

## INTEGRATION OF EXPERT SYSTEMS AND NEURAL NETWORKS FOR THE CONTROL OF FERMENTATION PROCESSES

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**Abstract.** Expert systems and neural networks are new tools for the control of fermentation processes. With expert systems the fermentation plant and the process itself is modelled via a generalized, qualitative system description based on the experience of human experts. On the other hand neural networks and interpolating associative memories can learn the process behaviour directly by process observation. The paper at hand reports, how both control techniques can be combined for purposes like process supervision, modelling and optimization of biological plants.

**Keywords.** Expert systems; neural networks; associative memories; learning control; fermentation processes; biotechnology.

### INTRODUCTION

The development and control of fermentation processes makes the integration of some research disciplines necessary. Organisms and substrate compositions are typically selected or modified by microbiologists. By empirical variation of environmental process parameters (e.g. temperature, pH, oxygen concentration) during some lab-scale fermentations the productivity of the process is improved. The optimized conditions are then applied to the real production plant by utilization of some scale-up criteria. In most cases the production process itself is then controlled by human operators. In summary the control of biotechnological processes is based on the knowledge of experts and human operators as well as on analysis and processing of numerical data (fig. 1).

For applications like process supervision and fault diagnosis of biological plants some expert systems were already developed [Halme, 1989]. Expert systems can handle that knowledge which can be acquired by human experts, but this knowledge describes the conscious thinking and decisions only. Modelling problems arise in case of unconscious decisions or complex input-output patterns.

Here learning control systems are an interesting system completion. Learning control loops can learn process models and control strategies automatically by observation. For the representation of the process behaviour neurally inspired storage devices (neural nets,

interpolating associative memories) have been established. The integration of expert systems and learning control techniques seems therefore promising, especially for intelligent control of fermentation processes.

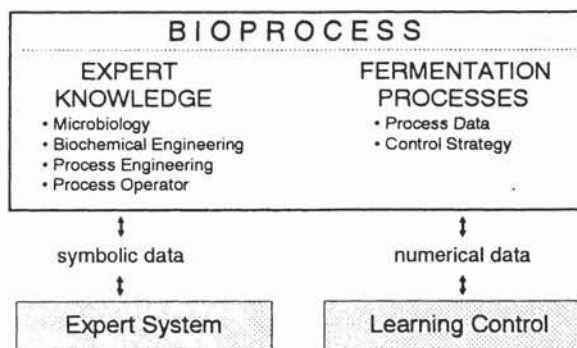


Fig. 1: Knowledge sources and problem solving strategies for development and control of bioprocesses.

### LEARNING CONTROL OF BIOTECHNOLOGICAL PROCESSES

Learning control has been developed in parallel to adaptive control systems and is advantageous especially in case of heavily nonlinear processes. Basic working mechanisms of learning control loops are briefly explained by describing the system LERNAS [Ersü and Tolle, 1984]. Within LERNAS (fig. 2) a predictive process model as well as an optimized control strategy is generated in parallel to the real process.

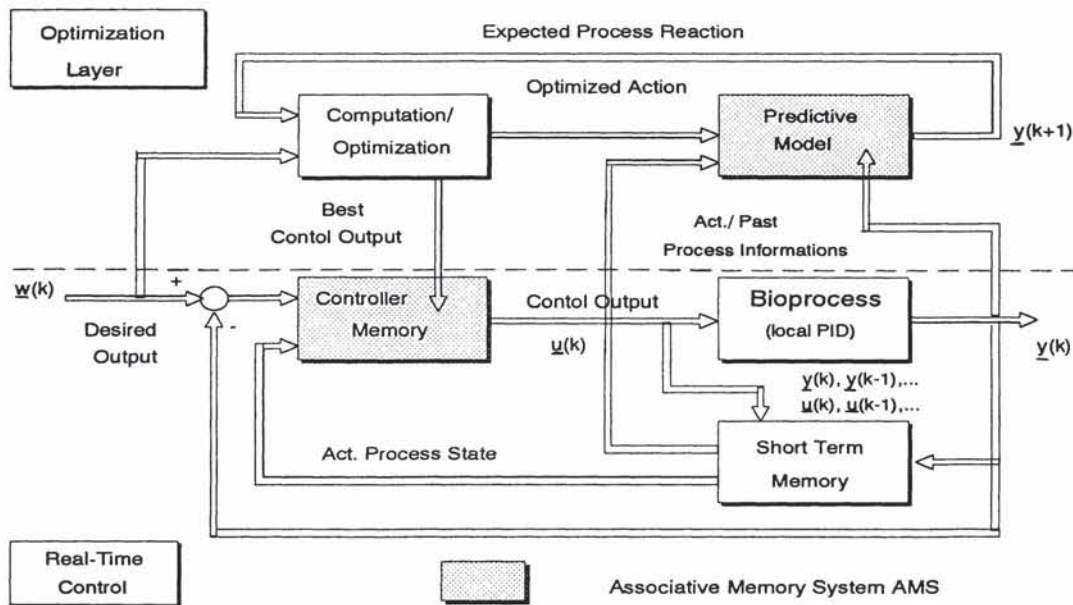


Fig. 2: Basic structure of the learning control loop LERNAS [Ersü and Tolle, 1984].

Both model and controller are realized by a general mathematical mapping  $I \rightarrow O : I \in \mathbb{R}^n, O \in \mathbb{R}^m$ . The predictive process model is generated by storing the process reaction  $y(k+1)$  as a function of the measured process inputs and outputs and some history of these values:

$$\begin{bmatrix} y^T(k), y^T(k-1), \dots, y^T(k-\alpha); \\ u^T(k), u^T(k-1), \dots, u^T(k-\beta) \end{bmatrix} \rightarrow y(k+1). \quad (1)$$

An advantageous control strategy is generated by applying different control inputs to the predictive process model and evaluating these results by a preselected optimization criterion. The so selected optimal control input  $u_{opt}(k)$  is then stored in a memory presenting the controller in dependence of the considered process situation:

$$\begin{bmatrix} w^T(k); y^T(k-1), \dots, y^T(k-\alpha); \\ u^T(k-1), \dots, u^T(k-\beta) \end{bmatrix} \rightarrow u(k). \quad (2)$$

For time-invariant processes the optimization becomes superfluous after sufficient training/optimization steps. Since the actual process situations are generated by chance, the memories must have the capability to interpolate the output values for scattered input values. According to this special locally interpolating associative memories – partially neurally inspired – have been generated [Tolle et al., 1988].

With LERNAS several investigations for the learning control of fermentation processes have been performed [Gehlen et al., 1988]. However, biotechnological processes show special properties, which motivate some fundamental extensions of the basic control structure.

a) During batch or fed-batch fermentation the cell metabolism modifies due to variations of extracellular conditions. Several process phases (lag phase, exponential growth, etc.) can be distinguished. The design of submodels and control strategies adapted

to the special characteristics of each "physiological state" [Konstantinov and Yoshida, 1989] instead of a global process view is efficient. The physiological state concept in coordination with process representation in neural nets/ interpolating associative memories is meaningful, because net inputs and outputs are reduced to key variables of each phase only. This leads to better convergence properties and savings in memory effort. The detection of physiological states with rule-based expert systems is possible [Halme, 1989].

b) In most cases where a biological plant has to be controlled the general process behaviour is known. Data of previous processes can serve as knowledge source, i.e. with this data predictive process models can be trained off-line in advance. With every process run the model is then further improved. Optimization of control strategies can be studied off-line, too.

c) In principle process errors (defect of plant components, contamination, etc.) can be detected with the help of a learned process model. However, an automatic reaction on such faults is only possible, if similar defects have been trained before. This is unlikely in case of complex fermentation plants. For this reason knowledge based fault detection can be an effective supplementation to learning control.

d) The variation of physical process parameters (temperature, pH, etc.) has to be bounded to avoid irreversible damage of organisms and products, i.e. the automatic search for optimal environmental parameters has to be limited by using the knowledge of experienced persons and process operators.

The coordination of learning control by an expert system is a powerful solution to include heuristic expert knowledge into a learning layer. This knowledge can be used for detection of process states, errors and physiological states.

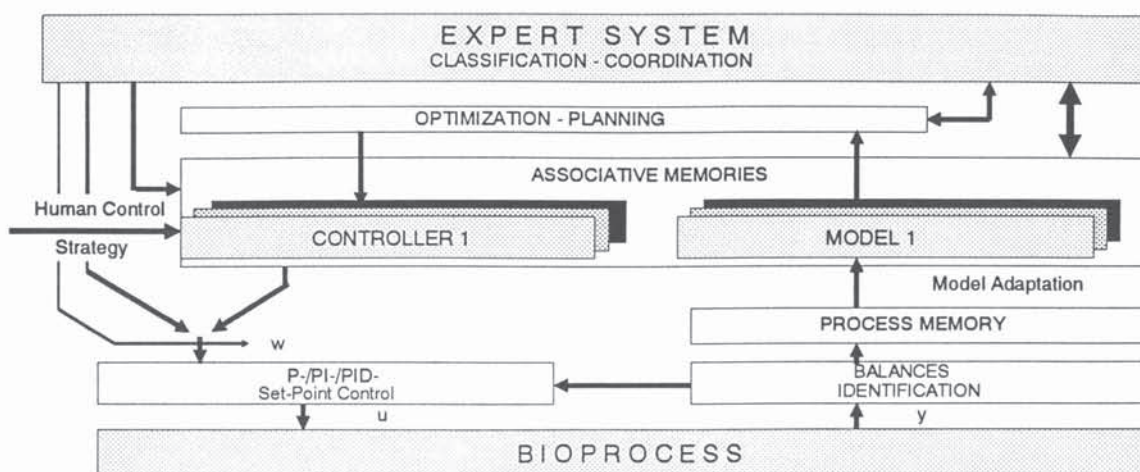


Fig. 3: Architecture of the intelligent control system *BioX* with integrated learning control mechanisms.

For these reasons an intelligent control system has been designed, which includes knowledge based and learning control algorithms. The basic architecture of this system is shown in fig. 3.

#### BASIC SYSTEM DESIGN

One main difference in known expert systems for control and supervision of fermentation plants is the kind of knowledge representation. Most systems use production rules for information storage. Uncertainties can be considered by introduction of certainty factors or by fuzzy approaches [Dohnal, 1985]. With qualitative techniques the gap between the exactness of numerical models and abstract system representation can be reduced.

For detection and analysis of process states rule based systems are a powerful solution. For this reason the expert system layer of *BioX* has been implemented as a production system. Process errors are detected by processing of special features (symptoms, measuring values, etc.). As the validation of errors can be a multistep procedure, hierarchies are allowed for the representation of faults. Results of one diagnostic step can serve another layer as a new feature. All diagnosis are treated uniformly as hypothesizes.

Several inference procedures, like forward and backward chaining and some special algorithms (e.g. "hypothesize & test") have been implemented. A transparent and efficient knowledge representation was possible by using frames. Special frame classes have been designed for storage of rules, hypothesizes, plant descriptions, process errors, process phases, measuring and control values, etc. The whole rule based layer of *BioX* was implemented in LISP.

Because the efficient implementation of (numerical) control algorithms is impossible while using LISP, algorithmic parts of *BioX* have been written in C. All important procedures of the learning layer can be controlled by the knowledge based procedures using a special LISP-C-interface. Several control monitors have been designed for all system components. In summary *BioX* can be regarded as a toolbox, which can

be applied for the control of the most fermentation processes.

#### APPLICATIONS

An industrial relevant bioprocess, the production of  $\alpha$ -amylase with *Bacillus subtilis*, serves as testbed for control applications with *BioX*. All fermentations have been performed in a 19 l fermenter with a coupled flow injection analyzer for on-line-monitoring of  $\alpha$ -amylase. Temperature, ph, stirrer speed,  $pO_2$ , air-flow and  $CO_2$ -fraction in the outlet are continuously measured with a sampling period of 1 minute. A complex medium was used leading to multiple growth phases and varying process behaviour. Three control applications with *BioX* are explained in detail:

a) Classification of process phases: The classification is performed by the expert system layer. All relevant informations for characterization and description of one phase/ physiological state are summarized in one frame. In each classification step the actual and all possible successor phases are tested, for each phase several features (e.g. numerical, symbolic or trend values of  $CO_2$  and  $pO_2$ , etc.) are checked. The phase with maximum likelihood is activated. In case of phase changes special demon functions are activated. These demons control the behaviour of the learning control algorithms. In this way process models (i.e. neural nets, interpolating memories), control strategies and optimization procedures are (de-)activated. The classification approach explained here has been shown to be very robust during several fermentations.

b) Learning of predictive process models: Three different architectures of self interpolating memories have been compared, the first memory device used is the associative memory system AMS, which is an improved version of the CMAC memory [Albus, 1975]. The second architecture uses a mathematical regression technique for interpolation. A detailed description of architecture and modelling experiments with these locally interpolating memories is found in [Gehlen and Bettenhausen, 1990; Gehlen and Kreuzig, 1991]. For comparison a globally interpolating backpropagation net [Thibault and van Breusegem, 1991; Willis et al.,

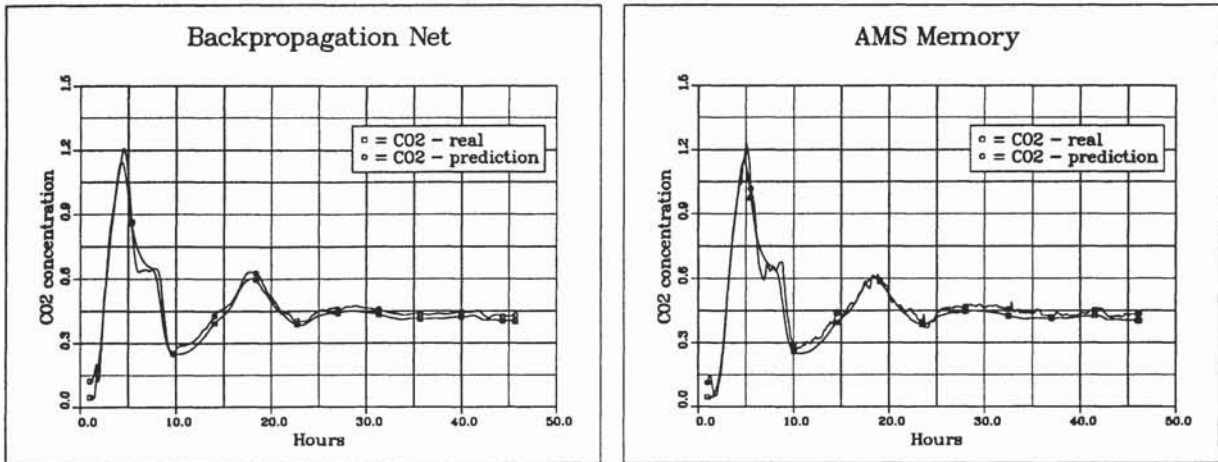


Fig. 4: Comparison between real ( $\square$ ) and predicted ( $\circ$ )  $\text{CO}_2$ -concentration in case of a) backpropagation net (1 hidden layer, 15 neurons, 500 training cycles), b) AMS-memory (16 active association cells, 20 training cycles).

1991] was tested. All nets have been trained with data of 16 fermentation runs. 8 inputs (temperature, pH,  $\text{CO}_2$ ,  $\text{pO}_2$ , amylase of the actual sampling step and past values of temperature, pH,  $\text{CO}_2$ ) have been selected, the values of  $\text{CO}_2$ ,  $\text{pO}_2$  and amylase have been predicted with a time horizon of 30 minutes. Fig. 4 shows the comparison between real and predicted  $\text{CO}_2$ -concentration in case of the backpropagation net and AMS for a previously unknown process. With all nets the prediction is possible, but the convergence of locally interpolating memories is much faster.

c) Optimizing the process productivity: In each sampling step a special optimization procedure (Hookes-Jeeves) searches for the best setpoints of underlying PID controllers, the predicted process reaction is calculated as explained before. The requirements of each phase/ physiological state can be taken into account using different optimization criteria, e.g. in the first growth phases the best environmental conditions for a maximum cell production, in the following phases conditions for a maximum production or product stabilization are searched. In case of our process the on-line optimization of temperature and pH leads to an increase in productivity (shorter production time/ higher final enzyme concentration) of more than 100 % in contrast to fermentations with constant setpoints.

## CONCLUSION

In this paper architecture and realization of an intelligent control system for process supervision, fault diagnosis and optimization of biotechnological plants has been presented. Main feature of *BioX* is the coordination of an expert system and learning control. The whole control system has been tested with a special fermentation process, the production of  $\alpha$ -amylase with *B. subtilis*. As *BioX* has been designed as a general framework, the adaptation to other fermentation processes is easily possible.

## REFERENCES

- [1] J.S. Albus (1975). The Cerebellar Model Articulation Controller. *Trans. on the ASME, Series G, Vol. 97, No. 3.*
- [2] M. Dohnal (1985). Fuzzy Bioengineering Models. *Biotechn. & Bioeng., Vol. 27.*
- [3] E. Ersü, H. Tolle (1984). A New Concept for Learning Control Inspired by Brain Theory. *9. IFAC World Congress, Budapest.*
- [4] S. Gehlen, M. Hormel, S. Bohrer (1988). A Learning Control-Scheme with Neuron-Like Associative Memories for the Control of Biotechnological Processes. *Int. Workshop on Neural Networks, Neuro-Nîmes, Nîmes (F).*
- [5] S. Gehlen, K.D. Bettenhausen (1990). Modelling of Biotechnological Processes with Interpolating Associative Memories. *IMACS-IFAC Symp. on Mathematical and Intelligent Models in System Simulation, Brussels.*
- [6] S. Gehlen, J. Kreuzig (1991). Learning by Interpolating Memories for Modelling of Fermentation Processes. *IFAC Symp. on Advanced Control of Chemical Processes, Toulouse, (F).*
- [7] A. Halme (1989). Expert System Approach to Recognize the State of Fermentation and to Diagnose Faults in Bioreactors, in *Computer Applications in Fermentation Technology*, ed. N.M. Fish, R.I. Fox, N.F. Thornhill, Elsevier.
- [8] K. Konstantinov, T. Yoshida (1989). Physiological State Control of Fermentation Processes. *Biotechn. & Bioeng., Vol. 33.*
- [9] J. Thibault, V. van Breusegem (1991). Modeling, Prediction and Control of Fermentation Processes via Neural Networks. *First Europ. Contr. Conf., Grenoble (F).*
- [10] H. Tolle, E. Ersü, J. Militzer (1988). Zur Leistungsfähigkeit lokal verallgemeinernder assoziativer Speicher und ihren Einsatzmöglichkeiten in lernenden Regelungen. *MSR, Berlin, 32*, [in german]
- [11] M.J. Willis, G.A. Montague, C. Di Massimo, M.T. Tham, A.J. Morris (1991). Artificial Neural Network Based Predictive Control. *IFAC Symp. on Advanced Control of Chemical Processes, Toulouse, (F).*