.

FasBack is characterised by several sintony parameters, which have clear physical meaning: vigilance parameters ρ_A and ρ_B which show how fine clustering of input and output, and fuzzyfication rates γ_A and γ_B indicating how fuzzy or crisp input and output clusters are.

2.2. Use of FasBack modules in AIMC

The main modules necessary for implementation of AIMC are a model of the plant to be controlled, and the actual controller, which most often is related to as inverse model of the plant. As shown previously, FasBack is specially adapted to build such modules.

The model module must capture direct dynamics of the plant. In the case of well known dynamics, a mathematical model of the plant can be developed, although this can be costly and inaccurate in many industrial plants, as is the case in the penicillin production plants. In this case, neural networks are a good approach, as shown in (Cano *et al.*, 1996c), where identification of a penicillin plant using simulated and real data is carried out.

To build the controller module (inverse model) the direct plant model should be inverted. However this is not always possible, due to the fact that either the inverse does not exist, or its implementation is not physically feasible. Some reasons for this are: the model is a non minimum phase model, has time delays, or using its inverse will require high gain loops. However, in most practical cases an analytical model is not available, and therefore neural networks can be used to learn inverse dynamics, taking as input signal the outputs of the system, and as supervision signal the inputs to the system, either in the expected operational range of the plant (Hunt and Sbarbaro, 1991), or in the whole operating space. FasBack neuro-fuzzy system can be used both **(a)** by inverting direct dynamics fuzzy rules, and **(b)** by learning inverse dynamics, and adaptation can be enabled in order to locally refine the general inverse model. In the case **(a)**, fuzzy rules inversion can be applied to rules extracted from FasBack plant model weights, as shown in (Cano *et al.*, 1996b). To build such a control module requires one model learning (direct), and also the availability of an inversion method. In the case **(b)**, a control module can be built with a single model learning (inverse). In this paper the second approach is adopted, and FasBack is used to learn direct dynamics to build the plant model, and inverse dynamics to build the control module. Adaptation of the plant model is carried out by learning input/output pair every time plant output is available. Adaptation of the controller follows a law similar to that proposed in (Hunt and Sbarbaro, 1991), which in a general form is:

$$\mathbf{p}(k+1) = \mathbf{p}(k) + \alpha \cdot \mathbf{e} \cdot \mathbf{J} \tag{1}$$

where $\mathbf{p}(k)$ is the parameter (weights) vector, $\mathbf{e}$ is the tracking error, $\mathbf{J} = \{j_{mn}\} = \dfrac{\partial y_m}{\partial u_n}$ is the Jacobian matrix of the plant, calculated numerically using the model, and α is an adaptation rate, which is 0.4 in all simulations.

3. AIMC APPLIED TO A SIMULATED PENICILLIN PLANT

In this section we present results of AIMC controller applied to the control of the biomass, one of the main variables in the penicillin problem. However, we keep in mind that the final objective of the process is penicillin production. It can be assumed that finding a good control for biomass can facilitate the control of penicillin production (Mou, 1979). Furthermore, it can also be assumed that the main control variable is feeding, and that biomass presents a two stage profile: an exponential growing stage, in which penicillin production can be neglected, and a production stage, of slow growing (Mou, 1979).

In order to achieve a better knowledge of the penicillin problem, and as an initial approach to the use of adaptive IMC to the control of a penicillin plant, a penicillin simulator has been used to generate data to build FasBack modules and to replace the actual plant within the AIMC structure. Among the several models existing in the literature, Tiller model (Tiller *et al.*, 1994) has been selected, because in our opinion, it is a good approximation to some real cases. It is a segregated model with parameters varying with time. The proposed system is not only able to learn parameters variation off-line during learning phase, but has also proved able to learn the effect of the time variation of some parameters in real time, as shown further in this section.

To test controller performance it must be considered that not any reference can be tracked by a biochemical plant. Here we use a reference inspired in (Mou-1979), which guarantees high growing rate at exponential growing stage (μ_{gr}), and low growing rate at production stage (μ_{pr}). Mathematically:

$$X^{ref} = \begin{cases} e^{\mu_{gr} t} & t \le t_1 \\ e^{\mu_{gr} t_1} + \Delta X_{pr} \dfrac{1 - e^{-\mu_{pr}(t - t_1)}}{1 + e^{-\mu_{pr}(t - t_1)}} & t > t_1 \end{cases} \tag{2}$$

where ΔX_{pr} is the total growing expected in the production stage, and t_1=25 is the time of change from the growing to the production stage. Due confidenciality reasons values of some parameters and plots are scaled in [0,1], both in the simulated and the real cases.

Before testing FasBack AIMC structure to control the simulator, a PID control was studied, according to the methodology proposed by Boskovic and Narendra (1995), in which simple controllers should be discarded before trying complex ones. Results of PID control are shown in figure 2 where the tracking is not good and the feeding law is not physically feasible. Increasing the derivative gain would lead to a better tracking but a rougher feeding law, even less feasible. Decreasing the derivative gain allows to find a feasible feeding, but with a very late tracking, thus strongly influencing penicillin production.

As seen in (Boskovic and Narendra, 1995) for an alcoholic fermentation, when the plant is complex and realistic (non linear, noise, time variant parameters) a PID control is not satisfactory, and more elaborated controllers should be used. In this sense the AIMC structure was applied. To identify

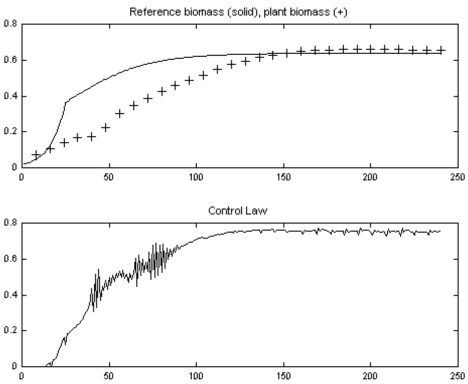

Fig. 2. PID control of the biomass. '+' signs show actual output at 8 time units sampling interval, and solid is the reference.

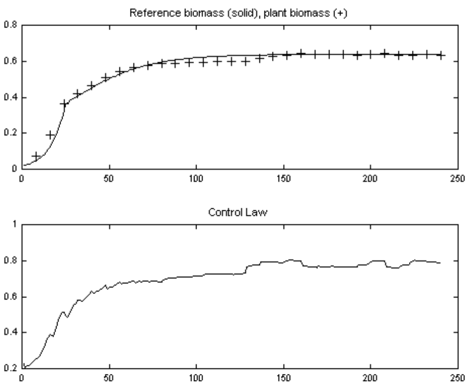

Fig. 3. AIMC for the nominal plant.

direct and inverse dynamics, 30 fermentations were generated, in which feeding law was selected randomly within bounds suggested by experience, and the rest of the input laws were kept fixed among fermentations. Gaussian noise was added to the output, with 0.1% amplitude for gas measurements, and 5% for laboratory analyses. Furthermore, although simulator can provide a continuous measurement of any variable, laboratory variables were down-sampled to realistic rates, and then interpolated, to have a more accurate approach to results that will be obtained when using real data, which are shown in next section.

Direct and inverse dynamics were learned using two FasBack neural networks with 10 training cycles (each of 30 fermentations of 240 instants). For direct dynamics *F(t)*, *CPR(t)*, *CPR(t*-1*)* and *CPR(t*-2*)* were used to predict *X(t*+1*)*, and for inverse dynamics *X(t*+1*)*, *CPR(t)*, *CPR(t*-1*)*, and *CPR(t*-2*)* were used to estimate *F(t*+1*)*, where *X* is the biomass concentration, CPR is the carbon dioxide production rate, and *F* is the sugar flow rate.

After training, the controller and model modules were generated using 50 nodes in ART_A and 39 in ART_B for the controller, and 47 nodes in ART_A and 34 in ART_B for the model. Satisfactory direct and

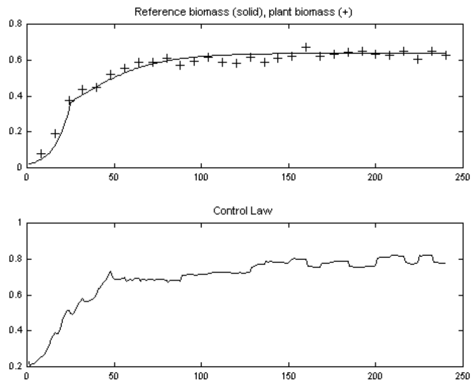

Fig. 4. AIMC for the nominal plant when there is 5% noise in the measurement of biomass and 0.1% noise in the measurement of CPR.

inverse results permit to build an AIMC strategy using these two modules. However the fact that the model reflects a general behaviour of the plant, rather than being accurately describing the actual plant, influences negatively control performance, and can be corrected by enabling adaptation, as shown in figure 3.

A more realistic approach can be made in the case of presence of noise in plant output. To test this the same experiments were run adding 5% gaussian noise to biomass *laboratory measurements*, and 0.1% gaussian noise to *CPR* measurement provided in reality by a gas spectrometer. Control results in figure 4 show AIMC capabilities to compensate noise in the output.

It is also interesting, to simulate the influence of cell damage by lysis and shear forces (Tiller *et al.*, 1994) and test on-line adaptation capability of the proposed system. It has been roughly assumed that these effects influence mainly biomass yield on sugar (Y_{XS} in (Tiller *et al.*, 1994)), supposing that it decreases from 0.5 g/g at time 100 to 0.1 g/g at the end of the fermentation. Results showed a better tracking of reference in adaptive case (figure 5) to obtain a similar penicillin production, whilst control law is smaller and smoother.

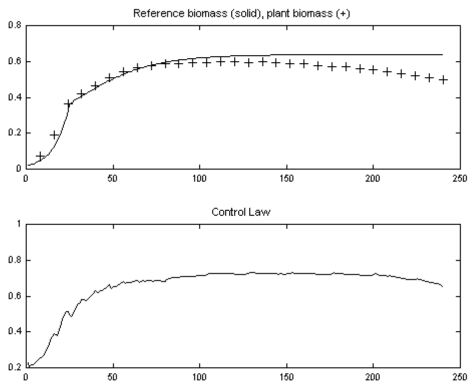

Fig. 5. AIMC for a time varying plant

4. AIMC WITH FasBack MODULES TRAINED WITH REAL DATA

One of the main problems to develop and test controllers is the necessity of a good mathematical model of the process, in order to test controller performance prior to actual implantation in industrial plant. However, biochemical processes are non-linear problems with time varying parameters, for which mathematical models are difficult and expensive to construct. Several approaches can be found in the literature (Tiller *et al.*, 1994) but they are very sensible in their parameters, i.e. parameters are conditions dependent (strain, type of feed...). Neuro-fuzzy systems are good candidates to replace mathematical models, due to the fact that performance equations need not be derived, parameters are automatically tuned by learning algorithm and empirical knowledge from experts can be added by the use of fuzzy rules. In this sense it was develop here a *FasBack plant* using real data collected from 8 standard fermentations. In these data sets continuous measurements are taken eight times faster than biomass measurements. This *plant* has feeding and state variables as inputs and produces biomass and state variables as outputs. To build the AIMC, the model and the inverse model were built using real data from the pilot plant. The model obtains biomass from feeding actions and state variables, and the inverse calculates feeding actions from reference biomass and state variables. Identification of unseen data is shown in figure 6, for one fermentation.

To follow a similar reference to equation 2, performance is satisfactory, and adaptation improves performance due to the refinement of both FasBack modules, as seen in figure 7.

In order to test performance in a plant with time varying parameters, we introduced a modification in the *plant* to reflect a gradual degradation of the yield of biomass in the feeding, as we did parametrically with simulated data. This negative effect can be solved enabling adaptation. Results are shown in figure 8 where tracking is achieved by increasing the main feeding.

Finally, noise influence is studied by adding 5% noise to the output of the *plant*. As posed in previous sections, AIMC show good noise rejection. It can also be seen in figure 9 how low level noise does not affect negatively adaptive IMC performance.

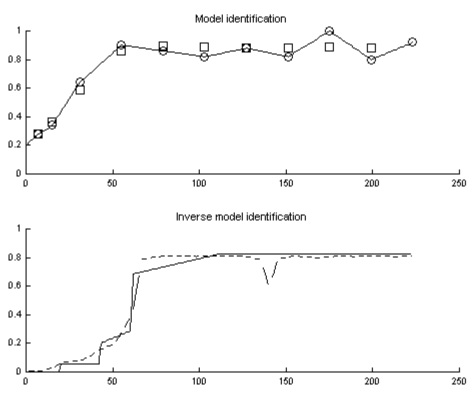

Fig. 6. Biomass identification (top) and inverse model prediction (bottom) for data from a real fermentation.

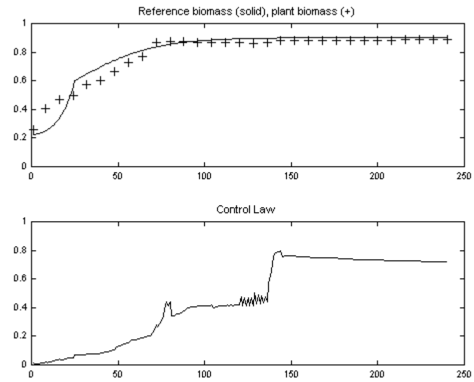

Fig. 7. AIMC for the nominal *FasBack plant.*

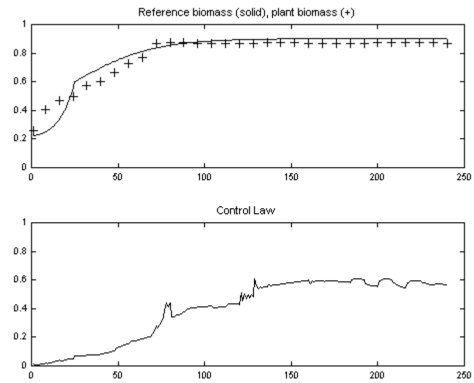

Fig. 8. AIMC for a time varying *FasBack plant.*

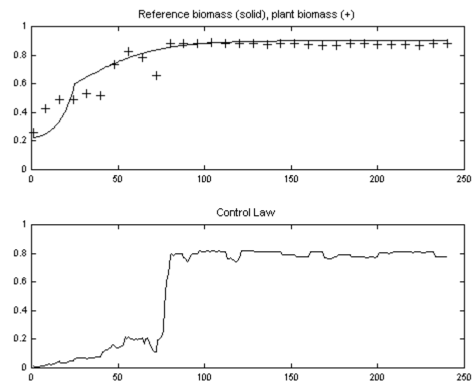

Fig. 9. AIMC for the nominal *FasBack plant* when there is 5% noise in the measurement of biomass.

5. CONCLUSIONS

In this paper, FasBack neuro-fuzzy system has been applied within an AIMC strategy in the problem of penicillin production. Such a problem is highly non linear, has time varying parameters, presents high levels of noise in the measurements, and suffers from a lack of good mathematical models considering the variability of the process. To solve this problems, IMC structure presents noise rejection, and can be easily extended to non linear problems with the use of FasBack neuro-fuzzy system. Furthermore, the use of this neural architecture is also a solution for the difficult task of building model and control modules, due to its fast stable learning from examples and good performance in plant identification.

In addition, on-line adaptive capability of FasBack has been used to add this feature to AIMC strategy, obtaining good results both in the case of the direct or inverse model are not accurate, and in the case of plant parameters varying with time, one of the fundamental difficulties of the biochemical problem. Application of FasBack based AIMC to a simulated penicillin plant has been very satisfactory, in the realistic cases of laboratory measurements are not available as often as control signal is required, there is presence of noise in plant output, and plant parameters vary with time. Furthermore, as a closer approach to real plant control, real data has been used to develop plant and inverse plant models, with satisfactory identification. These results suggest a simple efficient control strategy that can be of industrial interest if results can be extrapolated to a real plant. In this sense, the inclusion of experience based rules coming from the industry would facilitate the development of AIMC modules. FasBack, as a fuzzy system, presents the possibility of inclusion and manipulation of experts linguistic rules together with knowledge extracted from examples, and the interpretability of learned knowledge in terms of fuzzy rules. This is expected to be of use in the future application of this control strategy to a real pilot plant, which is the next objective of this research.

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